FEDERAL TRADE COMMISSION

I N D E X

IN RE POM WONDERFUL LLC, ET AL.

TRIAL VOLUME 12

PUBLIC RECORD

AUGUST 31, 2011


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UNITED STATES OF AMERICA

BEFORE THE FEDERAL TRADE COMMISSION

| | | |
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| In the Matter of | ) | |
| | ) | |
| POM WONDERFUL LLC and | ) | |
| ROLL GLOBAL LLC, | ) | |
| as successor in interest to | ) | |
| Roll International Corporation, | ) | |
| companies, and | ) | Docket No. 9344 |
| STEWART A. RESNICK, | ) | |
| LYNDA RAE RESNICK, and | ) | |
| MATTHEW TUPPER, individually | ) | |
| and as officers of the | ) | |
| companies. | ) | |
| | ) | |
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Wednesday, August 31, 2011

9:34 a.m.

TRIAL VOLUME 12

PUBLIC RECORD

BEFORE THE HONORABLE D. MICHAEL CHAPPELL

Administrative Law Judge

Federal Trade Commission

600 Pennsylvania Avenue, N.W.

Washington, D.C.

Reported by: Josett F. Whalen, RMR-CRR

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P R O C E E D I N G S

- - - - -

JUDGE CHAPPELL: Back on the record Docket 9344.

MS. EVANS: Good morning, Your Honor.

JUDGE CHAPPELL: Good morning.

MS. EVANS: One procedural matter initially.

I understand that Dr. Miller, who is going to testify next, is in the room. And as his testimony addresses some of the same subjects as Dr. Heber's testimony as pertains, for example, to standards of evidence, I would request that he be excused from the room until Dr. Heber's testimony is completed.

MR. FIELDS: Well, we didn't follow that procedure with their witnesses, Your Honor, but we have no objection to that if there's a place to sit down out there for Dr. Miller.

JUDGE CHAPPELL: So you're invoking the rule at this point?

MS. EVANS: Yes, sir. I don't believe that any of our expert witnesses observed the expert testimony of any of our other expert witnesses while they were testifying.

JUDGE CHAPPELL: Well, the rule generally doesn't apply to experts, but since there's no objection, your request is granted.

MS. EVANS: Thank you, sir.

JUDGE CHAPPELL: And Ironsides can find a place --

MR. GRAUBERT: Excuse me, Your Honor. I'll take him upstairs.

JUDGE CHAPPELL: Thank you.

- - - - -

Whereupon --

DAVID HEBER, M.D.

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

CROSS-EXAMINATION (resumed)

BY MS. EVANS:

Q. Good morning, Dr. Heber. How are you doing today?

A. Good morning.

Q. When we left off last night, we were discussing the fact that you had participated in representatives (sic) of respondents with regard to cardiovascular research; correct?

A. Yes.

Q. And these meetings would include Mr. Resnick on occasion, Mr. Tupper, Mr. Dreher, Dr. Kessler and other scientists and sometimes other experts in heart disease

or who had conducted heart disease research?

A. And also clinicians who were unconnected with any of the Resnicks' research to look at this area. Yes.

Q. Thank you.

And then you attended the POM summit most years?

A. Yes.

Q. And for example, you had told me during your deposition that you had seen Dr. Gerdi Weidner's presentations on Dr. Ornish's research?

A. One more time, please.

Q. I'm sorry.

I believe that you told me during your deposition that you had, for example, seen Dr. Gerdi Weidner's presentations on Dr. Ornish's research?

A. Yes.

Q. And you also had discussions with regard to Dr. Davidson's research with Dr. Dreher and later with Mr. Tupper and Mr. Resnick?

A. Yes.

Q. And you stated, did you not, that Mr. Resnick was speaking to the group of scientists --

(Admonition from the court reporter.)

BY MS. EVANS:

Q. And you stated that Mr. Resnick was looking to the group of scientists to tell him what did this study mean, referring to Dr. Davidson's study?

A. I believe that was in the context of your question about determining whether the research should be published, and I responded that the scientists discussed the science, and it was decided to allow the peer review process to proceed, that is, that the research would be submitted to other scientists and have them judge the competence of the science.

Q. And you testified that there was not --

MR. FIELDS: Could we have a page and line, Your Honor.

MS. EVANS: Oh, I'm sorry.

BY MS. EVANS:

Q. I'm sorry. Turning to page 201 of your deposition testimony in January of 2008, I asked you the question (as read): Did you have the impression from the conversations that were ongoing between the time Dr. Dreher -- the Davidson data was first --

(Admonition from the court reporter.)

BY MS. EVANS:

Q. "QUESTION (as read): Did you have the impression from the time -- from the conversations that

were ongoing between the time the Davidson data was first produced and the time it was ultimately decided to submit it for publication that Stewart Resnick had expressed the view that he didn't want that data in the public domain?

"ANSWER: Not to my recollection. I -- I always felt that we were trying to just get the truth about these results whether they were positive or negative. And I think Stewart was looking to the group of scientists to tell him what does this mean."

Now, indeed there was no general agreement among the group of scientists advising the respondents what the Davidson study meant, was there?

A. There was discussion. And as I indicated yesterday, the IMT measurement is a very difficult one, and this was an area that was discussed. But Dr. Davidson was very positive about his results in the IMT -- he is an expert in IMT -- and especially with regard to the subgroup analysis that was conducted.

And so this was -- you know, since there are other people in the cardiology community who are scientists who could judge the research, it was decided that for the people in the room that we didn't represent the full group of people that would look at this science, and so it was decided to then not only enlist

the outside group that we had enlisted for that purpose but to also then submit it to unrelated scientists in the field and let them judge the worthiness of the science, and they ultimately decided it should be published.

Q. Okay. The question I asked you was: There was not general agreement among the group of scientists advising the respondents about what the Davidson study meant, was there?

A. Not -- I wouldn't put it that way.

Q. There was --

A. That's stated incorrectly.

Q. At your deposition, on page 201 at line 21, you said (as read): "And since there was not general agreement among the group of scientists about this whole thing..."

A. Well, when I say that --

Q. There's no question pending.

Now --

MR. FIELDS: Your Honor, could we have the entire answer read rather than just part of it. I don't mean that there's anything improper about what was read, but we should have the whole answer read.

BY MS. EVANS:

Q. So the full answer was (as read): "And since

there was not general agreement among the group of scientists about this whole thing, they decided let's submit it to peer review."

Now, you attended two or three other meetings that looked at health claims assessments, human health claims assessments; correct?

A. Yes.

Q. And the meeting in 2008, for example, discussed -- could you bring up document CX 0959.

It's up.

Do you have that before you?

MR. GRAUBERT: Yes, we do.

BY MS. EVANS:

Q. And -- is that correct?

A. That's correct.

Q. Okay. And who attended those -- these meetings?

A. Dr. David Kessler, myself, Stewart Resnick and Matt Tupper and Mark Dreher.

Q. And the purpose of these meetings was to consider whether respondents' research was sufficient to get an FDA-approved health claim for pomegranate as an aspect of a healthy diet?

A. That's correct. But it was primarily to provide Dr. Kessler, as a former commissioner of the

FDA, with an opportunity to look at all of the research. And I was there really in the purpose of again as a scientific adviser to interpret the science. I did not hold myself out as the expert in that particular area. That was why Dr. Kessler was there.

Q. And now, you've previously testified that you're familiar with the FDA health claims rules; correct?

A. Where is that testimony? I don't recall that.

Q. If you could refer to -- can you bring this up -- PX 0353-A-12 at page 8.

MR. FIELDS: Is that deposition testimony?

Excuse me, Your Honor. Could we find out if that is in a deposition or a transcript or what.

BY MS. EVANS:

Q. And this was -- do you recall testifying in the matter of POM Wonderful versus Purely Juice on or about April 15, 2008?

MR. FIELDS: Again, Your Honor, may we have a page and line of the exact deposition we're talking about so we can read along with counsel.

JUDGE CHAPPELL: Right. You need to do that so they can follow along.

MS. EVANS: Yes, sir.

BY MS. EVANS:

Q. And turning to -- on the -- it's marked as exhibit page 8 at the bottom and it's page 202 of the actual transcript. I'm referring to line 20.

Did you testify there that you're familiar with the FDA health claim rules?

A. Could you just clarify for me, because I'm looking at the total context of my testimony, what is my answer on the next page after line 25.

Q. Well, first --

A. Because it says, "Am I drawing a legal conclusion?" Because that's an important distinction.

Q. Yes.

A. I am in many meetings.

Q. I'm first asking you what you testified.

Did you testify: It's a law that I'm familiar with on health claims --

A. Yes. But --

Q. -- because I have spent a good deal of time on discussions of what's necessary to obtain an FDA-approved health claim, and it's a considerable amount of work? You did testify to that?

A. Yes. But those discussions are with other scientists at scientific society meetings where there are general discussions of how, for example, you know,

randomized, controlled trials might or might not apply to nutritional substances and to nutrients.

Q. Well, these are the rules regarding food health claims; correct?

A. Well, in particular here I'm testifying and actually have to correct myself because I'm talking about a two-click rule and now, in further knowledge of reading in this area, I understand there is no such real rule as a two-click rule.

Q. But that is what you testified: I'm familiar with health claims because I have spent --

A. But I'm not a legal expert.

Q. -- on discussions of what's necessary to obtain an FDA-approved health claim, and it's a considerable amount of work; correct?

A. That is my general knowledge as a scientist, not as a lawyer --

Q. Yes. I'm not asking you --

A. -- certainly not as an FDA lawyer.

Q. But that was your testimony at that time.

A. That testimony, I stand by that testimony.

Q. Thank you.

Now, you were talking about the two or three meetings that looked at health claims assessments a moment ago.

What was the consensus of these meetings with regard to whether or not POM had -- respondents had sufficient evidence to get an FDA-approved health claim for pomegranate as an aspect of a healthy diet?

A. They -- I think that -- that in those meetings, you know, Dr. Kessler stated some opinions, and I can't recall exactly what he said.

Q. Well, what were the types of health claims you were -- that respondents were discussing seeking approval for?

A. Well, the reason for the discussions was that Mr. Resnick and, for example, the case that you pulled up my deposition is there were a number of manufacturers claiming to make pomegranate juice that was in fact adulterated or not real pomegranate --

MS. EVANS: Excuse me. I move to strike as that is not responsive.

THE WITNESS: I'm trying to be responsive because here the point is that the reason for the FDA was not to get a health claim for a drug approval, it was to differentiate the pomegranate juice which is also just pomegranate juice made by other manufacturers, not just POM Wonderful.

BY MS. EVANS:

Q. Did you --

A. And that is responsive to your question.

JUDGE CHAPPELL: By the way, you made a motion and then you just kept rolling.

MS. EVANS: Oh, I'm sorry, sir.

JUDGE CHAPPELL: Based on the open-ended question, I'm allowing his response. Your request is denied.

BY MS. EVANS:

Q. Okay. Did you discuss seeking approval at these meetings for a reduced risk of cardiovascular disease for POM Wonderful pomegranate juice?

A. I did not personally discuss that. There were discussions that Dr. Kessler made comments on. I was there to provide scientific advice.

Q. Well, after these meetings, were you aware of respondents seeking an FDA approval for a health claim for pomegranate juice?

A. I am not aware of that.

I did become aware, after Mr. Gillespie joined as the new scientific director, that an IND was put in, which is a permission for investigation of pomegranate X, and this was needed for the studies done at Johns Hopkins. But that's all secondary knowledge. That's not anything that I had primary knowledge of.

Q. Thank you.

Now, you also listed in by phone -- that is, listened in by phone on a May 12, 2000 (sic) meeting with regard to a cardiovascular research review?

A. That's correct.

Q. And -- excuse me.

Moving back to Dr. Kessler's discussions, what did he say with regard to and what did -- excuse me -- what did you hear discussed by Dr. Kessler with regard to food health claims?

A. He did not discuss that. Dr. Kessler was talking strictly about drug approval claims. He did not talk about a food claim.

Q. Now, the meeting that was attended on May 12, 2009 with regard to the cardiovascular research review, that meeting was attended by a number of outside experts, such as P.K. Shah and Gregg Fonarow and Sam Tsimikas?

A. That's correct.

Q. And it was intended to be an independent review of the respondents' cardiovascular research?

A. That's correct.

Q. Okay. Now, we discussed a moment ago that you're familiar with the FDA's rules for food health claims; correct?

A. Food health claims. We were talking about --

that wasn't the earlier question. I have general knowledge of food health claims, yes.

Q. Thank you.

And FDA requires significant scientific agreement to make an unqualified health claim for a food; correct?

A. There are -- there is an established health claim process within FDA with which I'm familiar. There are a very limited number of health claims generally issued for large food categories, such as fiber, protein, carbohydrate, saturated and unsaturated fat, and those limited health claims are for those nutrients when they're included in processed foods, et cetera.

For fruits and vegetables, they meet a large number of the existing food health claims already by virtue of being a fruit. They're rich sources of potassium, et cetera, et cetera, so that I am familiar with that.

MS. EVANS: I would move to strike that that was not responsive.

JUDGE CHAPPELL: I'll have to agree. You were asked if FDA requires scientific agreement, and your response was that you're familiar with that, so I will disregard that answer.

BY MS. EVANS:

Q. Now, sir, does FDA require significant scientific agreement to make an unqualified health claim for food?

MR. FIELDS: Objection, Your Honor. That calls for a legal conclusion and really is not something before this court.

MS. EVANS: May I respond?

JUDGE CHAPPELL: Go ahead.

MS. EVANS: The Federal Trade Commission 15 years ago issued a statement that we would generally follow the FDA's "significant scientific agreement" standard for making unqualified health claims for foods, so I believe that is very much before this court.

MR. FIELDS: It's still a legal conclusion as to whether the FDA requires it as a matter of law.

JUDGE CHAPPELL: Well, I'm going to sustain the objection on lack of foundation. We need to be clear. To the extent it is a legal issue, you're asking for a legal opinion, and you haven't established that he has any knowledge of what you're telling him about.

BY MS. EVANS:

Q. Are you aware that FDA requires significant scientific agreement for making unqualified health

claims for food?

A. I'm not clear what you mean by "an unqualified health claim." I'm aware that there are several levels of health claims, but I don't know what you mean by "unqualified health claim."

Q. Well, you never told the respondents, including Stewart Resnick or Matt Tupper or anybody else associated with these groups, that there was significant scientific agreement that pomegranate juice or POMx could prevent cardiovascular disease, did you?

A. I believe there is significant scientific agreement that pomegranate helps to reduce the risk of heart disease.

Now, when you say "prevent," I don't know what you mean by that. I mean, that could be something a drug might do. But, again, I'm not a lawyer, but I'm just saying that the scientific community believes that the research that's been done by Dr. Ornish and Dr. Aviram and Dr. Davidson on the basis of the basic science does provide a significant scientific agreement.

And I can't respond to your specific way that you proposed the question, so you'd have to clarify it for me.

MS. EVANS: I would move to strike because it

was not -- that question was not responsive to the question I asked.

JUDGE CHAPPELL: The question was whether you told the respondents. The answer is nonresponsive. The answer will be disregarded.

BY MS. EVANS:

Q. Now, sir, you never told respondents, including Stewart Resnick or Matt Tupper or anyone else with Roll or POM Wonderful, that there was significant scientific agreement that pomegranate juice or POMx could prevent cardiovascular disease.

A. I can't answer that question because I was never asked it in that way.

Q. Okay. At your deposition I asked you, did you ever tell the respondents --

MR. FIELDS: Could we again have a page and line.

MS. EVANS: I'm sorry. Page 244 of the deposition on January 28, 2001 (sic) at line 11 through 16.

BY MS. EVANS:

Q. And I asked you, did you ever tell the respondents -- I mean Stewart Resnick or Matt Tupper or anybody else with the Roll/POM Wonderful groups -- that there was this significant scientific agreement that

pomegranate juice or POMx could prevent cardiovascular disease?

And you responded:

"ANSWER: No. I never said that."

Now, you also, sir, never told them that there was significant scientific agreement that POMx or pomegranate juice could treat cardiovascular disease, did you?

A. I didn't have an opportunity to review your last piece of evidence. You just -- it just moved on and off the screen very quickly, so I can't respond.

Q. I was reading it into the record, sir. There was no question pending.

JUDGE CHAPPELL: Hold on a second. If you're going to ask him about his depo, he has the right to see if you're reading it correctly.

MS. EVANS: Okay.

JUDGE CHAPPELL: So you need to put that back up there, and I would suggest you have a follow-up question about whether that's the answer he gave that day if you want the record to make any sense.

BY MS. EVANS:

Q. Now, returning to my question, with regard to page 244 at line -- starting at line 11 and moving down to line 16, okay? Do you see that?

A. Could you put that back so I can see the full text, please.

(Pause in the proceedings.)

Yes. Well, of course I didn't because it says here "could prevent cardiovascular disease."

And you well know that there is a statement that drugs prevent, cure, mitigate or treat a disease. Now, a nutrient may help in the prevention, it may help in the treatment, but it's certainly not a cure. And certainly no one would tell someone to take pomegranate juice rather than to see their doctor.

So these answers that you asked me are drawn chapter and verse from the fact that nutrients may help prevent, may help to treat, but they do not prevent, cure or treat a disease or in any way do that on their own, and no one is saying that a pomegranate fruit is a substitute for a drug, and these are drawn from drug statements.

Q. Now, you also never told them that there was significant scientific agreement that POMx or pomegranate juice could treat cardiovascular disease, did you?

A. Again, that's very misleading and taken out of context. I'm sorry. I can't agree to your question.

Q. Okay. If you could turn to your deposition at

page 244 -- oh, I'm sorry. Excuse me.

And you never heard anyone else say that POMx or pomegranate juice could treat cardiovascular disease?

A. I never heard anyone say that pomegranate juice alone would treat cardiovascular disease, that's correct.

Q. Well, referring to your deposition transcript on page 2 -- excuse me.

One moment, Your Honor.

(Pause in the proceedings.)

You were talking earlier about your contacts and communications with respondents; correct?

A. Correct.

Q. Okay. In your many meetings and contacts with the respondents' representatives, such as with Dr. Dreher or Mr. Gillespie, you never reviewed or approved any advertising; correct?

A. That's correct.

Q. And you were never in fact shown any advertising in advance before it was run.

A. There is one instance where there was -- I was asked to provide information for a press release. Other than that, I was not participating in any of the advertising of POM Wonderful.

Q. Now, in your report, you state that it's important to consider the totality of the scientific evidence in order to decide what benefits a product is likely to provide?

A. You mumbled again at the end of your question. I'm sorry. I just can't understand you.

Q. I'm so sorry.

In your report, you state that it's important to consider the totality of the scientific evidence in order to decide what benefits a product provides?

A. Yes.

Q. And that includes in vitro animal studies and human studies along with basic science about nutritional uptake on metabolism?

A. Yes.

Q. And yesterday, when Judge Chappell asked you about having competent, reliable scientific evidence and what that meant, you said that meant looking at the totality of the evidence that exists for any scientific benefit?

A. That's correct.

Q. Okay. Now -- so you looked at all of the studies -- you -- that have been conducted on pomegranate juice and POMx; correct?

A. Well, there are hundreds of studies done in the

world. I can't say I've reviewed every one. I certainly have reviewed those that are relevant to our research, yes.

Q. And you evaluate the reliability of the results achieved in those studies?

A. I think when I read an article I do put it in the context of the other work that's been done in the field. Yes.

Q. Okay. Now, I'd just like to clarify what evidence you were considering in forming your opinions that competent, reliable evidence exists that POM juice and POMx are likely to reduce the risk of cardiovascular disease.

Yesterday, you testified about some hopeful results from Dr. Aviram's initial mouse studies; correct?

A. Yes.

Q. And you heard Dr. Liker explain that after Dr. Aviram did his animal studies, respondents turned to Dr. Rosenfeld, and he conducted another study to look at reduction of plaque in apoE mice with atherosclerotic disease?

A. Actually, no. Dr. Rosenfeld's model is a different model than the one that was studied by Dr. Aviram. Dr. Rosenfeld's model -- and I'd have to

review those papers now to see the details, but my recollection is it's a much more advanced stage of atherosclerosis in a specific -- I believe it's a rat model, not a mouse model, so it's not the apoE knockout mouse.

So it was a very different model, and he's a pathologist and looked at pathological changes, not the metabolic things that we were talking about in Dr. Aviram's study where the apoE knockout mouse is an established model for plaque stability.

Now, plaque stability, as I mentioned yesterday, is extremely important in prevention and helping to prevent heart disease because the event in a heart attack is the rupture of an unstable plaque. An unstable plaque contains oxidized LDL cholesterol and macrophages.

The lesions that Dr. Rosenfeld studied are far advanced from that. They have calcium. They have cholesterol crystals. And he was looking at it only histologically, so it was a very different model. When one uses different models you don't always get the same answer. But that certainly is part of the totality of the evidence.

But I would say that the basic mechanisms that I reviewed yesterday, oxidation, macrophage uptake of

cholesterol, plaque accumulation, the human studies on carotid stenosis, the myocardial perfusion studies, and so forth, provide a totality of scientific support that everyone would consider that pomegranate juice helps to reduce the risk of cardiovascular disease.

Q. So did you include Dr. Rosenfeld's result in your analysis of the totality of the evidence?

A. Yes.

Q. Now --

A. As I just explained.

Q. In your report at page 48 -- and I don't know if you need a copy of that before you -- you discuss -- do you need a copy?

A. Is it going to come up on here (indicating)?

Q. Okay. You discussed two human studies that were conducted by Dr. Aviram; correct?

A. Yes.

Q. And the studies that you're discussing, I just want to confirm that -- and, Will, if you could bring these up -- those are the studies that have been identified -- I just want to make clear that this one study -- one of the Aviram studies that you're discussing in your report has previously -- is the one that Will is going to bring up on the screen and is identified as CX 542.

Is that one of the studies you were discussing on page 48?

A. Can you go back to the expert report. I'm not sure --

Q. Certainly. We could also give you a paper copy if that would make it easier.

A. Well, okay. Let me say that I'll stipulate that. Go ahead and ask your question.

Q. Is the second of the Aviram studies the document that has previously been marked as CX 611?

May she approach and take him a paper copy of his report?

JUDGE CHAPPELL: Yes. Go ahead.

THE WITNESS: Thank you.

And what's your question?

BY MS. EVANS:

Q. Is this CISX -- is this the second study, CX 611, is that the second Aviram study that you're describing on page 48 of your report?

A. 48.

(Pause in the proceedings.)

Yes.

Q. And you previously testified, did you not, that Dr. Aviram's two human studies are unblinded and do not have a placebo control?

MR. FIELDS: Again, Your Honor, could we have a deposition, a line, a page.

MS. EVANS: Referring to CX 2007 at page 173.

JUDGE CHAPPELL: Or at least some context of where he supposedly testified. I doubt this is the first time he's been on the witness stand.

MS. EVANS: I'm sorry, sir.

Correct. You are absolutely right. He is -- I understand you've testified on several occasions for respondents?

THE WITNESS: That's correct.

MR. FIELDS: Could we have a copy of whatever this is. I don't think it's in evidence.

JUDGE CHAPPELL: As I said, would you inform the witness where you're claiming he testified if you're going to pursue this question --

MS. EVANS: Yes, sir.

JUDGE CHAPPELL: -- or move along.

BY MS. EVANS:

Q. You testified in this matter on March 30, 2001; correct?

A. What date?

Q. Do you recall your expert --

A. 2011?

Q. 2011.

March 30, 2011, you testified in your expert deposition in this matter?

A. Yes.

Q. And referring on page 178 -- 173 to lines 3 through 5, you testified that Dr. Aviram's human studies are unblinded and uncontrolled?

A. I obviously was in error there because there is a placebo in the carotid stenosis study, so I must have testified incorrectly there.

Q. So you question -- I'm going to read into the record the testimony at that point on page 173 starting at line 3 (as read):

"QUESTION: Well, Dr. Aviram's human studies are unblinded and uncontrolled; correct?

"ANSWER: They're unblinded.

"QUESTION: Right. And there's no placebo control."

A. I'm confused. Are you -- so you're referring to the acetylcholinesterase-inhibiting study on blood pressure, not the carotid stenosis study; is that correct?

Q. What was -- I used the plural, Dr. Aviram's human studies.

A. We have to break it up. Which study are you talking about?

Q. The question was (as read):

"Well, Dr. Aviram's human studies are unblinded and uncontrolled; correct?

"ANSWER: They're unblinded.

"QUESTION: Right. And there's no placebo control.

"ANSWER: That's correct."

A. That's incorrect. One is blinded and -- well, one is placebo-controlled. And I'd have to review the blood pressure study because I -- I would have to see that now, but I believe that when we were talking here, it was -- we were -- the word "thickness" there on the first line, I think we were talking about the carotid stenosis study.

Q. Well, so you're saying --

A. Where there was a placebo.

Q. Excuse me, sir?

(Admonition from the court reporter.)

BY MS. EVANS:

Q. I couldn't hear the response, and that's why I said -- so I'll read it again.

So you're saying in the -- are you testifying that in the blood pressure study that is CX 452 that that one was unblinded and un --

A. I can't recall. You'll have to bring me the --

you'll have to either show me the study or the evidence at this point. I'd have to go back. There's so many studies that I've reviewed, I'd have to look at it.

Q. Could you bring up CX 542.

(Pause in the proceedings.)

A. Okay.

Q. Turning to page --

A. Now --

Q. -- 2 under Methods?

A. Okay. So in this case, these patients served as their own controls, so this is not a -- this is not a placebo study, but it is a controlled study in that you had a small number of patients who were hypertensive. And hypertension in these patients, they were looking at a complex hormonal pathway, which is very common in prediabetes, which involves insulin, angiotensin, renin. And there are a number of drugs, as mentioned here, which inhibit that enzyme. And what they showed in this study was that pomegranate had an effect on this enzyme's activity. That was all that was shown here.

So the -- in this study, you have a controlled study where each person is their own control.

Now, in some studies it's not possible to find a matched control group. You would have to do a much

larger study.

So this was an original, as I had mentioned in my deposition, this was an exploratory study, and it did not have a placebo control, and I stand by that statement.

Q. Okay. And so all of the data in the -- this blood pressure/angiotensin-converting enzyme study, all of those results were compared to baseline; correct?

A. They're compared to the patient's own baseline level. That's correct.

Q. Thank you.

Now, you have previously described -- if you could -- did you testify with regard to Dr. Aviram's coronary artery stenosis in the -- in the Welch's deposition?

If you could refer the witness to the CX 2016 at TR 113 at page -- starting at page -- line 22 through line 6 on the next page.

Do you see that?

A. Yes, I see it.

Q. Did you previously describe Dr. Aviram's coronary artery stenosis study as a one-armed exploratory pilot that was not definitive?

A. That's the blood pressure study. Yes.

Q. Okay. Well, that was referring to page 13 of

your report in the Welch's matter; correct?

A. Yes.

Q. I'm going to -- I will return to that in a minute to tie it back up.

JUDGE CHAPPELL: What does a one-arm exploratory pilot mean?

THE WITNESS: It means that the patients were all not compared to another group. If you have a two-arm study, you're comparing a placebo to another group. And in some studies, it is hard to match the two groups or you need to start -- study a large number of people.

So often, when you're looking to see if there's a large effect, what we call an exploratory study, you'll take people as their own control over time.

And that's what was done here in this blood pressure study. It was a one-arm pilot exploratory study, a single arm. People were their own control.

BY MS. EVANS:

Q. And did you provide an expert report in the Welch's matter?

A. What's your question? I'm sorry.

Q. Did you provide an expert report in the Welch's matter?

A. Yes, I did.

Q. And on page -- the question -- the answer that you provided on CX 2016 at pages 113 that I just read back to you, the original question on page -- on line 22 was on page 13 of your report the pilot study by Aviram.

Now, on page 13 -- now, is the expert report that you provided in Welch's, is that previously marked as PX 0046?

Could somebody provide him with a copy.

(Pause in the proceedings.)

Is that the expert report that you provided in the Welch's case?

A. Yes.

Q. Okay. And turning to page 13 of that report, at the fractional paragraph at the bottom of that page, that -- that is talking about a pilot study by Aviram and colleagues and that -- that were -- where ten patients were supplemented with pomegranate juice for one year and five of them continued for up to three years.

That's the -- that's the carotid artery stenosis trial that you're referring to there, isn't it?

A. That's correct.

Q. Thank you.

So that's the one that on the next page you described as -- on line 10 of your deposition in the Welch's matter on page CX 2016-0114 as --

MR. FIELDS: Could you give us a deposition page -- Your Honor, I'm sorry. I shouldn't direct it to counsel. Could we have a deposition page, Your Honor.

MS. EVANS: Yes. Page 114.

MR. FIELDS: Thank you.

BY MS. EVANS:

Q. Do you have that before you?

A. Right.

JUDGE CHAPPELL: Hold on. She was in the middle I believe of a question, and there was an objection or a note, so nothing is pending. I suppose she was going to finish the question or maybe move on. I don't know.

BY MS. EVANS:

Q. So did you testify on page 114 of the Welch's deposition transcript that -- where you were asked, is your understanding of the mechanisms of that study, was there a real control group involved, and you answered, on line 10, I think it was a one-arm exploratory pilot was the one way I would put it?

A. Well, that may have been my recollection at the

time. But the term "exploratory pilot" is probably not appropriate here because of the fact that they actually got tissue in the study and demonstrated some more science that was in line with the basic mechanisms underlying what they had observed.

So although I characterized it that way at that time in that particular moment in that testimony, I really view that study as an important study because of the fact that they did get carotid tissue, so I would like to correct my earlier statement in a different case that was about adulterated pomegranate juice --

Q. Have respondents provided you with the transcript of Dr. Aviram's testimony at deposition?

A. I don't believe so. Not that I recall.

Q. So if Dr. Aviram testified in his testimony that there was no actual placebo product in this case, would you then think -- have a different answer?

In the Aviram CAS study?

A. I haven't seen that. I can't answer that.

Q. Thank you.

Now, turning to your report at page 49, you discuss -- and if you could refer to that -- the Ornish study?

A. Which report are you referring to?

Q. Oh, I'm sorry. We're back to this case.

A. Okay. Go ahead.

Q. Okay. So there, at the top of page 49, in the first paragraph, you say -- you're describing the Ornish study.

Now, when you're discussing -- making that reference, were you referring to the study document that has previously -- I ask you to bring it up, Will -- been identified as CX 1198?

A. You'd have to show me the -- I don't have your numbering system.

That is the Ornish study, yes.

Q. Yes. Thank you.

Now, one of the endpoints that's measured in CX 1198 was blood pressure; isn't that correct?

A. That was not a -- that was not measured as an outcome variable.

Q. But it was measured; correct?

A. Only in the sense of usual vital signs.

Q. And according --

JUDGE CHAPPELL: Hold on a second.

In an effort to make some sense of this down the road, you were asked if it was an endpoint. You responded it was not an outcome variable.

THE WITNESS: Right.

JUDGE CHAPPELL: Can you define what both of

those terms mean.

THE WITNESS: Sure.

When you're doing a study, one of the things you want to do is to look for a primary change in something. In this case, Dr. Ornish' study was directed at myocardial perfusion or blood flow within the heart.

In any clinical study, it's routine to take a blood pressure, pulse, body temperature, and so forth, to make sure the patients are healthy.

And as you'll note that the -- there's a sentence here at the end of the abstract that says the benefit was observed without changes in cardiac medications, blood sugar, hemoglobin A1c, weight or blood pressure in either group. Now, since these were patients with heart disease, that's an important secondary observation.

But as I testified earlier, to do a real blood pressure study is a -- is a specialized event. You have to get special nurses, special blood pressure equipment to see changes in blood pressure.

So this was not a blood pressure study per se, and one could therefore not conclude that since there was no change in blood pressure that there was no effect of pomegranate juice on blood pressure in this

study.

JUDGE CHAPPELL: Actually what I was looking for was how do you define "endpoint" versus "outcome variable."

THE WITNESS: Oh.

The primary outcome variable is defined prior to doing a study, and it is part of the statistical rules of how you evaluate a trial.

So you pick something that you're looking at, like myocardial perfusion. That doesn't invalidate the other observations you're making, but they would have to have some biological rationale in the discussion of the paper relative to your primary endpoint.

So an endpoint and a primary outcome variable are essentially the same thing.

BY MS. EVANS:

Q. Now, on page -- the next paragraph down, on page 49 of your report, you refer to a second Ornish study; correct?

A. Hold on a second.

JUDGE CHAPPELL: On the monitor it looks like one paragraph. How do you get the second paragraph?

MS. EVANS: On page 49, "The second report involved..."

THE WITNESS: So that's really a -- go ahead.

What's your question?

BY MS. EVANS:

Q. On the second paragraph on page 49, you discuss a second report under Ornish Studies.

A. I'm commenting on Dr. Stampfer's review of the Davidson study, is what I'm doing there.

Or is that -- I'm sorry. Or is that the second Ornish study? I guess it's the second --

JUDGE CHAPPELL: Why don't we wait and let her finish the question.

THE WITNESS: Okay. Go ahead. I'm guessing. I don't know. I'm confused.

BY MS. EVANS:

Q. Are you -- when you refer to the second report, are you referring to the document that has been marked in this matter -- and Will, if you could bring it up -- as CX 754?

A. Okay. I am familiar with this report.

Q. Okay. And is that the document that you are -- the report that you were referring to in the second paragraph on page 49?

A. Yes.

Q. Okay. And did I ask you about this report during your deposition on -- expert deposition on March 30, 2011?

A. You may have. I don't recall.

Q. Okay. And to refresh your recollection, if I can refer you to CX 2007 at pages 180 to 181.

MR. FIELDS: Could you identify it as the -- please, as the deposition. Because we don't remember all of those CX numbers, it's a little hard to pick out the deposition to track it.

MS. EVANS: I believe my question was: "Did I ask you about this report during your deposition on -- expert deposition on March 30, 2011?"

JUDGE CHAPPELL: You asked him to refer to a document. His counsel has a right to know with specificity what you're referring to.

BY MS. EVANS:

Q. Sir, referring to the transcript of Dr. Heber's expert deposition on 3-30-2011, which has been identified as CX 2007, at page 184 -- excuse me -- page 180, and looking at line 16, I asked you about Dr. Ornish's intima-media thickness study; correct?

A. Yes.

Q. And you testified that you understood that the study was not fully recruited and was terminated prematurely.

A. Correct.

Q. Okay. And who provided you with this

understanding?

A. I believe it was Mark Dreher.

Q. Okay. Did you do anything to determine whether or not it was true?

A. That wasn't my research, so I didn't.

Q. Okay. So -- thank you.

You also discuss briefly in your report on -- two studies by Dr. Davidson on page 49; correct?

A. Again, these were in response to Dr. Stampfer's criticisms.

Q. Okay. The two last lines of that paragraph under Davidson Studies reads, "In addition, the indeterminate results from a smaller 45-subject subpopulation showing no results with brachial reactivity as a measure of flow-mediated dilation are simply indeterminate."

When you said that, were you referring to the document that's been marked as CX 684?

Will, if you could bring that up.

A. Yes.

Q. Now, returning to page 19 of that document, CX 684-0019, was one of the measures in the study blood pressure?

A. The primary variable here, again, what we would call the primary outcome variable or endpoint, was

flow-mediated dilation, not blood pressure. One of the measures, secondary measures made in the study, was blood pressure, but again this was not a study focused on blood pressure.

So yes, blood pressure was measured, but the primary variable was the degree to which a large artery in the arm dilates following restriction and release of a blood pressure cuff (indicating). And this is done with a Doppler ultrasound device, and it is known to be a highly variable, operator-dependent measurement, as I testified.

So yes, blood pressure was measured, but no, it was not the primary outcome variable.

Q. And this study did not show any change in blood pressure, did it?

A. Yes. But, as I stated, it was not the primary outcome variable, and one could easily miss a change in blood pressure.

Q. Just to clarify, when I asked, "And this study did not show any change in blood pressure, did it," you responded, "Yes," and I just want to make clear that what you're saying is, no, it did not show a change in blood pressure?

A. I clarified that response by saying it was not a primary outcome variable and therefore cannot be relied

upon as negative evidence.

Q. But it did -- the study did not show a change in blood pressure, did it?

A. It failed to show a change in blood pressure.

Q. Thank you.

Now, do you know whether elevated blood pressure was one of the possible inclusion criteria in this Davidson study?

A. In the Davidson study, I would have to review the paper if you'd like to put it up, but I did not recall that as being an exclusion criteria or inclusion criteria.

Q. If you could refer to CX 1199 at page 1, and that -- counsel, that is Dr. -- the publication on Dr. Davidson's publication -- study.

Do you have that before you?

(Pause in the proceedings.)

A. Okay. So they had greater than one major coronary heart disease risk factor, yes.

Q. Okay. And one of those was increased blood pressure; correct?

A. One of those was increased -- let me just see here.

You'd have to go down in the methods here. Let me see.

To be eligible, men were required to have greater than one of the following risk factors. They mention cholesterol, HDL cholesterol. Increased blood pressure was one of the criteria, so not everyone in the study would have increased blood pressure. It would be a subgroup.

Q. Yes, sir.

A. Can I clarify my response there?

Q. Yes, sir.

A. This collection of signs and conditions is what's known as the metabolic syndrome, which I testified to yesterday. It's not really -- that each person wouldn't have all these things. They might have several of them but not all of them. The most risk-averse subgroup would be the high triglyceride/low HDL group.

Q. And referring to page CX 1199-005 of this same document in the right-hand column?

A. You have to magnify it.

Q. I'm going to ask him to enlarge it for you.

Okay.

Does this study conclude that there were no differences between treatment groups for changes from baseline in traditional cardiovascular risk markers, one of which was blood pressure?

A. That's correct.

Q. Thank you.

Now, did you consider the results of Dr. Ornish's blood pressure data in his myocardial perfusion study or his blood pressure data in -- or -- or the blood pressure data in Dr. Davidson's flow-mediated dilation study or the blood pressure data in Dr. Davidson's IMT study when you reached the conclusion stated in your report on page 40 that there is credible scientific evidence that pomegranate juice and pomegranate extract have significant benefits for human cardiovascular systems, including lowering of blood pressure?

A. Yes. Of course I considered it in the overall assessment of the evidence.

JUDGE CHAPPELL: You know, the way you asked that question, there were a lot of "ors." Did you want to find out which one he considered or --

BY MS. EVANS:

Q. Certainly.

Which ones did you consider, and how did you weigh them?

A. Well, in looking at a study, one always looks at the primary outcome variable and then at exploratory analyses based on the scientific background and

biological rationale for which the study was done.

And so in the case of the myocardial perfusion study by Dean Ornish, myocardial perfusion of the heart and small blood vessels would likely link to the basic biochemical mechanisms around nitric oxide; whereas, the large blood vessel blood pressure is affected by many other factors, such as the flexibility of the wall. With aging, the wall becomes less flexible. This affects systolic blood pressure. There are many other variables in blood pressure, including the renin-angiotensin system, which I mentioned earlier based on the earlier Aviram study.

So blood pressure is controlled by many things, whereas Dr. Ornish's study was directly looking at myocardial perfusion, so that weighed heavier in my consideration of the Ornish study.

Q. Okay. But I specifically asked you -- you stated on your report at page 40 that there is credible -- and if you'd like to refer to that -- that there's credible scientific evidence that pomegranate juice and pomegranate extracts have significant benefits for cardiovascular -- human cardiovascular systems, including lowering of blood pressure.

In reaching that, the part of that result that addresses including lowering of blood pressure, what

studies did you rely on for that?

A. Well, I think you have to look at the totality of the evidence.

So in looking at decreases in arterial plaque, I certainly was looking at the Aviram carotid study. And also in that study there was some decrease in blood pressure. There was the rationale related to the ACE enzyme in his earlier studies. This has not been followed up, but I think that the opinion here related to lowering of blood pressure was related to an overall assessment of the benefits on heart disease and simply listing these particular elements. There is no change in blood pressure observed in -- there's no change in systolic or diastolic blood pressure observed in the Ornish study since this was not the primary outcome variable.

Q. Now, you testified yesterday that one of the mechanisms through which pomegranate juice may likely benefit human health has to do with reducing oxidative stress and inflammation; correct?

A. That's correct.

Q. Okay. Now -- but -- and you have in fact yourself conducted research to determine whether or not pomegranate products act as an antioxidant in the human, haven't you?

A. Yes, I have.

Q. Okay. And you've also said that there's not a standardized method where you can say that a pomegranate is acting as an antioxidant in the human or not.

A. There are standard methods for testing the antioxidant potency of juices in the laboratory. And there -- the area of defining that antioxidant benefit in the human body as a pure antioxidant is something that is at the cutting edge of science because there are a lot of endogenous antioxidant mechanisms.

So the answer to your question is there's not an established method. There are a number of methods in use, a number of methods that are published, but they are still an area of cutting-edge investigation.

Q. Thank you.

Now, the fact that something acts as an antioxidant in an in vitro test does not mean that it acts as an antioxidant in a human, does it?

A. It depends what you mean by "acts as an antioxidant."

As I indicated yesterday, the term "antioxidant" is kind of an umbrella term, and antioxidants have specific effects in the body. In particular, pomegranate polyphenols have what are characterized as

antioxidant effects, such as inhibiting the oxidation of LDL cholesterol, inhibiting the uptake of LDL cholesterol by macrophages, and resulting in reduced amounts of oxidized cholesterol in arteries taken out of patients with carotid artery stenosis.

Now, if you ask me can you translate an antioxidant effect in the test tube into that same antioxidant effect in a human blood sample obtained in a fasting state or after a meal, that's a very difficult thing to do, and it's still an area of evolving science.

Q. Okay. And did you testify as to this issue in your deposition in the Welch's matter? Do you recall?

A. I don't recall.

Q. Okay. And if you could refer -- would it refresh your recollection if I showed you the transcript of that deposition?

A. Could you put it back up on the screen, please.

Q. If you could refer to CX 2016 on page 69, starting at line 16:

"QUESTION: And then you follow with your next sentence that begins (as read): 'Although in vitro antioxidants potency does not prove in vivo biological activity.' And that was a true statement when you wrote it?"

And you responded, "That's correct."

A. That's correct but again taken out of context because it does not refer to anything specific to pomegranate juice. That's a general statement about the umbrella nature of the term "antioxidants" and refers to my article Phytochemicals Beyond Antioxidation.

So the term "antioxidant" in vitro is well-known and well-characterized. In vivo, many antioxidants have other important effects, which I indicated.

Q. Well, were you one of the authors of an article reporting on a two-site study that was conducted in Denver and San Diego to evaluate the effects of consuming POMx on inflammatory markers?

A. Yes.

Q. Okay. And that -- and comes -- Will, could you bring that up.

That's the study that has previously been marked as CX 934?

A. Yes.

Q. Okay. And in CX 934 -- I believe it's on the last page -- you refer to TBARS.

A. That's right.

Q. Okay. And you said that -- did you rely on the TBARS results in the Denver site to conclude that POMx had efficacy?

A. I never said that.

Q. Well, if you refer to the last paragraph of this report on CX 934 page 4, you state there, "... these pilot studies demonstrate both the safety and efficacy of POMx..."

What were you relying on when you made that statement for the conclusion that this -- these pilot studies demonstrate the efficacy of POMx?

A. Well, certainly not conclusively. As you can see, this is one paragraph of a long discussion, which was: "Preliminary evidence of a reduction in TBARS was seen in the subjects who were studied at the Denver site. Further studies are underway to document the effects of this supplement in patients with type 2 diabetes, known to have a more marked increase in oxidant stress."

So the observation in Colorado was made in people who were gaining weight because the study was done in the late fall, over the holiday season, and that would be a time when you would expect to see an increase in weight and in oxidant stress, and in those people there was actually a reduction in the TBARS compared to the other group, so that was preliminary evidence that we subsequently followed up in a follow-up study.

Q. So when you said "these pilot studies demonstrate both the safety and efficacy of POMx," what were you relying on? What piece of data --

A. Well, this was primarily a safety study done at Accelovance in normal volunteers, and that's what I relied on.

Q. You relied on the Accelovance study for your --

A. The safety.

Q. -- conclusions?

A. I don't know what you mean -- well, I don't know why I used that term, but the term "efficacy" means the effects of, on antioxidants, so in that case I would rely on the Denver observation as a pilot study, a pilot demonstration. This is not a conclusive demonstration. And as I indicated, antioxidant activity is very difficult to study.

Q. Now, did this report -- this article, CX 934, does that include all of the results from both the Denver and San Diego site?

A. At that time. That were completed at that time.

Q. But it does not conclude all of the results from the Accelovance site, does it?

A. We subsequently went back and explored the Accelovance study population, which was a group of

normal volunteers, primarily studied for safety, with the idea that we would explore the idea of whether any inflammatory markers or oxidant stress markers were elevated in those subjects. And what we found was a great deal of variability between the baseline, that is, the -- a baseline and four-week measurements in the normals, because there was a lot of variation. And in this study we did not succeed in finding and in confirming an antioxidant effect or an anti-inflammatory effect. But this was again an exploratory study, and that's why those studies were subsequently not published because they were indeterminate results, not negative results.

Q. Okay. And I would move to strike --

A. So the answer to my question -- the answer to your question is yes.

Q. Yes, it does not include all of the results of the Accelovance arm of the study?

A. It does not.

Q. Okay. Now, the San Diego site of that study, that was randomized, and it did include a placebo group; correct?

A. Correct.

Q. Okay. And it showed no change in antioxidant and inflammatory markers?

A. I wouldn't put it that way. I would say that there was a great deal of variability and no significant difference between the two groups.

Q. So if I could refer you to CX 1254.

Do you have that?

MR. FIELDS: Your Honor, unfortunately we haven't memorized those numbers, so --

MS. EVANS: Okay.

MR. FIELDS: Your Honor, if we could just have a reference to the deposition in such and such a case, we'll find it.

MS. EVANS: That was -- it was Deposition Exhibit 1054 at the fact deposition on January 28, 2011, and Ms. Nach has provided you with that copy.

THE WITNESS: And what's the source of this? Could you clarify that for me.

BY MS. EVANS:

Q. Well, this document -- I'm looking at this document here, and it says "POMx in Heart Health: Antioxidant Effects."

A. Is this a report or a slide presentation? What is this exactly?

Q. Well, it has your name on it; right? David Heber, M.D., Ph.D.?

A. But I prepared interim reports sometimes for our

meetings with Mr. Resnick, so I'm not clear where this came from.

Q. Yes.

Can she approach?

JUDGE CHAPPELL: Yes. Go ahead.

THE WITNESS: Thank you.

Okay. So what this represents, if I can clarify the source of this --

JUDGE CHAPPELL: I don't think there's a question. There's no question --

THE WITNESS: Okay. No question. Go ahead. Ask me a question.

BY MS. EVANS:

Q. If you'd turn to page 6 of this document, it's entitled Study Design, 57 male or female 35 to 65 years of age with BMI 25 to 32 and a waist circumference --

A. Correct.

Q. And is that referring to the Accelovance site?

A. Yes.

Q. Okay. And in that, in that study, some of the endpoints that were measured were oxidative phospholipids by E6 Ab that's referred to on pages 13 --

A. I can't understand you. I'm sorry.

Q. If you'd turn to page 13, 14 and 15, do those

pages provide data for oxidized phospholipids by E06 Ab?

A. Yes. That's an antibody against an oxidized phospholipid from Dr. Tsimikas' group.

Q. And if you'd turn to pages 16 and 17?

A. Uh-huh.

Q. And 18?

A. Uh-huh.

Q. Does it provide lipoprotein(a) data --

A. Yes.

Q. -- from this study?

A. Uh-huh.

Q. That was something that was marked -- measured in this study?

A. Yes.

Q. And on pages 19, 20 and 21, does it contain data on nitric oxide?

A. Yes.

Q. Okay. And similarly, on pages 23, 24 and 25, does it include isoprostane data?

A. Uh-huh. Yes.

Q. If you'd refer to page 26 of this document -- and this is referring to the Accelovance study; correct?

A. That's correct.

Q. Okay. And it says in this study there were no changes in groups receiving one or two POMx capsules today -- per day in markers of antioxidant stress or inflammation that were studied.

Does it say that?

A. Yes.

Q. Okay. And you -- I asked you yesterday about CX 873, and CX 873 was one of the documents I asked you about when we were asking about funding for your studies?

And I'm going to ask Will if he could bring it up.

JUDGE CHAPPELL: I don't know who Will is, but I don't see anything on the screen.

BY MS. EVANS:

Q. Now, do you see that document now?

A. Yes, I do. Uh-huh. Correct.

Q. And in that study -- excuse me -- in that document, did you indicate that one of the things that was going to be discussed at the February 28, 2007 meeting with Mr. Resnick was a review of the Accelovance study in detail?

A. Yes.

Q. Okay. And so -- and that was on February of 2007, and what was the -- correct?

Correct?

A. I don't understand. I didn't hear the question.

Q. That meeting, that was scheduled for February 27 -- February 28, 2007?

A. Oh, I'm sorry. What's the question?

Q. That meeting was scheduled for February 28, 2007, the meeting to provide a review of the Accelovance study --

A. That's correct.

Q. And was the -- the results of the two-site study, CX 934, was that published in the 2007 -- a 2007 issue of the Journal of Agricultural and Food Chemistry?

A. What date was that? Do you have that?

Q. I'm looking --

A. I don't have that in front of me.

Q. -- 934.

Could you provide him with a copy of that.

A. Could you enlarge it and go to the bottom of the page, please.

Q. Actually it's at the very top left-hand corner.

A. Go back up again, please.

JUDGE CHAPPELL: Yes, you may approach.

THE WITNESS: Okay. So this was received for

review June 8, 2007, revised manuscript December 17, 2007, accepted September 21, 2007.

BY MS. EVANS:

Q. And all of those dates are subsequent to February 28, 2007?

A. They're prior to February 28.

Q. I thought you just said 2007.

A. I'm sorry. Was that 2008 that you had? Let me see your last e-mail, please.

JUDGE CHAPPELL: Are you asking Will?

THE WITNESS: I just can't -- she's asking me about a date, and I can't --

BY MS. EVANS:

Q. Yes.

On the very final page of this study, which is CX 934-005, it says, does it not, "Received for review June 8, 2007"?

A. Correct.

Q. Okay. And this meeting on February 28, 2007, that was before -- that's referred to in CX 873, that's before that manuscript was received for review?

A. Okay. Correct.

Q. Thank you.

Now, you also conducted some studies in -- you conducted one study in diabetics, and Dr. Hill also

conducted another study --

A. That's correct.

Q. -- in diabetics.

And I call it the study in diabetics, but you've explained to me that it was a glucose load study?

A. It was a what?

Q. A glucose load study?

A. It was a -- yes.

Q. Okay. Now, in that study, you measured malondialdehyde.

A. Correct.

Q. And you said that this is a way of actually measuring TBARS, didn't you, at your deposition?

A. Yes. TBARS and malondialdehyde are comparables.

Q. And in that study you were unable to show a statistically significant result?

A. That -- well, that's correct.

Q. Okay. And in fact, at your deposition on January 20, 2001, did you state that TBARS is an old colorimetric assay and is not considered as accurate as measuring malondial- -- malon- -- I did so well the first time -- malondialdehyde?

A. That's correct.

Q. Now, Dr. Davidson's IMT study, which has been previously marked as CX 1199 -- do you recall that study?

A. Yes.

Q. Okay. And one of the things -- there were several antioxidant and inflammatory markers that were measured in that study; correct?

A. Correct.

Q. And the markers included -- I'm referring to page 1165 of table 2.

Is one of those markers -- indicators of inflammation and oxidative stress, was one of them ferric reducing ability of plasma?

A. That's called a FRAP assay. That's also considered less specific than the malondialdehyde assay. As I said, this is a difficult area in which to look for oxidative stress.

Q. And is another one of those measures paraoxonase-1?

A. No. Paraoxonase-1 is an enzyme found in HDL cholesterol which actually has antioxidant activity, as I testified earlier.

Q. If you refer to CX 1065-003 at table 2, the -- one, two -- third measure down, was that paraoxonase-1?

A. Yes.

Q. And the next measure down was PD minus AAPH?

A. Yes.

Q. And the next measure down was PD plus AAPH?

A. Yes.

Q. The next measure down was thiobarbituric acid --

(Admonition from the court reporter.)

BY MS. EVANS:

Q. And the next measure down was thiobarbituric acid-reactive substances minus AAPH?

A. That's correct.

Q. And that is a TBARS measure; correct?

A. It's a variant of the TBARS measure, yes.

Q. And the last one on that chart is TBARS plus AAPH?

A. That's correct.

Q. Okay. And there were no statistically significant changes in any of these markers at the end of the study, were there?

A. That's correct.

Q. Okay. Now, you testified that you rely on Dr. Davidson's study for its implications of the totality of evidence on pomegranate juice and not specifically with regard to this component of how they had tested the antioxidant potency?

A. That's correct.

MS. EVANS: Okay. Your Honor, would it be a good time to take a break?

JUDGE CHAPPELL: How much time do you have remaining on cross?

MS. EVANS: At least an hour.

THE WITNESS: I'm fine. And I have an early flight back. I'd prefer to continue.

JUDGE CHAPPELL: Well, we're not going to finish before our next break.

THE WITNESS: Okay.

JUDGE CHAPPELL: We'll reconvene at 11:20.

(Recess)

JUDGE CHAPPELL: Back on the record.

Next question.

BY MS. EVANS:

Q. Dr. Heber, turning to page 40 of your expert report and referring to the last paragraph of your report there -- and I'm just going to read the section -- "In my expert opinion, there is credible scientific evidence that pomegranate juice and pomegranate extracts have significant health benefits for human cardiovascular systems, including," colon, and then one of the ones that you -- the next item there is decreases arterial plaque.

A. What's the question? I'm sorry.

Q. And were you testifying that you believe that pomegranate juice and pomegranate extracts are likely to have benefits, including decreases in arterial plaque?

A. Yes.

Q. Now, in support of that proposition, are you relying on Dr. Aviram's unblinded IMT study and -- which we've already discussed, and the subgroup data in Dr. Davidson's study?

A. I'm relying on the placebo-controlled trial of Dr. Aviram on carotid artery stenosis patients as well the totality of the science in Dr. Davidson's trial.

Q. Okay. Now -- and Dr. Davidson's study again is the one that we've -- that you're referring to here, you're referring to CX 1199?

A. That's correct.

Q. And that's the largest of POM -- respondents' pomegranate heart studies?

A. It had the largest number of subjects.

Q. It had 289 subjects.

It had 289 subjects?

A. That's correct.

Q. Okay. And you testified that the people in the study didn't have the -- maybe -- let me make sure I'm

correct, that you testified yesterday that these people didn't have the minimum level of IMT required to say that somebody actually "has plaque." Is that what you testified yesterday?

A. I testified yesterday that the official definition of plaque is 1.5 millimeters and that Dr. Davidson excluded everyone with a plaque -- with an IMT of greater than 2.0 millimeters and therefore was not a comparable study to that of Dr. Aviram. They're two different studies and need to be interpreted differently.

Q. Okay. But just to be clear, the subjects in this study, one of the inclusion criteria was that they had to have both one or more risk factors for heart disease and a posterior wall baseline IMT measurement of between .07 and 2.0 millimeters?

A. That would be an inclusion criteria. Yes.

Q. Thank you.

And this study is entitled the Effects of Pomegranate Juice on Carotid Intima-Media Thickness in Men and Women at Moderate Risk for Coronary Heart Disease; correct?

A. That's correct.

Q. Okay. Now, was this a well-conducted study?

A. Yes.

Q. Okay. And is the data regarding the overall IMT progression credible?

A. I would have to qualify that. I can't answer the question as asked.

The -- of course, it was collected accurately, executed accurately. The ability of any measurement to detect a difference in a human study depends on the characteristics of the patient and the characteristics of the test.

In this particular case, as I testified yesterday, the IMT is an extremely difficult measurement to make, and although these patients were at moderate risk of heart disease, their amount of plaque was relatively small and difficult to determine the differences.

So in answer to your question, and also the variability of the patient population, so yes, the results are credible in that there was a credible investigator, credible methods, but that does not mean that the study cannot be criticized. All studies can be criticized. But there's valuable, credible scientific information within this study.

Q. And at page 35 of your report, about the -- one, two, three, four, five, six -- seventh line from the bottom, you state: In conclusion, these results suggest

that in subjects with moderate coronary heart disease risk, pomegranate juice consumption had no significant effect on overall CIMT progression rate but may have slowed CIMT progression in subjects with increased oxidative stress and disturbances in the TG-rich lipoprotein/HDL axis.

That's what you say about this study?

A. Yes.

Q. And "TG" means triglycerides?

A. Pardon? I didn't understand the question.

Q. TG-rich. Where you used the phrase "TG-rich," that means triglyceride-rich?

A. Yes.

Q. Okay. And you have previously -- now, this -- this -- this discussion about CIMT progression in subjects with increased oxidative stress and disturbances in the TG-rich lipoprotein/HDL axis, that's the data with regard to the subgroup that Dr. Davidson identifies at 1199 page 5?

A. You'd have to put that up for me.

Q. Do you have that study before you -- oh, here it is.

The exploratory analysis of several subgroups, is this the information you're referring to when you say -- when you refer to subjects with increased

oxidative stress and disturbances in the triglyceride-rich lipoprotein/HDL axis?

A. That's correct.

Q. Okay. And Dr. Davidson's -- now, haven't you -- do you remember testifying about this study in the -- in your deposition in the Welch's matter, which I believe is CX 2016?

Oh, here it is. And I would refer you -- -- oh, do you remember testifying about this study in your deposition in the Welch's matter?

A. Yes.

Q. Okay. And if I could refer you to --

A. Page 14?

Q. There's too many numbers on all of these pages -- page 117.

Now, did you testify in the Welch's deposition that in what's called intent-to-treat analysis you look at the overall outcome between your intervention group and your placebo group and that on a strict intent-to-treat analysis there was no difference between the two groups at the end of the study?

A. Yes.

Q. Okay. And turning to the -- turning to that same deposition at page 137 line 13, were you there also discussing the IMT study?

Actually, strike that.

Did you say in that deposition, "Now, by the rules of statistical analysis, you're not allowed to report out that subgroup because one could, you know, randomly continue to divide a group of subjects until you found a positive result without rationale"?

A. Yes.

Q. And with regard to the subgroup analysis, starting at line 3, you said that the subgroup analysis now does two things, it generates a hypothesis for future studies where you would recruit everybody who had these characteristics, and it provides some substantiation when considered together with the total body of scientific evidence on the mechanisms around intimal medial thickness?

A. That's correct.

Q. Thank you.

And has Dr. Davidson's subgroup analysis been replicated in a later randomized clinical trial?

A. Can you repeat the question, please.

Q. Has Dr. Davidson's subgroup analysis in fact been replicated in a later randomized clinical trial?

A. No.

Q. Okay. Now, you already testified that you didn't review the results of Dr. Ornish's IMT study;

correct?

A. Yes.

Q. Okay. And so the totality of the evidence that you considered and about which you provide an opinion in your report, that did not include the null IMT data contained in that study, did it?

A. The opinion that I expressed was based on the totality of evidence, and as I indicated, that was an uncomplete -- incomplete study, so the answer is yes, it did not include that.

Q. And if that study was in fact completed, you don't know what your opinion would be?

A. That study was -- had inadequate power at that number of subjects.

Q. Now, how do you weigh the results of Dr. Davidson's well-controlled, well-conducted, large-population, published study conclusion against preclinical evidence such as the in vitro studies and a small pilot study like Dr. Aviram's?

A. A large study does not -- I rate them differently because a large study often has other issues, such as variability of the patient population, which was clearly the case in the Davidson study, so simply having a large study in a nutrition setting of a fruit juice or extract does not make it a better or

worse study.

So therefore, I would rate all of the evidence on mechanism as it relates to the subgroup analysis and the other supportive data in their totality when looking at the benefit for cardiovascular health.

Q. But the primary result of the Davidson study showed no overall improvement in IMT benefit; correct?

A. The -- from a clinical trial standpoint, if this were a drug, you would use what's called intent-to-treat analysis. And that is correct, that on the intent-to-treat analysis, a simple overall comparison of two highly variable groups, there's no difference.

Q. Thank you.

Now, what -- you have stated that one -- well, correct me if I'm wrong -- that you believe that one of pomegranate juice's beneficial effects is to increase paraoxonase and PON-1?

A. That's been shown in separate studies. Yes.

Q. And in support of this statement you rely on research by Drs. Aviram and Rock?

A. By Dr. Rock at UC San Diego.

Q. Well, I believe that you testified -- do you recall testifying about these studies in the Welch's deposition?

A. I may have. I don't specifically recall.

Q. Could I refer you to CX 2016 at page 136.

And with regard to Dr. Aviram's study on PON, did you testify that -- did you agree in that matter, starting on lane -- line 14 of page 136, that these were mechanistic studies and not intended to demonstrate convincing effects on cardiovascular disease?

A. The -- I'd have to see which study you're referring to. Because I was reviewing a critique by Dr. Blumberg, and it would depend on which of Dr. Aviram's paraoxonase studies you're referring to.

He has looked at paraoxonase in mechanistic studies in cell culture, and he's also looked at that ex vivo, taking blood samples from patients and showing that pomegranate increases the stability of paraoxonase's association with HDL or good cholesterol, so it would depend on the study.

Q. Which one is PX 192?

All right. You've previously stated that paraoxonase is not an intermediate marker for heart disease, although it is implicated in the pathogenesis of heart disease?

A. Again, I can't respond to the question as stated.

Q. Okay. Again turning to your deposition in Welch's, which is CX 2016, at page 128.

A. Well, what I meant by that comment -- is there a question?

Q. Well, actually let me read the questions and answers into the record, and then if you can --

A. Okay. Go ahead.

Q. You were asked the question (as read):

"And we were talking about cardiovascular disease before our break. I think if I could ask you, Dr. Heber, to look at page 17 on your report?

"ANSWER: Okay.

"QUESTION: Yes. On the top of that there's a reference to HDL --

(Admonition from the court reporter.)

BY MS. EVANS:

Q. I'm referring to the Welch's deposition, which is CX 2016 at page 127 -- actually it's page 128.

You were asked the question on line 1: Does anyone recognize the level of paraoxonase as a diagnostic tool for treatment of heart disease?

And you answered, starting on line 8: Again, I would say it is not an intermediate marker for heart disease, but it's implicated in the pathogenesis of heart disease based on basic and clinical

investigations.

Is that the --

A. That's correct.

Q. Thank you.

So -- now, you have tried to replicate the results of the Aviram and Rock studies in diabetic patients, haven't you?

A. We have, yes.

Q. Okay. But you were not able to do so?

A. The experiment -- okay. I have to clarify. It's not simple.

The paraoxonase level is stimulated by pomegranate juice under baseline conditions. And what we did in that study, we were looking for a change in paraoxonase-1 in diabetics given a glucose load to try to stimulate an oxidant stress. And we did not see a change.

Q. You did not see a change.

And paraoxonase also wasn't changed in the -- in the Denver site of the antioxidant study that's reported on CX 877 at page 7?

Do you have that?

A. Well, there's a decrease, but the variation between subjects is so great that it did not reach statistical significance; therefore, one could say that

there's no detectable change.

Q. And there was -- if you'd refer to the brachial artery reactivity study, CX 684 at page 12, there was no change in paraoxonase in that study?

A. Is that the Davidson study you're referring to?

Q. Yeah. It's the Davidson flow-mediated dilation study.

A. Yes.

Q. And in the primary -- the final Davidson report, which is CX 1199, at page 3, there was no change in the paraoxonase there either, was there?

A. No.

Q. Thank you.

Also on pages 31 and 32 of your report you talk about Dr. Aviram's 2001 study showing a reduction in ACE; correct?

A. Yes.

Q. Okay. And based on that and on page 32 of your report, you state -- it's at the bottom of the first paragraph at the top of the page -- because reduction in serum ACE activity even with no decrement in blood pressure has -- was previously shown to attenuate atherosclerosis, pomegranate juice can offer a wide protection against cardiovascular diseases which could be related to its inhibitory effect on oxidative stress

and on serum ACE activity?

A. Yes.

Q. Okay. But this ACE result, was that -- do you -- was that replicated in the brachial artery reactivity test on CX 684?

A. No.

Q. Okay. And that data is on page 11 of CX 684?

A. Yes.

Q. And to your knowledge, Dr. Aviram's data showing a reduction in ACE has never been confirmed or replicated in any of the double-blind, placebo-controlled studies on POMx or POM juice?

A. None of the studies confirmed it, no.

Q. Okay. Now, you also talked yesterday about Dr. Ignarro's evidence on nitric oxide?

A. Yes.

Q. And you proposed this as a possible mechanism for beneficial effects for the heart?

A. I said that pomegranate had been shown to lengthen the half-life of nitric oxide in vitro. Yes.

Q. Okay. Specifically you said that nitric oxide has a beneficial effect on blood flow?

A. Yes.

Q. Okay. Now, the evidence that you're relying on for the nitric oxide mechanism theory consists of

in vitro and animal studies; right?

A. There was also a 20 percent increase in plasma nitric oxide levels in the prostate cancer study that was done by Dr. Pantuck and levels measured by Dr. Ignarro.

Q. But that wasn't in any of the heart disease studies?

A. The heart disease studies did not -- I have to -- you'd have to show me in the studies where there was a measure of nitric oxide.

Q. Well, you testified at your second deposition on March 30, 2011 that brachial artery reactivity factor is a factor --

MR. FIELDS: Excuse me. Could we please, Your Honor, have a page so that we can follow along.

BY MS. EVANS:

Q. I'm referring to the second deposition, which is CX 2007, at page 187.

You testified, did you not -- turning to line 17, I asked you, is brachial artery reactivity -- brachial artery activity a factor of nitric oxide metabolism, and you answered it is?

A. Yes.

Q. Okay. But the brachial artery reactivity testing conducted by Dr. Davidson did not show a

statistically significant change in blood flow; correct?

A. That's correct.

Q. Okay. And you also measured nitric oxide in the Accelovance study, CX 859?

A. Yes. There's no difference.

Q. Okay. You stated yesterday, if I could turn you back to yesterday afternoon, that there is competent and reliable evidence showing that POM and POMx are likely to lessen, reduce, the risk of cardiovascular disease; correct?

A. Correct.

Q. And you did not opine that competent and reliable evidence supports a claim that pomegranate juice actually prevents or reduces the risk of heart disease, did you?

MR. FIELDS: Objection. Compound, Your Honor. Could we break down between prevents and reduces the risk of? They're very different.

BY MS. EVANS:

Q. Did you opine that competent and reliable evidence supports a claim that pomegranate juice actually prevents the risk of heart disease?

A. As I indicated yesterday, that question was not the one I was asked or answered. The question was does

it reduce the risk, and I did answer it does reduce the risk.

Q. Well, actually I was rereading your testimony, and I believe you said it would likely reduce risk?

A. I said that the scientific evidence supported the fact that it reduces the risk. Now, in any given individual, that risk is variable.

Q. When I asked you -- referring to CX 2007, which is your expert deposition, I asked you about the treatment claims, and I asked you whether or not the treatment claims that were alleged in the complaint were substantiated, and did you then say that -- and I can refer to --

MR. FIELDS: Your Honor, could we please have a page.

MS. EVANS: If I could finish the question, then I could say what I was referring him to.

JUDGE CHAPPELL: Actually, you need to give him a page and line number before you read it if you're asking him whether you asked that question.

MS. EVANS: Okay.

JUDGE CHAPPELL: You need to be fair to the witness and his counsel.

BY MS. EVANS:

Q. Turning to CX 2000 at page 80 -- excuse me --

page 81, the first line -- do you have that before you?

A. What's the question? I'm sorry.

Q. Okay. Did you testify: I've already indicated that nutrition is not a treatment for disease. It's not a drug or surgical procedure. So therefore, since you characterized it with the word "treatment," I'm not agreeing with your statement?

A. That's correct.

Q. Okay. And the question I had asked you was, turning to page 80 at line 20: Assuming for the purposes of argument that respondents' advertising makes the claim that competent and reliable scientific evidence supports the conclusion that drinking eight ounces of POM juice daily treats heart disease, including by decreasing arterial plaque, is that proposition supported in your opinion?

So that's the -- the answer on line (sic) 81 lines 1 to 5 was to that question?

A. Yes.

MR. FIELDS: Could we have an answer read rather than just the question.

BY MS. EVANS:

Q. And the answer again at line -- on page 81 at line 1 is:

"ANSWER: I've already indicated that nutrition

is not a treatment for disease. It's not a drug or surgical procedure. So therefore, since you characterized it with the word 'treatment,' I'm not agreeing with your statement."

A. I'll stand by that.

Q. Thank you.

And so you disagree that competent and reliable evidence supports the conclusion that pomegranate juice or POMx treats cardiovascular disease because, in your view, nutritional products don't treat disease.

A. Of course not.

Q. Okay. Yesterday you testified that there is competent and reliable evidence that POM and POMx are likely to lower the risk of prostate problems for men who have not been diagnosed with prostate cancer; correct?

A. That's correct.

Q. Now, you didn't actually opine that competent and reliable evidence supports a claim that pomegranate juice or POMx actually lowers the risk of prostate cancer in that population, did you?

A. What was my statement again? Could you review it.

Q. There is competent and reliable evidence that POMx and POM are likely to lower the risk of prostate

problems for men who have not yet been diagnosed for prostate cancer.

A. Well, the difference between "likely" and "actual" has to be defined, so I would say "in all medical probability," if that helps you, I would say that in all medical probability. The word "likely" is rather ambiguous, and if I used it in my deposition, I need to further clarify it. In all medical probability.

Q. And so yesterday when you testified that it likely reduced the risk that -- you didn't mean that word "likely" then?

A. The word "likely" is, in my estimation -- it's not a medical term. It's a probabilistic term.

So I would say that based on my review of all the evidence, the totality of scientific evidence, of which we have considerable evidence, which I'm very familiar with, then I would say that in all medical probability and in the general scientific community -- and this is well-supported -- that there is a reduction in the risk of prostate cancer, yes.

Q. Okay. Do you disagree that competent and reliable evidence supports the conclusion that pomegranate juice or POMx treat prostate cancer because nutritional products don't treat disease, just as you

did for heart disease?

A. Again, I can't answer your question as stated because you're misstating what I said yesterday, which was it could help to treat. I never said and would never opine that pomegranate juice should be substituted for medical or surgical treatment of prostate cancer.

Q. Turning to CX 2007 page 90.

MR. FIELDS: Again, Your Honor, we just can't remember these numbers, if counsel would please just tell us which deposition it is.

MS. EVANS: And that would be the deposition of March 30, 2011.

MR. FIELDS: Thank you.

BY MS. EVANS:

Q. I'm sorry. It was page 92.

At line 5 I asked you the question: And last but not least, assuming for the purposes of argument that respondents' advertising makes the claim that clinical studies, research and/or trials prove that -- excuse me. That's the wrong page. Oh, yes -- that POM juice daily -- that eight ounces of POM juice daily treats erectile dysfunction, is that proposition supported?

And on line 13 you said: Once again, I would

object to the term "treatment," and I would say that my professional opinion is that the body of research on pomegranate juice and extract revealing how they act in the body provides support for potential health benefits for prostate cancer.

And then I -- I asked the question: No. Erectile --

But you had given the answer for prostate cancer?

A. Correct.

Q. Okay.

A. You're reading the deposition correctly.

Q. Correct.

Now -- and have you refused to answer the question whether you believe that respondents have significant evidence to support an FDA health claim for pomegranate juice in reducing the risk of prostate cancer under the "significant scientific agreement" standard?

MR. FIELDS: Your Honor, if I may voice an objection, there was an objection to that question as ambiguous, and that was not of course ruled upon at the time of the deposition when the objection was made by counsel.

It is ambiguous in that the word "treat" is

ambiguous, as we talked about that in opening statement. "Treat" can mean a medical kind of treatment or it can mean help out. And I think without a definition of "treat" the question is ambiguous, and the objection made at the deposition should be sustained.

JUDGE CHAPPELL: Do you understand the question?

THE WITNESS: I think it's -- it's -- the way it's configured, I can't answer it.

JUDGE CHAPPELL: Sustained.

BY MS. EVANS:

Q. In your expert report you stated, on page 23, that it's your opinion that POM juice promotes prostate health; correct?

A. Correct.

Q. Okay. And you base this conclusion on a review of the Pantuck study and laboratory studies?

A. I base that opinion on the totality of evidence, including the basic mechanistic and cellular studies as well as the body of clinical evidence.

Q. Okay. Now, in the Pantuck study, there was only a single arm; correct?

A. That's correct.

Q. Okay. And all the -- all of the patients in

that study were taken -- were taking pomegranate juice.

A. That's correct.

Q. And if you could refer to your second deposition at page 151 and the -- turning then to page 152 down to page (sic) 22, if you could read that.

A. Which line are you referring to?

Q. Starting with the question on page -- at the very last line of page 151.

A. That's correct. There was no placebo group in this study, that is correct. The patient --

Q. And I asked you --

A. What's the question?

Q. I asked you, if instead of being an open-label study Dr. Pantuck had recruited both an active and a placebo group, you could not specify -- speculate on what would have happened to the PSA levels of the placebo group; correct?

A. That is correct because the level of rate of rise in patients with prostate cancer of their PSA after primary treatment is highly variable, and it would have been impossible to recruit matched groups for a placebo and control. Therefore, in this study, each patient established a rate of rise of PSA prior to recruitment into the study, and then that individual's course of rise of PSA was subsequently followed.

And this is standard methodology in urological research, and the PSA doubling time is an accepted variable by the vast majority of the urological community, including members of the American Urological Association and all the leading experts in prostate cancer research in the United States. This is not in dispute.

Q. But you did state on -- in that deposition on March 30, 2001, on page 152 on page (sic) 14, "I can't speculate on what would happen if they had recruited two groups"?

A. That's correct because, as I just indicated --

Q. Thank you.

A. -- such a study might recruit very different and highly variable patients in the two arms, so there would be no point.

Q. You also talk in your expert report about the -- Dr. Carducci's study?

A. Yes.

Q. Okay. Now, have the results of Dr. Carducci's study been published?

A. I believe that they were presented in abstract form. I'm not aware of publication.

Q. And do you have any firsthand knowledge of the responses of the subjects in the Carducci study or how

their prostate experience is linked to other patients with prostate cancer clinically?

A. As I testified, I'm not an expert in the detailed clinical assessment of prostate cancer patients, so the answer is no.

Q. Okay. Now, do you agree with Dr. Stampfer when he says that some recurring tumors do not produce prostate-specific antigen?

A. Certainly.

Q. Okay. And there haven't been any studies to evaluate whether or not pomegranate juice can prevent benign prostate hyperplasia?

A. That is a separate, common condition, like menopausal symptoms, et cetera, and it has not been separately studied. It's very common. Fifty percent of men over age 50 have benign prostatic hyperplasia.

It is not considered a precancerous lesion, by the way. It's simply a common condition among men.

Q. And have there been any human studies that have been conducted and completed in healthy men who have not yet been diagnosed with prostate cancer?

A. The answer is no because, as I indicated yesterday, that type of study would require a hundred thousand men over twenty to thirty years.

Q. Okay. Now, when you were talking a minute ago

about the ability to recruit patients for a two-arm study of pomegranate products for -- for prostate cancer benefits, are you aware that POM is currently conducting a large placebo-controlled study examining the effect of POMx in men with rising PSA?

A. Yes. And that study has been delayed significantly because it's very hard to recruit patients to a placebo arm with prostate cancer. That's correct.

Q. And did you -- referring to your second deposition at TR 155 -- actually strike that.

Looking at page 23 of your report...

(Pause in the proceedings.)

You said that the reason that the -- that the rationale for not having a placebo group in the Carducci study was that it was difficult to recruit prostate patients -- cancer patients to take a placebo based on the perception of the health benefits of pomegranate juice and extract based on the reading of the scientific literature; correct?

A. Correct.

Q. Okay. But did you refuse to answer the question in your deposition, CX 2007, page 156 starting at line 13 and proceeding to 157 starting at line 9?

MR. FIELDS: Could you give us a moment to get

there, please.

MS. EVANS: Yes, I will.

MR. FIELDS: We're there.

MS. EVANS: Good.

BY MS. EVANS:

Q. Did you refuse to answer the question whether the patients might have had this perception of potential benefits of the health benefit of pomegranates because of respondents' advertising?

A. I'm not -- as indicated by my counsel, I'm not a consumer ad expert and therefore refused to the answer the question, and I would take that same position now. I can't speculate on what impact advertising would have on consumers.

Q. Thank you.

And turning to your first deposition at page 326, did I ask you if there's a distinction between saying something may promote prostate health or a claim in advertising that it would treat prostate cancer, and did you respond that your selected phrase would be "promote prostate health"?

A. I positively stated "promote prostate health." Again, I think the use of the word "treat" is very problematic because no one is suggesting that pomegranate would be a substitute for the surgical or

medical treatment of prostate cancer.

Q. In that health claims assessment meeting that you attended with regard to the pomegranate and POMx science, what was the consensus -- was there -- was there a discussion about the prostate cancer evidence?

A. Can you repeat the question.

Q. Let me turn you to CX 959.

There's a -- do you see the document on page 2?

A. Yes.

Q. And is there a section in there on prostate health?

A. First of all, there is a section, yes.

Q. Okay. And you said previously with regard to heart disease that the purpose of those meetings was to consider whether or not there was enough evidence to support an FDA health claim; correct?

A. Correct.

Q. Okay. Now, was there a consensus about the evidence on --

A. Not that I recall.

Q. Can I finish the question first just so that we know that we have --

A. Oh, I thought you were done. Go ahead.

Q. Okay. Was there a consensus about what the evidence showed about the prostate cancer research at

that meeting or any of those meetings?

A. Oh, I think that there was a consensus that there's a significant body of scientific evidence to indicate that both pomegranate fruit juice and pomegranate extract can help to prevent or reduce the risk or help to treat prostate cancer by the various observations made in these studies.

Q. Well, what claims were respondents considering seeking FDA approval for?

A. The reason, as I understand it, was to differentiate this pomegranate juice and others that are made from whole fruit from the very prevalent practice of selling blends that contain small percentages of pomegranate juice or selling juices that have been adulterated with other juices and pretend to be pomegranate juice and so that people would not derive the benefits of pomegranate juice, so it was hoped that by getting an FDA approval that this would provide some unique character to the whole pomegranate juice area both for this product and for other products made from the whole fruit.

Q. Now, referring to your first deposition, at page 326 starting at line 19, 326 line 19, did you ever tell the respondents that there was a -- or anybody else at POM that there was significant scientific

agreement within prostate cancer research that -- researchers that pomegranate juice or POMx could prevent prostate cancer?

A. Again, I think there's -- I can't answer that question as stated.

But the term "significant scientific agreement" is quite ambiguous as is the term prevent. I can't answer it as asked.

Q. Now, you've attended meetings with the respondents about the prostate cancer research that were attended by Allan Pantuck and Phil Kantoff and Michael Carducci I believe --

A. Yes.

Q. And no one has ever made a comment to Mr. Resnick that the evidence showed that pomegranate juice or POMx could prevent prostate cancer?

A. That question -- that question I can't answer as stated.

Because there was a discussion of the scientific data, and it's not a black-and-white issue. Help to prevent, yes. Consideration of the studies done to date, yes. Enthusiasm from everyone, yes. Enthusiasm from Phil Kantoff from Harvard, yes.

Ultimately there's -- was substantial agreement on the body of evidence there that it could help to

prevent in the correct setting. When you say absolutely prevent, no, this would not be a substitute for a pharmaceutical prevention that some men might undertake, which also I might point out is not proven today. There are still questions about the use of certain preventive agents, whether they increase the risk of other types of prostate cancer.

So this is a complex area, and I can't answer the question as asked, and that was why it was judged to be vague and ambiguous before and I would say it is still and I can't answer it.

Q. And you testified at deposition -- if I could refer you to line (sic) 328 at line 8, you said: So I would say, from the totality of the evidence, I can really strongly agree with the statement that it promotes prostate health; correct?

A. Again, that's the same response as I had before.

Q. And when I asked you the question on that same page, 328, at line 12:

"QUESTION: Okay. Now, have you ever heard anybody else tell Stewart Resnick or the folks at POM that there was a substantial body of scientific agreement that pomegranate juice or pomegranate extract could prevent prostate cancer?"

And do you provide your response to that question at page 329 at line 3?

MR. FIELDS: Excuse me. Objection, Your Honor. Could we have the answer to the question that counsel read. She reads a question and then doesn't give the answer to the question.

MS. EVANS: I'm referring him to page 329 line 3.

MR. FIELDS: Well, Your Honor, counsel referred to page 327, as I understood it, and didn't read the answer. She said: I asked you about could it prevent prostate cancer. And then the answer is: I never used those specific words. And we're just getting a question and not the answer, and I -- that's my objection.

MS. EVANS: Okay. If I could just read into the record line 320 at page -- deposition -- that from the transcript of the first deposition, CX 1352, page 328 (as read):

QUESTION: Now, have you ever heard anybody else tell Stewart Resnick or the folks at POM that there was a substantial body of significant -- scientific agreement -- excuse me -- a substantial body of scientific agreement that pomegranate juice or -- or pomegranate extract could prevent prostate cancer?

ANSWER: No. I -- I think what happened is we had these meetings. You've kind of seen the agenda here.

QUESTION: Mm-hmm.

ANSWER: And Allan Pantuck presents all of the current state of knowledge. Other clinicians commented on it, like Phil Kantoff or others, like Michael Carducci, who had experience with patients --

QUESTION: Mm-hmm.

ANSWER: -- and how they feel about it, and then -- and that was all just thrown out there. No one made any comment to Mr. Resnick of the type you've indicated.

Now, when you say that nutrition is not a treatment for disease, it's not a drug or a surgical procedure, are you saying that nutrition is an adjunct therapy?

A. I didn't use those words. Those are your words.

I'm saying that nutrition via multiple things, including pomegranate juice, can help reduce the risk of prostate cancer, can help prevent, can help treat. But no one is saying that it is an adjunctive treatment. Adjunctive treatment is another category of drug use. You may often have an adjunct drug used with

another drug. I did not say adjunctive treatment.

Q. Well, in your experience, if somebody said that dietary -- actually made a --

(Admonition from the court reporter.)

THE WITNESS: I didn't understand the question. Could you repeat it, please.

BY MS. EVANS:

Q. Supposing --

A. Supposing.

Q. -- a manufacturer made a statement that a diet supplement or a food was making a treatment claim, would you then consider it to be a botanical drug, in your experience?

A. Okay. That's a -- I can't answer that.

MR. FIELDS: Objection. Now we view it as to what a treatment claim is.

JUDGE CHAPPELL: He already said he can't answer it.

MS. EVANS: Okay.

BY MS. EVANS:

Q. In your report at page 9, in the first full paragraph, you say it's not appropriate to require the results of double-blind, placebo-controlled studies for evaluating the health benefits of foods that have been consumed for their health benefits for thousands of

years; correct?

A. That is correct. I stand by that, that they are not necessary. They're part of the overall scientific totality of evidence, but they are not necessary.

Q. Okay. Now, given your age, I'm assuming that you don't actually have personal knowledge of why people living in the Mideast actually consumed pomegranates thousands of years ago.

A. Do you want to restate the question? I don't understand what your question is.

Q. You don't have personal knowledge of why people consumed pomegranates thousands of years ago?

A. I did not live thousands of years ago.

Q. Yeah.

A. So I --

Q. And the product that would have been available thousands of years ago, would that have been either whole pomegranates or hand-pressed, fresh pomegranate juice?

A. I can't answer the question.

Q. Okay. You have published a couple of books.

One of them is called The LA Shape Diet?

A. That's correct.

Q. And turning to page 74 of that book, I'm going

to read a section, and it says -- you said, at page 74: We all know that fruits and vegetables are healthy, but you need to strictly implement (sic) or avoid fruit juices; correct?

A. Where is this now?

Q. It's in your LA Shape Diet at 74.

A. This is in the context of weight loss.

Q. Uh-huh.

A. And the book that you held up is about weight loss and obesity. And for weight-loss promotion we need to limit calorically dense things like starchy vegetables, beans and potatoes. Beans may be very good food, nuts very good food, dried fruits very good food, fruit juices very good food, but if you're looking at your overall diet and trying to lose weight, you want to take in things with a low calorie density. That's less calories per bite. That was the context in which I'm saying that.

Q. And the reason you gave in the book for your statement was that it takes more than two oranges to make a glass of orange juice and I would rather you ate the whole orange?

A. That's correct.

Q. Now, POM Wonderful hundred percent juice contains a variety of polyphenols you've testified;

right?

A. Yes.

Q. Over 124 chemical constituents of POM have been identified?

A. 124 have been identified.

Q. Okay. And when you did research to identify real pomegranate juice as opposed to what you considered not to be real pomegranate juice, it was the anthocyanin profile of the juice that was the distinguishing factor?

A. Yes.

Q. And do you believe that there's universal agreement among pomegranate researchers in countries like Spain, Italy, Iran and Tunisia that the presence of six anthocyanins is indicative of real pomegranate juice?

A. There's significant agreement that pomegranate species from different areas around the world contain essentially the same profile of six anthocyanins, and that profile is different than for blueberries or elderberries and other similar red/purple fruit.

Q. And POMx pills and liquid don't contain anthocyanins; correct?

A. That's correct.

Q. And in your report at page 13, you say, "While a

unique pattern of anthocyanins contribute to the color of pomegranate juice (see authentication studies below) and undoubtedly contribute to the antioxidant capacity of pomegranate juice made from whole fruits," and that's the first half of the sentence; right?

A. Yep.

Q. Okay. Now, POM Wonderful also has a unique combination of glucose and fructose that are characteristic of pomegranate sugars?

A. It's naturally produced glucose and fructose at a ratio of approximately one to one.

Q. And POMx does not contain any sugars, does it?

A. That's correct.

Q. And POMx does not contain the anthocyanins?

A. That's correct.

Q. Yesterday afternoon, Mr. Fields asked you about an article written by Dr. Jeffrey Blumberg and Meir Stampfer; correct?

A. Correct.

Q. And that's the document we're referring to entitled Evidence-Based Criteria in the Nutritional Context?

A. Yeah.

Q. And if you could provide him with a copy of RX 5007.

Now, given that Drs. Blumberg and Stampfer are two of the articles -- two of the authors on this article, would they be in a better position than you to explain what they meant in the article?

A. Well, there are a number of authors here actually besides Dr. Blumberg and Stampfer, Connie Weaver --

(Admonition from the court reporter.)

THE WITNESS: Anyway, what my point is is this was a task force that include -- this was not the usual situation where you have one or two authors. These people are all leaders in nutritional research around the United States and members of the American Society for Nutrition. I know all of them personally. And we have had long discussions about this issue which is still in dispute about what should be the evidence-based criteria in the nutritional context, and there is wide agreement that RCTs are not necessary.

BY MS. EVANS:

Q. Okay. And so in response to my question, given that Drs. Blumberg and Stampfer are two of the authors on this article, would they be in a better position than you to explain what they meant in the article?

A. No.

Q. Dr. Blumberg has testified on several occasions

as the expert for some of the companies that have opposed the respondents in the Lanham Act cases?

A. That's correct.

Q. And has he ever in those cases stated that he interpreted this article to mean that RCTs were not needed to support advertising claims for pomegranate products?

A. As I said, that could be his opinion. I don't -- I don't -- I'm not aware of that.

Q. Okay. And this article talks about the kind of evidence needed to support development of nutrient requirements and dietary guidelines; correct?

A. That's part of what's in here. Yes.

Q. Okay. And an example of nutrient requirements would be the 1997 Dietary Reference Intakes?

A. That's a -- nutrient advice. Yes.

Q. And when this article talks about dietary guidelines, it identifies, for example, the dietary guidelines for Americans?

A. Yes.

Q. Okay. The article does say, does it not, that -- on page 479 in the left-hand column, the bottom, the first sentence of the last paragraph on the left-hand side (as read): Nevertheless, it is indisputable that the RCT in one of its variant forms is

the clinical design that best prevents strong causal inference concerning the relationship between an administered agent (whether drug or nutrient) and any specific outcome?

A. That's what the article says, yes.

Q. And does it also say that both drug indications and health claims for nutrients that are backed by one or more well-conducted RCTs are appropriately considered to have a more persuasive evidence base than corresponding data based primarily on observational data?

A. That is stated in the article. And what they mean by "observational data" are population studies.

Q. Right.

And that would be the large epidemiological studies that compare intake of different nutrients and endpoints over time; correct?

A. Correct.

Q. Okay. Is there any observational data of this sort on pomegranates, pomegranate juice or pomegranate extracts?

A. No.

Q. Now, turning to page 480, on the left-hand side, at the bottom, if you could read that, that section before I ask you a question.

(Pause in the proceedings.)

A. Yes.

Q. And that section is entitled Are Randomized, Controlled Trials Available to Test Nutrient Effects? Correct?

A. Yes.

Q. And one of the factors that they consider for relying more heavily on observational studies for nutrients is that if the nutrient in question is widely used, it will not be able to get a control group with sufficiently low intake of that nutrient to serve as an adequate contrast; correct?

A. That's what the article states, yes.

Q. Okay. Now, your hypothesis is that the active ingredient in pomegranates and pomegranate juice is the punicalagin; right?

A. It's the family of hydrolyzable tannins that most of our research has been addressed. They're called ellagitannins. And it is not unique. It is unique to the pomegranate to have the punicalagin, but it is not unique to have tannins, which I indicated also occur in walnuts and other foods.

Q. Okay. And so you have said that punicalagin is unique to the pomegranate.

A. Pardon? Could you repeat that.

Q. So you have said that punicalagin is unique to the pomegranate.

A. As to -- it's unique to pomegranate as an edible fruit, yes.

Q. Okay. And you've said that pomegranates have not been studied on -- in observational studies because they are not widely consumed in the United States?

A. That's also true for spices, and it is true for pomegranate.

Q. Okay. And this would suggest, since there could be an adequate control group, that RCTs for punicalagin would in fact be feasible?

A. It would depend on the question being asked, the size of the change, which I have indicated there are many problems -- not that RCT -- I'm not against RCTs, but they're not necessary for nutrient studies because they have significant issues, some of which are pointed out in this article.

Q. Well --

A. Observational studies also have significant issues.

So this is an area of great contention, as this task force discussion indicates. This paper came to no strong conclusion in that regard.

Q. And if you'd turn to table 1 of this study,

which is on page 482 in the middle of the page.

Do you see that?

A. Yes, I do.

Q. Now, this table is entitled Factors Affecting the Level of Certainty of Evidence Provided by Various Study Designs.

Correct?

A. Correct.

Q. Now, the three study designs they identify are randomized controlled trials, cohort designs and case control designs; correct?

A. Correct.

Q. Okay. Those are all human clinical studies; right?

A. All of the three are human clinical study designs, yes.

Q. So --

A. Oh, except -- excuse me -- the middle one. The cohort design, that's an observational study. That's an epidemiological study, not a clinical study.

Q. So in vitro and animal research is not included as a kind of evidence that provides any level of certainty in this table, is it?

A. Not in this table.

Q. Okay. Is there any indication in this article

that the authors concluded that the recommendations for nutrient -- that recommendations for nutrient intake would be considered appropriate where neither RCTs nor observational studies were available to support the recommendation?

A. In this particular article, the -- they did conclude that, because of the limitations inherent in RCTs, particularly of nutrients, it is suggested that nutrient policies will have to be made using the totality of available evidence. The article then goes on to discuss what they call a hierarchy of evidence that is established by this particular working group.

Q. And in vitro and animal studies were not on this chart, were they?

A. These are not the -- the basis of this article is to look at things such as the Dietary Reference Intake, which is a range of nutrient intakes for advice to the public. This is not related to evaluating the health benefits of a particular nutrient, so therefore, it's not a -- I disagree with your hypothesis.

Q. Thank you.

And if you'd turn to page 483 in the left-hand column, they actually -- I'll give you a minute to read that first full paragraph.

A. Where -- which paragraph?

Q. On page 43, left-hand column, starting with the word "offsetting."

And it says there: Offsetting that risk are the costs associated with action when the true effect is actually negligible or null. Any change -- and then I'm skipping a line -- Any change in nutritional policy creates work for both industry and regulators, efforts that have a cost and that may displace other action that might have been more productive.

Correct?

A. I think -- that is correct, you're reading it correctly. The last sentence is important. There is no single or simple correct answer to these questions about cost, and these are really questions about cost.

Q. Uh-huh. And cost is --

A. It is worthwhile to stress it must be factored into the decision matrix on a case-by-case basis.

Q. True.

Now, you have conducted randomized clinical trials on pomegranate juice and POMx, as we've discussed previously?

A. Could you repeat the question. I didn't understand.

Q. You have undertaken randomized clinical trials on pomegranate juice and POMx.

A. I have, yes.

Q. And you'll be delighted to know that we are on the last page.

Polyphenols are the largest class of phytochemicals that are known; correct?

A. Correct.

Q. And they're the primary antioxidant taken into the body.

A. Correct.

Q. And people take in 500 milligrams to a gram of them every day?

A. Correct.

Q. And most plants have flavonoids; correct?

A. There are about 5,000 different flavonoids in the plant world. Yes.

Q. And they're the largest category of antioxidants in the diet?

A. Yes.

Q. Okay. And you recommend that people eat a variety of colorful fruits and vegetables?

A. Yes.

Q. And you've done that in your book entitled What Color Is Your Diet?

A. Yes.

Q. And in that book you recommend that people

change their diet in simple ways to protect themselves from damage and replace bland, starchy foods with colorful fruits and vegetables using a color code system?

A. That's correct.

Q. Okay. And I don't -- among the -- well, the colorful fruits and vegetables you talk about, there's really a large number of them?

A. That's correct.

Q. And you recommend that the consumers replace foods with hidden oils and sugar with healthy foods that are high in fiber and filling?

A. Yes.

Q. And you recommend adequate protein at each meal?

A. Yes.

Q. And you concluded, putting all of these together in a healthy lifestyle that includes exercise and meditation will combine to reduce the damage to your DNA which affects aging, Alzheimer's disease, cancer, diabetes and heart disease; correct?

A. Correct.

Q. Now, you never speak of a single nutrient as making up for a bad diet or lifestyle?

A. Correct.

Q. Okay. And you're also one of the authors -- let me get -- pull it out for you so I don't get chewed out.

Previously -- previously in this matter on CX 1286 -- unfortunately, in referring to the documents last night, I realized that the copy of CX 1286 that was entered into evidence only contained the first eight pages. I'm requesting that we replace that --

JUDGE CHAPPELL: Could you please have this conference off the record.

MS. EVANS: Yes, sir.

BY MS. EVANS:

Q. Referring to the document that I've just handed you, is this a document of which you're the first author named on page 1?

A. Correct.

Q. And in this document -- it's entitled Nutrition, Exercise and Prostate Cancer?

A. Correct.

Q. And it offers advice to men who want to maintain a lifestyle that promotes prostate health?

A. Correct.

Q. Okay. And it recommends a -- really a comprehensive lifestyle approach, doesn't it?

A. I can't understand what you said. I'm sorry.

Q. Well, for example, does it recommend that you lose body fat?

A. Yes.

Q. Okay. That you maintain muscle mass?

A. Yes.

Q. That you exercise every day?

A. Yes.

Q. That you eat colorful fruits and vegetables?

A. Yes.

Q. And that you incorporate good nutrition and exercise into your daily nutrient --

A. Yes.

Q. -- routine?

A. Yes.

MS. EVANS: Thank you. I have no further questions.

JUDGE CHAPPELL: Redirect?

(Discussion off the record.)

JUDGE CHAPPELL: We'll reconvene at 1:45.

(Whereupon, at 12:43 p.m., a lunch recess was taken.)

A F T E R N O O N  S E S S I O N

(1:49 p.m.)

JUDGE CHAPPELL: Back on the record.

Redirect?

MR. FIELDS: Thank you, Your Honor.

First I'd like to thank you for your courtesy at the noon hour.

JUDGE CHAPPELL: You're welcome.

- - - - -

REDIRECT EXAMINATION

BY MR. FIELDS:

Q. Doctor, I'm going to kind of go in the order that we did earlier or that you followed on cross.

You talked about a case in Los Angeles before Judge Lett, a federal judge, and in that case you testified about RCTs.

Were you talking in that case about pure fruit juice or any other pure food?

A. No. It was a case about a dietary supplement. It was a mixture of a number of ingredients or herbals, and so forth.

Q. That's what I thought.

You said that you had participated in a number of RCTs over the years.

You're not against RCTs, are you?

A. No. Not in any sense at all.

Q. So what you're telling us is that they're not necessary, but they're fine; is that correct?

A. That's correct.

Q. And sometimes they're not feasible; is that correct?

A. They're often not feasible for nutrients or whole foods because of small changes that are seen, the issue with the number of patients that would have to be studied and the particular disease condition.

Q. Now, in this case, in our three areas, respondents had RCTs in two of those three areas. Let's review those.

In heart is it correct that they had three, at least three RCTs?

A. That's correct.

Q. Now, counsel read to you from a deposition in one of those cases -- I can't even remember which one, but it doesn't matter -- where you said that you had thought that Dr. Aviram's study, the CIMT study, did not have a placebo group.

Were you just wrong about that?

A. Yeah. I was incorrect in my deposition and didn't catch it. It clearly says in the article right on the face of it that there was a placebo group in the

carotid artery stenosis study where they got the tissue. There was definitely a placebo group in that study.

Q. Have you rechecked that in the --

A. I've rechecked that in the reprint, yes.

Q. Very clearly it was a placebo-controlled study.

A. Correct.

Q. Okay. Now, in the prostate area, neither Dr. Carducci nor Dr. Pantuck you said had a placebo group, but they had a control in that the -- each patient's own prior doubling time, PSA doubling time, was matched against what happened after they started taking the pomegranate juice; is that correct?

A. Yes. Pomegranate juice or extract in the Carducci case.

Q. And in your opinion, is it more feasible and efficient to use that kind of a control when studying PSA doubling time than to try to recruit and assemble a placebo group?

A. Yes. This is an accepted study design where you determine the PSA doubling time beforehand and then put patients on a treatment and then look at what happens.

Two reasons why it's difficult. One is that it's hard to get patients with prostate cancer to agree

to a placebo arm, as we found in a couple of the long-term studies, and that had been delayed because of that. And secondly, the variability between subjects would be significant.

Q. When you say "the variability," you mean the variability in their rate of doubling time going into the operation.

A. That's correct. It would be almost impossible to balance the two groups so that they have the same doubling times.

Q. And is it correct that they're encountering delay in trying to do that with the present study?

A. That's correct.

Q. You spoke about studies that you have done and studies that others have done sponsored by the Resnicks.

Are there other studies on pomegranate juice that are neither done by you or sponsored by the Resnicks?

A. Yes. Certainly. If one does a search on the PubMed, which is where these studies are found, you'll find NIH-supported studies on pomegranate and prostate cancer. You'll also find studies from many laboratories around the United States, University of Wisconsin, University of California at Davis, and then

many labs internationally as well in England and elsewhere.

Q. Now, just to get it totally clear, is it your opinion that experts in the field would consider competent and reliable science to support health claims for pomegranate juice based upon the totality of science that does not necessarily include RCTs?

A. That's correct. The totality of evidence would be what most experts would base their opinion on.

Q. All right. Now, there was talk about your payment, and I just want to make it clear.

Is it correct that you have not received any compensation from the Resnicks directly or indirectly?

A. That's correct. All of -- as was reviewed in detail yesterday, we've done a significant number of studies, and all of those were done either with monies from unrestricted gifts from the Resnick entities or for grants and contracts from them.

Q. And did -- go ahead.

A. I was also going to say we also utilized in those studies and credited our NIH grants that we had at the time because this was an area of reasonable investigation that met the mission of our botanical research center as well.

Q. Is it correct that your salary is strictly based

upon your academic rank?

A. Yes. It's through the University of California. I don't receive a salary of any kind from the Resnicks.

Q. And that salary has been fairly stable over the last --

A. Fairly stable except for some modest step increases. I'm now a professor step 8, so there have been, you know, some $1,000 per step type of increases from step 5 to step 8 perhaps in the last ten years.

Q. But that salary, those step increases have nothing to do with the Resnicks' contributions?

A. Not at all. It's based on a promotion committee reviewing my scientific work.

Q. Okay. Now, we talked about post hoc work -- pardon me -- you talked with counsel about post hoc -- and with me, post hoc analyses, things done that were not the prime objective as the study was applied for.

Now, is it correct that from a statistical point of view, those are not reported on typically?

A. Yeah. Typically in a drug-type trial or any other agent, the primary outcome variable in an intent-to-treat analysis, which is where you look at the comparison between two groups or even within one group, the statistical outcome is the one that would be reported in the paper for that primary outcome.

Q. But there are numerous papers doing post hoc analyses; isn't that correct?

A. Absolutely. Often in one of two directions, as I said yesterday, either if there's an adverse event that occurred that -- in a significant subgroup but was not statistically significant for the overall group or if there was a positive indication, then you would need to report either of those in the discussion and in the paper when you publish the full results of a study, and that would be part of the totality of the scientific evidence to be considered.

Q. And frequently those sub hoc analyses -- pardon me -- post hoc analyses are reported in peer-reviewed journals?

A. Absolutely. They're often included. As I mentioned, the Women's Health Initiative and other large studies funded by the NIH often report out things other than the primary outcome variable.

Q. Right.

And is it correct that frequently very important information is discovered through post hoc analyses?

A. Yes. Absolutely. Important clinical information is often obtained that way.

Q. And although one often does subsequent studies

to confirm that, do you deny the public the beneficial information of those important discoveries while you're waiting for the subsequent studies?

A. No. You report all the important aspects of the study and then launch into your confirmatory and future studies.

Q. Thank you.

Now, we talked -- or you talked a little bit about antioxidants. In fact, you talked a lot about antioxidants. And counsel asked you a couple of -- about a couple of studies that showed a null result with reference to that.

Is there widespread scientific acceptance of the biologic mechanisms by which antioxidants work as you testified?

A. Yes. There's a very wide acceptance that oxidant stress is a basic underlying mechanism for processes as diverse as aging, common forms of cancer, heart disease, diabetes, dementia, across the board. Oxidative stress and inflammation are common mechanisms now that cross different medical fields.

Q. Now, is it correct that the particular thing in pomegranate juice that creates the effect that you and others have discovered and testified to are the ellagitannins?

A. That's correct.

Q. And is it correct that anthocyanin -- I'm not pronouncing that correctly -- anthocyanins --

A. Anthocyanins, yes.

Q. -- anthocyanins are a minor factor, if any, in that contribution?

A. They make a minor contribution to the antioxidant effects, but they provide the color that distinguishes pomegranate, and that -- that's primarily -- it contributes to but in a very minor way to the antioxidant of the whole juice.

Q. Now, in the studies that you have done, has there been any difference between the antioxidant effect in pomegranate juice and that in POMx?

A. No. The antioxidant effect measured in the laboratory has not been different.

And also, when we give animals the purified pomegranate extract with the ellagitannins, we obtain the biological effects that we're studying that were similar to what would be in effect in animals getting pomegranate juice.

Q. Do you know of any study indicating that POMx and pomegranate juice do not have the same impact on oxidative stress?

A. No.

Q. Is it your firm belief that they do have the same impact?

A. Yes.

MR. FIELDS: That's all I have.

JUDGE CHAPPELL: Any recross?

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RECROSS-EXAMINATION

BY MS. EVANS:

Q. Thank you, Dr. Heber.

Are you an article on -- are you an author of an article entitled In Vitro Antiproliferative, Antipoptotic (sic) and Antioxidant Activities of Punicalagin -- In Vitro Antiproliferative, Apoptotic and Antioxidant Activities of Punicalagin, Ellagic Acid and a Total Pomegranate Tannin Extract Are Enhanced in Combination with Other Polyphenols Found -- as Found in Pomegranate Juice?

A. Yes.

Q. And did you find that the antioxidant activity of total pomegranate -- well, of the total pomegranate juice constituents are more potent than its separated and individual polyphenols?

A. We did.

Q. And did you state that this suggests synergistic and/or additive effects from the other phytochemicals

present in PJ?

A. We did speculate that, yes.

Q. Yes.

And did you say that "This finding is not surprising, as PJ also contains proanthocyanidins, anthocyanins (glycosides of delphinidin, peonidin and cyanidin) and flavonoid glycosides, phytochemicals that have all been shown to have antioxidant and antiproliferative activities"?

A. Yes.

MS. EVANS: Thank you.

No further questions.

MR. FIELDS: No questions, Your Honor.

JUDGE CHAPPELL: Thank you, sir. You're excused.

MR. GRAUBERT: Your Honor, could I have your indulgence for one second to go and get the other witness from the cafeteria?

JUDGE CHAPPELL: Okay.

(Pause in the proceedings.)

MR. FIELDS: Our next witness, Your Honor, is Dr. Denis Miller.

Dr. Miller, would you take the stand, please.

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Whereupon --

DENIS R. MILLER, M.D.

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

DIRECT EXAMINATION

BY MR. FIELDS:

Q. Good afternoon, Dr. Miller.

A. Good afternoon.

Q. I don't know if the reporter asked you, but would you state your full name, please.

A. Yes. Denis R. Miller.

Q. And Dr. Miller, you are a medical doctor; is that correct?

A. Yes, I am.

Q. And you have been practicing medicine for over 50 years; is that right?

A. That's correct.

Q. All right. And are you board certified in pediatric hematology and oncology?

A. Yes, I am.

Q. All right. And you're a clinical professor at the Robert Wood Johnson School of Medicine in New Jersey?

A. Yes, I am.

Q. All right. And is it correct that you graduated

from first Cornell and then Cornell Medical School?

A. That's correct.

Q. And you did your residency at Children's Hospital in Boston?

A. Yes.

Q. And also at Harvard Medical School; is that right?

A. Yes.

Q. And then you did a fellowship at Harvard in hematology/oncology?

A. Yes, that's correct.

Q. Okay. And you were a captain in the Air Force as a physician.

A. Yes, I was.

Q. You outranked me, so...

You've been a department chairman at Memorial Sloan-Kettering Cancer Center in New York?

A. Yes.

Q. And director of pediatric hematology/oncology at Cornell Medical School as well as the Strong Memorial Hospital at the University of Rochester?

A. Yes.

Q. Okay. And is it true you've been a consultant to a number of major pharmaceutical companies?

A. Yes, I have.

Q. And is that particularly in the area of oncology research?

A. Yes. It was primarily oncology/hematology and clinical research, yes.

Q. Okay. And is it correct that you've been the scientific director of the Cancer Research Foundation and have also directed the clinical research program at a national clinical cancer program?

A. Yes.

Q. Okay. And you were on the editor -- editorial board of the American Journal of Clinical Oncology?

A. That's correct.

Q. Is it correct that you've written and published 164 articles in peer-reviewed professional journals?

A. Yes.

Q. And you wrote 78 chapters in textbooks in your field?

A. Yes.

Q. Okay. Now, is it correct that you've been retained by the FTC as an expert in prior cases?

A. I have, yes.

Q. All right. And in those prior cases have you been accepted by the administrative law judge as an expert witness?

A. Yes.

MR. FIELDS: All right. Your Honor, we offer Dr. Miller as an expert, and we will offer his -- I guess his report is already in evidence, but we offer it again.

MS. VISWANATHAN: Your Honor, may we have articulation of the areas in which he's offering --

MR. FIELDS: He's going to be testifying about the applicable standards of substantiating evidence for fruit and fruit juice or food products in general as opposed to the standard that is applicable to drugs, just the standard.

MS. VISWANATHAN: Okay. With the understanding that he will not be testifying as to the reliability or strength of POM's particular studies, we have no objection.

MR. FIELDS: That's correct. He's not going to be testifying about the scientific studies. He's just going to testify about standards.

MS. VISWANATHAN: With that stipulation, we have no objection.

JUDGE CHAPPELL: What is the exhibit number of his expert report?

MS. VISWANATHAN: I believe it's PX 0206.

MR. FIELDS: Thank you.

JUDGE CHAPPELL: All right. Any opinions that

meet the proper legal standards will be considered.

BY MR. FIELDS:

Q. Is it correct, sir, that you testified as an expert for the FTC in the Daniel Chapter One case?

A. Yes, I did.

Q. And is it correct that in that case you testified that based on the standard of substantiation that you believe the -- was applicable to that case, to the evidence in that case, that respondents had insufficient science to support their claims? Is that correct?

A. Yes, that's correct.

Q. Okay. And what were the principal factors that led you to that conclusion or opinion in the Daniel Chapter One case?

A. Well, there were three main ones.

The first was that there was no reliable science supporting the claims that were made, nor were there any medical oncology/hematology experts that supported the position of Daniel Chapter One.

Secondly, the organization was making claims that their products could be taken in the place of and instead of conventional therapies to treat, prevent and cure cancer.

Thirdly, their products, a conglomeration of

different herbals and other materials, had side effects that were unsafe.

Q. Okay. Now, I'm going to ask you a hypothetical question.

Assume that we're talking about pure fruit or pure fruit juice and that it creates no material risk of harm and that it is not urged as a substitute for proper medical treatment. In that case, does the science to substantiate health claims for that fruit or fruit juice necessarily have to include RCT studies?

A. No, they don't have to include a randomized clinical trial.

Q. Is that because of the fact that it is safe and not urged as a substitute for proper medical treatment?

A. Yes.

Q. All right. Now, is it your opinion that the consensus of competent and reliable and experienced scientists would agree with the opinion you've just given, that when you're talking about a safe pure fruit juice that is not offered as a substitute for proper medical treatment, you look to the totality of the science and not require RCT tests?

A. Yes.

Q. All right. Dr. Miller, at the time you were retained as an expert in this case, you had also been

retained by the FTC to testify as an expert in still another case; isn't that correct?

A. That's correct.

Q. Is it correct that when the FTC learned that you were going to testify as an expert in this case, you got fired?

A. That's correct.

Q. Did you try to explain there was a difference between the two cases?

A. I did.

Q. All right. You got fired anyway?

A. Yes.

MR. FIELDS: All right. That's all I have.

JUDGE CHAPPELL: Any cross?

MS. VISWANATHAN: Yes.

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CROSS-EXAMINATION

BY MS. VISWANATHAN:

Q. Good afternoon, Dr. Miller.

A. Good afternoon.

Q. Dr. Miller, you agree that the claim being made about a product is relevant to the level of substantiation required, don't you?

A. Yes.

Q. And as you just discussed with Mr. Fields, you

prepared an expert report for the FTC in the Daniel Chapter One case; correct?

A. Yes, I did.

Q. And in your report in the Daniel Chapter One case, on page 7 -- that was January 28, 2009 -- didn't you state, "It is my opinion that to constitute competent and reliable scientific evidence, a product that purports to treat, cure or prevent cancer must have its efficacy and safety demonstrated through controlled clinical studies"?

A. Yes. I said that the key thing is what is the product.

Q. But you specifically said a product that purports to treat, cure or prevent cancer must have its efficacy and safety demonstrated through controlled clinical studies, did you not?

A. And as it applied to the Daniel Chapter One products, that statement is correct.

Q. Well, in that case didn't you also testify that if a sponsor of a potentially new therapy wishes to claim that their product is safe and effective in the treatment of a specific type and stage of cancer, a randomized, controlled clinical trial is mandatory, just as it would be for a new medicinal cancer therapy?

A. Again, it depends on the product. And when I

wrote that opinion, I wasn't discussing a food.

Q. You define treating cancer as causing a regression of the disease, putting somebody in remission, prolonging their disease-free remission or prolonging their survival; is that correct?

A. Yes.

MR. FIELDS: Objection. Oh, I'm sorry. Withdrawn.

BY MS. VISWANATHAN:

Q. And earlier when we were referring to RCTs, randomized, control -- that refers to randomized, controlled clinical trials; correct?

A. RCT means randomized clinical trial.

Q. Okay. And by "clinical trials" you mean trials done on human beings; correct?

A. Generally, that's the case.

Q. Which is distinct from nonclinical research which is done in either test tube or animal models; correct?

A. That's correct.

Q. You've stated in your report in this case on page 6 that "The regulatory requirements are much more rigorous when crossing the boundary between making a general health benefit claim, such as low-fat diets are healthier than high fat diets, and taking a general

statement to the next level and claiming efficacy in the treatment of a specific type of cancer"; correct?

A. Again, that's correct, but it depends on what the product is that we're talking about.

Q. I'm sorry.

A. I said --

Q. Oh, actually I'll just...

(Pause in the proceedings.)

So are you saying that if a dietary supplement were claiming to treat prostate cancer, it would require randomized, controlled clinical trials?

A. If -- are you talking about a food or are you --

Q. I'm talking about -- I said a dietary supplement.

MR. FIELDS: Objection. Ambiguity as to what "a dietary supplement" is. Some have pure foods. Some may be herbs. Some may be all kinds of things.

MS. VISWANATHAN: I'll withdraw the question.

BY MS. VISWANATHAN:

Q. If any product were claiming to treat prostate cancer, it would require randomized, controlled clinical trials; correct?

A. No, not correct. I don't believe that food requires a randomized clinical trial, and I believe that

the requirements and the stringency and the other things that we look at can be relaxed because it is a food and not a drug or a concoction of other herbs.

Q. Do you recall giving a deposition in this matter on April 5, 2011?

A. Yes.

Q. Okay. And in that deposition on page 110, do you recall giving the following testimony.

"QUESTION: Okay."

MR. FIELDS: Could we have just a moment to find it?

MS. VISWANATHAN: Oh, sure. We have a copy.

BY MS. VISWANATHAN:

Q. "QUESTION: Would you agree that a product of any type that purports to treat cancer should have its efficacy and safety demonstrated through controlled clinical studies?

"ANSWER: By treatment, a patient has to have a disease, a certain stage of disease, a certain extent of disease, and the treatment is going to have a beneficial effect on either eradicating the disease, getting it under control, prolonging someone's survival. If you're trying to make claims like that, there should be clinical trials to show that.

"QUESTION: And 'clinical trials' means trials

on humans.

"ANSWER: Again, if you're making a treatment claim, I've answered it already."

Do you recall giving that testimony?

A. Yes.

Q. Okay. So based on that testimony, if a fruit juice were claiming to treat prostate cancer, it would require clinical -- randomized clinical trials on humans; correct?

A. Not correct.

Q. And if a fruit juice were claiming to prevent prostate cancer, it would require clinical -- randomized, controlled clinical trials; correct?

A. No, not correct.

Q. And that's in contradiction to the testimony you gave earlier in this -- in your deposition in this case.

A. No, it's not.

In talking about a food, which is not being offered as a substitute or a replacement for a conventional therapy, that is known to be safe, for which there are reliable data to support a claim that it may be beneficial to patients with a number of different disorders, one can relax the requirement for a randomized clinical trial if the food has a high

benefit-risk ratio, a low or zero toxicity or safety profile, and has benefit to mankind.

Q. Sir, I'm asking you a question about a specific claim. I understand you're saying that you're talking about a claim that it may be beneficial to patients.

I'm asking you, if there's a specific claim that a fruit juice is treating prostate cancer, wouldn't it require randomized, controlled clinical trials?

A. Because it's a food, it would not require a randomized clinical trial.

Q. Even if there were a claim that it treats prostate cancer.

A. That's correct.

Q. And your answer is the same for if a fruit juice were claiming to prevent prostate cancer, you say it would not require randomized, controlled clinical trials?

A. That's correct. If there were reliable scientific data to support that.

Q. You defined "competent and reliable evidence" to mean a scientific hypothesis has been established; is that correct?

A. Yes.

Q. And you believe that nonclinical studies are hypothesis-generating; correct?

A. They're more than that. They -- you generate a hypothesis to begin with, but then you test the hypothesis in an animal model, in a test tube, in other laboratory or even in animal studies, so it goes beyond just hypothesis testing.

Q. Well, in fact you believe that if you see evidence of anticancer activity in a test tube or an animal test, then one goes to a clinical trial to see if there's any activities in humans; correct?

A. Assuming that the agent you're testing is safe and doesn't kill the animals, that's correct.

Q. And you believe that evidence from nonclinical settings does not mean that the product is effective in treating cancer patients; correct?

A. That may be the case, but also a lot of the evidence that we get from nonclinical trials gives us a direction to pursue that agent in potentially helping mankind.

Q. So -- yes.

So I understand, so you're saying that the nonclinical trials or the nonclinical evidence would provide a hint that needs to be investigated further; correct?

A. Yes. Understanding there are differences between the test tube or the mouse and man, but it gives

us important information to do further studies.

Q. Okay. You served as associate medical director at Cancer Treatment Centers of America; is that right?

A. That's correct.

Q. And when you were in that position, 80 percent of the patient population in your institution was using alternative or complementary medicine; correct?

A. That's correct.

Q. And some examples of the kinds of things they were using included fruit cocktails or fruit juice cocktails, shark cartilage and megavitamins; correct?

A. That's correct.

Q. And in the Daniel Chapter One case you testified in this court that if there is a claim that the alternative or complementary product is designed to prevent cancer, prevent the progression of cancer, cure cancer or specifically treat cancer, then those would have to go through the process of being tested in randomized, controlled clinical trials; correct?

A. Yes, that's correct. But again it depends upon what the product is.

Q. Was that your testimony in Daniel Chapter One?

A. Yes, it was.

Q. And in Daniel Chapter One you further stated that making claims that a particular product has

specific anticancer activity is different from saying it's just good nutrition like a vitamin; correct?

A. Run that one by me again. The acoustics in here are not very good. I'm sorry. I'm having trouble hearing you.

Q. No problem. I'll just reread it from the screen.

In Daniel Chapter One you further stated that making claims that a particular product has specific anticancer activity is different from saying the product is just good nutrition, as with a vitamin; correct?

A. Well, again, that applies -- yes, that's correct but again applied to a product that was being offered as a substitute for and a replacement for a conventional effective and safe anticancer therapy.

Q. So in Daniel Chapter One you said that claims about specific anticancer activity for alternative or complementary medicine products must go through the randomized, controlled testing process.

A. Yes, I said that. But then what is the alternative therapy, which is very important. "Alternative" means in place of or instead of conventional treatment for cancer and other diseases. And if that product is being offered in replacement for

known and safe agents, there better be some proof for that activity and safety.

Q. Okay. You believe that there shouldn't be a separate, different, less rigorous way of identifying the safety and efficacy of complementary medicine; correct?

A. I think we have to define "complementary medicine."

Q. Okay. Well, in Daniel Chapter One isn't it fair to say that you defined it as something that is being taken along with the patient's other cancer treatments?

A. Yes. If it's a food, I don't think you need a randomized clinical trial for it. If it's a drug that's going to improve a patient's tolerance to chemotherapy or lessen some of the toxic effects of chemotherapy by improving their blood counts, and it is a drug that is a complementary agent to cancer treatment, then that agent has to go through the process of clinical testing and randomized clinical trials. If it's a food, I don't believe it does have to go through that process.

Q. Okay. So previously when you testified in Daniel Chapter One that there shouldn't be a separate, different, less rigorous way of identifying the safety

and efficacy of so-called complementary medicine, you're saying that's no longer your opinion?

A. I'm saying that the product in Daniel Chapter One, again, had no reliable scientific evidence supporting it or reliable or competent medical oncologists supporting it. It was being offered as a replacement for and instead of conventional treatment for leukemia, for breast cancer. And thirdly, some of the products had concerns about safety issues so that they were not without safety concerns.

So for all of these reasons, my opinion was and it's -- it would -- my opinion was that that product required randomized clinical trials to support the claims that were being made.

It is not a food. It's not been around for thousands of years where there are no safety concerns, and so for that reason there's a huge difference between all of the different products that were being offered by and sold by Daniel Chapter One compared to the fruit juice we're discussing today.

Q. Well, in Daniel Chapter One you further stated that complementary medicine must go through the same rigorous process because, quote, we want to help cancer patients and we want to make sure what they're getting is safe and effective.

Was that your testimony?

A. Yes. But again, as I said, there are complementary medicines that diminish the severity of nausea and vomiting. They're drugs that need to be tested. There are other agents that improve the blood counts in patients who are getting chemotherapy. Because they're drugs or hormones, they also have to be tested. If it's a food, it doesn't have to go through the same stringency of a randomized clinical trial.

Q. Okay. In your report in this case, on page 11, you state that there may be some category of patients who do not have many or any alternatives, and for them a clinician may recommend, among other things, the consumption of pomegranate; correct?

A. That's correct.

Q. And that clinician's recommendation is for the purpose of benefiting the general well-being of the cancer patient; correct?

A. That's correct.

Q. The clinician is not recommending pomegranate as a treatment for their cancer; correct?

MR. FIELDS: Objection to "treatment" ambiguity. What does "treatment" mean?

MS. VISWANATHAN: Your Honor, I believe we have a question where he defined "treatment" earlier, where

he agreed to the definition of "treatment."

MR. FIELDS: I don't recall that, but if it could be repeated and if we have this defined, then I have no objection.

JUDGE CHAPPELL: Do you want to have her read it?

MS. VISWANATHAN: Yeah, let me -- if I can just go back and try and find it.

(Pause in the proceedings.)

I apologize, Your Honor. I'm just trying to find the previous question, unless the court reporter knows -- oh, here it is. Okay.

BY MS. VISWANATHAN:

Q. Earlier today I asked you, "You define treating cancer as causing a regression of the disease, putting somebody in remission, prolonging their disease-free remission or prolonging their survival; is that correct?"

And your answer was: "Yes."

A. Yes.

Q. So that is my -- that is the definition I'm using when I use the word "treatment." Is that fair?

A. Yes.

Q. Great.

So back to my -- where we were. Okay.

So my question was, where a clinician is recommending pomegranate for the purpose of benefiting the general well-being of a cancer patient, that's different from recommending pomegranate as a treatment for their cancer; correct?

A. When you started the question, you talked about a patient who seemed to have no other treatment options, where in the absence of any available therapy or standard of therapy for that patient would or could pomegranate juice be used to offer some benefit to the patient. I believe that's the way you started it.

Q. Uh-huh.

A. The answer to that would be yes. If there are no other standards, there is no available therapy, there is no other approved therapy, are there data to suggest that this agent would be safe and effective and not harmful, and in this case the answer would be yes, that could be used in that patient when there are no other treatment options in the absence of a randomized clinical trial to show that.

Q. And my understanding is -- my question is, the use of pomegranate in that case is for the patient's general well-being as opposed to a treatment for their cancer; correct?

A. Well, it might be for both. It might improve

the patient's well being, and it might provide some benefit to the patient.

Q. So you're assuming that this patient is a patient who's under the active care of an oncologist or oncological surgeon; correct?

A. Yes.

Q. And that patient is getting a recommendation from their physician; correct?

A. Yes.

Q. Okay. It's your opinion that you can't take the physician out of the formula; correct?

A. That's correct.

Q. You didn't actually evaluate any of the advertising claims made regarding the health benefits of POM's products; correct?

A. No, I did not.

Q. And as we've been discussing, your opinion is that the level of substantiation required for health claims for food is different from that required for a drug that is developed and marketed for the treatment, cure or prevention of certain diseases; correct?

A. That's correct.

Q. So, hypothetically, you would agree that if a food were marketed -- or were developed and marketed for the treatment, cure or prevention of disease that the

level of substantiation for a drug would apply?

A. I didn't understand the word "developed." I would think that foods are out here and don't have to be invented or developed today.

Q. Okay. Well, let's just say you agree that if a food were -- well, let me clarify it.

You would agree that -- hypothetically, you would agree that if a food were marketed for the treatment, cure or prevention for certain diseases that that level of substantiation for a drug would apply.

A. Again, there's a difference in my mind between a drug and the confidence that you have to have, the safety of the agent, the efficacy of the agent. The risk-benefit ratio is different for a drug than it would be for a food, and the stringency and requirement could be relaxed and made less rigorous than it would be for a drug.

Q. Okay. Well, in -- in Daniel Chapter One you testified that the dietary -- that dietary supplements marketed for the treatment, cure or prevention of cancer should meet the same level of substantiation as drugs; correct?

MR. FIELDS: Objection. Ambiguity to "dietary supplement" again. It could be just pure fruit or it could be a lot of herbs or it could be a drug.

"Dietary supplement" is very ambiguous term.

JUDGE CHAPPELL: Did you understand the question?

THE WITNESS: Yes, I did.

JUDGE CHAPPELL: Overruled.

THE WITNESS: I wasn't discussing in Daniel Chapter One the difference between a -- various concoctions of different herbs and other ingredients that made up the various Daniel Chapter One products. And by "a dietary supplement" I wasn't discussing or didn't mean to say a pure food substance. I was thinking about multivitamin substances. I was thinking about other things that would improve a patient's well-being, but I wasn't discussing a food.

Subsequently, since that Daniel Chapter One testimony, I've learned more and understood more and realize that there's a difference between a Daniel One -- a Daniel Chapter One product and a pure food substance, and thus my -- I don't think my opinion today has anything to do with the situation in Daniel Chapter One. They're totally different products; one is not a food and one is a food.

BY MS. VISWANATHAN:

Q. Okay. So is it your opinion that the level of substantiation required for health claims for a food is

different from the level of substantiation required for health claims for dietary supplements in some cases?

A. It depends on the dietary supplement. That's correct. Is it pure food and the other is a mixture of fifty different minerals and elements and vitamins and other things? Then I think there is a difference.

Q. Okay. Well, you are -- okay.

So you're aware that POM Wonderful has several products sold under the name POM Wonderful juice or POMx diet -- pills and POMx liquid; correct?

A. Yes. I understand that, and I understand they all come from the same, the same food substance.

Q. You have no independent knowledge of the ingredients of any of the POM products; correct?

A. You mean each of the individual ingredients of it?

Q. Yes.

A. I have some knowledge. I'm not here I don't believe to testify to the different ingredients and the milligrams or micrograms of each one of them.

Q. You have no specific knowledge of how those products are manufactured; correct?

A. That's correct.

Q. Okay. So what -- and is your knowledge based on what you were told by POM's representatives?

A. Well, I'm assuming that it's a food substance, and I'm assuming that it's a pure food substance without additives or supplements or other drugs that are added to it.

Q. Okay. So you're making an assumption about that there are no biological or chemical components added to the pure fruit; is that correct?

A. To the best of my knowledge, pomegranate and the other agents you've mentioned are from the pomegranate fruit.

Q. And in your opinion, all of the POM products regardless of the form they're in, whether it's in the juice form, the liquid extract or a pill form, are all the same for the purposes of determining the level of scientific substantiation required for their claims?

A. Since they all come from the same food substance, yes.

Q. And that's your opinion even though you don't specifically know the composition or the ingredients of the products; correct?

A. That's correct.

Q. And that's your opinion even though you don't know the bioequivalence of the different products; is that correct?

A. Well, I think others will -- may testify to

that. My understanding is that, again, it comes from the pomegranate fruit and juice, and within that are biological activities that are important in the indications and disorders that are under discussion.

Q. Dr. Miller, you're not an expert in studying the role of diet in the prevention or treatment of disease; correct?

A. I'm not a nutritionist. That's correct. I know enough about cancer epidemiology to know about the relationship between diet and other lifestyle factors that impact on the causation of cancer.

Q. But -- and you're not an expert in the role of foods specifically in the prevention and treatment of disease; correct?

A. I'm not an expert in that. I'm knowledgeable but not an expert. I'm not a nutritionist, that's correct.

Q. You've not published any articles on diet or foods in the prevention or treatment of cancer; correct?

A. That's correct.

Q. Is it fair to say that you have not read the Federal Trade Commission's advertising substantiation policy statement?

A. That's correct.

Q. And you've never read the Federal Trade Commission's Guidelines on Advertising of Dietary Supplements; correct?

A. That's correct.

Q. You've never read the Federal Trade Commission's Enforcement Policy Statement on Food Advertising; correct?

A. That's correct.

Q. You state in your report in this case on page 3 that you are familiar with the process of regulatory approval and post-approval fulfillment requirements.

A. I didn't hear the last.

Q. Sure. Let me restate the question.

You state in your report in this case on page 3 that you are familiar with the process of regulatory approval and post-approval fulfillment requirements.

A. I didn't hear your last word.

Q. It's post-approval fulfillment requirements.

A. Fulfillment, post-approval fulfillment.

Q. Yes.

A. Thank you.

Yes.

Q. And by that do you mean Food and Drug Administration regulatory requirements?

A. Yes.

Q. And that's from your experience in the pharmaceutical and biotechnology industries; correct?

A. Well, it's my experience in 50 years of practicing medicine and being involved in clinical research both from the clinical academic side as well as from the industry side.

Q. Okay. Okay. So is this -- and this experience with regulatory approval requirements is part of what qualifies you as an expert to offer your opinion on the standard for substantiating claims for the products in this case; correct?

A. That's correct.

Q. And you consider yourself an expert in the Food and Drug Administration's regulations governing approval for drug treatments for cancer; correct?

A. Yes. Having been involved in the approval of many of those agents, I'm aware of their requirements.

Q. You don't consider yourself an expert in the Food and Drug Administration's regulations concerning dietary supplements; correct?

A. I'm not an expert in that area, but I've reviewed some of the guidances relating to that subject matter.

Q. You're not aware of the Food and Drug Administration's regulations governing the standard for

health claims that can be made for a food, are you?

A. No, I'm not.

Q. You consider yourself an expert in the design of clinical research protocols; correct?

A. I certainly do.

Q. And you're relying on that expertise in presenting your opinions here today; correct?

A. Partly so, yes.

Q. Is it fair to say that your expertise is in designing clinical research protocols relating to treatment of cancer?

A. Some have been related to the treatment of cancer; others have been related to prevention of cancer.

Q. Do you have expertise in the design of clinical trials to prevent cancer in healthy people?

A. I haven't been involved directly in those. I'm aware of many of the studies that involve cancer prevention or attempts to study cancer prevention.

Q. Do you consider yourself an expert in the design of clinical research protocols for foods?

A. I haven't done any of those.

Q. You're here to testify specifically about the substantiation standard relating to foods and prostate cancer; correct?

A. It's more general, but my presence here today is to generally discuss what's required for accepting a food if for the benefit of mankind versus what's required for a drug or drug substance.

Q. Okay. But you're not here to testify about the substantiation standard related to foods and cardiovascular disease, are you?

A. No.

Q. And you're not here to testify about the substantiation standard for -- relating to foods and erectile dysfunction; correct?

A. That's correct.

MS. VISWANATHAN: Okay. May I just have one moment, Your Honor, to confer?

JUDGE CHAPPELL: Go ahead.

(Pause in the proceedings.)

BY MS. VISWANATHAN:

Q. Okay. Your current employer, Parexel, is a company that manages clinical research trials for the pharmaceutical and biotechnology industries; correct?

A. That's correct.

Q. And during the time you've been at Parexel, which I believe is 2006, you haven't been involved in any studies testing food in cancer; correct?

A. I realize now that I can't discuss it because

it's not -- we're not -- have not been awarded the project, but we're reviewing a project at this time that involves a food substance.

Q. Okay. But that -- in the time you've been at Parexel, that's the first one?

A. That's correct. We haven't managed a clinical trial regarding a food substance, that's correct.

Q. Okay. And so all of the trials that you've been involved in were for either drugs or biotechnology-type products?

A. Well, yes, that's true. But just to expand upon it, it includes conventional anticancer therapy. It would include new, what we call targeted therapies. And it could also include agents used as complementary medicine to support a patient undergoing cancer treatment. It also includes treatments for hematologic disorders as well.

Q. Okay. And I do have to ask, the one food study that's under proposal, is it -- it's not from any of the respondents in this case; correct?

A. That's correct.

Q. Okay. It's from a separate entity.

A. Separate entity.

Q. Okay.

A. Yes.

Q. In your report on page 15 -- and maybe we should bring this one up, if you don't mind, because it would be easier. We have a paper copy of your report as well if you want to look at that.

Your Honor, may we approach to --

JUDGE CHAPPELL: Go ahead.

MS. VISWANATHAN: Thanks.

BY MS. VISWANATHAN:

Q. Whichever you'd prefer to look at.

A. Oh, thank you.

Q. I'm looking at the top of page 15.

Where you state your opinion that the level and rigor of substantiation is quite different for a food than for a drug, you cite to an August 2010 paper that says "Beals"; correct, "Beals, et al."?

A. Yes.

Q. Okay. And that was a paper written by Howard Beals, Timothy Muris and Robert Pitofsky, entitled In Defense of Pfizer Factors; correct?

A. That's correct.

Q. You would agree that the Beals paper is not a medical article or review; correct?

A. Yes.

Q. And in fact it's a legal paper which describes how to look at foods compared to conventional treatments

and whether the same substantiation standard should be applied?

A. Yes.

Q. And that's essentially the scope of your opinion that you're offering here today as well; correct?

A. That's correct.

Q. And of course you're not an expert in the law; correct?

A. No, I'm not.

Q. You don't know anything about the background of the authors of that paper, do you?

A. No, I don't.

Q. You're not aware of whether they have medical backgrounds, for instance?

A. I'm not aware of?

Q. I'm sorry.

You're not aware of whether they have medical backgrounds, for instance?

A. I don't know what their background is. I haven't seen their CVs. That's correct.

Q. Is this the type of document that you as a medical doctor would typically rely upon in forming an opinion about whether claims for a cancer intervention were based in science?

A. I think in this area one needs to go beyond the

usual, conventional medical papers and scientific papers because it's a different area, and I think because of that one would welcome opinions or expansion of the processes whereby you determine whether a food is different from a drug, and an article like this helped me very much.

Q. Okay. But you were not familiar with this paper before you were asked to give an opinion in this case, were you?

A. I was not, that's correct.

Q. You -- it -- it wasn't something you came across in your independent literature review that you did for the case.

A. This paper, no. Other papers that relate to it, yes, since then.

Q. But this paper was provided to you presumably by representatives of POM; correct?

A. That's correct.

Q. Dr. Miller, you're being compensated at the rate of $500 an hour for your work on this matter; correct?

A. That's correct.

Q. And your rate for giving testimony is $5,000 a day; is that correct?

A. That's correct.

Q. And not counting today's testimony, have you been compensated approximately $10,000 for your work on this matter?

A. That's correct.

Q. You mentioned that you had consulted for the Federal Trade Commission in a case earlier this year in which you were fired; correct?

A. That is correct.

Q. Okay. And you prepared a declaration for the FTC in that case; correct?

A. That's correct.

Q. Had you signed a contract to serve as a consultant, expert consultant for the FTC?

A. For that case?

Q. Yes.

A. Yes.

Q. Okay. And that contract required you to report potential conflicts of interest, did it not?

MR. FIELDS: Objection. Best evidence, Your Honor. The document will speak for itself. I assume counsel has it.

JUDGE CHAPPELL: Overruled. She can inquire into this.

BY MS. VISWANATHAN:

Q. Would you like me to repeat the question?

A. No, no. I heard the question.

And I guess, to me, what is conflict of interest? Was I involved in a case that was in direct conflict with the case at hand, which involved a mixture of a number of different laxatives that were being put forth to cure constipation and basically prevent colon cancer, which I didn't think was a conflict of interest in presenting the health benefits of a food, so in my mind, there was no conflict of interest.

I would take a case based on its merits and whether I could support my opinions with a reasonable degree of medical certainty and probability, and I felt comfortable and confident that I could do it with the Seattle case with the laxatives as well as I could for this case which was totally different.

Q. Did that agreement also require you not to reveal nonpublic information?

A. I don't recall that in that contract.

Q. You don't recall.

So you're not aware of the fact that your expert report might have revealed information about a nonpublic investigation of the Federal Trade Commission at the time?

A. I just don't understand that language. I'm

sorry.

Are you asking me if I revealed that information?

Q. Well, in your expert report you did cite the fact that you prepared a declaration in the Pure Cleanse case; correct?

A. In which report?

Q. In your expert report in this matter.

A. Yes, I did.

Q. Okay. I have one more question.

In Daniel Chapter One, you said that if somebody is claiming that orange juice by itself has got anticancer activity and can be --

(Admonition from the court reporter.)

BY MS. VISWANATHAN:

Q. In Daniel Chapter One, didn't you state that if someone is claiming that orange juice by itself has got anticancer activity and can be taken by a cancer patient to treat their cancer, they'd better show you the scientific evidence for that?

A. Yes. But, again, what is -- you know, how much scientific evidence do you have to provide.

And I believe since providing that testimony in Daniel Chapter One I've had the opportunity to read other papers by scientists and physicians who have gone

into more detail about different standards required for a drug versus a food, and it's a position that I agree with. People's thinking and ideas about a subject matter can change and evolve, and I think mine has evolved somewhat since I provided my testimony in Daniel Chapter One.

MS. VISWANATHAN: Okay. Nothing further. Thank you.

JUDGE CHAPPELL: Any redirect?

MR. FIELDS: Very briefly, Your Honor.

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REDIRECT EXAMINATION

BY MR. FIELDS:

Q. Counsel asked you about food and cardiovascular health and prostate health and erectile dysfunction.

Is it correct that your testimony about the nonrequirement of RCTs when you're testing pure food like fruit juice applies to any health claim? Is that correct?

MS. VISWANATHAN: Your Honor, I object. This is beyond the scope of his disclosed expert testimony to us, which only referred to cancer.

MR. FIELDS: It doesn't only refer to cancer, Your Honor. He testified it applies to --

JUDGE CHAPPELL: Well, his question says he was

asked about it. If he was asked about it, I think it's within the scope.

BY MR. FIELDS:

Q. Is it correct, sir, that when you said that it's your opinion and in your opinion it would be the consensus of other scientists that to test the health claims of fruit juice that substantiating evidence need not include RCTs, you intended that to apply, and as you said in answer to the question, generally and not to any specific area as opposed to any other area? Is that correct?

A. That's correct. And again, it's because it's a food and not a drug.

Q. So that same standard of testing would apply whether you're talking about cardiology or prostate or erectile dysfunction or any other thing; isn't that correct?

A. That's correct.

Q. All right. And I don't know if you caught counsel's question, but is it correct that you are giving your best medical opinion rather than a legal opinion?

A. I'm a physician. I don't give good legal opinions.

MR. FIELDS: Thank you. That's all I have.

MS. VISWANATHAN: May I -- I have just a couple of recross questions.

JUDGE CHAPPELL: Go ahead.

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RECROSS-EXAMINATION

BY MS. VISWANATHAN:

Q. Dr. Miller, you're not an expert in cardiovascular disease; correct?

A. That's correct.

Q. You've never performed a clinical trial relating to cardiovascular disease; correct?

A. I did -- I was involved in a clinical trial on the adverse effects of iron overload in children with an inherited blood disorder called thalassemia where we looked at the effects of iron overload on cardiac function.

I've also been involved in clinical trials looking at the effects of chemotherapy agents on cardiac function.

Q. Okay. But that does not qualify you as an expert in cardiovascular disease, does it?

A. That's correct.

Q. You don't have any board certifications in cardiovascular disease?

A. No.

Q. You've never treated patients for cardiovascular disease. Unrelated to cancer.

A. That's correct.

Q. Okay. And you don't have any experience in erectile dysfunction -- or you don't consider yourself an expert in erectile dysfunction; correct?

A. That's correct.

Q. And you've never conducted any clinical trials or been involved in any clinical trials relating to erectile dysfunction; correct?

A. That's correct.

MS. VISWANATHAN: No further questions.

MR. FIELDS: No further questions, Your Honor.

JUDGE CHAPPELL: Thank you, sir. You're excused.

THE WITNESS: Thank you.

JUDGE CHAPPELL: Is that our last witness today?

MR. FIELDS: It is, yes, Your Honor. We tried to bring in another substitute witness, but he was taking out somebody's prostate, which we thought had priority.

So I apologize for the fact that we can't fill up the last couple of hours. We'll have our witness ready the first thing in the morning. He's flying in

from California.

JUDGE CHAPPELL: Okay.

MR. FIELDS: May we approach and discuss scheduling, Your Honor?

JUDGE CHAPPELL: Yes. Or we can do it on the record. Either way.

(Pause in the proceedings.)

MR. FIELDS: Forgive us for this, Your Honor. We're just making sure we're in sync.

MS. HIPPSLEY: Here's a proposal that we'd like to provide the court for we think our ability to complete the trial -- the hearing.

Given the fact that we were not going to be in session two days next week because of some personal issues, we would ask the court if we could have next week completely dark, and then we would return the week after, which is for one day for one expert witness, which is Wednesday, September 14.

MR. FIELDS: 13th.

JUDGE CHAPPELL: Wednesday is the 14th.

MS. HIPPSLEY: Okay. Wednesday, September 14, we have one expert. It's a rebuttal witness, and it would probably be a half day I'm guessing amount of court time.

And then we would come back on October 11 after

the court had to deal with the other matters, and respondents would present the rest of their case the week of October 11.

And we've been able to confirm that we can provide our rebuttal witness early in the week of October 17, and we'd be done that week. I'm not exactly sure how many days we need for the rebuttal case, but we would complete it that week.

JUDGE CHAPPELL: All right. Is there an objection to the rebuttal?

MR. FIELDS: There's no objection to that proposal, Your Honor.

MR. GRAUBERT: Excuse me. To the rebuttal.

MR. FIELDS: Oh, I'm sorry.

If it's the rebuttal of the -- I didn't hear Your Honor.

If it's the rebuttal to the expert witnesses and those are the rebutting witnesses who filed rebuttal reports, we have no objection, Your Honor.

JUDGE CHAPPELL: Okay. Let's see if I can follow this.

So we were going to be in trial next Tuesday and Friday, the 6th and 9th, and the request is that we're not here those two days. That's approved.

MS. HIPPSLEY: Okay. So no trial next week.

JUDGE CHAPPELL: What I'm unclear about, though, is the following week, are we here Tuesday through Friday?

MS. HIPPSLEY: No. We just have one expert rebuttal witness whose schedule the respondents have indulged that we keep that week, which would be he would come in for Wednesday, September 14, and it would be a half day I'm guessing.

JUDGE CHAPPELL: So respondent is anticipating completing their case by Friday, this Friday?

MR. FIELDS: No. We're going to finish up after October 11, Your Honor. It will be a very short case. We'll have probably -- I think we have two or three more witnesses to go. I don't think it will take more than a couple of days after the 11th. Then there will be another rebuttal witness.

JUDGE CHAPPELL: Okay. Why don't we do this. For now, I will approve what you're asking for generally, no trial next week, half a day on the 14th or whatever we need on the 14th.

MS. HIPPSLEY: Okay.

JUDGE CHAPPELL: Just get together. Send me an e-mail.

MS. HIPPSLEY: Yes.

JUDGE CHAPPELL: And we'll hash it out to be

precise.

MS. HIPPSLEY: Yes, Your Honor, we can do that.

JUDGE CHAPPELL: But for purposes of the record, in case the public wants to know, we'll be here the rest of this week and then we'll return on the 14th.

MS. HIPPSLEY: Correct.

MR. FIELDS: Correct, Your Honor.

MS. HIPPSLEY: For one day.

JUDGE CHAPPELL: All right. Anything else?

MR. GRAUBERT: No, sir.

JUDGE CHAPPELL: Until tomorrow at 0930 we're in recess.

(Whereupon, the foregoing hearing was adjourned at 3:12 p.m.)

# C E R T I F I C A T I O N  O F  R E P O R T E R

DOCKET/FILE NUMBER: 9344

CASE TITLE: In Re POM Wonderful LLC, et al.

HEARING DATE: August 31, 2011

I HEREBY CERTIFY that the transcript contained herein is a full and accurate transcript of the notes taken by me at the hearing on the above cause before the FEDERAL TRADE COMMISSION to the best of my knowledge and belief.

DATED: SEPTEMBER 7, 2011

JOSETT F. WHALEN, RMR

# C E R T I F I C A T I O N  O F  P R O O F R E A D E R

I HEREBY CERTIFY that I proofread the transcript for accuracy in spelling, hyphenation, punctuation and format.

ELIZABETH M. FARRELL