FEDERAL TRADE COMMISSION

I N D E X

POM WONDERFUL LLC

TRIAL VOLUME 6

PART 1, PUBLIC RECORD

JUNE 7, 2011

UNITED STATES OF AMERICA

BEFORE THE FEDERAL TRADE COMMISSION

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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TUESDAY, JUNE 7, 2011

9:30 a.m.

TRIAL VOLUME 6

PART 1

PUBLIC RECORD

BEFORE THE HONORABLE D. MICHAEL CHAPPELL

Administrative Law Judge

Federal Trade Commission

600 Pennsylvania Avenue, N.W.

Washington, D.C.

Reported by: Susanne Bergling, RMR-CRR-CLR

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P R O C E E D I N G S

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JUDGE CHAPPELL: Okay, back on the record, Docket 9344.

Anything before we start with the next witness?

MR. GRAUBERT: No, Your Honor.

MR. HOPPOCK: No, Your Honor.

JUDGE CHAPPELL: Regarding scheduling, we were talking about yesterday, I have taken the calendar that was, actually, the dates sent to me by the parties in this case and ProMedica and other cases, and I have just literally plugged conference calls and other things in every date that we're not up here.

And if this case isn't finished, if Respondents' case -- and if we have any rebuttal -- isn't finished by September 16th -- actually, the 15th, then we will just need to recess, and I'm thinking a couple of weeks, because that's the time for that other case, which could wrap in two weeks. So, if it helps you to know right now, because I know when we had the conference call I was told there were experts involved, and I know scheduling.

If it's better to know right now, rather than jump through hoops and force everything through, and I'm not trying to force -- you know, I'm not going to force

anybody to withdraw a witness that you need to testify here. But if it helps to know now, we can go ahead and plan that if we recess, say, on the 15th of September, if we're not finished, and we will reconvene on Tuesday, October 4th.

MR. GRAUBERT: I think that will be fine, Your Honor.

JUDGE CHAPPELL: All right.

MR. GRAUBERT: Is August 22nd and 23rd still available?

JUDGE CHAPPELL: They are, if necessary. I think I would actually prefer to go into October.

MR. GRAUBERT: All right.

JUDGE CHAPPELL: Because I've got -- I've got to be out of town on the 24th, and I was planning on leaving the 23rd, because you can't afford to fly somewhere the morning you have got to be somewhere anymore. So, it would be -- I think it would work better if we just -- if we have to, we bump it into October.

MR. GRAUBERT: All right.

JUDGE CHAPPELL: That will give you some idea of how to plan it with the witnesses.

MR. GRAUBERT: Thank you, Your Honor, yes. We will do so on that basis.

JUDGE CHAPPELL: The mic wasn't on. Did everyone hear me who needed to hear me? Okay.

Next witness.

MS. EVANS: Good morning, Your Honor. I'm Janet Evans for Complaint Counsel.

JUDGE CHAPPELL: Good morning.

MS. EVANS: And I would like to call Dr. Meir Stampfer to the stand, please.

Whereupon--

MEIR J. STAMPFER, M.D.

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

DIRECT EXAMINATION

BY MS. EVANS:

Q. Thank you, Dr. Stampfer.

Could you please state your full name for the record?

A. Meir Jonathan Stampfer.

Q. And how is that spelled?

A. M-E-I-R, Jonathan, Stampfer is S-T-A-M-P-F-E-R.

Q. And on the table before you is a document that's been marked as CX 1293. I believe that's your curriculum vitae.

A. Yes.

Q. Do you recognize this document?

A. Yes.

Q. And does it state your education, experience, training, and publications?

A. Yes, it does.

Q. Okay. Could you please summarize your education after high school?

A. I graduated Columbia University in New York with a bachelor's degree. Then I went to NYU Medical School for my M.D. degree. After that, I was an intern in internal medicine at Maimonides Hospital, and then a resident in community and environmental medicine at Mount Sinai School of Medicine. Then I went to Harvard for my MPH and followed that with my master's in public health.

Q. Excuse me. What does MPH stand for?

A. Master's in public health.

Q. And where are you currently employed?

A. Currently, I'm at the Harvard School of Public Health and the Brigham and Women's Hospital.

Q. Doctor, did you receive your master's in public health before or after your medical degree?

A. After.

Q. Now, is Harvard Medical School a part of Harvard University?

A. Yes.

Q. What do you do at Harvard Medical School?

A. I teach and do research.

Q. And what do you teach?

A. At the medical school, I teach the principles of epidemiology. At the Harvard School of Public Health, I teach the practice of epidemiology. I also advise doctoral students and supervise post-doctoral fellows and junior faculty.

Q. And what is epidemiology?

A. Epidemiology is the study of the determination and distribution of disease in humans.

Q. Have you held positions at other organizations within Harvard University?

A. Yes. So, I'm a professor of epidemiology and nutrition at Harvard School of Public Health; professor of medicine at Harvard Medical School; physician at Brigham and Women's Hospital; and director of the chronic disease epidemiology unit at Channing Laboratories at Brigham and Women's; and also a member of the Dana-Farber Harvard Cancer Center.

Q. In connection with your teaching responsibilities, do you also give lectures in connection with a preventative medicine course?

A. Yes.

Q. Now, during your career, have you engaged in

scholarly research?

A. Yes.

Q. And could you -- is it accurate to say that your research has focused on four human epidemiological studies?

A. Yes.

Q. Okay. Is one of these the Nurses' Health Study?

A. Yes.

Q. Could you describe the Nurses' Health Study?

A. This is a prospective cohort study of 121,700 U.S. female registered nurses, begun in 1976. We follow them every two years to collect information on diet and lifestyle and relate this to the occurrence of breast cancer, heart disease, and a host of other diseases. The study is still going on.

Q. And what is your relationship with that study?

A. I have been a coinvestigator since 1976 -- '79.

Q. And are you familiar with the term "endpoint"?

A. Yes.

Q. What does it mean?

A. It means the -- in an epidemiological study, the outcome of interest that you're studying.

Q. So, what endpoints does the -- has the Nurses' Health Study looked at?

A. A very wide range of disease outcomes: cancer at

a variety of sites, heart disease, stroke, fracture, diabetes, many, many outcomes.

Q. And have results from the Nurses' Health Study been published?

A. Yes.

Q. And have you been an author or coauthor on studies relating to that -- or articles?

A. Yes, many.

Q. Okay. For example, was one of them on competing risk factors for mortality, including glycemic load, cholesterol intake, and polyunsaturated fats in cereal fiber?

A. Yes.

Q. Does another one have to do with low-carb diets and mortality from cardiovascular disease and cancer?

A. Yes.

Q. And another one looks at -- has another one looked at drinking tea, high-density lipoproteins and myocardial perfusion?

A. Yes.

Q. Excuse me. Myocardial infarction. Thank you.

Is there also a study known as the Nurses' Health Study II?

A. Yes.

Q. Can you describe that study?

A. So, that's an identical design with younger nurses, so approximately 16,000 nurses that we followed in the same manner.

Q. And what is your relationship with the Nurses' Health Study II?

A. I helped -- I helped start that study in 1989 and remain a coinvestigator.

Q. Did you help design that study?

A. Yes.

Q. Now, what endpoints does the Nurses' Health Study II look at?

A. The same as the Nurses' Health Study I, but also includes reproductive outcomes.

Q. And have the results of the Nurses' Health Study II been published in articles that were authored or coauthored by you?

A. Yes.

Q. And so, for example, has the Nurses' Health Study looked at DASH diet scores and kidney stone markers?

A. Yes.

Q. And what is the DASH diet?

A. The DASH diet is a -- a recommended diet designed initially to reduce blood pressure, but it actually turns out to be a very powerful diet to

maintain good health overall. So, that was devised by Dr. Frank Sacks, my colleague at the Harvard School of Public Health.

Q. Thank you.

Did that study also look at the relationship between the intake of dietary fruits and vegetables with glioma?

A. Yes.

Q. And is glioma basically adult brain cancer?

A. Yes.

Q. And did the Nurses' Health Study II -- have you also published articles having to do with red meat intake and breast cancer?

A. Yes, um-hum.

Q. Okay. And also, have you published studies with regard to the Nurses' Health Study II having to do with the relationship between habitual caffeine intake and hypertension in women?

A. Um-hum. Yes.

Q. You have to say "yes" or "no." "Um-hum" does not translate.

Now, were you also involved with the Physicians' Health Study?

A. Yes.

Q. Could you describe the Physicians' Health Study?

A. This began as a randomized trial in 1982, beta-carotene and aspirin, for the prevention of cancer and cardiovascular disease.

Q. And what is beta-carotene?

A. Beta-carotene is a natural carotenoid substance that has a variety of disease-fighting properties. It occurs -- it's what gives carrots their characteristic color.

Q. And so what was your relationship with the Physicians' Health Study?

A. I helped start that.

Q. Did you help design it?

A. I helped design it and remain a coinvestigator.

Q. Okay. And have the results of the Physicians' Health Study been published in articles that you authored or coauthored?

A. Yes.

Q. Okay. For example, is one of the -- in addition to the endpoints you just mentioned, does the Physicians' Health Study -- have you published articles relating to fish intake and prostate cancer incidence and mortality?

A. Yes.

Q. And have you also published articles on C-reactive protein and lipids with -- and their

relationship with sudden cardiac death?

A. Yes.

Q. Okay. And as you said already, you looked at aspirin and myocardial infarction?

A. Yes.

Q. What is commonly -- myocardial infarction, what's the common term for that?

A. Heart attack.

Q. And did you also look at DNA damage and blood and lung cancer risk?

A. Yes.

Q. Now, were you also involved with a study known as the Health Professionals Follow-Up Study?

A. Yes.

Q. Could you describe that study for me?

A. That is essentially the identical design as the Nurses Health Studies I and II, except it's in males, in male health professionals. It started in 1986.

Q. And what is your relationship with that study?

A. I helped to start that one, also, and remain a coinvestigator.

Q. Okay. Now, what endpoints does the Health Professionals Follow-Up Study look at?

A. Again, a wide range of endpoints: cancer at various sites, cardiovascular disease, and other --

other endpoint -- common other diseases in men.

Q. And so -- and have you been an author or coauthor of articles arising out of this study?

A. Yes.

Q. And they would include, for example, an article very recently published on caffeine consumption and prostate cancer risk?

A. Yes.

Q. And another one -- have you published an article arising out of this study on long-term aspirin use and prostate cancer?

A. Yes.

Q. And what about the interplay of different polyunsaturated fats on coronary heart disease in men?

A. Yes.

Q. Now, aside from those studies we just mentioned, have you participated in other research to investigate -- and investigated risk factors associated with prostate cancer?

A. Yes.

Q. For example, were you involved in a study called "A Cancer of the Prostate: Strategic Urologic Research Endeavor"?

A. Yes.

Q. And what research did you do in connection with

this study?

A. I worked with my former student and now colleague, June Chan, who's one of the many investigators for that study, and my recently graduated student, Erin Richman, and they did an analysis looking at physical activity in relation to the occurrence of prostate cancer. They also looked at dietary factors.

Q. Okay. In connection with this study, did you author or coauthor a report addressing intakes of meat, fish, poultry, and eggs and the risk of prostate cancer progression?

A. Yes.

Q. Now, have you been involved in any randomized, controlled trials involving nutrition and health?

A. Yes.

Q. Could you describe these, please?

A. I have been involved in several. I was one of the investigators for the VISP study of B-vitamins in relation to incidence of recurrent stroke. I was the senior investigator for the DIRECT study which looked at comparing different diets for weight loss and also did a randomized trial of moderate alcohol consumption among diabetics to look at glucose metabolism.

Q. Now, in connection with the DIRECT study, did you publish -- excuse me, did you author or coauthor any

articles that were published?

A. Yes.

Q. And would -- for example, were you an author on an article discussing dietary interventions to reverse carotid atherosclerosis?

A. Yes.

Q. And what does "atherosclerosis" mean?

A. Build-up of plaque in arteries.

Q. Now, has your research involved nutrients that are characterized as antioxidants?

A. Yes.

Q. And we'll talk more about antioxidants later, but have you published any articles related to the intake of antioxidant nutrients and disease?

A. Yes.

Q. And could you give me some examples of those?

A. Well, we published, on the Physicians' Health Study trial, results of beta-carotene, which is an antioxidant nutrient; also, several papers on vitamin E consumption.

Q. Now, overall, is it accurate to say that you have authored or coauthored over 750 articles in the medical literature that describe original research?

A. Yes.

Q. And what proportion of these relate to

epidemiology?

A. Almost all.

Q. And what proportion of them relate to nutrition?

A. A big fraction.

Q. Okay. And what proportion relate to the relationship between nutrition and the prevention or treatment of cardiovascular disease or prostate cancer?

A. Over 300.

Q. Now, have you had any experience as an editor of medical journals?

A. Yes, um-hum.

Q. Can you tell me what editorial boards you've served on?

A. I've served as editor of the American Journal of Epidemiology and associate editor of that journal; the American Journal of Clinical Nutrition as an associate editor; Epidemiology, as an associate editor; American Journal of Medicine; and a bunch of others.

Q. Okay. In connection with your positions on these journals, have you had the opportunity to evaluate articles involving epidemiology, including the design and conduct of clinical trials?

A. Yes.

Q. And, for example, do you play a role in deciding what articles should or should not be published?

A. Yes, both as a reviewer and an editor.

Q. And in connection with your positions on these journals, have you had occasion to evaluate proposed or published articles involving nutrition and its relationship to the prevention of and treatment of cardiovascular disease?

A. Yes.

Q. And in connection with your positions on these journals, have you evaluated proposed or published articles involving nutrition and its relationship to the prevention and treatment of prostate cancer?

A. Yes.

Q. Now, do you belong to any professional organizations or societies relating to epidemiology?

A. Yes.

Q. And what would they be?

A. Society of Epidemiological Research; American Epidemiology Society; American College of Nutrition; the American Heart Association Council on Nutrition, Physical Activity, and Metabolism; and the American Association For Cancer Research; and several others.

Q. Okay. And do you belong to -- do some of these organizations also -- are they also involved in nutrition?

A. Yes.

Q. Okay. And do you also belong to any professional organizations or societies relating to cardiovascular disease?

A. Yes. As I mentioned, the American Heart Association and the International Society and Federation of Cardiology.

Q. And some of the organizations you belong to relate to cancer?

A. Yes.

Q. Now, have you consulted for the Government during your career?

A. I have.

Q. And can you give me some examples?

A. The -- the biggest one in terms of time and energy was my service on the U.S. Dietary Guidelines, to revise the 2000 guidelines.

Q. And that was looking at the overall nutritional recommendations contained in the 2000 Dietary -- that ultimately were contained in the 2000 Dietary Guidelines when they were issued?

A. Yes.

Q. And who publishes the dietary guidelines?

A. It's joint between HHS and the Department of Agriculture.

Q. Thank you.

In light of your education, training, and experience, do you believe yourself to be qualified as an expert in epidemiology?

A. I do.

Q. And in light of your education, training, and experience, do you consider yourself to be qualified as an expert in nutrition, including its relationship to the prevention and treatment of cardiovascular disease and prostate cancer?

A. Yes.

Q. And in light of your education, training, and experience, do you consider yourself to be qualified as an expert in clinical testing related to the prevention and treatment of cardiovascular disease and prostate cancer?

A. Yes. Sorry.

MS. EVANS: Now, based on Dr. Stampfer's education, extensive training, and experience, Complaint Counsel moves for Dr. Stampfer to be accepted as an expert in epidemiology, nutrition, including its relation to the prevention and treatment of cardiovascular disease, and prostate cancer, and the clinical testing relating to the progression of cardiovascular disease and prostate cancer.

MR. FIELDS: No objection, Your Honor.

JUDGE CHAPPELL: To the extent any opinions offered meet the proper legal standards, those opinions will be considered.

MS. EVANS: Thank you.

BY MS. EVANS:

Q. Dr. Stampfer, on the table before you is a document that's marked as CX 1293.

A. Yes.

Q. Can you identify this document?

A. Yes. This is my expert report.

Q. Does this document summarize the opinions that you have provided in connection with this matter?

A. Yes.

Q. Now, does your testimony in this matter relate, in part, to cardiovascular disease?

A. Yes.

Q. Can you briefly tell us what cardiovascular disease is?

A. In a broad sense, it's -- it relates to all of the diseases of the heart and blood vessels.

Q. Is coronary heart disease an aspect of cardiovascular disease?

A. That's a big subset, yes.

Q. And what about -- what other conditions are encompassed within that concept of cardiovascular

disease?

A. Well, in addition to coronary disease itself, cardiovascular disease also includes other forms of heart disease and other forms of vascular disease.

Q. Would stroke be included as a form of vascular disease?

A. Yes.

Q. Now, does your testimony in this matter relate, in part, to prostate cancer?

A. Yes.

Q. And can you tell us what prostate cancer is?

A. It's a malignant tumor that arises in the prostate gland.

Q. Now, based on your experience, do you have an opinion with regard to what kind of evidence is needed to support a claim that a product, like pomegranate juice or pomegranate extract, prevents, reduces the risk of, or treats cardiovascular disease or prostate cancer?

A. Yes.

Q. And what is that opinion?

A. To support a claim for a product like that, you need randomized trial data.

Q. Now, I would like to turn to page 9 -- I would like you to turn to page 9 of your report. And if you could bring up page 9 of the report.

On page 9, you say (as read), "The best evidence of a causal relationship between a nutrient or drug and a disease outcome in humans is a randomized, double-blind, placebo-controlled trial."

Do you see that paragraph?

A. Yes.

Q. I'd like to ask you some questions about that sentence. Now, is a clinical trial also known among researchers as a randomized clinical trial?

A. Sometimes people perform clinical trials that are not randomized, but they -- they shouldn't be.

Q. Does a clinical trial usually involve two or more groups of subjects?

A. Yes.

Q. Is one of these called the treatment group or the intervention group?

A. Typically.

Q. Okay. And is the other one typically called the control group or the placebo group?

A. Yes.

Q. Now, how are subjects in a randomized clinical trial assigned to one group or another?

A. If it's randomized, the mechanism for randomization nowadays would be a computer program for randomization; or they could do a coin toss or a sealed

envelope. There are various methods.

Q. And in that sentence I quoted, what do you mean by "placebo-controlled"?

A. Placebo is an alternative form that doesn't contain the active intervention. So, if it's a study of a pill, the placebo would be a pill that looks and seems like the real intervention, but does not contain the active ingredient.

Q. Is it the norm to use a placebo in a clinical trial?

A. It's the norm, when possible.

Q. And what's the purpose of the placebo?

A. The purpose is to be sure, to the extent that it's possible, that individuals don't know if they're taking the active agent or -- or the -- or they're in the control group. So, they approach the trial with the same mind-set and the same behavior.

Q. And what do you mean by "double-blind"?

A. Double-blind means that neither the participants nor the investigators know which group assignment is -- applies to any given individual.

Q. Now, if the subjects know what arm of a study they're in, can that affect the results of the trial?

A. Yes, that could, because this can alter their behavior in a variety of ways.

Q. For example, in a prostate cancer study, if you know you're going to be in the active group, how could that affect your behavior?

A. Well, you could imagine that if you know you're in the active group, you might relax your efforts to reduce risk in other ways; maybe you might think, well, I'm taking the active pill, so I won't bother with my morning exercise. It's hard to know in advance how that knowledge might affect behavior.

Q. If research -- excuse me. And if the researchers know what arm of a study they're in -- the patients are in, how can that affect the results of the trial?

A. If the researchers know, then subtle biases can creep in in terms of interpreting the endpoints. If they're -- if they want to see a positive result from the trial, they might be biased. So, to avoid that, blinding is often employed.

Q. Now, is there such a thing as a single-blinded study?

A. Yes. You could have a single blinded study in either direction where either the investigators don't know or the participants don't know.

Q. So, if the subjects are unblinded, is it important that the investigator be blinded?

A. If you can, it's a good practice.

Q. Okay. Now, turning to the bottom of page 9, if you could focus on the paragraph or the sentence that says, "A control group is necessary for the investigators to determine whether the incidence rate of the outcome observed in the treatment group was truly different from what would have been observed had the treatment group not been treated."

Do you see that sentence?

A. Yes.

Q. Now, in this sentence, what do you mean by "truly different"?

A. "Truly different" means -- in this sense, you're comparing the -- you want to know if an intervention works. So, it has to have a -- to be able to say that it works, you have to have an effect that's large enough to be measurable, and that's what truly different refers to.

So, that means that the effect has to be large enough that you believe that other causes for the difference are -- are implausible, such as -- such as chance or other explanations.

Q. And in clinical studies, is there an accepted measure of difference?

A. So, the -- in terms of the statistical testing,

the traditional accepted cut point is a P-value of 0.05.

Q. And what does this refer to?

A. So, the P-value refers to the probability that if there truly is no difference, that you would observe results as extreme or more by chance alone. So, by setting the cut point at 0.05, you're saying that results this extreme would occur at no more than one time out of 20 and that, therefore, chance is less likely as an explanation.

It doesn't rule out chance, because there's variability in biology, but you would more likely think that there's another explanation, that it's not just a coincidence.

JUDGE CHAPPELL: I have a question. When you were talking about double-blind, you said that the investigators didn't know, and then in a follow-up question, she asked you about researchers. In your answer, you again referred to investigators. Which is correct and what -- what's the difference, if any?

THE WITNESS: Well, I'm not sure -- is it possible to read back that question?

JUDGE CHAPPELL: I basically summarized it for you.

THE WITNESS: Okay.

JUDGE CHAPPELL: You're talking about

investigators and she's asking you about researchers and you're answering about investigators. Is there a difference?

THE WITNESS: Oh, no. Researchers and investigators are the same thing.

JUDGE CHAPPELL: Okay. At what point -- how high up does the double-blind go so that the researchers or investigators don't know which group is which? Somebody obviously has to know.

THE WITNESS: Right. So, anyone who's making a judgment about the outcome should be blinded. So, for example, if you're doing an imaging study and you're looking at, say, carotid artery intima-media thickness, the investigator who's making that judgment about whether there's an increase or a decrease or what the measurement is, should not know which group it is.

Then it goes to the statistician. Once the numbers are set, then there's no chance for the bias to creep in. So, the blinding is important only when there's a possibility for bias.

JUDGE CHAPPELL: All right. Thank you.

MS. EVANS: Thank you.

BY MS. EVANS:

Q. Now, when you're talking about a P-value of equal to or less than 0.05, can this be a before and

after change in the intervention group?

A. The P-value is just a function of the data. So, you can calculate a P-value for before and after or occurring within the control group, yes.

Q. When you're saying that a control group is necessary for the investigators to determine whether the incidence rate of the outcome observed in the treatment group was truly different from what would have been observed had the treatment group not been treated, are you referring to a difference between the active group and the placebo group?

A. Yes. The concept is that to know if something works, you give it to a group of people, and you observe a change, and you want to know would that change have -- would that change have occurred if you had not given them the intervention. So, that's the alternative path.

And you can't know that for those same individuals, so instead, what we do is we have the control group, which in an ideal setting is similar enough to the intervention group, which can be achieved by randomization, and then we see what happens in that group, and you draw the inference that that same result would have occurred in the intervention group but for the intervention. And that's the basis of the scientific inference.

Q. Now, if you just test an intervention in one group of subjects and then you compare the before values of the treatment group to the after values of that same group, what's the scientific value of such a test?

A. That is a much weaker test, because the basic assumption is that there would have been no change in that group, but we know that things change over time all the time. So -- so, that's -- you're -- it's a very strong assumption to assume that there's no change. So, in most settings, this would not be appropriate.

The only setting where it would be appropriate is -- for example, in the case at hand. If -- if one were to do a study of pomegranate juice and it -- among men with prostate cancer and all traces of prostate cancer completely vanished, that would be persuasive, because we know that although there's lots of changes that occur over time, that one is very unlikely to occur just by chance.

But in most settings, you need a control group that takes into account the changes that occur over time.

Q. Now, is the persuasiveness of a clinical study dependent, in part, on the number of patients studied? Excuse me, I swallowed that last word. Studied.

A. Um-hum, yes.

Q. All other factors being equal, is a clinical trial with a larger number of patients more persuasive than a clinical trial with a smaller number?

A. All things being equal, absolutely. Just like if you're tossing a coin and you've got one heads and one tails, you wouldn't assume that that's a fair coin. You would want to toss it 100 times and see something close to 50/50.

Q. Now, does the study have to be large enough that you can be confident that the results are broadly applicable?

A. The applicability of the results depends first on the validity. So, you need a large enough study to rule out other explanations for a difference. And then the applicability, once validity is established in some -- in the situation, the group that you studied, is that representative of the entire population?

Q. So, when you were talking about that coin toss example, is there a risk that with a small number of subjects, there's an increased possibility for chance results due to unknown factors?

A. Yes.

Q. Now, is the persuasiveness of a study -- a study's results also -- a clinical study's results also dependent on the length of the study?

A. It can be. The length has to be appropriate for the biology.

Q. Okay. So, does it depend what endpoint is being measured?

A. Yes.

Q. So, do some things settle into a pattern faster than other things?

A. It depends on the endpoint and the biologic mechanism for the intervention.

Q. Okay. Now, if a random -- if a clinical trial is randomized, double-blind, and placebo-controlled, and of sufficient size and with sufficient follow-up, with an appropriate dose of the treatment, is it possible to conclude a causal link between the nutrient and the disease under study?

A. Yes.

Q. Now, what do you mean by "causal"?

A. A causal link means a cause-and-effect relation, that the intervention reliably would make a change in -- when given, that would not have otherwise occurred.

Q. Okay. So, it's a but-for relationship?

A. Yes.

Q. Okay. Now, can you give me examples of when it would be appropriate to conclude that a study not meeting the description we just -- I just provided --

that is, double-blind, randomized, placebo-controlled, sufficient size, sufficient follow-up -- when would it be appropriate to conclude that a study not meeting this description -- excuse me -- can nonetheless demonstrate a causal link between a nutrient and a disease?

A. There are many things we know with a high degree of confidence that are not based on randomized trial data, and the characteristics of those situations are when the effect is very large and very uniform.

So, for example, you could -- you can have men with scurvy, and you give them vitamin C, and the scurvy will be treated, completely, and a cause-and-effect relation there could be strongly supported by that kind of observation.

Q. So, this applies to deficiency illnesses?

A. Either deficiency illnesses, or another example not from nutrition would be, say, smoking and lung cancer, where the effect is huge, and it's inconceivable that any other explanation, apart from a causal explanation, would be tenable.

Q. And in observational studies of the risk of lung cancer in smokers, how much higher is their risk of lung cancer than among nonsmokers?

A. For a heavy smoker, it would be 20-fold or more.

Q. Okay. Now, in contrast, when you're looking at

an outcome that often occurs in the presence or in the absence of an intervention, and what you're looking for is the level of that effect, then do you need more evidence to come to a causal inference?

A. Yes. Those situations are more difficult, so you need stronger evidence to --

Q. So, is this why you believe that randomized, double-blind, placebo-controlled studies are needed to show that products such as POM Juice, POMx Pills and POMx Liquid can prevent, reduce the likelihood, or treat cardiovascular disease and prostate cancer?

A. Yes.

Q. Now, do you believe that most scientists in the field of clinical trials, epidemiology, and the prevention of cardiovascular disease and prostate cancer would agree that this is the evidence that is required for products like these?

A. Yes.

Q. And why do you believe this?

A. This is -- this is what we teach in medical school and schools of public health. This is what we write about in journals. This is common -- common practice, common judgment.

Q. Now, I'd like you to turn to your expert report at page 8.

A. Yes.

Q. On that page, you discuss four different types of study designs that are used to examine the relationship between nutrition and health, correct?

A. Yes.

Q. Is one of these -- we just talked about the clinical trial. Can you tell me what an observational study is?

A. Observational studies are studies in humans where investigators measure the exposure and ascertain the outcome, but they don't assign the exposure. So, that's the difference between an observational study and a trial.

Q. So, in an observational study, for example, could you, like, look at a group of people and say these people have low vitamin C and these people have high vitamin C and let's see what happens next?

A. Yes.

Q. Okay. So, are there a couple of different ways that observational studies can be set up to evaluate potential relationships between diets or other factors and disease?

A. Yes.

Q. Is one of these a case control study?

A. Yes.

Q. Can you describe a case control study?

A. A case control study is a study where you start with the disease, and so you identify individuals who have the disease, and then you identify individuals, appropriate individuals, who don't have the disease. And then you go -- you ascertain their previous exposure from the past. If you're studying diet, you ask them, "Well, what did you used to eat before the diagnosis of the disease?" And you compare that to the people without disease to look at differences.

Q. Okay. And what are cohort studies?

A. Cohort studies take the opposite approach. They start with individuals before the occurrence of disease, so they ascertain, say, diet at some point in time, and then follow the people forward to see who gets sick and who doesn't and draw inferences based on their exposure.

Q. Okay. Now, can you generally conclude from an observational study that there is a causal relationship between nutrient intake and a health outcome?

A. Not -- no. You -- typically, it would not be sufficient to, on its own, to draw a causal conclusion.

Q. Okay. Is there a risk of any unidentified biases in observational studies?

A. Yes. For example, say, in studies of diet, we might say we studied broccoli, and the risk of prostate

cancer in people who eat broccoli often differ in other respects from people who eat it seldom. And sometimes we can measure these differences and adjust for them, but you're always concerned that there are differences that we cannot adjust for, and so this would be confounding. So, that's the kind of issue that gives people some hesitation about drawing a firm causal conclusion.

Q. And is there a risk of inadequate control confounding?

A. Yes. That's exactly what that is.

Q. Okay. Now, for example, did it used to be believed that coffee was a risk factor for heart disease?

A. Yes. And this is a good example of confounding. Many studies found that people who drank coffee heavily had a higher risk of heart disease and were wondering whether that was a causal relation, but as it happens, in many populations, heavy coffee drinking goes along with smoking.

And once -- once smoking was adjusted for, then it was revealed that actually coffee is not related to or does not -- has no adverse effect for risk of heart disease. That's an example of confounding where we were able to adjust for the confounding factor.

Q. Now, you said that an observational study generally can't prove a causal relationship, but at the same time, can a good observational study be better than a poorly conducted randomized, controlled trial?

A. Oh, yes.

Q. But is a good randomized control trial better than an good observational study?

A. Yes.

Q. Now, are there observational studies on pomegranate juice?

A. I'm not aware of any.

Q. Okay. Why is this?

A. Well, the consumption for -- we study diet in our cohorts, and consumption of pomegranate juice is relatively infrequent compared to other fruit items. So, there's just not enough out there to -- to -- to be able to study a population cohort.

Q. Okay. Now, another kind of study that you mention on page 8 of your report is animal studies. How are animal studies used to examine the relationship between nutrients and disease?

A. Animal studies can be very important to help learn about the biology, learn about the metabolism, biological pathways for the impact of a nutrient. Obviously, you can control the animal situation fully in

ways that aren't possible in humans. So, you can learn a lot of important biology through animal studies.

Q. What's the -- there's a term in the literature, mechanistic studies?

A. Um-hum, yes.

Q. Do these refer to animal studies?

A. They include animal studies. They also include in vitro studies.

Q. Okay. Can you -- now, can you -- do the results of animal studies correspond with what will occur in humans?

A. Sometimes, yes; sometimes, no.

Q. And can you predict in advance whether or not animal study results will be replicated in humans?

A. You can't predict accurately. If -- if an agent is -- has a strong effect on a basic fundamental biologic property that's common to all animals or all life, then you can predict with some degree of confidence. But for nutrients, things are very, very complicated because of different paths of evolution, so it's hard to judge.

Q. Okay. Could you provide an example of a -- actually, could you just tell me a little bit about -- you had an example that you talked about during your deposition involving aflatoxin. Can you explain what

the relationship is -- what -- how aflatoxin sort of explains the problems of -- of predicting from animal studies?

A. Yes. That's a -- there are many examples of this, but aflatoxin is a toxin that's produced by mold, so moldy peanuts would have aflatoxin. It's regulated. The levels are regulated for human food consumption.

And in rats, an intake of 15 parts per billion uniformly causes liver cancer in all rats. If you -- and that's the limit for human consumption or it was when I studied it a couple decades ago. If you give that same dose to mice, nothing happens. And, in fact, there are actually differences of strains of mice and rats in terms of their susceptibility to aflatoxin.

So, this just illustrates the perils of extrapolating results from animal studies to humans. We can learn a lot from animal studies, but we are not the same as animals.

Q. Okay. Now, can you tell us what the term "in vitro" means?

A. In vitro is a test tube study from a Petri glass, test tube, or Petri dish, and so these are studies that are done outside of an organism.

Q. And what do you mean by an organism?

A. In a test tube or dish, not in an animal or a

human.

Q. And what does the term "in vitro assay" mean?

A. It would just be a measurement of some function or level of concentration of a -- of a --

Q. Can you give me some examples of in vitro assays that are relevant to nutrition and health?

A. Well, you can -- you can look at blood levels of nutrients. You can look -- in -- in in vitro studies, you can look at the impact of nutrients on enzymatic activity or identify specific pathways.

Q. Are cell studies -- supposing you take human cells out of the body and put them in a laboratory dish. Are cell studies an example of an in vitro study?

A. That would be an example of in vitro study, yes.

Q. Now, if an in vitro assay shows a certain result, can you assume that the same will occur in the human body?

A. No, you really cannot.

Q. And why is that?

A. Because the situation in humans is much different and much more complex. So, you can, for example, grow tumor cells in a Petri dish and add an agent and kill them. That's -- you would not assume that that agent is now useful as a chemotherapy drug. It might be, but you would have to test it.

Q. In people?

A. In people.

Q. Now, do medical researchers fully know how cardiovascular disease and cancer originate and develop in the actual human body?

A. Not fully. We've learned a lot, but there's a lot unknown.

Q. And do these limitations in knowledge --

THE REPORTER: Excuse me. I'll need you to start that question over.

JUDGE CHAPPELL: You will need to consciously slow down when you're reading.

MS. EVANS: Yes, Your Honor.

BY MS. EVANS:

Q. Do these limitations in knowledge about how cardiovascular disease and cancer originate in the human body play a role in our -- do they impede the ability to reliably extrapolate from in vitro results to what happens in the human body?

A. Yes.

Q. I am going to switch gears right now, and at this point, I'd like to ask you about some concepts that relate to antioxidants.

Are you familiar with the term "free radicals"?

A. Yes, um-hum.

Q. And could you tell me what free radicals are?

A. They're atoms that have one or more unpaired electrons that are inherently unstable. It's formed -- they're formed naturally in the body, in humans and in every living thing, and it's part of normal physiology, but it also can cause damage.

Q. Electrons, they want to travel in twos, right?

A. So, they can cause chemical reactions that potentially can cause damage to DNA or protein.

Q. So, what are -- is rusting an example of free radical damage in the outside environment?

A. So, that would be an example of oxidation that occurs with that.

Q. And what is oxidation?

A. Oxidation is a -- is the consequence of this exchange of -- of unpaired electrons.

Q. And now, has oxidative damage been implicated in diseases associated with aging, such as cardiovascular disease and cancer?

A. Yes. That's a hypothesis.

Q. Okay. Can you tell me what antioxidants are?

A. So, antioxidants either help the body repair the damage that's caused by oxidation or prevent oxidation by absorbing the energy.

Q. And what's the characteristic of antioxidants

that gives them their name?

A. Having that property of opposing the effects of oxidation.

Q. Now, does the human body manufacture its own antioxidants?

A. Yes, and we also get some from diet.

Q. And can you give me some examples of antioxidants that come from diet?

A. So, dietary examples would be vitamin C and vitamin E.

Q. And are there minerals that are felt to be dietary antioxidants?

A. Some have antioxidant properties, yes.

Q. Such as zinc, copper, magnesium, and selenium?

A. Yes. In some situations, they can function as antioxidants.

Q. Now, do fruits and vegetables contain antioxidants?

A. Yes.

Q. And what about teas, legumes, and nuts?

A. Yes.

Q. Now, are antioxidants widespread in nature?

A. Yes.

Q. Okay. Is it accurate to say that everything that grows has to deal with oxygen in one way or

another?

A. That's right.

Q. Now, when you say that a food or a nutrient is an antioxidant, is that the only property of that substance?

A. No. An antioxidant just refers to the chemical properties. So, any given molecule -- for example, beta-carotene -- has antioxidant properties, but it also has other properties. So, a nutrient could be a source of fuel, it could be interacting with many different molecules or enzymes, and that functions apart from the antioxidant activity.

Q. Now, has it been hypothesized that diets high in antioxidants may prevent or treat chronic diseases, such as cardiovascular disease or cancer, by neutralizing free radicals?

A. Yes.

Q. Okay. And was this antioxidant effect on disease supported by in vitro testing?

A. Well, there are many in vitro tests that support it for specific conditions, yes.

Q. Okay. And was the antioxidant theory of disease supported by animal tests?

A. Well, I like to think of the antioxidant theory for a specific disease. I don't think of it as a theory

of all disease.

Q. Okay.

A. But -- so, the tests look at very specific effects, yes.

Q. And then did observational studies support the hypothesis that there was an association between nutritional antioxidant intake and cardiovascular disease?

A. Well, again, the studies look at specific factors, and whether it's due to the antioxidant property is an inference.

Q. Now, did the Nurses' Health Study show that women who had the highest vitamin E intake had lower coronary heart disease?

A. Yes.

Q. Okay. And that was an observational study?

A. Yes.

Q. Okay. And were there similar results in an observational study of Finnish citizens?

A. Yes.

Q. Now, did there come a time when randomized, controlled trials were conducted to evaluate whether there was a causal relationship between increased vitamin E consumption and reduced risk of major cardiovascular illness?

A. Yes. There have been several randomized trials.

Q. Is one of them the HOPE I and II studies?

A. Yes.

Q. And what were the results of the HOPE and HOPE II studies?

A. In those studies, there was no significant reduction in outcomes.

Q. And was the Women's Health Study another study that looked at vitamin E and cardiovascular disease?

A. Yes.

Q. And what were the results of the Women's Health Study?

A. Overall, there were no significant differences in cardiovascular events or all-cause mortality. There was a 24 percent reduction in cardiovascular death, but this was only one of the endpoints and it was not one of the primary endpoints.

Q. And the Physicians' Health Study also looked at vitamin E consumption and reduced risk of major cardiovascular events, didn't it?

A. Yes.

Q. Okay. And what were the results of that study?

A. There were no significant reductions in the incidence of major cardiovascular events.

Q. Now, turning to antioxidant intake and cancer,

were there observational studies that supported the hypothesis of an association between the consumption of foods rich in beta-carotene and the reduced risk of lung cancer?

A. Yes.

Q. Okay. And did there come a time when randomized, placebo-controlled trials were conducted to confirm a causal relationship between increased risk -- excuse me, increased intake of beta-carotene and lung cancer?

A. Yes. That was tested.

Q. And which trials were they and what were the results?

A. So, the main one was our -- our own randomized trial, the Physicians' Health Study, and we found no change in the risk of cancer by the administration of beta-carotene.

Q. Was there also evidence from observational studies supporting the hypothesis that there was a relationship between vitamin E and selenium and a reduced risk of prostate cancer?

A. Yes.

Q. Could you describe this observational research?

A. Well, for selenium, there were several studies showing that individuals with higher prevalence of

selenium had lower risk of cancer at various sites; also, regions of the country with higher selenium tended to be regions with lower cancer incidence. And several studies of that nature supported the hypothesis and led to randomized trials.

Q. And so -- and those randomized trials, were they conducted to evaluate whether or not there was a causal relationship between increased selenium or vitamin E consumption and reduced risk of prostate cancer?

A. Yes.

Q. And what was this research?

A. So, the biggest, most recent trial was the SELECT trial that was concluded recently, and they found no reduction in prostate cancer incidence with either agent.

Q. And when you say "either agent," you mean vitamin E or selenium?

A. Correct.

Q. Okay. Now, what was your reaction to the results of the vitamin E trials?

A. Well, I was disappointed that they stopped it so -- so soon. I felt that it should have gone on for another ten years or so to really test the hypothesis properly.

Q. Okay. Now, do the results of these -- the

randomized clinical trials on antioxidants, including the heart disease trials and the prostate cancer trials, did they reinforce your view that randomized clinical trials are reliably -- are needed to reliably show that consumption of a food or a supplement will prevent or reduce the risk of or treat a disease?

A. Yes.

Q. Okay. Now, did there come a time when you were asked by the Federal Trade Commission to review scientific evidence relating to POM Juice and POMx?

A. Yes.

Q. And in connection with that request, did the Federal Trade Commission provide you with voluminous materials to review?

A. Voluminous, yes.

Q. And did we advise you that they had been provided by the Respondents?

A. Yes.

Q. If you could turn in the binder before you to CX 1294, Exhibit E. Are you familiar with that document?

A. Yes.

Q. Okay. And what is -- what is that document?

A. That's an index of the materials that were sent.

Q. Was that 19 --

A. 2010.

Q. Excuse me. 2010?

Did you review these materials --

A. Yes.

Q. -- with an eye toward forming an opinion regarding whether they constituted reliable scientific evidence that POM Juice or the POMx extract prevents, reduces the risk of, or treats cardiovascular disease and prostate cancer?

A. Yes.

Q. And did you also conduct a literature search to find public -- published articles evaluating the efficacy of POM Juice -- pomegranate juice, any type, pomegranate extract, or the POM Wonderful products for the preventing or treating prostate cancer or heart disease?

A. Yes.

Q. Okay. And what did you find?

A. I found a bunch of articles, but they were all included in the materials that had been sent -- been sent to me. So, I didn't find anything new that was relevant.

Q. Okay. Now, in forming your opinions, did you also rely on your education, experience, and knowledge of the developments in the field of epidemiology,

nutrition, including its relationship to the prevention or treatment of prostate cancer and cardiovascular disease, and clinical research related to these diseases?

A. Yes.

Q. Okay. And just so there's no confusion on the record, in addition to the list of documents on the exhibit that's on the screen right now, you also read the deposition transcript of Dr. Michael Aviram?

A. Yes.

Q. And the expert report of Dr. Dean Ornish?

A. Yes.

Q. And did you advise counsel for the Respondents of this during your deposition?

A. Yes.

Q. Okay. And did you also see the results -- an abstract of the results of the dose-response study by Dr. Michael Carducci?

A. Yes.

Q. And that's been marked as CX 1174, correct?

A. Yes.

Q. Okay. Now, can you turn in your binder to the document that's marked as CX 541?

A. Yes.

Q. Is this one of the studies that you were

provided by Complaint Counsel?

A. Yes.

Q. Could you identify it, please?

A. The title is "Pomegranate juice consumption reduces oxidative stress, atherogenic modifications to LDL, and platelet aggregation: studies in humans and in atherosclerotic apolipoprotein E-deficient mice."

Q. And who is the author of that study?

A. The first author is Aviram.

Q. Now, can you summarize the animal and in vitro research done in that study?

A. The animal study was done in special mice that were genetically altered to make them highly susceptible to atherosclerosis, that they developed atherosclerosis rapidly, and these mice were given various doses of pomegranate juice, including a group with no pomegranate juice as the comparison, to look at atherosclerosis.

Q. And what conclusion did the author reach with regard to the animal and in vitro studies in this article?

A. They concluded that the -- in atherosclerotic mice, pomegranate juice may have anti-arthrosclerotic effect and atherogenic effects.

Q. And in this article, the authors also talk about some human research. Was that actually in vitro

research?

A. Well, in the human studies, pomegranate juice was given to humans, and then the blood samples were drawn from them to do various tests.

Q. So, was that actually in vitro research?

A. Yes.

Q. If you could turn to PX 008.

A. Yes.

Q. And is this also one of the studies you were provided by Complaint Counsel?

A. Yes.

Q. And could you identify this document?

A. The title is "Pomegranate Phenolics from the Peels, Arils and Flowers are Anti-atherogenic: Studies In Vivo in Atherosclerotic Apolipoprotein E-Deficient Mice and In Vitro in Cultured Macrophages and Lipoproteins." And the first author is Aviram.

Q. Now, what did this study find?

A. So, in this study, the same strain of mice that were in the previous study, in this case they consumed different extracts of pomegranate in relation to the development of atherosclerosis.

Q. And what conclusion did the authors reach?

A. They concluded that the attenuation of atherosclerosis development by some of the POM extracts,

and in particular POMf, which is the -- the -- the flower, could be related to the combined beneficial effects on certain macrophage atherogenic properties.

Q. And then could you turn to PX 0059.

A. Yes.

Q. And is this also a study you were provided by Complaint Counsel?

A. Yes.

Q. And can you summarize what was done in this study?

A. In this study, the pomegranate juice was provided or was used in cultured human coronary artery endothelial cells, the cells that bind the artery, that were exposed to sheer stress, and the effect of the pomegranate juice on the reaction to that stress in terms of nitric oxide, synthase activity, and other measures were assessed.

Q. And did they also test mice?

A. Yes.

Q. And what did they measure there?

A. They looked at progression of atherosclerosis.

Q. And this study was conducted on pomegranate juice?

A. Yes.

Q. Yes. Now, what did this study find?

A. Well, essentially, they found that pomegranate juice had an effect on increasing the expression of nitric oxide, synthase, and -- in the cultured endothelial cells, and also was -- caused a decrease in the atherosclerosis plaque in those mice.

Q. Okay. And what conclusions did the authors reach?

A. Well, their conclusion in the abstract was this approach may have implications for the prevention or treatment of atherosclerosis and its clinical manifestations.

Q. Okay. Now, did each of these last three studies on pomegranate juice or pomegranate extracts, they involve primarily in vitro and animal tests, correct?

A. Yes.

Q. Now, in your opinion, are the results from in vitro and animal testing alone enough to permit reasonable scientists to conclude that a tested product will prevent or treat disease in humans?

A. No.

Q. Okay. And in your view, do the results from in vitro and animal testing need to be confirmed in randomized human clinical trials before it can be concluded that the tested product will produce the same results in humans?

A. Yes.

Q. And why is this?

A. Because the physiology of humans is different than from these animals. These are highly specialized mice that it's not even clear whether you could extrapolate the results from these mice to regular, free-living mice, let alone to humans. The situation is -- is different.

So, you can learn interesting biology, but you can't draw the conclusion that the same thing that happens in these mice would happen in humans.

Q. Okay. If you could turn to PX 542.

A. Yes.

Q. Is this another document that you were provided by Complaint Counsel?

A. Yes.

Q. Would you identify this document?

A. The title is "Pomegranate juice consumption inhibits serum angiotensin converting enzyme activity and reduces systolic blood pressure."

Q. And who's the author?

A. That's Aviram.

Q. And can you summarize what was done in this study?

A. Yes. This was a study that reports on ten

patients with high blood pressure who were given pomegranate juice for two weeks.

Q. And how many patients were involved?

A. There were ten.

Q. And did some of them take pomegranate juice?

A. Yes. They all took pomegranate juice.

Q. Okay. Was the study blinded?

A. No.

Q. And was it controlled?

A. There was no -- there was no control -- there was no control group.

Q. And what tests were conducted?

A. So, in this study, the main result was looking at angiotensin converting enzyme activity and blood pressure.

Q. Okay. And what's angiotensin converting activity?

A. This is -- it's an enzyme that alters the functioning of angiotensin, which is -- relates to blood pressure.

Q. Okay. And what conclusion -- excuse me.

What were the results that were provided in this article?

A. So, compared to baseline, they observed a 36 percent reduction in the angiotensin converting enzyme

activity and a 5 percent reduction in systolic blood pressure.

Q. And what conclusions did the authors reach?

A. They concluded that pomegranate juice can offer a wide protection against cardiovascular disease which could be related to its inhibitory effect on oxidating stress and serum ACE activity.

Q. Okay. Could you turn to CX 611, please.

A. Yes.

Q. Were you provided this study by Complaint Counsel?

A. Yes.

Q. Could you identify it, please?

A. The title is "Pomegranate juice consumption for 3 years by patients with carotid artery stenosis reduces common carotid intima-media thickness, blood pressure, and LDL oxidation." And the first author was Aviram.

Q. Okay. Now, can you summarize what kind of research was conducted in this study?

A. This was a study that was reported to be a randomized, controlled study among 19 individuals, ten of whom consumed pomegranate juice daily, and the main measurement effect was the carotid intima-media thickness measured at 12 months compared to baseline.

Q. And did some of the patients also continue on

past 12 months?

A. Some continued for three years.

Q. Now, what was the health status of the patients in this study?

A. So, these were all individuals who had severe carotid stenosis. They had constricted carotid arteries.

Q. Okay. Now, was this study blinded?

A. No.

Q. Now, you said that IMT was --

A. Well, I -- I should qualify that. It's not clear if it was blinded. The authors refer to a placebo, so it's possible that it was blinded.

Q. Now, you said that one of the measures was IMT.

A. Yes.

Q. Is that also sometimes called CIMT?

A. C, for carotid, yes.

Q. Okay.

A. So, you could have IMT in other vessels.

Q. Okay. Now, in this -- this -- okay. So, if it's CIMT, does it relate to the intima-media thickness in your carotid artery?

A. Yes.

Q. Is that in your neck?

A. Yes.

Q. You have got two of them?

A. Yes.

Q. Hopefully.

A. Well, there's carotid intima and --

Q. So, you could also have the intima-media thickness of arteries elsewhere in your body?

A. Yes.

Q. Now, does IMT thickness have anything to do with atherosclerosis?

A. Yes. It reflects atherosclerosis.

Q. Okay. And is -- are IMT measures regarded as being a good measure of clinical outcome?

A. It's a strong predictor for clinical outcomes.

Q. Okay. Do you -- when you're talking about these kinds of markers, do you call them surrogate markers?

A. Well, surrogate markers refer to a marker that's in place of the marker -- the endpoint of interest. So, IMT thickness is a strong predictor of clinical outcomes, like stroke or heart attack, but not everyone with a high degree of IMT will get a stroke or a heart attack, and not everybody with a stroke or heart attack has a high IMT beforehand. So, it's an imperfect but strong predictor.

Q. Okay. Is blood pressure regarded as a surrogate marker for heart disease?

A. I wouldn't -- it's not a surrogate marker. It's a risk factor.

Q. A risk factor.

A. I -- I use the term "surrogate marker" as a marker that is -- could be in place of the clinical outcome. So, people with -- we know with certainty that people with high blood pressure are at high risk for stroke and heart disease, but, again, not everybody will get that.

Q. Now, what results were provided -- oh, was blood pressure also measured in this study?

A. Yes.

Q. Okay. Now, what results -- you can turn, if you want, to page 18 in your report -- what results were provided with regard to this study?

A. They reported that the carotid intima-media thickness was decreased by 35 percent and systolic blood pressure decreased by 12 percent over the -- over the 12 months compared to baseline.

Q. Okay. And do those appear to be before and after measures?

A. Those are before and after.

Q. Okay. Now, if you look at the abstract, what does it say there about what the blood pressure reduction was?

A. Just a moment. It says systolic blood pressure was reduced after one year of pomegranate juice consumption by 21 percent and was not further reduced along three years of pomegranate juice consumption.

Q. Is that basically consistent with the report -- with the data provided in the body of the study?

A. Yes.

Q. Does this study also look at before and after measures of oxidated LDL?

A. Yes.

Q. And what is oxidated LDL?

A. So, LDL is low-density lipoprotein, which carries cholesterol, and it is subject to oxidation, and that oxidation can be prevented by antioxidants. And what they found was that there was a significant reduction comparing before and after measurements in the pomegranate juice group.

Q. Now, these two studies by Dr. Aviram that we just discussed, I saw in your report, at page 18, that you called these pilot studies.

A. Yes.

Q. So, what do you mean by that?

A. What I mean by a pilot study is a small study that's typically done to demonstrate the feasibility of a larger study that could actually have the design

characteristics that could adequately test the hypothesis.

So, a pilot study is designed to be sure that people tolerate the pomegranate juice, that they would stick with it over a long time period, that it doesn't cause unexpected side effects or harm, and that paves the way for a more definitive trial.

Q. Now, in your opinion, do these two studies by Dr. Aviram provide sufficient evidence to support the claim that pomegranate juice, taken daily, will prevent or reduce the risk of or treat heart disease?

A. No.

Q. And why is that?

A. Mainly because they're too small, they don't have the proper control, and the -- the level of evidence falls far short of that required to make such a conclusion.

Q. Okay. And how would you characterize the blood pressure data from these two studies?

A. It -- if -- if this were all the data that we had, I would say it would be very interesting and would support the instigation of a trial that's big enough to actually test the hypothesis.

Q. Okay. Could you please turn to the document CX 1198?

A. Yes.

Q. Could you -- is this a study that you reviewed in connection with this matter?

A. Yes.

Q. Okay. Could you identify this document?

A. The title is "Effects of Pomegranate Juice Consumption on Myocardial Perfusion in Patients With Coronary Heart Disease."

Q. And who are the authors?

A. Sumner -- Michael Sumner is the first author and Dean Ornish is the last author.

Q. And by convention, does this mean he may be the lead author?

A. The senior author, yes.

Q. Now, can you summarize what was done in this study?

A. This was reporting the results of a randomized, double-blind, placebo-controlled trial to evaluate whether daily pomegranate juice for three months would affect myocardial perfusion, which is blood flow to the heart, in 45 patients who have coronary heart disease.

Q. Did it also look at lipids and blood pressure?

A. It looked at lipids, blood pressure, as well as the imaging of the blood flow.

Q. If you could turn to Table 2 of that study, I

believe it's on page 2.

A. Yes.

Q. Okay. Now, does this table summarize the findings on the blood flow measures that were taken?

A. Yes.

Q. Okay. And it has three tests there, SRS, SSS and SDS. What do those three abbreviations stand for?

A. SDS is the sum difference between those first two.

Q. Okay. And what were the results here of the SRS measures?

A. So, the SRS, that's the summed rest score, there were no statistically significant changes.

Q. And what were the results of the summed stress scores?

A. Likewise, there was no statistically significant difference there between groups.

Q. And what were the results of the summed difference scores?

A. There was a significant change.

Q. Now, would you consider the -- a change in this one of the three imaging measures to be a significant improvement?

A. Well, it's significant nominally in the narrow sense, the statistical sense of significant, but in

terms of the clinical significance, I do not regard this as a clinically significant finding for a couple of reasons.

The first is that you'll see at baseline, for the summed rest score in the pomegranate juice, their score is 1.9, whereas in the placebo, the score is 3.8, double that of the pomegranate juice. So, what this -- what this means is that although the participants were distributed at random, this illustrates the perils of small studies, that just by chance, apparently, it so happened that the placebo group was worse off for all of these measures of myocardial perfusion at the baseline. So, they weren't equivalent in -- in their baseline myocardial perfusion.

Ideally, in a randomized trial, you want to have your two groups be equivalent so you can draw the proper inference. Here, the placebo group was worse off at the start, and it's easy to imagine that if you're worse off at the start, you are going to get worse faster over time. So, the evidence isn't persuasive.

The second reason that I don't put a lot of weight on this is that the results were only slightly significant just for one of the three endpoints that was not specified as the primary outcome in advance.

Q. Okay. So, when you -- when you say that there

were differences in the baseline scores of the pomegranate-treated group and the placebo juice-treated group, does that look to you like a problem with randomization?

A. Yes. Assuming that the randomization was done properly, you could get this just by bad luck with small numbers. If -- had they done the study with several hundred people, it would be virtually impossible to get such an imbalance, and that's -- this goes back to why I was saying earlier that, all things being equal, a larger study is going to give you more reliable results, because you wouldn't have this kind of imbalance.

Q. Okay. And what were the blood pressure results in this test?

A. There were no differences.

Q. And that's a measure between the active and placebo groups at the end of the trial?

A. Yes.

Q. Now, what was this -- the duration of this study, according to CX 1198?

A. This was a three-month -- a three-month study.

Q. In your report, what do you -- what do you say about the duration of the study at page 19?

A. Yes. I reviewed internal documents that were provided to me that stated that the study was planned to

have measurements at three months and at 12 months.

Q. And was this fact reported -- mentioned in the published report?

A. No.

Q. Is it unusual to stop a study early and not mention that in the publishing?

A. That would be unusual.

Q. And do you recall at your deposition in this matter, counsel for Respondents asked you about the procedure for stopping a trial early?

A. Yes.

Q. When is it proper to start a trial early -- excuse me, stop a trial early?

A. Well, you could stop a trial early sometimes due to circumstances beyond your control, such as funding running out or some catastrophe, but in terms of a planned stopping of a trial early, it's only proper to do that if you have a high degree of confidence that no further information would emerge, so that that means either that you've answered your question, that you see a study result, and -- or that there's no effect of the agent and it's unlikely that -- it would be futile -- unlikely that any further information would change that conclusion.

Q. And in this case, where the results of the trial

were right at 0.05 at three months, is that a clear and conclusive result that would warrant ending a trial early?

A. No.

Q. If you can turn to CX 754.

A. Yes.

Q. Is this one of the studies you provided -- you were provided by Complaint Counsel?

A. Yes.

Q. And could you identify this document?

A. It's -- the title is "Bev 2 Summary."

Q. Okay. And can you summarize what was done in this study?

A. This was a randomized, placebo-controlled trial to assess the effect of pomegranate juice as compared to a placebo for carotid intima-media thickness and arterial elasticity, with a one-year -- one-year trial.

Q. And does elasticity reflect how much an artery expands and contracts?

A. Yes. So, a healthy artery, with a pumping of the heart, would distend and then contract; and a diseased artery would tend to be stiff and rigid.

Q. Okay. And did this study also look at blood pressure?

A. Yes.

Q. And you indicated the duration of the study was 12 months. When were -- when were measurements conducted?

A. At baseline and at the end.

Q. And also at six months?

A. There were measurements at six months as well, yes.

Q. Okay. What were the results of the study?

A. Essentially, they were null. There were no significant differences in the carotid intima-media thickness in the pomegranate juice group compared to the placebo. Likewise, there were no significant differences in blood pressure or lipids.

Q. And this was a test of pomegranate juice?

A. Yes.

Q. And how many patients were involved?

A. There were 73.

Q. Could we bring CX 1065 up on the screen?

Do you have CX 1065 before you, Dr. Stampfer?

A. Yes.

Q. Was this also a study that you were provided with by Complaint Counsel?

A. Yes. The title is "Effects of Consumption of Pomegranate Juice on Carotid Intima-Media Thickness in Men and Women at Moderate Risk For Coronary Heart

Disease." The first author is Davidson, and the last author is Aviram.

Q. And could you summarize what was done in this study?

A. This was an 18-month randomized, double-blind, placebo-controlled trial, with an initial enrollment of 383 participants, to examine the effect of pomegranate juice on progression of carotid intima-media thickness.

Q. Okay. And how many patients completed this study?

A. There were 289 that had baseline measurement and at least one postrandomization measurement for CIMT.

Q. Okay. And this was a pomegranate juice study?

A. Yes.

Q. And it was randomized, double-blind, and placebo-controlled?

A. Yes.

Q. Now, what tests were conducted?

A. Well, the main test was the carotid intima-media thickness, but they also examined blood pressure and measures of inflammation and oxidative stress.

Q. And lipids?

A. And lipids, yes.

Q. Are lipids fats?

A. Yes.

Q. Now -- and what was the duration of this study?

A. This was 18 months.

Q. Now, overall, what were the results of this study?

A. Overall, they were null.

Q. Okay. So, when you say "null," what were the results of the IMT test at 18 months?

A. So, at the end of the study, there were no significant differences in progression of intima-media thickness between the pomegranate juice and the placebo. Likewise, there were no significant differences in blood pressure or in the measures of inflammation and oxidative stress.

Q. Now, does the study also provide IMT results at 12 months?

A. Twelve months, yes.

Q. And where are they reported?

A. That would be in Table 3.

Q. And what does this show?

A. Table 3 shows three -- well, it shows the results for the anterior carotid, the posterior, and the pomegranate juice and the control group, and the composite that's based on both of those.

Q. Okay. And what was the -- what were the results for the anterior group at 12 months?

A. So, those were null in terms of the progression at both time points.

Q. At both 12 months and 18 months?

A. Yes.

Q. And what were the results for the posterior?

A. Those also were null.

Q. At both time points?

A. At both time points.

Q. Okay. And what about the composite?

A. For the composite, there was a statistically, but nominally statistically significant, difference in -- at the 12-month point, but at the end of treatment, there was no statistically significant difference.

Q. Okay. Now, is there any scientific merit to saying that pomegranate juice can reduce IMT because it did so at 12 months, even though it didn't do it at 18 months?

A. No.

Q. And why not?

A. The best and most reliable data would be the longer term results, and also, that was the a priori endpoint of the study. Inevitably, if you do lots of subgroup tests and look at a lot of measurements, by chance alone, you can see something that's statistically

significant. So, that's why typically, in a randomized trial, you identify, a priori, what your main endpoints are to be able to do the proper statistical test.

And also, if you actually look at the actual results, where the -- in the control group, the -- the average levels go from 0.79, 0.81, 0.80, over the -- from baseline, 12 months, and 18 months. Nothing much going on. And likewise, in the pomegranate juice, they go 0.78, 0.79, 0.79; nothing much going on there either. So, it seems clear that this is a null study, and that's what the authors concluded.

Q. Okay.

JUDGE CHAPPELL: We are going to take our morning break now.

MS. EVANS: Sure.

JUDGE CHAPPELL: We will reconvene at 11:30.

(A brief recess was taken.)

JUDGE CHAPPELL: Back on the record, Docket 9344.

Next question.

MS. EVANS: Thank you, Your Honor.

BY MS. EVANS:

Q. Dr. Stampfer, I realize before the break that we were using the term "a priori." What does a priori mean?

A. It means before.

Q. All right. And typically, does a clinical trial -- is it initiated with the development of a protocol?

A. Yes.

Q. And what is a protocol?

A. The protocol sets out the plans for how the trial will be conducted and how the analysis will be conducted and, in particular, the selection of the main outcome of interest a priori, meaning before the results are known.

Q. And why is it important to set out the endpoints ahead of time?

A. It's important to set those out because typically, in a -- in a large study, many things would be measured, and the more things that you measure, the more questions that you ask, the greater the likelihood that one would emerge by chance alone to meet the nominal P-value of 0.05.

So, that P-value cut-off has validity when it's for a single question, but if you're asking many, many questions, the chance is pretty high that one would hit that cut-off, just by chance alone.

Q. Okay. So, a protocol identifies ahead of time what endpoints will be measured and which ones will be

the primaries and secondaries?

A. Yes.

Q. Now, does this article, Dr. Davidson's report, which has been marked as CX 1065, does it also report on a subgroup analysis?

A. Yes.

Q. And was that subgroup analysis, was that a post hoc analysis?

A. Yes.

Q. And does post hoc -- is that like the opposite of a priori?

A. Yes. So, that's an analysis that's conducted after -- an exploratory analysis after the results are in.

Q. And what were the results of the post hoc analysis in this case?

A. In this case, they found that there were particular subgroups in which a reduction in IMT progression were observed; in particular, those with higher CV risk factors.

Q. "CV" meaning cardiovascular?

A. Cardiovascular risk factors. Sorry.

Q. Now, is it typical to find subgroups post hoc in which results differ in one direction or the other from the main result?

A. Yes, it is.

Q. And is it wrong to do subgroup analysis?

A. No, it's not wrong. It's good to do these kinds of analyses, because you want to explore the data fully and understand as much as possible what the biology is, but the danger is in the interpretation of the subgroup, and these -- this group of authors, Davidson, were -- can be considered exemplary in their recognition that this is a different type of analysis, and they -- they -- they explicitly point out that these are post hoc exploratory analyses and, therefore, must be interpreted with caution.

Q. Now, if you turn to CX 1065 at page 6, I believe it's -- it's about an inch and a half down. It starts with the word "Because." It says, "Because the decrease in CIMT progression in these subgroups was based on analyses that were not preplanned and had no correction for multiple comparisons (increasing the possibility of type I errors), these findings will need to be confirmed in future investigations."

Do you see where it says that?

A. Yes.

Q. Now, do you agree with the statement there?

A. Yes.

Q. Now, what is type I error?

A. Type I error is the -- when you erroneously conclude that a significant difference is present when it's not.

Q. All right. In your opinion, do the main null results from this study provide substantial evidence against the hypothesis that pomegranate juice protects against the progression of IMT?

A. Yes.

Q. Okay. And you said earlier that some of Dr. Aviram's studies showed improvements in LDL oxidation, correct?

A. Yes.

Q. And they also show increased peroxidase activity and decreased TBARS?

A. Yes.

Q. And were these results replicated in Dr. Davidson's study?

A. No, they are not.

Q. Okay. And where are the results of the various oxidation and inflammatory parameter data?

A. Those are set forth in Table 2.

Q. And could you tell me what you see there on Table 2?

A. Table 2 provides the results for change from baseline to three months, from baseline to 12 months,

and baseline to end of treatment for a range of inflammatory and oxidative markers in the two groups, and generally no significant results emerged. And in particular, looking at the best data, which is baseline to end of treatment, there were no statistically significant differences.

Q. Thank you.

Turning to CX 684.

A. Yes.

Q. Is this one of the studies that you reviewed in connection with this matter?

A. Yes.

Q. Can you summarize what was done in this study?

A. This analysis was a subgroup from the trial that we just talked about in which 45 of the participants in that trial also had a special measurement done to look at brachial artery reactivity.

Q. And is brachial artery reactivity, as referred to in CX 0684, as BART?

A. Yes.

Q. Okay. And do some people call this flow-mediated dilation testing, also?

A. Yes.

Q. Okay. Now, how many patients were involved?

A. There were 45.

Q. And as in the other Davidson studies, it was testing pomegranate juice as the intervention?

A. Yes. So, these were subjects who were in that study. So, this is an additional test that they had.

Q. And so what does BART testing measure?

A. That measures the -- it's another way to measure the status of the arteries, how elastic they are and how -- how well they react to stress.

Q. Is it a measure of blood flow?

A. Blood flow, yes.

Q. And did they also measure blood pressure in this test?

A. Well, they measured blood pressure both here and in the larger trial, and the results were null. There were no differences.

Q. Okay. Where are the blood pressure results, if you recall, in this report? Or should I direct you to Table 1?

A. Let's see. The blood pressure results --

Q. If I could refer you to 1.6? Did you find it?

A. One -- I'm sorry?

Q. Oh, it's page 19, numbered page 19 at the bottom.

A. Yes. So, that provides the blood pressure data in pulse, and there were no significant differences.

Q. Okay. Between the active and placebo groups?

A. Correct.

Q. Okay. And this was a 13-week trial?

A. This -- yes, a 13-week analysis.

Q. Okay. And you said that the results of the BART testing were null?

A. Right.

Q. If you look at page 21 of your expert report, you state that you looked at published and unpublished data examining the short-term effects of POM products on biomarkers. Is that correct?

A. Yes.

Q. Now, was one of these studies the report that has been marked as CX 934?

A. Yes.

Q. Could you identify that document?

A. The title is "Safety and Antioxidant Activity of a Pomegranate Ellagitannin-Enriched Polyphenol Dietary Supplement in Overweight Individuals with Increased Waist Size." The first author is David Heber.

Q. And was another one of the documents that you reviewed and that you're referring to as a biomarker study, was that the PowerPoint that has been marked as CX 1254?

A. Yes.

Q. So, what product did these studies measure?

A. These were measuring the pomegranate extract, POMx.

Q. And what endpoints did these studies look at?

A. In this -- in this study, they looked at a range of routine tests, including the complete blood count, blood chemistries, urinalysis, as well as antioxidant assessments, as reflected in the TBARS, the assays.

Q. Um-hum. And did the -- did CX 1254 also reflect results of a variety of anti-inflammatory markers?

A. Yes. They looked at a wide range of markers of oxidation and inflammation.

Q. And did those include oxidated phospholipids, nitric oxide, and peroxidase?

A. Yes.

Q. Now, even if the results of these studies were positive, could the biomarkers that were measured serve as an adequate surrogate for human disease?

A. No.

Q. And why not?

A. Because the -- well, first of all, they weren't positive, but even if they were, they wouldn't serve as an adequate marker, because the link between these biomarkers and actual clinical disease is not sufficiently strong that you could substitute one for

another.

Q. Okay. And you said that the results were not positive. Does CX 1254 reflect changes in biomarkers?

A. In that study, the -- the one that's on the screen, David Heber, "POMx in Heart Health," their conclusion was there were no changes in the groups receiving one or two POMx capsules per day in markers of oxidant stress or inflammation that were studied.

Q. Okay. And did the negative results, did they include -- that they discussed here include nitric oxide?

A. Yes.

Q. Now, based on your review of the evidence in this matter, including the data that we just discussed, all of the studies we just discussed, does competent and reliable scientific evidence show that drinking eight ounces of POM Juice daily prevents or reduces the risk of heart disease, including by decreasing arterial plaque, lowering blood pressure, and/or improving blood flow to the heart?

A. No.

Q. Based on your review of the evidence in this matter, including the data discussed above, does competent and reliable scientific evidence show that drinking eight ounces of POM Juice daily treats heart

disease, including by decreasing arterial plaque, lowering blood pressure, and/or improving blood flow to the heart?

A. No.

Q. Based on your review of the evidence in this matter, including what we have discussed above, do clinical studies, research, and/or trials prove that drinking eight ounces of POM Juice daily prevents or reduces the risk of heart disease, including through the mechanisms of decreasing arterial plaque, lowering blood pressure, and/or improving blood flow to the heart?

A. No.

Q. And based upon your review of the evidence in the matter, including the data discussed above, do clinical studies, research, and/or trials prove that drinking eight ounces of POM Juice daily treats heart disease, including through the mechanisms of decreasing arterial plaque, lowering blood pressure, and/or improving blood flow to the heart?

A. No.

Q. Okay. And based on your review of the evidence in the matter, I am going to ask you the same questions with regard to POMx Pills, eating -- taking one POMx Pill daily or one teaspoon of POMx Liquid daily.

Does the evidence discussed above provide

competent and reliable evidence showing that taking POMx Pills or POMx Liquid on a daily basis prevents, reduces the risk of, or treats heart disease, including through the mechanisms of decreasing arterial plaque, lowering blood pressure, and/or improving blood flow to the heart?

A. No.

Q. And finally, based on your review of the evidence in the matter, including the data discussed above, do clinical studies, research, and/or trials prove that taking one POMx Pill or one teaspoon of POMx Liquid daily prevents or reduces or treats heart disease, including by decreasing arterial plaque, lowering blood pressure, and/or improving blood flow to the heart?

A. No.

Q. Now, in reaching these conclusions, did you consider all of the data available to you, including in vitro, animal, and human study results?

A. Yes.

Q. Okay. Now, if you could turn to your report, page 22.

A. Yes.

Q. Can you read the second sentence of the first full paragraph?

A. "Although some promising results appear in several of the smaller studies with important design limitations, the weight of the evidence strongly favors the null hypothesis of no effect."

Q. Now, when you're talking about smaller studies with important design limitations, what studies were you referring to?

A. Basically, those are the two initial Aviram studies and the Ornish myocardial perfusion study.

Q. And what do you consider to be the important design limitations of those studies?

A. As discussed, the Aviram studies were small. The analysis was not correct in terms of comparison for a -- to a control group. In fact, the first study had no control group.

And in the Ornish study, it was larger, but still relatively small, and the imbalance of important factors at baseline between the placebo group and the intervention group rendered the results difficult to interpret, plus the finding of a marginal result for one of three endpoints and the trial results only being given at three months rather than at 12 months.

Q. Is blood flow to the heart a recognized surrogate marker for cardiovascular disease?

A. It's a research tool, but it's not a recognized

surrogate marker.

Q. Now, focusing on the blood pressure data in the studies that we've talked about and any other blood pressure data for pomegranate juice or POMx Pills that you're aware of, what's the weight of the evidence?

A. The weight of the evidence shows that there's no effect of pomegranate juice on blood pressure. The larger studies with proper control groups shows this conclusively.

Q. And focusing on the blood flow data, what's the weight of the evidence?

A. The evidence is more sparse, but it doesn't support a benefit.

Q. Okay. And focusing on the IMT data --

A. On the?

Q. -- what is the weight of the evidence there?

A. There, the weight of the evidence is strong and supports the null hypothesis of no effect.

Q. And by the "null hypothesis," what do you mean?

A. That there's no difference in effect between placebo and pomegranate juice.

Q. Okay. And have the positive results of the Respondents' animal and in vitro studies been confirmed in randomized, double-blind, placebo-controlled trials?

A. Oh, that would -- that would -- that would

change the whole picture. If, for example, the Davidson -- the Davidson study is a well-conducted, properly analyzed, randomized trial, and if those results were positive, we wouldn't be here.

Q. So, the results of the -- the positive results from the animal and in vitro studies were not confirmed in a randomized, double-blind, placebo-controlled trial?

A. Correct.

Q. You will be delighted to know that we are done with heart disease, and we are going to switch over to prostate cancer.

Now, did the Federal Trade Commission also ask you to look at evidence relating to pomegranate juice, POMx, and prostate cancer?

A. Yes.

Q. And before we talk about the studies, I'd like to make sure that we understand some of the terminology relating to prostate cancer.

What are androgens?

A. Androgens are male hormones, male steroid hormones, sex hormones.

Q. Okay. And do they regulate cell growth -- prostate cancer cell growth and differentiation?

A. Yes.

Q. Okay. And what are androgen receptors?

A. Those are proteins that bind the androgens and regulate their activity.

Q. Okay. And what's the relationship between androgen receptors and prostate cancer growth and differentiation?

A. Androgen receptor activity is very important for prostate cancer.

Q. Okay. And what is prostate-specific antigen?

A. That is a protein that's derived almost exclusively from the prostate.

Q. And is it used for -- a biomarker for some things?

A. Yes. So, it's abbreviated PSA, and it's used -- it can be -- it's widely used for screening. So, blood levels of PSA are measured in healthy men to assess their risk of prostate cancer, and it's also used after diagnosis of prostate cancer to monitor the progression of disease.

Q. And then what is prostate-specific antigen doubling time?

A. That refers specifically to prostate-specific antigen levels after diagnosis and treatment of prostate cancer, or it can also be in the absence of treatment, but it refers to the length of time for the levels to double.

Q. Okay. And can it be from a low level to just twice the low level or also a high level to twice the high level?

A. Yes. It's -- it's just the trajectory.

Q. Okay. If you could turn to PX 0068.

A. Yes.

Q. Is this one of the studies that you reviewed in connection with this matter?

A. Yes.

Q. Is it an in vitro study?

A. This -- yes. This is an in vitro study looking at the effect of the POMx Pills and POM Juice on expression of androgen receptors in prostate cancer cell lines.

Q. I'm sorry. What is the title of the report and who are the authors?

A. The title is "Pomegranate polyphenols down-regulate expression of androgen-synthesizing genes in human prostate cancer cells overexpressing the androgen receptor." And the first author is Hong, and the last author is Heber.

Q. Okay. And did the report that pomegranate polyphenols appear to inhibit gene expression of androgen-synthesizing enzymes in expression of the androgen receptor?

A. Yes.

Q. Okay. But this is in cell lines?

A. Yes.

Q. If you could turn to PX 0071.

A. Yes.

Q. Did you also review this study?

A. Yes.

Q. And could you identify this study?

A. The title is "Ellagitannin-rich pomegranate extract inhibits angiogenesis in prostate cancer in vitro and in vivo." And the first author is Sartippour and David Heber is the last author.

Q. And in this study, was human prostate cancer implanted in animals?

A. Yes.

Q. And why was prostate cancer -- why do you have to implant prostate cancer in order to study it in an animal model?

A. It's a commonly used animal model. Mice typically don't get prostate cancer, so it's -- you can't study naturally occurring prostate cancer in mice. The only animals that naturally get prostate cancer are dogs. So, if you want to do an animal model, a mouse model, then you have to do this kind of manipulation.

Q. And this study also looked at the proliferation

of human prostate cancer cells in the test tube?

A. Yes.

Q. Okay. And what does the author recommend at the conclusion of this trial?

A. They conclude that further studies in humans are needed to confirm that angiogenesis can be inhibited by an ellagitannin-rich pomegranate extract administered orally as a dietary supplement.

Q. And, I'm sorry, but could you tell me what angiogenesis is?

A. Angiogenesis is the formation of new blood vessels. So, this is a characteristic of tumors, because they need to have blood flow available to support their growth.

Q. Could you please turn to PX 0069.

A. Um-hum.

Q. Did you also consider this study in reaching your opinions in this matter?

A. Yes.

Q. Could you identify this document?

A. The title is "Pomegranate Ellagitannin-Derived Metabolites Inhibit Prostate Cancer Growth and Localize to the Mouse Prostate Gland." The first author is Seeram, and David Heber is the last author.

Q. And did this study conclude that POMx appears to

inhibit prostate tumor growth in the mouse prostate gland?

A. Yes.

Q. But that's -- that's an implanted prostate gland?

A. Yes.

Q. Okay. And it also concludes that ellagitannin is localized to the mouse prostate gland. Is that correct?

A. Yes.

Q. And in your view, what's the significance of that finding?

A. I'm not sure it has -- I don't know what its significance might be. It's hard to judge whether that has any biologic effect or not.

Q. Okay.

A. It's interesting, but...

Q. Okay. Now, these -- these three studies we just talked about, they are animal in vitro studies related to prostate cancer?

A. Yes.

Q. Can they be reliably extrapolated to humans?

A. No.

Q. And why or why not?

A. Because the situations are completely different

in terms of human prostate cancer is quite different from the mouse model. So, these are interesting to -- just to examine mechanisms. So, for example, the localization of the ellagitannin is interesting, but does that mean that it would promote prostate cancer growth or decrease prostate cancer growth or have no effect? You couldn't answer that from this kind of study.

Q. To your knowledge, would other experts in the field of prostate cancer agree with your assessment that the animal or in vitro prostate cancer studies cannot be reliably extrapolated to humans?

A. Yes. You can learn about human biology from studying animal biology, but you can't conclude that a particular agent will prevent or treat prostate cancer in humans unless you do the study in humans.

Q. And how do you know that other experts in the field of prostate cancer agree with you on this?

A. The same as -- the same as my answer for heart disease, through my discussion at scientific meetings, review of papers, literature, what -- what students and fellows are taught.

Q. So, do the results from animal and in vitro studies involving prostate cancer need to be confirmed by randomized clinical trials before you can draw firm

conclusions about the effectiveness of these agents in humans?

A. Correct.

Q. Okay. If you could please turn to CX 815.

A. Um-hum.

Q. Did you review this study in connection with this matter?

A. Yes.

Q. Could you please identify this document for me?

A. The title is "Phase II Study of Pomegranate Juice For Men with Rising Prostate-Specific Antigen Following Surgery or Radiation for Prostate Cancer." And the first author is Pantuck.

Q. Now, can you summarize -- well, first, can you tell me, what is a phase II study?

A. Well, a phase II refers to the progression -- the typical progression of agents used for -- for cancer. So, phase I is just initial testing in terms of product availability and initial safety. Phase II typically would be a bigger study to see whether it's acceptable to -- whether it's safe. It's not -- phase II studies are not designed to give the definitive result, but they're designed to pave the way for studies that would potentially give the definitive clinical result.

Q. And so can you summarize what was done in this phase II study?

A. In this study, 46 men who were diagnosed with localized, regional, low-grade prostate cancer, and had initial therapy, either with surgery or radiation, were then given pomegranate juice, eight ounces of pomegranate juice every day to see whether there would be changes in the PSA levels over time.

Q. And did the patients in the study have to have posttreatment PSA levels of between 0.2 and 5 nanograms per milliliter?

A. Yes.

Q. Now, were the patients in the study -- there were 48 of them?

A. Forty-six.

Q. Forty-six. Were they randomized into active and control groups?

A. No. They were just -- they were all given pomegranate juice. There was no control group.

Q. Okay. And was the study blinded?

A. No.

Q. No. So, was this a -- would you call this a before and after study?

A. Yes.

Q. Okay. Now, what measurements were taken --

undertaken in this research?

A. The main measurement was change in PSA doubling time.

Q. And did they also look at growth -- occurrence of metastatic disease and growth of cell lines?

A. Yes.

Q. Now, what were the findings of the study?

A. They found that before, the treatment -- the pretreatment PSA doubling time had an average of 16 months, and posttreatment had an average of 55 months.

Q. Was there any development of metastatic disease?

A. No.

Q. Do you have an opinion on whether this study supports a conclusion that POM Juice or any other POM product prevents or treats prostate cancer?

A. It does not.

Q. Okay. What factors cause you to reach that opinion?

A. Well, the main reason is there was no control group. So, we don't know what would have happened had there been no pomegranate juice in this -- in this group of patients. We know that PSA doubling time varies, and it's quite possible that we could have seen this result without any intervention.

Q. Now, is PSA doubling time accepted by experts in

the field of prostate cancer as an appropriate surrogate endpoint for overall survival?

A. No, it's not.

Q. And why or why not?

A. Because PSA doubling time does not predict prostate cancer mortality sufficiently well to serve as a surrogate in place of that outcome. So, in other words, many men with increase in PSA and increase in PSA doubling time don't die of prostate cancer. And likewise, sometimes men can succumb to prostate cancer without the PSA increase.

So, it's certainly a useful clinical marker of disease progression, and it's also a useful clin -- marker for research, but it doesn't substitute for PSA mortality in terms of, for example, testing chemotherapy drugs or other treatments. For those kinds of judgments, you need actual clinical progression.

Q. You were -- are PSA dynamics predictable?

A. They're not very predictable. So, these men all had an initial -- an initial rise of PSA after their initial treatment, but some of the men -- and not just these men, but in any study that looks at PSA, sometimes the levels go down; sometimes they go up slowly; sometimes they go up rapidly; they can go up and down. It's not -- it's not predictable. It's unstable.

Q. Okay. Could differences among labs impact PSA measures?

A. That could -- could play a role, but it's -- the biggest driver is just inherent biologic variability.

Q. Could PSA doubling time also be influenced by the number of PSA values that are used?

A. Yes. The more -- the more values, the more stable the result would be.

Q. Um-hum. And would they also be influenced by the length of time over which PSA values were ascertained?

A. Yes. The longer the time frame, again, the more stable.

Q. And do all recurrent tumors produce PSA?

A. They don't all.

Q. Now, when a man has a PSA doubling time of less than three months, is this an indicator of metastatic cancer?

A. It's a much stronger indicator, so that the -- the strength of the PSA doubling time as a predictor or a marker of metastatic disease is much stronger for very short doubling times. So, when PSA is rising rather quickly, then the predicted value of that PSA doubling time in terms of metastatic disease is much stronger. But when you get out to longer PSA doubling times, it --

the -- it becomes more wobbly and the prediction is less.

Q. So, is there any evidence that the increase in PSA doubling time seen in this unblinded, uncontrolled study, studying the PSADT from 16 months to 54 months, is there any evidence that that's clinically significant?

A. It's not clear that that -- even if that really were substantiated, as it would be if there was a control group that showed no change, even then, the clinical significance would be open to question.

Q. Now, in studies that you've conducted, do you use PSA measurements?

A. Yes.

Q. And what do you use them for?

A. Well, for example, we did a study looking at PSA values in men before diagnosis of prostate cancer to predict the risk of prostate cancer based on their PSA levels, and we found that PSA was, of course, a strong predictor of risk, which is the basis for its use in screening.

Q. Um-hum. And that's for -- a predictor in healthy men?

A. Pardon?

Q. That's a predictor in healthy men?

A. Yes, a predictor of prostate cancer, and I've also used PSA dynamics in assessing progression after diagnosis.

Q. Okay. And what -- did the lack of blinding in the study play any role in your conclusion that it's not a -- it doesn't support efficacy claims for pomegranate juice?

A. Well, there was no control group, so blinding is irrelevant.

Q. And what conclusions did the author of this study reach?

A. They conclude that further testing in a placebo-controlled study is warranted.

Q. Okay. Do you remember when these studies were originally provided -- presented to the scientific community?

A. Yes. That was long before I became a consultant to the Federal Trade Commission. I remember when these results were -- were presented and thinking, boy, this is quite interesting, and why didn't they have a control group?

Q. If you could turn to CX 1174.

A. Yes.

Q. Now, this is -- can you identify this document?

A. This is an abstract submitted to ASCO

Genitourinary Cancer Symposium, February 17 to 19, 2011.

Q. And what does it report on?

A. So, this is the -- it reports on a randomized trial of two different doses of the POMx on PSA doubling time.

Q. And what is an abstract when it's presented to a symposium?

A. Well, this was the meeting that was held earlier this year, so prior to the meeting, scientists have the opportunity to submit their work to present at the meeting, and it's done in the form of an abstract, which is just a brief summary of the results, typically would be presented before publication of the paper.

Q. And does it sort of give an opportunity for an informal peer review of the -- of the proposed findings?

A. Usually, there's some review of abstracts to -- that get accepted for presentation at the meeting, but typically, the idea is to present new, interesting findings for discussion at the meeting. So, there's not a terribly rigorous evaluation of the abstracts for acceptance.

Q. Okay. Now, in your report, you discuss the protocol and the results of this study, correct?

A. Yes.

Q. Okay. But we're just discussing this abstract

here since those other documents are in camera.

Now, do -- does this study, CX 1174, does that -- do this relate to an 18-month, double-blind clinical trial?

A. Yes.

Q. Now, was everybody in the trial taking POMx?

A. Everyone was taking POMx, and they either took one gram or three grams.

Q. So, was there a placebo control?

A. There was no untreated or placebo control group.

Q. Okay. And who were the subjects in this trial?

A. These were men with rising PSA after primary therapy.

Q. And by "primary therapy," you mean --

A. Radiation or surgery.

Q. Okay.

A. So, they were treated and now they have a rising PSA.

Q. Okay. And what were the primary and secondary study results?

A. So, the main analysis was to look at the median PSA doubling time from baseline to the end of the -- the end of the treatment, 18-month time point.

Q. And in the abstract, CX 1174, do they report that median PSA doubling time lengthened in the

intention-to-treat population from a baseline of about 12 months to 18.5 months after treatment?

A. Correct.

Q. Okay. Was there a significant -- and in your report, you provide slightly different numbers. Why are your numbers in your report different from the numbers in CX 1174?

A. In the report, I provide the mean values, and in the abstract, the authors provide the median abstract [sic]. So, the median is the middle value amongst all the values, whereas the mean is the arithmetic average, and so it's heavily influenced by outliers.

Q. Okay. And is there a -- what's a dose-response effect?

A. Typically, that means that the greater the dose of an agent, the more effect is observed.

Q. So, here, where they were comparing one dose of POMx to two doses -- to a two-pill dose of POMx, was there a dose-response effect?

A. There was no significant difference between the two groups.

Q. So, without a -- but without a placebo group, what's -- what's the most you can tell from this study?

A. All you can tell is that there's no difference between one gram a day of POMx and three grams a day of

POMx, and you can't tell whether there's an effect or no effect, because there's no untreated comparison group to make a judgment.

Q. So, does this study show a causal relationship between POMx treatment and a change in PSA doubling time?

A. No, it does not.

Q. Okay. And why is that?

A. Because there's no comparison group. So, we don't know what would have happened in the absence of POMx.

Q. You were asked by the Federal Trade Commission to evaluate whether the materials provided by the Respondents support claims that drinking eight ounces of POM Juice daily or taking one POMx Pill or one teaspoon of POMx Liquid daily prevents, reduces the risk of, or treats prostate cancer, including by prolonging prostate-specific antigen doubling time, correct?

A. Yes.

Q. In your opinion, did the available evidence provide competent and reliable scientific evidence in support of those claims?

A. No, it does not.

Q. Okay. Were you also asked by the Federal Trade Commission to evaluate whether the materials provided by

the Respondents supported claims that clinical studies, research, and/or trials proved that drinking eight ounces of POM Juice or taking one POMx Pill or one teaspoon of POMx Liquid daily prevents, reduces the risk of, or treats prostate cancer, including by prolonging PSA doubling time?

A. It does not.

Q. You said a little earlier that -- that Dr. Frank Sacks, who developed the DASH diet, was a colleague of yours?

A. Yes.

Q. Do you consider Dr. Sacks to be an expert in nutrition?

A. Absolutely.

Q. Okay.

A. He's a professor of nutrition in my department.

Q. Is it accurate to say that the conventional randomized clinical trials used for drugs are not an efficient or even effective scientific model by which to test nutrients or whole food products?

A. It is -- it's not true, no. It's difficult to do those trials, but they are what we do.

Q. Say you have a study that is not a randomized clinical trial. Does that mean it's a bad study?

A. Not necessarily.

Q. Because research proceeds by basically a stepwise fashion?

A. Steps and stutter steps.

Q. So, if it's not a randomized clinical trial, the issue isn't whether it was a good thing to do, is it? Is the issue whether -- what you can say about it?

A. Yes. We -- we learn from all kinds of study designs. The in vitro studies, the animal studies, the observational studies, they're all providing useful, important scientific information. It's not the case that you only learn from randomized trials and everything else is worthless. That is not true.

But when you want to draw a causal conclusion, you have to have the accumulation of data that's really sufficient to support that kind of claim. Randomized trials provide the best tool that we have to do that. It's not the only tool, but it's the best.

Q. Now, if you would turn to page -- the bottom of page 29 and the top of page 30 of your report.

A. Yes.

Q. There's a sentence that says, "I believe that it may be appropriate to use evidence short of randomized clinical trials for crafting public health recommendations regarding nutrient guidelines even when causality cannot be established, because everyone eats

and the public should be given advice based on the best evidence available."

Now, what do you mean there when you say "public health recommendations?"

A. What I mean is general advice to the public, such as what we did in the dietary guidelines committee, where you basically sift through all the available evidence, animal studies, in vitro, everything that is available, and come to a judgment. What can we tell people right now, who are making food choices, as to what they can do, to the best of our current knowledge, for their health?

In some cases causality will be established, and in other cases, it's just our best judgment based on imperfect data, but we have to act. So, in a setting like that, you do the best you can with the available evidence.

Q. And so when these public health recommendations are made, do a variety of scientists come together to look at the data overall?

A. Yes.

Q. Okay. And as a general matter, for example, the 2000 Dietary Guidelines, do they -- do they say things like "tests prove" if a position is not proven?

A. For the dietary guidelines committee, we have a

report, a long report for the Departments of Agriculture and HHS summarizing the views and why we supported those views, and they would give some discussion on the level of evidence. But in terms of the recommendations to the public, it would be more along the lines of "Eat more fruits and vegetables."

Q. Okay. And the discussions -- that long report you were talking about, is that sort of -- do you regard that scientists talking to scientists?

A. Yes.

Q. Okay. Now, do you believe that clinical decisions should be made on the best available evidence?

A. I do.

Q. Okay. And what's a clinical decision?

A. A clinical decision is any decision where an action is taken that affects health.

Q. Okay. Now, are your opinions here today in any way inconsistent with your statement that clinical decisions should be based on best available evidence?

A. No. There is no inconsistency.

Q. Now, would you look at the body of data relating to pomegranate juice and cardiovascular disease or pomegranate juice or -- excuse me, POMx and cardiovascular disease, and say, "This is the best available data, so I must recommend this product"?

A. No.

Q. Okay. And what about the data relating to POMx and pomegranate juice and prostate cancer?

A. The same -- the same answer. The data aren't strong enough, by any means, to support a recommendation in my view.

Q. Okay. Now, epidemiology is a public health discipline, correct?

A. Yes.

Q. Does that mean that all discussions about epidemiological studies constitute public health advice?

A. No. It also constitutes individual advice and study design analysis and many other things.

Q. And at your deposition, you were asked for your judgment about when it is proper to make public health recommendations, and you said that your opinion was offered as that of a scientist, correct?

A. Yes.

Q. Is it one that's based on regulatory or legal concerns?

A. I have no expertise in those matters.

Q. So, your expertise is always that of --

A. Only as a scientist, yes.

Q. And one last thought. At one point in your deposition, you said you were looking for evidence that

showed causality "beyond a reasonable doubt." When you said that, were you talking about the legal -- the criminal legal standard?

A. No. No, I meant -- I meant in a scientific sense, that the association could not plausibly be attributed to something other than a causal relation. So, I wasn't -- I'm not talking about it in the legal sense of how much evidence is required to convict a criminal or something like that.

Q. Thank you.

Could I have one moment?

JUDGE CHAPPELL: Go ahead.

MS. EVANS: Okay.

(Pause in the proceedings.)

MS. EVANS: No further questions. Thank you.

JUDGE CHAPPELL: Cross?

CROSS-EXAMINATION

BY MR. FIELDS:

Q. Good morning, Dr. Stampfer.

A. Good morning. Well, good afternoon.

Q. I am Bert Fields, and I'm one of the lawyers for the Respondents in this case. I think we met before in the courtroom.

Let's begin where we ended. You said, I think, that Respondents' science doesn't support their claims,

because there's insufficient evidence of causality. Is that -- is that correct?

A. Yes.

Q. Okay. And I think you said that to establish causality, you would have to prove the effect of their product beyond a reasonable doubt. Is that right?

A. Yes.

Q. Okay.

A. With the caveat that I didn't mean that in a legal sense.

Q. Well, in whatever sense you meant it, you did mean it, correct?

A. Of course I meant it.

Q. All right. So, beyond a reasonable doubt, they had to prove causality, right?

A. Right.

Q. Okay. Even though there was some evidence supporting their claims, that would be insufficient unless it was proved beyond a reasonable doubt. Is that what you're saying?

A. Yes, in the sense that I explained it.

Q. I understand. Okay.

Now, is that because they are making what you have called efficacy claims?

A. The -- there -- the claim is based on a causal

argument. So, they -- the proof needs to be provided that a causal link has been established.

Q. No, I understand. But is that because they're claiming the efficacy of their product in some way?

A. Correct.

Q. All right. Let's test what we mean by an efficacy claim. Is it an efficacy claim to say that a product reduces the risk of a disease?

A. Yes.

Q. Is it an efficacy claim to say that users of a product have a lower incidence of a particular disease?

A. No. That's different, because the way you phrased that is not a causal link. So, just because users of a product have a lower incidence doesn't mean that use of the product caused them to have a lower incidence.

Q. I see. So, when -- when you say it lowers the risk of the disease, then it's causal --

A. Yes.

Q. -- sorry about that mic -- but simply recording the fact that users have a lower incidence is not a causal matter, right?

A. Correct.

Q. Okay. Now, the standard of proof that you've talked about today for efficacy claims is not one you

consistently apply. Isn't that correct?

A. No. It is not correct.

Q. You apply it consistently?

A. Yes.

Q. And, sir, did you claim -- make claims for the efficacy of moderate alcohol consumption in reducing the risk of coronary heart disease, diabetes, and cognitive impairment?

A. Individuals with -- I don't believe that I have ever stated that a causal connection was established.

Q. Sir, did you -- do you recall doing an interview on national radio, a man named consider Norman Swan, and stating that -- and by the way, this is -- I am going to refer to RX 5000. Do we have that? Do we have it for the screen?

If you will turn to page 2 of that interview, I think you will find that you said that moderate alcohol consumption lowers the risk of both cognitive impairment and heart disease. Am I correct in that?

A. Let me just look through this.

Q. Do you see where it says "Meir Stampfer" on the bottom of page 2? "Moderate alcohol consumption does appear to raise the risk of breast cancer a little bit, but it is statistically insignificant. It also lowers risk not only of cognitive impairment but also heart

disease."

A. Yes.

Q. That's a classic -- classic efficacy claim, isn't it, sir?

A. Yes. And I do have to say I must have misspoken in that interview by not using the terms exactly correct.

Q. Yes. And did you say the same kind of thing about coronary heart disease and moderate alcohol consumption in an interview with the Modern Brewery Age? Do you recall that?

A. I don't recall it, but it could well have happened.

Q. Well, let's take a look at RX 5001, which I think is a publication called Modern Brewery Age. Do we have that up on the screen?

And, Your Honor, I have an associate approaching the Bench. I should ask your permission first.

JUDGE CHAPPELL: Yes, you may.

MR. FIELDS: Thank you, Your Honor. I take it we may do that with the exhibits without asking you each time, sir? Is that correct, Your Honor?

JUDGE CHAPPELL: I will give you that latitude.

MR. FIELDS: Thank you.

BY MR. FIELDS:

Q. Okay. Modern Brewery Age, do you see the same kind of --

JUDGE CHAPPELL: As long as it's within reason. As long as it's within reason and doesn't interrupt the flow.

MR. FIELDS: Yes. I will try not to, Your Honor, as well.

BY MR. FIELDS:

Q. Do you see, sir, where it says, "Stampfer" -- that refers to you, I take it -- "said his research has shown" -- your research has shown -- "that moderate alcohol consumption can lead to a reduction in the incidence of coronary heart disease"? Correct?

A. Well, this was what the reporter reported.

Q. Pardon me?

A. There was no quotation of me. It was --

Q. Well, are you denying you said that, sir?

A. No, I'm not denying it. I'm merely pointing out what the document says.

Q. Okay, good. All right. And those claims for the efficacy of moderate alcohol consumption in reducing the risk of coronary heart disease and cognitive impairment, those were based upon observational studies, isn't that correct, at the time you made those statements?

A. Yes.

Q. Okay. And they were not randomized, double-blind, placebo-controlled trials, correct?

A. That's correct.

Q. To shorten things, I am going to use the term "RCT trials." Do you understand that term?

A. RCT?

Q. Yeah. Some of you folks use that instead of what I just said, the randomized, double-blind, placebo-controlled studies, correct?

A. Yes.

Q. All right.

JUDGE CHAPPELL: "Some of you folks"?

MR. FIELDS: Well, I'm a little folksy, Your Honor. I'm from out on the Plains.

JUDGE CHAPPELL: Can we clear up on the record what you mean by "you folks"? Do you mean researchers or academia?

MR. FIELDS: I'm sorry. Scientists and researchers. Forgive me for --

JUDGE CHAPPELL: And he didn't take offense to that, so I guess...

MR. FIELDS: Okay.

BY MR. FIELDS:

Q. Now, it's correct that the causal link between

moderate alcohol consumption and various diseases that you said had a reduced risk, that causal link hadn't been established. Isn't that correct?

A. That's correct.

Q. Okay. Now, you made those efficacy claims about moderate alcohol consumption without proving the causal link and without RCT claims, because in the case of wine and beer, for example, you're talking about nutrients rather than pharmaceutical products. Is that correct?

A. I wouldn't characterize these comments in an interview setting as making an efficacy claim. It's far different from a prepared statement in the scientific literature or a prepared advertisement where one is thoughtfully watching each word.

These are interview setting quotations, and I did not use the proper terminology to make the distinction between a -- whether a causal link was established. And even in -- even in those quotations that you bring, you don't find me saying, "A causal link has been established between moderate alcohol consumption and cognitive function."

So, a slight misspeaking, the same way your earlier question, when you asked about people who use a drug have a lower incidence, this creeps into contemporary speech. It's not the same as making an

efficacy claim.

Q. Well, sir, you were talking to the public when you gave those interviews. Isn't that correct?

A. Yes.

Q. And are you now saying that moderate alcohol use does not lower the risk of cognitive impairment and coronary -- vascular -- cardiovascular disease?

A. What I'm saying is that that link is not -- the causal link is not established.

Q. I understand. But even though the causal link was not established, you felt free to tell the public that moderate alcohol consumption did, in fact, lower the risk of these diseases, right?

A. In an interview setting, that was my statement, and it was a poor choice of words. And if I had more time and thought about it, I would have chosen a more accurate way to raise the -- my opinion on this.

Q. Well, that's what I don't understand. Are you saying that, in fact, what you said in those interviews was untrue?

A. What I'm saying is that I used the wrong terminology, the wrong words. What I should have said was what I said earlier in the interview, that people with moderate alcohol consumption had lower cognitive decline, and I should not have used the term that

moderate alcohol use lowers risk. That was a mistake on my part. I admit it.

Q. Are you saying that things said in an interview are not the same as advertising?

A. I'm sorry? Say it again.

Q. Are you saying that things said in an interview are not the same as advertising?

A. I am saying that, yes. They are not the same.

Q. Okay, thank you.

Now, when you made those remarks about moderate alcohol consumption, Doctor, you were aware that moderate alcohol consumption is not totally safe. Isn't that correct?

A. It's -- moderate alcohol consumption is not totally safe. That is correct.

Q. Yeah. It's thought to tend to reduce breast cancer, right?

A. Yes, as I pointed out.

Q. Oh, I didn't hear you point that out. I'm sorry.

A. I think you actually said it yourself, but --

Q. You're right. You're right. I apologize. I did say it.

And also, if it slips from moderate alcohol consumption to immoderate alcohol consumption, it can

cause a lot of havoc and fatalities, right?

A. Absolutely.

Q. Now, wouldn't it be fair -- well, before I get to that, in fact, Doctor, you -- you or your school received a substantial payment from the Anheuser-Busch Beer Company. Isn't that correct?

A. I received nothing.

Q. Did you understand my question? I said "you or your school."

A. You or your school?

Q. Yes.

A. So, I'm answering the first part, is I received nothing, and the School of Public Health received a gift.

Q. They received a very substantial amount of money from the beer company.

A. 150,000.

Q. Yes. And you have also appeared and made presentations for the beer company, right?

A. I spoke on the risks and benefits of moderate alcohol consumption, yes.

Q. And those were presentations to the Anheuser-Busch Company, correct?

A. They were organized by Anheuser-Busch, yes.

Q. Well --

A. They were not presentations to the company. They -- but the company organized them.

Q. Okay. And they paid your expenses, the Anheuser-Busch people, right?

A. Pardon?

Q. They paid your expenses?

A. Yes.

Q. Okay. Now, you felt that when you made these statements about moderate alcohol consumption, the causal link between moderate alcohol consumption and these various diseases that you said had a reduced risk had not been firmly established. Isn't that correct?

A. Yes.

Q. You were relying strictly on observational studies; you didn't have RCTs to back that up.

A. Not for clinical endpoints.

Q. I'm sorry?

A. Not for clinical endpoints.

Q. Okay.

JUDGE CHAPPELL: Hold on. Hold on a second.

Let's go back to these presentations. You said you received no money?

THE WITNESS: Yes.

JUDGE CHAPPELL: They were arranged and everything was paid for by Anheuser-Busch?

THE WITNESS: Yes.

JUDGE CHAPPELL: At the time you were doing these, were they on your spare time or were they on Harvard time?

THE WITNESS: On my -- my own time.

JUDGE CHAPPELL: They weren't at any point when you should have -- you were on a leave or vacation status at the time?

THE WITNESS: The -- well, we don't have formal vacation status for professors, but it was on my own time.

JUDGE CHAPPELL: Okay. And you're currently a full-time employee of Harvard?

THE WITNESS: Yes. Well, Harvard and Brigham and Women's.

JUDGE CHAPPELL: And what do you consider your status today while you're sitting here?

THE WITNESS: Consultant to the Federal Trade Commission.

JUDGE CHAPPELL: Okay. And you don't have to be on vacation or anything for that?

THE WITNESS: Well, professors don't have a formal certain amount of vacation time, as long as --

JUDGE CHAPPELL: Right, but my point is, are you supposed to be lecturing students or teaching today?

THE WITNESS: No, not today. I'm on my own.

JUDGE CHAPPELL: Okay. Thank you.

BY MR. FIELDS:

Q. All right, sir. Now, is it correct that the same standard of proof that you've applied in making these statements about wine and beer apply to pomegranate juice?

A. The same standards, yes.

Q. Okay. So, it would be fair to say, without RCTs and without a causal link being proven beyond a reasonable doubt, that pomegranate juice may reduce the risk of certain diseases, correct?

A. Well, you used the -- you used the word "may," and if you use the word "may," then it would be correct, because "may" implies that it's possible. But if you say "will," then it is not correct, because "will" implies that a causal link has been established.

Q. So, the -- well, but you said that a causal link hadn't been established for moderate alcohol consumption, and yet you made a -- on two occasions that I cited to you, you made the statement that it lowered the risk of all kinds of diseases, right?

A. I think I answered that question previously, that it was a poor choice of words, and I do not hold the view that a causal link between moderate alcohol

consumption and reduced cognitive decline and reduced heart disease has been established.

So, you have found a quotation that was made in an interview setting that was incorrect, just as you yourself have already misspoken a couple of times in extemporaneous speech, and this is what happens with extemporaneous speech.

Q. Yes. And so you feel that a more rigorous standard should be applied to pomegranate juice than you've applied to wine and beer?

A. Absolutely not.

Q. The same, correct?

A. The same standard.

Q. Okay. Now, you've made a number of public health recommendations based upon what you call observational studies. Isn't that correct?

A. Yes.

Q. You've said that a number of food products result in a lowered risk of disease. Haven't you done that?

A. Yes.

Q. And also based on observational studies, correct?

A. Ah --

Q. No?

A. -- I made public health recommendations for various foods and diet in relation to risk of disease, that is correct.

Q. Well, I didn't say -- I don't think I said "in relation to."

A. Um-hum.

Q. Didn't you -- haven't you made statements to the public that various food items reduce the risk of certain diseases?

A. I -- I may have.

Q. You don't recall ever doing that, as we sit here today?

A. I don't recall a specific instance, but it's quite possible that it happened, as you pointed out for moderate alcohol.

Q. And let's --

A. But I have -- I don't believe that I have made a statement that a causal link has been established in the absence of evidence that would support that.

Q. Well, whether or not a causal link was established, you have said that various foods reduce the risk of specific diseases. Haven't you told the public that on a number of occasions?

A. That could well be.

Q. It could be -- well, isn't it?

A. Well, I don't recall a specific instance, but it very likely has happened, and I'm sure you can pull up some quotes.

Q. Let's take a look at page 31 of your deposition. I think your memory was clearer then. All right, I'm reading from line 19 at page 31.

JUDGE CHAPPELL: Hold on. Hold on. If you want him to read along, make sure he's with you.

MR. FIELDS: Pardon me?

JUDGE CHAPPELL: Make sure he's with you on the same page. I don't know that he --

MR. FIELDS: Okay.

BY MR. FIELDS:

Q. Do you have a copy of your deposition up there with you, sir?

A. No.

Q. It should be on the screen there.

A. It's not showing up.

Q. Oh, I'm sorry.

A. There we go.

Q. Thank you, Your Honor.

For some reason, my screen is blank, but maybe we can fix it at a recess.

All right. Now, the question at line 16, page 31, which I hope is on the screen:

"QUESTION: Now, you have made public recommendations on the basis of epidemiological research before?

"ANSWER: Yes.

"QUESTION: And you are aware that those recommendations have been propounded in television, the internet, magazines, and other forms of media?

"ANSWER: Yes.

"QUESTION: Those public health recommendations have been based on primarily epidemiological research, would you say?

"ANSWER: Yes.

"QUESTION: And those public health recommendations are primarily based on observational studies in particular?

"ANSWER: Most of them. Not all."

Now, sir, does that refresh your recollection that, in fact, based upon observational studies, you have made public health recommendations?

A. It's not a matter of refreshing my memory. Of course, I have made public health recommendations for nutrition, but you were asking specifically "result in." Those were the words you -- that you used, and that implies that I stated a causal link has been established.

Of course, I've made public health recommendations, and they're based in large part on observational studies because that's in many cases the best available evidence. That's not the same as stating that a causal link has been established. You should distinguish very clearly between recommendations that are based on the best available evidence that falls short of establishing a causal link.

So, yes, I've made -- I have made and continue to make many public health recommendations of diet and lifestyle, even when the data are not supported by randomized clinical trials or where a causal link has not been firmly established.

Q. Yes. I don't mean to suggest that you established a causal link; quite the contrary.

In fact, let's take some examples. Didn't you say, for example, that nuts lower the risk of heart disease and diabetes, sir?

A. If I used that exact wording, it would have been incorrect in implying that a causal link has been established.

Q. Well, let's look at -- you wrote an article called "Rebuilding the Food Pyramid." Do you remember that?

A. Yes.

Q. Could we take a look at RX 5003? And if you look at page 7 -- perhaps it's page 8. Let me take a look. Yes.

You said here that "Controlled feeding studies show that nuts improve blood cholesterol ratios, and epidemiological studies indicate that they lower the risk of heart disease and diabetes."

"They lower the risk of heart disease and diabetes," sir, that's pretty much an efficacy claim, isn't it?

A. No, it is absolutely not, because it's good to look at the whole sentence, and they say "indicate."

Q. Oh.

A. If it was a cause-and-effect relation, a stronger term would be used. An indication is a point-to; it is not proof. So, I am trying to draw this distinction between when a causal link is established and when it's not.

So, the controlled feeding studies show that because those are randomized trials, and they show that cholesterol is improved, and this provides a strong biologic rationale. And the epidemiologic studies indicate, not prove.

Q. So, you're telling me that when you tell the public that a study indicates that something lowers a

risk of disease, that's not an efficacy claim, correct?

A. It's -- it's not a proof of a causal link, right.

Q. Well, can you answer my question?

A. Yes.

Q. Is that what you call an efficacy claim, where somebody says that a study indicates that it lowers the risk of heart disease and diabetes?

A. Well, the term "efficacy claim" is a term that you're -- that you're using. I don't use that terminology in the scientific judgment. But the distinction I'm trying to make and continue to try to make is whether or not a causal link is established.

Q. Yes, I understand that. There was no causal link established for nuts --

A. That's right.

Q. -- lowering the risk of heart disease and diabetes.

A. Right.

Q. And so you say when you just use the word "indicate," that studies indicate, that is not -- that you don't need a causal link for that.

A. Well, it doesn't -- my interpretation of it is that I'm not claiming a causal link has been established when I use the word "indicate."

Q. So, if the Respondents said that studies indicate that pomegranate juice lowers the risk of cardiovascular disease or prostate cancer, they don't need a causal link for that in your view, right?

MS. EVANS: Objection.

JUDGE CHAPPELL: Legal basis?

MS. EVANS: It's beyond the --

JUDGE CHAPPELL: You need to stand up or I cannot hear you, Madam.

MS. EVANS: Oh, I'm very sorry. It is beyond the scope of his expertise. He has not claimed to be an advertising expert.

JUDGE CHAPPELL: Overruled.

THE WITNESS: Can you repeat the question?

BY MR. FIELDS:

Q. Yes. Yes, yes, yes.

You said that a causal link does not need to be established for statements that say that studies indicate that a product lowers the risk of heart disease and diabetes, right?

A. That that does not imply that a causal link is established, correct.

Q. So, you don't need to establish a causal link to say that, correct?

A. Correct.

Q. And therefore, sir, isn't it correct that if Respondents said that their studies indicate that drinking pomegranate juice -- indicate that drinking pomegranate juice lowers the risk of diseases, such as cardiovascular disease and prostate cancer, they don't need to establish a causal link, in your opinion, correct?

A. There's two parts to my answer. First, when you say the Respondents would say, if you're referring to the scientific literature, that's different from say in advertising, where, of course, I have no expertise and can't give an opinion.

But the other point is that the strength of the evidence for pomegranate is not sufficient to say that they indicate that -- a lower risk. For example, for the carotid IMT thickness studies, the evidence shows clearly that there's no benefit.

Q. Yes, we'll get to that.

A. So, they don't --

JUDGE CHAPPELL: Hold on a second.

All right, sir. Did I just hear you say that all of your expert testimony is about the scientific literature and testing and has nothing to do with advertising?

THE WITNESS: Right.

JUDGE CHAPPELL: Thank you.

Go ahead.

MR. FIELDS: All right.

BY MR. FIELDS:

Q. So, your article called "Rebuilding the Food Pyramid" is what you call scientific literature and testing?

A. Yes. It's a review.

Q. It's a what?

A. It's a review article.

Q. What do you mean by a "review article"?

A. It means that there's no new, original data that are put forth in this article; that it summarizes previous work.

Q. And where did this article appear?

A. I think that was in Scientific American.

Q. Yes. And in your opinion, this is merely, what, a review of your research and, therefore, it has a different standard from advertising? Is that your testimony?

A. Ah, I don't know anything about the standards required for advertising. So, I can't answer that question.

Q. Well, I understood you to answer the Court's question by saying that there was some difference

between what you say in this magazine article and what one might say in advertising. Are you drawing that distinction or did I misunderstand you?

A. I don't know anything about advertising, so I -- I can't -- this is not advertising. I'm not selling a product. This is a -- an article in a -- in a scientifically oriented magazine that I wrote. It's not advertising. I don't know anything about advertising.

JUDGE CHAPPELL: Also, for those that don't understand, can you state for the record the difference between a review article and a peer-reviewed article? Because I heard you say this was a review article.

THE WITNESS: Yes. That's an important distinction. So -- and they are separate issues. A peer-review article is an article that's submitted to a journal and it's sent out for review by other scientific experts for vetting and comments, and that constitutes a peer-review article.

A review article is an article that summarizes previous scientific work and doesn't bring in new, original work, and a review article either can be peer-reviewed or not peer-reviewed. So, the distinction between -- there's two distinctions: One is original research versus review, and a separate distinction is peer review versus not peer review.

JUDGE CHAPPELL: Thank you.

MR. FIELDS: All right.

BY MR. FIELDS:

Q. You've also made what you call public health recommendations on television?

A. Yes.

Q. Correct?

And the one that we saw before about beer was on radio -- one of them was on radio and one of them was in a newspaper, as I recall, right?

A. Yes.

Q. And you don't call those review materials, do you, sir?

A. No. Those are news reports.

Q. Yeah. And on television and in other media statements, you have talked about foods lessening the risk of diseases, haven't you?

A. Yes.

Q. And you did it based on observational studies, not RCTs.

A. Correct.

Q. And you did it without the causality link being established, correct?

A. Yes.

Q. Thank you.

I am about to move on to a new subject, Your Honor. Would this be a good time to take the noon recess or should I go forward?

JUDGE CHAPPELL: No, it's just past 1:00. Let's go ahead and take a break.

MR. FIELDS: Thank you, Your Honor.

JUDGE CHAPPELL: We will reconvene at 2:05. We're in recess.

(Whereupon, at 1:01 p.m., a lunch recess was taken.)

AFTERNOON SESSION

(2:05 p.m.)

JUDGE CHAPPELL: Back on the record, Docket 9344.

Go ahead.

MR. FIELDS: Thank you, Your Honor.

BY MR. FIELDS:

Q. Good afternoon, Doctor.

A. Good afternoon.

Q. We talked about or you talked about the requirement of RCTs -- you understand that abbreviation?

A. Yes.

Q. Yeah.

-- RCTs to provide evidence to support the Respondents' claims. Do you recall that?

A. Yes.

Q. Okay. Now, when you're doing nutritional research, aren't there feasibility limitations on randomized trials?

A. Yes.

Q. For example, the number of participants can be a problem.

A. Yes.

Q. And the time frame can be a problem, too. Isn't that true?

A. True.

Q. Okay. For example, if you're going to do a study about cancer and its relation to some nutritional substance, that's going to take a long time, right?

A. Yes.

Q. Okay. And isn't it also true that randomized tests are far more expensive than, for example, observational studies?

A. Typically.

Q. Yeah. And, in fact, in general, even simple randomized tests are very expensive. Isn't that true?

A. Well, everything's relative, but on -- when you compare randomized trials to observational studies, typically, if they're the same size, the trial will be more expensive.

Q. Yes. I am going to refer you to your deposition at page 77, where you said that -- and I quote from line 16:

"ANSWER: Typically randomized trials, even simple ones, of nutrition are very expensive."

Right?

A. Yes.

Q. Okay. In fact, you've called them a huge expense. Isn't that true?

A. I probably did.

Q. And even governments and major institutions tend to lack interest in funding randomized trials because of that, as you put it, huge expense. Isn't that true?

A. True.

Q. Okay. Now, you are really asking Respondents in this case to take on those really huge expenses, isn't that correct, in order to substantiate their claims?

A. I'm not asking them to do anything. I'm merely evaluating the scientific merit of the findings.

Q. Well, but as I understand your testimony, you're saying that RCT tests, these hugely expensive tests, would be required to substantiate their claims, right?

A. They're -- the tests are expensive, but the tests that were mounted, in aggregate, were completed, and had they shown the benefit that was hoped for, then the establishment of evidence would be -- would be present.

So, yes, the trials are expensive, but, for example, in aggregate, the data from the Ornish IMT study, in aggregate with the Davidson IMT study, is a substantial number of subjects and had sufficient statistical power to observe a certain benefit if one were present.

So, in this instance, although the trials are expensive, they're not prohibitive, and, in fact, they

were even done.

Q. Well, you are saying that in order to substantiate their claims, further, hugely expensive tests would be required. Isn't that what you're saying?

A. No. To -- not quite. What I'm saying is to substantiate the claims, you need to have evidence and data, and that data can come from trials that are expensive. Thus far, the trial data have not substantiated. So, it's not the case that -- even if a very expensive trial were mounted, that doesn't mean that the case would be substantiated.

Q. Well, I understand that, and we'll get to the tests in a few minutes, but you are saying, right now, they haven't got sufficient -- Respondents haven't got sufficient science to satisfy you or your tests. So, if they wanted to satisfy those tests, they would have to undertake these very expensive additional tests. Isn't that correct?

A. That's correct.

Q. Okay. And it is also true, is it not, that in dealing with nutrition, as opposed to pharmaceutical products, there usually is no intellectual property to that, right?

A. Correct.

Q. So, you don't have the benefit of a patent to

reward you for undertaking that huge expense, correct?

A. That's correct.

Q. Okay. And I suppose the risk of harm is something else that has to be considered in evaluating the standard of evidence. Isn't that right?

A. The risk of harm, of course, has to be evaluated in terms of recommendation and how the agent might be used, but in terms of evaluating a causal link, it's distinct. That issue is distinct from safety.

So, the overall recommendation or use of the product obviously has to -- there has to be more benefit than harm, but -- but to establish the causal link for benefit is a separate issue from safety.

Q. Well, when you're evaluating what standard of evidence should apply, what degree of evidence should be required, isn't the risk of harm one of the factors you consider?

A. You don't consider risk of harm in terms of evaluating causality. You consider risk of harm in whether it should actually be used.

Q. So, you -- I'm sorry. Finish your answer.

A. So, those are just -- the risk of harm is terribly important, but it's different from evaluating a causal link.

Q. I see. Now, haven't you said, in connection

with some of your public health recommendations, that when the risk of harm is slight, you don't want to hold up information from the public and you would err on the side of giving them that information?

A. Yes, I have said that. I hold that view.

Q. Even without causality, right?

A. Right.

Q. Okay. So, the risk of harm is a factor that weighs upon the decision of what standard of evidence is required to support a claim, correct?

A. No, not correct. So, we will go through it one more time.

The risk of harm is -- plays into a recommendation whether or not to use the agent, but it does not play into making that causal -- a judgment about a causal link. So, those are two separate issues.

Q. Well, putting aside causal link for the moment, in deciding whether you can give information to the public about a product and its effect, doesn't the risk of harm enter into that decision?

A. The decision of whether you can give information to the public? I'm always in favor of giving information.

Q. Yes.

A. I oppose withholding information.

Q. And --

A. Unless there's some very strong reason not to -- to withhold it.

Q. So, when you're talking about a product, if there is a slight or a known risk of harm and a potential benefit, you are a strong advocate of giving that information to the public. Isn't -- isn't that true?

A. Yes, that is true.

Q. Okay.

JUDGE CHAPPELL: Hang on a second.

You were talking about the risk of harm, and you said whether to use the agent. Are you talking about whether you're talking -- testing the effect of spring water versus the risk of arsenic? Is that what you mean by "the agent," what you're testing? What did you mean by that?

THE WITNESS: What I meant by that is whatever it is that you're recommending, the food or the drug or the product, whatever it is you're recommending, you have to take into account risk of harm.

JUDGE CHAPPELL: So, something that's generally considered safe, like spring water, low risk.

THE WITNESS: Right.

JUDGE CHAPPELL: Okay.

BY MR. FIELDS:

Q. Okay, I think we understand each other.

Now, isn't it your opinion that generally, in dealing with nutrition and food that bears nutrients, that RCT trials are not and should not be required?

A. Required for what?

Q. To substantiate health claims based on those products.

A. If -- if the health claim is -- presumes a causal link, then in many instances, you would do a randomized trial. If the -- if the claim is there's some evidence to suggest the possibility that nuts may reduce risk of diabetes, I would say that was -- would support such a statement. But if you ask do -- is there a causal link that has proven that if you eat nuts, you'll lower your risk of diabetes, I would say not yet.

Q. Well, don't you consider it appropriate to rely on evidence short of RCT trials --

A. Absolutely.

Q. -- for --

A. Oh, I'm sorry.

Q. -- for claims regarding nutrients in food, even when causality cannot be established?

A. Well, it depends on what the claim is.

Q. You mean if it's an efficacy claim, like the one

you made about moderate alcohol use, then you have to have causality? Is that what you're now saying?

A. If the claim implies that a causal link has been established, then you have to have evidence to back it up.

Q. I see. Well, when -- do you recall coauthoring an article with Dr. Blumberg on evidence-based criteria?

A. I do.

Q. Yes. And in that article, did you express the opinion that the general principles of evidence-based medicine can provide a sufficient foundation for establishing dietary requirements and dietary guidelines in the absence of RCTs?

A. Yes.

Q. Okay. And, in fact, isn't it true that a hypothesis about disease causation can rarely, if ever, be directly tested in humans using the RCT design?

A. Can -- can -- well --

Q. Do you want me to read it again, if you didn't follow?

A. Sure, please.

Q. The statement is, "A hypothesis about disease causation can rarely, if ever, be directly tested in humans using the RCT design." Is that your opinion, sir?

A. I believe this was in the context of nutritional factors?

Q. Yes. We're talking about nutrition, right, pomegranate juice or beer and wine.

A. Yes. It's rare. It's rare to do that. That is -- that is the case. Rare, but not -- not impossible.

Q. I didn't ask you if it was rarely done. I said, isn't it correct that disease causation can rarely, if ever, be directly tested using the RCT design?

A. Correct, yes.

Q. If ever.

A. Well, that's the statement.

Q. Those are your words, right?

A. Well, my words along with the coauthor's.

Q. Yeah. All right.

You also agree, do you not, that there are very striking differences between what's needed to test for drugs and what's needed to test for nutrients?

A. Very striking -- I didn't catch that word.

Q. Pardon me?

A. Very striking -- I didn't catch the word that you said.

Q. Differences.

A. Differences? There's -- there's differences

between drugs and nutrients, yes.

Q. Well, and didn't you -- isn't it your opinion that in testing drugs, we must apply the highest standards, because they can be dangerous and they can also tend to bring a high price in the marketplace and they also have protection by way of intellectual property? Correct?

A. We need to have the high standards, and the reasons that you gave apply, but that's not the reasons for having the high standards. We need to have high standards because we want to know the truth, and as a -- an effect of those treatments is the possibility for harm and the other -- and the high cost and the other things that you mentioned.

Q. Wouldn't this be true: That those same concerns that we just mentioned are substantially less pressing for nutrients. Is that correct?

A. The concerns are, but the -- the necessity for having the standards of evidence is similar. So, the concerns are different, but it's not that -- it's not those concerns that drive the necessity to have a high standard of evidence for causality. The evidence for causality remains, but the -- the worries about harm and cost are different.

Q. Sir, wasn't it the entire thesis of your article

with Dr. Blumberg that for nutritional matters, nutritional issues, we should not require RCT trials, as we do with drugs?

A. I -- I'm -- I must have failed in the way I wrote the article, because no, that was not the point of the article.

Q. Oh, I see. Okay.

Didn't you -- isn't it your opinion that in dealing with nutrition and dietary claims, the evidence will necessarily be based on observational studies, rather than RCT trials?

A. Yes.

Q. So, you're saying it will necessarily be based on observational studies rather than RCT trials, but at the same time, you're saying RCT trials are necessary in the case of Respondents and pomegranate juice?

A. They're necessary to establish a causal link. What I'm saying in the article is that we have to recognize that that high standard to which we should aspire will, of necessity, because of feasibility reasons, often not be reached for diet and nutritional substances, but -- and this was the point of the article -- but this doesn't mean that we should fail to make recommendations based on the best possible evidence. We just need to distinguish the level of

evidence that supports those recommendations. So, that was the point of the article.

Q. Well, sir, you didn't say "often" in the article, did you, when you made the statement about evidence having to be based on observational trials? You said, "It will necessarily based on observational trials." Isn't that correct?

A. Necessarily because of constraints -- practical constraints, not necessarily conceptually.

Q. Okay. Well, putting aside conceptually, because of practical constraints, isn't it correct that pomegranate juice can sustain its claims based upon observational studies? It necessarily has to if your article is right, correct?

A. No. No, that is not correct. It just will have to -- it will have to reduce its claims to match the data. It's not -- you don't just take the best data that you have and say, "Well, this is the best data that I have, so, therefore, I can claim a cause-and-effect relation." You say, "This is the best data I have, so, therefore, I can claim this but not that."

Q. Well, sir, you said such claims will necessarily be based on observational studies, rather than RCT tests. "Necessarily" means that's all we have to deal with. Isn't that correct?

A. That is correct.

Q. And so you're saying it would be impossible, then, for them ever to sustain, by any kind of test, because observational studies are the only thing that can present a case here, and you're saying that's not enough.

A. No. That's -- that is not what I'm saying. First of all, there have been and are today randomized trials of nutritional factors, and some show benefit and some show no benefit, and the, in fact, randomized trials of a reasonable size have been done with pomegranate and show no benefit.

So, it is not the case that you can never have randomized trials of nutritional factors. But the level of the claim has to match the level of the data. That's all I'm saying.

Q. So, when you said it would necessarily be based on observational studies and not RCT trials, you didn't mean -- you didn't mean what I just said; you meant sometimes, not necessarily. Is that right?

A. I did not mean, by "necessarily," that there never could be a trial on nutritional factors, and I don't think the sentence implies that.

Q. Do you recall -- do you recall quoting from Dr. Sackett, who is, according to you, one of the

intellectual fathers of evidence-based medicine? Do you recall quoting from Dr. Sackett?

A. Yes.

Q. And do you recall Dr. Sackett saying, "Evidence-based medicine is not restricted to randomized trials"? Right?

A. I don't recall the exact wording, but something along those lines.

Q. And that's part of your opinion, too; evidence-based medicine is not restricted to randomized trials. Is that right?

A. Oh, I -- yes. I agree with that.

Q. And isn't it your opinion that the failure to act, in the absence of conclusive RCT evidence, increases the risk of forgoing benefits to the public that might have been achieved with little risk and little cost?

A. Yes, absolutely.

Q. So, when we've got little risk and little cost, we should err on the side of getting the information to the public. Isn't that true?

A. Cost and risk, to me, are not the driving factors of whether the public has access to information.

Q. Well, didn't you say that the failure to act in the absence of conclusive RCT evidence, when there's

little risk and low cost, shouldn't forgo the public getting the information?

A. Yes. I did say that, but I'm not talking about withholding or not withholding information. I'm talking about making recommendations based on available evidence.

Q. When you say the risk of withholding available evidence from the public, you're talking about withholding the information. What's the difference?

A. I -- I'm -- I'm not in favor of withholding information.

Q. Yes, that I gather from your article, but that's the point I'm making. You said -- and I'm in total agreement -- that when there's little risk and little cost involved and a potential benefit, that we should make that information available to the public rather than withhold it. Isn't that correct?

A. We definitely should.

Q. Okay. Let's turn to science, where you really have the edge on me.

Okay. How many of Respondents' studies did you review?

A. I don't know the exact number, but the list is --

Q. Approximately.

A. Gee, I don't -- 25 or some -- 30. I don't know exactly, but the list is in the -- in the materials. And some of the documents were repeated documents where they had the same studies, so it's hard to actually --

Q. Were you aware that Respondents sponsored 90 separate scientific studies?

A. I know that there are -- many studies were sponsored, but I didn't know the exact count.

Q. Did you know that 67 of those 90 studies were published?

A. Again, I knew many were published, but I didn't know the exact count.

Q. So, you read 25. You read a little bit more than a third of the published studies, correct?

A. Well, I'm guessing at the numbers.

Q. Pardon me?

A. I'm guessing at the numbers.

Q. Oh, okay. I don't want you to guess.

Did you know that the 90 studies, separate scientific studies, were done at 44 different medical institutions?

A. No. I didn't know that number.

Q. Okay. And did you ask to see more studies?

A. I reviewed all the studies that were provided for me, and I also did a -- my own literature search to

see if there were others that were relevant that I missed.

Q. And your best estimate is you -- if there were 67 published studies, you probably read around 25, right?

A. It's -- it's a rough estimate. I -- I -- you know, if we -- if you want me to take the time, I could count them up, but I'm just guessing here.

Q. All right. Now, you know that Respondents did numerous in vitro and animal studies, correct?

A. Yes.

Q. You've had little experience in in vitro research. Isn't that correct?

A. That's correct.

Q. Okay. And isn't it true that you can get very useful information from both in vitro and animal studies?

A. You can get very useful information from those studies, yes.

Q. Thank you.

And those studies allow an examination of the biological mechanisms, correct?

A. Yes.

Q. In highly controlled settings, correct?

A. Correct.

Q. Okay. In fact, you're not opining on the in vitro studies for the antioxidant affecting pomegranate juice. Isn't that correct? Isn't that what you said?

A. I'm opining on the claims.

Q. Just on their claims, but not on the in vitro studies?

A. Well, the in vitro and animal studies are part of the body of evidence.

Q. And you're not opining, as I understand it, on the strength of antioxidants in Respondents' products?

A. That is correct.

Q. Or on how antioxidants in pomegranate juice are metabolized in the body?

A. Correct.

Q. Okay. Did you review Dr. Aviram's in vitro and animal studies?

A. I reviewed all of the papers that were provided to me, which I understand were provided by the Respondents.

Q. So, you don't know whether or not they included all of Dr. Aviram's studies?

A. No, I don't.

Q. Okay. Now, the studies you mentioned this morning all showed a -- that is, Dr. Aviram's in vitro and animal studies -- all showed pomegranate juice

having a beneficial effect on heart health. Isn't that correct?

A. You're referring to the animal studies?

Q. Well, both the in vitro and animal. Let's take in vitro first. They all -- they all showed a beneficial effect, correct?

A. Well, in vitro studies, by their nature, can't show a beneficial effect on heart health, because there is no heart. So, they -- they show results of chemical mechanisms that could be interpreted as favorable toward heart health, but that's different from actually showing heart health.

Q. Okay.

A. It may be a fine distinction.

Q. So, they were interpreted by Dr. Aviram as being consistent with pomegranate juice helping the heart, correct?

A. Yes, um-hum.

Q. And the same is true with his animal studies, correct? They also showed a positive effect?

A. Yes.

Q. All right. And these animal and in vitro studies, is it your position that even though there's some evidence of benefit from pomegranate juice, that standing alone, they can't be sufficient? Does that

accurately summarize your position?

A. They can't be sufficient to make a claim -- a causal link in humans, yes.

Q. Right.

A. Or even a recommendation in humans.

Q. Now, you've done animal studies yourself, correct?

A. Many.

Q. Yes. And you did one on vitamin E deprivation on --

A. Oh, animal? I'm sorry.

Q. Animal studies.

A. Animal studies? Oh, very few.

Q. Very few?

A. Maybe one that I can think of.

Q. Well, you did one about vitamin A --

JUDGE CHAPPELL: Hold on a second. Earlier, you were asked the question about animal studies, and you said you've done many -- I'm sorry, many. So, what were you answering to, just so the record's clear?

THE WITNESS: I'm sorry, yes, thank you for the clarification. I misheard the "animal." I thought he said, "You have done many studies." So, I have done many studies, but not animal studies. I did one in college quite a few years ago.

BY MR. FIELDS:

Q. Well, didn't you do an animal study on vitamin A deprivation?

A. Yes, when I was in college.

Q. Um-hum. And that was on rats?

A. Yes.

Q. And you showed the curve along which vitamin A deprivation caused night-blindness?

A. Yes.

Q. Okay. And your assumption was that this could tell us the effect of vitamin A deprivation in humans at the time, correct?

A. No, no. The -- that wasn't the -- I mean, even -- even though that was ancient days, it was already known that vitamin A deficiency caused blindness. So, it wasn't a matter of testing whether vitamin A caused blindness. We know that. It was a matter of looking at the kinetics. And I'm a little hazy on the details since that paper was done in 1972 or so.

Q. Okay. We will pass on that given those limitations.

A. Thank you.

Q. But you reviewed Dr. Aviram's human clinical trials?

A. Yes.

Q. Okay. His CIMT trials, for example?

A. Yes.

Q. And that was blinded and controlled, as I understand your testimony.

A. The -- well, there were two -- there were two small studies. We should just be clear which one we're talking about. So, you're talking about the trial of 19 individuals? Is that the one?

Q. Yes.

A. Yes.

Q. Okay. And it showed a 30 percent reduction in plaque found in the walls of the coronary artery?

A. Let me look back.

Q. Maybe it was 35 percent.

A. I'm sorry. Just a second.

Q. Sure.

A. (Document review.) Yes, 30 percent, right, at one year.

Q. Thirty percent, okay.

A. Um-hum.

Q. And your criticism was, as I recall your testimony this morning, was that the number of participants was small. Is that correct?

A. Yes.

Q. Okay. And isn't it also your opinion that a larger study is not necessarily better than a smaller one; sometimes a smaller one can be more efficient?

A. A large, poorly conducted study can be worse than a small, well-conducted study, but all factors held equal except for size, the larger study is better.

Q. Okay. And here again, Dr. Aviram's study showing the 30 percent decrease in plaque on the walls of the artery, coronary artery, may be some evidence of support for his claims or for Respondents' claims, but it's not sufficient, standing alone. Is that your testimony?

A. Yes.

Q. Okay. Now, you read Dr. Ornish's coronary perfusion study, right, or you reviewed it?

A. Yes.

Q. Okay. And as you said, that was an RCT study, a randomized, double-blinded, placebo-controlled trial.

A. Yes.

Q. Okay. And it showed a statistically significant improvement in the pomegranate juice over the placebo group, right?

A. Yes.

Q. And you said -- I think you referred to it as a slightly statistical -- statistically significant

increase. Am I correct?

A. I'm not sure I used that exact word, but -- but yes, it was --

Q. In any event, it showed a --

A. -- it was --

Q. -- a statistically significant increase, correct?

A. Correct.

Q. Okay. And you talked about -- I think your criticism was that there was a difference in baseline in the SSS measure. Is that correct?

A. In that trial, there were -- there were three measures that they used as the outcome, and the placebo group was worse at baseline than the intervention group for each of those three --

Q. Each of the three, sir?

A. Each of the three, sir.

Q. Are you telling me the SDS and the placebo group was worse?

A. Yes.

Q. Are you sure?

A. Yes.

Q. All right. SDS you're talking about?

A. SDS, SRS, and SSS.

Q. Okay. Let's focus on SDS, because that's what

he reported.

A. Well, he reported all three.

Q. I realize he gave you the numbers for all three, but what he was basing his conclusions on and measuring for the purpose of his study, as important in his study, was SDS, correct?

A. Well, that was -- that was what he -- that was where he found his statistically significant result, but it wasn't the a priori, main endpoint specified in advance of the trial.

Q. All right.

A. So, the only reason to highlight that one was the post hoc finding of that statistically significant finding.

Q. But, again, have you read his protocol?

A. I read some materials of it. I can't recall --

Q. Well, I assume --

A. -- I can't recall if I read the entire protocol.

Q. If you're not sure you read his protocol, can you really tell us what he specified as his objective in the experiment?

A. In the materials that I read, I didn't see any specification of that endpoint as an a priori, main endpoint.

Q. But you don't know. Isn't that correct?

A. I -- I can't say for certain.

Q. That's what I thought.

Now, would you give me the numbers on the SDS at baseline?

A. Yeah. For the pomegranate juice, it was 4.5; for the placebo group, the baseline was 5.9.

Q. Okay. So, the placebo group had a somewhat higher start, right?

A. That's right.

Q. Okay. Now, firstly, Dr. Ornish was measuring the degree of change. Isn't that right?

A. Right.

Q. If he's measuring the degree of change, it doesn't matter, does it, if everybody starts at the same place?

A. You don't know if it doesn't matter. What you know is that the placebo group, for whatever reason, was worse off than the -- than the pomegranate juice. And one easily could imagine that a group that starts off worse can progress more than a group that starts off better, and we all know this.

Q. It could be the opposite, couldn't it?

A. It could be the opposite.

Q. Yeah.

A. And -- and what we like to see in a trial is a

balance so that you can draw that kind of inference.

Q. All right. Well, let's come back to it could be the opposite, because you know the principle of regression to the mean, don't you?

A. Yes, I do.

Q. And isn't it likely that people who start out sicker are going to show more improvement rather than less improvement?

A. I don't know about that. Usually people who start off sicker get sicker quicker.

Q. Really?

A. Yeah, really.

Q. So, what is regression to the mean?

A. Well, it doesn't refer to getting sicker.

Q. Well, doesn't it mean that if you have a condition that is far removed from the ultimate objective, you are going to show more movement toward that objective? In other words, if you are ill, you are going to -- the chances are that your response will be more dramatic than someone who is not ill?

A. No, that's -- that -- that's not what regression to the mean is. If you're -- if you're ill, there's a -- more chance that you're going to get more sick.

Q. Really? You're sure of that?

A. Yes, I am.

Q. Okay. So, you think someone who is more ill at the time the experiment starts is less likely, rather than more likely, to show improvement? I want to make sure that we understand each other, because we're going to have experts testifying on this.

A. Right. It depends on the exact clinical situation that you're talking about, and for this particular instance, I do not know whether the group is more prone or less prone to get a worsening of their perfusion. But when you have imbalances at baseline, it casts serious doubt on the validity of the study.

Q. Isn't it quite common that when you randomly select people, that you're going to get some difference in baseline?

A. The -- the -- that's one of the main reasons why you need large numbers. It's quite common when you have a small sample, because by chance alone, they'll differ in some respects. But if you have big numbers -- and that's why big numbers are so important -- these differences will even out, and then it will be very uncommon to have any important differences.

Q. Well, let's approach it this way: You -- you say -- if I understood the last couple of answers, you don't really know whether those people were more or less likely to show improvement.

A. Right.

Q. It could have been either way.

A. Right.

Q. But you were ready to throw out Dr. Ornish's RCT trial because of that slight imbalance at baseline, right?

A. No.

Q. Why are you willing to throw it out?

A. No. Let me respond to two points.

Q. Yeah.

A. First, I'm not throwing it out. It contains evidence, studies -- but this is a serious defect. I don't throw out the study, but you have to weight the evidence that it's providing with the recognition that there are serious flaws.

So, it's a matter of degree. So, I take it into account, I recognize that there's a serious flaw, and weigh that evidence in my judgment. I don't throw it out.

And secondly, I wouldn't characterize the difference as slight, because it's actually double.

Q. Yeah. Well, when you say you don't throw it out, you say you're not giving it weight, if that study -- let's assume that was the only study --

A. Um-hum.

Q. -- and based upon that study, it really shows a definite improvement based upon pomegranate juice, doesn't it?

A. No.

Q. I see you shaking your head.

A. No, it does not.

Q. Oh. You don't find a 0.05 P-value a statistically significant improvement?

A. That -- it is statistically significant, but that's a somewhat different wording from what you used in the previous phrasing.

Q. Okay. So, we have a statistically significant improvement in the coronary perfusion test which affects the blood flow to the heart, correct?

A. Yes.

Q. And you are saying you would not permit a -- that information to be given to the public as a heart health benefit because there's some disparity at baseline in the people who were starting the experiment, right?

A. No.

Q. Well, then, I don't understand you. Are you -- do you think that, based upon this experiment, it would be appropriate to tell the public that we found a statistically significant benefit?

A. This -- these data are available, as appropriate, to the public. So, it's -- of course, the public should have -- has a right to this information. What I am saying, though, is that this evidence does not provide sufficient basis to draw a causal link.

That's different from whether the public -- whether information is or is not withheld. And as I said before, I'm against withholding information.

Q. Well, how about information that says there is a -- pomegranate juice has shown a statistically significant improvement in heart health? Would that be an appropriate thing to tell the public based upon this experiment?

A. I can't give an opinion on how the public might interpret that, but I think I'd be concerned.

Q. I'm not asking you about how the public would interpret it. I'm asking you, would it be appropriate to tell the public -- you've made many public statements about benefits --

A. Um-hum.

Q. -- and would it be appropriate to tell the public that the -- there is a statistically significant improvement in pomegranate juice -- in using pomegranate juice for heart health based upon this study?

A. If that was the only information that was

provided about this study, then I would say it is not appropriate, because it's misleading and doesn't provide the full results of the study. So --

Q. Well, are you -- I'm sorry. Go ahead. Finish.

A. So, there was -- one out of the three measures was statistically significant. So, if one were to give this information to the public, then you would have to give all of the relevant information to the public.

So, you -- you'd have to say that there was no statistically significant benefit in the summed difference score or the summed stress score and explain what those things are, so...

Q. Sir, isn't the -- isn't the SDS the result of subtracting the SRS from the SSS?

A. Right.

Q. So, you don't have to go back to the two building blocks to avoid stating the conclusion, do you?

A. No, I think you do.

Q. You think you do?

A. Yes.

Q. So, you think you'd have to put all of that in, we got this SDS by subtracting the SRS from the SSS. You don't think the conclusory, summary figure would be sufficient?

A. That's correct. It's not sufficient.

Q. Okay. All right. Now, let's turn to Dr. Davidson's study. You referred to it as a null result.

A. Null. Null result, yes.

Q. Null result, N-U-L-L?

A. Correct.

Q. Well, that wasn't true at the end of 12 months, was it?

A. Well, when I referred to result, I meant the final result of the study, not at some single time point or every single assay.

Q. Well, didn't Dr. Davidson say that he was going to measure at 12 months and at 18 months?

A. Yes.

Q. Well, then, at 12 months, it was a very positive result, no?

A. I wouldn't call it very positive, but there --

Q. I'm sure you wouldn't -- go ahead.

A. Pardon?

Q. Go ahead. I'm sorry.

A. There was a statistically significant result at -- at 12 months but not at 18 months.

Q. I understand. And you call it a null result, and I don't even think you mentioned the 12 months in your report, did you?

A. I'd have to check. (Document review.) I'm sorry. That's correct. I did not.

Q. Yeah. You omitted it.

A. Pardon?

Q. You were aware there was a very positive result -- strike "very."

There was a positive result for 12 months, and you left it out of your report, right?

A. It was an interim result.

Q. Well, you say "interim." The doctor said he was going to measure it at 12 months and 18 months, and you look at the 18-month measurement and say it's a null, and you simply left out the 12-month that was very positive, correct?

A. I wouldn't call it "very positive." I left out that result. I left out lots of results. I provided a summary of the key findings.

Q. Yeah. Well, do you think it's fair and not misleading to say it was a null result when the result at 12 months was hardly null? Sir?

A. Yes, I do. And, in fact, if you look at that -- at the paper, the first line of the discussion reads, "Results of the present study showed no significant influence of about 18 months of pomegranate juice consumption on CIMT progression in the overall study

sample." So, that was his initial summary of his own data, and I echoed that in my report.

Q. Yes, but he didn't leave out the result at 12 months, and you did, right?

A. Well, I boil it down in my summary to one paragraph, and he's got seven pages.

Q. Yes. You boiled it down by leaving out the good parts, right?

A. That's absolutely false.

Q. Okay. The Court will decide.

Now, there was -- let's stay with the 12 months for a moment.

A. Sure.

Q. Let's assume that we're doing a study of cancerous tumors, and the doctor says he's going to measure at 12 months and 18 months, and at 12 months, the tumor necroses factor rolls back the tumors, but stops working at the end of 12 months, and at 18 months, no more tumors. Do we simply said, "Oh, gosh. Let's ignore the fact that it gave somebody 12 additional months of life"?

A. No, we do not ignore that.

Q. But you're ignoring it in this case, even though it's not quite as dramatic.

A. Excuse me, it's not even close to as dramatic.

We are not talking about adding life here.

Q. Well, we're talking about what could be adding life if, in fact, this slowed the progression of a cardiac arrest for 12 months, and didn't slow it anymore, somebody might have gotten 12 additional months of life. Isn't that right?

A. No, that's not right.

Q. Okay.

A. Because it's a -- you said it didn't slow it anymore. In fact, the differences disappeared at 18 months.

Q. Well, I understand. It stopped working according to this. We don't know why, but it no longer created improvement.

A. I -- I would interpret it differently.

Q. Yes, I'm sure you would.

Now, often, studies are stopped before they're done. Isn't that right? You told us that this morning.

A. Yes.

Q. And sometimes they're stopped because there seems to be an answer that's right there, correct?

A. Yes.

Q. Okay. Now, if Dr. Davidson had stopped his trial after 12 months because he had an affirmative result, he would have been an unqualified success, and

you couldn't be here to say it was null, right?

A. That would be speculation on my part, that I would not characterize it -- it's hard to know what the result would have been at 12 months, but I -- I don't think I would characterize it as --

Q. Well --

A. -- an unqualified success.

Q. I'm sorry. I didn't mean to cut you off.

Okay, let's talk about the subgroup.

A. Yes.

Q. Now, there was a very definite benefit to a subgroup of people who were at the greatest risk, isn't that correct, high-risk people?

A. No, that is not correct. It was not a very definite benefit.

Q. Was there a benefit, sir?

A. They -- they -- there was a -- a difference in the IMT in post hoc subgroups, yes.

Q. They -- they did --

A. But the -- the -- my argument is with the terms "very definite."

Q. Oh. But it was a benefit, correct?

A. Yes.

Q. And --

A. Apparent benefit.

Q. Pardon me?

A. Apparent benefit.

Q. Apparent benefit?

A. Yes.

Q. What's the difference between a benefit and an apparent benefit, sir?

A. It's the degree of certainty of the truth of it.

Q. Well, you say certainty is the truth? You don't think Dr. Davidson's lying about the benefit, do you?

A. Of course I don't.

Q. So, we're not talking about the truth of what he's reporting. He's reporting numbers, and numbers show a benefit to the high-risk patients, right?

A. I was referring to whether there was a true benefit underlying this observation.

Q. Well, if you've got less plaque in your artery or the blood is flowing to your heart better, that's generally considered a benefit, right?

A. That is considered a benefit, yes.

Q. Okay. And that's what he was measuring, correct?

A. Actually, it was carotid artery, but --

Q. Carotid. Forgive me. All right.

Now, in the United States alone, there could be millions of people in that subgroup that were benefited,

correct?

A. Yes.

Q. And all of those people might really want to know Dr. Davidson's result, right?

A. Well, I'd like to know the true result myself.

Q. Well, you -- you don't know the true result, huh?

A. Well, as Dr. Davidson points out, what these post hoc exploratory findings are -- what you can conclude from these post hoc exploratory findings is to identify subgroups for future study. So, were they to do another trial like this and focus on that subgroup and find that, indeed, the IMT thickness was reduced, it would be wonderful, I would go over to your side, and we would support the claim.

Q. And --

A. But we don't have that data.

Q. Because it's called post hoc.

A. No -- well, right now it's post hoc, but hey, let's do another study. If they think that that's -- that that's a plausible subgroup that might benefit, if -- if that were -- if the data backed that up, great.

Q. So, haven't there been post hoc analyses that have been announced to the public from various studies that have been very beneficial to the public?

A. I don't know, actually. I'd have to think about that. Did you have an example in mind?

Q. I will be presenting some examples.

A. Okay.

Q. But let's just take a hypothetical for a moment.

A. Um-hum.

Q. Let's assume that the stated endpoint of an experiment is to discover if a particular substance lowers blood pressure.

A. Um-hum.

Q. And in the course of that, we find it doesn't low blood pressure at all, but it eliminates cancerous tumors, but it's post hoc. We don't tell the world about that? Is that --

A. Of course we tell the world.

Q. Well, but it's post hoc. Don't we have to have another study before we can tell the world?

A. No. No, the world should be told about all the study results.

Q. So, the world should be told about the benefit to the high-risk patient from Dr. Davidson's experiment, right?

A. I'm having trouble understanding -- when you say -- when you're talking about withholding information and what the world could or should be told. So, I know

I'm repeating myself, but I am in favor of the world having access to all the results of all the studies.

Q. So --

A. I don't have a problem with the world being told things.

Q. So, it follows that the world should be told that on the basis of Dr. Davidson's study with high-risk patients, there is at least strong evidence that your likelihood of having a heart attack is reduced.

A. No.

Q. You don't think that better blood flow to the heart indicates that a -- a lower likelihood of a heart attack?

A. If that were demonstrated, but what you're talking about telling the world is a small little slice, and if you're going to tell the world something about a study, then you need to tell the world about the whole study, and that's why I'm in favor of the world having access to the scientific literature. But it's grossly misleading to take one little slice out and proclaim that a causal relation has been established.

Q. But we talked about the fact that there could be millions of people in this subgroup that was shown to be benefited by this study.

A. But it would --

Q. My question is, don't those millions of people get to be told without waiting for future, very expensive studies to be done over a period of years?

A. The problem is that the finding has not been shown. It's suggested, it's interesting, and when the randomized trial was done -- just for an example, we have the small study of Aviram, and there, they showed a 30 percent reduction in carotid intima-media thickness.

And so maybe the world should have been told that, but instead, the right thing was done, which was to do a larger study, and where did that finding go?

Q. But Dr. Davidson's was a large study, wasn't it?

A. Right, and it was a large null result.

Q. And it showed a benefit for this high-risk group of patients, didn't it, sir?

A. It did not show it. It suggested it.

Q. It suggested it?

A. Yes.

Q. Are you saying that it didn't show that those high-risk patients had improvement over the placebo people?

A. In that subgroup, they had -- they had improvement, but this was a post hoc analysis, and, therefore, the interpretation of the statistics is different.

Q. All right.

A. As they -- as they acknowledged very nicely in the article themselves.

Q. They acknowledged that it was different?

A. That the interpretation was different, yes.

Q. Did you review the work of Dr. Hill from Heart Health?

A. Dr.?

Q. Dr. Hill, H-I-L-L.

A. Can you refer me to the paper?

Q. I don't have the number in front of me.

A. Or the title or the other authors?

Q. If you don't know, you don't know.

A. Well, I mean --

Q. Do you know if they referred --

A. -- if you refer me to a paper, I can respond to the question.

Q. I'm not trying to hide the number from you, Doctor. I just don't know what the number was.

A. Well, here's a paper by Dr. Hill --

Q. Yes.

A. -- "Safety and Antioxidant Activity in a Pomegranate Ellagitannin-Enriched Polyphenol." Is that the one you're referring to?

Q. You did read that?

A. Yes. The first author is Heber and James Hill is the last author.

Q. So, you are referring to what is Dr. Heber's study?

A. I'm trying to answer your question.

Q. No, I understand. Did you review that study?

A. This one?

Q. Yes.

A. Yes.

Q. The one that -- go ahead.

A. The one where the first author is Heber, the safety and antioxidant activity?

Q. Yes.

A. Yes, I reviewed that one.

Q. And that showed a positive result?

A. This did not have any clinical endpoints. This was --

Q. And it showed a positive result?

A. Well, you have to -- it showed a positive result in that there was a statistically significant finding for antioxidant activities as evidenced by TBARS, but that's not the same as a heart attack.

Q. Did you review the study by Dr. Rosenblatt and others?

A. I don't recall.

Q. Okay.

A. I don't recall.

Q. Tobahtz, and I may have the spelling wrong, I think it's T-O-B-A-H-T-Z, but we will find out the spelling.

I don't mean to burden you with looking through the pile of papers. If you can't recall, we'll move on.

A. Pardon?

Q. If you can't recall, we'll move on.

A. Well, I don't have all of the papers memorized.

Q. Okay. Let's talk about -- you are not a cardiologist, are you?

A. Pardon me?

Q. You are not a cardiologist, are you?

A. No.

Q. And you are not a urologist either?

A. No, I am not.

Q. Let's talk about prostate a little bit.

A. Okay.

Q. You reviewed two separate studies by two urologists, Dr. Pantuck at UCLA and Dr. Carducci at Johns Hopkins, correct?

A. Yes.

Q. Sir? Is that correct?

A. Oh, yes. I'm sorry, yes.

Q. Okay. And they both showed that pomegranate juice in patients have a marked limiting of PSA doubling times?

A. Comparing before -- comparing baseline to after treatment, there was a prolonging in PSA doubling time, yes.

Q. Right.

And PSA doubling times are a predictor of recurrence of disease and mortality. Isn't that correct?

A. Yes. An imperfect predictor of mortality, but they do predict, yes.

Q. Perhaps an imperfect predictor, but nonetheless, a predictor.

A. Yes.

Q. And that doubling time was slowed down in the case of the people who took pomegranate juice, both at Johns Hopkins and at UCLA, correct?

A. It was slowed down in the people who took -- who drank pomegranate juice. That is correct.

Q. And that's a decided benefit, right?

A. It's a benefit if the pomegranate juice caused that to happen; otherwise, it's a coincidence.

Q. Yes. And the people who drank the pomegranate juice got this benefit, and you were asking whether

maybe that benefit would have accrued even if they hadn't drunk the pomegranate juice. Is that your point?

A. Well, yeah. I mean, I wouldn't call it a benefit, but yes, the point is we don't know if it would have happened without the pomegranate juice.

Q. Well, you say you don't know what benefit. Certainly it's a benefit --

A. Well, that --

Q. -- if your predictor of mortality and recurrence has been slowed down. That's a benefit, right?

A. It's a good thing.

Q. Yeah. And that good thing -- your only question is, when the pomegranate juice people got that benefit, whether it was caused by pomegranate juice or some extraneous factor, right?

A. Right.

Q. Okay. And here again, you wouldn't refrain from telling the public about that benefit, would you?

A. I wouldn't characterize it as a benefit of pomegranate juice.

Q. You wouldn't characterize -- well, what if we just said the people who drank pomegranate juice had their PSA doubling time substantially lengthened? Shouldn't that information go to the public?

A. By itself, I could -- again, I'm not an expert

on public information, but by itself, that information could easily be misconstrued. I think an educated audience might well say, "Oh, that's good," but how about people who -- who drank tomato juice or who didn't drink any juice at all? What happened to them? That question might not occur to everyone.

Q. Okay. Now, you have expressed an opinion that a placebo group is not always required or even ethical. Isn't that correct?

A. Correct.

Q. Okay. But in this instance, your criticism is there was no placebo group.

A. Yes. In this instance, it was -- it certainly would have been easy to do and would have -- would have not violated any ethical constraints. So, to my mind, it's really a pity that they didn't have a placebo group, because if they showed this -- if they showed this difference in the pomegranate juice people and in a placebo group there was no change in PSA doubling time, that would have been a very important finding. But now, one can't interpret whether the pomegranate juice had any effect or not. Well, this was POMx, but still.

Q. If the pomegranate juice, when it appeared to have this effect, if the doctors believed it would have this effect, wouldn't it have been unethical not to give

it to a placebo group?

A. No.

Q. Haven't you testified that there are some things that benefit where it would be unethical to have a placebo group?

A. Yeah, sometimes that's true, and -- but this is not an instance where that's true. That's true in the setting where you are withholding standard of care from a patient or you are causing known harm to a patient. Ethically, you cannot do that.

So, right now, in this country, pomegranate juice is not standard of care for patients with prostate cancer, so it's entirely ethical to give them placebo, just as it was ethical to give placebo in the randomized trials of carotid intima-media thickness.

Q. Well, if -- once Dr. Pantuck's study had shown a doubling time for those who drank pomegranate juice that appears to go up four-fold, you're telling me that it would have been proper not to tell the people in the placebo group that you hypothesized, "Boy, you guys ought to be drinking this, because your life may be saved"?

A. To the contrary. I -- to my mind, it's unethical not to do the randomized, placebo-controlled trial, to delay getting the truth out. If -- if this --

if this most recent trial had shown -- had shown the same result with either of those doses of POMx against a control group where there was no change in PSA doubling time, then -- then there would have been a finding that could potentially change practice.

Q. If this PSA doubling time extension, let's say four-fold as shown in the UCLA study, or I think it was two-fold in the Johns Hopkins study, if that's true, that really could substantially prolong lives, correct?

A. It -- it could, and so it's a pity that they didn't include a proper control group.

Q. But aside from that, you're telling me you wouldn't want the public to be told that it's been shown that people who drink pomegranate juice got doubling time four times, just in case maybe -- maybe that was because of the pomegranate juice?

A. That is correct. You -- I wouldn't want the public to be misled about a causal link being established.

Q. All right. Now, you did a recent study on coffee. Is that right?

A. Yes.

Q. And you came to the conclusion that people who drank a good bit of coffee, because of the antioxidants in coffee, their inflammation was reduced, and as a

result, they did better with regard to prostate cancer, correct?

A. The concept is right but not the wording. So, I did not conclude that a causal link was established. What we found was that men who drank coffee had a lower risk of lethal prostate cancer. That's what we found. We discussed the potential for antioxidants in coffee to -- to be a potential mechanism for this but did not conclude that a causal link had been established.

And I would not support a claim by the coffee industry to start advertising coffee to reduce the risk of lethal prostate cancer. Instead, they should sponsor a study to test that hypothesis.

Q. Yes. Now, actually, pomegranate juice is richer in antioxidants than coffee. Isn't that right?

A. Well, there are different -- different forms of -- there are different antioxidants and there are different tests for antioxidants. So, it's not -- it's -- it's not -- you can't really compare sort of the broad terms of antioxidants. So, pomegranate juice has more of certain antioxidants than coffee; coffee has more of certainty antioxidants than pomegranate juice. So, they are different compounds.

Q. All right.

A. But there is no question, they are both good

sources of antioxidants.

Q. All right.

That's all I have, Your Honor.

JUDGE CHAPPELL: Redirect?

MS. EVANS: Yes, sir, brief.

REDIRECT EXAMINATION

BY MS. EVANS:

Q. Mr. Fields asked you several questions relating to the article that you published with Dr. Blumberg, correct?

A. Yes.

Q. And he -- Dr. Blumberg is at Tufts?

A. Yes.

Q. Now, that article, what was the -- what was the subject of that article?

A. Well, the main subject was standard -- standards of evidence in nutritional studies as compared to studies of drugs, and pointing out the differences in studies of drugs and studies of nutrition.

Q. And is that -- was that article one of your contributions to an ongoing discussion about what the basis for public health recommendations should be?

A. Yes.

Q. And so when you're talking about public health recommendations, everyone needs food, right? Is there a

question whether or not you want to push people towards saturated fats as opposed to unsaturated fats, and fruits and vegetables as opposed to meats?

A. Well, the issue is making sound recommendations in the face of imperfect information, which -- which we have to do in the case of diet, because as you say, everyone eats, so we want to give the best advice we can with the data at hand.

And the challenge is to distinguish between the findings where a causal link is established between a nutrient and a disease outcome and whether it's just based on lesser evidence, where we think it might be beneficial, but we don't know for sure.

Q. And when Mr. Fields was asking you questions about whether "such claims" should be supported by evidence that was lower than a randomized clinical trial, you were talking about claims related to public health recommendations?

A. You don't need randomized trial data for making public health recommendations, but if you're going to make a claim based on an establishment of a causal link, then you need evidence that supports that type of claim. So, you don't have to demonstrate a causal link to make a public health recommendation.

Q. And when you're talking about those public

health recommendations, do they relate primarily to the prevention or the reduction of the risk of disease?

A. Mainly. Yes, because that's what the general -- yes, that is certainly the broadly applicable, general public health recommendations. So, there are different recommendations for people who have established disease.

Q. And Mr. Fields also asked you some questions with regard to -- with regard to when you speak. Now, when you're speaking, are you providing public health guidelines?

A. I try to.

Q. Because you are a public health expert?

A. Yes.

Q. Okay. And when you speak on the radio and television, those instances that he identified for you, were you providing those messages as a paid endorser for any particular brand of product?

A. No. I have never done that.

Q. And Mr. Fields also asked you about alcohol claims, and you and I have actually talked about that stuff, right?

How many observational studies have been conducted looking at the relationship between alcohol consumption and -- and disease risk?

A. Many dozens.

Q. How many observational studies have been conducted regarding the relationship between alcohol consumption and a reduction in the risk of cardiovascular disease?

A. Also many dozens.

Q. And what about alcohol consumption and all-cause mortality?

A. Many, probably several dozen.

Q. Overall, how many people would be involved in these studies?

A. Oh, over a million in aggregate.

Q. Over how many?

A. Over a million in aggregate.

Q. Over a million.

And what is the duration of these studies?

A. Well, some of them have gone on for decades.

Q. Do the dietary guidelines for Americans recognize the possibility of a link between alcohol intake and cardiovascular disease?

A. The guidelines basically say that if you drink, do so in moderation.

Q. Do they also say, referring to the 2010 guidelines that were just released, do they say that strong evidence from observational studies has shown that moderate alcohol consumption is associated with a

lower risk of cardiovascular disease; moderate alcohol consumption also is associated with reduced risk of all-cause mortality among middle-aged and older adults and may help to keep cognitive function intact with age?

A. Yes, I agree with those statements.

Q. And those dietary guidelines, as we talked earlier about dietary guidelines, those are formulated by bringing experts together to consult with government?

A. Yes.

Q. Now, to your knowledge, have observational studies been conducted with regard to nut consumption?

A. Yes.

Q. And is that with regard to nut consumption and heart disease or prostate cancer?

A. For heart disease.

Q. To your knowledge, has the Food and Drug Administration authorized a claim about the relationship between nut consumption and cardiovascular disease?

A. I don't know.

Q. Now, we provided you with a several-inch deep pile of published studies relating to pomegranate juice and prostate cancer or heart disease, correct?

A. Yes.

Q. Okay. Did we provide you with published studies that were on subjects not related to prostate cancer or

cardiovascular disease, to the best of your recollection?

A. No.

Q. Okay. Dr. Aviram's 19-person trial, that was a within-group analysis?

A. Within -- yes, a before and after analysis, right.

Q. Okay. When you were talking about Dr. Ornish's study, if, in fact, the protocol for Dr. Ornish's study did not expressly identify SDS as the primary study endpoint, would this support your conclusion that the SSS and SRS data are important results from the Ornish trial?

A. Yes, that would support it.

Q. Now, Mr. Fields asked you if you thought that Dr. Davidson was lying when he presented his study results. Do you recall that?

A. Yes.

Q. Now, did Dr. Davidson expressly state, in his results, that in the subgroup analysis, he couldn't tell if the results were statistically significant, because there was a lack of correction for multiple factors being available?

A. He raised that issue explicitly.

Q. Okay. And if Dr. Davidson had testified in his

deposition that he has never done a correction for multiple conclusions, does this confirm your belief that the results of the subgroup analysis must be confirmed in a later trial?

A. It supports that, yes.

Q. Yes. Supposing we follow Mr. Fields' advice and just eliminate controls from clinical trials, would this -- this would substantially reduce the cost of doing research, right?

A. I don't know that that was his explicit advice.

Q. Would we ever really learn --

JUDGE CHAPPELL: It sounded like an objection that you're misstating the evidence, so you'll need to rephrase.

BY MS. EVANS:

Q. Do -- if there were no controls in -- in nutritional research related to the treatment of disease, would we ever know whether or not the product actually treated the disease?

A. You have to have a control to draw inferences, and the control is either explicit or implied. So, in a before and after study, the control is implied, and the assumption is that things otherwise would have stayed the same over time but for the intervention, and that's a heavy assumption.

And when you have a concurrent placebo control, you don't have to make that assumption. All you have to do is have enough people so that you're confident that the people in your control group have the same experience that would have happened to the intervention group but for the intervention. And then that would obviously draw a firm conclusion.

Q. Okay. And if -- oh, I see it now. I lost my spot.

When Mr. Fields was referring you to pages 31 to 32 of your deposition at line 16 -- and I think we have to bring you your deposition, because I don't think you have a copy before you.

A. Oh, no. I don't have it.

Q. Okay. You are going to have to take your tabs off.

Excuse me, this will take 30 seconds.

(Pause in the proceedings.)

THE WITNESS: Where should I be looking?

JUDGE CHAPPELL: That's what happens when you don't ask for permission to approach.

MR. HOPPOCK: Forgive me, Your Honor. I recalled your earlier approval of approaching the witness just to give them an exhibit, and I didn't think I had to ask.

JUDGE CHAPPELL: Oh, I believe that was for this attorney over here.

MR. HOPPOCK: Okay.

MR. GRAUBERT: As long as you don't interrupt the flow.

MR. HOPPOCK: I apologize.

JUDGE CHAPPELL: Good work, Ironsides. The trap worked.

BY MS. EVANS:

Q. Okay. So, where were we?

I was asking you -- okay. When you -- Mr. Fields was referring you to pages 31 to 32 of your deposition, and I believe the questions he was asking about started at line 16.

A. Yes.

Q. Let me know when you have found that.

A. Okay.

Q. You were asked about making public health recommendations on the basis of epidemiological evidence, right?

A. Yes.

Q. You were not at that point in your deposition being asked whether food items, specific food items would reduce the risk of specific diseases.

A. Yes.

Q. Do you know how consumers interpret terms like "may" or "indicate" or "suggest"?

A. I do not.

Q. That's not your area of expertise?

A. No.

Q. And your testimony, it relates to what scientists would require to conclude that pomegranate juice or POMx has been shown to prevent, reduce the risk of, or treat cardiovascular disease or prostate cancer. Is that correct?

A. Correct.

Q. Thank you.

No further questions.

JUDGE CHAPPELL: Recross?

MR. FIELDS: We do move the document I talked about, Exhibit 5007, with this witness.

MS. EVANS: Oh, we have no objection.

JUDGE CHAPPELL: Right. In the future, go ahead and consult with the other side before you offer it.

So, we have an offer of Exhibit -- was that RX?

MR. GRAUBERT: Yes.

JUDGE CHAPPELL: And what's the number?

MR. GRAUBERT: 5007.

JUDGE CHAPPELL: No objection?

MS. EVANS: No objection, sir.

JUDGE CHAPPELL: So admitted.

(RX Exhibit Number 5007 was admitted into evidence.)

JUDGE CHAPPELL: Thank you, sir. You're excused.

All right, we will start with the next witness right after our afternoon break. We will reconvene at 3:50, 3-5-0.

(A brief recess was taken.)

JUDGE CHAPPELL: Okay. Back on the record, Docket 9344.

Who's the next witness?

MS. VISWANATHAN: Your Honor, Complaint Counsel calls Matthew Tupper.

Whereupon--

MATTHEW TUPPER

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

DIRECT EXAMINATION

BY MS. VISWANATHAN:

Q. Good afternoon, Mr. Tupper.

A. Good afternoon.

Q. Can you state and spell your full name for the record?

A. Sure. It's Matthew Tupper, M-A-T-T-H-E-W,

T-U-P-P-E-R.

Q. Mr. Tupper, where are you currently employed?

A. POM Wonderful.

Q. What's your title at POM Wonderful?

A. President.

Q. Does POM also have a chief executive officer?

A. No.

Q. Are you effectively serving in the role as chief executive officer?

A. I believe so.

Q. How long have you been an employee at POM?

JUDGE CHAPPELL: Hold on. The bailiff is adjusting the mic.

Thank you, Ironsides.

BY MS. VISWANATHAN:

Q. Okay. Mr. Tupper, how long have you been a POM employee?

A. Since 2003.

Q. And approximately when in 2003 did you join POM?

A. It was sometime in the summer.

Q. In the spring?

A. In the summer.

Q. Summer.

And did you join POM as a full-time employee in the summer of 2003?

A. Yes.

Q. And when you started at POM, what was your title?

A. My title was chief operating officer.

Q. And at what point did that title change to president?

A. I believe that was in 2005, in the middle of the year. I don't remember which month.

Q. Were your responsibilities different as chief operating officer versus president?

A. No, they weren't.

Q. Prior to starting work with POM Wonderful, were you employed by Roll International?

A. Yes.

Q. And when did you start at Roll International?

A. I started at Roll in May of 2001.

Q. What was your title when you joined Roll International?

A. Vice president of strategy.

Q. Is Roll International now called Roll Global?

A. Yes, it is.

Q. So, if I refer to Roll, you'll understand what I mean?

A. I think so.

Q. Are Roll and POM located in the same building?

A. The headquarters of POM are located in the same building as Roll.

Q. Does POM share services with Roll?

A. Roll provides services in some areas for POM, yes.

Q. And can you give me examples of the areas in which Roll provides services to POM?

A. Sure. An example -- one example would be human resources. Another example would be tax and treasury services. Another example would be legal.

Q. Would the IT and computer systems also be another area where there are shared services?

A. Not currently, no.

Q. But in the past, there have been?

A. At certain points in the past, yes.

Q. As president of POM Wonderful, would you describe your job as being responsible for managing the day-to-day affairs of the business?

A. Yes.

Q. Approximately how many employees does POM Wonderful have?

A. Worldwide, we have roughly 350 employees.

Q. Approximately how many people at POM report directly to you?

A. I currently have nine or ten direct-reports.

Q. Is one of the people who reports to you directly the vice president of marketing for POM Wonderful?

A. Yes.

Q. And who currently holds that position?

A. Jan Hall.

Q. Is another person who reports to you the vice president of clinical development?

A. Yes.

Q. And who currently holds that position?

A. Brad Gillespie, G-I-L-L-E-S-PI-E.

Q. Does POM have a sales department?

A. No, not per se.

Q. Did POM have a sales department in the past?

A. Yes.

Q. Is there a department that currently performs the functions of the prior sales department?

A. There are multiple departments that have sales functions.

Q. Does POM have an operations department?

A. Yes, we do.

Q. Would the heads of -- excuse me.

Would the head of the operations department report to you?

A. Yes.

Q. And is there also a department at POM that does

the manufacturing, taking the fruit and turning it into juice?

A. Yes. That's the operations department that you referenced earlier.

Q. Okay. Would your responsibilities at POM Wonderful include monitoring the sales figures for POM products?

A. Yes.

Q. And increasing sales of products, presumably?

A. Yes.

Q. Does the -- excuse me. Strike that.

Does POM have its own corporate communications department?

A. No, not currently.

Q. Okay. And it did in the past?

A. Yes.

Q. Can you tell me at what point POM ceased to have its own corporate communications?

A. Sure. I'm trying to remember the year. I want to say 2007 or 2008.

Q. Are the corporate communications functions now done by Roll?

A. Correct, by an organization called Fire Station, which is a creative agency.

Q. Overall, are you ultimately responsible for the

sales and marketing for POM Wonderful?

A. Yes. The individuals who head up the marketing department reports to me. And as I said, there are various departments who have sales responsibilities, and those individuals report to me.

Q. Do you report to Stewart Resnick?

A. Yes, I do.

Q. Did you also report to Stewart Resnick when you were hired at Roll in 2001?

A. Yes, I did.

Q. Do you interact with Mr. Resnick every day?

A. No.

Q. Well, how often, per week, would you say you interact with Mr. Resnick?

A. It varies. It can range from once a week to several times a week. Sometimes it can be every day or so.

Q. And just to be clear, when I say "interact" with him, I mean by any means, you know, not just telephone, but email, telephone, in-person. So, your answer is once a week to several times a week?

A. Correct, by all those means.

Q. What aspects of POM Wonderful's business do you interact with Mr. Resnick on?

A. All aspects.

Q. The financial status of the company? Is that one aspect?

A. Yes.

Q. Marketing?

A. Yes, on occasion.

Q. Manufacturing, as we discussed, the production of the juice and the POMx?

A. Yes.

Q. Medical research?

A. Yes.

Q. Is it fair to say that as president of POM, that you also frequently interact with Lynda Resnick on marketing and product development?

A. Yes, I have.

Q. Is it fair to say that Mrs. Resnick has been very active in the marketing and product development for POM Wonderful?

A. She's been active.

Q. Is it fair to say that she's also been active in communications or public relations for POM Wonderful?

A. Yes, she has been active.

JUDGE CHAPPELL: Let me ask you a couple questions.

You were previously with Roll?

THE WITNESS: That's correct.

JUDGE CHAPPELL: And now you're with POM?

THE WITNESS: That's correct, Your Honor.

JUDGE CHAPPELL: All right. Who replaced you at Roll?

THE WITNESS: When I left Roll for POM, that was in 2003, it was a gentleman named John Cochran who took my place at Roll as the vice president of strategy.

JUDGE CHAPPELL: Okay. And who's there now?

THE WITNESS: As the vice president of strategy? It's actually an open position. There is a search ongoing as we speak.

JUDGE CHAPPELL: All right. And what's the title of the highest-ranking person at Roll?

THE WITNESS: That's a good question.

JUDGE CHAPPELL: Did you have a boss at Roll when you were the vice president?

THE WITNESS: I did, yes.

JUDGE CHAPPELL: And who was that?

THE WITNESS: And that was Stewart Resnick.

JUDGE CHAPPELL: And who does he work for or did he work for at the time? Was he Roll or was he POM?

THE WITNESS: Well, collectively, my understanding is that Stewart Resnick and Lynda Resnick are the co-owners of Roll. What their titles are, I'm not exactly sure.

JUDGE CHAPPELL: Are you aware of what the corporate or legal status or relationship actually is between POM and Roll? Is one a subsidiary? Is one a sister company? Are you aware of what their status is as to each other?

THE WITNESS: Specifically, no, in terms of how they're organized with shareholdings and what the relationships are. But I would say generally that we refer to it as -- Roll as the parent company of POM.

JUDGE CHAPPELL: Okay.

THE WITNESS: But the exact sort of legal --

JUDGE CHAPPELL: Right.

THE WITNESS: -- I'm not...

JUDGE CHAPPELL: And you said you are in the same building. Who owns or controls that building?

THE WITNESS: Roll or an affiliate company of Roll owns the building.

JUDGE CHAPPELL: Okay. Thank you.

BY MS. VISWANATHAN:

Q. Actually, let me just ask one more question. Are there other Roll companies also located in that building, for example, the Fire Station agency, that you mentioned earlier?

A. Yes.

Q. POM Wonderful has provided support and funding

for research on pomegranate juice, correct?

A. Correct.

Q. And POMx -- excuse me. And POM has supported -- provided support and funding for research on other POM products, such as POM Pills or POM Liquid, correct?

A. Correct.

Q. Does Brad Gillespie, who you identified as vice president of clinical development, work with the medical researchers who are conducting investigations on POM products?

A. Yes.

Q. And is it -- is that basically his job duties, to stay apprised of the scientific evidence with respect to POM products?

A. That's a very important part of his job, yes.

Q. And you yourself have a significant degree of involvement in the medical and scientific research aspect of POM's business. Is that correct?

A. Yes.

Q. As part of your responsibilities, do you discuss with Mr. Resnick and Mr. Gillespie research areas that are appropriate for funding, for example?

A. Correct.

Q. And you participate in decisions made by POM Wonderful as to whether or not to fund particular

medical research?

A. Yes. I am involved with those decisions.

Q. How long has Brad Gillespie been in his position?

A. If my memory serves, I believe we hired Brad in the earlyish part of 2009, but I -- I can't remember what -- specifically what day or month.

Q. And is he -- does he go by Dr. Gillespie or Mr. Gillespie? Do you know?

A. I call him Brad.

Q. Okay.

A. Yeah.

Q. What would I call him?

A. You would probably call him Brad as well. He -- he does have a doctorate degree, so technically speaking, he's Dr. Gillespie.

Q. And POM hired Dr. Gillespie in 2009 to assist POM in pursuing drug development type projects. Is that right?

A. Correct.

Q. And one of the reasons Dr. Gillespie was hired was, in fact, he has a background in drug development? Is that right?

A. Correct.

Q. And the decision to hire Dr. Gillespie was made

at that time because the research that POM was contemplating was, in fact, more in line with drug development research. Is that right?

A. That's -- yes, I think that's correct.

Q. Essentially, Dr. Gillespie's experience in drug development was more in line with the direction you wanted to take for the business at that time, correct?

A. That's a better way to phrase it, yes.

Q. Who was Brad Gillespie's -- excuse me, Dr. Gillespie's predecessor?

A. When Brad was hired, there was -- that was the first time we had had that position. So, there was no predecessor with that title. We had a -- a different gentleman who was heading up our scientific research program, whose name was Dr. Mark Dreher. Mark held a different title.

Q. What was the title that Dr. Mark Dreher held?

A. I believe Dr. Dreher's title was vice president of scientific affairs or scientific research, one of those two.

Q. Is it fair to say that Dr. Dreher's background was in food science?

A. I believe Dr. Dreher had a Ph.D. in something having to do with food science. I don't remember the exact area of his research.

Q. But as far as you can recall, it was not necessarily drug development, like Dr. Gillespie?

A. That's correct.

Q. And so Dr. Dreher's expertise and qualifications were not necessarily in keeping with the direction of the business that the company wanted to go in?

A. We were looking for a different skill-set, that's correct.

Q. Can you tell me what is your educational background after high school?

A. Sure. I have a undergraduate college degree from Stanford University, and I have a graduate MBA degree from Harvard University.

Q. Is your undergraduate degree in science or biology?

A. My undergraduate degree was a bachelor's in political science.

Q. So, you have no formal training or education in science or physiology or biology, correct?

A. No. Just a very high level of interest.

Q. Well, a high level of interest. I mean, is it fair to say that you consider yourself knowledgeable about health issues? Correct?

A. Yes.

Q. And physiology, nutrition, nutrition science?

A. Yes.

Q. Okay. And is one source of the knowledge that you've gained about science over the years the fact that your wife actually went to medical school and works in drug development?

A. The very same wife who is sitting behind you.

Q. Have you also gained your knowledge about health, nutrition, and physiology from working closely with research scientists who have worked with POM over the years?

A. Yes.

Q. Did you have direct contact with the research scientists who were working on POM products?

A. Yes.

Q. You also, obviously, supervised Dr. Mark Dreher when he was at POM, correct?

A. Correct.

Q. And you currently supervise Dr. Gillespie?

A. Correct.

Q. And how often do you interact with -- well, I guess it may be different.

Let's start with, how often did you interact with Dr. Dreher when he was at POM?

A. With Dr. Dreher, as with all my direct-reports, we have a scheduled weekly update meeting, which happens

more often than not. Sometimes it can't happen due to travel and so forth. And then we'll interact on an ad hoc basis, however often is necessary, which could be every day or several times a day to nothing more than our weekly meeting.

Q. And so that would be the same when Dr. Gillespie joined the company?

A. Correct.

Q. And you -- you know who Dr. Harley Liker is, correct?

A. Yes.

Q. And he -- I believe you heard his title was medical director. Is that accurate?

A. Correct.

Q. Do you interact with him on a -- the same basis as you would with any of your other direct-reports?

A. No.

Q. Okay. And how often do you interact with Dr. Liker?

A. It varies and it's much more on an ad hoc basis. So, it could be, you know, once a month; it could be -- it could be once a week if there was lots of stuff going on; it could be once every couple months if there's not much going on.

JUDGE CHAPPELL: Hold on a second.

Does it sound right that I've heard this Dr. Liker referred to as a medical consultant for POM?

THE WITNESS: So, Dr. Liker is not an employee of POM, and in that respect, he's a contractor or a consultant, although he carries with him the title of medical director.

JUDGE CHAPPELL: That's what threw me off when I heard he had a title. Most consultants, I don't believe, have a title in the company, do they?

THE WITNESS: I can't speak to that. I don't know.

JUDGE CHAPPELL: So, he is not a full-time employee, but that's his title within the company?

THE WITNESS: Correct.

JUDGE CHAPPELL: And that's within Roll and POM or one or the other?

THE WITNESS: I believe just POM.

JUDGE CHAPPELL: And do you know that he has other employment, other jobs, other consultancies, or not?

THE WITNESS: I do, yes.

JUDGE CHAPPELL: Okay. Is it something you can tell us or is it something he wouldn't want in public?

THE WITNESS: Well, I think I've read his deposition where I think he describes his -- his trade,

what he does. He's a practicing physician.

JUDGE CHAPPELL: All right.

THE WITNESS: He's an M.D. He -- so, part of his time is spent treating patients. And then part of his time is spent working, for example, with POM. And I believe he also serves on one or more advisory boards as an M.D. for pharmaceutical companies.

So, for example, I forget -- I actually forget the pharmaceutical company, maybe AstraZeneca. But he is a specialist in gastroenterology, and so he serves on an advisory board for one of those drugs that pertain to that. So, that's my understanding of what occupies his time.

JUDGE CHAPPELL: Does he have an office in your building?

THE WITNESS: No.

JUDGE CHAPPELL: Thank you.

BY MS. VISWANATHAN:

Q. From working with Drs. Dreher, Gillespie, and Liker, is that another source of knowledge that you've gained about nutrition and science?

A. Yes.

Q. Do you have the authority to hire and fire people at POM Wonderful?

A. It is my job to hire and fire people, and I do

so either on my own or in consultation with either of the Resnicks, depending on the situation.

Q. And is it the case that you have, in fact, hired and fired people during your tenure at POM?

A. Yes, I have.

Q. In the past, have you made the decision to fire a head of the marketing department?

A. Yes.

Q. And similarly, you -- do you have the authority to eliminate positions and restructure the organization at POM Wonderful?

A. Again, I would carry out those duties, and for any major restructuring, I would consult with the owners.

Q. I'm sorry. I didn't hear the last -- you would consult with --

A. I would consult with the owners, the Resnicks.

Q. The Resnicks, okay.

Okay. And, in fact, when you brought in Dr. Gillespie, that was part of a restructuring of the management team at POM, correct?

A. Correct.

Q. Do you have authority to sign checks on behalf of POM Wonderful?

A. Yes, I do.

Q. And you have -- have you, in fact, signed checks on behalf of POM Wonderful?

A. Yes, I have, every week.

Q. Do you have authority to sign contracts or agreements on behalf of POM Wonderful?

A. Yes, I do.

Q. And have you, in fact, signed contracts or agreements on behalf of POM Wonderful?

A. Yes, I have.

Q. Would that include agreements with institutions to conduct research on POM product?

A. Yes.

Q. Are you familiar with an entity called The Stewart and Lynda Resnick Revocable Trust?

A. Vaguely familiar.

Q. Are you aware that the trust entered into agreements with research institutions to perform scientific research on POM's products?

A. Vaguely aware, yes.

Q. Let me show you one of these agreements. It's Exhibit CX 606. And it will come up on the screen, but you can also look at it in the notebook, whichever is easier.

Okay. In the top paragraph of this document, it says that this is an agreement for Preventive Medicine

Research Institute, or PMRI, to perform two clinical trials on behalf of Stewart and Lynda Resnick, as trustees of this trust that I mentioned.

Do you see that?

A. I see that, yes.

Q. And the trust is defined as the sponsor in this agreement, correct? It's in the same paragraph.

A. I'm sorry. The screen is cutting off on the left side.

JUDGE CHAPPELL: Someone needs to go over there and hit the auto-adjust button.

THE WITNESS: Someone just did.

BY MS. VISWANATHAN:

Q. Can you read this now?

A. Yes, I can.

Q. And the trust is defined as the sponsor in this document?

A. Correct.

Q. And if you could turn to page 2, at the top of the document. At the very top of that paragraph 3, there's a section called "Payment Terms."

Do you see that?

A. I see that.

Q. And then it says, "Sponsor shall pay to PMRI various amounts as set forth in the schedule below."

Do you see that?

A. Yes.

Q. And let's just go to the last page, which is page 3. On this page, as you can see, there are signature lines. One is Stewart Resnick, Lynda Resnick, Dr. Dean Ornish on behalf of PMRI, and yourself as chief operating officer of POM Wonderful. Is that correct?

A. Correct.

Q. Do you know why the trust was a sponsor of this agreement?

A. No, I don't.

Q. Do you know why POM signed the agreement?

A. No, I don't.

Q. Okay. Were these -- was the research that was being contemplated in this agreement, was it on a POM product?

A. I believe so, yes.

Q. Was it part of your responsibilities at POM Wonderful to oversee the clinical trials on POM products that would have been done by this institution?

A. Yes.

Q. I'd like to show you one other agreement that's been admitted into evidence. This is an agreement with a company called Radiant Research, and it's CX 604.

You're familiar with the company Radiant

Research?

A. Yes, I am.

Q. And is Dr. Michael Davidson associated with Radiant Research?

A. I'm sorry, Dr. Who?

Q. Dr. Michael Davidson.

A. Yes, he is.

Q. And as we've heard today, Dr. Davidson has conducted studies on POM Juice, correct?

A. Correct.

Q. Okay. If we could look at page 3 of this agreement, or at least of this document, okay, and, again, at the top, under "Research Agreement," this is an agreement that The Stewart and Lynda Resnick Trust is a sponsor, correct?

A. Correct.

Q. If you would turn to page 16, which is one of the signature pages of the document, as you can see, there's a signature block for the trust, The Stewart and Lynda Resnick Trust, correct?

A. Correct.

Q. And below that there's a signature block for Radiant Research, correct?

A. Yes.

Q. Okay. And then if we go to the next signature

page, which is 18, it looks like there's a signature block for principal investigators, including Dr. Davidson, correct?

A. Yes.

Q. Okay. And if you would like, you can look through the paper copy in the book, but I can represent to you that there's no signature line in this agreement for POM Wonderful.

Are you aware of why there wouldn't be a signature line for POM in this agreement with Radiant?

A. No, I'm not.

Q. If we look at a later page of this agreement, page 26. At the very top, it says, "Radiant Development, Study Timeline," and underneath, it says, "Roll/POM Wonderful," with a number.

Do you see that?

A. Oh, I see what you're talking about. Up at the top?

Q. Yeah.

A. Yes, I see that.

Q. Do you know why the agreement said "Roll/POM Wonderful" at the top if the trust was the sponsor?

A. No, I don't.

Q. Okay. All right. And at the bottom, it appears that this page was signed by someone on behalf of

Stewart Resnick. Is that correct?

A. Correct.

Q. Okay. I just want to look at one more page in this document, if we can turn to page 28. And, again, at the top, it says, "Roll International" only. It doesn't say "Roll/POM."

Do you know why that would be?

A. No, I don't.

Q. If you look at the entire document again, it appears to be a task list with specific responsibilities with respect to various aspects of the study, including protocol, case report forms, et cetera. Is that right?

A. Correct.

Q. And there are columns to the right which say "Sponsor, Radiant, or Joint," correct?

A. Yes.

Q. So, for example, under "Protocol," if we can go up to the "Protocol" section, it says that -- there's a checkmark under "Approval," it says, "Protocol approval, number 3."

Do you see that? There's a check -- an X mark under "Sponsor"?

A. Yes.

Q. Okay. So, would that indicate that the sponsor was responsible for approval, to your knowledge?

A. That's what it appears.

Q. Okay. Do you know whether POM Wonderful approved a protocol for a study with Radiant Research?

A. I believe we would have, yes.

Q. Okay. Did Roll also approve the protocol?

A. Not that I'm aware.

Q. And were you aware of whether the trust had approval of the protocol?

A. I don't believe so.

Q. Okay. So, for the tasks that are listed as the sponsor's responsibility under this agreement, would those have actually been done by POM --

A. Yes, I believe so.

Q. -- with respect to the study?

A. Correct.

Q. Okay. Okay. Actually, for one sec, let's just go to the published paper from Dr. Davidson from Radiant Research, which is CX 1199. And if we look at the bottom left, the "Acknowledgment" section, if we could enlarge it.

In the first paragraph, it says, "This study was funded by Roll International Corporation, Los Angeles, California."

Are you aware of whether there was funding for this study -- whether the funding for this study came

from Roll?

A. I don't know specifically which entity the study -- the funding would have come from, no.

Q. So, do you know whether it would have come from POM?

A. It may have.

Q. Are you -- we can put that down.

Are you aware of any other research agreements for studies on POM products in which the trust was the sponsor?

A. I believe there were others. Specifically which ones, I don't recall.

Q. Are you aware of any other research agreements for studies on POM products in which Roll is the sponsor?

A. I don't know.

Q. Were there some research agreements -- research agreements in which POM itself -- POM Wonderful itself was the sponsor?

A. I believe there were, yes.

Q. As far as your responsibilities as president of POM Wonderful, did they differ with respect to the medical research studies depending on who signed the agreement?

A. Not any studies that involved POM products, no.

Q. Okay. And it did not depend upon who was listed as the sponsor?

A. Correct.

Q. Okay. Is overseeing the budget for POM Wonderful also within your responsibilities as president?

A. Yes.

Q. And that would include the budget for all departments, I assume?

A. Yes.

Q. So, you're responsible for the marketing budget for POM, correct?

A. Responsible for administering it, yes.

Q. Were you also -- well, what do you mean by "administering it"? I just want to be clear -- make the record clear.

A. I don't have the unilateral authority to say, "Okay, we're going to spend $5 million on marketing versus 3 versus 10," as an example.

Q. And so what is your role as president in terms of administering the budget?

A. Once we have agreed upon an amount that we're going to spend over a given period of time, I make sure I work with the team, no matter what department it would be, to ensure that we, in fact, execute according to

that budget, spend the amount that we said we were going to spend, et cetera.

Q. Okay. Were you also responsible for administering the budget for scientific research on POM products?

A. Yes, in that same sense.

Q. Was it the case -- well, we've discussed that there were -- as we saw in another study, that some of the payments for research may have come from another entity, like the trust, correct?

A. Correct.

Q. Was it still the case that you were responsible for administering the budget for research on POM products, even if POM wasn't the sponsor of that research?

A. I believe so, but I -- I don't believe that many of those studies that were funded by the trust have occurred in recent times. I think those were all fairly early on; some of them, I think, before I actually became involved with POM.

Q. As president of POM Wonderful, would it be part of your job responsibilities to be aware of the status of medical research on POM products?

A. Yes.

Q. You had said before that you had interaction --

direct interaction with the researchers, correct?

A. Yes.

Q. Did your interaction with those researchers involve substantive discussions of the underlying science?

A. Yes.

Q. So, is it fair to say that you have some working knowledge of medical terminology?

A. Some.

Q. Well, specifically, you have some knowledge with respect to medical terminology that were used in the studies on POM products, at least, correct?

A. Correct.

Q. So, for instance, some of the terms that we've heard during the proceeding, you would be familiar with, such as protocol? Do you know what that --

A. Yes, I know what a protocol is.

Q. Or IMT?

A. Yes, I know what IMT is.

Q. BART?

A. I think I know what BART means.

Q. And PSA or PSADT?

A. Yes. I know what those mean.

Q. Endpoints or biomarkers, are you familiar with those?

A. Yes.

Q. And also statistical terms like P-value?

A. Yes.

Q. Your wife has reviewed some protocols for studies on POM products. Is that correct?

A. I believe she's reviewed one or two, correct.

Q. Would she give suggestions or comments on those protocols?

A. Yes.

Q. Was this done informally or did she have a defined consulting role at POM?

A. It was informal.

Q. So --

A. A favor from her to me.

Q. Pro bono?

A. I'm sorry?

Q. Pro bono.

Would she give her suggestions or comments to you directly or to other people at POM as well?

A. I believe to -- for example, in the one instance where she provided feedback to Dr. Liker.

Q. But presumably you would be CC'd on any kind of communications?

A. I think so, yes.

Q. Would she also participate in any

teleconferences or meetings in person?

A. I don't believe ever any meetings in person, and I'm not sure about phone calls. Possibly.

Q. And your wife reviewed a protocol for a cardiovascular study by Dr. Dean Ornish. Do you recall that?

A. Vaguely, but -- yeah, I -- I don't recall that specifically, but that could have been one of the studies.

Q. Okay. Let me show you, just to see if this will refresh your recollection, if you can look at CX 573. We can either show it on the screen or -- yes.

At the very -- oh, this is an email from you to Mr. Resnick, dated February 2003, and at the top, the email from you says, "Here are my wife's initial thoughts on maximizing patient enrollment in the Ornish study."

Do you see that?

A. I will whenever the -- there you go. Thank you. Yes, I see that.

Q. You see that, okay.

Okay. So, does this refresh your recollection that your wife did provide comments on a protocol for a Dr. Ornish study?

A. I had actually forgotten that she had provided

feedback on this study, but it looks like she did back in 2003.

Q. You -- strike that.

Were any of her suggestions or comments implemented in the final protocol for Dr. Ornish's study?

A. I don't know. Since my wife is here, I mean, I'm sure they were all excellent suggestions. That's for my own record.

Q. In the past, POM's Web site has had --

JUDGE CHAPPELL: You know, that -- what you just did, we want to encourage peaceful marital situations, so good for you.

THE WITNESS: I am being trained slowly but surely. It's taken a while.

JUDGE CHAPPELL: You will be trained well enough in time, I'm sure.

THE WITNESS: With pleasure.

BY MS. VISWANATHAN:

Q. Okay. In the past, POM's Web site has had a blog page where the company itself would post content. Is that correct?

A. That's right.

Q. And that part of the Web site allowed consumers to post their comments or feedback as well, correct?

A. I believe so, yes.

Q. Okay. And let me just show you so you can confirm if this is the type of document I'm talking about. Look at CX 336. It shows up on the page. Can you make it a little larger at the top?

This is a URL at -- it says pomwonderful.com/community, and it's dated December 10, 2009. At the top, there's a Web page -- the Web page title "is POM's Health Benefits: Fact or Fiction"?

Do you see that?

A. Yes.

Q. At the top there's a statement attributed to you, Matt Tupper, president. Do you see that?

A. I do.

Q. And are these statements that you would have written before they were posted on the Web site?

A. I believe these are actually statements that I made verbally to someone on the team who then transcribed them, yes.

Q. And would you have reviewed this statement before it went up on the Web site?

A. I believe so, yes.

Q. And from time to time, you would contribute to this blog, this Web site page, in your capacity as president?

A. I'm not sure that I did this more than once. I think it was the intention to do it multiple times, but I think it may have -- it may not have gotten that much traction. I also don't know whether this page is still on the Web site.

Q. Okay. Mr. Tupper, you have appeared on the Fox Network Business Channel program in your capacity as president of POM Wonderful, correct?

A. Correct.

Q. Have you made other media appearances on behalf of POM Wonderful?

A. I'm not sure what you mean by "media appearances."

Q. Other television --

A. That sounds very glamorous, but --

Q. I'm sorry?

A. That sounds very glamorous.

JUDGE CHAPPELL: Was that on the Fox News Channel or their new cable business channel?

THE WITNESS: I think it was Fox Business News, which I don't know if that's a -- like a show on their Fox channel or if that's, like, a separate channel. It may be a separate channel, actually.

BY MS. VISWANATHAN:

Q. Well, I -- for example, any other kind of

television interviews?

A. I believe I did one other television interview several years ago, yes.

Q. Or podcasts, radio, anything like that?

A. I don't think I've ever done anything on the radio.

Q. And do you have any more specific recollection of when that other television interview was?

A. No. It was -- I believe it was prior to Fox.

Q. Okay. You have given comments to media outlets, such as newspapers, in your role as president, correct?

A. Yes. I have been interviewed many times by newspapers or magazines.

Q. Okay. We've heard testimony earlier in the proceeding about the creation of marketing materials. Is it fair to say that the creation of POM Wonderful's marketing materials is a collaborative effort between Fire Station Agency and POM Wonderful?

A. In a manner of speaking, yes.

Q. Would the collaboration of marketing materials, that would include creating advertising, correct?

A. Yes.

Q. In terms of creating advertising, does POM use the Fire Station in-house ad agency for all or virtually all of its ad agency needs?

A. Yes, for our domestic needs, that's correct.

Q. We've also heard testimony earlier on creative briefs. Are you familiar with the term "creative briefs"?

A. I am.

Q. And is it accurate to say that the creative briefs are developed by the POM marketing people in order to give the Fire Station employees insight on how to start a particular marketing project?

A. I think that's fair to say.

Q. Are creative briefs done for new marketing campaigns that POM undertakes?

A. Yes.

Q. And these new marketing campaigns will sometimes be given names, I think we have heard like Dress Bottle or Comic Book or Superhero, correct?

A. They would be given names after the fact, yes.

Q. When you say "after the fact," do you mean -- can you just explain what you mean by "after the fact"?

A. Sure. For example, in the case of what we have -- what we call -- what we did call our Superhero Campaign, we didn't -- when I say "we," the creative process didn't start with a vision that said, "We want to create a Superhero Campaign." That was one of many options that was offered up. That was the one that was

chosen, and then -- you pick it, you like it, you know, and you give it a name.

Q. So, as the concept developed, then it might get a name. Is that fair to say?

A. No. Typically, it would be after -- once -- once something had been chosen as a direction we wanted to head, although I guess I should also say, who knows? It may be that the employees of Fire Station internally would refer to different campaigns with a nickname or something like that. I'm not aware -- I wouldn't be aware of that.

Q. Was -- you just mentioned the Superhero Campaign. The Superhero Campaign and the Comic Book Campaign, are they the same -- different names for the same campaign?

A. Yes, I think so.

Q. Does POM's marketing department maintain an archive of creative briefs from past campaigns?

A. Yes, they do.

Q. Okay. And how are those creative briefs stored at POM?

A. How meaning like electronic versus paper or --

Q. Yes. If you know.

A. I don't know specifically. I would imagine that they're probably a combination of -- of both, but I

don't know.

Q. Who's responsible for maintaining the creative briefs?

A. The marketing department.

Q. Do you know how long they're kept? Are they just archived indefinitely?

A. I don't know.

Q. Do you know if there's any kind of a document retention procedure, you know, people are required to keep certain documents?

A. No.

Q. As president of POM Wonderful, would you ever review creative briefs?

A. No.

Q. Okay. Let's look at CX 0084. I'm focusing on the middle email. It's from Staci Glovsky to Mrs. Resnick, and you are CC'd on this email. It's dated October 2006. And the subject line is, "Creative Strategy Briefs - POMx Pills & Liquid."

Ms. Glovsky's email in the middle of the page says, "Per our discussion last week, attached please find draft Creative Strategy Briefs for POMx pills and liquid. These have been reviewed by Liz and Matt. Thanks! Staci."

Do you know if by "Matt," Ms. Glovsky is

referring to you?

A. It looks like it, yes.

Q. So, in this case, did you review creative briefs -- draft creative briefs for POMx Pills and Liquid?

A. I don't know.

Q. So, you don't recall ever offering suggestions or comments on any creative briefs?

A. No. No, the -- no.

Q. Even if it was -- well, okay, let me back up.

Would you be one of the decision-makers in terms of choosing headlines or graphics to be used in a marketing campaign?

A. Actually, let me just be clear on what I meant by not reviewing briefs. When I -- I interpreted you -- I interpreted your question as would I look at the template that says "Creative Brief" on it. So, in this case, I -- I have no recollection of reviewing this template from top to bottom. But would I have discussions with the marketing department about individual parts or elements of marketing briefs? I'm sure I would, yes.

Q. Do you know how often you would discuss creative briefs with the marketing people, for instance?

A. No. I can't -- I can't give you a good answer

on that one.

Q. Would it be more than once a month?

JUDGE CHAPPELL: Just so we're clear, do you mean various creative marketing briefs or a particular one that may come in?

MS. VISWANATHAN: No, I'm sorry. I'm referring to creative briefs in general.

THE WITNESS: Yeah. That's -- that's the question I'm answering.

BY MS. VISWANATHAN:

Q. Okay. Would you be one of the decision-makers in terms of choosing the headline or graphic to be used in a new marketing campaign?

A. Yes.

Q. So, for a new campaign, would you review the headlines being considered?

A. Yes.

Q. And by "headlines" -- does "headlines" have a specific meaning within POM Wonderful marketing?

A. It did and it does, yes.

Q. Okay. What -- just so we're on the same page, how did you -- how do you understand the word "headlines" in terms of POM Wonderful marketing?

A. To me, a headline would be, for example, the phrase that would appear on a billboard, where that's

really the only text that you see; or a headline could also be, for example, in a magazine ad, the sort of large statement at the top. That would be a headline as well.

Q. And that would be distinguished from the body copy -- is that the term? -- for any smaller copy in the ad? Is that correct?

A. Correct.

Q. So, you would review and provide input on headlines. And would you also review and provide input on graphics?

A. Typically not. The creative people like to keep me away. I'm not particularly artistic.

Q. Have you ever provided input on graphics?

A. I've provided my opinion on graphics, but input during the creative process, definitely not.

Q. Okay. Would you ever review -- let me strike that.

Would you ever review and approve specific ad copy for advertisements?

A. Yes.

Q. And how often, if you can estimate, would you review ad copy for advertisements for a POM product?

A. Again, it's difficult to say, you know, I did it once every week on Friday or, you know, a couple times a

month. It varied. It could -- you know, in a given month, there could be several times, and then there could be a stretch of four months with -- with nothing.

Q. We also have heard testimony that POM has done magazine wraps for Time Magazine that were distributed through urologists' offices. Are you familiar with these magazine wraps?

A. Yes, I am.

Q. Did you help draft the ad copy for the magazine wraps?

A. Yes, I did.

Q. POM Wonderful has reached out to bloggers to make them aware of POM, the company, and its products, correct?

A. Correct.

Q. And as part of this outreach, POM provides POM product and information to bloggers?

A. That's correct.

Q. Was the POM outreach done by the marketing department?

A. It was.

Q. Does POM Wonderful have a Facebook page?

A. We do.

Q. Does POM Wonderful have a Twitter page or a Twitter feed?

A. I'm not sure. That's somewhat beyond me, but I believe we do, yes. We "tweet," I think, as the saying goes.

Q. That's correct.

Are these run by the marketing department as well?

A. Yes, they are.

Q. And the marketing department would provide the content or the posts on the Facebook and Twitter pages?

A. That's correct.

Q. Are there any other type of social media that POM's involved in? I'm not --

A. Those are the main ones that I'm aware of.

Q. The bloggers, the Facebook, and the Twitter feeds?

A. Those are the ones that I'm aware of. I'm sure the marketing department would scold me for not remembering other great things, but I think those are the main ones.

Q. Does POM hold regularly scheduled marketing meetings?

A. We do, yes.

Q. And do you typically attend each of these marketing meetings?

A. No, not all.

Q. Do you attend most of the marketing meetings?

A. I attend the semiregular marketing review meetings where Lynda Resnick also attends. Beyond that, I don't attend marketing meetings with any regularity.

Q. Okay. So, you're saying -- like if the marketing department was having an internal meeting, you wouldn't typically attend?

A. No.

Q. But if there's a meeting that Lynda Resnick was attending, then you would attend?

A. I typically do.

Q. And these meetings that you're talking about that you would attend and Lynda Resnick attends, who else would typically be there?

A. A number of people, including several members from the POM marketing team, the head of the marketing team, several members within the marketing team. There would be typically someone from Fire Station, the creative agency, as well as the corporate communications representative from Fire Station. And depending on the nature of the agenda, there may be other people as well.

Q. Is there a product design department?

A. There is a product design department, yes.

Q. Okay. And what do they do?

A. They typically do designs for -- we sort of --

we call it three-dimensional objects. So, in the case of POM, if we're going to do a new bottle or a new package, anything with multiple dimensions, that's what the -- the design agency would be involved with.

Q. So, depending on the agenda of the meetings that we've been discussing, product design people might be present?

A. That's correct.

Q. Would representatives from the science department, I guess, be there, Dr. Gillespie or Dr. Dreher prior to him, ever be present at these meetings?

A. Yes.

Q. Would Dr. Gillespie or Dr. Dreher be a regular attendee at these meetings?

A. If there -- if there was an agenda item to discuss research, then either one of them would have attended, yes.

Q. And these marketing meetings that we're discussing, are they also what we've heard referred to as the LRR meetings?

A. Correct. The ones that I'm referring to, that I've attended, those are the LRR meetings.

Q. As far as the product POMx Pills, the company sells POMx Pills via direct order from its Web site or a

toll-free number. Is that correct?

A. Yes.

Q. And do most -- strike that.

And most POMx purchasers buy it via the Web site or direct-order in some way, correct?

A. That's correct.

Q. And because it's available by direct-order, is POM able to track the number of orders generated by particular POMx ads?

A. Yes.

Q. So, does that mean --

A. In an approximate way.

Q. Well, does that mean that POMx -- excuse me.

Does that mean that POM could tell if a specific pill ad was more successful in generating orders than another?

A. Directionally, yes.

Q. I'm sorry. I didn't hear that word. Directionally?

A. Directionally, yes.

Q. Can you explain what you mean by "directionally"?

A. Sure. So, in a -- in a magazine ad or a newspaper ad, there's a Web site listed where you would go place the order or there's -- and that -- the URL for

that Web site contains a suffix at the end, which is a code, that on the one hand enables the person to -- if there's some sort of a deal that we're advertising, they can take advantage of the deal, and that also allows us to know which ad it came in from.

Similarly, with the phone number. If they call the 800 number, it tells them to mention the code. That's how we track which orders go with which ads. Not all orders that come in, however, not all of them have a code associated with them. People can't remember which ad they saw, and so forth. So, our accounting is -- is approximate and directional, but it is not precise.

Q. I understand.

Would each specific magazine ad have its own individual code?

A. No.

Q. Okay. I guess what I'm trying to get at is, would -- if the same ad appeared in two different magazines, would they have two different codes?

A. Typically, they would.

Q. Okay. As president of POM, are you informed in meetings or by other communications whether particular pill ads were more successful than others in terms of generating orders?

A. Yes.

Q. We've talked about the fact that POM or Roll and the trust sponsor specific scientific research on POM's products. For simplicity's sake, going forward, if I refer to studies that POM has funded or sponsored, I'll be referring to studies -- I'll be including studies that are sponsored by the trust or Roll as well, just to keep it simple, because what I'm really interested in is the fact that the studies were done on POM products. Is that okay?

A. Yes.

Q. Okay. Is that understandable? Great.

Is it fair to say that some of the research that POM has funded and has been conducted on POM products has involved human physiology?

A. I think so. I'm not quite sure what you mean, but I think so.

Q. Well, is other -- and other research has involved basic chemistry, including chemical analysis of POM's product?

A. Yes, that's right.

Q. And what's the purpose of the basic chemistry chemical analysis research on POM's products?

A. Well, the active polyphenol components in pomegranate juice and extract are -- they're multiple, they're varied, and it is important to us to know -- to

be able to characterize them, to know what they are, what quantities they occur in, what their chemical structures are, and so forth. That is an important underpinning of all the -- the entire scientific program that we do, is knowing what -- what substance we're studying.

Q. So, identifying the components, is that what you're describing?

A. Yes.

Q. Is it also the case that some of the research that POM has funded has involved animal and livestock physiology rather than on humans?

A. Yes. Many of our studies are using various animal models.

Q. Okay. I'm not -- I guess I'm not talking about animal models specifically. I'm talking about studies on, say, cattle health or the health of cattle. Is that one of the areas that POM's done research in?

A. Yes.

Q. And just to be clear, the studies that POM has funded on the cattle health, that's not an animal model for human research, correct?

A. No. It's to see if there's a benefit to the cattle themselves.

Q. Okay. In terms of human -- POM's effect on

human physiology, is it accurate to say that one of those specific areas that has been studied is the cardiovascular system?

A. Yes.

Q. And has POM also worked with scientists to investigate various aspects of the urological system?

A. Yes.

Q. I want to just -- right now, I want to talk specifically about studies on humans. In the urological area, some studies on POM products have involved men who were previously treated for prostate cancer, correct?

A. Correct.

Q. As far as you're aware, however, there have been no human studies on men who have not been diagnosed yet with prostate cancer, correct?

A. Correct.

Q. Okay. So, in other words, you're not aware of any human clinical studies on prevention of prostate cancer in normal men, correct?

A. All the patients in the clinical studies have been diagnosed and treated for prostate cancer, that's correct.

Q. Okay. Also, within the urological area, is it accurate to say there has been one human study looking at the effect of POM Juice on erectile dysfunction?

A. Correct.

Q. In terms of studies involving humans in the cardiovascular area, you would agree that one specific subarea has been the effect of POM products on arterial plaque, correct?

A. Correct.

Q. And another subarea of the cardiovascular system has been the effect of POM on blood flow, correct?

A. Correct.

Q. And a third subarea has been the effect of POM on blood pressure. Is that right?

A. Correct.

Q. Is it fair to say that POM has funded studies by researchers where no publication resulted from the study?

A. Yes, that's correct.

Q. Is it your belief that if a study isn't published, it's because the study had no conclusions and there was nothing more?

A. That's certainly why studies don't reach a medical journal, that's correct.

Q. So, it's your testimony that the reason a study doesn't get published is because there were no conclusions from the study?

A. Not quite, no.

Q. Well, do you recall giving a deposition in this case on February 2nd, 2011?

A. I do.

Q. And at that deposition, starting on page 83, line 17, you gave the following testimony:

"QUESTION: So, POM has sponsored studies that were not published. Isn't that correct?

"ANSWER: That is correct.

"QUESTION: And there were conclusions made in those studies, right?

"ANSWER: No. I believe I testified that the reason a study doesn't get published is that there's nothing learned, no conclusions drawn."

Was that your testimony at the time?

A. I believe so. Which page is that in here? I don't --

Q. I don't think we -- maybe you could show him that.

A. I'll take your word for it. It sounds right.

Q. Okay. Would POM see the final data from a study before the data are turned into a manuscript?

A. Typically, yes, but not always.

Q. Would POM sometimes see the interim data results from a study before the study was completed?

A. Sometimes.

Q. Do the researchers POM works with consult with POM in deciding whether to submit a study to a journal for publication?

A. Sometimes, yes.

Q. Would POM also typically review drafts of study manuscripts before they're submitted to publications?

A. Yes. Sometimes we do.

Q. Would you say you typically see those manuscripts?

A. Typically, yes. Not always.

Q. You have helped put together summaries of POM's medical research, together with either Dr. Dreher or Dr. Gillespie. Is that right?

A. That's correct.

Q. Was the purpose of these types of medical studies to provide a basis for future studies?

A. I suppose. I'm not quite sure what you're -- what your question is getting at, but in a manner of speaking, I guess.

Q. Okay. Well, let me show you, actually, one summary, and then we can ask questions about it. It's CX 262, an email. This is an email from you to Diane Kuyoomjian and Martin Shreeves, dated December 16, 2008. It's attaching a PowerPoint, "Medical Research Results Summary."

Do you see that? Do you have the document?

A. Yeah, I have got it right here. Thank you.

Q. And the first line is that, "Mark" -- presumably Mark Dreher -- "and I have assembled a summary of POM medical research results that we are using as the basis to chart our future studies."

Do you see that?

A. Yes.

Q. And what did you mean by "chart our future studies" in that email?

A. Well, the purpose of these reviews is to take stock of the portfolio research both which has occurred in the past and what we have learned from that to tell us what's going on now, and then to facilitate a discussion about where we go in the future, both with respect to launching new studies and continuing existing studies and so forth.

Q. Okay. And Ms. Kuyoomjian and Mr. Shreeves, are they a part of -- or were they at the time -- part of POM's marketing department?

A. That's correct.

Q. The second part of your email says, "I wanted to share a portion of that document with both of you, as it may help with future marketing communications."

How are the medical research summaries intended

to help with future marketing communications?

A. Well, I suppose it's -- it's to help educate the marketing team about the body of science that lies behind POM, so that as we're communicating various aspects of that science, they are familiar with it.

Q. So, you would agree that POM cites to medical research studies in its marketing for its products, correct?

A. Yes, that's correct.

Q. And POM's marketing and advertising has stated that its products have benefits in the areas of cardiovascular, prostate, and erectile dysfunction, correct?

A. I'm not sure that's the precise language, but directionally, yes.

Q. When POM's ads refer to health benefits, is it POM's position that all of those benefits are supported by published research?

A. We believe that the benefits are supported by the entire body of research, published or unpublished.

Q. Is it also POM's position that all of these health benefits are supported by clinical human research?

A. We believe that the benefits and the insight are supported by, again, the entire body of research, which

includes in vitro, it includes animal, and, yes, it includes clinical as well.

Q. Okay. Well, did you testify at your deposition that you were not aware of ads that POM had run or talked about published research where the area of health didn't involve clinical research?

A. I believe that's correct, yes.

Q. Okay. Clinical meaning human?

A. Correct.

Q. As president of POM, do you read the published papers that result from studies on POM products?

A. I do.

Q. As president of POM, do you review any unpublished data or manuscripts that result from studies on POM product?

A. I do.

Q. Okay. I'd like to show CX 1029. It's a document that is in evidence and that you have testified about in your deposition, and it's entitled "Medical Research Portfolio Review," and dated January 13, 2009.

Is this a document that you're familiar with?

A. Yes, I am.

Q. And, in fact, did you edit this document and work on it with Dr. Dreher?

A. I did, yes.

Q. Have similar medical research portfolios been prepared from time to time during your tenure at POM Wonderful?

A. Not in this format, but we have done reviews from time to time, yes.

Q. And was this medical research portfolio used as a discussion document during meetings with Mr. Resnick to discuss current and future research?

A. Mr. Resnick as well as other scientific advisors of POM, yes.

Q. And were these medical research portfolios also used to make decisions about funding medical research in the future?

A. They were used to facilitate discussions, and the discussions were obviously intended to lead to decisions in many cases, yes.

Q. If we could turn to page 2 of this document, at the top, the title says, "Portfolio Summary - January, 2009," and along the left column, it says "Research Area," and it's divided it looks like into five categories, for lack of a better word, with subcategories underneath. Is that accurate?

A. Yes.

Q. Okay. And the five categories being chronic diseases, infectious disease, quality of life, product

research, and other costs, correct?

A. Correct.

Q. And then going -- looking at the columns going across, it looks like there's a column that says "Current Plan of Action," and the last two columns appear to be budget estimates. Is that right?

A. That's right.

Q. So -- and this is what we had talked about in terms of using the document to discuss future plans, research plans, correct?

A. No. I believe in this case, this document was a summary of the discussion after the fact.

Q. When you say "after the fact," you mean after the research summary was created or after the research summary was used at a meeting?

A. I'm sorry. I should be more -- I meant the latter. After we had the dialogue in the meeting, during which the portfolio review document was used to facilitate discussion, I believe that this particular page summarized some of the discussion that happened in that meeting. That's my recollection.

MS. VISWANATHAN: Your Honor, I'm actually at a stopping point. I don't know if you want to stop.

JUDGE CHAPPELL: Okay.

MS. VISWANATHAN: It probably makes sense to

stop at this point.

JUDGE CHAPPELL: All right. You can have a seat.

MS. VISWANATHAN: Thank you.

JUDGE CHAPPELL: How much more time do you anticipate needing on direct?

MS. VISWANATHAN: I would estimate probably another 2, 2 1/2 hours.

JUDGE CHAPPELL: All right.

Any estimates on cross?

MS. DIAZ: Short, Your Honor. Short, Your Honor.

JUDGE CHAPPELL: Okay. We'll reconvene in the morning at 0930. We're in recess.

(Whereupon, at 5:12 p.m., trial was adjourned.)

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 NAME: POM WONDERFUL LLC

DATE: JUNE 7, 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: 6/12/2011

SUSANNE BERGLING, RMR-CRR-CLR

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.

SARA J. VANCE, CMRS