

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25

IN THE UNITED STATES DISTRICT COURT

IN AND FOR THE DISTRICT OF DELAWARE

- - -

ELAN PHARMA INTERNATIONAL : Civil Action  
LIMITED, :

Plaintiff, :

v. :

ABRAXIS BIOSCIENCE INC., :

Defendant. :

No. 06-438-GMS

- - -

Wilmington, Delaware

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

1 APPEARANCES CONTINUED:

2 ELENA C. NORMAN, ESQ., and  
3 MICHELLE SHERETTA BUDICAK, ESQ.  
4 Young Conaway Stargatt & Taylor, LLP

5 -and-  
6 MICHAEL A. JACOBS, ESQ.,  
7 EMILY A. EVANS, ESQ.,  
8 ERIC S. WALTERS, ESQ.,  
9 DIANA KRUZE, ESQ., and  
10 ERIK J. OLSON, ESQ.  
11 Morrison & Foerster  
12 (San Francisco, CA)

13 Counsel for Defendant

14 - - - - -

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

17 (Counsel respond "Good morning.")

18 THE COURT: Mr. Jacobs.

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

23 We have seen a graphic displayed on the screen  
24 in which Mr. Scheve would display those privilege log  
25 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.

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

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

10           THE COURT: Okay. Mr. Scheve.

11           MR. SCHEVE: Thank you, Your Honor.

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

15           THE COURT: He took the day off. Huh?

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

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

20           MR. SCHEVE: Yes.

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

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

25           THE COURT: Yes.

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

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

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

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

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

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

1 regarding product composition.

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

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

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

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

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

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

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

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

11 MS. GLOVER: No. 1.

12 MR. JACOBS: No. 1.

13 THE COURT: By Abraxis?

14 MR. JACOBS: Correct.

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

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

25 THE COURT: Okay.

1 Mr. Jacobs.

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

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

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

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

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

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

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

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

12 THE COURT: Your memo is?

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

16 THE COURT: Go ahead.

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



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

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

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

7 THE COURT: Mr. Scheve, your reaction?

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

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

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

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

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

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

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

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

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

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

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

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

3 So...

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

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

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

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

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

18 THE COURT: And I expressed concern with that  
19 representation.

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

25 That was the predicate for then -- and at that

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

3 When Elan produced Dr. Brittain at his  
4 deposition, the night before we got this lengthy  
5 466-reference log, I took that deposition, I examined  
6 Dr. Brittain on what he had done for Elan in testing. The  
7 only question he was allowed to answer was that he had  
8 tested Abraxane.

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

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

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

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

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

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

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

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

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

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

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

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

21 THE COURT: Last word, Mr. Scheve.

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

25 Your Honor, the record needs to be clear. What

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

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

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

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



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

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

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

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

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

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

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

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

1 Dr. Soon-Shiong as a couple of their next witnesses.

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

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

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

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

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

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

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

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

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

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

1 THE COURT: Mr. Scheve?

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

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

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

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

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

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

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

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

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

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

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

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

25 So what they knew exactly in their head in 1996

1 versus what they have --

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

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

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

11 We will take a break.

12 (Recess taken.)

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

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

1 circumstances.

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

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

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

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

1 MR. SCHEVE: I have, Your Honor.

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

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

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

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

12 MR. JACOBS: Thank you.

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

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



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

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

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

11 All right. We are prepared to proceed with  
12 Abraxis.

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

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

17 THE COURT: You may proceed, Mr. Jacobs.

18 MR. JACOBS: Thank you, Your Honor.

19 DIRECT EXAMINATION

20 BY MR. JACOBS:

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

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

25 Q. Could we please bring up DX-96.

Desai - direct

1                   What is DX-96, Dr. Desai?

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

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

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

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

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

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

23          Q.     Your formal training was in chemical engineering.

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

Desai - direct

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

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

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

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

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

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

Desai - direct

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

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

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

14 Q. Are you an inventor on any patents?

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

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

22 A. That's correct.

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

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

Desai - direct

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

7 Q. How many total scientific publications do you have?

8 A. I have about 35 or so scientific publications.

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

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

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

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

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

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

Desai - direct

1 least 15 presentations at scientific meetings.

2 Q. Do you also organize symposia or conferences?

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

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

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

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

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

25 Q. Have you received any special recognition for your

Desai - direct

1 work in cancer nanomedicine?

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

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

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

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

17 So I was called to speak on those topics.

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

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

Desai - direct

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

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

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

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

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



Desai - direct

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

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

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

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

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

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

Desai - direct

1 blood and into the tumor in a very quick fashion.

2 Therefore, prevent toxicities, but maybe even help fight the  
3 tumor.

4 So that was, really, how it all began.

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

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

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

11 What does Abraxis place in a vial of Abraxane?

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

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

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

Desai - direct

1 Q. So, in sum, what is in the vial?

2 A. In the vial, there is about ten times as much albumin  
3 as there is the drug paclitaxel, so it's a ratio of roughly  
4 nine or ten to one. And the paclitaxel is in the form of  
5 these amorphous nanoparticles. And around the nanoparticles  
6 is a thin layer of the albumin, which is cross-linked.

7 Q. What is Abraxane approved for today?

8 A. Today it is approved for the treatment of breast  
9 cancer.

10 Q. What other areas are being explored?

11 A. The other types of cancers that have been tested for,  
12 and are in clinical trials this very moment, are in lung  
13 cancer, in melanoma, in ovarian cancer, people have interest  
14 in brain cancer, and, right now, we are getting some very  
15 exciting results in pancreatic cancer.

16 Q. Breast cancer was the first disease for which it was  
17 improved?

18 A. That's correct, yes.

19 Q. Why did you, at Abraxis, pursue breast cancer first?

20 A. Breast cancer, as you know, like all other cancers, is  
21 a terrible disease. It affects a large population of women.  
22 And we thought this might be a good place to test the drug,  
23 since there is a big need for new drugs in breast cancer.

24 The drug Taxol, which was approved in 1993, was  
25 a big advance in breast cancer, but it had lots of

Desai - direct

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

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

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

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

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

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

Desai - direct

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

11           You have to have it sufficiently smaller than  
12 200 nanometers, about 150, 130 nanometers, so you can pass  
13 the entire drug through, thereby sterilize it and have it  
14 safe. That is why the size is very important.

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

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

Desai - direct

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

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

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

13 The idea of having albumin as a cross-linked  
14 shell around it helps to stabilize that structure. And by  
15 "cross-linked," I mean it's like a mesh or a net so the  
16 individual albumin molecules are linked together to create  
17 this net or mesh that holds the structure together.

18 Those are the critical features, sort of, of  
19 Abraxane.

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

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

Desai - direct

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

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

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

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

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

Desai - direct

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

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

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

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

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

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



Desai - direct

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

3 Q. How long have you been working with paclitaxel?

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

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

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

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

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

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

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

Desai - direct

1 no foundation.

2 BY MR. JACOBS:

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

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

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

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

17 We have two components --

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

19 (The following took place at sidebar.)

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

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

Desai - direct

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

4 THE COURT: Did you hear what he said?

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

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

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

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

20 THE COURT: He doesn't object to that.

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

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

Desai - direct

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

3 MR. JACOBS: Exactly.

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

6 THE COURT: Both of you well understand.

7 (End of sidebar conference.)

8 BY MR. JACOBS:

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

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

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

25 So all of the crystalline character completely

Desai - direct

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

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

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

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

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

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

Desai - direct

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

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

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

8 A. Yes. We can see that here.

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

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

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

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

Desai - direct

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

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

6 That will be seen in a second.

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

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

Desai - direct

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

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

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

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

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



Desai - direct

1 the albumin.

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

4 A. Yes, I do.

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

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

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

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

17 A. Yes, I did.

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

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

Desai - direct

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

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

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

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

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

Desai - direct

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

8 That is what scale up is all about.

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

11 What is JX-31, Dr. Desai?

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

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

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

Desai - direct

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

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

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

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

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

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

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

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

Desai - direct

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

5 Q. You are an inventor on this patent?

6 A. Yes, I am an inventor.

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

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

11 A. VivoRx.

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

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

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

Desai - direct

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

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

4 What is JX-28, Dr. Desai?

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

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

18 A. In the time period when we filed the patent, we were  
19 thinking that the useful sizes of these particles could be  
20 in a range of about .1 micron to about five micron. Again,  
21 .1 micron is 100 nanometers, the same thing, all the way to  
22 five micron, which is 5,000 nanometers. That is the size  
23 range we were thinking of.

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

25 Was there anything else interesting about the

Desai - direct

1 face page here, Dr. Desai?

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

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

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

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

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

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

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

Desai - direct

1 short form for that, it is removed very slowly.

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

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

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

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

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

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

25 This is exactly what we were steering away from.



Desai - direct

1 Q. Let's go back to the previous page.

2 A. This was the second experiment in the series. So I  
3 have written here in my notebook, Redo the experiment and  
4 give no time for crystallization. So we wanted to do that  
5 evaporation very quickly to see if we can completely avoid  
6 formation of the crystals.

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

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

20 Q. We are looking at Page 78 and 80 of your notebook, 198  
21 and 200.

22 A. Yes, that's correct.

23 Q. Dr. Desai, let's go back to the timeline. Where are  
24 we now in the development of what became Abraxane as you  
25 were just describing to us?

Desai - direct

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

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

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

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

12 A. Well, at this time, you know, we had gotten what we  
13 thought was a good first step. So we had the amorphous  
14 particles. But there is, of course, you don't stop  
15 development. You have to find all kinds of different  
16 conditions. You try to still further keep optimizing the  
17 formulation. You do several different types of experiments  
18 to make sure you can reduce the particle size down to below  
19 200 nanometers. So there was a lot of work still ahead that  
20 eventually led to Abraxane.

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

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

Desai - direct

1 effect on the characteristics.

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

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

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

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

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

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

Desai - direct

1 milligrams per milliliter Taxol arrow human dose.

2 A. Yes.

3 Q. What are you describing there?

4 A. Here, I am already thinking about, now that we have  
5 got, you know, what we feel is, we are making headway in  
6 terms of this formulation.

7 So I am thinking ahead about what the possible  
8 human dose could be and how we could give this to humans.

9 I put in here that five milligrams per mil  
10 Taxol. What I am referring to is the concentration of the  
11 drug when we would ultimately go into humans, this is the  
12 concentration we would give the drug at, into the vein.

13 It turns out, if you look at the package insert,  
14 that is, the instructions for Abraxane today, that is  
15 exactly that. That is what we ended up giving the drug, at  
16 five milligrams per mil.

17 Q. Let's go to Page 243 of your lab notebook, JX-21,  
18 Dr. Desai. What are you representing here?

19 A. First I should apologize for all these complex  
20 notations here. I will try and simplify it the best I can.

21 Here we are looking at yet another parameter.  
22 There is many things we have to test to get to the right  
23 place with this formulation.

24 So this is in April of 1995, where we are  
25 testing the effect of the amount of albumin. We talked

Desai - direct

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

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

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

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

Desai - direct

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

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

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

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

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

19 (The following took place at sidebar.)

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

22 MR. JACOBS: Let's take a break.

23 (End of sidebar conference.)

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

Desai - direct

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

2 (Recess taken.)

3 THE COURT: All right. Ms. Walker.

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

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

7 BY MR. JACOBS:

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

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

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

12 Q. And in September of 1995, you -- in the summer of  
13 1995, you started sending some samples out?

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

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

25 We sent samples, subsequent to this, we sent

Desai - direct

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

3 Q. Let's take a look at JX-41. JX-41, dated September  
4 25th, 1995, from VivoRx to Bristol Myers Squibb.

5 What does this letter represent?

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

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

17 What are you showing on this, Dr. Desai?

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

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



Desai - direct

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

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

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

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

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

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

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

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

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

Desai - direct

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

2 What is JX-7, Dr. Desai?

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

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

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

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

12 Q. Let's take a look at 462.

13 What is his notebook reflecting here, Dr. Desai?

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

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

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

Desai - direct

1 nanometers. There were several experiments here that show  
2 130 nanometers, 150, 140. So what we are trying to show you  
3 is that, at that time, we had achieved, more or less, our  
4 target of being at about 150 nanometers or below.

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

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

10 Q. What is the date of this work?

11 A. This is dated July 19th, 1996.

12 Q. You confirmed that?

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

15 Q. Let's take a look, again, at your notebook, JX-21, at  
16 296.

17 What are you describing here, Dr. Desai?

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

Desai - direct

1 Q. You dated this to July 22, 1996?

2 A. That's correct (did he say 22? )

3 Q. Let's take a look at 298, July 15th, 1996.

4 What are you showing here?

5 A. Here I am showing several notations I put down in my  
6 notebook. This indicates we are ready for scale up. That  
7 is, as I mentioned, going from the small laboratory scale to  
8 the larger scale that was more important for actual use in  
9 clinical trials. I make that notation there that we have to  
10 scale up from the small volume, 100 cc, 100 milliliters.

11 I am talking about a preparation of a package  
12 for the FDA. And that I am giving about a month for myself  
13 to prepare the package, that it should be ready in about a  
14 month, and that I need to call the FDA to set up what's  
15 known as a pre-IND meeting. That is, "IND" stands for  
16 investigational new drug.

17 When you first approach the FDA that you are  
18 ready to do testing in the clinical setting, that is in  
19 human patients, you need to compile a big package for the  
20 FDA with all the information.

21 So I wanted to set up that meeting. That's what  
22 this refers to.

23 Q. Let's go to Page 329 of JX-21. August 27, 1996.

24 What are you describing here?

25 A. This is some results of those scale up experiments

Desai - direct

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

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

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

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

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

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

19 What were you describing here, Dr. Desai?

20 A. In this notebook page, which is dated August 26 of  
21 1996, after we had made the formulation of what we believed  
22 were amorphous nanoparticles, we wanted to confirm that by a  
23 technique that's known as x-ray powder diffraction. And  
24 this is a technique that is used all over the pharmaceutical  
25 industry, it's a standard technique that's used to determine

Desai - direct

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

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

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

9 I will just explain to you briefly what this  
10 means.

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

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

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

25 There is a complete lack of sharp peaks,

Desai - direct

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

4 So the conclusion of this experiment is that the  
5 paclitaxel in our preparation is amorphous and we were able  
6 to confirm it with a standard technique by August 26th of  
7 1996.

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

9 A. That's correct.

10 Q. How did that happen?

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

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

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

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

Desai - direct

1 Dr. Desai?

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

5 Q. This is from your files?

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

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

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

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

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

18 So there was an exchange of information.

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

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

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



Desai - direct

1 Q. What is the date on the slide, sir?

2 A. The date on the slide is, it's August 28 of 1996.

3 Q. Did you study these slides and develop an  
4 understanding of what Elan was seeking to convey by them?

5 A. Yes, definitely. We looked at these slides carefully,  
6 and I formed an impression of what their technology was all  
7 about, as indicated in these materials.

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

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

13 BY MR. JACOBS:

14 Q. What was the impression that you formed, while we are  
15 bringing that up, Dr. Desai?

16 A. As indicated in this slide here, if you can blow that  
17 up, so they talk about parenteral NanoCrystal applications.  
18 Clearly, this technology was focused on crystals in the nano  
19 form, so small crystals. The key features were outlined in  
20 this slide, A, B, C, D.

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

Desai - direct

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

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

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

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

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

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

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

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

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

Desai - direct

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

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

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

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

14 What was this, Dr. Desai?

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

25 So we had indicated to them that we are working

Desai - direct

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

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

6 Did you make a note on this patent?

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

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

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

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

Desai - direct

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

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

12 Q. Let's go to JX-20 at 656. This is a page from the  
13 '363 patent.

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

16 A. Yes, I do.

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

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

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

Desai - direct

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

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

7 Q. Patrick is Dr. Soon-Shiong?

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

10 Q. When did you hire Raj Selvaraj?

11 A. Raj Selvaraj we hired more than, I think it was three  
12 years -- this is in 1996, so this is three years later, in  
13 1999, I think it was May 1999.

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

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

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

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

25 It was interesting to note this coincidence,

Desai - direct

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

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

6 When did you file your IND?

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

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

15 A. That's correct.

16 Q. When did you file that?

17 A. So the New Drug Application is the final application.  
18 After you have finished all your clinical testing and you  
19 are ready for commercialization, you file a huge packet of  
20 information. That's called a New Drug Application. So it  
21 comes several years after the IND application. That  
22 application was filed, NDA application, was in, I believe in  
23 2004.

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

25 What is JX-64, Dr. Desai?

Desai - direct

1 A. This is the cover page of an application for the new  
2 drug Abraxane that we had filed with the FDA.

3 Q. Could you give the jury a sense of what one of these  
4 things looks like if you were to assemble it in a single  
5 place, one of these NDAs?

6 A. Well, it represents a huge amount of testing that is  
7 done, because to get a new drug out into the market, you  
8 need to do all of the clinical testing, you need to do all  
9 of the toxicity testing in animals, you need to show your  
10 manufacturing processes in every detail so the FDA can look  
11 at this and analyze it. It would probably fill the whole  
12 side of this courtroom if you were to put it all together.

13 Q. Let's take a look at 117473 of JX-6.

14 What is this, Dr. Desai?

15 A. This is one small part of that huge package of  
16 information. And this is a report that did several  
17 characterization studies on Abraxane. This is the Table of  
18 Contents. So it lists here things like x-ray diffraction,  
19 differential scanning calorimetry, electron microscopy, et  
20 cetera, all the different techniques that we used to analyze  
21 Abraxane to understand its physical form and its chemical  
22 features.

23 Q. Some of these -- actually, I should step back.

24 Did you participate in the preparation of this  
25 application?



Desai - direct

1 A. Yes, I did, actually.

2 Q. How heavily were you involved?

3 A. I was very heavily involved right from the beginning.

4 Q. Have you had personal experience with the techniques  
5 listed under physical analysis, or some of them?

6 A. Yes. I have had personal experience with some of  
7 them. I have, myself, done electron microscopy as part of  
8 my graduate career and myself done differential scanning  
9 calorimetry as part of my graduate career and have published  
10 on these techniques. And I, myself, have done not x-ray  
11 diffraction but a very similar technique that's called x-ray  
12 photo electron spectroscopy, which, in that sense, uses the  
13 same principles of using x-rays to analyze samples, and I  
14 published on those techniques as well.

15 Q. Let's go to 483 of 484 of your NDA.

16 What do these pages represent, Dr. Desai?

17 A. This is part of that characterization report that  
18 focuses on the x-ray diffraction testing, which, as I  
19 mentioned, is the standard method of testing or to analyze  
20 if the material is crystalline or not.

21 Q. What are you describing here? What are you  
22 representing by this information?

23 A. Well, it says here that there were different lots of  
24 material. We talk about stability lots and there are  
25 numbers here. Each one of these numbers represents a

Desai - direct

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

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

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

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

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

Desai - direct

1 remain amorphous and that was the conclusion of this  
2 testing.

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

4 What is this, what are these pages showing?

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

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

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

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

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

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

Desai - direct

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

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

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

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

13 Q. What have the results shown in each case?

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

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

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

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

Desai - direct

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

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

4 What did the report conclude?

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

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

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

19 Q. Do you regard this as an achievement?

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

Desai - direct

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

6 So I think that's quite an achievement.

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

9 A. No, we did not do that.

10 Q. Why not?

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

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

25 For testing of that kind, where you want to know

Desai - direct

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

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

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

11 Q. What do you mean by an artifactual result?

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

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

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

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

Desai - direct

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

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

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

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

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

21 We never did that for this type of testing.

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

24 What is shown here?

25 A. There is two types of electron microscopy studies done



Desai - direct

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

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

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

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

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

Desai - direct

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

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

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

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

16 A. No, not at all.

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

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

21 THE COURT: See counsel.

22 (The following took place at sidebar.)

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

25 MR. JACOBS: Because he drew a conclusion based

Desai - direct

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

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

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

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

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

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

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

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

Desai - direct

1 if he rephrases there.

2 MR. SCHEVE: It needs to be rephrased.

3 (End of sidebar conference.)

4 THE COURT: If you could rephrase.

5 BY MR. JACOBS:

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

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

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

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

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

Desai - direct

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

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

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

7 THE COURT: All right.

8 BY MR. JACOBS:

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

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

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

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

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

Desai - direct

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

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

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

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

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

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

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

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

Desai - direct

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

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

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

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

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

21 THE COURT: Rephrase the question, please.

22 BY MR. JACOBS:

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

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

Desai - direct

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

4 Q. Let's take a look at 397, 705 to 706. That is PX-397,  
5 705 to 706.

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

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

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

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

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

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

25 So in these notebooks, this is one of those



Desai - direct

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

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

9 A. Sure.

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

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

20 THE COURT: Doctor, this is Abraxis testing?

21 THE WITNESS: Yes.

22 THE COURT: I think you said Elan.

23 MR. JACOBS: That Elan showed to the jury.

24 THE COURT: I misunderstood. Sorry.

25 THE WITNESS: Yes, this is in our notebooks.

Desai - direct

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

4 BY MR. JACOBS:

5 Q. This is the lot that you did what?

6 A. We rejected this lot.

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

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

11 Q. It's PX-400, is what is represented there. It's from  
12 1996. Needle-like crystals. Leslie Louie?

13 A. Maybe we can just blow it up.

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

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

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

Desai - direct

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

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

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

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

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

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

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

24 Can you explain what is going on in this  
25 exchange?

Desai - direct

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

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

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

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

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

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

Desai - direct

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

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

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

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

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

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

17 (The following took place at sidebar.)

18 (Question read as follows:

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

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

Desai - direct

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

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

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

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

12 (End of sidebar.)

13 THE COURT: I am going sustain that objection.

14 BY MR. JACOBS:

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

16 What is DX-112?

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

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

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

Desai - direct

1           Could you jump to what you understood this,  
2           these test results to be demonstrating to you at Abraxis?

3           A.     Yes. So we measured in this test the percentage of  
4           cross-linking, that is the percentage of where you have two  
5           or multiple or several albumin molecules linked together.

6                     What we found in our testing, that there was at  
7           least 55 percent of the albumin that's on the surface of the  
8           particles that are cross-linked to each other in this  
9           technique.

10          Q.     Did Abraxis do any experiments to investigate the  
11          nature of the cross-linking between albumin molecules on the  
12          surface of Abraxane?

13          A.     Yes, we did.

14          Q.     What this showed to you precisely was what, Dr. Desai,  
15          when you did it?

16          A.     This helped us just quantify, give an idea of what  
17          percentage of all of albumin that is on the surface of the  
18          particle was cross-linked, and the determination that was  
19          made from this study was that 55 percent on average, through  
20          multiple, multiple batches, of that albumin on the surface  
21          is cross-linked.

22          Q.     Now let's go to DX-76, and DX-76 is Young Trieu's  
23          notebook. It has an initial date of July 2, 2007.

24                     Let's go to 586.

25                     In a nutshell, Dr. Desai, why did you do this

Desai - direct

1 experiment and what did you conclude from it?

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

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

10 And I will try and describe very briefly.

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

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

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

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



Desai - direct

1 albumin.

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

6 Q. DX-70 at 17002, please.

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

10 October 10, 2006, did you give a presentation?

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

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

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

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

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

Desai - direct

1 Did you give that statement?

2 A. Yes, I did.

3 Q. What did you mean by that statement?

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

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

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

17 BY MR. JACOBS:

18 Q. So if you --

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

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

25 MR. JACOBS: If I misspoke, I sincerely

Desai - direct

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

2 BY MR. JACOBS:

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

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

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

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

14 Q. You were there?

15 A. I was present.

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

19 Do you see that?

20 A. Yes, I do.

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

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

Desai - direct

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

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

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

12 Q. Let's look at JX-11.

13 What is JX-11, Dr. Desai?

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

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

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

Desai - direct

1 mediator transport, which is another feature of albumin.

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

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

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

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

25 What I mean by that, I am referring here to

Desai - direct

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

7 So that's what I was referring to.

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

11 A. In my view, it is amorphous.

12 Q. And do you believe that is important?

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

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

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

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

Desai - direct

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

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

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

7 BY MR. JACOBS:

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

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

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

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

25 Q. Did the Nano Systems or Elan NanoCrystal work

Desai - direct

1 contribute anything to your development of Abraxane?

2 A. No. It did not contribute anything. In fact, it was  
3 clear that the pathways were completely different. I give  
4 them credit for developing the oral drugs that they did with  
5 their technology in the NanoCrystal form. Clearly, ours was  
6 a different approach.

7 Q. Did the Elan '363 patent, when you read it over in  
8 1996, or whenever, contribute anything to the development of  
9 Abraxane?

10 A. No, it did not. It just showed that the approaches  
11 were quite different.

12 Q. In view of the understanding that you had developed  
13 over time about the path that Elan was on as compared with  
14 the path that Abraxis was on, what was your reaction when  
15 you were sued for patent infringement?

16 MR. SCHEVE: Objection, Your Honor.

17 THE COURT: Sustained. I think I know what you  
18 want to do, but you can't. Rephrase.

19 BY MR. JACOBS:

20 Q. When you were sued for patent infringement, what did  
21 you reflect back on in terms of your understanding of the  
22 Elan technology and what you had come to know about it?

23 A. Well, first of all, I was shocked to hear about a  
24 lawsuit, given that I had seen Elan's presentations at  
25 public meetings, given that I was familiar, to an extent,



Desai - direct

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

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

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

11 MR. SCHEVE: Objection, Your Honor.

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

14 Go ahead.

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

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

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

Desai - direct

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

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

8 MR. JACOBS: Thank you, Dr. Desai.

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

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

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

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

15 (Recess taken.)

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

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

23 THE COURT: All right. We will see.

24 (Jury enters courtroom at 12:05.)

25 THE COURT: Please take your seats.

Desai - cross

1 Mr. Scheve, you may cross-examine.

2 MR. SCHEVE: Thank you.

3 CROSS-EXAMINATION

4 BY MR. SCHEVE:

5 Q. Slide 67.

6 Excuse me.

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

9 (Pause.)

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

12 BY MR. SCHEVE:

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

15 Thank you for being patient with me.

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

18 A. Yes.

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

21 A. Yes, I am.

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

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

Desai - cross

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

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

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

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

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

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

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

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

24 Do you have that notebook in front of you?

25 A. Which exhibit?

Desai - cross

1 Q. Plaintiff's Exhibit 211.

2 Did you find it, sir?

3 A. Yes.

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

5 A. Yes.

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

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

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

15 Is it listed in the Orange Book as covering  
16 Abraxane?

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

19 Q. Are you familiar with this patent?

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

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

25 A. Did you say 030?

Desai - cross

1 Q. Yes, sir. Do you see the face page there?

2 A. Yes. I see it.

3 Q. Is it applicable to Abraxane?

4 A. It is applicable to Abraxane. I am not sure if this  
5 was specifically an Orange Book listed patent.

6 Q. Is it applicable to Abraxane?

7 A. Yes, it is.

8 Q. If we go to Column 6, does this patent -- this  
9 Abraxane or Abraxis patent says, quote, "While it's  
10 recognized that particles produced according to the  
11 invention can either be crystalline, amorphous, or a mixture  
12 thereof, it is generally preferred that the drug be present  
13 in the formulation in an amorphous form"?

14 A. Yes, that is what it says there. Again, what we were  
15 referring to is that if you increase the loading beyond a  
16 certain point, you cannot do that to maintain amorphousness.  
17 In Abraxane, it's below that limit. We keep it so that we  
18 maintain amorphousness.

19 Q. Just so I understand your direct testimony, sir, did  
20 you go through any formal formulation sciences curriculum  
21 when you were in school?

22 A. I did chemical engineering, which teaches all the  
23 basics of the principles that go into formulation science,  
24 which include basic chemistry of drugs and different  
25 molecules, polymers, et cetera. So I feel I have a

Desai - cross

1 background strong enough to work in formulation science.

2 Q. Didn't you testify in your deposition, sir, in this  
3 case that you have no formal training and no degree in  
4 formulation science?

5 A. That's true. My degree is in chemical engineering.

6 Q. Is that still the same today?

7 A. Yes, it is.

8 Q. Now, you graduated from the University of Texas in  
9 what year?

10 A. That was in 1991.

11 Q. Is the first time you ever had anything to do with  
12 trying to formulate paclitaxel was 1992?

13 A. Yes. I think late '91 to early 1992.

14 Q. Is it true, sir, that you and Dr. Patrick Soon-Shiong  
15 went to a conference in September of 1992 sponsored by the  
16 National Cancer Institute?

17 A. Yes, we did.

18 Q. Is that the first time that you and Dr. Soon-Shiong  
19 decided you were going to try and develop a formulation of  
20 paclitaxel?

21 A. No. It was well after. We had already started  
22 working on paclitaxel early in 1992. If I remember right,  
23 the conference was in September of 1992.

24 Q. So approximately when in '92 were you hired?

25 A. I was hired in 1991, in April.

Desai - cross

1 Q. When, then -- I misspoke. I apologize. When in early  
2 '92 did you begin working on paclitaxel?

3 A. I don't remember the exact date. But it was early  
4 1992.

5 Q. How many years had the scientific and pharmaceutical  
6 industry been trying to find some way to formulate  
7 paclitaxel that didn't incorporate solvents?

8 A. Well, there has been a couple of other companies that  
9 have tried and failed. I don't know how many years they  
10 worked on it.

11 Q. Did Dr. Soon-Shiong have a degree in formulation  
12 science?

13 A. No. He is a surgeon, an M.D.

14 Q. He had been an assistant professor of surgery at UCLA.  
15 Correct?

16 A. That's correct.

17 Q. So the two of you, were you the only two people  
18 working internally to develop a formulation of paclitaxel  
19 beginning in early 1992?

20 A. Well, there was other scientists on the team. It was  
21 a small group. But, certainly, there were other scientists  
22 present.

23 Q. Well, sir, during your deposition, didn't you tell me  
24 that the company had a total of five to ten people and that  
25 you and Dr. Soon-Shiong were the only two that were working



Desai - cross

1 in the beginning to develop a formulation of paclitaxel?

2 A. I don't think I said that. But there were other  
3 scientists, and, in fact, they are even listed as inventors  
4 on the patent. All of us worked on the idea of paclitaxel.

5 Q. So you started in early '92. How soon thereafter did  
6 you come up with a formulation?

7 A. Well, we filed the first patent in early '93. So  
8 within a year of our work. So within a year, we had  
9 something that was good enough to file as a patent.

10 Q. So you were able to do within a year something that  
11 nobody else in the pharmaceutical industry or any other  
12 inventor had been able to do. Is that correct?

13 A. Well, let me just expound on that. The development of  
14 Abraxane didn't occur in a year. We found some key features  
15 that were patentable that we found in the early periods.  
16 But it was a long, arduous, several years before we came to  
17 a, what we recognized what we recognize as Abraxane today.  
18 It wasn't overnight.

19 Q. Let's begin to look and piece this story together.

20 If you could get me the Slide No. 3, please.

21 I will put my glasses on.

22 Sir, do you recognize this patent '686? You  
23 mentioned you came up with a formulation and you issued a  
24 patent. Is this this patent here sir, that was filed in  
25 February 1993 called the '686 patent?

Desai - cross

1 A. Yes, this was our first patent.

2 Q. In terms of trying to figure what it is, the  
3 formulation, that you had created, if we read that patent,  
4 isn't it true, sir, that what you described there was a  
5 procedure for preparing chemically cross-linked microspheres  
6 that involved glutaraldehyde. Correct, sir?

7 A. No, that is incorrect. You are mischaracterizing what  
8 we had in the patent. That was referring to what other  
9 people do. They add in the chemicals and things that, in  
10 fact, I testified in front of the FDA, and that's what this  
11 is referring to, that they used chemicals like  
12 glutaraldehyde to chemically cross-link the microsphere.  
13 This was not our work. We were differentiating what other  
14 people do from what we do.

15 Q. Sir, it says, In accordance with the present  
16 invention, the polymer, for example, a protein, is  
17 selectively chemically cross-linked.

18 Isn't that what your patent said in 1993?

19 A. Yes. Again, but what that refers to is the  
20 cross-linking of the protein itself through the disulfide  
21 bonds. I specifically mentioned there disulfide bonds.  
22 This is not by adding any extraneous agent.

23 Q. So your position was, in your first patent, that there  
24 was an actual chemical cross-linking. Correct?

25 A. Of course, it's chemical. It's disulfide that is a

Desai - cross

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

6 Q. Is that a yes, sir?

7 A. I don't remember your question now.

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

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

17 So do the best you can.

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

22 BY MR. SCHEVE:

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

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

Desai - cross

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

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

10 Did I read that correctly?

11 A. Yes, you read that correctly.

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

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

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

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

Desai - cross

1 five microns at the top end is even more preferred.

2 Q. So the only patent you had through 1993, you couldn't  
3 get below five microns, at least as described here, correct,  
4 according to this embodiment of the present invention?

5 A. No, that's not correct. Somewhere else in the patent,  
6 there is a range of .1 to 5 microns. I would ask you to  
7 refer to that.

8 Q. Well, sir, does this language say --

9 A. This is in reference to the upper limit of ten  
10 microns, yes. So the upper limit, what this says is that  
11 the upper limit is ten microns. And a more preferred upper  
12 limit would be five microns.

13 Q. All right. Now, did you, in this patent, describe  
14 anything below a thousand nanometers?

15 A. Can I look at the patent, please?

16 Q. Sure.

17 A. Which exhibit would that be?

18 Q. It's Plaintiff's Exhibit 212.

19 A. Okay. I would refer you to Example 9, Column 15 in  
20 the patent.

21 Q. Is it in the claims, sir, in terms of what you claim?  
22 Is there anything in the claims of your patent that claim  
23 something below a thousand nanometers?

24 A. Sir, I thought your question to me was: Was there  
25 anything in the patent that showed a size below a thousand

Desai - cross

1 nanometers?

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

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

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

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

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

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

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

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

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

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

Desai - cross

1 A. Again, I point you to Example 9.

2 Q. Well, I see the patent, sir. Let's go to the claims  
3 of this patent. Where in the claims --

4 MR. JACOBS: Your Honor, objection.

5 MR. SCHEVE: I will rephrase it.

6 THE COURT: You are withdrawing the question?

7 MR. SCHEVE: I withdraw the question.

8 MR. JACOBS: Sidebar, Your Honor.

9 (The following took place at sidebar.)

10 MR. JACOBS: This is very thick stuff, this  
11 patent stuff. If Mr. Scheve wants to burn his time, I guess  
12 I should say, Fine, let him go. If he means in the claims,  
13 he should say the claims. If he means in the specification,  
14 he should say the specification. The witness ought to be  
15 given time to study the patent. It requires that you look  
16 at something very carefully.

17 MR. SCHEVE: I will be more precise.

18 THE COURT: It is just the nature of the subject  
19 matter.

20 MR. SCHEVE: That is the first time I am forcing  
21 myself into a satellite. That's what I will do.

22 (End of sidebar conference.)

23 BY MR. SCHEVE:

24 Q. Now, where, sir, in that patent, in the claims, do you  
25 see solvent precipitation? I am talking about the '686,

Desai - cross

1 which is referred to as Plaintiff's Exhibit 212.

2 A. In the claims, we don't talk about the process. The  
3 claims just cover the final composition.

4 Q. Let's move to the next patent, the '421 patent, sir.  
5 It's Exhibit 213. A copy of it is here.

6 Is the '421 a patent that's listed in the Orange  
7 Book and certified by Abraxis to cover Abraxane?

8 A. Yes, I believe it is.

9 Q. Now, this time I do want to go look at one of the  
10 examples. Do you make reference, sir, in Example 46, in  
11 Column 53, of using a ball mill to grind down crystalline  
12 particles?

13 A. You say Example 46?

14 Q. 46, on Column 53.

15 A. Yes, I do.

16 Q. Did you disclose to the Patent and Trademark Office in  
17 this patent anything about contamination using a ball mill  
18 to grind down crystalline particles?

19 A. No. These were just approaches we were taking in the  
20 early days to see how we could get small particles. We had  
21 the approach that we already talked about of the solvent and  
22 removal of solvent to create the particles.

23 There was other approaches we were  
24 investigating, like sizing the particles down, maybe ball  
25 mill or sonication and other techniques. This was all



Desai - cross

1 disclosed in the patent.

2 Q. And this example of using a ball mill to grind down  
3 crystalline particles, was that disclosed to the Patent and  
4 Trademark Office?

5 A. Yes, it's right in Example 46.

6 Q. Did you raise with the Patent and Trademark Office any  
7 potential problems that you or others at Abraxis saw with  
8 contamination using that method?

9 MR. JACOBS: Objection?

10 THE WITNESS: No, we --

11 THE COURT: Sustained.

12 BY MR. SCHEVE:

13 Q. Did Abraxis disclose to the Patent and Trademark  
14 Office anything about contamination?

15 THE COURT: Perhaps I can help. Sidebar.

16 (The following took place at sidebar.)

17 MR. JACOBS: Our patents are not on trial here.  
18 It is the Elan patents for which inequitable conduct is at  
19 issue, Your Honor.

20 MR. SCHEVE: Well, but they are contending that  
21 our patents are invalid because they failed to disclose.

22 THE COURT: But you don't -- we are not going to  
23 do a tit for tat in that regard. He is correct. His  
24 patents are not on trial. It's Elan's patents.

25 MR. SCHEVE: It goes to, directly to credibility

Desai - cross

1 of them criticizing --

2 THE COURT: I disagree. The objection is  
3 sustained.

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

8 (End of sidebar conference.)

9 BY MR. SCHEVE:

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

12 A. As far as I remember, there was the very first patent,  
13 the '686 patent, which we already talked about. And there  
14 was this '421 patent which was filed within a year of the  
15 '686 patent. So it was filed in 1994.

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

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

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

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

Desai - cross

1 1994. Do you remember this abstract that was presented at  
2 the annual meeting of the Society For Biomaterials in Boston  
3 in April of 1994?

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

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

9 Was this reduced to written form?

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

11 Q. It was presented at this meeting?

12 A. That's correct.

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

15 A. Yes, it does.

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

18 A. Yes.

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

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

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

Desai - cross

1 distribution of .5 to two microns"?

2 A. Yes, I did.

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

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

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

11 MR. JACOBS: Objection, Your Honor. Vague.

12 BY MR. SCHEVE:

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

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

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

Desai - cross

1           It just says what we are going to present at the  
2 meeting, the data we are going to present at the meeting are  
3 on microspheres that can be consistent with, prepared in the  
4 .5 to two micron size range.

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

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

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

11 Q.     Do you recognize this Joint Exhibit, 027?

12 A.     Yes, I do.

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

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

19 Q.     Liquid?

20 A.     Liquid.

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

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

Desai - cross

1 the microsphere.

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

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

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

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

13 A. Yes, I do.

14 Q. What year was this again, sir?

15 A. I am sorry?

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

19 A. I am not sure exactly. Maybe in the '95 time frame,  
20 '94-'95.

21 Q. Would you be comfortable suggesting, sir, that this  
22 description of your technology was at least after January of  
23 1995?

24 A. It's possible.

25 Q. Well --

Desai - cross

1 A. I mean, I don't know the date where we received the  
2 notice of allowance. I can't remember that.

3 Q. Would that be a reasonable assumption?

4 A. I think it's a reasonable assumption.

5 Q. Just so we understand here, what you were describing  
6 as of at least January of 1995 was still a particle that was  
7 two microns large, according to this diagram. Is that  
8 correct?

9 A. Yes. Again, as I mentioned, this is not Abraxane.  
10 This is a particle which inside it has a liquid. It says  
11 right there, This is non-aqueous liquid. And this falls  
12 into the range of our earlier patents where we said we were  
13 interested in down from .1 micron or a hundred nanometers  
14 all the way to five microns.

15 Q. I am just asking, sir, does this reflect your  
16 technology as of January 2005?

17 MR. JACOBS: Your Honor, it is a vague question.

18 THE COURT: Yes. You are going to have to be  
19 more specific.

20 BY MR. SCHEVE:

21 Q. Does this image here, sir, reflect what you understood  
22 your particles to look like in your technology as of January  
23 2005?

24 A. As a general theme, yes.

25 Q. And so that we understand this, this wasn't a solid

Desai - cross

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

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

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

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

17 A. "In vivo" is in the body.

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

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



Desai - cross

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

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

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

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

7       A.     Yes, I am familiar with this patent.

8       Q.     Do you see that diagram called Figure 1?

9       A.     Yes, I do.

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

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

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

16      A.     Yes, I do.

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

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

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

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

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

Desai - cross

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

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

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

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

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

11 A. Yes, it is.

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

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

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

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

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

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

Desai - cross

1 Q. Does it contain the word "amorphous"?

2 A. Again, I can't go through the whole document. It's 40  
3 pages. But I think the focus of this was really on the  
4 cross-linked shell. So it may not have the word "amorphous"  
5 in there.

6 Q. Does any patent that had been filed by Abraxis, for  
7 which you were the inventor through June of 1996, state  
8 anything about it being amorphous? Did the word "amorphous"  
9 appear in any patent filed through that date and time?

10 A. I don't believe we had amorphous specifically as a  
11 word. But the technique to generate amorphous particles is  
12 definitely in the patent.

13 Q. Okay. Now, sir, I want to go forward then to this  
14 Liversidge package.

15 You acknowledge that you received a package from  
16 Dr. Liversidge in August of 1996?

17 A. Yes.

18 Q. Did you sign a confidentiality agreement?

19 A. Sure, we did.

20 Q. Now, do you see this handwriting here on -- let's make  
21 sure we are clear.

22 Did you receive with that packet a proposed  
23 clinical development submitted by a Dr. Daniel van Hoff?

24 A. Yes. I think it was one-page summary of a clinical  
25 plan proposed for a drug called piposulfan.

Desai - cross

1 Q. Did you get a slide presentation from Dr. Liversidge?

2 A. Yes, we did.

3 Q. Did you get three patents from Dr. Liversidge?

4 A. I think there were two or three patents in that  
5 packet, yes.

6 Q. Do you recognize this handwriting here, where it says,  
7 Note: Prosecute our grinding claims for Taxol?

8 A. Yes, that's my handwriting.

9 Q. Now, did you write this here, sir, in the left-hand  
10 column of this page, Copy, and then put that line?

11 A. I wrote that. What that refers to is that, this was a  
12 list of drugs that are contemplated as part of the  
13 invention. When I saw that list, it looked very similar to  
14 the list that we had in our own patent.

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

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

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

23 BY MR. SCHEVE:

24 Q. Okay. With regard to the NanoCrystal technology, sir,  
25 the '118, the '684, the '025, the '363 patent, did all of

Desai - cross

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

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

5 Q. You don't remember?

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

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

9 A. That's correct. Our first patent was February of  
10 1993.

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

17 MR. JACOBS: Your Honor, sidebar?

18 (The following took place at sidebar.)

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

Desai - cross

1 sideshow.

2 THE COURT: I am tending to agree with that. I  
3 have an idea what you are trying to do. I have a concern  
4 about it.

5 MR. SCHEVE: For example, he put an asterisk  
6 next to this particular microfluidizer, Your Honor, and he  
7 incorporated it into their manufacturing methods. I would  
8 think I would have an opportunity to show how he lifted  
9 certain parts of the technology.

10 THE COURT: Go ahead.

11 MR. JACOBS: There is no lifting of the  
12 technology. There is a published patent. If he wants to  
13 walk into this one, terrific, but I object.

14 THE COURT: I understand your objection. I  
15 think he is entitled to make an effort to do what I think he  
16 is trying to do, what he has described. I don't know where  
17 it comes out.

18 Your objection is noted. I am going to overrule  
19 it at this point.

20 I think you need to mind your time, though.

21 MR. SCHEVE: I will, Your Honor.

22 (End of sidebar conference.)

23 BY MR. SCHEVE:

24 Q. Did you put this asterisk down here, sir, about Model  
25 M 140 K, which is a high-pressure micro fluid diver?

Desai - cross

1 A. Yes, I did. What that refers to, again, is a type of  
2 equipment that is known in the art, it's known in the field.  
3 It's a microfluidizer or a fluidizer. And we had some  
4 references to that in our very own lab notebooks. It's an  
5 instrument that's used to shear, sort of like an analogy,  
6 would be a blender, to break up things and make them into  
7 small particles.

8 So that was the reference to that instrument.

9 Q. Did you make reference here to the particle size being  
10 less than 400 nanometers?

11 A. Yes. All of these were notations I was making as I  
12 was reading it. Some of them, to me, were very striking,  
13 because they were either, for example, when I saw the list  
14 of drugs, I said, Okay, this looks very much like what we  
15 had in our own patent.

16 When I saw cross-linked or I -- rather  
17 non-cross-linked, I made an exclamation point there because  
18 it was different from our technology.

19 I was just underlining the key features as I  
20 went along and read the patent.

21 Q. Did you highlight here, sir, This processing  
22 temperature of between 30 and 40 degrees Centigrade are  
23 preferred?

24 A. Sure, I did, yes.

25 Q. Let's go on then, sir, to the next patent in the

Desai - cross

1 sequence, which was filed on September 9th, 1997, the  
2 so-called '331 patent.

3 Is this a patent that marks Abraxane according  
4 to the Orange Book?

5 A. Please give me the exhibit.

6 Q. This would be Plaintiff's Exhibit 594.

7 A. Yes, this is one of our patents.

8 Q. Is this the first time, sir, that you had a patent  
9 that actually refers to this thing called Capxol?

10 A. For the first time, the word "Capxol" is used in a  
11 patent?

12 Q. Correct.

13 A. It's possible. I don't know without going through the  
14 text of all the patents.

15 Q. Is Capxol a name that was eventually used to  
16 substitute for that word Proto-sphere?

17 A. No, it's not.

18 Q. What is the difference between Proto-sphere and  
19 Capxol?

20 A. Proto-sphere is a general word referring to  
21 protein-based microsphere. So it encompasses the technology  
22 in general. You can use different proteins. You can use  
23 different drugs. You can have oil inside the particles or  
24 you can have a solid amorphous particle on the inside.

25 All of that is covered by the word



Desai - cross

1 "Proto-sphere."

2 Capxol is a name that we had given at the time  
3 to the particular formulation with paclitaxel.

4 Q. I don't mean to cut you off, sir. Did you finish?

5 A. That's okay.

6 Q. Is it true, sir, that then this patent that was filed  
7 in 1997 describes a Capxol as forming a stable colloidal  
8 solution of paclitaxel. The size of the colloidal  
9 suspension may range from 20 nanometers to eight microns  
10 with a preferred range of about 20 and 400 nanometers?

11 A. Yes, that is stated in the patent. And the reason for  
12 that, if we can just go back, so the reason for that is it's  
13 a general description of what Capxol is. You give a general  
14 range. Then you typically, in patents, you give a more  
15 preferred range.

16 So both of those general ranges, all the way  
17 down from 20 nanometers up to eight microns, are here. Even  
18 the more preferred range of 20 to 400 nanometers, which is a  
19 smaller size range, is mentioned in this patent.

20 Q. Does this patent have the word "amorphous" anywhere in  
21 it, sir?

22 A. You know, I don't believe it does, because this patent  
23 was really focusing in on clinical application. How do you  
24 administer this drug to a patient? Do you give it in one  
25 hour or three hours? How often do you repeat the treatment

Desai - cross

1 cycle? Is it three weeks? One week?

2 It's a method of administration and treatment.

3 We covered the other aspects, like cross-linking, in the  
4 first patent. There was other patents that covered the  
5 amorphous aspect. This particular patent covered the  
6 administration to the patient.

7 Q. So, through the filing of this patent in 1997, had a  
8 single one of your patents, of the patents marking Abraxane,  
9 contained the word "amorphous"?

10 A. I am sorry. Could you repeat the question?

11 Q. Certainly. Through the time that this '331 patent was  
12 filed in September of 1997, the application was filed, had  
13 any of the patents marking Abraxane contained the word  
14 "amorphous"?

15 A. Absolutely. We had patents, if I remember correctly,  
16 it was filed in October of 1996, that, in fact, had the  
17 definitive data that showed amorphousness in Abraxane. That  
18 was filed as a separate patent, like I said, you file  
19 patents on different aspects. We covered cross-linking  
20 already. We then filed, in '96, amorphousness, even though  
21 we had examples in the earlier patents, that clearly made  
22 amorphous particles. So by this time in 1997, I think more  
23 than a year before this, we had already filed a patent with  
24 amorphous.

25 Q. What was the number of that patent, sir?

Desai - cross

1 A. 5,916,596.

2 Q. '596 were the last three digits?

3 A. '596 were the last three digits.

4 Q. Okay. Now, sir, with regard to this '405 patent, I am  
5 just about ready to move on to a new topic here, is it true  
6 you filed then another new patent in 2000, called the '405  
7 patent?

8 A. Yes. We filed several patents along the way. This  
9 is, okay, the '405 patent. I don't believe your filing date  
10 of August 2000 is correct.

11 Q. Okay. And it's referred to as Defendant's Exhibit  
12 029. Again, is it describing suspension ranging from 20  
13 nanometers to eight microns, and then providing a preferred  
14 range?

15 A. Did you say 029?

16 Q. It's '405, sir. It's Defendant's Exhibit 029, 029.

17 THE COURT: Mr. Scheve, would you signal when  
18 you are moving into this next topic? We will break at that  
19 point.

20 THE WITNESS: Yes. This was, that language is  
21 in that patent.

22 MR. SCHEVE: Do you want to break, Your Honor?

23 THE COURT: Sounds like a good time. Let's take  
24 our lunch.

25 (Jury leaves courtroom at 12:59 p.m.)

Desai - cross

1 (Luncheon recess taken.)

2 THE COURT: We will work until 4:00 o'clock  
3 today.

4 Ms. Walker.

5 (Jury enters courtroom at 2:10 p.m.)

6 THE COURT: Mr. Scheve.

7 BY MR. SCHEVE:

8 Q. Good afternoon, Doctor.

9 A. Good afternoon.

10 Q. I am going to put up this image. You mentioned during  
11 direct examination that there was a mutual exchange of  
12 information between you and Dr. Liversidge?

13 A. Yes, Doctor there was.

14 Q. Is this the image you gave to Dr. Liversidge of your  
15 technology as of August of 1996?

16 A. It's either this one or something that looked very  
17 similar.

18 Q. Very similar to this?

19 A. Yeah. Maybe it's, Doctor I can't be exactly sure.  
20 Could you show me the exhibit?

21 Q. Yes, Doctor sir. I believe it is Joint Exhibit 025.  
22 It also says Joint Exhibit 028. Apparently, Doctor it's  
23 found in two places.

24 (Pause.)

25 A. Which one is it? Because it's not in one and I think

Desai - cross

1 it's in the other.

2 Q. Which one do you find it in, Doctor sir?

3 A. 028.

4 Q. Is this the image that you exchanged with  
5 Dr. Liversidge?

6 A. Probably. My book looks like a big block. I am sorry  
7 about that.

8 Q. To the best of your memory, Doctor sir, Doctor would  
9 this be the image that you exchanged?

10 A. It could be.

11 Q. I need to establish if this is what you gave him or  
12 not, Doctor sir. We will quickly look for that.

13 A. There is another image in here, Doctor if you would  
14 like to refer to that, Doctor which may be clearer.

15 Q. Is it this image here?

16 A. No. It's a different one. It's on 025262.

17 Q. Let's just establish, Doctor you sent an image to  
18 Dr. Liversidge. Is that correct?

19 A. Yes, Doctor I did.

20 Q. Now, Doctor would you go to 20, Doctor Slide 20.

21 Sir, Doctor I just want to establish some  
22 things. Did Dr. Liversidge give you this slide as part of  
23 his slide deck?

24 A. Yes, Doctor I remember that slide.

25 Q. Let's move to the next one, Doctor Plaintiff's Exhibit

Desai - cross

1 363.

2 Did this become an image that was utilized  
3 internally at Abraxis to describe its Abraxane  
4 nanoparticles?

5 A. Yes. This is a typical cartoon that we have used for  
6 a long time.

7 Q. Was this being used in 2006?

8 A. I don't recall specifically.

9 Q. To the best of your memory, Doctor approximately when  
10 was it being utilized within Abraxane to depict the  
11 particles -- within Abraxis to depict the particles within  
12 Abraxane?

13 A. My guess is we have used that cartoon for probably at  
14 least ten years.

15 Q. Ten years?

16 A. Maybe.

17 Q. Do you know for sure?

18 A. No, Doctor I don't.

19 Q. Let's go on here. Did Dr. Liversidge give you these  
20 charts relating to release profiles and dissolution profiles  
21 as part of the technology exchange?

22 A. Could you please point me to that?

23 Q. Absolutely. I am looking at Joint Exhibit 020. It's  
24 Pages 15 and 18.

25 A. All of these slides are in that package.

Desai - cross

1 Q. I hate to backtrack, Doctor if you would be kind  
2 enough to go back to Exhibit 025, Doctor Joint Exhibit.  
3 It's a Bates number ending in 305.

4 If you would be kind enough to bring it up,  
5 Doctor Jonathan. 67, Doctor please.

6 I apologize, Doctor sir, Doctor for making you  
7 go back and forth.

8 A. Just to clarify, Doctor it is in there. But 025 is  
9 not something we sent to Nano Systems.

10 Q. 025 is not?

11 A. No.

12 Q. Does this image here in 025, Doctor was that an image  
13 of your technology?

14 A. Yes. This was taken very early on during the  
15 development.

16 Q. Is it found in a packet of materials that has a date  
17 on it?

18 A. It's in that packet of materials that, Doctor you see  
19 a fax page as the first page of that exhibit, Doctor there  
20 is a June 1993.

21 Q. '93?

22 A. Yes.

23 Q. Okay. Now, Doctor this image, Doctor was it something  
24 that was done internally at Abraxis?

25 A. No, Doctor we did not do this internally.

Desai - cross

1 Q. Where was it done?

2 A. It was done at University of Illinois.

3 Q. I want to move on, Doctor if I could get Slide 27,  
4 Doctor please.

5 Is it true, Doctor sir, Doctor that the  
6 manufacture of Abraxane is carried out at a low temperature  
7 with chilling throughout the process?

8 A. Yes. The chilling throughout the process is important  
9 because you have albumin, Doctor and albumin is a protein.  
10 Proteins are very sensitive to different temperatures.  
11 Also, Doctor you can get, Doctor you have to be very careful  
12 not to contaminate it with microbes, Doctor so you keep it  
13 at a low temperature. If you keep it at high temperature,  
14 Doctor you can get a lot of microbial growth, Doctor because  
15 that condition is very useful for microbes to grow. So we  
16 chilled that entire process.

17 Q. Then I would like to go to Slide 29, Doctor please.

18 Is it true, Doctor sir, Doctor that in terms of  
19 homogenization to reduce the particle size, Doctor that you  
20 were using a certain emulsifier up until February of 1975  
21 and that your process switched over to M 140 K  
22 microfluidizer?

23 A. Yes. We used different types of equipment to make the  
24 particles. I think I explained before that homogenizer or  
25 fluidizer is the type of equipment that can achieve the



Desai - cross

1 smaller size in particles.

2 Initially, we were using, when we were at small  
3 scale, at lab scale, in the test tube, we were using what's  
4 known as this Avestin (phonetic) unit, which can handle  
5 small samples. Then as this necessity for scaleup began,  
6 that we needed to make bigger and bigger units, we went to  
7 what was standard and available at the time.

8 For the bigger size, we used M 140 K. Then, at  
9 the commercial size, we used yet another unit that is even  
10 bigger than that particular unit.

11 Q. Actually, the first human clinical trial batch wasn't  
12 made until clear down here in 1998, was it, sir? 1998?

13 A. I think there was clinical batches that were made  
14 prior to that date.

15 Q. Well, let's go look at this page. I don't want to  
16 delay us. But please look at it, Plaintiff's Exhibit '017.  
17 Do you have that in front of you?

18 A. Yes, I have it here.

19 Q. Are you able to find it, sir? Do you have that page?

20 A. Is it Page 324 in this?

21 Q. It's Table 1. Did you find it?

22 A. Yes.

23 Q. If you look at the top, doesn't it say, "Used For  
24 Preclinical Studies Listed Below"?

25 A. Yes, I see it.

Desai - cross

1 Q. Preclinical means animal?

2 A. That's correct.

3 Q. Isn't it true that the first human study, the first  
4 batch wasn't made until March of 1998?

5 A. The first clinical batch, which was used in our  
6 clinical trials, as identified in this table, is down here.  
7 (Indicating.)

8 Q. Sir, isn't it true that you began using this very  
9 specific model of microfluidizer, the M 140 K, clear in the  
10 first week of February of 1997, 13 months before the first  
11 clinical batch?

12 A. Well, this data just represents the batches that were  
13 used for testing that was sent to the FDA, meaning if we did  
14 any animal tests, we had to identify which particular lots  
15 were used for the animal test.

16 So there was a lot of other development work  
17 that was going on at the same time, just in finding the  
18 right experimental conditions and to produce the product.  
19 So that information is not represented on this table. So I  
20 would say that even prior to this date, that we were using  
21 equipment such as this to produce nanoparticles of  
22 paclitaxel.

23 Q. Can you find it on this page, sir?

24 A. No, it wouldn't be on this page, because this  
25 reference the specific lots, as indicated in the title, that

Desai - cross

1 are used for preclinical, that is for animal studies, and  
2 for clinical studies.

3 Q. When was the first clinical study started, sir?

4 A. It was started in May of 1998.

5 Q. May of 1998?

6 A. I beg your pardon. The IND was filed in May '98. The  
7 clinical trials started in July.

8 Q. In July of '98?

9 A. Yes.

10 Q. This chart shows that the first Phase 1 batch was made  
11 in March of '98. Correct?

12 A. That's correct.

13 Q. The jury has seen a number of images of crystals.

14 Would you please put up No. 45.

15 Do you see this here, sir? Microscope!

16 Needles! Pretty damn small! Normal

17 sample-microscope-needles.

18 Do you see that, sir?

19 A. Can you tell me which exhibit it is?

20 Q. Yes, it's Joint Exhibit 62.

21 THE COURT: What's the Bates page, Mr. Scheve?

22 MR. SCHEVE: It ends in 191, Your Honor, I am  
23 sorry.

24 MR. JACOBS: Your Honor, we are having trouble  
25 tracking the exhibit and the Bates page.

Desai - cross

1 THE COURT: I am, too. JX-62?

2 MR. SCHEVE: 062.

3 THE COURT: I have that.

4 THE WITNESS: I don't think it's in here. All  
5 the Bates pages start with 527.

6 THE COURT: Yes. The last three numbers,  
7 Mr. Scheve, on the first page, 474 through -- well, it goes  
8 on from there.

9 MR. SCHEVE: Let me go forward. I apologize to  
10 the Court and the witness for that. I have it marked as  
11 that. If I am wrong, I stand corrected. I apologize.

12 BY MR. SCHEVE:

13 Q. Let's go forward to the next one, please.

14 Do you recall, sir, the discussion that you had  
15 with counsel for Abraxis about these references to crystals?  
16 I am now looking at Joint Exhibit 021.

17 A. Yes. This, I testified this morning about this  
18 particular example from my notebook.

19 Q. If we go forward in 1995, you will acknowledge, sir,  
20 that there are references to crystals being observed at  
21 different stages, in other words, some in the manufacturing  
22 process and then later on, actually, after they were  
23 reconstituted with saline solution.

24 Do you agree with that, sir?

25 A. No, actually, that is a mischaracterization.

Desai - cross

1 Let me clarify.

2 This is a notebook from Dr. Shlomo Magdassi's  
3 notebook, who used to work for me. In this particular case,  
4 on this date, this was in early '96, he is doing an  
5 experiment where he uses a surfactant, a surface active  
6 agent or a surface modifier. If somebody could blow this  
7 up. It says, Cremophor. I can see right here. He uses  
8 Cremophor in this formulation. Here we are, when I talked  
9 to you earlier about testing all kinds of different  
10 conditions, all kinds of different components, in this case,  
11 we are testing Cremophor for. The results that he got was  
12 crystals. And he identified right here that, "The problem:  
13 Crystal growth. How to prevent it"?

14 So this is clearly a result that we did not want  
15 or striving to get away from crystals. This is a condition  
16 that we did not want, using this particular component,  
17 Cremophor. And we completely steered away from that. In  
18 fact, in the patent that we filed later, in this very same  
19 year, which had the amorphous x-ray diffraction data in  
20 there, there are specific examples in that patent, this is  
21 one of the examples in there, it clearly shows and  
22 identifies that this is a technique that is not to be used  
23 for the invention. That the addition of surfactants should  
24 not be done.

25 Q. If we move forward, you told us here now that you

Desai - cross

1 started clinical trials with ABI-007 in July of 1998.

2 Correct?

3 A. That's correct.

4 Q. Let's move forward to Slide 53.

5 A. What exhibit?

6 Q. Slide 53, please. It's Plaintiff's Exhibit 334. In  
7 2000, July of 2000, this is two full years, is it not, sir,  
8 after this drug is being administered to humans in clinical  
9 studies?

10 A. Yes, that's correct. Let me just get to that notebook  
11 page, please.

12 Q. Sure, Plaintiff's Exhibit 334.

13 A. Do you have a Bates number, please?

14 Q. The page that is in your lab notebook, sir, did not  
15 contain a Bates number when it was produced to us.

16 THE COURT: Mr. Scheve, would you check your  
17 copy? Is the cover, Second Nature, notebook, something  
18 along those lines? So we know we are talking about the same  
19 exhibit. I have, in the notebook you provided me, PX-334.  
20 Behind that tab, I see Neil Desai, handwritten, American  
21 Bioscience, and then, Second Nature.

22 MR. SCHEVE: Yes, Your Honor.

23 THE COURT: What we are trying to determine is  
24 what page. I do see Bates number pages. Are we talking  
25 about the same exhibit?

Desai - cross

1 THE WITNESS: Sir, the last entry date on this  
2 exhibit is only from 1999. There is nothing in 2000.

3 THE COURT: You are talking about August 19,  
4 Doctor?

5 THE WITNESS: Yes, that's right.

6 BY MR. SCHEVE:

7 Q. Let me move to the next one.

8 A. I remember this, so I can talk about it.

9 Here, what we are doing, this is a conversation,  
10 a conference call that I am having with this company Bristol  
11 Myers Squibb. As you know, Bristol Myers Squibb made the  
12 original Taxol. They are now interested in some aspects of  
13 our technology. So at this time, I had a whole probably  
14 four or five people from Bristol Myers Squibb on the line.  
15 And I was walking them through our technology.

16 We talked not only about Abraxane but other  
17 applications. If you look here, that says inhalation, so  
18 looking at other applications of drugs. And we talked about  
19 Abraxane also.

20 What Mr. Scheve has highlighted here for you is  
21 this statement, Change of amorphous to crystalline. And it  
22 says something about PK.

23 So I was making notes of what they were telling  
24 me and asking me. One of the questions they raised, very  
25 valid question, is, upon reconstitution, which is shown

Desai - cross

1 right here, upon reconstitution, which means when you take  
2 the vial of Abraxane, which is a powder, and put saline in  
3 it, or water in it, in essence, does it change from  
4 amorphous to crystalline?

5 The reason they were interested in that was  
6 because -- and I put here "PK" -- so PK of amorphous versus  
7 PK of crystalline. What PK refers to is a word in the  
8 medical field called pharmacokinetics, which describes how  
9 the behavior -- what is the behavior of the drug once it  
10 enters the bloodstream.

11 So when you change the PK, what they are  
12 referring to is that an amorphous material would behave  
13 differently when administered to the bloodstream from a  
14 crystalline material. Of course, I fully agreed with it,  
15 because, as I have described to you before, an amorphous  
16 material leaves the bloodstream very quickly and crystalline  
17 materials stay in the bloodstream.

18 In fact, this is their statement to me, asking  
19 me, or, rather, question to me, Does the Abraxane, after  
20 reconstitution, change from amorphous to crystalline? They  
21 were very interested in that because, as you know, PK would  
22 change if that does happen. My response to that was, No, it  
23 does not change and it remains amorphous. What I have done  
24 here is just noted down their questions to me in that  
25 telephone call.



Desai - cross

1 Q. Here, sir, there was a question, and a question mark.  
2 What you are telling me now is even though this doesn't say  
3 question mark, that this was a question?

4 A. Yes. That was a Bristol Myers question to me.

5 Q. This is Leslie Louie's notebook from September of  
6 2000, Plaintiff's Exhibit 397, if you can find that.

7 Do you see up here, Reconstitution study?

8 A. Yes, I do.

9 Q. Isn't it true, sir, that when Leslie Louie  
10 reconstituted Abraxane in September of 2000, which was two  
11 years and two months after you had began putting this drug  
12 in humans, and her observation was, Few random crystals, at  
13 five hours. Correct, sir? At differing strengths?

14 A. Okay. Let me clarify for you.

15 MR. SCHEVE: Your Honor, I would really  
16 appreciate an answer to my question.

17 THE COURT: I think he is getting ready to.

18 THE WITNESS: I agree with you that she put that  
19 notation there.

20 But this is the same page that was brought up in  
21 my direct testimony. This is lot No. 197079. This is that  
22 same first lot that we produced at 20 liter scale. This was  
23 done over that July 4th weekend. This is the same lot that  
24 was rejected, that failed all our testing for Abraxane,  
25 because it has very high solvent levels.

Desai - cross

1 We never utilized that lot. It was thrown away.

2 So this is from 1997 to 2000, first of all.

3 This is three years later. Of course, that doesn't have any  
4 bearing. But the fact is that this was a rejected lot with  
5 very high solvent levels.

6 BY MR. SCHEVE:

7 Q. It was using the method that was illustrated during  
8 your direct where you poured two things together into --  
9 first you dissolved it in a solvent and poured it together,  
10 and that method, even though I hear you say now that you  
11 think the solvent was too high, that method was used when  
12 these crystals were observed. Correct?

13 A. First of all, I don't think the solvent -- I know for  
14 a fact that the solvent levels were extremely high and it  
15 was rejected. That method was used. But there was  
16 something wrong in that particular lot in the manufacturing  
17 process. And we could not get out all the solvent that we  
18 wanted to. That was the problem with this lot.

19 Q. That method that was being utilized -- again, this is  
20 two years and two months after -- you have already got  
21 humans getting the drug. Correct?

22 A. Yes.

23 Q. This was the observation by Ms. Louie within Abraxis.  
24 Is that correct?

25 A. Sir, again, back to the point --

Desai - cross

1 THE COURT: I think he has answered that  
2 question, Mr. Scheve. You can argue it.

3 BY MR. SCHEVE:

4 Q. May I go on, then, to the next one, which was -- I  
5 think this is Mr. Ron -- is it not? Do you know the  
6 gentleman named Ron who continued this experiment?

7 A. I think this is still Louie's notebook.

8 Q. At her deposition, she talked about it. So I won't  
9 belabor the point.

10 When I took your deposition, you told me that  
11 you are not an expert in crystallography. Is that still  
12 true?

13 A. That is true.

14 Q. You told me you were not an expert in x-ray  
15 diffraction. Is that still true?

16 A. I have used x-ray techniques hands-on before and  
17 published on them. Not specifically x-ray diffraction, but,  
18 as I mentioned, x-ray photo electron spectroscopy, which  
19 utilizes some of the very similar equipment.

20 So I know about these techniques. I have  
21 studied about these techniques. I have utilized them and  
22 published data based on these techniques. But I do not  
23 perform these techniques every day and I would not qualify  
24 myself as an expert.

25 Q. Thank you, sir. And you told me you were not an

Desai - cross

1 expert in cryo-transmission electron microscopy, or  
2 cryo-TEM. Is that still true?

3 A. That is still true.

4 Q. You are not an expert in terms of looking at shapes or  
5 sizes of particles to express opinions as to whether or not  
6 they are crystals. Is that correct?

7 A. Well, my experience resides with my hands-on  
8 experience with paclitaxel. And I know a paclitaxel crystal  
9 when I see one. It is a very characteristic needle-shaped  
10 crystal.

11 Q. Is it correct, sir, you are still not an expert in  
12 that?

13 A. It depends on how you define expert. I have 15 years  
14 of experience on observing these crystals. If you use the  
15 definition "expert" in the highest sense of the word, have I  
16 published extensively in that particular field?, no, I am  
17 not an expert. But I have experience.

18 Q. You told me during the deposition there really weren't  
19 any people within Abraxis who were necessarily experts in  
20 any of those fields. Isn't that correct, sir?

21 A. I think I have to say it is the same answer. You may  
22 not qualify them as experts. But a lot of the people in  
23 Abraxis have been working for a long time in these areas.

24 Q. And you told me during the deposition that Abraxis had  
25 not submitted Abraxane or any aspect of Abraxane to any

Desai - cross

1 outside expert to ask them whether or not the particles  
2 within Abraxane were amorphous before this product was  
3 marketed.

4 Isn't that correct?

5 A. Yes, I think that's correct.

6 Q. Now, I want to show you an image, sir. Then I will  
7 try to bring my examination to a close.

8 I want to address briefly the cross-linking  
9 issue. But I want to show you an image that I found in some  
10 of the materials. First off, could we go to Page 36,  
11 please.

12 Sir, was this the image that was reflected in  
13 this presentation here? Who selected it? This image, this  
14 round one up here in the top, Plaintiff's Exhibit 363.

15 A. I am sorry. What was your question?

16 Q. Who selected this round image here for purposes of  
17 this presentation that's found on Plaintiff's Exhibit 363?

18 A. I think this is an image I had in my files. And this  
19 was used for, I believe this was an ODAC presentation, so we  
20 utilized that.

21 Q. When you say "ODAC," that is the Oncology Drugs  
22 Advisory Committee to the FDA?

23 A. That's correct.

24 Q. Was it selected from this image?

25 A. No. It was selected from a series of tests that were

Desai - cross

1 done earlier.

2 Q. Well, this here, sir, is supposedly a cryo-TEM image,  
3 isn't it?

4 A. Yes. The particle that we are looking at here, just  
5 for clarification, this little bar-like thing has got  
6 nothing to do with the particles. It is part of the grid  
7 that you put the samples on.

8 Q. When it says, Amorphous confirmed by x-ray  
9 diffraction, that is not an x-ray diffraction pattern, is  
10 it, sir?

11 A. No. We are referring to the fact that this is a  
12 particle and that we have a separate, different technique by  
13 which we have proved amorphousness. And that technique is  
14 x-ray diffraction.

15 Q. So this is cryo-TEM. Was it selected from this  
16 cryo-TEM image? Can you find that nanoparticle there?

17 A. Like I said, it's not from this image. This is images  
18 we had done several years earlier.

19 Q. What about this one here, do you see this nice round  
20 particle anywhere in this cryo-TEM image?

21 MR. JACOBS: Could we have the exhibit number?

22 BY MR. SCHEVE:

23 Q. Plaintiff's Exhibit 330 and the one before that was  
24 also Plaintiff's Exhibit 330?

25 A. These are again cryo-TEM images. Remember what I said

Desai - cross

1 about the prune, that when you create the droplet, it is  
2 more or less spherical, you shrink it when you pull the  
3 solvent off so you get more or less spherical but slightly  
4 irregular shapes. So this is what that represents.

5 Q. Was that nice round image taken from either of these  
6 two cryo-TEM images, sir; that was my question?

7 A. No. It was taken from a series of studies we had done  
8 several years before.

9 Q. These cryo-TEM images, are these images of  
10 reconstituted Abraxane?

11 A. They are.

12 Q. Sir, going back to this image here, this presentation  
13 of yours to ODAC said, Example of needle-shaped crystals.  
14 Is that correct?

15 A. Yes.

16 Q. You actually pulled that image from an article by  
17 someone named Barrett Rabinow, didn't you, sir?

18 A. Yes, we did.

19 Q. At the top of that Rabinow paper, there is raw  
20 material. There is material after precipitation and before  
21 homogenization.

22 You mentioned precipitation earlier, did you  
23 not, in your testimony?

24 A. Can I please go to that exhibit?

25 Q. Absolutely. It's Plaintiff's Exhibit 729.

Desai - cross

1 A. What was your question?

2 Q. My question is: This image here says, After  
3 precipitation. You described precipitation in your earlier  
4 testimony in describing how Abraxane was manufactured, did  
5 you not, sir?

6 A. Yes, we did.

7 Q. Now, there is also a picture about what these  
8 NanoCrystals look like after they are homogenized.

9 Did you include this in your slide presentation?

10 A. There was no need to. What we are trying to  
11 demonstrate is the difference, if you go back to that  
12 previous slide, if you would, please, our slide, all we are  
13 trying to say is that we have shown you an example, it says  
14 there, Example of needle shape, and then show the  
15 needle-like crystals. And we are trying to differentiate  
16 from what is Abraxane to what is standard needle shapes.

17 That is what was in the presentation on that  
18 slide.

19 Q. When we reduce it by homogenization, do you still see  
20 needles there, sir?

21 A. Sir, I have no idea what was done in this process, who  
22 did it, who has done it, what they have used for  
23 homogenization. So, you know, this is a low magnification,  
24 this is a 20 micron scale. I would like to see this at  
25 probably a hundred nanometer resolution. Then you could see



Desai - cross

1 that. This is very low magnification.

2 Q. Do you see needles, sir?

3 A. I see some shapes that look like needles.

4 Q. That look like crystals?

5 A. These are very large. Please understand, they showed  
6 magnification. The very large particles are being looked at  
7 as the same magnifications as the small particles. Here is  
8 a shape that looks like a rod or needle. In fact, there are  
9 several others I can point out to you on this, what I am  
10 looking at, my screen here, that look just like that.

11 Q. What about with regard to these images here, sir? Do  
12 you see anything in here that maybe looks like it's got some  
13 angularity, it's the shape of a triangle or arrow head?

14 THE COURT: PX-330?

15 MR. SCHEVE: Yes, sir. PX-330.

16 BY MR. SCHEVE:

17 Q. Do you see any angularity in those, sir?

18 A. Again, I may see some angularity and irregular shapes  
19 but there is no needles in them.

20 Q. Now, with regard to this cross-linking issue, sir, I  
21 am going to ask you to look at Joint Exhibit 071. Would you  
22 go to Slide 42, please.

23 Now, as part of the New Drug Application to the  
24 FDA, did you submit data from what are called pivotal  
25 stability batches relating to the monomeric content of the

Desai - cross

1 albumin contained in vials of Abraxane? That is, again,  
2 Joint Exhibit 71, sir.

3 A. Yes, we did.

4 Q. Did you report to the FDA, sir, that the monomeric  
5 content from these three batches here -- and you made  
6 reference earlier about this Melrose Park facility in  
7 Illinois -- did you represent to the FDA, sir, that with  
8 one, it was 90.2, give or take 0.6 percent monomer?

9 A. Yes. This is looking at the entire Abraxane, what is  
10 in the vial, the entire contents of it. If you analyze the  
11 albumin that's in the vial, this is what you get in terms of  
12 monomer, dimer, oligomer, and polymer.

13 Q. And with regard to the other value that is down here  
14 at the bottom, for all of these lots here, was the average  
15 monomer reported to the FDA 82.2 plus or minus 0.6 percent?

16 A. Yes, it was.

17 Q. Now, did you also submit to the agency data on monomer  
18 content for batches that were produced in a New York  
19 facility, Grand Island?

20 A. Yes. The objective of that was to show that from  
21 facility to facility, there was no difference, or the  
22 product, essentially, was very similar.

23 Q. And were the values reported to the agency 92.5  
24 percent plus or minus 0.2, 86.4 percent plus or minus 0.2,  
25 86.7 plus or minus 0.1 percent, and 86.8 plus or minus zero?

Desai - cross

1 A. Yes. That data was information sent to the FDA.

2 Q. Has that data ever been retracted from what was  
3 submitted to the FDA?

4 A. No, it was not. I would like to point out one thing  
5 additional that we reported to the FDA. That albumin is  
6 cross-linked and that it is cross-linked via the cystine in  
7 the albumin, that is, the disulfide linkages. This was  
8 clearly identified in this document.

9 Q. With regard, sir, so we understand the last series of  
10 my questions, then I will sit down, with regard to what  
11 Abraxis has done or not done, is it true, sir, that Abraxis  
12 has never commissioned anyone to use a test for  
13 crystallinity with reconstituted Abraxane powder?

14 A. Well, you can't do that, because the standard  
15 technique for analysis for crystallinity is x-ray powder  
16 diffraction. And powder necessarily means it's not  
17 reconstituted, it's not in water. So you have to do it for  
18 a dry powder.

19 Q. Is it true, sir, that you have commissioned no studies  
20 after it was reconstituted to test for crystallinity?

21 A. We have done -- I beg your pardon. We have done no  
22 x-ray diffraction studies on reconstituted material. That's  
23 correct.

24 Q. And isn't it true, sir, that you have separated the  
25 particles from free albumin within Abraxis?

Desai - cross

1 A. We have done that, but in the context of another  
2 study, where we are looking for the amount of cross-linkages  
3 on the particle, not for an x-ray diffraction.

4 Q. After those particles were separated, isn't it true,  
5 sir, that neither Abraxis or anyone commissioned by Abraxis  
6 has ever tested those nanoparticles that were separated from  
7 the free albumin to determine their levels of crystallinity?

8 A. That's correct. And it would not make sense to do  
9 that, because, as I mentioned, when you remove all of that  
10 free albumin from the particles, you destabilize the  
11 particles. You can get all kinds of artifacts. You can get  
12 aggregates. You can get agglomerates. So we wouldn't do  
13 that type of testing.

14 Q. But you felt comfortable relying on that separation  
15 data to report to the FDA that the particles are 82 percent  
16 paclitaxel and 18 percent albumin. Correct?

17 A. Absolutely, because, in that case, it makes sense.  
18 All you are doing is looking at the total content. You are  
19 not looking at structural information. You are just  
20 measuring what's in the particles.

21 Q. No crystallinity testing, I am putting under this  
22 column.

23 Is it true, sir, that the only crystallinity  
24 testing you did of freeze-dried powder was x-ray powder  
25 diffraction?

Desai - cross

1 A. X-ray powder diffraction is a standard technique. We  
2 utilize Abraxane as is from the vial. It is a powder  
3 diffraction which means you have to use powder. That is the  
4 test we did with Abraxane.

5 Q. Is it also then correct, sir, that it's tenfold  
6 amorphous albumin in what you tested using x-ray powder  
7 diffraction?

8 A. That's true. But it doesn't matter. We ran the  
9 appropriate controls, where we had the tenfold albumin and  
10 we had the crystalline paclitaxel from the manufacturer. We  
11 mixed the two up, and we ran the same x-ray diffraction  
12 tests, and there it was. You could see the peaks of  
13 crystalline material. So we ran the appropriate controls in  
14 those experiments.

15 Q. So is the answer yes, sir, tenfold?

16 A. Yes. I already said it was yes at the beginning of my  
17 answer.

18 Q. Thank you. With regard, then, sir, isn't it true we  
19 are dealing with 130-nanometer particles?

20 A. Yes, give or take a little bit.

21 Q. You just told the jury that, as the control, you did a  
22 physical mixture of paclitaxel with albumin for your  
23 control. Is that correct?

24 A. That's correct.

25 Q. Now, isn't it true, sir, that those particles that you

Desai - cross

1 used as a control, the raw paclitaxel mixed with this  
2 tenfold amorphous albumin had particles up to 500 microns in  
3 size?

4 A. Well, we didn't measure the particles, for one, in the  
5 control. But I would just assume they are very much larger  
6 than the nanoparticles.

7 Q. So this jury understands, did you ever use as a  
8 standard, or a control, a mixture of this tenfold amorphous  
9 to particles that were 130 nanometers?

10 A. It wouldn't make sense to use that as a control. And  
11 neither do you need to, because whether you have big  
12 particles or small particles, if it is crystalline, it is  
13 crystalline, it will show up on the x-ray method. If it is  
14 not crystalline, the peaks will not show up. So size really  
15 has no bearing on that method.

16 Q. Is this a correct statement, sir: You used no  
17 130-nanometer control?

18 A. Could you please describe what exactly you mean by the  
19 "control" there?

20 Q. The physical mixture of raw paclitaxel and this  
21 tenfold amorphous albumin that you used as a control, isn't  
22 it true, sir, that that was not -- the paclitaxel in that  
23 was not reduced to 130 nanometers?

24 A. That is absolutely true.

25 Q. Isn't it true, sir, your own patents say that raw

Desai - cross

1 paclitaxel ranges from 20 to 500 microns in size?

2 A. I don't remember the exact range. They are very large  
3 crystal particles.

4 Q. 500 microns would be 3500 times bigger than 130  
5 nanometers. Is that correct?

6 A. Yes. But it doesn't matter. Again, because if, in  
7 your control, you put in the same amount of paclitaxel as  
8 you do with, as is seen with Abraxane, that is the whole  
9 point of the control. If you have ten milligrams of  
10 paclitaxel in the Abraxane sample, you have to make sure you  
11 have at least ten milligrams of paclitaxel in the control  
12 sample. So then, as long as those amounts are the same, the  
13 size has no value in that experiment.

14 Q. Can you just confirm for me, sir, that raw paclitaxel  
15 is up to 3500 times larger than the size of the particles  
16 that are in Abraxane?

17 A. It could be, yes.

18 Q. Then I want to ask you one last question, sir. Isn't  
19 it true that you performed, or the company performed  
20 differential scanning calorimetry or DSC?

21 A. Yes, absolutely.

22 Q. Isn't it true, sir, that there was not found to be a  
23 glass transition temperature for Abraxane?

24 A. It's true. And that's easily explainable. Let me  
25 explain it.

Desai - cross

1           Glass transition, first of all, I don't know if  
2 the jury is familiar with that, is something you see for  
3 amorphous materials. And because we have albumin complex  
4 with the paclitaxel, that property of glass transition of  
5 paclitaxel is lost, because it's complexed with albumin  
6 molecules and it's not complexed with itself.

7           And glass transition is a bulk property, so you  
8 need bulk material, that is, a lot of paclitaxel molecules,  
9 to be associated to each other, to be able to see that.  
10 Because we have albumin, and the albumin is complexed to the  
11 paclitaxel, you wouldn't expect to see that.

12 Q.     Isn't true, sir, when you applied differential  
13 scanning calorimetry, that Abraxis did not find a glass  
14 transition temperature for that product, for the paclitaxel  
15 in that product? Yes or no?

16 A.     I just said we did not.

17 Q.     Okay. Three more slides, then I am sitting down.  
18 Would you please pull up Slide 32.

19           Isn't it true, sir, you represented to the  
20 Oncology Drugs Advisory Committee, to the Food & Drug  
21 Administration --

22 A.     Could I pull up the exhibit, sir?

23 Q.     I am sorry. It is Plaintiff's Exhibit 112. I  
24 apologize.

25           Did you make this statement to the Oncology



Desai - cross

1 Drugs Advisory Committee, to the FDA, that the albumin  
2 particles rapidly dissociate into individual albumin  
3 molecules and then circulate with the paclitaxel still  
4 attached?

5 A. Yes. That's exactly what I am talking about, the  
6 complexation, where the paclitaxel stays attached to the  
7 albumin.

8 Q. And then, sir, at that same FDA meeting on October  
9 10 -- yes, the FDA meeting of October 10th, 2007, did you  
10 state, sir, in your remarks to the FDA, with regard to  
11 Abraxane, that it says, quote, "You've got soluble albumin  
12 bound drug floating around very soon after administration"?

13 A. This is now a different exhibit?

14 Q. Yes, sir. It's Exhibit 070. Do you see it? It's  
15 Page 184 of your testimony to the FDA.

16 A. Okay. I am there.

17 Q. Did you make those three statements there?

18 A. Yes, I did.

19 Q. My last exhibit, and I will sit down. Is it true,  
20 sir, that in this presentation, does this presentation here  
21 depict what happens to the -- and I am looking at  
22 Plaintiff's Exhibit 363 -- what happens to the surface  
23 modifier once it's put in the blood? Once it's injected  
24 into a human?

25 A. Well, this is just a cartoon to indicate that when we

Desai - redirect

1 take Abraxane and administer it, the drug -- this particle  
2 rapidly dissociates, this goes to the point of its  
3 amorphousness. Remember, it quickly dissolves. So it  
4 dissolves into these complexes of albumin with the drug  
5 attached. And you can see these little stars there. Again,  
6 this is a little cartoon depiction. It is then these  
7 complexes that can piggy-back onto the albumin and rapidly  
8 get out of the bloodstream. That is what we are trying to  
9 indicate here.

10 Q. And indicating that, sir, is it correct, at the top,  
11 it says, In the circulation, the nanoparticles rapidly  
12 dissociate?

13 A. Absolutely. That is a key feature of Abraxane.

14 MR. SCHEVE: Your Honor, with that, I pass the  
15 witness.

16 THE COURT: Mr. Jacobs.

17 REDIRECT EXAMINATION

18 BY MR. JACOBS:

19 Q. Let's take that last sequence in reverse order,  
20 Dr. Desai.

21 Is there anything inconsistent between the idea  
22 of rapidly dissociating and the amorphousness of the  
23 paclitaxel?

24 A. No. In fact, not at all. I think a key feature of  
25 the amorphous is that we want it to rapidly dissolve and

Desai - redirect

1 dissociate so it can get out of the bloodstream. If it is  
2 not doing that, it is not doing its job that we planned.

3 Q. Is there anything inconsistent with the idea of  
4 rapidly dissociating and disulfide bond based cross-linking?

5 A. Not at all. There is disulfide cross-linked albumin  
6 in our natural blood circulating around all the time. If  
7 you have disulfide cross-linked albumin, the particle, the  
8 body does not see that as foreign. That is the whole point.

9 We did not want to denature -- remember the egg  
10 white concept. So it's very important, in fact, that we  
11 have this cross-linking to help stabilize the particle, and  
12 very important, in fact, that we have the amorphous nature  
13 so that it dissociates very rapidly.

14 Q. Did you rely on DSC for the conclusion at Abraxis that  
15 Abraxane, the paclitaxel in Abraxane, was amorphous?

16 A. No, absolutely not. DSC is not the definitive test  
17 for crystallinity or amorphousness. X-ray diffraction is.

18 DSC is a standard test to look at thermal  
19 behavior of materials. So you increase the temperature, see  
20 what happens; decrease the temperature, see what happens.  
21 It's got nothing to do with crystallinity.

22 Q. Can we take a look at JX-21, at 325, please.

23 Dr. Desai, again, this is August -- the actual  
24 test data on this page is 23rd of August. Correct?

25 A. That's correct.

Desai - redirect

1 Q. This is before you got the materials from Nano  
2 Systems?

3 A. That's right.

4 Q. I think we all know by now, this is an x-ray powder  
5 diffraction?

6 A. That's correct, yes.

7 Q. You made a point about five questions towards the end  
8 of Mr. Scheve's examination that I wanted to be sure we  
9 capture. You talked about the total quantity of paclitaxel  
10 in the physical mixture and addressed that as compared with  
11 the question of the size of those paclitaxel particles. Can  
12 you just explain that one more time, please?

13 A. Okay. So what's important here is that when we test  
14 Abraxane, you have all the appropriate controls in place.  
15 By "controls," we mean appropriate other samples that you  
16 test along with it to confirm something.

17 When we test Abraxane, which is the curve right  
18 on top, you have no crystalline peaks, as you can see, no  
19 sharp peaks.

20 We want to make sure that our testing is not  
21 flawed. So we put in a control sample, which is just  
22 albumin and paclitaxel from the manufacturer, and we mix  
23 them up together in the same ratio as you would have in the  
24 actual Abraxane sample.

25 The importance of that same ratio, it's actually

Desai - redirect

1 very important to do that in the right ratio, because if you  
2 had more or less paclitaxel in that control sample, then you  
3 would get a different picture when you looked at the  
4 chromatograms.

5 So from that perspective, having the same amount  
6 of paclitaxel in the control sample is important. That's  
7 what we did.

8 When we ran that control sample, we could still  
9 see the crystalline peaks, meaning that there were crystals  
10 in that sample, and that control sample, or having the same  
11 amount of drug in that sample was adequate for a control, so  
12 that we could see, or have a definitive answer for our  
13 Abraxane sample.

14 The other point was on the issue of the size of  
15 those particles. Now, when you have crystalline material,  
16 whether it's a hundred microns or 200 microns, or it's 200  
17 nanometers or a hundred nanometers, it really doesn't  
18 matter. Because, if there is crystallinity, you will pick  
19 it up on this method.

20 There is a reason x-rays are used in this  
21 method. The reason for that is, again, I am getting into  
22 technical concepts here, but the reason for that is the  
23 wavelengths of these x-rays are extremely, extremely small.  
24 Much, much smaller than the smallest nanoparticle that we  
25 have talked about today.

Desai - redirect

1           The point is that if it's -- if an x-ray is  
2 penetrating a particle, scale wise, the x-ray may look like  
3 this, but that smallest particle, nanoparticle, looks like  
4 that. (Indicating.) So there is no chance that the x-ray  
5 is not going through the particle.

6           When you have a bigger particle that, in the  
7 context of the nanoparticle is even as big as this room,  
8 that x-ray is still going to go through and penetrate, no  
9 matter what.

10           Whether you have a big particle or a small  
11 particle, the x-ray is so much smaller than either of those  
12 that it makes no real difference to whether the particle is  
13 big or small.

14 Q.     And the important point, then, in setting up the  
15 physical control was to match what to what in terms of the  
16 paclitaxel?

17 A.     So the control was matched to Abraxane. So we had the  
18 same amount of paclitaxel in the control as we had in  
19 Abraxane.

20           For the control, we could see the crystalline  
21 peaks. And for Abraxane, we could not.

22 Q.     Did you ever file a patent application with the x-ray  
23 powder diffraction data we just saw?

24 A.     Yes. Soon after this data was obtained, we were  
25 already in the process of compiling a patent application,

Desai - redirect

1 which, in fact, contained all of the information from the  
2 previous year or year and a half.

3 And within, I think, a month after we got this  
4 final definitive data, we filed the application.

5 This was literally the last piece of the  
6 information that went into the patent application.

7 Q. So let's pull up DX-605. Is this the patent  
8 application that led to the 5,916,596 patent that you were  
9 referring to, sir?

10 A. Yes. This is the exact one that we filed soon after  
11 we got the x-ray diffraction data.

12 Q. If you go to Example 13, does Example 13 of this  
13 patent reflect the x-ray pattern diffraction data that you  
14 just showed the jury?

15 A. Yes. It's that very same data that we obtained by  
16 August 23rd of that year.

17 Q. Did you report to the Patent Office your conclusion  
18 about amorphousness?

19 A. Yes. We, in fact, up here in the introduction to that  
20 data, we said that it is advantageous that the formulation  
21 contain the drug in amorphous form, because of the issue of  
22 bioavailability, which we have talked about a lot, that it  
23 dissolves very quickly, like cotton candy.

24 In this paragraph, we actually presented the  
25 data, Sample 1, Sample 2, Sample 3, Sample 4. Those are the

Amiji - direct

1 four curves that you saw in that graph.

2 The conclusion here is that the presence of, in  
3 Sample 4, which is the formulated paclitaxel, showed no  
4 evidence of crystallinity which is characteristic of the  
5 standard raw material paclitaxel. And that was essentially  
6 the conclusion.

7 MR. JACOBS: Thank you. No further questions,  
8 Your Honor.

9 THE COURT: Thank you, Dr. Desai. You are  
10 excused.

11 THE WITNESS: Thank you.

12 (Witness excused.)

13 THE COURT: Ms. Kruze, who is your next witness.

14 MS. KRUZE: Dr. Mansoor Amiji.

15 ...MANSOOR AMIJI, having been duly sworn as a  
16 witness, was examined and testified as follows...

17 DIRECT EXAMINATION

18 BY MS. KRUZE:

19 Q. Good afternoon, Dr. Amiji.

20 A. Good afternoon, Ms. Kruze.

21 Q. Could you please introduce yourself to the jury?

22 A. My name is Mansoor Amiji. I am a professor of  
23 pharmaceutical sciences at Northeastern University in  
24 Boston.

25 Q. Are you testifying here today as an expert witness?



Amiji - direct

1 A. Yes, I am.

2 Q. What is your area of expertise?

3 A. I am in the pharmaceutical sciences department. I am  
4 an expert in the area of drug delivery systems,  
5 specifically, looking at nanoparticulate drug delivery, as  
6 well as nanotechnology applications in medical problems.

7 Also, my research interest is in polymeric  
8 biomaterials.

9 Q. Could you please turn to Defendant's Exhibit 474 in  
10 your binder. Mr. Broyles, if you could bring that up on the  
11 screen as well.

12 Would you identify this document for the jury?

13 A. Yes. This is a copy of my curriculum vitae, referred  
14 to as CV.

15 Q. And where did you do your undergraduate work?

16 A. I did my undergraduate work at Northeastern  
17 University, the same institution that I am currently  
18 employed at.

19 Q. And could you tell the jury if you have any advanced  
20 degrees?

21 A. Yes. I do. I have a doctoral philosophy degree, a  
22 Ph.D. degree in pharmaceuticals from Purdue University.

23 Q. What was the subject of your dissertation?

24 A. I worked on an area called surface modification of  
25 biomaterials, specifically in the area of hydrophobic or

Amiji - direct

1 materials that we have already heard in this trial. These  
2 are materials that do not like water.

3 So I looked at surface modification of these  
4 materials using what we call a stearic propulsion approach.

5 Q. Could you please tell the jury your current position?

6 A. I am currently the professor of pharmaceutical  
7 sciences. I am also the associate chair of the department.  
8 I also co-direct a program that we have at Northeastern,  
9 called the nano medicine consortium.

10 Q. What types of classes do you teach?

11 A. I teach both in the pharmacy program, this is the  
12 professional program, which we call sometimes the  
13 undergraduate program. I also teach in the graduate  
14 program, Master's and Ph.D. students.

15 In the undergraduate pharmacy program, I teach a  
16 course called Pharmaceutics 2. This course specifically  
17 deals with the application of physical and chemical  
18 principles in drug development.

19 For the graduate students, I teach a course  
20 called advanced drug delivery. I also teach in another  
21 program that we have, which is called the nanomedicine  
22 program. This program, I teach a course called introduction  
23 to nanomedicine.

24 We also have a course called nanosystems design.

25 Q. What is the focus of your research?

Amiji - direct

1 A. My research is focused on the application of  
2 nanotechnology for various diseases, both in the diagnosis,  
3 as well as in therapy. Most of our work is in therapy. We  
4 are looking at, specifically in cancer, but we also have  
5 interest in other diseases, such as cardiovascular disease  
6 and infectious disease.

7 Q. Have you written any books on drug delivery?

8 A. I have written several. I have written a book called  
9 Applied Physical Pharmacy, that I use in my teaching. I  
10 have also written a book called Polymeric Gene Delivery  
11 Systems. And I have written a book called Nanotechnology  
12 For Cancer Therapy.

13 Q. Mr. Broyles, could you bring up DD-112 on the screen.

14 Is this the book that you were just referring  
15 to?

16 A. Yes. This is the pride and joy of my work. It is  
17 actually, nanotechnology is an area, as we heard in this  
18 trial, that is receiving a lot of attention. This book was  
19 written specifically because of the interest that came from  
20 the National Cancer Institute of the National Institutes of  
21 Health. It is a 38-chapter treatise. I was involved in the  
22 editing of this book. We also have two chapters in there.  
23 It also has a forward from Peter Gryzinski (phonetic), who  
24 is a program manager at the National Cancer Institute.

25 Q. Let's turn back to DX-474. Have you also written any

Amiji - direct

1 articles on drug delivery?

2 A. I have written extensively. I have got about 80  
3 peer-reviewed articles. And you have heard about  
4 peer-reviewed process in this trial. It's where you submit  
5 an article and someone who is a peer of yours in an academy  
6 or industry gets a chance to review or critique. I have  
7 also written a number of book chapters and various abstracts  
8 in conference proceedings.

9 Q. Are you a referee of any of those peer review boards?

10 A. Yes. There are various trade journals I am referee  
11 for. On a weekly basis, I get asked to review an article  
12 typically for various journals, including Pharmaceutical  
13 Research, Journal of Controlled Release, and various other  
14 distinguished journals that are scientific in nature.

15 Q. Can you tell the jury about any awards that you  
16 received?

17 A. Yes, I have. I have been very fortunate, again, to  
18 receive awards. In 2006, I received the Nanoscience and  
19 Technology Institute's Fellowship Award. This was in  
20 recognition of our work in the area of nanotechnology, micro  
21 technology, and biotechnology.

22 Last year, in 2007, I received the American  
23 Association of Pharmaceutical Scientists, this is the agency  
24 that many of us in the pharmaceutical sciences belong to,  
25 and it is the largest society of the pharmaceutical science,

Amiji - direct

1 I received the meritorious manuscript award from the AAPS.  
2 They recognized our manuscript from 2005 as having received  
3 the highest number of citations and they bestowed upon us  
4 this wonderful award.

5 In the same year, 2007, I became the AAPS  
6 fellows.

7 Q. Those ones haven't made it to your CV yet. Right?

8 A. Those did not get into the CV, correct.

9 Q. What about grants, have you received any grants?

10 A. Yes. Again, I am very fortunate to have received -- I  
11 am one of the few pharmacy faculty in the country to have  
12 multiple awards from the National Institutes of Health. I  
13 have currently three awards and three grants from the  
14 National Institutes of Health. Our first one is in the area  
15 of nanotechnology, specifically focusing on this problem,  
16 it's a huge problem, called drug resistance in cancer.

17 We are trying to address this by having enhanced  
18 delivery of drug to the tumor cite. Also asking the  
19 question, how widely these cancer cells become resistant to  
20 chemotherapy and what we can do about it.

21 The second grant that we have, again, it is a  
22 distinction to have this because only four are awarded  
23 throughout the country, is the training grant. This is a  
24 grant to actually fund students, doctoral students, who are  
25 going to receive a Ph.D. degree, so that they can be trained

Amiji - direct

1 in the area of nanomedicine.

2 We, at Northeastern, have received this grant  
3 from the National Cancer Institute and it is administered by  
4 the National Science Foundation. We have close to six or  
5 seven doctoral students a year, which is in their third year  
6 of this grant, so we have funded close 15 or 16 Ph.D.  
7 students.

8 Q. Let's turn to cross-linking. If we can bring up  
9 JX-81.

10 Dr. Amiji, do the claims of the '363 patent  
11 require that the surface modifier molecules in the  
12 nanoparticles be non-cross-linked?

13 A. Yes, it did. Here we can see clearly in the first  
14 claim of the '363, it says that the non-cross-linked surface  
15 modifier --

16 MR. SCHEVE: Your Honor, this term has been  
17 construed by Your Honor specifically. If he is saying that  
18 this is the construction, it clearly is not the Court's  
19 construction of the term.

20 THE COURT: Let me see counsel.

21 (The following took place at sidebar.)

22 THE COURT: What is your response?

23 MS. KRUZE: My very next slide is going to the  
24 patent talking about that. It is exactly what Your Honor  
25 says in the Court's claim construction.

Amiji - direct

1 THE COURT: For the jury's benefit, we should  
2 avoid questions that might confuse them as to this issue.  
3 As we know, this has been hotly contested. The other side  
4 disagrees with my construction. They are entitled to. We  
5 don't want this fact-finder confused.

6 MS. KRUZE: No problem. I will just refer to  
7 how the patent talks about it. Or have him read from the  
8 patent.

9 THE COURT: I have construed contested terms.

10 MR. SCHEVE: Free of intermolecular  
11 cross-linkages.

12 MS. KRUZE: The very next slide is exactly that.

13 THE COURT: That is fine. I think the objection  
14 is to this slide.

15 MS. KRUZE: We will move directly on then.

16 THE COURT: So do you want to withdraw that  
17 question? Do you want to rephrase that question?

18 MS. KRUZE: Let me rephrase.

19 THE COURT: Do you want to move into the next  
20 slide?

21 MS. KRUZE: Yes.

22 (End of sidebar conference.)

23 BY MS. KRUZE:

24 Q. If you could bring up DD-33, which is based on JX-81.

25 Could you please read the highlighted term?

Amiji - direct

1 A. Yes. So here, again, in the patent itself, it says,  
2 essentially, free of intermolecular cross-linkages.

3 Q. Let's move to DD-70. When protein molecules exist in  
4 a non-cross-linked form, what do scientists call them?

5 A. Here we have heard this already, the terms in this  
6 trial, when you have single protein molecules, these are  
7 called monomers. When protein molecules associate and form  
8 two protein molecules associate, that is called a dimer.  
9 When you have three, that is a trimer. Many would be an  
10 oligomer. Even more would be polymers.

11 Q. Are dimers another word for cross-links?

12 A. Yes. Anything, once the proteins associate with each  
13 other, dimers, trimers, oligomers, and polymers would be  
14 considered cross-linked.

15 Q. Are there different types of cross-linking?

16 A. Yes. There are two types of cross-linking. There is  
17 a physical cross-linking and what's called chemical or  
18 covalent cross-linking.

19 Q. What is an example of physical cross-linking?

20 A. The best example I can give is the favorite of our  
21 children, the gelatin. We make gelatin, we take gelatin,  
22 put it in warm water. You take that, put it in a mold, put  
23 it in the refrigerator and it gels and forms this squiggly  
24 gel. That is a physical cross-link because you have changed  
25 the temperature and now the gel has solidified.



Amiji - direct

1           If you reverse that by heating that gel, it will  
2 become liquid again.

3       Q.     You also mentioned chemical cross-linking.

4           What does that involve?

5       A.     Chemical cross-linking involves formation of these  
6 bonds, what I would call covalent bonds.

7       Q.     Does the '363 patent distinguish between those two  
8 different types of cross-linking?

9       A.     No, it doesn't. The '363 patent was very clear in the  
10 fact that all types of cross-linking were included.

11       Q.     Can you pull up DD-71, Mr. Broyles. This is a 1006  
12 exhibit based on JX-81, JX-39 and DX-16.

13           What are these, Dr. Amiji?

14       A.     Here are some of the comments from the patent file  
15 history, as well as the patent itself. Both the '363 patent  
16 and the '684 patent, and we have heard the '684 being  
17 referred to as the mother patent for the '363.

18           You look at different comments. Let's start  
19 with the first one on the top, where we see -- this pointer  
20 is probably blinking. I can't see from here.

21           The top one there is the '288 prior art. That's  
22 the Oppenheim prior art. It says, The particle comprised a  
23 cross-linked matrix of macro-molecules having the active  
24 material supported on or incorporated into the matrix.

25           Here, the '363 applicants were distinguishing

Amiji - direct

1 their invention from this prior art, the Oppenheim prior  
2 art, based on the fact that it was cross-linked and theirs  
3 was not cross-linked.

4 The second comment, looking at the '294 patent,  
5 that's the Motoyama patent, again, the applicant  
6 distinguished their invention, the '363 applicants  
7 distinguished their invention based on the fact that the  
8 Motoyama patent had this crystallized carbohydrate matrix  
9 and these carbohydrates were cross-linked. Here is a case  
10 where it was physically cross-linked.

11 MS. KRUIZE: Permission to approach the witness,  
12 Your Honor?

13 THE COURT: Yes.

14 BY MS. KRUIZE:

15 Q. Dr. Amiji, is the albumin coating on the surface of  
16 Abraxane particles non-cross-linked?

17 A. No. The albumin coating, as we just heard, is  
18 significantly cross-linked on the surface of the Abraxane  
19 nanoparticle.

20 Q. How do you know?

21 A. I have looked at a number of different documents from  
22 Abraxis, documents that I have reviewed, experiments that I  
23 have reviewed. And all the documents that I have seen show  
24 that the surface of the Abraxane nanoparticle, the albumin  
25 that is on the surface, is substantially cross-linked.

Amiji - direct

1 Q. Let's discuss some of those. Dr. Amiji, could you  
2 turn to DX-107 in your binder.

3 Mr. Broyles, could you bring that up on the  
4 screen?

5 What are these documents?

6 A. This first one is a document from Abraxis. It  
7 specifically deals with a test that is called size exclusion  
8 chromatography. It is a fancy way of saying sieving  
9 experiment. The only difference between this type of  
10 experiment and a standard sieve is a sieve separates from a  
11 particle and basically gets out smaller particles. In this  
12 case, the larger particles get out first.

13 What you see at the bottom in the table is the  
14 composition of the albumin that is present. Here we see the  
15 polymer, having approximately 38.9 percent of the  
16 composition, the oligomer having 3.8 percent of the  
17 composition, and the dimer having 11.3 percent of the  
18 composition.

19 If you add the three numbers, the total  
20 composition of the cross-linked albumin is going to be about  
21 55 percent.

22 Q. Could you go back to the original screen.

23 When were these tests conducted?

24 A. These tests were conducted, it's in the upper part of  
25 the document, in January of 2003.

Amiji - direct

1 Q. Before this lawsuit?

2 A. Yes, they were conducted before this lawsuit.

3 Q. Let's bring up DD-104, which is based on DX-112.

4 What is this?

5 A. So here, again, we see the -- there are, in this table  
6 that you see in this slide, the monomer, dimer, oligomer,  
7 and polymer compositions from 17 different experiments that  
8 were done with different lots of Abraxane on different days,  
9 in certain cases, with triplicate or duplicate experiments.

10 All of them report the fact that there is a high  
11 degree of cross-linking in the albumin with an average at  
12 the bottom there showing about 55 percent of the  
13 surface-bound albumin on the nanoparticle being  
14 cross-linked.

15 Q. Did you investigate the nature of these bonds,  
16 Dr. Amiji?

17 A. Yes, I did.

18 Q. Let's turn to DX-76. Could you tell the jury what  
19 this is?

20 A. This is the lab notebook of an Abraxis investigator by  
21 the name of Voung Trieu. It's dated July 2007.

22 Q. If you could turn to Page 10 of the document, also  
23 Bates numbered 523594. Could you explain to the jury what  
24 sorts of tests are on this page?

25 A. This is an experiment that was done at Abraxis to

Amiji - direct

1 confirm the type of bond that's formed in these cross-linked  
2 albumins. What you see here is what we referred to in the  
3 protein chemistry art as polyacrylamide gel electrophoresis,  
4 abbreviation PAGE, P-A-G-E.

5 Basically, these gels are made from a polymer  
6 called polyacrylamide and proteins are then run in these  
7 gels to create various lanes.

8 So what you see are, in each of those, are the  
9 lanes of proteins, so 15, 17 and so forth. And the lane  
10 will have -- in this case, the lane is designated by this  
11 dye called coomassie blue or coomassie staining. That  
12 basically stains for the protein. It doesn't sustain the  
13 gel.

14 When these proteins are run, what you see in the  
15 non-reduced state, which is when the cross-linking still is  
16 in tact, is the fact that the protein has higher molecular  
17 weight. It's greater than the albumin control that you see  
18 down here.

19 All this on the top, the bands that you see on  
20 the top correspond to the higher molecular weight. Those  
21 are the cross-linked albumin.

22 When these same proteins are taken and run under  
23 reduced conditions, in this case, now, the disulfide bonds  
24 that form with these cross-links are intentionally broken  
25 with a chemical that breaks those bonds, and now we see that

Amiji - direct

1 the lane that these proteins migrate to is exactly the same  
2 as albumin.

3 So you are intentionally breaking the bond,  
4 using this disulfide bond breaking agent, and the reduced  
5 condition, to get the free albumin back.

6 So based on these results, it's clear that the  
7 bonds that are formed in these cross-linked albumin is by  
8 disulfide bonds.

9 Q. Is this a typical type of experiment to determine the  
10 presence of disulfide or covalent bonds?

11 A. Yes, it is. It is actually the standard test that's  
12 used to confirm disulfide bonding.

13 Q. Did you review the lab notebooks and other materials  
14 that were associated with these experiments?

15 A. Yes. So, again, as I looked into the lab notebook, at  
16 one part of the lab notebook, there was a standard operating  
17 procedure that was used, and I reviewed that standard  
18 operating procedure, and it's very characteristic of the  
19 experiments that I have done for these types of analyses.

20 Q. Were these experiments conducted well?

21 A. They are conducted extremely well. I was able to find  
22 all the information that I needed to make my interpretation  
23 and my analysis and my conclusions.

24 Q. Let's bring up DD-75, Mr. Broyles. This is from  
25 Defendant's Exhibit 107.

Amiji - direct

1           Have you reviewed any tests conducted by Elan or  
2 its experts regarding cross-linking?

3 A.     No. I have not seen a single test done by Elan or its  
4 expert in regard to the cross-linking Abraxane.

5 Q.     To the best of your knowledge, did any Elan expert  
6 conduct testing of cross-linking in Abraxane?

7 A.     No. I have not seen a single test from an Elan expert  
8 on cross-linking in Abraxane.

9 Q.     Were you here when Dr. Manning testified?

10 A.    Yes, I was.

11 Q.    Could you remind the jury who Dr. Manning was?

12 A.    Dr. Manning was an expert from Elan's side. He  
13 testified on this area of cross-linking. I believe he was  
14 on the faculty at the University of Colorado. Currently, he  
15 has his own company. I believe it is called Legacy  
16 BioDesigns.

17 Q.    Do you recall when Dr. Manning gave testimony  
18 regarding 15 to 20 percent cross-linking?

19 A.    Yes, I do.

20 Q.    What is the discrepancy between the number you were  
21 just talking about, 55 percent cross-linking, and the number  
22 he testified to, 20 percent?

23 A.    So he was talking about the entire Abraxane  
24 formulation. As we just heard a few minutes back from  
25 Dr. Desai, Abraxane has this free albumin and there is also

Amiji - direct

1 albumin that is on the surface of the nanoparticle.

2 When you look at the entire composition of  
3 Abraxane, there is about 20 percent cross-linking. However,  
4 when you look at the surface of the nanoparticle itself,  
5 it's actually got about five percent cross-linking.

6 Q. And which one is the relevant number for this  
7 analysis?

8 A. So the relevant number for this analysis is what's on  
9 the surface, because that's really what's in the claim of  
10 the '363 patent, how much of the surface modifier is on the  
11 surface of the nanoparticle.

12 Q. Let's go to JX-81, Claim 1. What is the language here  
13 that shows you the relevant amount?

14 A. If we look at the fifth line -- starting from the  
15 fourth line, it says, Non-Cross-Linked surface modifier  
16 adsorbed on the surface thereof.

17 What this refers to, clearly, in the claim  
18 language, that this is the surface of the nanoparticle.

19 Q. And have you reviewed any documents where Dr. Manning  
20 agrees with your analysis that the free albumin can be  
21 different than the absorbed albumin, for example?

22 A. Yes, I have. Actually, in review of various  
23 documents, I came across a chapter that Dr. Manning wrote  
24 that when the nanoparticle, or when you have surfaces, there  
25 is higher concentration of the protein on the surfaces, and



Amiji - direct

1 Dr. Manning clearly identified that on surface of various  
2 hydrophobic surfaces, there is greater concentration, and,  
3 therefore, you do have this cross-linking phenomenon.

4 Q. Mr. Broyles, can we bring up DD-115 on the screen, and  
5 the source of this is PX-493.

6 Is this the article that you were referring to?

7 A. Yes. This is Manning article from 1992. It is more  
8 than a thousand times more concentrated protein in the  
9 surface than on the bulk phase. Bulk refers to basically  
10 the free albumin.

11 Because the albumin concentrates significantly  
12 on the surface, there is a higher probability of formation  
13 of this cross-linking, and that is really what we observed  
14 with Abraxane.

15 Q. Did Dr. Manning contest your opinion that 55 percent  
16 albumin is cross-linked in the nanoparticles?

17 A. No. I haven't seen a single comment or any opinions  
18 from Dr. Manning that contests that.

19 Q. Did Dr. Manning review any Elan tests when he was  
20 giving his testimony?

21 A. No, I don't believe Elan did any tests.

22 Q. Did you also hear his testimony that Abraxane behaves  
23 like a non-cross-linked particle?

24 A. Yes, I did.

25 Q. Did you agree with his opinion?

Amiji - direct

1 A. Again, as we just heard a few minutes back, when you  
2 put Abraxane in the body, it dissociates very fast. Once it  
3 dissociates, the fact that these nanoparticles, and the  
4 disulfide bonds is not because you are putting a chemical  
5 in, it's formed because of the fact that there is inherent  
6 formation of these linkages in proteins, and that  
7 dissociates in the presence of blood. There is no  
8 discrepancy between the fact that albumin and Abraxane is  
9 able to go into blood very quickly and this idea that the  
10 surface is cross-linked.

11 Q. Bring up DD-75 again. In summary, Dr. Amiji, what is  
12 your opinion regarding cross-linking of the albumin on the  
13 surface of the Abraxane particles?

14 MR. SCHEVE: Objection to the form of the  
15 question, Your Honor.

16 THE COURT: Repeat the question.

17 BY MS. KRUZE:

18 Q. In summary, what is your opinion regarding  
19 cross-linking on the albumin on the surface of the Abraxane  
20 nanoparticles?

21 THE COURT: Form, you object to why?

22 MR. SCHEVE: There is a certain standard that  
23 has to be announced by the witness before the opinion  
24 becomes evidence or admissible as opposed to submittable.  
25 There has not been an appropriate question asked.

Amiji - direct

1 THE COURT: Let's go to sidebar.

2 (The following took place at sidebar.)

3 THE COURT: I think Mr. Scheve is going with  
4 this you need to ask the witness, Do you have an opinion to  
5 a reasonable degree of scientific certainty.

6 MR. SCHEVE: That's part of what is missing.

7 THE COURT: Where else are you going,  
8 Mr. Scheve?

9 MR. SCHEVE: There is a series of two or three  
10 questions there that she has to ask and she hasn't done it.  
11 I am objecting for the record.

12 MS. KRUZE: I am sorry. This is my first time  
13 with an expert.

14 (End of sidebar conference.)

15 BY MS. KRUZE:

16 Q. Do you have an opinion, to a reasonable degree of  
17 scientific certainty, regarding non-cross-linking?

18 A. Yes, I do.

19 Q. What is your opinion regarding cross-linking of the  
20 albumin on the Abraxane nanoparticles?

21 A. I believe based on all the studies that I have  
22 analyzed and looked at and the conclusion that I draw that  
23 the surface of the Abraxane nanoparticle has substantial  
24 cross-linking of albumin.

25 Q. Let's turn to -- actually, one more question. Do you

Amiji - direct

1 have an opinion regarding the nature of those cross-links to  
2 a reasonable degree of scientific certainty?

3 A. Yes, I do. I believe that the nature of the  
4 cross-linking in the Abraxane nanoparticle surface is  
5 through that disulfide bond.

6 Q. Let's turn to crystallinity. Could you turn to  
7 DDX-15. Could you tell the jury what this is?

8 A. Again here, we are looking at different comments from  
9 the patent abstract, the patent itself, the '363 patent.

10 Here, the patent, itself, distinguishes, that it  
11 is for crystalline anticancer agent. And crystalline phase  
12 differs from the amorphous phase.

13 Q. This comes from JX-81, for the record.

14 Dr. Amiji, is an amorphous drug equivalent to a  
15 crystalline drug?

16 A. No, it is not. Amorphous drug is exactly the opposite  
17 of a crystalline drug.

18 Q. Can you bring up DD-84, Mr. Broyles.

19 What are some of the differences between a  
20 crystalline and amorphous drug?

21 A. Here, we have seen this before, when the molecules are  
22 packed in a crystal, you have this very nice order of  
23 packing of molecules; whereas, in amorphous, you don't have  
24 that nice packing that we observe in crystalline.

25 This occurs because of the fact this packing

Amiji - direct

1 order leads to --

2 MR. SCHEVE: Your Honor, I thought we were  
3 limited to one expert each per issue in the lawsuit. This  
4 is clearly testimony that's already been covered by a  
5 previous expert for Abraxis.

6 MS. KRUZE: Your Honor, he is going to be  
7 covering different issues, including the biology of these  
8 differences.

9 THE COURT: So, Mr. Scheve objects that this is  
10 a re-do of previous expert testimony.

11 MR. SCHEVE: This was used with Dr. Atwood. I  
12 only object because I am of the impression I am limited to  
13 one witness per topic.

14 THE COURT: You are.

15 MS. KRUZE: I will be happy to switch to the  
16 functional differences. This is more background.

17 THE COURT: We have enough background.

18 BY MS. KRUZE:

19 Q. Let's go to DD-76.

20 Do crystalline solids function differently than  
21 amorphous solids in pharmaceutical compositions?

22 A. Yes, they do. Crystalline solids dissolve a lot  
23 slower than amorphous solids. Amorphous solids dissolve a  
24 lot faster. I believe we have heard the analogy many times  
25 between cotton candy and rock candy.

Amiji - direct

1 Q. Let's go to DD-77. How do these differences in  
2 dissolution affect the performance of an anticancer drug?

3 A. When you have a crystalline drug, the fact that the  
4 crystalline drug would circulate in the bloodstream with, it  
5 would not resolve, it would still remain as a crystal. But  
6 in the case of an amorphous drug, like Abraxane, it  
7 dissolves very fast, and that dissolved drug is able to be  
8 carried by blood into the tumor. It is really the  
9 dissolved, the molecular form of the drug that gets into the  
10 cell. And that's the one that's therapeutically most  
11 effective.

12 Q. Are there any scientific treatises that agree with you  
13 about this difference between crystalline and amorphous drug  
14 in anticancer pharmaceutical compositions?

15 A. Yes. One of the classic scientific treatises that we  
16 use in pharmaceutical science is the Remington's. It is  
17 sort of considered to be the authority in the area of  
18 pharmaceutical science.

19 If you look at Remington's, there is clearly a  
20 passage that differentiates amorphous and crystalline drugs  
21 that says amorphous has higher solubility and also higher  
22 bioavailability.

23 Q. Could you pull up DD-78, Mr. Broyles.

24 This is based on DX-407.

25 Is this the article that you were referring to?

Amiji - direct

1 A. Yes. Here is a passage from Remington's, Amorphous  
2 versus Crystalline. Clearly, the crystalline state of  
3 hydration and polymorphic structure -- this is when you have  
4 different crystalline structures -- have been shown to have  
5 a significant influence on the dissolution rate.  
6 Investigators Mullin and Macek showed that this drug,  
7 novobiocin, has higher solubility, higher dissolution rate.  
8 The dissolution rate is basically a measure of how fast  
9 something dissolves than the crystalline form.

10 Additionally, the blood levels, this is an  
11 indicator of the bioavailability because now you are seeing  
12 how much drug is in the blood, is three to four times more  
13 in the amorphous form as compared to the crystalline form.

14 Q. At the bottom of the slide, that was also observed in  
15 four other compounds?

16 A. Yes. Here we can see that it's not a drug dependent  
17 -- it is not dependent on novobiocin. It's actually  
18 independent of the type of chemical. As long as you have  
19 these differences between crystallinity and amorphousness,  
20 it really doesn't matter which drug it is.

21 Q. Mr. Broyles, can you switch to DD-113. This is based  
22 on 627.

23 Are there any Elan experts that agree with your  
24 opinion?

25 A. Yes, here is one of the articles from Dr. Munson.

Amiji - direct

1 Dr. Munson was an expert from Elan. He also agrees that  
2 amorphous state has a higher dissolution rate, higher  
3 solubility than does the crystalline state.

4 Q. Let's switch to DD-79. Is there anything in the '363  
5 patent that teaches that the inventors believed that their  
6 invention had prolonged circulation in the blood pool?

7 A. Yes. There are two places in the '363 patent that  
8 mentions this issue of prolonged circulation.

9 It is clear that crystalline drug will have  
10 prolonged circulation in the blood pool after IV or  
11 intravenous injection in the blood. Similarly here, we see  
12 prolonged circulation in the blood pool.

13 Q. Are these statements consistent with an amorphous drug  
14 like Abraxane?

15 A. No, they are not. A drug like Abraxane or amorphous  
16 drug like Abraxane would dissolve very quickly and it would  
17 then be available at the tumor site much more rapidly.

18 Q. Are you familiar with Dr. Danishefsky's testimony?

19 A. Yes, I am. I wasn't here physically for his  
20 testimony. But I read the transcript of the testimony.

21 Q. Could you remind the jury who Dr. Danishefsky is?

22 A. Dr. Danishefsky is a professor, I believe at Memorial  
23 Sloan Kettering Institute in New York.

24 Q. Did you hear Dr. Danishefsky disagree with anything  
25 that you said today on these differences?



Amiji - direct

1 A. No. I don't believe -- from the testimony that I  
2 read, I don't believe there was anything that he disagreed  
3 on.

4 Q. Are you aware of any statements made by Elan that  
5 confirm your understanding of these differences between  
6 crystallinity and amorphousness?

7 A. Yes. I have seen several of the reports in this  
8 trial, and in various parts by looking at all the evidence,  
9 that there has been comments about this.

10 Q. Mr. Broyles, can you bring up DD-80.

11 Dr. Amiji, can you explain to the jury what this  
12 is?

13 A. So here are some of those comments. We see the first  
14 one is that e-mail from -- excuse me, a memo from Glenn  
15 Portmann to Dr. Gary Liversidge. He clearly says, Amorphous  
16 state has been known to have enhanced bioavailability. This  
17 is the measure of how much drug that's going to be available  
18 at the disease site.

19 Distinct from particle size considerations, as  
20 you are well-aware, and then it says, Amorphous form usually  
21 possesses higher thermodynamic energy. This just means that  
22 they are in the unstable state than the crystalline  
23 counterparts resulting in solubilities and dissolution rates  
24 of much higher magnitude.

25 They also go on to say, in the '684 patent file

Amiji - direct

1 history, that amorphous forms are highly unstable. But this  
2 is true of only the drug itself, not when it's in the  
3 formulation, like Abraxane.

4 And then crystalline particles exhibit improved  
5 stability. In itself, this is a true statement. Amorphous  
6 materials tend to have exhibited unacceptable or poor  
7 stability and/or short shelf life.

8 Q. When the Elan scientists were making these statements,  
9 were they making them in the context of nano-sized drugs?

10 A. Yes. In the case of the '684 patent file history as  
11 well as the '363 file history, these are both dealing with  
12 nano-sized drugs.

13 Q. Do you have an opinion, to a reasonable degree of  
14 scientific certainty, as the equivalency between crystalline  
15 and amorphous drugs?

16 A. Yes, I do.

17 Q. Based on the list you have reviewed, are crystalline  
18 and amorphous drugs equivalent?

19 A. No, they are not. Amorphous drugs are exactly the  
20 opposite of crystalline.

21 Q. Would scientists in the field have considered Abraxane  
22 to have been interchangeable with the crystalline drug  
23 claimed in the '363 patent?

24 MR. SCHEVE: Objection. There is no foundation,  
25 Your Honor.

Amiji - direct

1 BY MS. KRUZE:

2 Q. Based on the evidence that you have reviewed,  
3 Dr. Amiji, would the amorphous drug in Abraxane be  
4 interchangeable with a crystalline drug?

5 A. No, it wouldn't be.

6 Q. Let's talk about drug surface modifier combinations.

7 Do you have any testimony, Dr. Amiji, relevant  
8 to whether the claims are enabled?

9 A. Yes, I do.

10 Q. Is this testimony also relevant to whether the claims  
11 are invalid?

12 A. Yes.

13 Q. Let's turn to DD-88. This is from JX-81.

14 What types of drugs do the '363 claims cover?

15 A. So the '363 patent, the Claim 1 of the '363 patent  
16 covers drugs that are anticancer and having solubility of  
17 less than ten milligrams per ml. And then specifically  
18 going into various classes such as alkylating agents, with  
19 these group of alkylating agents, drugs like vinca  
20 alkaloids. There are also antibiotics, like daunomycine and  
21 bleomycin, and then going into biological response  
22 modifiers. We talked about Taxol. There is also hormones,  
23 radiosensitizers, platinum compounds. Those are in Claim 1.

24 In Claim 5, it's limited to eight different  
25 drugs: Puposulfan, puposulfam, camptothecin, etoposide,

Amiji - direct

1 Taxol, these triazine derivatives and retinoic acids.

2 Q. How many drugs are in these claims, approximately?

3 A. For Claim 1, there is a large number of drugs, because  
4 these deals with classes of compounds, and not necessarily a  
5 single drug. For instance, an enzyme, there could be a  
6 large number of enzymes. Enzyme is a class. It is not a  
7 single drug. Biological response modifier, again, it's a  
8 class of drugs, it's not a single agent.

9 Radiosensitizers, again, it's a class of  
10 compounds.

11 And so you have hundreds of compounds in Claim  
12 1.

13 In Claim 5, it is limited to eight compounds.

14 Q. Do all these drugs have the same structural and  
15 chemical characteristics?

16 A. No, they don't. So an enzyme, for instance, could be  
17 a protein; whereas, you know, platinum compound is something  
18 that has platinum in it. So these are very different from  
19 each other.

20 Q. Let's pull up DD-89, which is also from JX-81.

21 Turning to the surface modifier portion of the  
22 claim, what sort of surface modifiers does the patent cover?

23 A. The patent covers any non-cross-linked surface  
24 modifier. The list goes on. For instance, in this case, we  
25 see both the pages having this list of surface modifier.

Amiji - direct

1 Q. Let's pull up JX-81 at the end of Column 3 to 4.  
2 Starting at the last paragraph, then going all the way down  
3 until I think about Line 60.

4 How many surface modifiers, approximately, are  
5 called out by the patent?

6 A. Here we can see, in both of these columns, there is a  
7 large number of surface modifiers, just absolutely  
8 significantly large, because some of these are actually  
9 classes of surface modifiers. For instance, we are looking  
10 at anionic surfactant, and that would be a class of surface  
11 modifiers. And each of these classes would have a large  
12 number of individual surface modifiers.

13 If we focus on the second, on Column 4, from the  
14 top, again, we see classes of surface modifiers. For  
15 instance, fourth line from the top is a surface modifier  
16 called polyoxyethylene castor oil derivatives. That is the  
17 Cremophor that we heard of. Again, it is a class of surface  
18 modifier.

19 There is Tweens. Again, that's a class of  
20 surface modifier. Again, there is a large number of  
21 Tweens -- there is specific types of Tweens that are part of  
22 that class.

23 Q. And do all of these surface modifiers have the same  
24 chemical and structural characteristics?

25 A. No, they don't. They are very different. For

Amiji - direct

1 instance, again, looking at gelatin is a protein. Whereas  
2 stearic acid is just a fatty acid. Whereas tragacanth is a  
3 polysaccharide or made from various sugars. Cholesterol is,  
4 again, another type. If you go here, the synthetic  
5 materials, like Tween, and there are also natural surface  
6 modifiers. So they are very different from each other.

7 Q. Are there any surface modifiers in this list that  
8 surprise you in terms of a pharmaceutical formulation?

9 A. Yes.

10 MR. SCHEVE: Objection, Your Honor. The word  
11 "surprise" is without foundation.

12 THE COURT: Do you want to rephrase that?

13 MS. KRUZE: Certainly.

14 BY MS. KRUZE:

15 Q. Are there any surface modifiers that would be toxic to  
16 use in a pharmaceutical composition?

17 A. Yes. Looking at Column 4, at the top, we see  
18 polyoxyethylene castor oil derivatives. And I remember in  
19 this trial testimony here, we talked about the fact that  
20 Bristol Myers Squibb's Taxol product has this Cremophor  
21 inside. This is exactly the same. Polyoxyethylene is  
22 Cremophor. Seeing something like this is very surprising.  
23 Coming down the list is colloidal silicon dioxide. That is  
24 a fancy name for sand. I can't imagine anybody with cancer  
25 getting sand in their body.

Amiji - direct

1           Coming down the list, we see something called  
2 phosphates. Again, what type of phosphates? There are so  
3 many different types of phosphates. One wonders what kind  
4 of phosphate is claimed in the '363 patent.

5           Then, going down the list, in the area of what  
6 is called particularly preferred surfactant or surface  
7 modifier, you see this interesting chemical called Triton X,  
8 and Triton X is actually a product that's used in  
9 laboratories, we use this in our laboratory to break apart  
10 cells. So seeing that being put in a patent composition for  
11 anticancer drug was very surprising.

12 Q.     Let's go to DD-92. You testified that the patent  
13 covers these crystalline drugs and any surface modifier.

14           How many sorts of combinations are we talking  
15 about here?

16 A.     From Claim 1, we saw that there were a significant  
17 number of drugs. Claim 5 restricted to about eight drugs.  
18 Any of the surface modifier that we just talked about could  
19 be in any of these -- can be mixed with any anticancer drug.

20           Then you have this ratio of drug to surface  
21 modifier that is also in Claim 1, which is also in other  
22 claims of the '363 patent.

23           So there are millions and millions of  
24 possibilities. It's like looking at a product that -- or a  
25 food product that you do, you go to one grocery store to buy

Amiji - direct

1 one product and another grocery store to buy another  
2 product, and saying, you know, you can make a dish out of  
3 that. It is just impossible to really imagine how many  
4 possible combinations exist here.

5 Q. Looking and turning back to the patent, which is  
6 JX-81, would a scientist have known whether any given  
7 combination would work?

8 A. No, they would not know that.

9 Q. And does the patent specification tell a scientist  
10 which surface modifiers will work?

11 A. No, it doesn't.

12 Q. What kinds, if any, does the patent give a scientist?

13 A. There is, in the patent, what is called a simple  
14 screening test.

15 Q. Let's go to DD-103.

16 Is this the screening method you are referring  
17 to?

18 A. Yes. Here in the patent, there is this simple  
19 screening test, which says that you take this combination,  
20 which, you know, you basically choose from the drug itself,  
21 from the surface modifier, the list that was previously  
22 shown, and you take the two, and whatever ratio, you have to  
23 figure out yourself what the ratio is, and then you mill  
24 that or grind that for 120 hours. After it's been ground,  
25 you take that product and look at it under naked eye for 15



Amiji - direct

1 minutes for up to two days or with a microscope.

2 Q. From this procedure, how would you know which surface  
3 modifiers to try?

4 A. You wouldn't. You would have to basically do a trial  
5 and error.

6 Q. And is there any indication of which drugs to try?

7 A. No. Again, there is no indication of which drugs to  
8 try. It is basically any drug that is listed in the claims,  
9 as well as any surface modifier that's non-cross-linked and  
10 listed in the specification.

11 Q. You mentioned 120 hours. Is that to mill one  
12 combination?

13 A. Yes. So this would be for one combination would be  
14 milling for 120 hours, for more than five days.

15 Q. How long would it take someone to try out all the  
16 combinations that are covered by the '363 patent?

17 A. It's almost impossible to say, because you are looking  
18 at 120 hours for one, and there is so many possible  
19 combinations, it would be more than our lifetime.

20 Q. Claims 10 and 11, if we could go briefly there.

21 What do these cover?

22 A. Claim 10 covers the method of treating a mammal  
23 comprising of this product from Claim 1 in an effective  
24 amount of anticancer agent where the efficacy is increased.

25 And Claim 11 is where the same product is

Amiji - direct

1 administered to a mammal where the toxicity is reduced.

2 Q. Let's go back to DD-103.

3 Is there any way you can tell from this  
4 screening method whether something is going to be effective  
5 or non-toxic?

6 A. No, you can't. There is nothing in this screening  
7 method that will say anything related to the safety and  
8 efficacy of the final product.

9 Q. Stability to the naked eye, what sort of end point is  
10 that for a pharmaceutical product?

11 A. It's a very trivial end point, because when you are  
12 dealing with pharmaceutical products, you want to make sure  
13 they are stable for a long period of time. Up to 15 minutes  
14 to the naked eye, especially with nanoparticle formulation,  
15 these are very, very small particles, you can't see them  
16 with the naked eye or even with the microscope.

17 Q. To a scientist, does this screening method amount to  
18 extensive experimentation?

19 A. Yes, it does. Because you are basically grinding  
20 something for 120 hours and then you are looking at it for  
21 15 minutes, and you are trying to see if it is actually  
22 going to be a product that is going to be used. I think it  
23 doesn't work that way.

24 Q. And have you reviewed documents where Elan, itself,  
25 has admitted that doing these combinations requires

Amiji - direct

1 extensive experimentation?

2 A. Yes, I have.

3 Q. Let's pull up DD-105.

4 Are these some of the comments that you were  
5 thinking of?

6 A. That's correct. So looking back from '92, not all  
7 surface stabilizers will function to stabilize all active  
8 agents.

9 December of '93, this document says, Few  
10 surfactants meet the criteria necessary for a successful  
11 drug formulation.

12 In '94, there is no surfactant of choice for  
13 parenteral or this drug that is administered into the  
14 bloodstream. In 2003, the choice of a surface stabilizer is  
15 not trivial and usually requires extensive experimentation.

16 Then again in 2007, the art of formulating drugs  
17 into nanoparticles is highly unpredictable.

18 Q. And the source of those quotes is DX-490, DX-327,  
19 DX-528 and DX-607.

20 Let's go to the next slide, which is DD-93, the  
21 source for that is DX-544.

22 Is this another Elan statement regarding the  
23 extensive experiments required?

24 A. Yes. Here is another patent from Elan, which is filed  
25 in 2003, and it says clearly in this patent that the choice

Amiji - direct

1 of surface stabilizer is non-trivial and requires extensive  
2 experimentation to realize a desirable formulation.

3 Q. The patent also talks about examples. Correct?

4 A. Yes, it does.

5 Q. And how many different drugs did the patent examples  
6 cover?

7 A. I believe there are about six different drugs in the  
8 patent examples.

9 Q. How many different surface modifiers are shown in the  
10 patent examples?

11 A. There are about 12 different surface modifiers shown  
12 in the examples.

13 Q. Given your earlier testimony about the breadth of the  
14 combinations that the claim covers, what sort of a  
15 percentage of the coverage is that of the examples?

16 A. It is a very small percentage. It is actually  
17 minuscule, compared to the possibilities. You see the list  
18 of surface modifiers, and in that list is a class of surface  
19 modifiers. You also see on the left side all the different  
20 anticancer drugs. So 20 is a very, very small percentage.

21 Q. Do these the examples contain any failures?

22 A. No, they do not.

23 Q. Dr. Amiji, did you review any Elan internal documents  
24 regarding Elan's efforts to make NanoCrystal formulations?

25 A. Yes, I did. I reviewed a large number of documents.

Amiji - direct

1 Q. Let's turn to Defendant's Exhibit 193.

2 Could you please explain to the jury what this  
3 document is?

4 A. So here is one of the documents that I reviewed. It's  
5 a presentation on a drug called piposulfan, which is an  
6 anticancer drug belonging to the class of the alkaloid. And  
7 it's dated August of '93.

8 Q. Could you turn to Bates No. 10921.

9 Would you confirm that this is a memo dated May  
10 1992 to Pramod Sarptodar?

11 A. It is a memo to Pramod Sarptodar.

12 Q. Is Pramod Sarptodar an inventor of the '363 patent?

13 A. Yes, he is.

14 Q. Dr. Amiji, did you compare this document with the  
15 patent?

16 A. Yes, I did.

17 Q. Let's see if we can pull up the comparison.

18 Did this document supply some of the data that  
19 went into the '363 patent?

20 A. Yes, it did. Specifically, in Example 2 and 4, the  
21 use of this surfactant called Tween 80 and Span 80 came from  
22 this document.

23 Q. Did Elan disclose all of the information that came  
24 from this document?

25 A. No, it did not.

Amiji - direct

1 Q. Let's do an example. Say, for example, Tween 80,  
2 which is the top one, that is a surface modifier. Is that  
3 correct?

4 A. That's correct, yes. Tween 80 is a surface modifier.

5 Q. What is the size that Elan got with Tween 80?

6 A. With Tween 80, they got a size of 3,000 nanometer.  
7 That is three times the 1,000 nanometer limit from Claim 1  
8 of the '363 patent.

9 Q. But Elan doesn't disclose that failed experiment to  
10 the Patent Office?

11 A. That's correct.

12 Q. Let's go back to the last page of the document, which  
13 is DX-193.

14 Could you please read the second line for the  
15 jury?

16 A. The second line in the conclusion section, it says,  
17 "Combination of Tween 20/Span 20 and Tween 40/Span 40 failed  
18 to reduce the average particle size below 400 nanometer."

19 Q. And did Elan disclose that information to the Patent  
20 Office?

21 A. No. I don't believe Elan disclosed that to the Patent  
22 Office.

23 Q. But these were the same tests that were under the  
24 examples for pipsulfan listed in the patent?

25 A. That's correct, yes.

Amiji - direct

1 Q. Did you review any other documents regarding Elan's  
2 efforts to make a piposulfan, a NanoCrystal piposulfan?

3 A. Yes, I did review a lot of other documents.

4 Q. Let's go to DD-106?

5 THE COURT: Counsel, I think we are going to  
6 have to leave it there.

7 Ladies and gentlemen, we have come to the end of  
8 our day. Travel safely. We will see you back here at 9:00  
9 a.m. tomorrow morning.

10 (Jury leaves courtroom at 4:02 p.m.)

11 THE COURT: Counsel, where are we with the jury  
12 instructions and the verdict form?

13 MR. SULLIVAN: Your Honor, if I may, we have  
14 prepared both examples with objections and law and also what  
15 we understood the Court's preference, also clean copies that  
16 really just present either undisputed or in some cases  
17 disputed instructions, very clean.

18 Also, each side has its own verdict form and we  
19 are prepared to pass these up, if we may.

20 THE COURT: You have not been able to merge your  
21 discussions with regard to the verdict form?

22 MR. SULLIVAN: We tried. It became pretty  
23 apparent last night that there was a divergence of at least  
24 a couple of points.

25 On the jury instructions, I will note for Your

Amiji - direct

1 Honor that there has been significant progress, up to and  
2 including last night. I hope the Court will be pleased to  
3 see a lot of undisputed instructions.

4 THE COURT: The Court is always pleased to see  
5 undisputed instructions.

6 The rest of counsel is excused. We are done for  
7 the day.

8 MR. WALTERS: Your Honor, we seem to be short  
9 one form of our verdict form, which we will send a messenger  
10 right over.

11 THE COURT: You can just give Ms. Walker what  
12 you have.

13 MR. WALTERS: Okay.

14 (Court recessed.)

15 (Reporter: Kevin Maurer)

16

17

18

19

20

21

22

23

24

25