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
Monday, June 9, 2008
8:30 a.m.
SIXTH 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.,
LISA A. CHIARINI, ESQ.
ROBERT RIDDLE, ESQ., and
PAUL FEHLNER, ESQ.
Baker Botts LLP
(Houston, TX)
-and-
GREGORY BOKAR, ESQ.
Counsel - Elan Drug Delivery

Counsel for Plaintiff

APPEARANCES CONTINUED:

ELENA C. NORMAN, ESQ., and
MICHELLE SHERETTA BUDICAK, ESQ.
Young Conaway Stargatt & Taylor, LLP
-and-
MICHAEL A. JACOBS, ESQ.,
EMILY A. EVANS, ESQ.,
ERIC S. WALTERS, ESQ.,
DIANA KRUZE, ESQ., and
ERIK J. OLSON, ESQ.
Morrison & Foerster
(San Francisco, CA)

Counsel for Defendant

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THE COURT: Good morning, counsel. Please be seated for a moment.

(Counsel respond "Good morning.")

THE COURT: Mr. Jacobs.

MR. JACOBS: Thank you, Your Honor. Mr. Scheve has signaled an intent to examine Dr. Desai, our first witness this morning, about privilege log entries in Dr. Desai's notebook.

We have seen a graphic displayed on the screen in which Mr. Scheve would display those privilege log entries or notebook pages with privilege redactions on them.

Mr. Scheve's contention is because the Court has decreed that an adverse inference will be drawn from Dr. Brittain's related privilege assertions, Elan should be able to develop a record that Abraxis asserted the privilege over, in this case, Dr. Desai's notebook entries.

The two are not parallel. The Court made findings with respect to Dr. Brittain in order to even get into examining a witness on the stand about topics that bear on attorney-client privilege. Our position is the Court would have to make similar findings.

We think Mr. Scheve, Elan, should be directed not to raise any such issues or any such implication to examine Dr. Desai on any topics that bear on attorney-client privilege issues during the cross-examination of Dr. Desai.

THE COURT: Okay. Mr. Scheve.

MR. SCHEVE: Thank you, Your Honor.

If I could, beforehand, Mr. Day couldn't be here today. He says there is a small event going on this evening.

THE COURT: He took the day off. Huh?

MR. SCHEVE: Or at least half the day. He is dealing with some issues Your Honor may be familiar with.

THE COURT: Indeed. Our children's graduation from high school.

MR. SCHEVE: Yes.

Your Honor, if I may put up a slide, what this is about, and there has been a Bench brief filed by Abraxis that cites the case authority.

MR. JACOBS: May we provide that to Your Honor?

THE COURT: Yes.

MR. SCHEVE: And that case authority on Page 2, Your Honor, if I may quote from, in the first instance, from Weinstein's federal evidence, saying, The claim of a privilege is not a proper subject of comment by judge or counsel. No inferences may be drawn therefrom.

Then, later on in the Ninth Circuit, they cite another case, that there could be no negative inference from a defendant witness' claims of attorney-client privilege.

I raise that because what we did with Dr. Brittain is create a privilege log. You will recall, he signed an agreement with an attorney named Sipio and was providing consultation with Mr. Sipio. Every one of those was placed on a privilege log.

I think the record, and Your Honor will recall, the position we urged upon the Court is it would be inappropriate for an inference to be drawn from the fact that we claimed those are privileged.

Your Honor has, to this date, said that you will allow that inference to be drawn. This is what has occurred during discovery, which is the image up here.

What Abraxis has done, Your Honor, has claimed privilege over, quote, results from experiments that they, "to" communicate to the counsel. Not reflecting anything that was communicated to counsel, or Desai lab notebook reflecting information to communicate to patent counsel

regarding product composition.

They have, I don't remember what the number is there, it is page after page after page of testimony results from the lab notebook that I can't see because they are claiming it's privileged.

I don't understand how they are now going to call Dr. Desai, who is going to testify, and be able to claim that a lab notebook is privileged when it clearly doesn't say, Reflects communication with attorney. This is lab results.

My view, Your Honor, is while we think the proper ruling, and I say this, Your Honor, because none of us want to come back and try this case again, we think it is legal error for an inference to be drawn when counsel, when Mr. Brittain's gave us those documents, that he consulted with Mr. Sipio on, we put them on a privilege log. There was never a motion brought to compel. Never a request that Your Honor look at it to determine whether, in fact, it was privileged.

And now they have asked you, they want a negative inference to be drawn from the fact we put it up there. If you look at the cases cited in their brief, it's error.

But they want to be able to pull Dr. Brittain in here tomorrow and go through that. I am saying, If that's

Your Honor's ruling, why can they make reference to a privilege log that's never been reviewed, for which there has never been a ruling, and our contention is, as we have argued in the past, and I don't mean to rehash, but our view is that you can't draw -- there can't be -- what's the right word -- a repercussion until there is first a predicate act.

THE COURT: Which motion in limine was this? Does anybody remember?

MR. SCHEVE: They attempted to limit us to Mr. Brittain.

MS. GLOVER: No. 1.

MR. JACOBS: No. 1.

THE COURT: By Abraxis?

MR. JACOBS: Correct.

MR. SCHEVE: If they are going to be able to call Dr. Brittain tomorrow and Mr. Jacobs has advised me he has got him under subpoena, he would be here today but he is taking care of his grandchild, that they are putting him on solely to put up that privilege log and argue that there must be something there that is being withheld from somebody and get a negative inference.

Our view is, while we don't think it is appropriate either way, why should they be allowed to do it and then I can't do the same thing? That's just not fair.

THE COURT: Okay.

Mr. Jacobs.

MR. JACOBS: So there are a couple of issues now getting rolled up into one. No. 1, we are very comfortable with the record on Motion in Limine No. 1. We are very, very comfortable with the record, including the observation by the Court about the seriousness of the violation that led to the ruling on Motion in Limine No. 1.

No. 2, we can't, in the ten minutes before witness' testimony is supposed to start, we can't go through each of the privilege log entries and have a reargument about these privilege log entries. I can tell you several things, if it will comfort the Court. We went through each of these entries on a one-by-one basis with Dr. Desai to make sure that the privilege was properly being asserted. We did it because there was back and forth between counsel about the privilege log entries.

Dr. Desai's notebooks relate to a wide variety of topics, some of them related to the litigation. We will be talking about those in his testimony. But they cover any number of other research areas, other patent issues.

When we are talking about test results, for example, it might be that Abraxis was conducting a test specifically related to some patent proceeding that was going on somewhere in the world. But I can't get into each of those now. It would be unfair to try to get into each of

those now. That's why it's inappropriate to do exactly what Elan's counsel is doing right here. That's why Weinstein's directive is so compelling, because it can look bad when you splash it up on the screen.

So, No. 1, we are very comfortable with the record on Motion in Limine No. 1.

No. 2, we shouldn't be getting into Abraxis' assertions of privilege.

No. 3, the question of what to do about -- it is useful, I think. That is the Bench memo on what they propose to do, I believe.

THE COURT: Your memo is?

MR. JACOBS: Yes. There are a couple of Brittain issues coming up. So we have a couple of pieces of paper.

THE COURT: Go ahead.

MR. JACOBS: No. 3, if Mr. Scheve's concern is the specific concern that I would raise the word "privilege" with Dr. Brittain as opposed to a log of documents that were not produced to us, if that would enable us to get past this little imbroglio we are having here, I don't need to use the word "privilege" in examining Dr. Brittain. All the jury needs to understand is Dr. Brittain did some testing, he did it on Abraxane. The entries on the log that we got leave aside the word "privilege," describe that not in very much

detailed, nothing like this, testing, you may recall the log testing, testing related to the litigation.

I do want the jury to see the lengthy list of documents that we didn't get, because it does have a substantial impact.

But I don't need to use the word "privilege."

THE COURT: Mr. Scheve, your reaction?

MR. SCHEVE: I didn't fall off the turnip truck yesterday, Judge, in order to preserve my appeal. Clearly, they are trying to invade the privilege with regard to Mr. Brittain, I shouldn't be saying that, but with regard to Dr. Brittain, when you put it on a privilege log, I am not going to be coerced by opposing counsel, very good counsel, to now disclose that privilege, but them assume that everything on that list was Abraxane, that Dr. Brittain did. I can tell you, that is not the case.

What they are trying to do is whipsaw me in and stand up and, if you will, waive the privilege that existed between Mr. Sipio and Dr. Brittain. And I have already told Your Honor that to the extent there was any testing done by Dr. Brittain on Abraxane, he didn't do any x-ray powder diffraction, and what he would like to do is point to a privilege log and ask this, Your Honor, to instruct the jury there is an inference that somehow all of this was done and he found some negative results and the only relevant issue

would be on crystallinity, when I have already represented to Your Honor he didn't test Abraxane using x-ray powder diffraction, or solid state NMR.

So his relationship was with Mr. Sipio. If they want to draw that inference, and, frankly, Your Honor, I don't believe, I think it's error and none of us want to come back, I don't know how they can draw an inference from a privilege log. But look at these entries. Lab notebooks, it's information to communicate resulting results of experiments.

If Your Honor wants briefs, I can show and this has been part of the problem in this lawsuit, we have heard about how much work there is. I can show you examples where they put something on their privilege log. It's still there. And then they inadvertently gave it to us. And there is nothing privileged in there other than it says, Entries of crystallinity, but it's still on the privilege log. I can go through it, if we have a further hearing, I can show you those sorts of materials.

All I am urging, Your Honor, our position, again, that this is error and neither side ought to be getting into stuff that is put on a privilege log.

Your Honor has rules that we have attempted to abide by. I would love to have been able to bring to Your Honor's attention these claims that a lab notebook is

privileged. But Your Honor had said, I am not going to hear anymore discovery disputes. That's why we are where we are.

THE COURT: After a point, counsel, as all of you know, our resources are limited. We can only devote so much time to any one dispute. This case has, quite frankly -- I am not going to get on a soapbox this morning. In point of fact, this case has been one of the more litigious patent matters over which I have presided during my almost ten years on the Bench. And I have presided over a lot of patent cases.

It has been a disappointment in that regard, especially because we have such good lawyers here, especially lead counsel, to take nothing away from associate counsel and second seats and all that. But it makes it difficult, two very able advocates, who make reasonable appeals to the Court's rationale or at least hopefully to its intellect. I am going to try to sort through this a little bit. Most especially, the word "fairness" resonates with me, as some of you may know or not.

So, Mr. Jacobs, could you, just for a moment, address that issue that Mr. Scheve raises, the issue of, that this just isn't fair, Judge, because we didn't have the time, and even at the pretrial conference -- we could have said at our pretrial conference, I could have delved into what really happened here in these discovery disputes, what

was -- who was really the bad actor? Was it both of you, my suspicion? Who deserves to suffer, as they say?

So...

MR. JACOBS: I don't want to try the Court's patience, regarding go --

THE COURT: Don't worry about trying the Court's patience. It is an important issue.

MR. JACOBS: Let me go through how we got to Motion in Limine No. 1.

Mr. Walters was here at a discovery conference. We had raised for Your Honor the fact that their privilege log seemed not to contain testing references on it. And that we had not gotten Elan's testing documents.

Elan's counsel stood before Your Honor and said, The privilege log is complete. I am tired of being, my figurative words for him, I am tired of being beat up about my privilege log.

THE COURT: And I expressed concern with that representation.

MR. JACOBS: He said the privilege log was complete and that we have maintained clear walls between consulting and testifying experts, as noted in the Court's order on Motion in Limine No. 1. Both of those representations were incorrect.

That was the predicate for then -- and at that

hearing, the Court said, No more discovery disputes, and we understood that.

When Elan produced Dr. Brittain at his deposition, the night before we got this lengthy 466-reference log, I took that deposition, I examined Dr. Brittain on what he had done for Elan in testing. The only question he was allowed to answer was that he had tested Abraxane.

Every other question: What kind of tests did you do? What was the purpose of the testing? Did it relate to crystallinity? Did it relate to this? Did it relate to that? There was an instruction not to answer.

We wrote to Elan several times and said, You can't possibly do this; he is a testifying expert. It says on the log he was doing testing related to this litigation. You proceed with Dr. Brittain at your own risk. I scripted those words, Your Honor, because I wanted to be really clear to Elan very early on what the consequences of the assertion they were making with respect to Dr. Brittain were.

We then wrote our Motion in Limine. We said, Here's the history. Elan shouldn't be allowed to criticize our x-ray powder diffraction when there is all this testing evidence that suggested to us, based on the information we had then, Dr. Brittain had done precisely what we had done, used x-ray powder diffraction in various ways, whether on

Abraxane or a fraction of Abraxane or a sample, we didn't know. We knew only what we knew. We shifted the burden to them in that motion to demonstrate that the privilege was properly asserted.

They came forward with a declaration from Dr. Brittain. That declaration said no more than, What I did in the litigation was a different subject than what I am testifying to as an expert. It provided no underlying rationale for that distinction. It provided no subject matter basis. We argued that precise issue at the Motion in Limine hearing before Your Honor.

Your Honor observed that you had noted in the margin of one of the briefs the possibility of an order to show cause for contempt. Your Honor said, We are not going there, counsel. But I want to let Elan know that I view this as a very serious matter. And then we worked out, over the course of the Motion in Limine hearing, what's the right remedy here, given the violation of Federal Rule 26.

Then we proposed an order for the Court. Elan took a run at the proposed order with a letter brief. We responded to the letter brief. Then the Court adopted the proposed order, which, itself, lays out the rationale for the adverse inference that the Court is going to instruct the jury on.

There is none of that run up for this. They are

just showing up at trial and saying, Privilege log, privilege log. Look at these entries on Dr. Desai in particular.

Your Honor knows what these cases are like. Here is Elan's privilege log (indicating). These are huge cases, which where we over-sweep in documents to make sure we don't under-produce. Then we go through these documents, both sides, this is not unique to us, one by one, and we say, No proper assertion of attorney-client privilege. Then we have some back and forth.

Then, in this case, for example, with respect to communicate to patent counsel, our team went through each of those and confirmed that it was, in fact, communicated. It was, in fact, communicated.

I don't know how else, absent appointment of Special Masters and all those other things that we do to delve more deeply into this, I don't know how else to suggest this could have been addressed, Your Honor, given where we are. It is unfair to show up at trial and throw this up on the screen in front of the jury.

THE COURT: Last word, Mr. Scheve.

MR. SCHEVE: I will just address two points. I am pleased to hear they finally addressed the word "fairness" at the very end other than just a rehash.

Your Honor, the record needs to be clear. What

Dr. Brittain did was in his consultation with Mr. Sipio. His contract was to help Mr. Sipio understand some issues. He is continually characterizing what Mr. Brittain did, Dr. Brittain did, as Elan testing. And then they said, Well, you proceed with Dr. Brittain at your own risk.

I have reviewed the law on, Can an inference be drawn from the fact that things were put on privilege? And the law is, There can't be any inference drawn from that, which is what they have invited Your Honor to do. So we didn't put Dr. Brittain up, because if I had, I would hear on appeal it's waived, that the issue is waived.

We would simply say, Your Honor, we don't think it is appropriate either way for people to be instructed that there is an inference to be drawn when lawyers get information, look at it, and I don't doubt that they looked at stuff, although in one of the discovery conferences, Your Honor said, I don't know how a lab notebook can be claimed to be privileged. But they did it.

We put materials on a privilege log, and Your Honor has never been -- again, it's because Your Honor is burdened -- but we reached a point where there was no vehicle for either party to get this in front of you for review. Is this really privileged? You know, entry about, Well, these are results of experiments, but I plan to tell counsel about it. Of course, you can't hide facts by

saying, somehow cloaking it is something I think I am going to tell them in the future. Our point is if they are going to be able to do it with Dr. Brittain, and we think that is error, in fairness, how can they claim, shield from us experiments and claim that it wouldn't be fair for us to show the jury that they have done -- that they have shielded experiments under claims of privilege.

THE COURT: Let me think about this a bit. Is there anything else?

MR. JACOBS: One more fact that is useful, I think, Your Honor, to understanding the picture here.

DX-186 is the actual engagement letter with Dr. Brittain from Mr. Sipio.

THE COURT: Mr. Sipio is the fly in this ointment to a degree, I think, as I recall.

MR. JACOBS: Except two things, Your Honor. No. 1 it's cc Mr. Bokar, cc Mr. Bokar, and it states as follows, it's dated November 23, 2005: This letter will confirm that I have retained you as a consultant for your expertise in x-ray crystallography and other analytical techniques suitable for the characterization of chemical compounds present in human pharmaceutical compositions.

THE COURT: Are there any other issues that are more easily disposed than this?

MR. SCHEVE: They do plan to call Dr. Desai and

Dr. Soon-Shiong as a couple of their next witnesses. Dr. Soon-Shiong, who is the CEO, it is a series of newspaper articles about him that they plan to throw up about his work in diabetes and things of sort. It really becomes character evidence.

He is a good man. Look what he has done to fight diabetes, et cetera.

Character evidence shouldn't be coming in. If it does, it clearly opens the door to the fraud lawsuit brought by his brother against him. We go down the path, the fraud lawsuit brought against him by Mylan, the securities fraud action that is currently pending against him in California. I raise it with Your Honor so that if I have to ask for an opportunity for sidebar, you know where I am going.

Secondly, it is pretty clear from what they intend to do that they are trying to make comparisons of the embodiment of the '363 patent to the accused infringing product. And the case law there is very clear that they can't do that.

So they are not -- they have not been designated as experts. Clearly, they can come on as fact witnesses and talk about what they saw, heard, smelled, touched. But I believe, Your Honor, there will be many instances where what this devolved into with these two individuals commenting on

Elan's technology, it is clearly in the nature of expert testimony. I note to Your Honor we object to that. I am asking if you want to deal with that in realtime by sidebar.

We think they have clearly crossed the line between fact witness and trying to give expert testimony on their perceptions of the failings of Dr. Liversidge's invention.

THE COURT: Let's deal with that in realtime. Did you want to react to that?

MR. JACOBS: On the first one, it actually wasn't about character evidence. I didn't mean to suggest by those documents that we were going to put his character in play, although we have no regrets about that in any respect whatsoever.

But, rather, when Mr. Scheve took his deposition, his qualifications to have made the invention in question on our side, that is, his qualifications to have developed Abraxane, were called into question. What we intended to with demonstrate to the jury that Dr. Soon-Shiong is -- I hope they take away the inference that maybe I have taken away, that the man is a genius for his inventive capabilities. That is why we had it in there. I definitely don't intend to open the door to other litigation involving matters unrelated to this dispute. And I would ask Your Honor to patrol that during the testimony.

THE COURT: Mr. Scheve?

MR. SCHEVE: Your Honor has already requested the jury repeatedly, Don't go be influenced by what the media says. Now I have got a stack of at least ten newspaper articles about him.

I would suggest that if it's a game of what has the newspaper written, for every one that praised him, I can find one that criticized him and accused him of a lot of devious things. I think we have crossed the line.

If they want to ask him, I would like to talk with you about what you have done, sir, great. But to put up the newspaper, that this newspaper or that newspaper has interviewed him, I don't believe that is appropriate.

MR. JACOBS: That is fine, Your Honor. We don't have to use the newspaper.

THE COURT: That eliminates that. There was a second.

MR. JACOBS: The expert issue, it is a fine line but it's one that, I think, falls our way. We don't intend them to do an expert comparison in the way that the experts have. Elan has put their state of mind into play with their willfulness allegation, What did you think when you saw the Elan patents? What did you think when you saw the Elan presentation that you were faxed in 1996? How did you evaluate it compared to the technology path you were on?

That is very much in play and we have to elicit that testimony from them.

So that is not a real issue. We do not intend to ask them, In your expert opinion, Dr. Desai or Dr. Soon-Shiong.

Where I would ask for a little bit of leeway is that the words of the witnesses, because they are typically in front of scientists and they are typically making presentations, may not always say, My understanding is that. But I am happy to try to set this up so that when I ask them a series of questions, I will start out with, Was it your understanding that, so that it's factual and not expert.

MR. SCHEVE: I agree with him that how they perceived something in 1996 or 1995 is fact testimony. I am not here to argue against that. If this gets into, Let's go to Example 1 in the Liversidge patent, Doctor, why doesn't that do this, that, or the other, that crosses the line to expert testimony. And it is not reflecting what they saw or thought, heard back in '95-'96.

THE COURT: I think what you just described Mr. Jacobs would agree. Go ahead.

MR. JACOBS: Yes. Except I think it continues because the lawsuit is filed, and they have kind of put their state of mind in general in play.

So what they knew exactly in their head in 1996

versus what they have --

THE COURT: We are talking about comparisons, comparisons, either directly or indirectly, that are inappropriate, that Mr. Scheve has identified, and you know as fundamental, patent cannot be done, embodiment comparison, that is.

MR. JACOBS: Yes. I don't think we are actually going to get into this, Your Honor.

THE COURT: Well, let's see how that works out. Let me take a look at this.

We will take a break.

(Recess taken.)

THE COURT: Please, take your seats for a moment.

As I indicated earlier, Mr. Scheve, the issue of fairness does resonate with me quite profoundly. Having said that, I am going to rule in Elan's favor on this, in the brief time we have available to us, because now I have had a jury waiting in a very hot and overheated room. You may or may not know that the rest of this building is not as comfortable as this courtroom and I am going to let them out of that box. Given the limited amount of time that I have had to consider and reconsider Brittain and now the issue raised with regard to, it's Desai, I believe, I believe there are some material factual differences and

circumstances.

But I want to redial back to an option that I gave you during the pretrial conference, Mr. Scheve. That was to select the Motions in Limine that you felt were most critical. This, with all respect, I would have suggested might have been one better heard at that time when we had more time, when you would have had more time to write, I would have had more time to have the benefit of those writings around further argument.

That aside, you made the election you made. You did review it at sidebar. That doesn't send me off on an aimless, mindless search willy-nilly trying to anticipate what your arguments may or may not be. Elan has presented the Court, I think, a position that is legally correct.

You may be right, and at the end of the day, the Federal Circuit may say, Sleet, you blew it. It won't be the first time. I don't say that blithely. But we do what we do as trial judges, that is, make the best call that we can make under, oftentimes, rather stressful circumstances. This is one of them.

I am going to make the call to agree with Abraxis in this situation and grant the request that is provided in their conclusion at Page 3 of their Bench brief. You have been provided a copy of that, have you not, Mr. Scheve?

MR. SCHEVE: I have, Your Honor.

THE COURT: That is how this examination will proceed, without forcing the invocation of the privilege. And we will proceed from there.

MR. SCHEVE: Understood. Thank you, Your Honor.

MR. JACOBS: Your Honor, so the record is clear, I think I heard Elan a couple of times in there. You are ruling in favor of Abraxis.

THE COURT: Yes. If I misspoke at any point and transposed the parties, it should be clear that I meant that I am granting Abraxis' motion.

MR. JACOBS: Thank you.

THE COURT: Ms. Walker, I think we are ready for the jury.

I should also say, while the jury is coming in, reflecting back on one of the concerns I had, and I mentioned that Sipio may be the fly in the ointment, it was one of the concerns I recall having at the time, was the transformation, the morphing, the metamorphosis of Mr. Sipio, that is, permitting him to morph Brittain from a testifier into -- from a non-testifier, consultant, to a testifier, in a way that I felt was, perhaps, I am not accusing Elan of anything inappropriate, but just not a policy that I thought was one that I was prepared to sanction.

I am not going to redial and go back over all of that again. That was on my mind and is on my mind today.

(Jury enters courtroom at 9:29 a.m.)

THE COURT: Good morning, ladies and gentlemen. You will notice it is cooler in here. You are the most important people in the building, not the lawyers. I am being a little facetious. It's just happenstance that they were able to bring this room up more quickly than the other portions of the building. I hope it's getting a little better.

All right. We are prepared to proceed with Abraxis.

MR. JACOBS: Your Honor, Abraxis calls Dr. Neil Desai.

...NEIL DESAI, having been previously sworn as a witness, was examined and testified further as follows...

THE COURT: You may proceed, Mr. Jacobs.

MR. JACOBS: Thank you, Your Honor.

DIRECT EXAMINATION

BY MR. JACOBS:

Q. Now that you are seated in the witness box, could you introduce yourself to the jury, please?

A. Yes. My name is Neil Desai. I am the vice president of research and development for Abraxis Bioscience.

Q. Could we please bring up DX-96.

What is DX-96, Dr. Desai?

A. DX-96 is part of my CV. It's the initial part which has the biography of my work.

Q. I would like to discuss your background with you, now, Dr. Desai.

Mr. Broyles, could you follow along. We will go to 264.

Dr. Desai, tell the jury a little bit about your formal education.

A. I started off in Bombay, India, where I got, after my formal high school education, I received my Bachelor's in chemical engineering from one of the premier institutes of chemical technology in Asia. It's called the University and Institute of Chemical Technology. It is a very competitive institute to get in. I was there from 1982 to 1986. And I got my Bachelor's degree.

Following that, I got a full academic scholarship to the University of Texas at Austin. So I moved from India to Texas. That was a big move for me. And I pursued my graduate career, and I got my Master's degree in chemical engineering and my Ph.D. in chemical engineering at UT Austin. I finished up in '91.

Q. Your formal training was in chemical engineering.

How did you happen to work in the area of drug delivery?

A. Okay. Well, in my research area, I focused my efforts on medical applications, even though I was a chemical engineer. And the reason for that, really, is my prior background is I grew up with medicine in my background. Both my parents were doctors. Especially my father, he was an eminent cancer surgeon and head of one of the largest cancer centers in Asia. And growing up, I often went to the hospital, accompanied him to surgeries. I walked with him in the wards. I saw the patients at a very young age. I saw their suffering on the one hand and I saw their great satisfaction and their joy at being cured or being treated of the terminal disease, cancer. This left a very deep impression on me for the longest time, until today.

When I had an opportunity, as I was pursuing my research area in my Ph.D., I quickly focused my area towards medicine, so that maybe some day I could help patients with cancer.

Q. Have you published any of your thesis work, Dr. Desai?

A. Yes. In fact, I have. During my Ph.D., I think we did about ten or 11 publications. I think they are highlighted here on the board.

Q. Some of them refer to surface modifying or surface modifiers. What was that about?

A. Well, the focus of my thesis there was really to try and understand what happens when different materials come in

contact with the body, like blood and tissue. So it was very important to look at the interface, "interface" meaning the place where the one fluid contacts the other.

So if we are looking at materials, for example, that are used in medical devices that all of you are familiar with, you need to understand that when these devices get into the body, what happens to them, how they interact. And proteins play a very, very big role in this interaction.

So a lot of my study was on proteins and on interfaces of these materials that eventually come in contact with the body. That is what a lot of my publications involve.

Q. Are you an inventor on any patents?

A. Yes. I am an inventor on several patents. I think at the time of my graduate career, by the time I left, we had about seven patents that we had filed on different devices and different modifications to these devices. And these were subsequently licensed by some pharmaceutical companies.

Q. These are patents dating from your University of Texas days?

A. That's correct.

Q. Did you happen to study the concept or the topic of cross-linking during your graduate thesis work?

A. Yes, in fact, I did. We were one of the first groups

to show a unique type of cross-linking in some of these medical materials that are used today, in fact. And this was a, developed a method to make these materials sensitive to light so that upon exposure to light, they would cross-link and link all the molecules together for different applications in medicine.

Q. How many total scientific publications do you have?

A. I have about 35 or so scientific publications.

Q. And then since the University of Texas days and your graduate work there, have you been named as an inventor on other patents?

A. Yes, there are several other patents. I have a total of about 45 issued U.S. patents, probably another 20 or 30 international patents. And there is many, about 20 or 30 that are still pending that have not yet issued.

Q. Explain to the jury about the life, about your life as a scientist by telling them a little bit about the scientific presentations you give.

A. Yes. As part of my career, and as part of the career of most scientists, you go to scientific meetings and present your work. So over the course of the years, I probably presented at scientific meetings, I think about 80 or 90 times to date.

Q. How about in the past year, Dr. Desai?

A. In the past year, probably about, I would say, at

least 15 presentations at scientific meetings.

Q. Do you also organize symposia or conferences?

A. Yes, I have done that. I have organized several symposia, probably seven to eight or nine symposia where I, myself, chaired and organized and invited speakers to participate in.

Q. Do you review manuscripts submitted by other scientists for publication?

A. Yes, I do. Over the years, I have reviewed several manuscripts for different journals, like the Journal of Biomedical Materials Research, Journal of the Controlled Release Society, Clinical Cancer Research. In fact, just last week, I was reviewing an article for Clinical Cancer Research.

Q. How about awards for your academic performance, have you received any of those?

A. Yes. I did, at the time when I was in India, before coming to graduate school, I received an award for the highest scores in board examinations in the science area. I also received, after I finished my Bachelor's degree, a national endowment award, it's called Tata Endowment For Higher Education. That is supposed to help students with graduate studies abroad. That is usually given to a select few nationally from India.

Q. Have you received any special recognition for your

work in cancer nanomedicine?

A. Just this last year, I was asked to be a distinguished lecturer as part of the Center for Cancer Nanotechnology Excellence that is funded by the National Cancer Institute.

I have also been invited to give lectures in the area of nanomedicine and nanotechnology in about six or seven other conferences throughout the year.

Q. Do you talk to the Food & Drug Administration about these topics?

A. Yes. I have talked to the FDA in an advisory capacity on two occasions, one in 1996 -- I beg your pardon, in 2006, and one just a few months ago where they are trying to set standards for nanotechnology drugs. As you know, this is a very new field, and, in fact, we are fortunate enough to have one of the first cancer nanotechnology drugs through the FDA.

So I was called to speak on those topics.

Also, very recently, I was appointed as part of an advisory panel for the United States Pharmacopeia, which is an organization that sets standards for medicines, that is to make them safe, to see what kind of purity and to prevent unnecessary contamination or inadvertent contamination in materials.

So I am part of that advisory panel, which deals with blood products.

Q. **Explain to the jury, please, how you came to work with Dr. Soon-Shiong?**

A. **Yes. That was a long time ago. We were presenting our work when I was still in graduate school, I had some scientific meetings, and I think he saw the work that we were doing and we got talking. It was very interesting and exciting for me, because here I was as a Ph.D. student, involved in proteins, in cross-linking, and such ares.**

Dr. Soon-Shiong, at the time, was focusing on trying to cure diabetes. His approach there was to try and use eyelet cells, which are the cells in your body that produce insulin. They are from your pancreas. The idea was to encapsulate these cells, that is, coat them, and put them in these tiny microcapsules and put them in the body of the diabetic patient so that they can have insulin produced within their bodies. In diabetics, as you know, insulin is absent.

When I learned of this, it was very exciting because I immediately felt I could use my cross-linking background, use my background of protein and interactions with different devices that are put in the body to help this effort.

I think Dr. Soon-Shiong also felt the same way. That is how I got to know and work with Dr. Soon-Shiong after I graduated from the university.

Q. Was there a relationship between the work you did in your doctoral work and the work you did beginning with Dr. Soon-Shiong?

A. Yes. In fact, there was a definite overlap. As I mentioned, the cross-linking expertise was important for generating the microcapsules that he was working on. And the protein-based experience was important for trying to avoid adverse reactions to these implanted capsules once you put it in the body.

Q. How did you start to work on Abraxane? How did that develop?

A. Well, that sort of developed once I got together and started working with Dr. Soon-Shiong. We were looking at different strategies, focused on what we call biopolymers or natural polymers or natural materials for diabetes and for other applications.

Really, I think the light bulb went off when we talked about different proteins, and, in particular, a specific protein called albumin, which is in our bodies and does a lot of interesting functions.

We realized at that time that albumin can get out of the bloodstream very fast by some unique mechanisms. Really, the thinking was, Can we utilize this in application to cancer? That if we somehow managed to link or combine a drug with that albumin, that we could get it out of the

blood and into the tumor in a very quick fashion. Therefore, prevent toxicities, but maybe even help fight the tumor.

So that was, really, how it all began.

Q. When did you actually begin working on a paclitaxel drug delivery system?

A. That would have been, I think, 1992, to the best I remember.

Q. Let's go to the other end of the chronology and talk about Abraxane and what's actually in an Abraxane vial.

What does Abraxis place in a vial of Abraxane?

A. Well, Abraxane is really composed of only two components. It has a lot of albumin, which is the protein that I just talked about, and it has the drug paclitaxel.

The drug paclitaxel, or Taxol, as it is known as, is in the form of these very tiny particles, which are amorphous in nature, that is, they are not crystalline. And these are nanometer sized particles. To be specific, they are about 130 nanometers.

Just to calibrate you, I am not sure if you are familiar with nanometer size range, but it's about, if you think of the thickness of a human hair, and that is a common example that everybody uses, and you think of the size of the nanoparticle, it is about 10,000 times smaller than the thickness of the human hair.

Q. So, in sum, what is in the vial?
A. In the vial, there is about ten times as much albumin as there is the drug paclitaxel, so it's a ratio of roughly nine or ten to one. And the paclitaxel is in the form of these amorphous nanoparticles. And around the nanoparticles is a thin layer of the albumin, which is cross-linked.
Q. What is Abraxane approved for today?
A. Today it is approved for the treatment of breast cancer.
Q. What other areas are being explored?
A. The other types of cancers that have been tested for, and are in clinical trials this very moment, are in lung cancer, in melanoma, in ovarian cancer, people have interest in brain cancer, and, right now, we are getting some very exciting results in pancreatic cancer.
Q. Breast cancer was the first disease for which it was improved?
A. That's correct, yes.
Q. Why did you, at Abraxis, pursue breast cancer first?
A. Breast cancer, as you know, like all other cancers, is a terrible disease. It affects a large population of women. And we thought this might be a good place to test the drug, since there is a big need for new drugs in breast cancer.
The drug Taxol, which was approved in 1993, was a big advance in breast cancer, but it had lots of

limitations. One of the big limitations was the toxicity of that drug, and toxicity was really not due to the active drug itself, but due to what was a solvent that was given with the drug, just to help make it soluble, so that it could be injected into the bloodstream of cancer patients.

And patients actually died from receiving that, because of the toxicity of the solvent.

So there was a big need at that point. And we decided that using our approach of albumin to get the drug out of the bloodstream very fast to the tumor would be appropriate in this setting, so that we could make it safe and we could also make it more effective.

Q. You mentioned the size of the nanoparticles in the Abraxane formulation.

Why is it important that the size of those particles be what it is?

A. It's actually critical that the size be in the range, or well below 200 nanometers, because when you think about drugs that are administered directly into the bloodstream, you have to be -- it's a very high standard of safety you need to achieve because you cannot have any contaminants. You cannot have any microorganisms. You cannot have bugs accidentally in the preparation, because since the drug goes directly into the bloodstream, you can have very adverse events for the patient.

So the size is very important, because the FDA has demanded that for a drug to be injected in the bloodstream, it needs to be sterile, that is, it cannot have any bacterial contamination. The way to avoid that is to pass the drug through tiny pore filters which have very tiny pores, which are 200 nanometers. Since most microorganisms are bigger than 200 nanometers, you would filter them out. This drug needs to be put through these filters. Therefore, if the size is greater than 200 nanometers, it is not getting through the filter.

You have to have it sufficiently smaller than 200 nanometers, about 150, 130 nanometers, so you can pass the entire drug through, thereby sterilize it and have it safe. That is why the size is very important.

Q. Can you tell the jury why Abraxane was designed to be the way you described it, amorphous, cross-linked, and maybe any other reasons why you designed it to be nano-sized?

A. So the amorphous nature has really got to do with how fast you can get the drug to the tumor. When you have something amorphous, that is, amorphous really means that you have a lack of structure, and when you have that kind of molecule as opposed to a crystalline molecule, which is the opposite of amorphous, amorphous molecules dissolve very fast. It's like taking the analogy of cotton candy. You put cotton candy on your tongue, it just goes away and

dissolves right away, versus the rock candy example. These are big crystals of rock, of candy that take a long time to dissolve.

So using that analogy, we thought of amorphous as being very useful for dissolving the drug very fast, and because we use albumin, it helps to get the drug right out of the bloodstream like that, very quickly.

The second aspect to it is the cross-linking aspect. We are creating these structures, which are small spherical balls, if you will, of about 130 nanometers in size. We need something to keep that structure in place as we produce through our manufacturing process.

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.

Q. Any other reasons besides sterility why you made it so small?

A. Yes. Other than the sterility aspect, it was well-known at the time that if you had small particles in the hundred nanometer size range, this is important for getting out of the bloodstream into the tumor, as opposed to

larger particles, which may go into other organs, like the liver and spleen. We did not want these particles to get into these other organs, but we wanted to get them into the tumor.

Q. Over time, have you developed your own understanding of Elan's approach to nano-sized particles?

A. Yes. Certainly over time, through presentations that I have heard and through other materials, we have come to understand Elan's technology as being very interesting and novel, but focused on a different aspect. They focus on crystals. And their technology focuses on breaking down crystals to small size. So you start from a big crystal and end up with a smaller crystal in the nano-size range.

As compared to that, our technology is different, we actually build the nanoparticle to make an amorphous nanoparticle.

The other thing I learned about Elan's technology is that they put surface modifiers on the surface of the crystal, and that these surface modifiers, it turns out, are non-cross-link. They are not linked to each other. The individual molecules of the surface modifier are separate, which is again different from the approach we used, that our surface modifiers of proteins is a protein albumin, and is linked together to form this shell around the particle.

Q. Let's use a slide to explain this to the jury, Dr. Desai. Does this reflect your understanding of the differences between Elan's technology, as you came to learn it, and Abraxis' technology?

A. That's correct. It does. On the left side is Elan's technology, and on top left first, so these are crystals of the drug paclitaxel. And the paclitaxel crystals, a very characteristic feature of paclitaxel, they form needle-like or rod-like crystals. That is why this shape.

And then on the, those crystals are adsorbed, which means just stuck there without any chemical interaction, these molecules of a surface modifier that are non-cross-linked, that is, they are not attached to each other in any way.

So that forms the basis of Elan's technology as it relates to paclitaxel.

On the other hand, Abraxane, as I tried to describe to you, is more, sort of a spherical structure. It's like a little ball of paclitaxel where the drug, itself, in the core of the particle is amorphous. So we don't have crystals. And as I mentioned, crystals of paclitaxel look like this, like little rods.

On the surface of the particles, this is designed to have albumin, the protein albumin on the surface that is cross-linked to each other. That is the individual

molecules of albumin are linked to each other to stabilize this particle.

Q. How long have you been working with paclitaxel?

A. I have been working with paclitaxel from about 1992. That would probably make it, what, 16 years or so.

Q. Have you ever seen it in a form different than the form you are describing it here, that is, needle shaped or rod shaped?

A. In my entire career working with paclitaxel, any time you look at paclitaxel crystalline material that is from many different manufacturers that we have looked at, it's always in the form of needle-shaped crystals. In fact, in the textbooks, it's even described as needle-shaped crystals for paclitaxel. That is a very characteristic feature.

Q. Did you develop an understanding of how Elan manufactures its nanoparticles?

A. Well, from the information that was out in the literature, it was evident that Elan uses some techniques where we start with big crystals, which may have come from a manufacturer, from a manufacturer of this drug, and these crystals are then ground up into small particles.

One of the ways of grinding that I think Elan uses is using what's called a ball mill. In essence --

MR. SCHEVE: Excuse me, Your Honor. To the extent he just expressed what he thinks Elan does, there is

no foundation.

BY MR. JACOBS:

Q. Can you explain how you came to have the understanding about Elan's technology reflected on this slide?

A. Yes. From reading in the literature, from reading in published patents, and from some materials that they sent to us, I think, in 1996. And from presentations that I have heard at scientific meetings.

So at any rate, the technology, as I understand it, involves grinding of large crystals to make them into small crystals, and then, also, in the presence of a surface modifier to help stabilize these crystals.

On the other side is, just so you can get a comparison of the different process that we use for making Abraxane, here is how we make Abraxane. Again, this is simplified, so that we can easily understand it.

We have two components --

MR. SCHEVE: Your Honor, may we have a sidebar.

(The following took place at sidebar.)

MR. SCHEVE: This is clear comparison of the embodiment of the '363 to the Abraxane product. We object that that is inappropriate.

MR. JACOBS: I don't see how it can possibly be inappropriate for him for compare and contrast the manufacturing information when Mr. Scheve, in his opening

statement, placed into question whether somehow Abraxis had copied manufacturing details from the information that Elan received in 1996.

THE COURT: Did you hear what he said?

MR. SCHEVE: I did. He is saying, Here is what Elan's product looked like, these needles. Now he is going to compare it to the accused product, the accused infringing product. That's clearly not appropriate.

MR. JACOBS: That is a different issue from manufacturing, which is what I think we are on right now.

MR. SCHEVE: He didn't put up a slide comparing manufacturing. He put up needles and he is going to compare it to Abraxane. That is inappropriate.

MR. JACOBS: I think the objection is, now he is about to explain the Abraxane manufacturing process. I think we are past the description of the Elan process. We are on to Abraxis now. We are about to move into a discussion of how Abraxane is made. I think it is very relevant to the jury.

THE COURT: He doesn't object to that.

MR. SCHEVE: No, not to how they make Abraxane. He has made a comparison, that is what I object to.

MR. JACOBS: He is describing his understanding, having worked in the field. They have put his state of mind at issue.

THE COURT: You are finished now, on the manufacturing?

MR. JACOBS: Exactly.

MR. SCHEVE: As long as there is no comparison of their invention to their infringing --

THE COURT: Both of you well understand.

(End of sidebar conference.)

BY MR. JACOBS:

Q. Let's proceed with where we were. You were describing the manufacturing process for Abraxane by Abraxis.

A. On the right side here, we have the manufacturing process for Abraxane. It essentially starts with two components. One is albumin, the protein. This protein is dissolved in water. So you have a solution of albumin.

On the other hand, the other component is paclitaxel. So we start with large crystals of paclitaxel that we obtain from the paclitaxel manufacturer, not unlike what is shown here, the needle-shaped crystals. And we completely dissolve them in a solvent. So there are certain solvents that can dissolve paclitaxel so all the crystalline character is gone, it's completely dissolved. It's a solution. It's like taking sugar and putting it in water, and after some time, you can't see anything anymore. You can't see the particles.

So all of the crystalline character completely

disappears. It's now entirely just molecules floating around in solution.

Now, the second step is to combine these two in a process, where you can disperse or make tiny droplets of this paclitaxel solution inside the albumin solution.

This is shown here as the little red dots. You make these tiny little droplets of the solution of paclitaxel inside this albumin solution. And then what you do is rapidly evaporate this solvent. So the idea is you only use this solvent initially to dissolve the material. But then you want to take it out. So you put it under a vacuum, and under vacuum, the solvent can evaporate off, or boil off, and leaving behind the drug.

What this does is, because it's in solution, and you take the solvent away, it actually precipitates the drug in an amorphous form. So when it comes out of the solution, you do what's known as a solvent precipitation, that is, the solvent goes away, and you precipitate or create solid particles off the paclitaxel, which is amorphous in character.

This is a well-recognized theme, that is, solvent precipitation can be used to create amorphous materials. So we used that theme.

After we evaporated the solvent, you end up with tiny solid particles, and here you have those solid

amorphous particles. In that process here, the albumin settles around the surface of the nanoparticles and you get cross-linking.

So that's how you end up with these particles that are cross-linked and be amorphous.

Q. Have you prepared an animation to describe the Abraxis manufacturing process?

A. Yes. We can see that here.

Q. Why don't you explain to us what this animation is describing?

A. Okay. So this actually takes you through the process. As I mentioned, the first step, you take the paclitaxel crystals. You completely dissolve them in solvent. And the raw material you get for this is in the form of crystals. You put this into the solvent and stir it up and shake it up. Eventually, these crystals are completely gone. There is no more crystal structure. It is essentially a clear solution.

Now you have got the paclitaxel solution, which has no more crystals.

The second step to this is taking the albumin solution. Remember, there are two components, albumin and the drug, so here is the albumin dissolved in water, here is the paclitaxel dissolved in solvent, and we mix these up and we take the crystal-free paclitaxel solution and homogenize

or mix it or fluidize it with the two together. The idea, as was seen in the previous picture, was to get these tiny droplets of the mixed solution.

So this is mixed up under high shear conditions so you get a very fine droplet size.

That will be seen in a second.

At this stage, you get the cross-linking of albumin. Around the droplets, the albumin accumulates. Then the cross-linking occurs. After this step is done, what we want to do, remember, the solvent is still here, we want to get rid of all the solvent. So if you look at this microscopically now, these are tiny droplets, as indicated here in the dark red, which contain the drug. And then these yellow particles, or these yellow molecules are actually the albumin that is beginning to accumulate on the surface and start cross-linking.

When you look at it close up, you can see that this is shown that there is individual molecules of paclitaxel that are still dissolved inside the droplet in the solvent. That's indicated here. And, again, there is no crystal structure here, remember. This is completely dissolved. And then on the surface of these particles is the albumin that starts to accumulate and coat the surface and cross-link to each other or link to each -- the molecules of albumin linked to each other.

Now you have got these droplets and you do evaporation. You, in effect, under vacuum, you are removing all of the solvent. So the solvent goes away. And because of that, you precipitate, that is, you create these solid particles by solvent precipitation. These particles are amorphous.

Essentially, you have created, now you have cross-linked albumin coating on these solid particles, amorphous particles.

Now you have nanoparticles suspended in albumin solution. The next step is to filter. Remember I talked to you about the importance of filtration, to make sure that it become sterile. So it's filtered and then filled into the vials that we use for making Abraxane. At this point, you freeze dry it. That is, you freeze it rapidly, and you put it again under a vacuum, so all of the water evaporates off to leave you with a dry powder.

Here is the water coming off under high vacuum. And then all you are left with is a dry powder that has the two components, the albumin and the drug paclitaxel, and then the nanoparticles of paclitaxel, which are amorphous, and have a cross-linked coating.

Of course, we put a cap on the vial. And this is what becomes Abraxane. And then the 100 milligrams of drug in there, paclitaxel, with about ten times as much of

the albumin.

Q. Dr. Desai, I am sure you recall, you had your deposition taken in this case. Do you remember that?

A. Yes, I do.

Q. Do you recall that Elan asked you a lot of questions suggesting that you had somehow used Elan's ideas from a packet of material that Gary Liversidge sent you around August 28th, 1996, to develop Abraxane. Did you do that?

A. Not at all. In fact, the approaches were completely different. By that time, we were well under way to developing Abraxane.

Q. I would like to run through with you a chronology of some of the milestones in the development of Abraxane before the exchange with Nano Systems in late August 1996.

This is a timeline, Dr. Desai. Did you help prepare this?

A. Yes, I did.

Q. Can you walk us through briefly what this timeline is showing?

A. Okay. So this timeline starts with early 1992, when we first think about and start to work on what eventually became Abraxane, all the way to here, which is the end of August, beginning of September, 1996, where we had a phone call with Nano Systems and some materials were exchanged and we had a discussion.

In between that, it shows that within these four years, we were actually working hard on the development of Abraxane during that time period. And there were some critical milestones achieved during that time period. I will just point to a few here.

The first was in February, 1993, we filed our own patent, which is called the '686 patent, that covers cross-linking of albumin-based paclitaxel nanoparticles. Also, in February, 1995, we actually achieved a formulation of Abraxane which was amorphous. And we believed that it was amorphous and I have this notation in my lab notebook. We continued further development. We, in fact, contacted the FDA in April of 1996 to tell them that we had developed this novel form of paclitaxel and that we were wanting to go into the clinic with that. And we were able to scale up the process to make large amounts, and we put together a clinical plan with the FDA and we, in fact, confirmed that the particles were amorphous.

This was all occurring before we ever talked to Nano Systems.

Q. Dr. Desai, you have used that word "scale up" a couple times. Can you explain what that means?

A. Yes. That is a common word that's used in the pharmaceutical industry. When you first start with a new preparation of a drug, for example, and you start in the lab

on the lab bench and you're working on very small test tube quantities of material. But, eventually, in thinking of going into the clinic, thinking of testing these, the drug in human patients and then eventually going commercial to sell the drug, you need to, of course, scale up, that is, you need to be able to not just manufacture in a test tube but maybe make it in large vats of material.

That is what scale up is all about.

Q. Let's take a look at some documents from the development of Abraxane.

What is JX-31, Dr. Desai?

A. This is an entry from my lab notebook. Pardon my handwriting. But I will try and explain to you what's there.

This is October of 1992 from my lab notebook. This says, the title says, Albumin MIC, which is short for microcapsules, with the drug Taxol, with Taxol.

Here, what we have done is -- this is -- we have created these nanoparticles here, which we call prunes. The reason we use the word "prunes," I will explain that to you in a minute, but the process here is using the solvent as you saw in that little animation. And, incidentally, we use the solvent benzene in this case. We made the little particles of the drug by pulling the solvent off, or evaporating it, very much like was seen in that animation.

This resulted in solvent precipitation or precipitation of the amorphous particles from the solvent.

Then we took this material, which is the nanoparticles, and we actually put it into animals at this early stage in 1992. So this refers to two rats here that were tested with this particular formulation back in 1992.

Q. You mentioned prunes, Dr. Desai. What is a prune?

A. Well, that's sort of a nickname that we gave the structure that we were trying to create, because, at that point, we imagined it to be sort of spherical in nature, but the process that we were using was to first use the solvent and make the droplets. Then we were evaporating, or, in fact, drying out that process.

It is like, think of a grape that you dry out and you get a raisin or a plum that you dry out and you get a prune. So I guess we affectionately called this structure we were making a prune.

Q. You mentioned your '686 patent. Let's take a quick look at that.

This is DX-552. Can you just explain to the jury what the title of that patent is referring to, Delivery of Water-Insoluble Agents?

A. Yes. This patent covers, this is the first patent that we filed on Abraxane back in February 1993. And this patent, the title of it covers water-insoluble

pharmacologically active agents, which means water-insoluble drugs. And useful compositions and methods for invivo delivery, meaning methods for giving this drug to an animal or humans. That's what we covered in this patent.

Q. You are an inventor on this patent?

A. Yes, I am an inventor.

Q. Let's take a look at Column 4, Lines 18 to 33.

Were you putting in your patent applications some of the work you were actually undertaking at the company you were then at, I guess it was called?

A. VivoRx.

Q. What is described, what does this reflect about capturing what you guys were thinking about at that time?

A. Well, this is in the section of the invention that talks about the detailed description. It gives a summary of what the invention is all about. Maybe if we can sort of expand this box a little bit.

So this invention talks about a polymeric shell, and the polymer here that we used is albumin, is the molecule we used, so we are creating a shell of albumin. Around a, particles of albumin, that is less than about ten microns, and the important thing that is covered in this patent is that this polymeric shell that is around the particles is cross-linked, and that the cross-linked -- that is, these molecules are linked together by a very specific

linkage called the disulfide bond. So we cover that aspect of the invention in this patent.

Q. Let's take a look at JX-28.

What is JX-28, Dr. Desai?

A. This is an electron micrograph. So we did electron microscopy, looking at very high magnifications, to look at our particles. This was, again, done in the early days. So this gives an indication of what the particle looked like. It was more or less spherical, and it had a thin shell, which is not very visible, unfortunately, on this. But this shell, we could actually measure the thickness of that cross-linked shell. We have indicated that here, that the cross-linked shell was only about 25 nanometers thick. So it's a very thin layer. But it's there and it's cross-linked.

Q. Let's go back to the patent. What sizes were you thinking about in this time period?

A. In the time period when we filed the patent, we were thinking that the useful sizes of these particles could be in a range of about .1 micron to about five micron. Again, .1 micron is 100 nanometers, the same thing, all the way to five micron, which is 5,000 nanometers. That is the size range we were thinking of.

Q. Let's go back to the face page of the '686 patent.

Was there anything else interesting about the

face page here, Dr. Desai?

A. Yes. If we can blow up that part right there. It was very interesting that the primary examiner and the assistant examiner -- these are examiners at the United States Patent Office in Washington, D.C., are Thurman Page and William Benston.

Q. Let's turn to JX-21 at 0525198.

What is interesting about this lab notebook entry, Dr. Desai?

A. This lab notebook entry is from early 1995. I believe the date on this was about February 1995. Here, we use the word again "prunes." But what we are testing here is a couple of things. And, in fact, this was a series of experiments. There are two experiments in this series. We were trying to evaluate one condition of making the particles. And that particular condition is the evaporation step.

When you do that evaporation step that removes the solvent, you can either remove it slowly over time or you can remove it in a flash, very quickly.

We were trying to see if that affected the outcome, that is, what kind of particles we would get if we did that slowly versus we did that very quickly.

So this first experiment talks about removing the solvent, in this case it's ethyl acetate, that is the

short form for that, it is removed very slowly.

What I also note here, by removing it slowly, we give it time for crystallization. That is sort of a well-known process, that when you evaporate things slowly, the drug or the molecule that is inside has time to crystallize and make its crystal.

So we tested that here. And I think the results are shown on the next page.

Q. Let's go to the next page, please.

A. That is over here. So here is that first experiment, and then we do the evaporation very slowly. And this, what I have written here is the microscope, meaning I am looking through the microscope and observing what we see. We see these needle shapes, that I have drawn here, these are the characteristic needle shapes of paclitaxel crystals.

I confirm that by using polarizing microscopy, which is a type of microscopy where you use a polarizing lens, so you can tell if these things are crystals or not crystals.

Under the polarizer, I make the notation that these are mostly crystals. So what I proved here in this experiment is that if you evaporate slowly, if you take the solvent out slowly, you are giving time for crystallization and you will end up with crystals.

This is exactly what we were steering away from.

Q. Let's go back to the previous page.
A. This was the second experiment in the series. So I have written here in my notebook, Redo the experiment and give no time for crystallization. So we wanted to do that evaporation very quickly to see if we can completely avoid formation of the crystals.

The results are, we have two pages down, on this page, this is blown out here, my observations, with the second experiment, and I looked through the microscope, and I see, I make a notation that most of the Taxol is probably amorphous. And that this is a good result. Meaning that this is what we were after right from the beginning. And we seem to have achieved this goal in this experiment.

Here we have now determined that at least one condition of the process, that is, evaporation, a very important step in the process, and if you do take time and do it slowly, you are going end up with crystals, which is not what we want. So you have to do it very quickly and prevent the crystal formulation.

Q. We are looking at Page 78 and 80 of your notebook, 198 and 200.
A. Yes, that's correct.
Q. Dr. Desai, let's go back to the timeline. Where are we now in the development of what became Abraxane as you were just describing to us?

A. This is in February 1995. That notebook entry which you just saw is February 1995. I made the notation, Amorphous, good. And that's what's indicated here in this timeline.

Q. Had you even heard of the Nano Systems people by this point?

A. No. I was not even aware of Nano Systems at that point.

Q. Tell the jury, please, about some of the challenges you and your team encountered in developing Abraxane from this time forward.

A. Well, at this time, you know, we had gotten what we thought was a good first step. So we had the amorphous particles. But there is, of course, you don't stop development. You have to find all kinds of different conditions. You try to still further keep optimizing the formulation. You do several different types of experiments to make sure you can reduce the particle size down to below 200 nanometers. So there was a lot of work still ahead that eventually led to Abraxane.

Q. Let's go back to your notebook, JX-21, at 227. So this entry, March 9, 1995, what are you doing here, Dr. Desai?

A. This is a different experiment. Now we are testing if the amount of albumin in that formulation affects, has any

effect on the characteristics.

So, here, we have tested and looked at, if you use a ten to one ratio, meaning you have ten times as much albumin as you have paclitaxel, so here it's 50 milligrams of HSA, which is human serum albumin, and five milligrams of Taxol that is used in this experiment. And the result of this, fortunately, I observed it. I made a notation, Looks pretty good.

So this was a good result I did obtain when you have ten to one ratio, that is ten times as much albumin as you have the drug. So this is yet another parameter or a condition that we were looking at to try and make the amorphous particles.

Q. There is a reference at the bottom, See the Brownian Dance, Dr. Desai. What is that?

A. That is a sort of note that I made because I was observing these particles under the microscope. When particles get very small, they sort of dance around and they are not sitting still in one place but they are vibrating. This effect was noted about more than 200 years prior, the famous scientist, with the name Brown. That effect was subsequently called the "Brownian" motion.

I am just making a notation there that I was happy to see that Brownian Dance.

Q. If you go over to the middle right, it says, Five

milligrams per milliliter Taxol arrow human dose.
A. Yes.
Q. What are you describing there?
A. Here, I am already thinking about, now that we have got, you know, what we feel is, we are making headway in terms of this formulation.
So I am thinking ahead about what the possible human dose could be and how we could give this to humans.
I put in here that five milligrams per mil Taxol. What I am referring to is the concentration of the drug when we would ultimately go into humans, this is the concentration we would give the drug at, into the vein.
It turns out, if you look at the package insert, that is, the instructions for Abraxane today, that is exactly that. That is what we ended up giving the drug, at file milligrams per mil.
Q. Let's go to Page 243 of your lab notebook, JX-21, Dr. Desai. What are you representing here?
A. First I should apologize for all these complex notations here. I will try and simplify it the best I can.
Here we are looking at yet another parameter. There is many things we have to test to get to the right place with this formulation.
So this is in April of 1995, where we are testing the effect of the amount of albumin. We talked

about the ratio, the performance of the ratio in the previous couple of note pages in my notebook. Here we specifically tested a range of ratios going from .5 percent to 5 percent. That is varying the amount of albumin in there by tenfold. So the five percent on top refers to that ten to one ratio that we tested. And then here we are testing it as very low amounts of albumin.

The bottom line here was, if you look under the microscope and observe these particles, when you have very little amount of albumin, you end up with large chunks. These are five micron chunks or five microliter chunks, which is well above the size range that we want. We wanted it way down at around 200 nanometers or in the nanometer size range.

In contrast, when you use five percent, that is that ten to one ratio of albumin, there is enough albumin in this formulation to get nice, stable particles. And my notation here is, essentially, nothing visible under the microscope, that this is submicron. That is, these particles were so small that even at high magnification, under a microscope, you can barely see them. This is exactly what we were looking for.

On the right side here is also the filtration, and, again, this is the complex notation, but here, this is the .2 micron or 200 nanometer sterile filter that's used to

sterilize Abraxane. And when we filter this, it goes straight through. And that's why I indicated here, Goes straight through, without any problem.

In contrast, when you have very little albumin, you have a big problem filtering, and I think what I have said here down below is, Major resistance to filtration, and I have also made a notation, Bust, this experiment is bust, this condition does not work.

Q. Dr. Desai, just to explain your notebooks a little bit, there is a name and date at the bottom of this, Paul Sanford, May 22nd, 1996. What does that represent?

A. Well, that is just when these notebooks were signed off or witnessed. Also, there is a date of 5/20/96. That is when I signed the notebooks. But the actual experiment, as can be confirmed from just a few pages prior in this notebook or a couple of pages further up, the experiment was conducted in April 15, 1995.

MR. SCHEVE: Your Honor, may I approach, please?

(The following took place at sidebar.)

MR. SCHEVE: I apologize, Your Honor. I am about to die. I got to go to the rest room.

MR. JACOBS: Let's take a break.

(End of sidebar conference.)

THE COURT: Ladies and gentlemen, let's take a short break.

(Jury leaves courtroom at 10:29 a.m.)

(Recess taken.)

THE COURT: All right. Ms. Walker.

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

THE COURT: All right, ladies and gentlemen. We will pick up where we left off.

BY MR. JACOBS:

Q. Mr. Broyles, if we could put up the timeline again.

Dr. Desai, where are we in the development of Abraxane in this timeline?

A. Well, we still are around April of '95.

Q. And in September of 1995, you -- in the summer of 1995, you started sending some samples out?

A. That's right. We sent samples out to different groups. These were third parties that were outside of our organization. And we did this to send samples out for testing.

After we had created what we thought was amorphous particles and we had a ratio of about one to ten that we had identified as a good ratio, we sent samples to the National Cancer Institute for some testing. We also sent samples to BMS, or Bristol Myers Squibb, which is a pharmaceutical company, because they were interested in Taxol.

We sent samples, subsequent to this, we sent

samples to Southern Research Institute and to the biological test center to do further studies with our drug.

Q. Let's take a look at JX-41. JX-41, dated September 25th, 1995, from VivoRx to Bristol Myers Squibb.

What does this letter represent?

A. This is a cover letter which goes with the samples that we sent to the Bristol Myers Squibb for testing. It says that we sent it to Jim Bergey, who is the director of licensing in Bristol Myers. It says the package includes several things, and there is five vials of encapsulated Taxol, which we called Capxol, which is short for encapsulated Taxol. That is the name we had given it at the time. And that each vial contains 40 milligrams of Taxol and about roughly 300 or so HSA or human serum albumin.

Q. Let's look at Page 649 in this packet. DX-117 or JX-41.

What are you showing on this, Dr. Desai?

A. This is what we call Fact Sheet, meaning this has a little more information about the drug that we are sending to Bristol Myers Squibb so the personnel at Bristol Myers Squibb has all the information on how to use the drug and what is in the drug.

So we said, This is a Capxol, and it's about 50 milligrams, it has about roughly tenfold the amount of albumin, and, more importantly, we identify the particle

diameter, the size of the particles here, to be about 470 nanometers. We measured this by laser light scattering. So we provided them with this information, along with the package of materials.

Q. Was this before or after you received materials from Nano Systems?

A. This is almost a year before we ever received any information from Nano Systems.

Q. Let's take a look at DX-60, Dr. Desai.

What is DX-60, April 18th, 1996?

A. So this represents, in fact, one of our first contacts with the FDA. This is now in 1996, April. I write them a letter, this is from myself, to the person at the FDA, saying that we have developed a new formulation for the anticancer agent Taxol. In this letter, I also identify that our formulation comprises nanoparticles of Taxol that can be freely suspended, for example, in saline, which is just a salt solution.

The reason I sent them this is because I was asking them some advice on the solvents that we used in our process. That was the basis of this letter.

Q. Was this before or after your first contact with Nano Systems?

A. This is well before. This is in April of 1996, several months before our contact with Nano Systems.

Q. Let's take a look at JX-7.

What is JX-7, Dr. Desai?

A. This is a notebook of one of the scientific staff that worked for me. His name is Shlomo Magdassi.

Q. Let's move to Page 462, please.

Dr. Magdassi was in what capacity as compared with you in the organization at this time?

A. He reported to me. Actually, he was a professor from Israel who was working with us at the time. And he is an expert in colloidal science. That is his field. He reported to me for that period of time.

Q. Let's take a look at 462.

What is his notebook reflecting here, Dr. Desai?

A. Again, there is a lot of information here. This is results of testing of several formulations that he was working on of our nanoparticles. He was also trying and testing all these different conditions to try and find the best condition.

And the focus in this testing is really looking at the size aspect. So after each preparation was made, you would measure the size by this instrument that's called laser light scattering. It is a technique that is used to measure size.

Clearly, at this time, you see several different numbers here. All of these numbers are the size in

nanometers. There were several experiments here that show 130 nanometers, 150, 140. So what we are trying to show you is that, at that time, we had achieved, more or less, our target of being at about 150 nanometers or below.

Roughly around 150 nanometers, as I explained, is important for the filtration. So we have to get the particles through the filter in order to sterilize them.

So it needs to be well below the 200 nanometer range.

Q. What is the date of this work?

A. This is dated July 19th, 1996.

Q. You confirmed that?

A. Yes, through the previous page, I think, of this notebook.

Q. Let's take a look, again, at your notebook, JX-21, at 296.

What are you describing here, Dr. Desai?

A. Okay. This is, again, we sent samples out for testing, as I mentioned before. This is one of those institutes that we sent the testing samples to, it's called Southern Research Institute, it's a famous institute in Alabama, Birmingham, Alabama, that does these types of tests in animals. It clearly indicates that we have 150-nanometer preparation of Capxol that we are going to send to them for testing.

Q. You dated this to July 22, 1996?
A. That's correct (did he say 22?)
Q. Let's take a look at 298, July 15th, 1996.
What are you showing here?
A. Here I am showing several notations I put down in my notebook. This indicates we are ready for scale up. That is, as I mentioned, going from the small laboratory scale to the larger scale that was more important for actual use in clinical trials. I make that notation there that we have to scale up from the small volume, 100 cc, 100 milliliters.
I am talking about a preparation of a package for the FDA. And that I am giving about a month for myself to prepare the package, that it should be ready in about a month, and that I need to call the FDA to set up what's known as a pre-IND meeting. That is, "IND" stands for investigational new drug.
When you first approach the FDA that you are ready to do testing in the clinical setting, that is in human patients, you need to compile a big package for the FDA with all the information.
So I wanted to set up that meeting. That's what this refers to.
Q. Let's go to Page 329 of JX-21. August 27, 1996.
What are you describing here?
A. This is some results of those scale up experiments

that I referred to in the previous notebook page, and that we have actually conducted those experiments, and those scale up experiments result in a size of about 150 nanometers. And I noted that with an exclamation point here, indicating that we seem to have achieved our target when we scaled up from the small scale to the larger scale.

Q. Had you done that work that is reflected here before you first received information from Nano Systems?

A. Yes, definitely. This is August 27, 1996. This is before we ever received any information from Nano Systems.

Q. And the "this" is the work that led up to this notebook entry?

A. Correct. This is the scaleup work. It talks about the different conditions, how much Taxol is in the preparation. There are some details about what we did, actually did in the experiment.

Q. Let's take a look now, still in JX-21, still in your notebook, at Page 325.

What were you describing here, Dr. Desai?

A. In this notebook page, which is dated August 26 of 1996, after we had made the formulation of what we believed were amorphous nanoparticles, we wanted to confirm that by a technique that's known as x-ray powder diffraction. And this is a technique that is used all over the pharmaceutical industry, it's a standard technique that's used to determine

whether a material is crystalline or whether it's amorphous.

So we utilized that very same technique, x-ray powder diffraction, and tested our own samples. And this was done by a third party. We sent out the samples for analysis.

This were the results. The results are actually dated 23rd August of 1996. So that's when the results became available.

I will just explain to you briefly what this means.

The number of curves here, there is four different samples. The first sample is just straight paclitaxel from the manufacturer. So we haven't done anything to that sample. We take the sample from the manufacturer. This is the thing that goes into our process, which ultimately becomes the nanoparticles.

So that sample shows all these peaks, which you can see, they are sharp peaks here. And that represents crystalline character. So it is absolutely clear that this material has crystalline material in it.

On the other hand, the final curve up here is the curve that represents the analysis on our nanoparticles, what we call Capxol preparation or what ultimately became Abraxane.

There is a complete lack of sharp peaks,

indicating that it is amorphous. I have noted here that amorphous materials show broad humps as opposed to these sharp peaks.

So the conclusion of this experiment is that the paclitaxel in our preparation is amorphous and we were able to confirm it with a standard technique by August 26th of 1996.

Q. At some point, you came in contact with NanoSystems?

A. That's correct.

Q. How did that happen?

A. I saw a presentation by them at a scientific meeting. And then I thought it was very interesting technology. As, in my normal way, when I am interested about a scientific idea or presentation, I went and talked to the person who was presenting, and I said, Maybe we should have some discussions, there could be some collaborations, et cetera. That is basically the first contact with Nano Systems.

Q. Let's take a look at JX-28. What is this document, Dr. Desai? You have it in your notebook if you want to look at it?

A. This appears to be a fax transmittal on the 21st of August of 1996. And this is from Nano Systems to us. I believe this is the confidentiality agreement that we ended up signing.

Q. Let's take a look at JX-20 at 602. What is this,

Dr. Desai?

A. This is the cover page of the Nano Systems packet of information that was sent to us, and that's why I indicated here "Nano Systems."

Q. This is from your files?

A. Yes. I found it in my files when I was doing discovery for this lawsuit.

Q. So let's take a look at 625 and 626 -- did we miss this? Let's go -- let's have that back up.

Was this a one-way or two-way confidentiality agreement, Dr. Desai?

A. As it states in this part of the agreement, each party may provide the other with certain information which the submitter considers confidential.

This was a two-way agreement. So Nano Systems was providing us with some information. We were providing them with some information.

So there was an exchange of information.

Q. So now let's go back to JX-20 and 625 and 626.

These are some slides from that presentation, Dr. Desai?

A. Yes. Correct. This is the information that was provided to us by Nano Systems. It was a packet of slides. There were several slides in the presentation. These are a few of them.

Q. What is the date on the slide, sir?
A. The date on the slide is, it's August 28 of 1996.
Q. Did you study these slides and develop an understanding of what Elan was seeking to convey by them?
A. Yes, definitely. We looked at these slides carefully, and I formed an impression of what their technology was all about, as indicated in these materials.

While they are bringing that up, my impression, after looking at that technology, which I, of course, appreciated --

MR. SCHEVE: Your Honor, excuse me. There is no question pending.

BY MR. JACOBS:
Q. What was the impression that you formed, while we are bringing that up, Dr. Desai?
A. As indicated in this slide here, if you can blow that up, so they talk about parenteral NanoCrystal applications. Clearly, this technology was focused on crystals in the nano form, so small crystals. The key features were outlined in this slide, A, B, C, D.

The thing that I looked at and formed an impression on me was it's a platform of technology to restrict the compound to the vasculature. So their focus was to engineer their NanoCrystals, but when administered into an animal or human, the goal was to keep that

NanoCrystal in the circulation, that is, in the bloodstream.

This struck me as being quite different from our approach, which was complexing with the albumin and using the albumin to get the drug out of the bloodstream as fast as possible.

So this was one of the key sort of take-away messages that I formed an impression on.

Q. Let's go back to the document itself.

Were there other slides on this presentation that reinforced that impression?

A. Yes. There was, I think it's this slide here, which also, in effect, talked about the same thing, about the NanoCrystal technology to parenterals. That is any drug that is administered into the body is called a parenteral.

The focus of their technology was especially in the area of cancer, that is oncologics, that means dealing with cancer, so the focus of their technology was on cancer drugs that may benefit from prolonged vascular circulation.

Again, all that means is that it stays in the bloodstream for a long time after you inject it into the bloodstream.

Again, this was very different from our approach, where we are trying to get the drug out of the bloodstream. In fact, later on, we proved that approach to be more effective, because since our drug gets out of the

bloodstream, when we did our big clinical trial to compare with Taxol, which tends to stay in the bloodstream a lot longer than our drug, we found that the bone marrow toxicity of our drug was three times less, even though we could give more drug than the Taxol.

This was a very important feature that, if you keep drugs in the bloodstream, you will end up with high bone marrow toxicity. We saw that in our clinical results.

It sort of validated our approach. And, also, clearly, it differentiated for us that this is not an approach that we want to use. We want to get the drug out of the blood.

Q. So let's take a look at 271, JX-28.

What was this, Dr. Desai?

A. So this was the part of the packet that was exchanged. This was our information that we sent to Elan, or Nano Systems at the time. And it gave a little cartoon of what our technology was about. We gave them this picture, which shows a cross-linked protein shell, and that one of the components of the cross-linked shell can be albumin. That is highlighted here. The other aspect is that what's contained inside this shell could be several different types of drugs, and one of the drugs that's highlighted here is Taxol.

So we had indicated to them that we are working

with Taxol, and that our approach is to use proteins and to form tiny capsules and cross-link the protein that's around the capsules.

Q. Going back to JX-20, this is the '684 patent that was included in the materials that Nano Systems sent to you.

Did you make a note on this patent?

A. Yes, I did. I made a note on the patent, identifying to myself that this is a crystalline drug substance, that is, this patent is about crystalline materials. When I read the patent, that was obvious to me.

Q. Let's take a look at 685. This is actually the '363 patent.

If you go to 692, did you make any notations there?

A. Yes. This is Claim 1 of the patent. As you may know, all patents have some claims. And the key features are usually identified in those claims, as I understand it. So what I read in the claims, in Claim 1, the very first claim, was that this patent was about particles that consisted essentially of crystalline medicament. That is a medicine that is made of crystals. And the other key message that I took away from this is that this crystalline medicament has on it, on its surface, a surface modifier that is non-cross-linked, meaning that is not cross-linked, that the surface modifier, molecules on, that decorate the surface of

these particles, these crystalline particles, are not linked together in any way. They are individual molecules that are stuck on.

Upon looking at this, to me, it was quite obvious that the approaches that were outlined in this patent are very different from the approaches that we were using at the time, and continue to use today. That is, we focus on materials that are not crystalline. They are amorphous. And we focus on a surface modifier which is albumin, and that surface modifier is cross-linked as opposed to not cross-linked as identified in this patent.

Q. Let's go to JX-20 at 656. This is a page from the '363 patent.

Do you see, there is a notation, Raj, 30K, at the top there?

A. Yes, I do.

Q. Does the Raj here refer to Raj Selvaraj, the Abraxis employee?

A. No, it does not. At the time, I didn't even know who Raj Selvaraj was.

This Raj here, his name is Raj Vaidyanathan. He is a completely different person. We were thinking of hiring him as a GNP consultant, which is a consultant to help us with the manufacture, this person was familiar with the FDA requirements, so to make sure that we met all the

guidelines for the FDA, we, in fact, hired him as a consultant to help us with that aspect.

And this "30K" refers to a discussion between me and Patrick -- in fact, this was Patrick's handwriting, where he wrote down, 30K, that we would pay him 30,000 for his consulting efforts for Abraxis.

Q. Patrick is Dr. Soon-Shiong?

A. Yes. Patrick is Dr. Patrick Soon-Shiong, who I worked for at the time.

Q. When did you hire Raj Selvaraj?

A. Raj Selvaraj we hired more than, I think it was three years -- this is in 1996, so this is three years later, in 1999, I think it was May 1999.

Q. Now, if you look at the primary examiner and the assistant examiner on the Nano Systems patent, what did you notice?

A. Well, it was very interesting because I noticed that the primary examiner -- these are the people in the United States Patent Office who look at patents and decide ultimately whether these patents can be issued as patents.

So Thurman Page and William Benston are the same two examiners who examined our patents.

And our patents were also filed in the early part of the '90s, 1993 time frame. They issued in 1995.

It was interesting to note this coincidence,

that the same people in the Patent Office were looking at the Nano Systems patent and they were looking at our patent at the same time.

Q. Dr. Desai, you mentioned earlier an IND, an Investigational New Drug Application for Abraxane.

When did you file your IND?

A. The IND was filed in, we first had the pre-IND with the FDA. That is a standard process. That was in December '96. Then we worked on several things after that, where we had been asked to do some additional animal studies. And we ultimately filed the IND, which is the actual final application, in May of, I believe it was May of 1998.

Q. And then you, at some point, filed an NDA, a New Drug Application?

A. That's correct.

Q. When did you file that?

A. So the New Drug Application is the final application. After you have finished all your clinical testing and you are ready for commercialization, you file a huge packet of information. That's called a New Drug Application. So it comes several years after the IND application. That application was filed, NDA application, was in, I believe in 2004.

Q. Let's take a look, JX-64.

What is JX-64, Dr. Desai?

A. This is the cover page of an application for the new drug Abraxane that we had filed with the FDA.
Q. Could you give the jury a sense of what one of these things looks like if you were to assemble it in a single place, one of these NDAs?
A. Well, it represents a huge amount of testing that is done, because to get a new drug out into the market, you need to do all of the clinical testing, you need to do all of the toxicity testing in animals, you need to show your manufacturing processes in every detail so the FDA can look at this and analyze it. It would probably fill the whole side of this courtroom if you were to put it all together.
Q. Let's take a look at 117473 of JX-6.
What is this, Dr. Desai?
A. This is one small part of that huge package of information. And this is a report that did several characterization studies on Abraxane. This is the Table of Contents. So it lists here things like x-ray diffraction, differential scanning calorimetry, electron microscopy, et cetera, all the different techniques that we used to analyze Abraxane to understand its physical form and its chemical features.
Q. Some of these -- actually, I should step back.
Did you participation in the preparation of this application?

A. Yes, I did, actually.
Q. How heavily were you involved?
A. I was very heavily involved right from the beginning.
Q. Have you had personal experience with the techniques listed under physical analysis, or some of them?
A. Yes. I have had personal experience with some of them. I have, myself, done electron microscopy as part of my graduate career and myself done differential scanning calorimetry as part of my graduate career and have published on these techniques. And I, myself, have done not x-ray diffraction but a very similar technique that's called x-ray photo electron spectroscopy, which, in that sense, uses the same principles of using x-rays to analyze samples, and I published on those techniques as well.
Q. Let's go to 483 of 484 of your NDA.
What do these pages represent, Dr. Desai?
A. This is part of that characterization report that focuses on the x-ray diffraction testing, which, as I mentioned, is the standard method of testing or to analyze if the material is crystalline or not.
Q. What are you describing here? What are you representing by this information?
A. Well, it says here that there were different lots of material. We talk about stability lots and there are numbers here. Each one of these numbers represents a

different batch of Abraxane that was prepared at a different time. And each of these are tested under rigorous conditions when you do stability. The goal is to test them at high temperatures, like 40 degrees, at very high humidity, like 75-percent humidity. The whole idea is to stretch these samples as much as you can, to see, under the worst conditions, what could happen.

So this ensures the stability of your drug when it is really out in the field, it may be transported here or there under very rigorous conditions, et cetera.

So this is part of the stability testing. As part of the stability testing, we looked at the crystalline or amorphous character. And we were -- so that was the x-ray diffraction testing that was done here.

Q. What was the result, what did you understand the results of these experiments to show?

A. Well, the results are highlighted in the conclusion. And, really, the first part of it says it all, that the nanoparticles of ABI-007, which is a code name we use for Abraxane, are amorphous. So under these rigorous conditions, which included testing over six months, where you store these samples at these high temperatures and high humidities and take vials and put them upside-down and do all kinds of things, that even after those rigorous conditions, after long periods of time, that the particles

remain amorphous and that was the conclusion of this testing.

Q. Let's review 485 to 486, the next couple of pages.

What is this, what are these pages showing?

A. This is similar to the x-ray diffraction patterns that I have shown you just a little bit earlier which were in my notebook from 1996. This was testing done much later at the time of the NDA filing. This was included in the packet of information that was sent to the government, the FDA. Same type of test. This is the starting material. That is the raw paclitaxel drug which we get from the manufacturer, clearly shows you all these sharp peaks, indicating crystallinity.

On the other hand, these top two represent ABI-007, which is Abraxane that is tested under the different stability conditions.

And there is no sharp peak here. There are these broad humps, which are characteristic of amorphous material. So none of these materials are crystalline.

Q. Let's look at DX-41, Dr. Desai. Can you take a look at DX-41 in your binder, please.

Can you tell us what DX-41 represents, Dr. Desai?

A. Yes. DX-41 is a report of results on x-ray diffraction testing. And this was done not in house, in our

company, but these samples were sent out to a laboratory called Micron, Inc. And they were tested for x-ray diffraction to show if they were amorphous or crystalline.

This is pages after pages of information on several different lots or batches of Abraxane that were produced. And every piece of data that's in there shows that each Abraxane lot that is tested was amorphous.

Q. How many times has Abraxis sent out samples for x-ray powder diffraction testing?

A. I don't know the number. But probably 20 or more, maybe more than 20 times. A lot of those samples are in this exhibit.

Q. What have the results shown in each case?

A. In each and every case, they have always shown amorphous results. There is no evidence of crystallinity in Abraxane.

Q. Let's just take a look at one page out of this, 103. So this is in May of 2006. What is this document?

A. This is the sign off sheet on the final report that resulted from all of this testing of Abraxane commercial and stability lots.

And there is a number of signatories here. I am one of them. And by signing here, you indicate that you agree with what's in the document and you agree with the conclusions and you have reviewed the testing. I had

reviewed all the report. And I agreed with the testing and the conclusions that were in this report.

Q. 109 of DX-41, Mr. Broyles.

What did the report conclude?

A. So the report, the conclusion is very much similar to the one we saw earlier, that nanoparticles of Abraxane are amorphous, and that, when tested, these particular lots are tested, that it shows that Abraxane is amorphous.

Moreover, there was another aspect to this. We were manufacturing Abraxane at two different manufacturing factories, or sites. One was Ruby Street in Chicago. Another was Grand Island in New York.

We tested the product, Abraxane, from both of these sites, independently, and it showed that it didn't matter which site this came from, they were equivalent, and, in fact, no matter how you manufactured it, whether one site or the other, they are still amorphous after all the stability testing.

Q. Do you regard this as an achievement?

A. Actually, I do. And this is very interesting, because typically, amorphous materials are not very stable. And they can change over time, just because of their amorphous character. This showed under rigorous conditions, with that albumin present to help bolster the structure of these nanoparticles, that these nanoparticle character remain

unchanged. That under high temperatures, under long periods of time, under high humidity, nothing changed. This is just one character of it, which is amorphous. There is probably ten other things that we measured and everything was consistent.

So I think that's quite an achievement.

Q. Did Abraxis separate the nanoparticles from the free albumin before doing x-ray powder diffraction?

A. No, we did not do that.

Q. Why not?

A. Because in a technique like x-ray diffraction or any technique where you want to know the characteristic of these particles, as is, as the, in the vial, you do not want to manipulate the sample in any way, because you could potentially change those characteristics due to that manipulation.

Since we had already determined early on that the amount of protein present is very important to the integrity and structure and characteristic of these nanoparticles, and we had shown that when you remove the protein, if you have very little protein present to help keep the particles stable, they are not stable anymore. They form these chunks and aggregates and can change structure.

For testing of that kind, where you want to know

really the characteristics of those particles like in electron microscopy, you want to see how these particles look like. If you take away the albumin, then you potentially can get an artifactual result.

Similar, for this crystallinity/amorphous aspect. If you take way the albumin, you could destabilize it, and maybe what you end up seeing is not the real thing.

So we were very careful, at least in the case in x-ray diffraction, that we did not mess with Abraxane. We looked at it as is.

Q. What do you mean by an artifactual result?

A. Artifactual result is -- the word "artifact" is used in scientific terminology to determine things that occur during your process of experimentation. So you say, if something changes, and when you observe it, it looks different than what you had thought and you know what that change was, then you say, That was an artifact of the experimentation.

So that type of experimentation can be misleading, which is why you want to be very careful with it.

Q. Why did you do x-ray powder diffraction the way you did on the, that is on the intact Abraxane sample?

A. For the very reason I just explained, that we did not want to remove components, we did not want to sediment out

the particles and separate them out because they know they will aggregate.

For that purpose, we did not want to change the character, because we were looking for a specific characteristic of Abraxane.

Q. What would happen if you took a pellet of separated nanoparticles and tried to reconstitute that pellet into Abraxane?

A. Well, first of all, it wouldn't be Abraxane anymore, because one of the key features of Abraxane is that excess protein. You know, we have ten times as much protein as we do drug. It's there for a very good reason, to help keep the particles stable.

So when you sediment or you centrifuge or you pellet out the particles from all of this free protein, you are taking away that stability. And, therefore, it is no longer Abraxane, one, and, two, if you tried to re-disperse that sedimented pellet, it is very hard to do that. You would get big chunks and aggregates and that would lead to artifactual results.

We never did that for this type of testing.

Q. Let's look at some of Abraxis' electron microscopy of Abraxane now. Let's look at JX-8 and 885.

What is shown here?

A. There is two types of electron microscopy studies done

here. One is what is called just regular transmission electron microscopy. On the right is what is known as cryo-transmission electron microscopy, "cryo" meaning low temperature, so this is done at very low temperatures.

In this technique, we were trying, again, to visualize the particles and what we hoped was in their actual state as they are in the vial. So we did not separate the protein out. We kept it as it is. This is an actual sample of Abraxane. No manipulation other than putting it into the instrument and trying to visualize it.

We see these little balls of material. And you can size the size of this, it is in the hundred or so nanometer size range, which is what we measured by independent technique. This, in fact, confirms the size. And it confirms for us the shape, roughly spherical shape, of these particles.

On the right side is, again, an electron microscopy technique. This is done by cryo-techniques. That is, you rapidly freeze the sample. And then you observe it. And the idea of rapidly freezing is, again, to literally freeze the sample in its native state so you don't get any changes as a result of the procedure itself.

In this technique, we, again, see these little, more or less, spherical particles. By the way, I should explain that this fat black line here has nothing to do with

the sample, but it's actually a grid on which the samples are mounted.

What we are looking at only are these little spherical dots here. Some of them are spherical. Some of them are sort of irregular. If you remember, I explained to you how these particles are formed, that you start with the droplets, you have the solvent in there, and then you evaporate, so then you sort of shrink the droplets and you form these prunes.

So they are slightly irregular shaped but still, more or less, somewhat spherical. You can, in fact, see that here, not only some nice spherical, round shapes, but there is some prune-like shapes, if you will.

Q. The prune-like shapes, are they indicative to you of crystallinity?

A. No, not at all.

MR. SCHEVE: Your Honor, I object. This is now crossing the line to expert testimony.

MR. JACOBS: I am asking him for the conclusion he drew, Your Honor.

THE COURT: See counsel.

(The following took place at sidebar.)

THE COURT: Why isn't that objection well-taken, Mr. Jacobs?

MR. JACOBS: Because he drew a conclusion based

on this work. And Abraxis has made representations based on this work about what you can glean from this. This is very much part of his analysis of his own particles.

THE COURT: You are saying as a matter of fact he drew a conclusion. He is not offering an opinion as an expert.

MR. SCHEVE: He testified in his deposition that the only test that they relied upon for crystallinity was x-ray powder diffraction.

Now he is asking for an opinion of whether these SEM and cryo-TEM images provide a basis for him to conclude it is crystalline. That is clearly an opinion.

MR. JACOBS: It is true he did rely, because even as their own expert testified, these are suggestive. But he will testify that he drew the conclusion that this was consistent with x-ray powder diffraction at the time he saw them.

THE COURT: Do you object to him testifying as a matter of fact that that's what happened, that's the conclusion he drew?

MR. SCHEVE: He asked him the question in present day terms, Your Honor, which is it's formed as an opinion. He testified in his deposition, as I will show, he concedes, I am not an expert in any of these techniques.

THE COURT: You will cross-examine him on that,

if he rephrases there.

MR. SCHEVE: It needs to be rephrased.

(End of sidebar conference.)

THE COURT: If you could rephrase.

BY MR. JACOBS:

Q. On or about the time you saw these pictures, did you form a conclusion about what these pictures represented by way of crystallinity or amorphousness?

A. Well, this technique, the microscopy technique, I should say, is not a definitive technique for measuring crystals or the lack thereof. You really have to look at what these particles, what the shape of these particles and all of that; because x-ray diffraction is the definitive technique. But sometimes you can make some assumptions from what you see. And there may be suggestions.

From my background, all those years I worked on paclitaxel, any time I had seen paclitaxel crystals, they were always needle shaped. That is characteristic of paclitaxel. And that is published, also, by other people.

So when I looked at this, I see no needle shapes. My assumption is, Okay, this looks like what we think it is. These are the little round particles of Abraxane.

To me, even sitting here today, this does not look crystalline.

MR. SCHEVE: Objection, Your Honor. Move that that be stricken.

THE COURT: I will strike that last part of the response. Ask an additional question, if you can.

MR. JACOBS: I don't need to, Your Honor. Thank you.

THE COURT: All right.

BY MR. JACOBS:

Q. During this lawsuit, Dr. Desai, Elan has pointed to snapshots of notebook pages from people working under you on Abraxane where there are references to crystals. I would like to look at a couple of those and ask you to tell us what was actually going on in those instances. Let's take a look at PX-19 at 292, a slide from Elan's opening presentation.

Can you tell us, based on your work with Nilesh Ron, what is going on in this notebook page?

A. Nilesh Ron was one of the members of my group. He reported to me and he did a lot of testing on Abraxane, like many of the other members of the team.

So here, he is testing -- can we blow this up, please?

I believe -- this is a lot number. This is a specific lot of Abraxane that was produced. This is, this lot was manufactured in 1997, on July 2nd. The reason I

remember this lot very well is this was the first lot of Abraxane that we produced at the 20-liter scale.

We had done some scale up and increase in size. This is the first time we went to 20 liters.

Q. A liter is about how much, Dr. Desai?

A. A liter is about maybe that much. (Indicating.) Imagine 20 of those in a big vessel.

So this is the first time we had produced this lot. The second reason I remember this is because this was over the July 4th weekend. We spent the entire weekend sequestered in our labs making this first lot, this large lot of Abraxane.

When this was subsequently tested, after we made it, in fact, to our dismay, because we had put so much effort into it, it was found to have very high levels of the solvent that we were using in that process.

And we ended up rejecting that lot because we had certain criteria of what we mean by Abraxane, and to meet those criteria, it was way above, I don't remember the exact number, but probably 20, 30 times above the allowable limit for that solvent, which means it could be toxic if we put it into patients.

Based on that criteria, we rejected this lot. So this did not meet the criteria for Abraxane. And because we were not able to evaporate out all the solvent that we

wanted, something clearly went wrong in the process. This was a rejected lot. We threw it away.

Subsequently, we also were interested in it. And, in fact, three years later, I believe, which is when this notebook is dated, in 2000, some of my colleagues were testing this. And they found a couple of things. They found the presence of some crystals. In fact, during the course of that testing that they did, it was also inadvertently, by mistake, contaminated. I think the samples were left on the lab bench.

So you see where it says "moldy." And, really, I think you can't really draw any conclusions out of this, other than they observed some crystals and other than there was a lot of solvent present, which, in Abraxane, it has to be at very low ppm levels.

Q. Does this have anything to do, in your judgment, Dr. Desai, with the question of whether Abraxane has crystals in it?

MR. SCHEVE: Objection, Your Honor. That is asking for opinion.

THE COURT: Rephrase the question, please.

BY MR. JACOBS:

Q. What happened to this sample, in the end?

A. Well, this sample was thrown away. As I mentioned, it was a rejected sample. It was never used. Just sort of

stayed there in the back of our labs. At some point, we were testing some of it much later. But, clearly, this is not Abraxane as we know it today.

Q. Let's take a look at 397, 705 to 706. That is PX-397, 705 to 706.

Leslie Louie is the person doing the work on these notebook pages. She reports, for example, in 2000, few random crystals.

What is your understanding of what was going on in this work, Dr. Desai?

A. Okay. Can we expand those pages so I can look at them? Look at the individual pages.

Q. Let me ask you a general question, first of all. What kind of work goes on at Abraxis that is not the actual testing, it's different from the actual testing of Abraxane?

A. Well, we are a research group. I run the research group at Abraxis. These people whose notebooks you are seeing, they were part of the group. As part of ongoing research, we continuously are testing, even testing today, different drugs, different formulations, different aspects.

So even with Abraxane, once we got even to the clinical trials, we were constantly trying to further improve, to look at all the possible variations, to make sure we ultimately ended up with the right formulation.

So in these notebooks, this is one of those

entries. She mentions, Few random crystals. What I would like to point out is, again, this is that same lot that we just talked about that had very high solvent levels. This is the lot we made over that July 4th weekend. And it had the same issues, that it had too much solvent present and we had rejected it and we had seen some crystals in that lot.

Q. Let's go to the next page. I could hand you the whole notebook if that would help you.

A. Sure.

Q. So what else do we see on these pages that Elan highlighted for the jury, Dr. Desai?

A. Okay. So, again, there is some evidence of crystals here. Again, this is testing on that same lot. So this is just further information. This was being tested over time, just to see what would happen if we just let the vial sit there over time, after you reconstitute the vial, that is put in saline, and re-disperse the particles and then let the vial sit, then, periodically, you would come back to look at the particles and see if there was any changes.

THE COURT: Doctor, this is Abraxis testing?

THE WITNESS: Yes.

THE COURT: I think you said Elan.

MR. JACOBS: That Elan showed to the jury.

THE COURT: I misunderstood. Sorry.

THE WITNESS: Yes, this is in our notebooks.

Again, the appearance of a few crystals. This, again, is that same lot that we just talked about, which had very high solvent levels.

BY MR. JACOBS:

Q. This is the lot that you did what?

A. We rejected this lot.

Q. Let's go back to that first slide. There are a -- have you covered all of the entries on here, Dr. Desai?

A. I think we can see that. I will just look at it in my notebook.

Q. It's PX-400, is what is represented there. It's from 1996. Needle-like crystals. Leslie Louie?

A. Maybe we can just blow it up.

Okay. This talks about fluidizer recycling. Here we are using this equipment that is well-known to generate small particles. It is a fluid diver, or homogenizer is another word for it. Here we are testing the effect of different modifiers. We have albumin there. But in addition, we are adding other surface modifiers.

In this particular case, it's a surface modifier called Cremophor. When we add that in, we see the formulation of needle-like crystals.

So, again, this condition, or this particular experiment, showed us what not to do. That is, when we added Cremophor, we ended up with crystals. There is many

experiments like this where we add other surface modifiers in, other than albumin, and we generate crystals. This is part of the full testing, to know what components we can add and not add to generate the formulation.

Q. And what you are describing, Dr. Desai, is that listed right on the page of the notebook?

A. It says right here, you can see needle-like crystals. And you can see we have added Cremophor, which is a surfactant or a known surface modifier.

Q. How does this bear -- how did this bear in 1996 on the development of Abraxane?

A. Well, in 1996, we were testing a lot of things. Amongst them, this was one aspect of it.

Since then, we completely moved away from using these type of agents, these type of surface modifiers. The only thing we use is just albumin with the drug. There is no other component.

Q. Let's turn to the topic of cross-linking, and let's take a look at JX-15. JX-15 is an e-mail that has been in court already, Dr. Desai. Let me quickly set it up. There is an e-mail from Zachary Yim to you dated January 17, 2006, and then an e-mail from you back to him just a few minutes later, and this is about cross-linking.

Can you explain what is going on in this exchange?

A. Zachary Yim was a relatively new employee at that time. He worked for me in the formulation group, the group that does work on these type of products.

I had mentioned to him something about cross-linking. So he refers to that.

So I respond to him to clarify his thinking, to this e-mail, that when I was talking about cross-linking, I say, yes, but not heat-induced cross-linking, which is usually construed as denaturation. Denaturation is a word that is used in the context of proteins. And the most common example that all of you know is if you take egg white, which is albumin protein, and you heat it up, you make your scrambled eggs, you end up with denatured protein. So it turns into that fluff, white stuff.

So that's what I am talking about. When I am talking about cross-linking, I am not talking about heat-induced cross-linking, which is called denaturation or egg white, but I am talking about the mechanism that occurs on Abraxane.

I say that cross-linking results from unfolding of the protein, which is albumin, on the hydrophobic solvent/particle surface.

When I showed you that animation, as the protein is getting onto the surface of those droplets, that's what I was talking about. The protein accumulates on those

droplets. And by its nature, it unfolds. And when it unfolds, this exposes certain chemical groups within the protein.

When that happens, the protein that's nearby, and also exposing its group, can link up, that's called a cross-linking. That's the process that I was describing.

And the cross-linking occurs through spontaneous disulfide interchange, that is, these disulfide bonds are the ones that link together.

Q. Do you believe that to be the mechanism by which cross-linking occurs on the surface modifier particles on Abraxane nanoparticles?

MR. SCHEVE: Objection, Your Honor. That calls for an expert opinion. The question was, "Do you believe"?

THE COURT: I didn't hear the question. Let's have a sidebar.

(The following took place at sidebar.)

(Question read as follows:

Q. Do you believe that to be the mechanism by which cross-linking occurs on the surface modifier particles on Abraxane nanoparticles?

MR. JACOBS: I am establishing that is a prior consistent statement. It is an e-mail he wrote in 2006. I could ask it a little differently. I could say, Do you believe that e-mail to be true.

MR. SCHEVE: If it is being offered for prior consistent statement, clearly, there has to have been a confrontation with an inconsistent statement. There is no predicate.

THE COURT: There has been no attack. You can bring it back.

MR. JACOBS: Can I offer it as an explanation of his understanding of the mechanism by which he designed --

THE COURT: Now that you have told me you want to offer it as a prior consistent statement, I will say no. But you will get another chance, I am sure.

(End of sidebar.)

THE COURT: I am going sustain that objection.

BY MR. JACOBS:

Q. Let's turn to DX-112, please, Dr. Desai.

What is DX-112?

A. This is a summary table of evaluating of whether there is cross-linking on the Abraxane particle.

So there were several tests done, and all of the rows, all of the rows in this table represent different tests that were done to determine cross-linking. And they represent different lots of Abraxane, so Abraxane produced at different types.

Q. The jury has heard about what a dimer and oligomer and a polymer are, Dr. Desai.

Could you jump to what you understood this, these test results to be demonstrating to you at Abraxis?
A. Yes. So we measured in this test the percentage of cross-linking, that is the percentage of where you have two or multiple or several albumin molecules linked together.
What we found in our testing, that there was at least 55 percent of the albumin that's on the surface of the particles that are cross-linked to each other in this technique.
Q. Did Abraxis do any experiments to investigate the nature of the cross-linking between albumin molecules on the surface of Abraxane?
A. Yes, we did.
Q. What this showed to you precisely was what, Dr. Desai, when you did it?
A. This helped us just quantify, give an idea of what percentage of all of albumin that is on the surface of the particle was cross-linked, and the determination that was made from this study was that 55 percent on average, through multiple, multiple batches, of that albumin on the surface is cross-linked.
Q. Now let's go to DX-76, and DX-76 is Voung Trieu's notebook. It has an initial date of July 2, 2007.
Let's go to 586.
In a nutshell, Dr. Desai, why did you do this

experiment and what did you conclude from it?

A. Well, this was to look at the nature of the cross-linking. As I mentioned before, we believed that the cross-link was due to a special chemical bond called a disulfide bond. And we wanted to confirm that.

We had done earlier studies many years before to show that. But in the final Abraxane, as it is today, to confirm that, in fact, it was the disulfide link, we did this experiment.

And I will try and describe very briefly.

These bands here that you see represent monomer albumin, that is single molecules of albumin.

On the other hand, these large smears represent polymers, that is, large molecules of albumin that are linked together.

This experiment showed us, clearly, that these large polymers of albumin or cross-linked albumin existed in Abraxane, which sort of confirmed the previous experiments that we had done where we showed 55 percent cross-linking. And to confirm, in fact, it was disulfide links, we put in a special chemical that selectively breaks disulfide links.

So if you had those polymers all together, which is represented here, and you put the chemical in, you would now break these apart and reduce them. That's the reference to reduce, reduce them to the single band of monomeric

albumin.

So this proves, in effect, two things; one which we had already proved before, that there are cross-linked albumins on the particle, and, two, that these cross-linked albumins are cross-linked through a disulfide bond.

Q. DX-70 at 17002, please.

Dr. Desai, your testimony before the FDA has come up in the trial so far and comments you made about Abraxane. So we need to look at that quickly.

October 10, 2006, did you give a presentation?

A. Yes, this was one of the presentations I made at the FDA nanotechnology meeting.

Q. In what capacity were you invited, or for what purpose were you invited?

A. Well, this was an open forum to discuss issues with nanotechnology drugs, because this was such a new field, emerging field.

We had put in, Abraxis, that is, had put in a request to be able to present that at that meeting. We were granted that request. That is the context of this meeting.

Q. Let's go to 202 and 203 of the transcript, 203 and 204 of the Bates pages, and you are quoted there as saying, We use the native albumin. And if you start cross-linking the albumin with chemicals and things, I think you might run into problems but we don't do that.

Did you give that statement?

A. Yes, I did.

Q. What did you mean by that statement?

A. Well, this was in response to a question that related to immunogenic behavior or immune response. What I was clarifying by responding to that question is that the albumin in the particle, we have talked about albumin being cross-linked. But what I was saying is that we do not add any chemicals, any special chemicals to cause that cross-linking to occur.

That cross-linking occurs as a spontaneous part of our process.

And if you start adding chemicals, additional chemicals that can cause cross-linking to the albumin and modify the albumin, then you might run into problems of this immunogenic or immunological responses.

BY MR. JACOBS:

Q. So if you --

MR. SCHEVE: Your Honor, if I could. Mr. Jacobs read the last line to say, But we don't want to do that. And for purposes of the record, it really needs to be read as it was.

THE COURT: You can read it yourselves, ladies and gentlemen.

MR. JACOBS: If I misspoke, I sincerely

apologize. It reads, But we don't do that.

BY MR. JACOBS:

Q. Were you saying anything in this particular comment about the kind of cross-linking you referred to a few minutes ago referring to disulfide bond interchange?

A. I did not talk about disulfide bonds here. All I was saying is that we did not add anything, any other chemicals to the process to chemically modify the albumin.

Q. Let's take a look at PX-156, at 3712. Did you give a presentation at this ODAC?

A. Yes. It wasn't myself who gave the presentation. But our company did make a presentation at this advisory meeting.

Q. You were there?

A. I was present.

Q. It says, We combined water-insoluble compounds such as paclitaxel with human albumin, without altering either component or forming covalent bonds.

Do you see that?

A. Yes, I do.

Q. What were you conveying by that information? What was the context here?

A. Well, it's a common misconception that, in Abraxane, the albumin molecule is chemically linked to the paclitaxel molecule in some fashion.

I have been asked that on numerous occasions, when I speak at scientific meetings, et cetera.

Really, this was a clarification of that context, that the paclitaxel that we put into the process stays as paclitaxel. We are not altering the chemical structure of paclitaxel. And the albumin that we put into the paclitaxel is not in any way linked to the paclitaxel. It just surrounds it in the shell.

So that is what we clarify here, saying that neither albumin nor paclitaxel are linked together through a covalent bond.

Q. Let's look at JX-11.

What is JX-11, Dr. Desai?

A. JX-11 is a response to another e-mail from Zachary Yim. This is dated May of 2005. Maybe if I can see his question, please.

So in that e-mail to me, he is asking me the following: That there, or stating the following. That there are at least a number of companies, such as Baxter, Dow, Elan, which make nanoparticles, stabilized by something non-toxic, other than albumin.

So would it be important for us to check their efficacy, meaning how well those nanoparticles worked, versus our nab technology -- nab refers to our Abraxane type technology -- to see in the context of some receptor

mediator transport, which is another feature of albumin.

To that, I responded, if we can blow that up, I said here, With the current resources, that I did not want him to spend time getting into other company's formulations. And what I did say here, that most of the stabilizers that these other companies are utilizing are surfactant like, that these surface modifiers form a class of compounds that are known as surfactants, which is really a short term for surface active agent, surfactant. And because we do not use these type of molecules, we use albumin, I was trying to steer him away from that.

The other fact that I put in here, my statement was that, in fact, it is well-known that Elan or Nano System's paclitaxel acts more like a blood pool agent rather than getting transported into the tissue.

This goes back to my understanding of their technology, which restricted the drug into the bloodstream, that it stays in the bloodstream. That's what I mean by "acts as a blood pool agent," rather than getting out of the blood circulation into the tissue.

I also made a statement here that, so far, none of these technologies have made it to clinic with a major drug in the injectable form, meaning referring to the other companies' technologies.

What I mean by that, I am referring here to

injectable form, which is a form that can be administered into the vein of a patient, which is different from administering, say, a pill, which you take by mouth, because the standards are very different. There is a much higher standard of safety for a drug that you put into a vein as opposed to something you put into the body by mouth.

So that's what I was referring to.

Q. To summarize, Dr. Desai, this testimony that you gave today, in Abraxis' view, is the paclitaxel in Abraxane amorphous or crystalline?

A. In my view, it is amorphous.

Q. And do you believe that is important?

A. I believe that's very important, because it actually defines our technology. It allows the drug to get rapidly out of the bloodstream into the tumor. And we have demonstrated and proven the benefits of this in patients.

For example, in our clinical trials versus Taxol for breast cancer, twice the number, roughly twice the number of women with breast cancer responded to our drug as opposed to those who responded to Taxol.

We also showed a benefit in survival in these patients. And I think, clearly, and, luckily, we adopted that amorphous strategy, which allows the drug to get to the tumor where it really needs to act.

Q. And, in your view, is the human serum albumin on the

surface of the Abraxane nanoparticles cross-linked or non-cross-linked?

MR. SCHEVE: Objection, Your Honor. That is clearly asking for an opinion.

THE COURT: I am going to sustain the objection as to the question as phrased.

BY MR. JACOBS:

Q. Did you intend to develop Abraxane so that it had surface modifier molecules that were cross-linked or non-cross-linked?

A. Clearly, our intention was to develop a cross-linked albumin on the surface of the particle. We wanted to use albumin because we felt it was a very important part of getting the drug out of the blood very quickly. In all the testing that we did, that I was personally involved with, we saw the presence of crosslinks.

Q. Did you believe that was important to your strategy for Abraxane?

A. Yes, absolutely. It's a key feature, we feel, on the aspect of keeping the particles stable. We demonstrated the particle is stable through rigorous testing. And the only reason that, I believe, that it is is because it has that cross-linked albumin and it also has a lot of the additional albumin, the tenfold excess of albumin, to keep it stable.

Q. Did the Nano Systems or Elan NanoCrystal work

contribute anything to your development of Abraxane?
A. No. It did not contribute anything. In fact, it was clear that the pathways were completely different. I give them credit for developing the oral drugs that they did with their technology in the NanoCrystal form. Clearly, ours was a different approach.
Q. Did the Elan '363 patent, when you read it over in 1996, or whenever, contribute anything to the development of Abraxane?
A. No, it did not. It just showed that the approaches were quite different.
Q. In view of the understanding that you had developed over time about the path that Elan was on as compared with the path that Abraxis was on, what was your reaction when you were sued for patent infringement?
MR. SCHEVE: Objection, Your Honor.
THE COURT: Sustained. I think I know what you want to do, but you can't. Rephrase.
BY MR. JACOBS:
Q. When you were sued for patent infringement, what did you reflect back on in terms of your understanding of the Elan technology and what you had come to know about it?
A. Well, first of all, I was shocked to hear about a lawsuit, given that I had seen Elan's presentations at public meetings, given that I was familiar, to an extent,

with their technology from the materials that were sent to us back in 1996, and given that we had always pursued independently a completely different path. Our path was amorphous and cross-linked. Their path was crystalline and non-cross-linked, as was clear from the reading of those patents and their presentations.

Really, it didn't make sense to me. I said, Well, where is this infringement? I didn't have any idea.

The second part of it was, I took it at a more personal level --

MR. SCHEVE: Objection, Your Honor.

THE COURT: No. I will permit him to continue. I recall similar testimony from Elan.

Go ahead.

THE WITNESS: So the second aspect that I was thinking was really more a personal level. I knew Gary Liversidge and I had taken special efforts when I organized certain symposia and chaired meetings in 1998 and in 2002 to invite Gary to speak at these symposia. These symposia were focused on drug delivery in general, where I had multiple speakers come together and present their scientific data.

I presented myself on our technology. Gary presented on his technology.

And, to me, this was almost like a slap in the face. After all these years where I have invited him, I

recognized him as a good scientist coming to make presentations at meetings at the same venues that I was making presentations, it seemed impossible to me that he wouldn't be able to grasp the issue of the differences. Amorphous, crystalline, cross-linked, non-cross-linked.

So I really don't know what was behind this. But I think -- I was quite upset at the time.

MR. JACOBS: Thank you, Dr. Desai.

THE COURT: Mr. Scheve, you may cross-examine.

MR. SCHEVE: Would there be any opportunity for a short break?

THE COURT: Sure. Ladies and gentlemen, let's take a very short break.

(Jury leaves courtroom at 11:55 a.m.)

(Recess taken.)

MR. JACOBS: Before Mr. Scheve's cross, he represented when he played Dr. Desai's deposition testimony, that he would not be recrossing on topics that he played. And I just wanted to remind him.

MR. SCHEVE: I am not going to re-ask any questions I asked. There are clearly some things that I didn't ask that I hope to get into in cross.

THE COURT: All right. We will see.

(Jury enters courtroom at 12:05.)

THE COURT: Please take your seats.

Mr. Scheve, you may cross-examine.

MR. SCHEVE: Thank you.

CROSS-EXAMINATION

BY MR. SCHEVE:

Q. Slide 67.

Excuse me.

MR. SCHEVE: Your Honor, I apologize. My thumbs again.

(Pause.)

MR. SCHEVE: It is not my thumbs. It's my eyes, Judge.

BY MR. SCHEVE:

Q. Doctor, I blocked you off, I apologize. Let me move this a little bit.

Thank you for being patient with me.

In examination by Mr. Jacobs, you made reference to some patents covering Abraxane. Is that correct?

A. Yes.

Q. Are you familiar with something called the Orange Book?

A. Yes, I am.

Q. Is the Orange Book a book in which you have to sign certain forms representing certain things to the FDA in order to get your patent listed there?

A. To my best understanding, the Orange Book is when you

have a drug approved, you have to identify to the FDA which patents cover the drug. So you send them a list of the patents and there are some forms that are signed for that purpose.

Q. This patent, the '868 patent, is that one of your more recent patents that's listed in the Orange Book as covering Abraxane?

A. Yes. I believe that's an Orange Book patent, that's correct.

Q. Isn't it true, sir, in your own patent covering Abraxane, it is stated in Column 8, quote, "While it's recognized that particles produced according to the invention can be either crystalline, amorphous, or a mixture thereof, it is generally preferred that the drug be present in the formulation in an amorphous form"?

A. Yes, I see that written in the patent.

Q. Is it also stated in your patent covering Abraxane, quote -- this is Column 32 -- "It is also known that as the loading of the drug and the formulation is increased, the tendency for crystallization also increases"?

A. I am not sure about that. If I can see that page, please.

Q. Okay. This would be Plaintiff's Exhibit 211, sir.

Do you have that notebook in front of you?

A. Which exhibit?

Q. **Plaintiff's Exhibit 211.**

Did you find it, sir?

A. **Yes.**

Q. **Could you go over to Column 32. Are you there, sir?**

A. **Yes.**

Q. **Do you see on the fifth line, quote, "It is also known that as the loading of the drug in a formulation is increased, the tendency towards crystallization also increases"?**

A. **Yes, I see that. That is in reference to as you try and pack more and more drug into the particles, at some point, you reach a limit, and then you may see crystallization beyond the limit.**

Q. **Let's go to the next patent you have, the '579.**

Is it listed in the Orange Book as covering Abraxane?

A. **I am not sure about the -- I don't remember all the numbers. Maybe you could just identify if it is or not.**

Q. **Are you familiar with this patent?**

A. **Can I see the face page, please?**

Q. **Certainly. It's in Defendant's Exhibit, this would be Abraxis' Exhibit 030. I am probably going to have to review back to one of those heavy notebooks. I apologize for the heavy lifting.**

A. **Did you say 030?**

Q. Yes, sir. Do you see the face page there?
A. Yes. I see it.
Q. Is it applicable to Abraxane?
A. It is applicable to Abraxane. I am not sure if this was specifically an Orange Book listed patent.
Q. Is it applicable to Abraxane?
A. Yes, it is.
Q. If we go to Column 6, does this patent -- this Abraxane or Abraxis patent says, quote, "While it's recognized that particles produced according to the invention can either be crystalline, amorphous, or a mixture thereof, it is generally preferred that the drug be present in the formulation in an amorphous form"?
A. Yes, that is what it says there. Again, what we were referring to is that if you increase the loading beyond a certain point, you cannot do that to maintain amorphousness. In Abraxane, it's below that limit. We keep it so that we maintain amorphousness.
Q. Just so I understand your direct testimony, sir, did you go through any formal formulation sciences curriculum when you were in school?
A. I did chemical engineering, which teaches all the basics of the principles that go into formulation science, which include basic chemistry of drugs and different molecules, polymers, et cetera. So I feel I have a

background strong enough to work in formulation science.
Q. Didn't you testify in your deposition, sir, in this case that you have no formal training and no degree in formulation science?
A. That's true. My degree is in chemical engineering.
Q. Is that still the same today?
A. Yes, it is.
Q. Now, you graduated from the University of Texas in what year?
A. That was in 1991.
Q. Is the first time you ever had anything to do with trying to formulate paclitaxel was 1992?
A. Yes. I think late '91 to early 1992.
Q. Is it true, sir, that you and Dr. Patrick Soon-Shiong went to a conference in September of 1992 sponsored by the National Cancer Institute?
A. Yes, we did.
Q. Is that the first time that you and Dr. Soon-Shiong decided you were going to try and develop a formulation of paclitaxel?
A. No. It was well after. We had already started working on paclitaxel early in 1992. If I remember right, the conference was in September of 1992.
Q. So approximately when in '92 were you hired?
A. I was hired in 1991, in April.

Q. When, then -- I misspoke. I apologize. When in early '92 did you begin working on paclitaxel?
A. I don't remember the exact date. But it was early 1992.
Q. How many years had the scientific and pharmaceutical industry been trying to find some way to formulate paclitaxel that didn't incorporate solvents?
A. Well, there has been a couple of other companies that have tried and failed. I don't know how many years they worked on it.
Q. Did Dr. Soon-Shiong have a degree in formulation science?
A. No. He is a surgeon, an M.D.
Q. He had been an assistant professor of surgery at UCLA. Correct?
A. That's correct.
Q. So the two of you, were you the only two people working internally to develop a formulation of paclitaxel beginning in early 1992?
A. Well, there was other scientists on the team. It was a small group. But, certainly, there were other scientists present.
Q. Well, sir, during your deposition, didn't you tell me that the company had a total of five to ten people and that you and Dr. Soon-Shiong were the only two that were working

in the beginning to develop a formulation of paclitaxel?
A. I don't think I said that. But there were other scientists, and, in fact, they are even listed as inventors on the patent. All of us worked on the idea of paclitaxel.
Q. So you started in early '92. How soon thereafter did you come up with a formulation?
A. Well, we filed the first patent in early '93. So within a year of our work. So within a year, we had something that was good enough to file as a patent.
Q. So you were able to do within a year something that nobody else in the pharmaceutical industry or any other inventor had been able to do. Is that correct?
A. Well, let me just expound on that. The development of Abraxane didn't occur in a year. We found some key features that were patentable that we found in the early periods. But it was a long, arduous, several years before we came to a, what we recognized what we recognize as Abraxane today. It wasn't overnight.
Q. Let's begin to look and piece this story together.
If you could get me the Slide No. 3, please.
I will put my glasses on.
Sir, do you recognize this patent '686? You mentioned you came up with a formulation and you issued a patent. Is this this patent here sir, that was filed in February 1993 called the '686 patent?

A. Yes, this was our first patent.
Q. In terms of trying to figure what it is, the formulation, that you had created, if we read that patent, isn't it true, sir, that what you described there was a procedure for preparing chemically cross-linked microspheres that involved glutaraldehyde. Correct, sir?
A. No, that is incorrect. You are mischaracterizing what we had in the patent. That was referring to what other people do. They add in the chemicals and things that, in fact, I testified in front of the FDA, and that's what this is referring to, that they used chemicals like glutaraldehyde to chemically cross-link the microsphere. This was not our work. We were differentiating what other people do from what we do.
Q. Sir, it says, In accordance with the present invention, the polymer, for example, a protein, is selectively chemically cross-linked.
Isn't that what your patent said in 1993?
A. Yes. Again, but what that refers to is the cross-linking of the protein itself through the disulfide bonds. I specifically mentioned there disulfide bonds. This is not by adding any extraneous agent.
Q. So your position was, in your first patent, that there was an actual chemical cross-linking. Correct?
A. Of course, it's chemical. It's disulfide that is a

covalent chemical bond. But that occurs with the protein, itself, from protein to protein. We don't have to throw in any additional chemicals, like glutaraldehyde or anything else to cause it to occur. It is a native property of the natural albumin.

Q. Is that a yes, sir?

A. I don't remember your question now.

MR. SCHEVE: Your Honor, if I could ask that the witness answer my questions today, it may facilitate him remembering what my question is.

THE COURT: Doctor, understanding all of the answers to these questions are not necessarily susceptible to a yes or no response, if you can indicate yes or no and then explain; however, I will tell you that Mr. Jacobs will have an opportunity to ask further questions after Mr. Scheve is finished.

So do the best you can.

THE WITNESS: Okay. So we did not add any extraneous chemicals. So if the answer was -- if the question was whether we were adding other things in there to make it cross-linked, the answer is no.

BY MR. SCHEVE:

Q. Actually, the question was, sir: Did you not, in this patent, describe a chemical cross-linking?

A. So the answer to that is, Yes, it is through disulfide

bonds. But it's got nothing to do with additional chemicals added. It occurs through the protein, too.

Q. If we go to Column 5, it says, According to this embodiment of the present invention, particles of substantially water-insoluble pharmacologically active agents are contained within a shell having a cross-examination sectional diameter of no greater than about ten microns. A cross-sectional diameter of five microns is more preferred.

Did I read that correctly?

A. Yes, you read that correctly.

Q. These ten microns, that would be particles that are approximately 70 times larger than the particles within Abraxane. Is that correct?

A. Yes, that is correct. And the reason we are interested in large particles, but we are also interested in small particles. It depends on the application. In the very same patent, we cover applications not only for intravenous, that is, injecting it into the vein, but we talk about inhalation and other types of applications where you may want larger particles.

So we are covering a range, and I believe, in my direct testimony, I mentioned that range of .1 to 5.

This just says that ten microns is the largest size. We look interested in below ten microns, and that

five microns at the top end is even more preferred.
Q. So the only patent you had through 1993, you couldn't get below five microns, at least as described here, correct, according to this embodiment of the present invention?
A. No, that's not correct. Somewhere else in the patent, there is a range of .1 to 5 microns. I would ask you to refer to that.
Q. Well, sir, does this language say --
A. This is in reference to the upper limit of ten microns, yes. So the upper limit, what this says is that the upper limit is ten microns. And a more preferred upper limit would be five microns.
Q. All right. Now, did you, in this patent, describe anything below a thousand nanometers?
A. Can I look at the patent, please?
Q. Sure.
A. Which exhibit would that be?
Q. It's Plaintiff's Exhibit 212.
A. Okay. I would refer you to Example 9, Column 15 in the patent.
Q. Is it in the claims, sir, in terms of what you claim? Is there anything in the claims of your patent that claim something below a thousand nanometers?
A. Sir, I thought your question to me was: Was there anything in the patent that showed a size below a thousand

nanometers?

Q. In terms of what you claimed, I am sorry.

A. Sir, just to clarify, in Example 9 of that patent, the particles that are created are definitely less than a thousand nanometers. And in the claim, which is Claim 1, for example, Claim 1 only talks about the upper limits. So we are interested in particles that are no greater than about ten microns, which identifies the upper limit, we are interested in everything below that.

Q. Your next patent was called the '421 patent, was it not, sir?

Before we go to that, let's go back to the '686.

Can you find the word "amorphous" anywhere in that patent?

A. I would have to read the whole patent. But my guess is, we haven't talked about amorphous in here.

Q. Well, I really don't want you to guess, sir. I want you to tell the jury what the facts are.

Do you believe the word "amorphous" is found anywhere in the '686 patent?

A. I don't see it at a glance. But we are using solvent precipitation, which is well-known in the art, to create amorphous structures.

Q. Where does it say solvent precipitation in that patent, sir?

A. Again, I point you to Example 9.
Q. Well, I see the patent, sir. Let's go to the claims of this patent. Where in the claims --
MR. JACOBS: Your Honor, objection.
MR. SCHEVE: I will rephrase it.
THE COURT: You are withdrawing the question?
MR. SCHEVE: I withdraw the question.
MR. JACOBS: Sidebar, Your Honor.
(The following took place at sidebar.)
MR. JACOBS: This is very thick stuff, this patent stuff. If Mr. Scheve wants to burn his time, I guess I should say, Fine, let him go. If he means in the claims, he should say the claims. If he means in the specification, he should say the specification. The witness ought to be given time to study the patent. It requires that you look at something very carefully.
MR. SCHEVE: I will be more precise.
THE COURT: It is just the nature of the subject matter.
MR. SCHEVE: That is the first time I am forcing myself into a satellite. That's what I will do.
(End of sidebar conference.)
BY MR. SCHEVE:
Q. Now, where, sir, in that patent, in the claims, do you see solvent precipitation? I am talking about the '686,

which is referred to as Plaintiff's Exhibit 212.
A. In the claims, we don't talk about the process. The claims just cover the final composition.
Q. Let's move to the next patent, the '421 patent, sir. It's Exhibit 213. A copy of it is here.
Is the '421 a patent that's listed in the Orange Book and certified by Abraxis to cover Abraxane?
A. Yes, I believe it is.
Q. Now, this time I do want to go look at one of the examples. Do you make reference, sir, in Example 46, in Column 53, of using a ball mill to grind down crystalline particles?
A. You say Example 46?
Q. 46, on Column 53.
A. Yes, I do.
Q. Did you disclose to the Patent and Trademark Office in this patent anything about contamination using a ball mill to grind down crystalline particles?
A. No. These were just approaches we were taking in the early days to see how we could get small particles. We had the approach that we already talked about of the solvent and removal of solvent to create the particles.
There was other approaches we were investigating, like sizing the particles down, maybe ball mill or sonication and other techniques. This was all

disclosed in the patent.
Q. And this example of using a ball mill to grind down crystalline particles, was that disclosed to the Patent and Trademark Office?
A. Yes, it's right in Example 46.
Q. Did you raise with the Patent and Trademark Office any potential problems that you or others at Abraxis saw with contamination using that method?
MR. JACOBS: Objection?
THE WITNESS: No, we --
THE COURT: Sustained.
BY MR. SCHEVE:
Q. Did Abraxis disclose to the Patent and Trademark Office anything about contamination?
THE COURT: Perhaps I can help. Sidebar.
(The following took place at sidebar.)
MR. JACOBS: Our patents are not on trial here. It is the Elan patents for which inequitable conduct is at issue, Your Honor.
MR. SCHEVE: Well, but they are contending that our patents are invalid because they failed to disclose.
THE COURT: But you don't -- we are not going to do a tit for tat in that regard. He is correct. His patents are not on trial. It's Elan's patents.
MR. SCHEVE: It goes to, directly to credibility

of them criticizing --

THE COURT: I disagree. The objection is sustained.

Just to further articulate the Court's rationale for its ruling, we would be here all day with that. I am going to exercise my discretion. We aren't going to have a trial within a trial on this issue.

(End of sidebar conference.)

BY MR. SCHEVE:

Q. How many different patents that cover Abraxane or that mark Abraxane make reference to this ball milling method?

A. As far as I remember, there was the very first patent, the '686 patent, which we already talked about. And there was this '421 patent which was filed within a year of the '686 patent. So it was filed in 1994.

Again, that same example covers alternative techniques, ball milling. It talks about solvent precipitation in that very same example, 46. It talks about sonication and it talks about spray drying. All potentially different techniques to get small particles.

Q. Now, at the same time that these patents were being filed, were you publishing papers describing your technology?

A. No, I don't believe we published papers at that time.

Q. Let's look at this presentation of this abstract from

1994. Do you remember this abstract that was presented at the annual meeting of the Society For Biomaterials in Boston in April of 1994?

A. Yes. This was an abstract that we sent to a meeting. Just to clarify it, it is not a publication. It is just an abstract.

Q. Thank you for that clarification. We are looking at Plaintiff's Exhibit 353.

Was this reduced to written form?

A. Yes. You are required to submit it in written form.

Q. It was presented at this meeting?

A. That's correct.

Q. And does it show down below the 20th Annual Meeting of the Society For Biomaterials?

A. Yes, it does.

Q. Now, if I look at the very first line, it talks about microspheres. Do you see that?

A. Yes.

Q. It doesn't say nanoparticles, does it, sir?

A. Microspheres was a term in the art at the time. So we used it to refer to everything as microspheres irrespective of the size. It just means that it's microscopic.

Q. I want to be clear, then: Did this paper that you presented in '94 contain this entry, quote, "The microspheres may be prepared with a consistent narrow

distribution of .5 to two microns"?

A. Yes, I did.

Q. Did that describe the technology that you were working on at that point in time, 1994?

A. Well, it describes specifically for the purpose of this abstract and what was presented at the meeting that the microspheres that we disclosed at the meeting had the .5 to two micron size range.

Q. It actually says, "consistently narrow." That was the size range that you were as of 1994. Is that correct?

MR. JACOBS: Objection, Your Honor. Vague.

BY MR. SCHEVE:

Q. As of this presentation in 1994, is that .5 to two micron range, does that reflect the particle size that you were able to consistently come up with as of that point in time?

A. No. I think you are mischaracterizing what is in this abstract. When you present an abstract at a meeting, you have to be very specific about the thing you are talking about. So there is no generalizations.

What we are talking about here is a particular type of microspheres that could be consistently prepared in this size range. So it doesn't necessarily talk about all the work we are doing globally, that we were restricted to this size range.

It just says what we are going to present at the meeting, the data we are going to present at the meeting are on microspheres that can be consistent with, prepared in the .5 to two micron size range.

Q. All right. Now, let's go to the next exhibit I have, sir, which is the Joint Exhibit 027.

Did you come then to call your technology as you moved forward something then called Protosphere?

A. Yes, we used that terminology to indicate protein-based spheres. So Protosphere.

Q. Do you recognize this Joint Exhibit, 027?

A. Yes, I do.

Q. And is this a document a document that described your internal technology in trying to formulate paclitaxel?

A. Yes. This -- I am sorry. This described one aspect of the technology, which was as it's identified in that figure. It talks about a version of the technique where you have liquid in the microspheres.

Q. Liquid?

A. Liquid.

Q. Do you show any adsorbed on the surface modifier in this image?

A. Yes. It says, Cross-Linked protein albumin, and this is, again, as I said, this is a version of the microspheres that we were working on that have non-aqueous liquid inside

the microsphere.

Q. My question is: Do you see the word "adsorbed" onto the surface anywhere in this discussion or description of your technology as of the date of this document?

A. That word is not there. But I think anybody who knows the science can understand that molecules like proteins, that's what they do, they adsorb on surfaces.

So to anybody in the art, it would be evident that proteins adsorb on a surface, which is this non-aqueous liquid. Let's make sure we are clear and I understand this.

Do you see this reference here to an allowance of a patent?

A. Yes, I do.

Q. What year was this again, sir?

A. I am sorry?

Q. What year would this have been, sir, the first notice of allowance in the U.S. of this patent covering this technology?

A. I am not sure exactly. Maybe in the '95 time frame, '94-'95.

Q. Would you be comfortable suggesting, sir, that this description of your technology was at least after January of 1995?

A. It's possible.

Q. Well --

A. I mean, I don't know the date where we received the notice of allowance. I can't remember that.
Q. Would that be a reasonable assumption?
A. I think it's a reasonable assumption.
Q. Just so we understand here, what you were describing as of at least January of 1995 was still a particle that was two microns large, according to this diagram. Is that correct?
A. Yes. Again, as I mentioned, this is not Abraxane. This is a particle which inside it has a liquid. It says right there, This is non-aqueous liquid. And this falls into the range of our earlier patents where we said we were interested in down from .1 micron or a hundred nanometers all the way to five microns.
Q. I am just asking, sir, does this reflect your technology as of January 2005?
MR. JACOBS: Your Honor, it is a vague question.
THE COURT: Yes. You are going to have to be more specific.
BY MR. SCHEVE:
Q. Does this image here, sir, reflect what you understood your particles to look like in your technology as of January 2005?
A. As a general theme, yes.
Q. And so that we understand this, this wasn't a solid

particle of paclitaxel, it was non-aqueous liquid containing dissolved or dispersed drug. That's what you were describing it as of January 1995. Is that correct?

A. Again, this is one specific aspect of the technology. If you look at our patents, it says that it can be a solid core of material in there, which is, today, Abraxane. You can have liquids in the particles, which is some other application.

This clearly shows that there is liquid in here. So this is referring to that piece of the technology.

Q. And, then, if I go further and look in there, with regard to this Proto-sphere technology, again, reference to this notice of allowance, isn't it true, sir, that in this document that reflected that aspect of your technology, it said that the gradual breakdown of the protein shell in vivo -- does that mean in living, in a living entity?

A. "In vivo" is in the body.

Q. -- results in the release of encapsulated drug and provides controlled release of the compound? Is that correct? Is that what it says?

A. That's what it says. But, again, I would remind you that this refers to when you have liquids like oils inside the microcapsules. So this is a different application. If you go back to the '686 patent, the specific examples of that application, with oil inside there, and those

microspheres are larger, about one micron or two microns in size.

Q. If we go to the next one, which is your next patent, are you familiar with the '382 patent?

A. Can you tell me where the exhibit is, please?

Q. Yes, sir. It's Plaintiff's Exhibit 214.

A. Yes, I am familiar with this patent.

Q. Do you see that diagram called Figure 1?

A. Yes, I do.

Q. And does this purport to describe the technology that you were patenting?

A. Let me just look at what is meant by A, B, C, D in there.

Q. Let me do that for you, sir. If you would go to Column 7, do you see Column 7, sir?

A. Yes, I do.

Q. Does it describe what A and B and C and D reflected?

A. Yes. This is a general -- it is referring to the general picture which describes the technology again in general.

Q. Let's go back to the image here. B is pointing to these dots. Correct? Inside of this particle. Correct?

A. Well, it's pointing to the inside of the particle.

Q. Now, if we go back to the next exhibit, where it describes what "B" is, do you see anywhere there where it

says that's a solid particle, paclitaxel, or, excuse me, a solid particle of drug, not paclitaxel, any of drug?

A. Well, the word solid particle is right here.

Q. Does it say solid particles dispersed in a liquid, a suspension of solid particles dispersed in a liquid?

A. Well, I think that suspension refers to when you have the entire particle suspended in a liquid, which is what you need to administer the drug into a patient.

Q. Sir, the "B," as you recall here, is pointing to the inside of a single particle. Correct?

A. Yes, it is.

Q. And if we go to the next one, "B" refers to the interior of the polymeric shell.

Where do you see here, sir, in this invention, or in this patent, where it covers a solid particle?

A. Well, it may not be there. But it's in the rest of the patent.

Q. Does this patent contain the word "amorphous"?

A. Again, this patent is a continuation-in-part of the first filed patent, which is the '686 patent. In fact, it has all the same examples that were in the '686 and probably more.

So, while it may not contain the word "amorphous," it has the technique in there of generating amorphous particles.

Q. Does it contain the word "amorphous"?
A. Again, I can't go through the whole document. It's 40 pages. But I think the focus of this was really on the cross-linked shell. So it may not have the word "amorphous" in there.
Q. Does any patent that had been filed by Abraxis, for which you were the inventor through June of 1996, state anything about it being amorphous? Did the word "amorphous" appear in any patent filed through that date and time?
A. I don't believe we had amorphous specifically as a word. But the technique to generate amorphous particles is definitely in the patent.
Q. Okay. Now, sir, I want to go forward then to this Liversidge package.

You acknowledge that you received a package from Dr. Liversidge in August of 1996?
A. Yes.
Q. Did you sign a confidentiality agreement?
A. Sure, we did.
Q. Now, do you see this handwriting here on -- let's make sure we are clear.

Did you receive with that packet a proposed clinical development submitted by a Dr. Daniel van Hoff?
A. Yes. I think it was one-page summary of a clinical plan proposed for a drug called piposulfan.

Q. Did you get a slide presentation from Dr. Liversidge?
A. Yes, we did.
Q. Did you get three patents from Dr. Liversidge?
A. I think there were two or three patents in that packet, yes.
Q. Do you recognize this handwriting here, where it says, Note: Prosecute our grinding claims for Taxol?
A. Yes, that's my handwriting.
Q. Now, did you write this here, sir, in the left-hand column of this page, Copy, and then put that line?
A. I wrote that. What that refers to is that, this was a list of drugs that are contemplated as part of the invention. When I saw that list, it looked very similar to the list that we had in our own patent.

So I made a note there, this looks like a copy of our patent.

Q. Which was first in time, sir, the '363 patent or any of your patents?

MR. JACOBS: Objection, Your Honor. It says right up there it's the '118. Let's at least be clear what we are talking about. It's the patent that is not in the lawsuit.

BY MR. SCHEVE:
Q. Okay. With regard to the NanoCrystal technology, sir, the '118, the '684, the '025, the '363 patent, did all of

those, were they filed prior in time to your patent, any of your patents?

A. Well, I don't remember their filing dates. Maybe you can put them up and we can verify it.

Q. You don't remember?

A. I don't remember their clear filing dates.

Q. Would it be certain, sir, that you didn't file any patent before 1992?

A. That's correct. Our first patent was February of 1993.

Q. Okay. Now, in addition, sir, did you make other notations in this patent, other than writing the word "copy," did you write here with an exclamation mark and with this, these lines, No cross-link in surfactant, individually adsorbed molecules of the surface modifier are essentially free of intermolecular cross-linkages?

MR. JACOBS: Your Honor, sidebar?

(The following took place at sidebar.)

MR. JACOBS: You may recall the discussion we had at the Motion in Limine hearing. Mr. Scheve had said, Don't do this, I said, I am happy to not contend that creating generic drugs is improper. I think we should have an agreement that reading public patents is not improper. And that suggests that reading public patents is improper. This is the '118 patent. It is not in the lawsuit. It is a

sideshow.

THE COURT: I am tending to agree with that. I have an idea what you are trying to do. I have a concern about it.

MR. SCHEVE: For example, he put an asterisk next to this particular microfluidizer, Your Honor, and he incorporated it into their manufacturing methods. I would think I would have an opportunity to show how he lifted certain parts of the technology.

THE COURT: Go ahead.

MR. JACOBS: There is no lifting of the technology. There is a published patent. If he wants to walk into this one, terrific, but I object.

THE COURT: I understand your objection. I think he is entitled to make an effort to do what I think he is trying to do, what he has described. I don't know where it comes out.

Your objection is noted. I am going to overrule it at this point.

I think you need to mind your time, though.

MR. SCHEVE: I will, Your Honor.

(End of sidebar conference.)

BY MR. SCHEVE:

Q. Did you put this asterisk down here, sir, about Model M 140 K, which is a high-pressure micro fluid diver?

A. Yes, I did. What that refers to, again, is a type of equipment that is known in the art, it's known in the field. It's a microfluidizer or a fluidizer. And we had some references to that in our very own lab notebooks. It's an instrument that's used to shear, sort of like an analogy, would be a blender, to break up things and make them into small particles.

So that was the reference to that instrument.

Q. Did you make reference here to the particle size being less than 400 nanometers?

A. Yes. All of these were notations I was making as I was reading it. Some of them, to me, were very striking, because they were either, for example, when I saw the list of drugs, I said, Okay, this looks very much like what we had in our own patent.

When I saw cross-linked or I -- rather non-cross-linked, I made an exclamation point there because it was different from our technology.

I was just underlining the key features as I went along and read the patent.

Q. Did you highlight here, sir, This processing temperature of between 30 and 40 degrees Centigrade are preferred?

A. Sure, I did, yes.

Q. Let's go on then, sir, to the next patent in the

sequence, which was filed on September 9th, 1997, the so-called '331 patent.

Is this a patent that marks Abraxane according to the Orange Book?

A. Please give me the exhibit.

Q. This would be Plaintiff's Exhibit 594.

A. Yes, this is one of our patents.

Q. Is this the first time, sir, that you had a patent that actually refers to this thing called Capxol?

A. For the first time, the word "Capxol" is used in a patent?

Q. Correct.

A. It's possible. I don't know without going through the text of all the patents.

Q. Is Capxol a name that was eventually used to substitute for that word Proto-sphere?

A. No, it's not.

Q. What is the difference between Proto-sphere and Capxol?

A. Proto-sphere is a general word referring to protein-based microsphere. So it encompasses the technology in general. You can use different proteins. You can use different drugs. You can have oil inside the particles or you can have a solid amorphous particle on the inside.

All of that is covered by the word

"Proto-sphere."

Capxol is a name that we had given at the time to the particular formulation with paclitaxel.

Q. I don't mean to cut you off, sir. Did you finish?

A. That's okay.

Q. Is it true, sir, that then this patent that was filed in 1997 describes a Capxol as forming a stable colloidal solution of paclitaxel. The size of the colloidal suspension may range from 20 nanometers to eight microns with a preferred range of about 20 and 400 nanometers?

A. Yes, that is stated in the patent. And the reason for that, if we can just go back, so the reason for that is it's a general description of what Capxol is. You give a general range. Then you typically, in patents, you give a more preferred range.

So both of those general ranges, all the way down from 20 nanometers up to eight microns, are here. Even the more preferred range of 20 to 400 nanometers, which is a smaller size range, is mentioned in this patent.

Q. Does this patent have the word "amorphous" anywhere in it, sir?

A. You know, I don't believe it does, because this patent was really focusing in on clinical application. How do you administer this drug to a patient? Do you give it in one hour or three hours? How often do you repeat the treatment

cycle? Is it three weeks? One week?

It's a method of administration and treatment. We covered the other aspects, like cross-linking, in the first patent. There was other patents that covered the amorphous aspect. This particular patent covered the administration to the patient.

Q. So, through the filing of this patent in 1997, had a single one of your patents, of the patents marking Abraxane, contained the word "amorphous"?

A. I am sorry. Could you repeat the question?

Q. Certainly. Through the time that this '331 patent was filed in September of 1997, the application was filed, had any of the patents marking Abraxane contained the word "amorphous"?

A. Absolutely. We had patents, if I remember correctly, it was filed in October of 1996, that, in fact, had the definitive data that showed amorphousness in Abraxane. That was filed as a separate patent, like I said, you file patents on different aspects. We covered cross-linking already. We then filed, in '96, amorphousness, even though we had examples in the earlier patents, that clearly made amorphous particles. So by this time in 1997, I think more than a year before this, we had already filed a patent with amorphous.

Q. What was the number of that patent, sir?

A. 5,916,596.
Q. '596 were the last three digits?
A. '596 were the last three digits.
Q. Okay. Now, sir, with regard to this '405 patent, I am just about ready to move on to a new topic here, is it true you filed then another new patent in 2000, called the '405 patent?
A. Yes. We filed several patents along the way. This is, okay, the '405 patent. I don't believe your filing date of August 2000 is correct.
Q. Okay. And it's referred to as Defendant's Exhibit 029. Again, is it describing suspension ranging from 20 nanometers to eight microns, and then providing a preferred range?
A. Did you say 029?
Q. It's '405, sir. It's Defendant's Exhibit 029, 029.
THE COURT: Mr. Scheve, would you signal when you are moving into this next topic? We will break at that point.
THE WITNESS: Yes. This was, that language is in that patent.
MR. SCHEVE: Do you want to break, Your Honor?
THE COURT: Sounds like a good time. Let's take our lunch.
(Jury leaves courtroom at 12:59 p.m.)

(Luncheon recess taken.)

THE COURT: We will work until 4:00 o'clock today.

Ms. Walker.

(Jury enters courtroom at 2:10 p.m.)

THE COURT: Mr. Scheve.

BY MR. SCHEVE:

Q. Good afternoon, Doctor.

A. Good afternoon.

Q. I am going to put up this image. You mentioned during direct examination that there was a mutual exchange of information between you and Dr. Liversidge?

A. Yes, Doctor there was.

Q. Is this the image you gave to Dr. Liversidge of your technology as of August of 1996?

A. It's either this one or something that looked very similar.

Q. Very similar to this?

A. Yeah. Maybe it's, Doctor I can't be exactly sure. Could you show me the exhibit?

Q. Yes, Doctor sir. I believe it is Joint Exhibit 025. It also says Joint Exhibit 028. Apparently, Doctor it's found in two places.

(Pause.)

A. Which one is it? Because it's not in one and I think

it's in the other.
Q. Which one do you find it in, Doctor sir?
A. 028.
Q. Is this the image that you exchanged with Dr. Liversidge?
A. Probably. My book looks like a big block. I am sorry about that.
Q. To the best of your memory, Doctor sir, Doctor would this be the image that you exchanged?
A. It could be.
Q. I need to establish if this is what you gave him or not, Doctor sir. We will quickly look for that.
A. There is another image in here, Doctor if you would like to refer to that, Doctor which may be clearer.
Q. Is it this image here?
A. No. It's a different one. It's on 025262.
Q. Let's just establish, Doctor you sent an image to Dr. Liversidge. Is that correct?
A. Yes, Doctor I did.
Q. Now, Doctor would you go to 20, Doctor Slide 20.
Sir, Doctor I just want to establish some things. Did Dr. Liversidge give you this slide as part of his slide deck?
A. Yes, Doctor I remember that slide.
Q. Let's move to the next one, Doctor Plaintiff's Exhibit

363.

Did this become an image that was utilized internally at Abraxis to describe its Abraxane nanoparticles?

A. Yes. This is a typical cartoon that we have used for a long time.

Q. Was this being used in 2006?

A. I don't recall specifically.

Q. To the best of your memory, Doctor approximately when was it being utilized within Abraxane to depict the particles -- within Abraxis to depict the particles within Abraxane?

A. My guess is we have used that cartoon for probably at least ten years.

Q. Ten years?

A. Maybe.

Q. Do you know for sure?

A. No, Doctor I don't.

Q. Let's go on here. Did Dr. Liversidge give you these charts relating to release profiles and dissolution profiles as part of the technology exchange?

A. Could you please point me to that?

Q. Absolutely. I am looking at Joint Exhibit 020. It's Pages 15 and 18.

A. All of these slides are in that package.

Q. I hate to backtrack, Doctor if you would be kind enough to go back to Exhibit 025, Doctor Joint Exhibit. It's a Bates number ending in 305.

If you would be kind enough to bring it up, Doctor Jonathan. 67, Doctor please.

I apologize, Doctor sir, Doctor for making you go back and forth.

A. Just to clarify, Doctor it is in there. But 025 is not something we sent to Nano Systems.

Q. 025 is not?

A. No.

Q. Does this image here in 025, Doctor was that an image of your technology?

A. Yes. This was taken very early on during the development.

Q. Is it found in a packet of materials that has a date on it?

A. It's in that packet of materials that, Doctor you see a fax page as the first page of that exhibit, Doctor there is a June 1993.

Q. '93?

A. Yes.

Q. Okay. Now, Doctor this image, Doctor was it something that was done internally at Abraxis?

A. No, Doctor we did not do this internally.

Q. Where was it done?
A. It was done at University of Illinois.
Q. I want to move on, Doctor if I could get Slide 27, Doctor please.
Is it true, Doctor sir, Doctor that the manufacture of Abraxane is carried out at a low temperature with chilling throughout the process?
A. Yes. The chilling throughout the process is important because you have albumin, Doctor and albumin is a protein. Proteins are very sensitive to different temperatures. Also, Doctor you can get, Doctor you have to be very careful not to contaminate it with microbes, Doctor so you keep it at a low temperature. If you keep it at high temperature, Doctor you can get a lot of microbial growth, Doctor because that condition is very useful for microbes to grow. So we chilled that entire process.
Q. Then I would like to go to Slide 29, Doctor please.
Is it true, Doctor sir, Doctor that in terms of homogenization to reduce the particle size, Doctor that you were using a certain emulsifier up until February of 1975 and that your process switched over to M 140 K microfluidizer?
A. Yes. We used different types of equipment to make the particles. I think I explained before that homogenizer or fluidizer is the type of equipment that can achieve the

smaller size in particles.

Initially, we were using, when we were at small scale, at lab scale, in the test tube, we were using what's known as this Avestin (phonetic) unit, which can handle small samples. Then as this necessity for scaleup began, that we needed to make bigger and bigger units, we went to what was standard and available at the time.

For the bigger size, we used M 140 K. Then, at the commercial size, we used yet another unit that is even bigger than that particular unit.

Q. Actually, the first human clinical trial batch wasn't made until clear down here in 1998, was it, sir? 1998?

A. I think there was clinical batches that were made prior to that date.

Q. Well, let's go look at this page. I don't want to delay us. But please look at it, Plaintiff's Exhibit '017. Do you have that in front of you?

A. Yes, I have it here.

Q. Are you able to find it, sir? Do you have that page?

A. Is it Page 324 in this?

Q. It's Table 1. Did you find it?

A. Yes.

Q. If you look at the top, doesn't it say, "Used For Preclinical Studies Listed Below"?

A. Yes, I see it.

Q. Preclinical means animal?
A. That's correct.
Q. Isn't it true that the first human study, the first batch wasn't made until March of 1998?
A. The first clinical batch, which was used in our clinical trials, as identified in this table, is down here. (Indicating.)
Q. Sir, isn't it true that you began using this very specific model of microfluidizer, the M 140 K, clear in the first week of February of 1997, 13 months before the first clinical batch?
A. Well, this data just represents the batches that were used for testing that was sent to the FDA, meaning if we did any animal tests, we had to identify which particular lots were used for the animal test.

So there was a lot of other development work that was going on at the same time, just in finding the right experimental conditions and to produce the product. So that information is not represented on this table. So I would say that even prior to this date, that we were using equipment such as this to produce nanoparticles of paclitaxel.

Q. Can you find it on this page, sir?
A. No, it wouldn't be on this page, because this reference the specific lots, as indicated in the title, that

are used for preclinical, that is for animal studies, and for clinical studies.

Q. When was the first clinical study started, sir?

A. It was started in May of 1998.

Q. May of 1998?

A. I beg your pardon. The IND was filed in May '98. The clinical trials started in July.

Q. In July of '98?

A. Yes.

Q. This chart shows that the first Phase 1 batch was made in March of '98. Correct?

A. That's correct.

Q. The jury has seen a number of images of crystals.

Would you please put up No. 45.

Do you see this here, sir? Microscope! Needles! Pretty damn small! Normal sample-microscope-needles.

Do you see that, sir?

A. Can you tell me which exhibit it is?

Q. Yes, it's Joint Exhibit 62.

THE COURT: What's the Bates page, Mr. Scheve?

MR. SCHEVE: It ends in 191, Your Honor, I am sorry.

MR. JACOBS: Your Honor, we are having trouble tracking the exhibit and the Bates page.

THE COURT: I am, too. JX-62?

MR. SCHEVE: 062.

THE COURT: I have that.

THE WITNESS: I don't think it's in here. All the Bates pages start with 527.

THE COURT: Yes. The last three numbers, Mr. Scheve, on the first page, 474 through -- well, it goes on from there.

MR. SCHEVE: Let me go forward. I apologize to the Court and the witness for that. I have it marked as that. If I am wrong, I stand corrected. I apologize.

BY MR. SCHEVE:

Q. Let's go forward to the next one, please.

Do you recall, sir, the discussion that you had with counsel for Abraxis about these references to crystals? I am now looking at Joint Exhibit 021.

A. Yes. This, I testified this morning about this particular example from my notebook.

Q. If we go forward in 1995, you will acknowledge, sir, that there are references to crystals being observed at different stages, in other words, some in the manufacturing process and then later on, actually, after they were reconstituted with saline solution.

Do you agree with that, sir?

A. No, actually, that is a mischaracterization.

Let me clarify.

This is a notebook from Dr. Shlomo Magdassi's notebook, who used to work for me. In this particular case, on this date, this was in early '96, he is doing an experiment where he uses a surfactant, a surface active agent or a surface modifier. If somebody could blow this up. It says, Cremophor. I can see right here. He uses Cremophor in this formulation. Here we are, when I talked to you earlier about testing all kinds of different conditions, all kinds of different components, in this case, we are testing Cremophor for. The results that he got was crystals. And he identified right here that, "The problem: Crystal growth. How to prevent it"?

So this is clearly a result that we did not want or striving to get away from crystals. This is a condition that we did not want, using this particular component, Cremophor. And we completely steered away from that. In fact, in the patent that we filed later, in this very same year, which had the amorphous x-ray diffraction data in there, there are specific examples in that patent, this is one of the examples in there, it clearly shows and identifies that this is a technique that is not to be used for the invention. That the addition of surfactants should not be done.

Q. If we move forward, you told us here now that you

started clinical trials with ABI-007 in July of 1998. Correct?

A. That's correct.

Q. Let's move forward to Slide 53.

A. What exhibit?

Q. Slide 53, please. It's Plaintiff's Exhibit 334. In 2000, July of 2000, this is two full years, is it not, sir, after this drug is being administered to humans in clinical studies?

A. Yes, that's correct. Let me just get to that notebook page, please.

Q. Sure, Plaintiff's Exhibit 334.

A. Do you have a Bates number, please?

Q. The page that is in your lab notebook, sir, did not contain a Bates number when it was produced to us.

THE COURT: Mr. Scheve, would you check your copy? Is the cover, Second Nature, notebook, something along those lines? So we know we are talking about the same exhibit. I have, in the notebook you provided me, PX-334. Behind that tab, I see Neil Desai, handwritten, American Bioscience, and then, Second Nature.

MR. SCHEVE: Yes, Your Honor.

THE COURT: What we are trying to determine is what page. I do see Bates number pages. Are we talking about the same exhibit?

THE WITNESS: Sir, the last entry date on this exhibit is only from 1999. There is nothing in 2000.

THE COURT: You are talking about August 19, Doctor?

THE WITNESS: Yes, that's right.

BY MR. SCHEVE:

Q. Let me move to the next one.

A. I remember this, so I can talk about it.

Here, what we are doing, this is a conversation, a conference call that I am having with this company Bristol Myers Squibb. As you know, Bristol Myers Squibb made the original Taxol. They are now interested in some aspects of our technology. So at this time, I had a whole probably four or five people from Bristol Myers Squibb on the line. And I was walking them through our technology.

We talked not only about Abraxane but other applications. If you look here, that says inhalation, so looking at other applications of drugs. And we talked about Abraxane also.

What Mr. Scheve has highlighted here for you is this statement, Change of amorphous to crystalline. And it says something about PK.

So I was making notes of what they were telling me and asking me. One of the questions they raised, very valid question, is, upon reconstitution, which is shown

right here, upon reconstitution, which means when you take the vial of Abraxane, which is a powder, and put saline in it, or water in it, in essence, does it change from amorphous to crystalline?

The reason they were interested in that was because -- and I put here "PK" -- so PK of amorphous versus PK of crystalline. What PK refers to is a word in the medical field called pharmacokinetics, which describes how the behavior -- what is the behavior of the drug once it enters the bloodstream.

So when you change the PK, what they are referring to is that an amorphous material would behave differently when administered to the bloodstream from a crystalline material. Of course, I fully agreed with it, because, as I have described to you before, an amorphous material leaves the bloodstream very quickly and crystalline materials stay in the bloodstream.

In fact, this is their statement to me, asking me, or, rather, question to me, Does the Abraxane, after reconstitution, change from amorphous to crystalline? They were very interested in that because, as you know, PK would change if that does happen. My response to that was, No, it does not change and it remains amorphous. What I have done here is just noted down their questions to me in that telephone call.

Q. Here, sir, there was a question, and a question mark. What you are telling me now is even though this doesn't say question mark, that this was a question?

A. Yes. That was a Bristol Myers question to me.

Q. This is Leslie Louie's notebook from September of 2000, Plaintiff's Exhibit 397, if you can find that.

Do you see up here, Reconstitution study?

A. Yes, I do.

Q. Isn't it true, sir, that when Leslie Louie reconstituted Abraxane in September of 2000, which was two years and two months after you had began putting this drug in humans, and her observation was, Few random crystals, at five hours. Correct, sir? At differing strengths?

A. Okay. Let me clarify for you.

MR. SCHEVE: Your Honor, I would really appreciate an answer to my question.

THE COURT: I think he is getting ready to.

THE WITNESS: I agree with you that she put that notation there.

But this is the same page that was brought up in my direct testimony. This is lot No. 197079. This is that same first lot that we produced at 20 liter scale. This was done over that July 4th weekend. This is the same lot that was rejected, that failed all our testing for Abraxane, because it has very high solvent levels.

We never utilized that lot. It was thrown away.

So this is from 1997 to 2000, first of all. This is three years later. Of course, that doesn't have any bearing. But the fact is that this was a rejected lot with very high solvent levels.

BY MR. SCHEVE:

Q. It was using the method that was illustrated during your direct where you poured two things together into -- first you dissolved it in a solvent and poured it together, and that method, even though I hear you say now that you think the solvent was too high, that method was used when these crystals were observed. Correct?

A. First of all, I don't think the solvent -- I know for a fact that the solvent levels were extremely high and it was rejected. That method was used. But there was something wrong in that particular lot in the manufacturing process. And we could not get out all the solvent that we wanted to. That was the problem with this lot.

Q. That method that was being utilized -- again, this is two years and two months after -- you have already got humans getting the drug. Correct?

A. Yes.

Q. This was the observation by Ms. Louie within Abraxis. Is that correct?

A. Sir, again, back to the point --

THE COURT: I think he has answered that question, Mr. Scheve. You can argue it.

BY MR. SCHEVE:

Q. May I go on, then, to the next one, which was -- I think this is Mr. Ron -- is it not? Do you know the gentleman named Ron who continued this experiment?

A. I think this is still Louie's notebook.

Q. At her deposition, she talked about it. So I won't belabor the point.

When I took your deposition, you told me that you are not an expert in crystallography. Is that still true?

A. That is true.

Q. You told me you were not an expert in x-ray diffraction. Is that still true?

A. I have used x-ray techniques hands-on before and published on them. Not specifically x-ray diffraction, but, as I mentioned, x-ray photo electron spectroscopy, which utilizes some of the very similar equipment.

So I know about these techniques. I have studied about these techniques. I have utilized them and published data based on these techniques. But I do not perform these techniques every day and I would not qualify myself as an expert.

Q. Thank you, sir. And you told me you were not an

expert in cryo-transmission electron microscopy, or cryo-TEM. Is that still true?

A. That is still true.

Q. You are not an expert in terms of looking at shapes or sizes of particles to express opinions as to whether or not they are crystals. Is that correct?

A. Well, my experience resides with my hands-on experience with paclitaxel. And I know a paclitaxel crystal when I see one. It is a very characteristic needle-shaped crystal.

Q. Is it correct, sir, you are still not an expert in that?

A. It depends on how you define expert. I have 15 years of experience on observing these crystals. If you use the definition "expert" in the highest sense of the word, have I published extensively in that particular field?, no, I am not an expert. But I have experience.

Q. You told me during the deposition there really weren't any people within Abraxis who were necessarily experts in any of those fields. Isn't that correct, sir?

A. I think I have to say it is the same answer. You may not qualify them as experts. But a lot of the people in Abraxis have been working for a long time in these areas.

Q. And you told me during the deposition that Abraxis had not submitted Abraxane or any aspect of Abraxane to any

outside expert to ask them whether or not the particles within Abraxane were amorphous before this product was marketed.

Isn't that correct?

A. Yes, I think that's correct.

Q. Now, I want to show you an image, sir. Then I will try to bring my examination to a close.

I want to address briefly the cross-linking issue. But I want to show you an image that I found in some of the materials. First off, could we go to Page 36, please.

Sir, was this the image that was reflected in this presentation here? Who selected it? This image, this round one up here in the top, Plaintiff's Exhibit 363.

A. I am sorry. What was your question?

Q. Who selected this round image here for purposes of this presentation that's found on Plaintiff's Exhibit 363?

A. I think this is an image I had in my files. And this was used for, I believe this was an ODAC presentation, so we utilized that.

Q. When you say "ODAC," that is the Oncology Drugs Advisory Committee to the FDA?

A. That's correct.

Q. Was it selected from this image?

A. No. It was selected from a series of tests that were

done earlier.
Q. Well, this here, sir, is supposedly a cryo-TEM image, isn't it?
A. Yes. The particle that we are looking at here, just for clarification, this little bar-like thing has got nothing to do with the particles. It is part of the grid that you put the samples on.
Q. When it says, Amorphous confirmed by x-ray diffraction, that is not an x-ray diffraction pattern, is it, sir?
A. No. We are referring to the fact that this is a particle and that we have a separate, different technique by which we have proved amorphousness. And that technique is x-ray diffraction.
Q. So this is cryo-TEM. Was it selected from this cryo-TEM image? Can you find that nanoparticle there?
A. Like I said, it's not from this image. This is images we had done several years earlier.
Q. What about this one here, do you see this nice round particle anywhere in this cryo-TEM image?
MR. JACOBS: Could we have the exhibit number?
BY MR. SCHEVE:
Q. Plaintiff's Exhibit 330 and the one before that was also Plaintiff's Exhibit 330?
A. These are again cryo-TEM images. Remember what I said

about the prune, that when you create the droplet, it is more or less spherical, you shrink it when you pull the solvent off so you get more or less spherical but slightly irregular shapes. So this is what that represents.

Q. Was that nice round image taken from either of these two cryo-TEM images, sir; that was my question?

A. No. It was taken from a series of studies we had done several years before.

Q. These cryo-TEM images, are these images of reconstituted Abraxane?

A. They are.

Q. Sir, going back to this image here, this presentation of yours to ODAC said, Example of needle-shaped crystals. Is that correct?

A. Yes.

Q. You actually pulled that image from an article by someone named Barrett Rabinow, didn't you, sir?

A. Yes, we did.

Q. At the top of that Rabinow paper, there is raw material. There is material after precipitation and before homogenization.

You mentioned precipitation earlier, did you not, in your testimony?

A. Can I please go to that exhibit?

Q. Absolutely. It's Plaintiff's Exhibit 729.

A. What was your question?
Q. My question is: This image here says, After precipitation. You described precipitation in your earlier testimony in describing how Abraxane was manufactured, did you not, sir?
A. Yes, we did.
Q. Now, there is also a picture about what these NanoCrystals look like after they are homogenized.
Did you include this in your slide presentation?
A. There was no need to. What we are trying to demonstrate is the difference, if you go back to that previous slide, if you would, please, our slide, all we are trying to say is that we have shown you an example, it says there, Example of needle shape, and then show the needle-like crystals. And we are trying to differentiate from what is Abraxane to what is standard needle shapes.
That is what was in the presentation on that slide.
Q. When we reduce it by homogenization, do you still see needles there, sir?
A. Sir, I have no idea what was done in this process, who did it, who has done it, what they have used for homogenization. So, you know, this is a low magnification, this is a 20 micron scale. I would like to see this at probably a hundred nanometer resolution. Then you could see

that. This is very low magnification.
Q. Do you see needles, sir?
A. I see some shapes that look like needles.
Q. That look like crystals?
A. These are very large. Please understand, they showed magnification. The very large particles are being looked at as the same magnifications as the small particles. Here is a shape that looks like a rod or needle. In fact, there are several others I can point out to you on this, what I am looking at, my screen here, that look just like that.
Q. What about with regard to these images here, sir? Do you see anything in here that maybe looks like it's got some angularity, it's the shape of a triangle or arrow head?
THE COURT: PX-330?
MR. SCHEVE: Yes, sir. PX-330.
BY MR. SCHEVE:
Q. Do you see any angularity in those, sir?
A. Again, I may see some angularity and irregular shapes but there is no needles in them.
Q. Now, with regard to this cross-linking issue, sir, I am going to ask you to look at Joint Exhibit 071. Would you go to Slide 42, please.
Now, as part of the New Drug Application to the FDA, did you submit data from what are called pivotal stability batches relating to the monomeric content of the

albumin contained in vials of Abraxane? That is, again, Joint Exhibit 71, sir.

A. Yes, we did.

Q. Did you report to the FDA, sir, that the monomeric content from these three batches here -- and you made reference earlier about this Melrose Park facility in Illinois -- did you represent to the FDA, sir, that with one, it was 90.2, give or take 0.6 percent monomer?

A. Yes. This is looking at the entire Abraxane, what is in the vial, the entire contents of it. If you analyze the albumin that's in the vial, this is what you get in terms of monomer, dimer, oligomer, and polymer.

Q. And with regard to the other value that is down here at the bottom, for all of these lots here, was the average monomer reported to the FDA 82.2 plus or minus 0.6 percent?

A. Yes, it was.

Q. Now, did you also submit to the agency data on monomer content for batches that were produced in a New York facility, Grand Island?

A. Yes. The objective of that was to show that from facility to facility, there was no difference, or the product, essentially, was very similar.

Q. And were the values reported to the agency 92.5 percent plus or minus 0.2, 86.4 percent plus or minus 0.2, 86.7 plus or minus 0.1 percent, and 86.8 plus or minus zero?

A. Yes. That data was information sent to the FDA.
Q. Has that data ever been retracted from what was submitted to the FDA?
A. No, it was not. I would like to point out one thing additional that we reported to the FDA. That albumin is cross-linked and that it is cross-linked via the cystine in the albumin, that is, the disulfide linkages. This was clearly identified in this document.
Q. With regard, sir, so we understand the last series of my questions, then I will sit down, with regard to what Abraxis has done or not done, is it true, sir, that Abraxis has never commissioned anyone to use a test for crystallinity with reconstituted Abraxane powder?
A. Well, you can't do that, because the standard technique for analysis for crystallinity is x-ray powder diffraction. And powder necessarily means it's not reconstituted, it's not in water. So you have to do it for a dry powder.
Q. Is it true, sir, that you have commissioned no studies after it was reconstituted to test for crystallinity?
A. We have done -- I beg your pardon. We have done no x-ray diffraction studies on reconstituted material. That's correct.
Q. And isn't it true, sir, that you have separated the particles from free albumin within Abraxis?

A. We have done that, but in the context of another study, where we are looking for the amount of cross-linkages on the particle, not for an x-ray diffraction.

Q. After those particles were separated, isn't it true, sir, that neither Abraxis or anyone commissioned by Abraxis has ever tested those nanoparticles that were separated from the free albumin to determine their levels of crystallinity?

A. That's correct. And it would not make sense to do that, because, as I mentioned, when you remove all of that free albumin from the particles, you destabilize the particles. You can get all kinds of artifacts. You can get aggregates. You can get agglomerates. So we wouldn't do that type of testing.

Q. But you felt comfortable relying on that separation data to report to the FDA that the particles are 82 percent paclitaxel and 18 percent albumin. Correct?

A. Absolutely, because, in that case, it makes sense. All you are doing is looking at the total content. You are not looking at structural information. You are just measuring what's in the particles.

Q. No crystallinity testing, I am putting under this column.

Is it true, sir, that the only crystallinity testing you did of freeze-dried powder was x-ray powder diffraction?

A. X-ray powder diffraction is a standard technique. We utilize Abraxane as is from the vial. It is a powder diffraction which means you have to use powder. That is the test we did with Abraxane.

Q. Is it also then correct, sir, that it's tenfold amorphous albumin in what you tested using x-ray powder diffraction?

A. That's true. But it doesn't matter. We ran the appropriate controls, where we had the tenfold albumin and we had the crystalline paclitaxel from the manufacturer. We mixed the two up, and we ran the same x-ray diffraction tests, and there it was. You could see the peaks of crystalline material. So we ran the appropriate controls in those experiments.

Q. So is the answer yes, sir, tenfold?

A. Yes. I already said it was yes at the beginning of my answer.

Q. Thank you. With regard, then, sir, isn't it true we are dealing with 130-nanometer particles?

A. Yes, give or take a little bit.

Q. You just told the jury that, as the control, you did a physical mixture of paclitaxel with albumin for your control. Is that correct?

A. That's correct.

Q. Now, isn't it true, sir, that those particles that you

used as a control, the raw paclitaxel mixed with this tenfold amorphous albumin had particles up to 500 microns in size?

A. Well, we didn't measure the particles, for one, in the control. But I would just assume they are very much larger than the nanoparticles.

Q. So this jury understands, did you ever use as a standard, or a control, a mixture of this tenfold amorphous to particles that were 130 nanometers?

A. It wouldn't make sense to use that as a control. And neither do you need to, because whether you have big particles or small particles, if it is crystalline, it is crystalline, it will show up on the x-ray method. If it is not crystalline, the peaks will not show up. So size really has no bearing on that method.

Q. Is this a correct statement, sir: You used no 130-nanometer control?

A. Could you please describe what exactly you mean by the "control" there?

Q. The physical mixture of raw paclitaxel and this tenfold amorphous albumin that you used as a control, isn't it true, sir, that that was not -- the paclitaxel in that was not reduced to 130 nanometers?

A. That is absolutely true.

Q. Isn't it true, sir, your own patents say that raw

paclitaxel ranges from 20 to 500 microns in size?
A. I don't remember the exact range. They are very large crystal particles.
Q. 500 microns would be 3500 times bigger than 130 nanometers. Is that correct?
A. Yes. But it doesn't matter. Again, because if, in your control, you put in the same amount of paclitaxel as you do with, as is seen with Abraxane, that is the whole point of the control. If you have ten milligrams of paclitaxel in the Abraxane sample, you have to make sure you have at least ten milligrams of paclitaxel in the control sample. So then, as long as those amounts are the same, the size has no value in that experiment.
Q. Can you just confirm for me, sir, that raw paclitaxel is up to 3500 times larger than the size of the particles that are in Abraxane?
A. It could be, yes.
Q. Then I want to ask you one last question, sir. Isn't it true that you performed, or the company performed differential scanning calorimetry or DSC?
A. Yes, absolutely.
Q. Isn't it true, sir, that there was not found to be a glass transition temperature for Abraxane?
A. It's true. And that's easily explainable. Let me explain it.

Glass transition, first of all, I don't know if the jury is familiar with that, is something you see for amorphous materials. 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.

Q. Isn't true, sir, when you applied differential scanning calorimetry, that Abraxis did not find a glass transition temperature for that product, for the paclitaxel in that product? Yes or no?

A. I just said we did not.

Q. Okay. Three more slides, then I am sitting down. Would you please pull up Slide 32.

Isn't it true, sir, you represented to the Oncology Drugs Advisory Committee, to the Food & Drug Administration --

A. Could I pull up the exhibit, sir?

Q. I am sorry. It is Plaintiff's Exhibit 112. I apologize.

Did you make this statement to the Oncology

Drugs Advisory Committee, to the FDA, that the albumin particles rapidly dissociate into individual albumin molecules and then circulate with the paclitaxel still attached?

A. Yes. That's exactly what I am talking about, the complexation, where the paclitaxel stays attached to the albumin.

Q. And then, sir, at that same FDA meeting on October 10 -- yes, the FDA meeting of October 10th, 2007, did you state, sir, in your remarks to the FDA, with regard to Abraxane, that it says, quote, "You've got soluble albumin bound drug floating around very soon after administration"?

A. This is now a different exhibit?

Q. Yes, sir. It's Exhibit 070. Do you see it? It's Page 184 of your testimony to the FDA.

A. Okay. I am there.

Q. Did you make those three statements there?

A. Yes, I did.

Q. My last exhibit, and I will sit down. Is it true, sir, that in this presentation, does this presentation here depict what happens to the -- and I am looking at Plaintiff's Exhibit 363 -- what happens to the surface modifier once it's put in the blood? Once it's injected into a human?

A. Well, this is just a cartoon to indicate that when we

take Abraxane and administer it, the drug -- this particle rapidly dissociates, this goes to the point of its amorphousness. Remember, it quickly dissolves. So it dissolves into these complexes of albumin with the drug attached. And you can see these little stars there. Again, this is a little cartoon depiction. It is then these complexes that can piggy-back onto the albumin and rapidly get out of the bloodstream. That is what we are trying to indicate here.

Q. And indicating that, sir, is it correct, at the top, it says, In the circulation, the nanoparticles rapidly dissociate?

A. Absolutely. That is a key feature of Abraxane.

MR. SCHEVE: Your Honor, with that, I pass the witness.

THE COURT: Mr. Jacobs.

REDIRECT EXAMINATION

BY MR. JACOBS:

Q. Let's take that last sequence in reverse order, Dr. Desai.

Is there anything inconsistent between the idea of rapidly dissociating and the amorphousness of the paclitaxel?

A. No. In fact, not at all. I think a key feature of the amorphous is that we want it to rapidly dissolve and

dissociate so it can get out of the bloodstream. If it is not doing that, it is not doing its job that we planned.

Q. Is there anything inconsistent with the idea of rapidly dissociating and disulfide bond based cross-linking?

A. Not at all. There is disulfide cross-linked albumin in our natural blood circulating around all the time. If you have disulfide cross-linked albumin, the particle, the body does not see that as foreign. That is the whole point.

We did not want to denature -- remember the egg white concept. So it's very important, in fact, that we have this cross-linking to help stabilize the particle, and very important, in fact, that we have the amorphous nature so that it dissociates very rapidly.

Q. Did you rely on DSC for the conclusion at Abraxis that Abraxane, the paclitaxel in Abraxane, was amorphous?

A. No, absolutely not. DSC is not the definitive test for crystallinity or amorphousness. X-ray diffraction is.

DSC is a standard test to look at thermal behavior of materials. So you increase the temperature, see what happens; decrease the temperature, see what happens. It's got nothing to do with crystallinity.

Q. Can we take a look at JX-21, at 325, please.

Dr. Desai, again, this is August -- the actual test data on this page is 23rd of August. Correct?

A. That's correct.

Q. This is before you got the materials from Nano Systems?
A. That's right.
Q. I think we all know by now, this is an x-ray powder diffraction?
A. That's correct, yes.
Q. You made a point about five questions towards the end of Mr. Scheve's examination that I wanted to be sure we capture. You talked about the total quantity of paclitaxel in the physical mixture and addressed that as compared with the question of the size of those paclitaxel particles. Can you just explain that one more time, please?
A. Okay. So what's important here is that when we test Abraxane, you have all the appropriate controls in place. By "controls," we mean appropriate other samples that you test along with it to confirm something.

When we test Abraxane, which is the curve right on top, you have no crystalline peaks, as you can see, no sharp peaks.

We want to make sure that our testing is not flawed. So we put in a control sample, which is just albumin and paclitaxel from the manufacturer, and we mix them up together in the same ratio as you would have in the actual Abraxane sample.

The importance of that same ratio, it's actually

very important to do that in the right ratio, because if you had more or less paclitaxel in that control sample, then you would get a different picture when you looked at the chromatograms.

So from that perspective, having the same amount of paclitaxel in the control sample is important. That's what we did.

When we ran that control sample, we could still see the crystalline peaks, meaning that there were crystals in that sample, and that control sample, or having the same amount of drug in that sample was adequate for a control, so that we could see, or have a definitive answer for our Abraxane sample.

The other point was on the issue of the size of those particles. Now, when you have crystalline material, whether it's a hundred microns or 200 microns, or it's 200 nanometers or a hundred nanometers, it really doesn't matter. Because, if there is crystallinity, you will pick it up on this method.

There is a reason x-rays are used in this method. The reason for that is, again, I am getting into technical concepts here, but the reason for that is the wavelengths of these x-rays are extremely, extremely small. Much, much smaller than the smallest nanoparticle that we have talked about today.

The point is that if it's -- if an x-ray is penetrating a particle, scale wise, the x-ray may look like this, but that smallest particle, nanoparticle, looks like that. (Indicating.) So there is no chance that the x-ray is not going through the particle.

When you have a bigger particle that, in the context of the nanoparticle is even as big as this room, that x-ray is still going to go through and penetrate, no matter what.

Whether you have a big particle or a small particle, the x-ray is so much smaller than either of those that it makes no real difference to whether the particle is big or small.

Q. And the important point, then, in setting up the physical control was to match what to what in terms of the paclitaxel?

A. So the control was matched to Abraxane. So we had the same amount of paclitaxel in the control as we had in Abraxane.

For the control, we could see the crystalline peaks. And for Abraxane, we could not.

Q. Did you ever file a patent application with the x-ray powder diffraction data we just saw?

A. Yes. Soon after this data was obtained, we were already in the process of compiling a patent application,

which, in fact, contained all of the information from the previous year or year and a half.

And within, I think, a month after we got this final definitive data, we filed the application.

This was literally the last piece of the information that went into the patent application.

Q. So let's pull up DX-605. Is this the patent application that led to the 5,916,596 patent that you were referring to, sir?

A. Yes. This is the exact one that we filed soon after we got the x-ray diffraction data.

Q. If you go to Example 13, does Example 13 of this patent reflect the x-ray pattern diffraction data that you just showed the jury?

A. Yes. It's that very same data that we obtained by August 23rd of that year.

Q. Did you report to the Patent Office your conclusion about amorphousness?

A. Yes. We, in fact, up here in the introduction to that data, we said that it is advantageous that the formulation contain the drug in amorphous form, because of the issue of bioavailability, which we have talked about a lot, that it dissolves very quickly, like cotton candy.

In this paragraph, we actually presented the data, Sample 1, Sample 2, Sample 3, Sample 4. Those are the

four curves that you saw in that graph.

The conclusion here is that the presence of, in Sample 4, which is the formulated paclitaxel, showed no evidence of crystallinity which is characteristic of the standard raw material paclitaxel. And that was essentially the conclusion.

MR. JACOBS: Thank you. No further questions, Your Honor.

THE COURT: Thank you, Dr. Desai. You are excused.

THE WITNESS: Thank you.

(Witness excused.)

THE COURT: Ms. Kruze, who is your next witness.

MS. KRUZE: Dr. Mansoor Amiji.

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

DIRECT EXAMINATION

BY MS. KRUZE:

Q. Good afternoon, Dr. Amiji.

A. Good afternoon, Ms. Kruze.

Q. Could you please introduce yourself to the jury?

A. My name is Mansoor Amiji. I am a professor of pharmaceutical sciences at Northeastern University in Boston.

Q. Are you testifying here today as an expert witness?

A. Yes, I am.
Q. What is your area of expertise?
A. I am in the pharmaceutical sciences department. I am an expert in the area of drug delivery systems, specifically, looking at nanoparticulate drug delivery, as well as nanotechnology applications in medical problems.
Also, my research interest is in polymeric biomaterials.
Q. Could you please turn to Defendant's Exhibit 474 in your binder. Mr. Broyles, if you could bring that up on the screen as well.
Would you identify this document for the jury?
A. Yes. This is a copy of my curriculum vitae, referred to as CV.
Q. And where did you do your undergraduate work?
A. I did my undergraduate work at Northeastern University, the same institution that I am currently employed at.
Q. And could you tell the jury if you have any advanced degrees?
A. Yes. I do. I have a doctoral philosophy degree, a Ph.D. degree in pharmaceutics from Purdue University.
Q. What was the subject of your dissertation?
A. I worked on an area called surface modification of biomaterials, specifically in the area of hydrophobic or

materials that we have already heard in this trial. These are materials that do not like water.

So I looked at surface modification of these materials using what we call a stearic propulsion approach.

Q. Could you please tell the jury your current position?

A. I am currently the professor of pharmaceutical sciences. I am also the associate chair of the department. I also co-direct a program that we have at Northeastern, called the nano medicine consortium.

Q. What types of classes do you teach?

A. I teach both in the pharmacy program, this is the professional program, which we call sometimes the undergraduate program. I also teach in the graduate program, Master's and Ph.D. students.

In the undergraduate pharmacy program, I teach a course called Pharmaceutics 2. This course specifically deals with the application of physical and chemical principles in drug development.

For the graduate students, I teach a course called advanced drug delivery. I also teach in another program that we have, which is called the nanomedicine program. This program, I teach a course called introduction to nanomedicine.

We also have a course called nanosystems design.

Q. What is the focus of your research?

A. My research is focused on the application of nanotechnology for various diseases, both in the diagnosis, as well as in therapy. Most of our work is in therapy. We are looking at, specifically in cancer, but we also have interest in other diseases, such as cardiovascular disease and infectious disease.

Q. Have you written any books on drug delivery?

A. I have written several. I have written a book called Applied Physical Pharmacy, that I use in my teaching. I have also written a book called Polymeric Gene Delivery Systems. And I have written a book called Nanotechnology For Cancer Therapy.

Q. Mr. Broyles, could you bring up DD-112 on the screen.

Is this the book that you were just referring to?

A. Yes. This is the pride and joy of my work. It is actually, nanotechnology is an area, as we heard in this trial, that is receiving a lot of attention. This book was written specifically because of the interest that came from the National Cancer Institute of the National Institutes of Health. It is a 38-chapter treatise. I was involved in the editing of this book. We also have two chapters in there. It also has a forward from Peter Gryzinski (phonetic), who is a program manager at the National Cancer Institute.

Q. Let's turn back to DX-474. Have you also written any

articles on drug delivery?

A. I have written extensively. I have got about 80 peer-reviewed articles. And you have heard about peer-reviewed process in this trial. It's where you submit an article and someone who is a peer of yours in an academy or industry gets a chance to review or critique. I have also written a number of book chapters and various abstracts in conference proceedings.

Q. Are you a referee of any of those peer review boards?

A. Yes. There are various trade journals I am referee for. On a weekly basis, I get asked to review an article typically for various journals, including Pharmaceutical Research, Journal of Controlled Release, and various other distinguished journals that are scientific in nature.

Q. Can you tell the jury about any awards that you received?

A. Yes, I have. I have been very fortunate, again, to receive awards. In 2006, I received the Nanoscience and Technology Institute's Fellowship Award. This was in recognition of our work in the area of nanotechnology, micro technology, and biotechnology.

Last year, in 2007, I received the American Association of Pharmaceutical Scientists, this is the agency that many of us in the pharmaceutical sciences belong to, and it is the largest society of the pharmaceutical science,

I received the meritorious manuscript award from the AAPS. They recognized our manuscript from 2005 as having received the highest number of citations and they bestowed upon us this wonderful award.

In the same year, 2007, I became the AAPS fellows.

Q. Those ones haven't made it to your CV yet. Right?

A. Those did not get into the CV, correct.

Q. What about grants, have you received any grants?

A. Yes. Again, I am very fortunate to have received -- I am one of the few pharmacy faculty in the country to have multiple awards from the National Institutes of Health. I have currently three awards and three grants from the National Institutes of Health. Our first one is in the area of nanotechnology, specifically focusing on this problem, it's a huge problem, called drug resistance in cancer.

We are trying to address this by having enhanced delivery of drug to the tumor cite. Also asking the question, how widely these cancer cells become resistant to chemotherapy and what we can do about it.

The second grant that we have, again, it is a distinction to have this because only four are awarded throughout the country, is the training grant. This is a grant to actually fund students, doctoral students, who are going to receive a Ph.D. degree, so that they can be trained

in the area of nanomedicine.

We, at Northeastern, have received this grant from the National Cancer Institute and it is administered by the National Science Foundation. We have close to six or seven doctoral students a year, which is in their third year of this grant, so we have funded close 15 or 16 Ph.D. students.

Q. Let's turn to cross-linking. If we can bring up JX-81.

Dr. Amiji, do the claims of the '363 patent require that the surface modifier molecules in the nanoparticles be non-cross-linked?

A. Yes, it did. Here we can see clearly in the first claim of the '363, it says that the non-cross-linked surface modifier --

MR. SCHEVE: Your Honor, this term has been construed by Your Honor specifically. If he is saying that this is the construction, it clearly is not the Court's construction of the term.

THE COURT: Let me see counsel.

(The following took place at sidebar.)

THE COURT: What is your response?

MS. KRUZE: My very next slide is going to the patent talking about that. It is exactly what Your Honor says in the Court's claim construction.

THE COURT: For the jury's benefit, we should avoid questions that might confuse them as to this issue. As we know, this has been hotly contested. The other side disagrees with my construction. They are entitled to. We don't want this fact-finder confused.

MS. KRUZE: No problem. I will just refer to how the patent talks about it. Or have him read from the patent.

THE COURT: I have construed contested terms.

MR. SCHEVE: Free of intermolecular cross-linkages.

MS. KRUZE: The very next slide is exactly that.

THE COURT: That is fine. I think the objection is to this slide.

MS. KRUZE: We will move directly on then.

THE COURT: So do you want to withdraw that question? Do you want to rephrase that question?

MS. KRUZE: Let me rephrase.

THE COURT: Do you want to move into the next slide?

MS. KRUZE: Yes.

(End of sidebar conference.)

BY MS. KRUZE:

Q. If you could bring up DD-33, which is based on JX-81. Could you please read the highlighted term?

A. Yes. So here, again, in the patent itself, it says, essentially, free of intermolecular cross-linkages.
Q. Let's move to DD-70. When protein molecules exist in a non-cross-linked form, what do scientists call them?
A. Here we have heard this already, the terms in this trial, when you have single protein molecules, these are called monomers. When protein molecules associate and form two protein molecules associate, that is called a dimer. When you have three, that is a trimer. Many would be an oligomer. Even more would be polymers.
Q. Are dimers another word for cross-links?
A. Yes. Anything, once the proteins associate with each other, dimers, trimers, oligomers, and polymers would be considered cross-linked.
Q. Are there different types of cross-linking?
A. Yes. There are two types of cross-linking. There is a physical cross-linking and what's called chemical or covalent cross-linking.
Q. What is an example of physical cross-linking?
A. The best example I can give is the favorite of our children, the gelatin. We make gelatin, we take gelatin, put it in warm water. You take that, put it in a mold, put it in the refrigerator and it gels and forms this squiggly gel. That is a physical cross-link because you have changed the temperature and now the gel has solidified.

If you reverse that by heating that gel, it will become liquid again.

Q. You also mentioned chemical cross-linking.

What does that involve?

A. Chemical cross-linking involves formation of these bonds, what I would call covalent bonds.

Q. Does the '363 patent distinguish between those two different types of cross-linking?

A. No, it doesn't. The '363 patent was very clear in the fact that all types of cross-linking were included.

Q. Can you pull up DD-71, Mr. Broyles. This is a 1006 exhibit based on JX-81, JX-39 and DX-16.

What are these, Dr. Amiji?

A. Here are some of the comments from the patent file history, as well as the patent itself. Both the '363 patent and the '684 patent, and we have heard the '684 being referred to as the mother patent for the '363.

You look at different comments. Let's start with the first one on the top, where we see -- this pointer is probably blinking. I can't see from here.

The top one there is the '288 prior art. That's the Oppenheim prior art. It says, The particle comprised a cross-linked matrix of macro-molecules having the active material supported on or incorporated into the matrix.

Here, the '363 applicants were distinguishing

their invention from this prior art, the Oppenheim prior art, based on the fact that it was cross-linked and theirs was not cross-linked.

The second comment, looking at the '294 patent, that's the Motoyama patent, again, the applicant distinguished their invention, the '363 applicants distinguished their invention based on the fact that the Motoyama patent had this crystallized carbohydrate matrix and these carbohydrates were cross-linked. Here is a case where it was physically cross-linked.

MS. KRUZE: Permission to approach the witness, Your Honor?

THE COURT: Yes.

BY MS. KRUZE:

Q. Dr. Amiji, is the albumin coating on the surface of Abraxane particles non-cross-linked?

A. No. The albumin coating, as we just heard, is significantly cross-linked on the surface of the Abraxane nanoparticle.

Q. How do you know?

A. I have looked at a number of different documents from Abraxis, documents that I have reviewed, experiments that I have reviewed. And all the documents that I have seen show that the surface of the Abraxane nanoparticle, the albumin that is on the surface, is substantially cross-linked.

Q. Let's discuss some of those. Dr. Amiji, could you turn to DX-107 in your binder.

Mr. Broyles, could you bring that up on the screen?

What are these documents?

A. This first one is a document from Abraxis. It specifically deals with a test that is called size exclusion chromatography. It is a fancy way of saying sieving experiment. The only difference between this type of experiment and a standard sieve is a sieve separates from a particle and basically gets out smaller particles. In this case, the larger particles get out first.

What you see at the bottom in the table is the composition of the albumin that is present. Here we see the polymer, having approximately 38.9 percent of the composition, the oligomer having 3.8 percent of the composition, and the dimer having 11.3 percent of the composition.

If you add the three numbers, the total composition of the cross-linked albumin is going to be about 55 percent.

Q. Could you go back to the original screen.

When were these tests conducted?

A. These tests were conducted, it's in the upper part of the document, in January of 2003.

Q. Before this lawsuit?
A. Yes, they were conducted before this lawsuit.
Q. Let's bring up DD-104, which is based on DX-112.
What is this?
A. So here, again, we see the -- there are, in this table that you see in this slide, the monomer, dimer, oligomer, and polymer compositions from 17 different experiments that were done with different lots of Abraxane on different days, in certain cases, with triplicate or duplicate experiments.
All of them report the fact that there is a high degree of cross-linking in the albumin with an average at the bottom there showing about 55 percent of the surface-bound albumin on the nanoparticle being cross-linked.
Q. Did you investigate the nature of these bonds, Dr. Amiji?
A. Yes, I did.
Q. Let's turn to DX-76. Could you tell the jury what this is?
A. This is the lab notebook of an Abraxis investigator by the name of Voung Trieu. It's dated July 2007.
Q. If you could turn to Page 10 of the document, also Bates numbered 523594. Could you explain to the jury what sorts of tests are on this page?
A. This is an experiment that was done at Abraxis to

confirm the type of bond that's formed in these cross-linked albumins. What you see here is what we referred to in the protein chemistry art as polyacrylamide gel electrophoresis, abbreviation PAGE, P-A-G-E.

Basically, these gels are made from a polymer called polyacrylamide and proteins are then run in these gels to create various lanes.

So what you see are, in each of those, are the lanes of proteins, so 15, 17 and so forth. And the lane will have -- in this case, the lane is designated by this dye called coomassie blue or coomassie staining. That basically stains for the protein. It doesn't sustain the gel.

When these proteins are run, what you see in the non-reduced state, which is when the cross-linking still is in tact, is the fact that the protein has higher molecular weight. It's greater than the albumin control that you see down here.

All this on the top, the bands that you see on the top correspond to the higher molecular weight. Those are the cross-linked albumin.

When these same proteins are taken and run under reduced conditions, in this case, now, the disulfide bonds that form with these cross-links are intentionally broken with a chemical that breaks those bonds, and now we see that

the lane that these proteins migrate to is exactly the same as albumin.

So you are intentionally breaking the bond, using this disulfide bond breaking agent, and the reduced condition, to get the free albumin back.

So based on these results, it's clear that the bonds that are formed in these cross-linked albumin is by disulfide bonds.

Q. Is this a typical type of experiment to determine the presence of disulfide or covalent bonds?

A. Yes, it is. It is actually the standard test that's used to confirm disulfide bonding.

Q. Did you review the lab notebooks and other materials that were associated with these experiments?

A. Yes. So, again, as I looked into the lab notebook, at one part of the lab notebook, there was a standard operating procedure that was used, and I reviewed that standard operating procedure, and it's very characteristic of the experiments that I have done for these types of analyses.

Q. Were these experiments conducted well?

A. They are conducted extremely well. I was able to find all the information that I needed to make my interpretation and my analysis and my conclusions.

Q. Let's bring up DD-75, Mr. Broyles. This is from Defendant's Exhibit 107.

Have you reviewed any tests conducted by Elan or its experts regarding cross-linking?

A. No. I have not seen a single test done by Elan or its expert in regard to the cross-linking Abraxane.

Q. To the best of your knowledge, did any Elan expert conduct testing of cross-linking in Abraxane?

A. No. I have not seen a single test from an Elan expert on cross-linking in Abraxane.

Q. Were you here when Dr. Manning testified?

A. Yes, I was.

Q. Could you remind the jury who Dr. Manning was?

A. Dr. Manning was an expert from Elan's side. He testified on this area of cross-linking. I believe he was on the faculty at the University of Colorado. Currently, he has his own company. I believe it is called Legacy BioDesigns.

Q. Do you recall when Dr. Manning gave testimony regarding 15 to 20 percent cross-linking?

A. Yes, I do.

Q. What is the discrepancy between the number you were just talking about, 55 percent cross-linking, and the number he testified to, 20 percent?

A. So he was talking about the entire Abraxane formulation. As we just heard a few minutes back from Dr. Desai, Abraxane has this free albumin and there is also

albumin that is on the surface of the nanoparticle.

When you look at the entire composition of Abraxane, there is about 20 percent cross-linking. However, when you look at the surface of the nanoparticle itself, it's actually got about five percent cross-linking.

Q. And which one is the relevant number for this analysis?

A. So the relevant number for this analysis is what's on the surface, because that's really what's in the claim of the '363 patent, how much of the surface modifier is on the surface of the nanoparticle.

Q. Let's go to JX-81, Claim 1. What is the language here that shows you the relevant amount?

A. If we look at the fifth line -- starting from the fourth line, it says, Non-Cross-Linked surface modifier adsorbed on the surface thereof.

What this refers to, clearly, in the claim language, that this is the surface of the nanoparticle.

Q. And have you reviewed any documents where Dr. Manning agrees with your analysis that the free albumin can be different than the absorbed albumin, for example?

A. Yes, I have. Actually, in review of various documents, I came across a chapter that Dr. Manning wrote that when the nanoparticle, or when you have surfaces, there is higher concentration of the protein on the surfaces, and

Dr. Manning clearly identified that on surface of various hydrophobic surfaces, there is greater concentration, and, therefore, you do have this cross-linking phenomenon.

Q. Mr. Broyles, can we bring up DD-115 on the screen, and the source of this is PX-493.

Is this the article that you were referring to?

A. Yes. This is Manning article from 1992. It is more than a thousand times more concentrated protein in the surface than on the bulk phase. Bulk refers to basically the free albumin.

Because the albumin concentrates significantly on the surface, there is a higher probability of formation of this cross-linking, and that is really what we observed with Abraxane.

Q. Did Dr. Manning contest your opinion that 55 percent albumin is cross-linked in the nanoparticles?

A. No. I haven't seen a single comment or any opinions from Dr. Manning that contests that.

Q. Did Dr. Manning review any Elan tests when he was giving his testimony?

A. No, I don't believe Elan did any tests.

Q. Did you also hear his testimony that Abraxane behaves like a non-cross-linked particle?

A. Yes, I did.

Q. Did you agree with his opinion?

A. Again, as we just heard a few minutes back, when you put Abraxane in the body, it dissociates very fast. Once it dissociates, the fact that these nanoparticles, and the disulfide bonds is not because you are putting a chemical in, it's formed because of the fact that there is inherent formation of these linkages in proteins, and that dissociates in the presence of blood. There is no discrepancy between the fact that albumin and Abraxane is able to go into blood very quickly and this idea that the surface is cross-linked.

Q. Bring up DD-75 again. In summary, Dr. Amiji, what is your opinion regarding cross-linking of the albumin on the surface of the Abraxane particles?

MR. SCHEVE: Objection to the form of the question, Your Honor.

THE COURT: Repeat the question.

BY MS. KRUZE:

Q. In summary, what is your opinion regarding cross-linking on the albumin on the surface of the Abraxane nanoparticles?

THE COURT: Form, you object to why?

MR. SCHEVE: There is a certain standard that has to be announced by the witness before the opinion becomes evidence or admissible as opposed to submittable. There has not been an appropriate question asked.

THE COURT: Let's go to sidebar.

(The following took place at sidebar.)

THE COURT: I think Mr. Scheve is going with this you need to ask the witness, Do you have an opinion to a reasonable degree of scientific certainty.

MR. SCHEVE: That's part of what is missing.

THE COURT: Where else are you going, Mr. Scheve?

MR. SCHEVE: There is a series of two or three questions there that she has to ask and she hasn't done it. I am objecting for the record.

MS. KRUZE: I am sorry. This is my first time with an expert.

(End of sidebar conference.)

BY MS. KRUZE:

Q. Do you have an opinion, to a reasonable degree of scientific certainty, regarding non-cross-linking?

A. Yes, I do.

Q. What is your opinion regarding cross-linking of the albumin on the Abraxane nanoparticles?

A. I believe based on all the studies that I have analyzed and looked at and the conclusion that I draw that the surface of the Abraxane nanoparticle has substantial cross-linking of albumin.

Q. Let's turn to -- actually, one more question. Do you

have an opinion regarding the nature of those cross-links to a reasonable degree of scientific certainty?

A. Yes, I do. I believe that the nature of the cross-linking in the Abraxane nanoparticle surface is through that disulfide bond.

Q. Let's turn to crystallinity. Could you turn to DDX-15. Could you tell the jury what this is?

A. Again here, we are looking at different comments from the patent abstract, the patent itself, the '363 patent.

Here, the patent, itself, distinguishes, that it is for crystalline anticancer agent. And crystalline phase differs from the amorphous phase.

Q. This comes from JX-81, for the record.

Dr. Amiji, is an amorphous drug equivalent to a crystalline drug?

A. No, it is not. Amorphous drug is exactly the opposite of a crystalline drug.

Q. Can you bring up DD-84, Mr. Broyles.

What are some of the differences between a crystalline and amorphous drug?

A. Here, we have seen this before, when the molecules are packed in a crystal, you have this very nice order of packing of molecules; whereas, in amorphous, you don't have that nice packing that we observe in crystalline.

This occurs because of the fact this packing

order leads to --

MR. SCHEVE: Your Honor, I thought we were limited to one expert each per issue in the lawsuit. This is clearly testimony that's already been covered by a previous expert for Abraxis.

MS. KRUZE: Your Honor, he is going to be covering different issues, including the biology of these differences.

THE COURT: So, Mr. Scheve objects that this is a re-do of previous expert testimony.

MR. SCHEVE: This was used with Dr. Atwood. I only object because I am of the impression I am limited to one witness per topic.

THE COURT: You are.

MS. KRUZE: I will be happy to switch to the functional differences. This is more background.

THE COURT: We have enough background.

BY MS. KRUZE:

Q. Let's go to DD-76.

Do crystalline solids function differently than amorphous solids in pharmaceutical compositions?

A. Yes, they do. Crystalline solids dissolve a lot slower than amorphous solids. Amorphous solids dissolve a lot faster. I believe we have heard the analogy many times between cotton candy and rock candy.

Q. Let's go to DD-77. How do these differences in dissolution affect the performance of an anticancer drug?
A. When you have a crystalline drug, the fact that the crystalline drug would circulate in the bloodstream with, it would not resolve, it would still remain as a crystal. But in the case of an amorphous drug, like Abraxane, it dissolves very fast, and that dissolved drug is able to be carried by blood into the tumor. It is really the dissolved, the molecular form of the drug that gets into the cell. And that's the one that's therapeutically most effective.
Q. Are there any scientific treatises that agree with you about this difference between crystalline and amorphous drug in anticancer pharmaceutical compositions?
A. Yes. One of the classic scientific treatises that we use in pharmaceutical science is the Remington's. It is sort of considered to be the authority in the area of pharmaceutical science.

If you look at Remington's, there is clearly a passage that differentiates amorphous and crystalline drugs that says amorphous has higher solubility and also higher bioavailability.
Q. Could you pull up DD-78, Mr. Broyles.

This is based on DX-407.

Is this the article that you were referring to?

A. Yes. Here is a passage from Remington's, Amorphous versus Crystalline. Clearly, the crystalline state of hydration and polymorphic structure -- this is when you have different crystalline structures -- have been shown to have a significant influence on the dissolution rate. Investigators Mullin and Macek showed that this drug, novobiocin, has higher solubility, higher dissolution rate. The dissolution rate is basically a measure of how fast something dissolves than the crystalline form.

Additionally, the blood levels, this is an indicator of the bioavailability because now you are seeing how much drug is in the blood, is three to four times more in the amorphous form as compared to the crystalline form.

Q. At the bottom of the slide, that was also observed in four other compounds?

A. Yes. Here we can see that it's not a drug dependent -- it is not dependent on novobiocin. It's actually independent of the type of chemical. As long as you have these differences between crystallinity and amorphousness, it really doesn't matter which drug it is.

Q. Mr. Broyles, can you switch to DD-113. This is based on 627.

Are there any Elan experts that agree with your opinion?

A. Yes, here is one of the articles from Dr. Munson.

Dr. Munson was an expert from Elan. He also agrees that amorphous state has a higher dissolution rate, higher solubility than does the crystalline state.

Q. Let's switch to DD-79. Is there anything in the '363 patent that teaches that the inventors believed that their invention had prolonged circulation in the blood pool?

A. Yes. There are two places in the '363 patent that mentions this issue of prolonged circulation.

It is clear that crystalline drug will have prolonged circulation in the blood pool after IV or intravenous injection in the blood. Similarly here, we see prolonged circulation in the blood pool.

Q. Are these statements consistent with an amorphous drug like Abraxane?

A. No, they are not. A drug like Abraxane or amorphous drug like Abraxane would dissolve very quickly and it would then be available at the tumor site much more rapidly.

Q. Are you familiar with Dr. Danishefsky's testimony?

A. Yes, I am. I wasn't here physically for his testimony. But I read the transcript of the testimony.

Q. Could you remind the jury who Dr. Danishefsky is?

A. Dr. Danishefsky is a professor, I believe at Memorial Sloan Kettering Institute in New York.

Q. Did you hear Dr. Danishefsky disagree with anything that you said today on these differences?

A. No. I don't believe -- from the testimony that I read, I don't believe there was anything that he disagreed on.

Q. Are you aware of any statements made by Elan that confirm your understanding of these differences between crystallinity and amorphousness?

A. Yes. I have seen several of the reports in this trial, and in various parts by looking at all the evidence, that there has been comments about this.

Q. Mr. Broyles, can you bring up DD-80.

Dr. Amiji, can you explain to the jury what this is?

A. So here are some of those comments. We see the first one is that e-mail from -- excuse me, a memo from Glenn Portmann to Dr. Gary Liversidge. He clearly says, Amorphous state has been known to have enhanced bioavailability. This is the measure of how much drug that's going to be available at the disease site.

Distinct from particle size considerations, as you are well-aware, and then it says, Amorphous form usually possesses higher thermodynamic energy. This just means that they are in the unstable state than the crystalline counterparts resulting in solubilities and dissolution rates of much higher magnitude.

They also go on to say, in the '684 patent file

history, that amorphous forms are highly unstable. But this is true of only the drug itself, not when it's in the formulation, like Abraxane.

And then crystalline particles exhibit improved stability. In itself, this is a true statement. Amorphous materials tend to have exhibited unacceptable or poor stability and/or short shelf life.

Q. When the Elan scientists were making these statements, were they making them in the context of nano-sized drugs?

A. Yes. In the case of the '684 patent file history as well as the '363 file history, these are both dealing with nano-sized drugs.

Q. Do you have an opinion, to a reasonable degree of scientific certainty, as the equivalency between crystalline and amorphous drugs?

A. Yes, I do.

Q. Based on the list you have reviewed, are crystalline and amorphous drugs equivalent?

A. No, they are not. Amorphous drugs are exactly the opposite of crystalline.

Q. Would scientists in the field have considered Abraxane to have been interchangeable with the crystalline drug claimed in the '363 patent?

MR. SCHEVE: Objection. There is no foundation, Your Honor.

BY MS. KRUZE:

Q. Based on the evidence that you have reviewed, Dr. Amiji, would the amorphous drug in Abraxane be interchangeable with a crystalline drug?

A. No, it wouldn't be.

Q. Let's talk about drug surface modifier combinations.

Do you have any testimony, Dr. Amiji, relevant to whether the claims are enabled?

A. Yes, I do.

Q. Is this testimony also relevant to whether the claims are invalid?

A. Yes.

Q. Let's turn to DD-88. This is from JX-81.

What types of drugs do the '363 claims cover?

A. So the '363 patent, the Claim 1 of the '363 patent covers drugs that are anticancer and having solubility of less than ten milligrams per ml. And then specifically going into various classes such as alkylating agents, with these group of alkylating agents, drugs like vinca alkaloids. There are also antibiotics, like daunomycine and bleomycin, and then going into biological response modifiers. We talked about Taxol. There is also hormones, radiosensitizers, platinum compounds. Those are in Claim 1.

In Claim 5, it's limited to eight different drugs: Piposulfan, piposulfam, camptothecin, etoposide,

Taxol, these triazine derivatives and retinoic acids.
Q. How many drugs are in these claims, approximately?
A. For Claim 1, there is a large number of drugs, because these deals with classes of compounds, and not necessarily a single drug. For instance, an enzyme, there could be a large number of enzymes. Enzyme is a class. It is not a single drug. Biological response modifier, again, it's a class of drugs, it's not a single agent.

Radiosensitizers, again, it's a class of compounds.

And so you have hundreds of compounds in Claim 1.

In Claim 5, it is limited to eight compounds.
Q. Do all these drugs have the same structural and chemical characteristics?
A. No, they don't. So an enzyme, for instance, could be a protein; whereas, you know, platinum compound is something that has platinum in it. So these are very different from each other.
Q. Let's pull up DD-89, which is also from JX-81.

Turning to the surface modifier portion of the claim, what sort of surface modifiers does the patent cover?
A. The patent covers any non-cross-linked surface modifier. The list goes on. For instance, in this case, we see both the pages having this list of surface modifier.

Q. Let's pull up JX-81 at the end of Column 3 to 4. Starting at the last paragraph, then going all the way down until I think about Line 60.

How many surface modifiers, approximately, are called out by the patent?

A. Here we can see, in both of these columns, there is a large number of surface modifiers, just absolutely significantly large, because some of these are actually classes of surface modifiers. For instance, we are looking at anionic surfactant, and that would be a class of surface modifiers. And each of these classes would have a large number of individual surface modifiers.

If we focus on the second, on Column 4, from the top, again, we see classes of surface modifiers. For instance, fourth line from the top is a surface modifier called polyoxyethylene castor oil derivatives. That is the Cremophor that we heard of. Again, it is a class of surface modifier.

There is Tweens. Again, that's a class of surface modifier. Again, there is a large number of Tweens -- there is specific types of Tweens that are part of that class.

Q. And do all of these surface modifiers have the same chemical and structural characteristics?

A. No, they don't. They are very different. For

instance, again, looking at gelatin is a protein. Whereas stearic acid is just a fatty acid. Whereas tragacanth is a polysaccharide or made from various sugars. Cholesterol is, again, another type. If you go here, the synthetic materials, like Tween, and there are also natural surface modifiers. So they are very different from each other.

Q. Are there any surface modifiers in this list that surprise you in terms of a pharmaceutical formulation?

A. Yes.

MR. SCHEVE: Objection, Your Honor. The word "surprise" is without foundation.

THE COURT: Do you want to rephrase that?

MS. KRUZE: Certainly.

BY MS. KRUZE:

Q. Are there any surface modifiers that would be toxic to use in a pharmaceutical composition?

A. Yes. Looking at Column 4, at the top, we see polyoxyethylene castor oil derivatives. And I remember in this trial testimony here, we talked about the fact that Bristol Myers Squibb's Taxol product has this Cremophor inside. This is exactly the same. Polyoxyethylene is Cremophor. Seeing something like this is very surprising. Coming down the list is colloidal silicon dioxide. That is a fancy name for sand. I can't imagine anybody with cancer getting sand in their body.

Coming down the list, we see something called phosphates. Again, what type of phosphates? There are so many different types of phosphates. One wonders what kind of phosphate is claimed in the '363 patent.

Then, going down the list, in the area of what is called particularly preferred surfactant or surface modifier, you see this interesting chemical called Triton X, and Triton X is actually a product that's used in laboratories, we use this in our laboratory to break apart cells. So seeing that being put in a patent composition for anticancer drug was very surprising.

Q. Let's go to DD-92. You testified that the patent covers these crystalline drugs and any surface modifier.

How many sorts of combinations are we talking about here?

A. From Claim 1, we saw that there were a significant number of drugs. Claim 5 restricted to about eight drugs. Any of the surface modifier that we just talked about could be in any of these -- can be mixed with any anticancer drug.

Then you have this ratio of drug to surface modifier that is also in Claim 1, which is also in other claims of the '363 patent.

So there are millions and millions of possibilities. It's like looking at a product that -- or a food product that you do, you go to one grocery store to buy

one product and another grocery store to buy another product, and saying, you know, you can make a dish out of that. It is just impossible to really imagine how many possible combinations exist here.

Q. Looking and turning back to the patent, which is JX-81, would a scientist have known whether any given combination would work?

A. No, they would not know that.

Q. And does the patent specification tell a scientist which surface modifiers will work?

A. No, it doesn't.

Q. What kinds, if any, does the patent give a scientist?

A. There is, in the patent, what is called a simple screening test.

Q. Let's go to DD-103.

Is this the screening method you are referring to?

A. Yes. Here in the patent, there is this simple screening test, which says that you take this combination, which, you know, you basically choose from the drug itself, from the surface modifier, the list that was previously shown, and you take the two, and whatever ratio, you have to figure out yourself what the ratio is, and then you mill that or grind that for 120 hours. After it's been ground, you take that product and look at it under naked eye for 15

minutes for up to two days or with a microscope.
Q. From this procedure, how would you know which surface modifiers to try?
A. You wouldn't. You would have to basically do a trial and error.
Q. And is there any indication of which drugs to try?
A. No. Again, there is no indication of which drugs to try. It is basically any drug that is listed in the claims, as well as any surface modifier that's non-cross-linked and listed in the specification.
Q. You mentioned 120 hours. Is that to mill one combination?
A. Yes. So this would be for one combination would be milling for 120 hours, for more than five days.
Q. How long would it take someone to try out all the combinations that are covered by the '363 patent?
A. It's almost impossible to say, because you are looking at 120 hours for one, and there is so many possible combinations, it would be more than our lifetime.
Q. Claims 10 and 11, if we could go briefly there.
What do these cover?
A. Claim 10 covers the method of treating a mammal comprising of this product from Claim 1 in an effective amount of anticancer agent where the efficacy is increased.
And Claim 11 is where the same product is

administered to a mammal where the toxicity is reduced.
Q. Let's go back to DD-103.
Is there any way you can tell from this screening method whether something is going to be effective or non-toxic?
A. No, you can't. There is nothing in this screening method that will say anything related to the safety and efficacy of the final product.
Q. Stability to the naked eye, what sort of end point is that for a pharmaceutical product?
A. It's a very trivial end point, because when you are dealing with pharmaceutical products, you want to make sure they are stable for a long period of time. Up to 15 minutes to the naked eye, especially with nanoparticle formulation, these are very, very small particles, you can't see them with the naked eye or even with the microscope.
Q. To a scientist, does this screening method amount to extensive experimentation?
A. Yes, it does. Because you are basically grinding something for 120 hours and then you are looking at it for 15 minutes, and you are trying to see if it is actually going to be a product that is going to be used. I think it doesn't work that way.
Q. And have you reviewed documents where Elan, itself, has admitted that doing these combinations requires

extensive experimentation?

A. Yes, I have.

Q. Let's pull up DD-105.

Are these some of the comments that you were thinking of?

A. That's correct. So looking back from '92, not all surface stabilizers will function to stabilize all active agents.

December of '93, this document says, Few surfactants meet the criteria necessary for a successful drug formulation.

In '94, there is no surfactant of choice for parenteral or this drug that is administered into the bloodstream. In 2003, the choice of a surface stabilizer is not trivial and usually requires extensive experimentation.

Then again in 2007, the art of formulating drugs into nanoparticles is highly unpredictable.

Q. And the source of those quotes is DX-490, DX-327, DX-528 and DX-607.

Let's go to the next slide, which is DD-93, the source for that is DX-544.

Is this another Elan statement regarding the extensive experiments required?

A. Yes. Here is another patent from Elan, which is filed in 2003, and it says clearly in this patent that the choice

of surface stabilizer is non-trivial and requires extensive experimentation to realize a desirable formulation.

Q. The patent also talks about examples. Correct?

A. Yes, it does.

Q. And how many different drugs did the patent examples cover?

A. I believe there are about six different drugs in the patent examples.

Q. How many different surface modifiers are shown in the patent examples?

A. There are about 12 different surface modifiers shown in the examples.

Q. Given your earlier testimony about the breadth of the combinations that the claim covers, what sort of a percentage of the coverage is that of the examples?

A. It is a very small percentage. It is actually minuscule, compared to the possibilities. You see the list of surface modifiers, and in that list is a class of surface modifiers. You also see on the left side all the different anticancer drugs. So 20 is a very, very small percentage.

Q. Do these the examples contain any failures?

A. No, they do not.

Q. Dr. Amiji, did you review any Elan internal documents regarding Elan's efforts to make NanoCrystal formulations?

A. Yes, I did. I reviewed a large number of documents.

Q. Let's turn to Defendant's Exhibit 193.

Could you please explain to the jury what this document is?

A. So here is one of the documents that I reviewed. It's a presentation on a drug called piposulfan, which is an anticancer drug belonging to the class of the alkaloid. And it's dated August of '93.

Q. Could you turn to Bates No. 10921.

Would you confirm that this is a memo dated May 1992 to Pramod Sarptodar?

A. It is a memo to Pramod Sarptodar.

Q. Is Pramod Sarptodar an inventor of the '363 patent?

A. Yes, he is.

Q. Dr. Amiji, did you compare this document with the patent?

A. Yes, I did.

Q. Let's see if we can pull up the comparison.

Did this document supply some of the data that went into the '363 patent?

A. Yes, it did. Specifically, in Example 2 and 4, the use of this surfactant called Tween 80 and Span 80 came from this document.

Q. Did Elan disclose all of the information that came from this document?

A. No, it did not.

Q. Let's do an example. Say, for example, Tween 80, which is the top one, that is a surface modifier. Is that correct?
A. That's correct, yes. Tween 80 is a surface modifier.
Q. What is the size that Elan got with Tween 80?
A. With Tween 80, they got a size of 3,000 nanometer. That is three times the 1,000 nanometer limit from Claim 1 of the '363 patent.
Q. But Elan doesn't disclose that failed experiment to the Patent Office?
A. That's correct.
Q. Let's go back to the last page of the document, which is DX-193.
Could you please read the second line for the jury?
A. The second line in the conclusion section, it says, "Combination of Tween 20/Span 20 and Tween 40/Span 40 failed to reduce the average particle size below 400 nanometer."
Q. And did Elan disclose that information to the Patent Office?
A. No. I don't believe Elan disclosed that to the Patent Office.
Q. But these were the same tests that were under the examples for piposulfan listed in the patent?
A. That's correct, yes.

Q. Did you review any other documents regarding Elan's efforts to make a piposulfan, a NanoCrystal piposulfan?
A. Yes, I did review a lot of other documents.
Q. Let's go to DD-106?
THE COURT: Counsel, I think we are going to have to leave it there.
Ladies and gentlemen, we have come to the end of our day. Travel safely. We will see you back here at 9:00 a.m. tomorrow morning.
(Jury leaves courtroom at 4:02 p.m.)
THE COURT: Counsel, where are we with the jury instructions and the verdict form?
MR. SULLIVAN: Your Honor, if I may, we have prepared both examples with objections and law and also what we understood the Court's preference, also clean copies that really just present either undisputed or in some cases disputed instructions, very clean.
Also, each side has its own verdict form and we are prepared to pass these up, if we may.
THE COURT: You have not been able to merge your discussions with regard to the verdict form?
MR. SULLIVAN: We tried. It became pretty apparent last night that there was a divergence of at least a couple of points.
On the jury instructions, I will note for Your

Honor that there has been significant progress, up to and including last night. I hope the Court will be pleased to see a lot of undisputed instructions.

THE COURT: The Court is always pleased to see undisputed instructions.

The rest of counsel is excused. We are done for the day.

MR. WALTERS: Your Honor, we seem to be short one form of our verdict form, which we will send a messenger right over.

THE COURT: You can just give Ms. Walker what you have.

MR. WALTERS: Okay.

(Court recessed.)

(Reporter: Kevin Maurer)