Pages 771 - 1012

UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

Before The Honorable Vince Chhabria, Judge

IN RE: ROUNDUP PRODUCTS LIABILITY LITIGATION,) NO. M. 16-02741 VC

San Francisco, California
Friday, March 9, 2018

TRANSCRIPT OF PROCEEDINGS

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Also Present: The Honorable Ioana Petrou
Leonora Lynham
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INDEX

Friday, March 9, 2018 - Volume 5

PLAINTIFFS' WITNESSES	PAGE	VOL.
NABHAN, CHADI		
(SWORN)	794	5
Direct Examination by Mr. Miller	794	5
Cross-Examination by Mr. Griffis	830	5
ReDirect Examination by Mr. Miller	851	5

DEFENDANT'S WITNESSES	PAGE	VOL.
CORCORAN, CHRISTOPHER (RECALLED)		
Cross-Examination by Ms. Robertson	775	5
MUCCI, LORELEI		
(SWORN)	852	5
Direct Examination by Mr. Lasker	853	5
Cross-Examination by Mr. Miller	952	5

Friday - March 9, 2018 **9:10 a.m.**

P R O C E E D I N G S

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THE COURT: All right. Anything to discuss before we resume?

MS. WAGSTAFF: There is, your Honor.

THE COURT: Okay.

MS. WAGSTAFF: So I just -- we were reading the daily transcripts last night -- which you're doing a great job on, by the way -- and I just wanted to clear something up so we didn't have to waste time on it next Wednesday, but I made a comment when I was crossing Dr. Rosol that plaintiffs were not challenging all of the methodologies of Dr. Rosol. Of course we are, as shown in the *Daubert* brief. And I just wanted to make that clear in case I misspoke, so there was no question about that.

THE COURT: Yeah. No problem. All right.

MS. ROBERTSON: Hi.

THE COURT: Good morning. All right. You can take it away.

CHRISTOPHER CORCORAN,

called as a witness for the Defendant, having been previously duly sworn, testified further as follows.

CROSS-EXAMINATION

BY MS. ROBERTSON

Q. Good morning, Dr. Corcoran.

A. Good morning.

Q. Dr. Corcoran, prior to this litigation did you ever design a rodent carcinogenicity study to assess the ability of a chemical to cause cancer?

A. No, as I said yesterday in my testimony, a large part of my career and my work has been spent on developing methodologies that can be used to analyze data from these experiments, including, you know, especially focused on methods that are useful when the outcomes are rare or the sample sizes are small, which is certainly true in this case.

And when I published on this in the past, I've used examples from rodent carcinogenicity experiments that could be analyzed using the methods I've developed.

Q. Prior to this litigation, did you ever perform a rodent carcinogenicity study to assess the ability of a chemical to cause cancer?

A. No, but as I said, I've been pretty heavily involved in methodological developments in this area that are highly applicable, I guess, in this case.

Q. Dr. Corcoran, prior to this litigation, did you ever oversee a rodent carcinogenicity study to assess the ability of a chemical to cause cancer?

THE COURT: Got to slow down. Got to slow down.

Did you get the question?

MS. ROBERTSON: Ms. Court Reporter, would you like me to repeat?

(Record read by reporter.)

THE WITNESS: Yeah, no. As I've been saying, I'm a biostatistician, so I'm not a pathologist, I'm not a toxicologist. What I do is I analyze data. I don't actually design experiments, I work with people who do, and I analyze the data that come from those experiments that's my job.

BY MS. ROBERTSON:

Q. Dr. Corcoran, prior to this litigation, did you ever design a study that addresses the optimal dosing pattern for rodent carcinogenicity studies to assess the ability of a chemical to cause cancer?

A. No. I understand from Dr. Portier's testimony that, you know, that's what he -- that's what his dissertation was focused on when he was getting his doctorate in biostatistics. My Ph.D. was focused on developing methods that can be used to analyze data from these kinds of experiments. That was my focus.

So we're both biostatisticians. That was his emphasis. Analyzing data from these experiments, that's my emphasis.

Q. Dr. Corcoran, you are aware that Dr. Portier developed the Poly-3 Trend test, correct.

A. Yeah, I'm aware.

Q. Is it your testimony that you believe Dr. Portier relied solely on pooling analysis here?

A. I'm sorry, can you repeat that?

Q. Is it your testimony that you believe Dr. Portier relied solely on pooling for his analysis here?

A. No, that's not my testimony.

Q. Isn't it true, Dr. Corcoran, that you didn't run logistic regression with the full dataset in this case?

A. How do you mean? What do you mean by "full dataset"?

Q. Using all of the p-values from the animal carcinogenicity studies that are at issue in this case, did you conduct a logistic regression test?

A. I'm sorry. The question's kind of confusing, because you don't apply logistic regression to p-values, you apply logistic regression to data.

Q. Thank you for that clarification. Did you apply a logistic regression to the data in this case?

A. In my expert report, I demonstrated how, if you were going to actually combine datasets in the appropriate way, in the way that Dr. Portier's references dictated, that I showed the steps that would be required to do that, using, I think, the Brammer, Suresh and Wood data. That's what I used. So I stepped through those procedures the way that they were outlined in Dr. Portier's references to show how you would do that appropriately.

Q. So aside from Brammer, Suresh and Wood, you did not conduct a logistic regression and apply the logistic regression to the data and the other animal carcinogenicity studies, the nine, not counting Wood, Suresh and Brammer; is that correct?

A. Well, it's an interesting question because, as Dr. Portier testified, the Cochran-Armitage Trend Test is -- more or less for statisticians it's the same thing as logistic regression.

So in other words, you can get a dose-response assessment using either logistic regression or a trend test. That's, you know, what he understands and that's correct. That's what I understand, as well.

The reason why somebody would use logistic regression is that you would have to control for other things, besides dose. So if --

Q. One moment.

I'm sorry, your Honor, to interrupt the witness, but that really wasn't my question.

THE COURT: I think it's appropriate for him to be answering the way he is.

MS. ROBERTSON: Okay.

THE WITNESS: So in other words, you know, if you're going to be "pooling" data from different studies, and I use "pooling" in quotes, because, you know, I don't think he did it correctly, but if you're going to be combining information from different datasets using logistic regression, it's like you're

doing a trend test, but you're adding in other factors in the model that allow you to account for the fact that there are these study differences that we've been talking about over the past few days.

(Clears throat.) Excuse me.

So if in other words, in essence, yes, I -- you know, the trend test represents the answer that you would get if you did an exact logistic regression for dose-response.

What I was criticizing in his expert report is the fact that you can't just throw data together if you're going to combine information from different studies; that if you were going to do that, you'd have to extend the trend test to somehow account for those differences, and which he kind of attempted to address in his rebuttal, but he did not address adequately, as you know, I stepped through yesterday in my own testimony. He didn't follow the steps that his own references outlined for doing that correctly.

Q. Okay, I think we're still missing each other a little bit. My question was whether you ran the logistic regression to the data, aside from those three that you've already -- those three studies, Brammer, Suresh and Wood, that you've already pointed out, did you run logistic regression in your expert report, is there something in your appendices that shows you us you applied it to the rest of the dataset?

A. Right, let me step through this again, in two parts, just

to make sure that.

THE COURT: Well, first, it seems like you could answer yes or no to that question.

THE WITNESS: Well, yeah, but the answer's a little bit difficult because, like I said, for a statistician, the Cochran-Armitage Trend Test is kind of a version of logistic regression, and so from a -- you know, from a technical standpoint the answer is yes. I did --

THE COURT: Okay.

THE WITNESS: -- I used -- I used -- in fact, just for the record, even though I know this is kind of a technical detail, but just to make sure it's in the transcript in case somebody goes back and looks at this, the trend test -- and I think Dr. Portier alluded to this as well in his testimony -- the trend test is in statistics what we called a scored test from a logistic regression model. So every time you're doing a trend test, in essence, you're performing a logistic regression.

So yes, in that sense, I performed a logistic regression in computing every single p-value that was in all of my tables.

BY MS. ROBERTSON

Q. So you agree, Dr. Corcoran, that the Cochran-Armitage test is a logistic regression test? Is that what you're testifying?

A. It's a scored test -- and again, I'm sorry, you'd have to, you know, sit through one of my really exciting categorical

data analysis classes or, you know, any such class at a university and learn how that is, but yes, it's a score test for logistic regression model.

Q. Thank you. Now, Dr. Corcoran, the tumor counts referenced in your expert report come from the Greim summary tables, correct?

A. Yes.

Q. And from the Greim summary tables, you counted 1,016 tumors, is that right?

A. That's right, yeah, 1,016 tumors that had at least one observed, er -- 1,016 types that had at least one observed tumor.

Q. Thank you. And so then you took that tumor count, the 1,016, and you plugged those into your computer program to create the appendices we see at the end of your expert report, right? You didn't write that out by hand. It went into a computer program and generated the tables.

A. The p-values themselves were computed using software, yes, they were computed using the SAS statistical software program.

Q. And then for your Tables C and D that you talked about yesterday, Tables C and D include all 1,016 tumors, is that correct?

A. C and D, with the false discovery rate adjustments?

Q. Yes, sir.

A. Well, let me make sure I'm clearing about what you are

asking. Are you asking whether the adjustment was made with respect to all 1,016 tumors simultaneously?

Q. Table C and D show the --

A. Right.

Q. -- computation of the 1,016 total tumor types, correct?

A. No. Tables C and D show only a subset of the tumor types for which the individual EXACT trend test p-value was less than .05, with the associated adjustment for multiple testing, the false discovery rate adjustment.

So, no, Tables C and D do not contain all 1,016 p-values.

JUDGE PETROU: Can you tell us why it says, in Tables C and D, computed across 1,016 total tumor sites?

THE WITNESS: Oh. Thanks, okay.

JUDGE PETROU: I think that's why the question keeps coming up.

THE WITNESS: I understand that, yeah, and I'm glad you actually raised this point, because when Dr. Portier was testifying, he said -- he said something like, well, Dr. Corcoran adjusted the, you know -- for the green jelly bean problem we're talking about yesterday.

By the way, I was curious, have you ever actually transcribed green jelly beans in this courtroom?

THE REPORTER: Yesterday.

THE WITNESS: Yesterday was the first? That's good.

Anyway, for that green jelly bean problem I was talking

about yesterday, you know, we -- there's a conventional approach for adjusting for all of those p-values to make sure that you -- you know, that you account for all of the tests that you're doing.

And when Dr. Portier was testifying the other day, I was listening, and he said that -- that you might have adjusted for all 1,016 tumor types, and I hasn't done it in, I think, the way that he was suggesting, and I apologize if the -- if the title for these appendices was unclear.

Let me make sure that you know exactly how I did the FDR adjustment for those tables.

What I did, for example -- can we just turn to my report so I can show you?

MS. ROBERTSON: Sure, I have it.

THE WITNESS: Which tab is it, again, my own expert in my binder?

MR. GRIFFIS: It's 2, I believe.

THE WITNESS: Oh, it's number 2, sorry.

MR. GRIFFIS: I think it was 3.

THE WITNESS: So for example, in my expert report, you know, let's look at the Wood table B.3, so the mouse data.

BY MS. ROBERTSON:

Q. Excuse me, B.3? I thought we were talking about Tables C and D.

A. Yeah, we are, but this relates to how the p-values were

computed for C and D.

Q. Okay.

A. So that's why I have to talk about this. So B.3, which is on page 42 of my report.

Now here are -- two, four, six, eight, ten, twelve, fourteen, sixteen, eighteen, twenty -- 21 tumors for males, 21 tumor types, starting with adrenal adenoma and ending with lymphoma.

So what I did when I made the FDR adjustment, because I wanted to err on the safe side, I wanted to make sure I wasn't -- I wasn't, I guess, incurring too large a penalty for all of the multiple tests.

So what I did was, for these mice, and the Wood data, and the male group, when I made my multiple-test correction, when I applied the FDR, it was only for these 21 tumor types. So it wasn't for all 1,016.

Now, again, remember what I talked about with the green jelly bean problem yesterday. The more tests that you're doing -- really, some statisticians would argue, well, you should throw -- you know, if I'm talking about just tumors with three or more -- with an incidence of three or more, or if I'm talking about all 1,016, I should throw all three or four hundred or all 1,000 in the same mix, and make the adjustment simultaneously for all of the p-values that I computed.

What I did, to make sure that I was being safe, in other

words, is I actually only adjusted within sex within study.

So in other words, what you see in the Appendices C and D, these p-values adjusted for false discovery rate, like, for example, on page 46, for all of the mouse and rat studies, these adjusted rates are only within study within sex.

So, in other words, I'm not -- I'm not, you know, penalizing the p-values as much as you would think. I'm actually erring, you know, kind of on the other side, if anything. So that's how these were computed.

MS. ROBERTSON: Judge, I don't want to continue unless it answered your question.

JUDGE PETROU: You can go ahead.

MS. ROBERTSON: Okay.

THE WITNESS: So -- just to make sure you're clear, I want to make sure I'm clear on this, I looked at all 1,016, but as I made the adjustment, I only made them within the study.

JUDGE PETROU: No, I understand that.

THE WITNESS: So, just so you know.

BY MS. ROBERTSON

Q. Dr. Corcoran, would you agree that there is a difference between primary and secondary tumors?

A. Yeah. I think you asked me about this during my deposition, and -- and I agree with that.

Q. You agree there's a difference?

A. Yeah. You -- I think there was some dialogue in my deposition that --

THE COURT: Don't worry about your deposition, just go ahead and answer the question.

THE WITNESS: Oh, okay. Yeah, there's a difference between primary and secondary tumors.

BY MS. ROBERTSON:

Q. At the time you formed your opinion in this case, did you know the difference between primary and secondary tumors?

A. I -- yeah, I think -- I think I understood that. I mean, I wouldn't call myself an expert in pathology, but -- but I understood, in looking at the data from Greim that I was using, that -- that the -- that the -- there were differences between those two.

MS. ROBERTSON: Can we please pull up deposition at page 150, lines 12 to 17?

Your Honors, I have hard copies if you'd would like them, or we're going to put it on the screen.

THE WITNESS: Got it.

BY MS. ROBERTSON

Q. Okay, and there, Dr. Corcoran, you were asked the same question about primary and secondary --

JUDGE PETROU: May I see the hard copy, please?

MS. ROBERTSON: Absolutely.

(Whereupon a document was tendered to the Court.).

THE COURT: Thank you.

MS. ROBERTSON: It's page 150.

THE WITNESS: Could I have a copy of my deposition as well --

MS. ROBERTSON: Absolutely.

THE WITNESS: -- please? Thanks.

MS. ROBERTSON: And for the record, this is Exhibit 379.

BY MS. ROBERTSON

Q. We're at page 150.

A. Got it.

Q. All right, and there, you were asked if you knew the difference between primary and secondary tumors.

A. Uh-huh.

Q. And your response was, "I am not really kind of familiar with the differences between primary and secondary tumors." Isn't that correct?

A. Yes.

MR. GRIFFIS: Could we have 18 through 22 read, please?

THE COURT: Sure.

MS. ROBERTSON: Absolutely.

"QUESTION: So you don't know what a primary tumor is.

"ANSWER: Answer: Well I do. I mean, I

wouldn't say that I'm expert in tumor pathology, no."

Q. So, in fact, the only way you get to the tumor count 1,016 is by counting primary and secondary tumors, correct?

A. Well, what I did to get the 1,016 is I transcribed all of the data from the Greim supplement, and that's how I actually -- those are -- those are the data that I used for my analysis.

JUDGE PETROU: So Dr. Corcoran, are secondary tumors included in the 1,016, or not?

THE WITNESS: Yes, yeah. So whatever was listed in the Greim supplement, that's what I used.

BY MS. ROBERTSON

Q. Dr. Corcoran, can you cite to me a single peer-reviewed article that applies false discovery rate to animal bioassays?

A. Well, the false discovery rate approach is actually now one of the most cited papers in science, and so it's been, you know, very influential. It's very widely applied across all of the sciences.

I think, you know, in 2014, I think it was just a few years ago, the journal Nature, which is one of the most respected journals in our scientific research, they actually listed the 100 most cited papers, not just statistical papers, but papers, period, and the paper that actually suggested the false discovery rate approach was the 60th most cited paper in

science for, you know, the last at least century, and it's the fifth most cited paper in statistics.

So when I say that it's accepted in our field by, you know, people in statistical practice, I think that goes without saying.

The ASA in that statement on p-values that I alluded to yesterday, they actually specifically mentioned it, as well.

Q. Dr. Corcoran, are you an ASA fellow?

A. No.

Q. Can we please look at deposition page 169, lines 21 to 25? Dr. Corcoran, at your deposition you were asked the same question I asked previously,

> **"QUESTION:** Can you cite to a single peer-reviewed article that applies false discovery rate to animal bioassays?"

Your answer was,

> **"ANSWER:** I don't think so. Not off the top of my head."

A. Mm-hm.

Q. Is that still true today?

A. Well, since that deposition, I was interested to see that the EPA actually came out with their -- I can't remember what it's called exactly, but it was a -- it was a report that they issued about glyphosate this past fall, after my deposition, and the false discovery rate approach was actually mentioned.

And so I -- you know, with respect to the toxicology studies of glyphosate and, in fact, that paper -- it's Benjimini and Hochberg.

So I guess I should spell that for you. B-E-N-J-I-M-I-N-I, and Hochberg is H-O-C-H-B-E-R-G.

That's the seminal paper from 1995 that actually gave rise to the false discovery rate and the one that's so widely cited now.

But that paper was actually cited in that EPA report, and so I was interested in what they had to say about it, and so I, you know, I looked at some of the minutes, as well, and Dan Zelterman, who's a colleague of mine at Yale, he actually suggested that it would -- that it was used for the glyphosate toxicology data.

So it was discussed by that Scientific Advisory Panel with respect specifically to toxicology data.

Q. Thank you. My question was whether the statement on the screen is true today. Can you give us a peer-reviewed article?

A. Peer-reviewed article?

Q. To an animal bioassay, sir.

A. It's kind of a funny question, because when you're talking about one of the 60 most influential scientific papers of all time, what that means -- and it's, you know, that's a list that's published by Nature.

It doesn't have anything to do with, you know, the

specific branch of science. It has to do with all of the sciences.

I mean, if a toxicologist would -- would publish in Nature, which he or she would, of course, then, you know, you have to consider that's a paper that, you know, would be useful.

Q. Dr. Corcoran --

THE COURT: Well, but could you -- I mean, could you just answer the question? And then, if you need to explain your answer, that's fine.

THE WITNESS: Oh, okay. Thanks.

THE COURT: You didn't even answer this question.

THE WITNESS: No, but as far as the use of bioassays --

THE COURT: Okay, so the answer is no, right? I take it, the answer is no.

THE WITNESS: No, but I think --

THE COURT: You can now explain why the answer is no --

THE WITNESS: Right.

THE COURT: -- or why you think it doesn't matter, but try to answer her question. So if you need to time to explain your answer to provide context, feel free to do so, but you've got to at least answer the question.

THE WITNESS: Okay. Sure.

So, no, not off the top of my head, with all of that added context.

BY MS. ROBERTSON:

Q. Thank you. And Dr. Corcoran, isn't it true that National Toxicology Program, the NTP, does not use multiple comparisons, including FDR?

A. I really don't know what, you know, what the NTP's requirements are.

You know, what I'm tasked to do in this case is just provide my kind of own independent evaluation just based on my own background and my own expertise, my own experiences.

So, you know, that's what I'm applying here, not -- not regulatory requirements that -- that are esoteric to particular agencies.

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

THE COURT: Any redirect?

MR. GRIFFIS: No, your Honor.

THE COURT: Okay. Thank you very much.

THE WITNESS: Okay. Thanks very much.

(Witness excused.)

THE COURT: Okay, what's next?

MR. MILLER: I think Dr. Nabhan. Your Honor, with the Court's permission, we would call Dr. Nabhan.

THE COURT: Great, and then what's -- just curious,

what's the plan for the defendants after that?

MR. LASKER: We're not calling Dr. Goodman, so we will be calling Dr. Mucci.

THE COURT: Okay, and for Dr. Nabhan, how long do you expect the direct to go?

MR. MILLER: I'm sorry, your Honor. I would say the direct is an hour or less.

THE COURT: Okay, great. Thank you.

MR. MILLER: Depending on what the Court might ask.

THE CLERK: Please raise your right hand.

CHADI NABHAN,

called as a witness for the Plaintiffs, having been duly sworn, testified as follows:

THE WITNESS: I do.

THE CLERK: Please be seated. Speak clearly into the microphone, and spell your last name for the record.

THE WITNESS: Chadi Nabhan. First name C-H-A-D-I, last name N-A-B-H-A-N.

MR. MILLER: Now, I'm going to hand you this water, Doctor, should you get thirsty.

THE WITNESS: Should I trust you?

THE COURT: I have a glass of glyphosate here, if you want.

(Laughter.)

DIRECT EXAMINATION

BY MR. MILLER

Q. How do we pronounce your last name?

A. N-A-B-H-A-N, "NAH-ban."

Q. Nabhan, all right. And Dr. Nabhan, good morning.

A. Good morning.

Q. You have never been an expert witness before?

A. It's my first time. I'm a rookie.

Q. All right, and in order to explain and articulate your opinions here today, did you assist in preparing a PowerPoint?

A. I did.

Q. Okay. Let's go to slide 2, and look at your background, and you can please explain some of this to us?

A. So for the past year and a half, I've been working in administrative and health outcomes research at Cardinal Health as Chief Medical Officer of Specialty Solutions, which is one the divisions within Cardinal Health.

Q. Okay, not too fast, and loud enough for everyone to hear you.

A. And prior to that, I was at the University of Chicago as an Associate Professor of Medicine in Hematology-Oncology. I'm a hematologist and medical oncologist by training. I ran the Clinical Cancer Center, I was director of the cancer clinics, which oversaw all disciplines within cancer care, and I was the Medical Director of the international program, as well, which

looked at getting international patients into the cancer center.

Q. All right, so you're a medical doctor.

A. I am.

Q. And you're a hematologist-oncologist.

A. I am.

Q. And now, you are board-certified in these subspecialties of hematology-oncology?

A. I am.

Q. And how long have you been board-certified in oncology and hematology?

A. Since 2002.

Q. Uh-huh. All right.

A. And in internal medicine since 1998.

Q. Very well, sir. Let's go to the next page of our slide.

A. So this is just a background. The University of Chicago, when I was there, it remains one of 42 institutions of the NCI comprehensive centers which, you know, for the NCI to designate a comprehensive cancer center, it requires good clinical translational basic and preventive medicine research.

Q. You're going to have to slow down, because this lady has been working all week, all right?

So NCI means, of course, National Cancer Institute, right, Doctor?

A. All right, I'll be slow.

Q. Okay.

A. During my tenure there, the last fiscal year we had 48,000 visits, over 5,000 new cases, while I was the Medical Director of the Cancer Center.

Q. It's not on your slides, but I'll ask you now: How many of those were lymphoma cases?

A. I actually don't remember top of my head, so I don't want to misstate. I don't remember the exact number of lymphoma cases.

Q. Estimate?

A. But it's in the thousands.

Q. Okay. So while you were at the University of Chicago, is it fair to say, or not, that you treated non-Hodgkin's lymphoma patients every day?

A. Eighty percent of my practice throughout my career has been lymphoid malignancy and CLL, 80 percent of my publications and research is lymphomas and CLL, which is a form of lymphoid malignancy, as well. So my practice was dedicated to lymphoma is 80 percent of the cases, but 20 percent I did some GU pathology, seeing prostate cancer as well.

Q. Okay, so the thrust of your practice --

THE REPORTER: I'm sorry, I lost you. You did some GU...?

THE WITNESS: GU, which stand genitourinary, so I -- about 20 percent of my practice was prostate, with about 80 to

85 percent was in lymphomas.

BY MR. MILLER:

Q. And before you were a professor at the university of Chicago -- let's go to the next page, please -- if you could tell us about your experience there.

A. So prior to that, I was at Advocate Lutheran General Hospital. It's a large community tertiary hospital, with Advocate Health Care, and in Chicago. I was the Chief of Oncology and Hematology for the five years immediately prior to being recruited to the University of Chicago.

The Director of the Hematology-Oncology program. So I was in charge of training and educating fellows who are going to be future hematologists or oncologists, and the Director of the Cancer Institute at that institution. Then I was recruited to University of the Chicago.

Q. How many future board-certified hematologists-oncologists have you trained in your career, approximately?

A. Many. I mean, I think we all, in oncology we all pride ourselves for being mentors. I think it's probably one of the most satisfying things, to train future physicians who are going to care for patients.

I would say, you know, directly, probably at least 25 to 30 oncologists I have mentored and I've helped in publishing, and writing research and so forth; but we are, you know, as a team, we are indirectly involved in training many of the

oncologists.

Q. Sure, and I don't want you to leave your scientific common sense at the door. Will you only give us your opinions today if you would feel giving comfortable giving those same opinions to the fellows that you train to become future oncologists?

A. Absolutely.

Q. All right, so you were, from 2003 to 2013, at Advocate Lutheran General Hospital.

Let's go to the next slide, if we could.

A. Just start to give you a background of that particular hospital, because it's a little bit different than the University of Chicago. It's over 600-bed community teaching tertiary referral hospital for regional -- for other regional institutions within the area, one of the top hundred hospitals in the U.S.

And my role was there really to, essentially, aside from training and educating fellows, to improve various cancer service lines.

So we've actually built a very robust bone marrow transplant program, neuro-oncology programs, and we received the QOPI certification, which is the Quality Oncology Practice Initiative, which is the highest quality award by the American Society of Clinical Oncology. We did that both at the University of Chicago and at Advocate, which basically it's an award that testifies that these patients are receiving quality

and safe care for cancer.

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

A. So I'm board-certified in internal medicine, hematology, and medical oncology, as we just said. I am licensed in five states.

The reason I received the California license is because I think at some point I'm going to move to California because of the weather. Not sure.

Again, my practice is really focused on lymphomas and CLL, About 80 to 85 approximate percent of the time.

I have seen 30 lymphoma patients a week, at least four to five new patients a week.

All of the community oncologists in the regional area have my cell phone and e-mail, and I was a referral or resource for them, seeing patients, difficult cases mainly, that was referred to me.

Q. Very good, sir. Could we go to the next page of the slide?

A. So really, my past and current research continues to focus on lymphoma; couple of areas, disparities in lymphoma care, very interested in real world evidence.

I think we all can agree that clinical trials don't always represent what happens in the real world. Clinical trials often enroll younger patients, healthier patients, patients who are able to travel, even, to academic sites to get in studies.

So I'm very interested in what happens for the 90 to 95 percent of lymphoma patients who are not in clinical trials.

Q. All right, sir.

A. Heavily engaged in health outcomes research. I have authored or coauthored over 200 peer-reviewed publications, manuscripts and abstracts, and presented my research at national and international meetings.

In fact, I am going to present some of my lymphoma research in Stockholm for the European Hematology Association this summer.

And some of my research are in very high journals such as *JAMA, Journal of Hematology and Blood,* and so on.

Q. Let's go to the next page, please. Are these some samples of the kind of research you've done and published in the peer-reviewed literature?

A. Yes, just one or two, a few there.

Q. And are these in lymphoma?

A. Yes, and all peer-reviewed, obviously.

Q. Very well, sir. Before we get to your general causation opinions, you and I have never worked together before, right, sir?

A. We have not.

Q. In fact, we met last night, but you've been working with our law firm because we asked you to review these issues, right, sir?

A. Yes. Yes.
Q. All right, let's go. And you've reviewed a lot of stuff, let's put it this way. It's in your report.
A. Yes.
Q. All right. Let's go to your general causation opinions, please.
A. So there's a lot of literature out there, and I think, you know, at the end of the day, as a clinician, as someone who treats patients, who sees patients, and who has to decide what is the best approach for patients in terms of treatment, prognosis and prevention -- which is very important -- I'm convinced that there is enough literature and enough evidence to suggest that Roundup® can cause and be a substantial contributor to the development of non-Hodgkin's lymphoma.
Q. And do you hold that opinion to a reasonable degree of medical certainty?
A. I do.
Q. And let me ask you this: If I was a fellow and I came to you and I said, Dr. Nabhan, should I look only at the epidemiology or should I look only at the -- at the biomechanical animal data, or should I look at everything, as a scientist, in order to reach my conclusions, what would you tell me?
A. You really have to look at the totality of evidence. I think it's one of my pet peeves when someone would look at

one part of the evidence, ignores the rest. It's similar to some of my fellows who would -- who used to read the abstract of an actual paper, and not read the actual paper, not read the actual methods, and not read the supplement tables, and the -- the things that are posted online, that are usually just -- are buried, because you're just too busy, you just get to the conclusions.

So you look at the totality of evidence. You cannot just look at one thing versus another.

Q. All right, sir. Now your second bullet point here, we've talked about some in this courtroom this week. Please tell us what this opinion is, sir.

A. Again, there are no -- there are no case-control studies that will be perfect. I think we can critique every single paper that is published. It's part of our role as peer reviewers, and I peer-review every week several articles.

So you can always find the good and bad, in every study. That's always the case, as we --

Q. We didn't -- I'm sorry to interrupt. We didn't go over that in your qualifications. You are actually a peer reviewer for peer-reviewed journals?

A. For clinically-oriented journals, like, again we're looking --

Q. Example?

A. *Blood, Journal of Medical Oncology, JAMA, JAMA Oncology,*

annals of internal medicine. These are clinical journals.

Q. Yes, sir.

A. So in the literature I reviewed, there are some case-control studies that suggested a dose-response effect, which again, confirms my opinion about the association.

Q. All right.

THE COURT: Could I ask a question about that slide? You know, we have those two bullets.

Am I to interpret this slide as saying that the reason you have the opinion in the first bullet is, in insignificant part, because of what is said in the second bullet, that is, the dose-response effect is seen in some case-control studies?

THE WITNESS: Not necessarily, no.

THE COURT: All right.

THE WITNESS: I think in some studies there was evidence of dose-response in terms of the amount of exposure and the duration, and in others not, but I don't believe that -- in other words, even with the lack of -- even if there were no dose-response, I think there's enough evidence from the other studies that I saw and I read to suggest a causation and correlation.

THE COURT: Okay, thanks.

BY MR. MILLER

Q. Let's go on to the next slide, if we could. Explain this slide, three bullet points, for us, please.

A. You know, I honestly think the most important part in this one is bullet three, which is -- again, I'm a clinician, I'm not an epidemiologist or a statistician, but we're on the front line with patients.

At the end of the day, we have to look at what we -- the evidence that we have, when you're sitting in front of a patient who has cancer, and they're asking you, what do I do next, what treatment do I get, et cetera, you need to look at everything and provide an opinion.

So all clinicians -- excuse me -- will look at the totality of evidence, especially when looking at epidemiology studies, and the -- you know, when you look at the totality of evidence and what has been written and published, it is supportive of causality between glyphosate and non-Hodgkin's lymphoma.

Q. And asking you to not leave your real world experience at the door, the Court has asked a question of other witnesses this week:

Have people, in your opinion, knowing what you know now, gotten non-Hodgkin's lymphoma in real world exposures from exposure to glyphosate-based products?

A. In my opinion, absolutely, yes.

Q. And in fact, have you been asked to review files of people who have non-Hodgkin's lymphoma who have been exposed to glyphosate-based products, and put your professional reputation

on the line about whether they, in fact, have a causal connection between the two?

A. I have been asked to do so, and if I didn't believe that, I wouldn't be here.

Q. So -- and we haven't heard this concept in the courtroom yet, but what is a differential diagnosis?

A. Well, differential diagnosis is when you're faced with a patient who have certain signs and symptoms suggestive of a disease, you have to look at what these signs and symptoms might be in relation to. There could be several other diseases that have similar signs and symptoms, right? A person could present with a cough and it could be lung cancer, but it could be just simple bronchitis.

So I think differential diagnosis, when a clinician is faced with a patient who has signs and symptoms but does not know yet the diagnosis and, in his or her mind, goes through what are the possibilities of what this patient might have.

Q. If --

A. And then you go through tests and imaging and so forth to get to the proper diagnosis.

Q. If I were to walk into your office, independent of this courtroom, and say, Dr. Nabhan, you've told me I have non-Hodgkin's lymphoma, and I spent 15 years working on a farm, I've been exposed to Roundup®, would that on your differential now, knowing what you know?

A. So it would be on the differential of possible etiology or possible triggering event developing the disease. The patient -- if I -- if the patient already has the disease, then there's no differential diagnosis for the diagnosis.

Q. Sure.

A. I already know that the person has lymphoma. But in every patient who walks in every physician's office -- and I will challenge any physician -- you always ask about occupational exposure. You always ask, what you do for a living? Do you smoke? Do you drink? Do you do drugs? You ask about these things.

And unless you ask, because you're trying to identify and modifiable risk factor to tell you your patient, maybe you should stop drinking, maybe you should stop smoking, then why are we asking these questions?

And we spend a lot of time asking these questions for a reason, because there are scenarios where patients have certain risks that, if we try to mitigate, we are going to do a better job.

Q. Let's take a look at the next slide. All right, thank you. Yeah, we could go -- I think we've been through that. Yeah, let's go to the next slide, please.

(Pause in proceedings.).

THE WITNESS: Computer malfunction. I can have water.

MR. MILLER: A little machine issue here.

Q. Well, let's not spend a lot of time here. I have a hard copy.

What we're trying to do, since you're the only non-Hodgkin's lymphoma expert who treats patients, I just wanted you to explain to the Court some basic concepts about non-Hodgkin's lymphoma.

A. So I mean, I would say I go through this -- it's back (indicating) it's back.

Q. There it is, all right.

A. So it's a very --

Q. Thank you, your Honor.

A. -- it's a very typical question, and I promise you that anybody in this courtroom that, God forbid, they ever have any type of disease or cancer, the first question that they will ask an oncologist is, Why did I get that? And number two is, What do I do next? And number three, What's my prognosis? And number four, What's the impact on my family? I've done this many times, and these are the four common questions asked.

So I oftentimes answer these questions before being asked this, because I know this is what goes through a patient's mind.

So to simply find non-Hodgkin's lymphoma, just, you know, as a big category, is divided in to T-cell and B-cell, and each one of them, the T-cell non-Hodgkin's lymphoma and the B-cell

non-Hodgkin's lymphoma, they are divided into two major categories. One we call indolent, and one we call aggressive.

So indolent means you might discover it by chance. It's not very fast growing. It may not cause a lot of symptoms right away. And aggressive, obviously, is the opposite.

The classifications have evolved over the years, of non-Hodgkin's lymphoma.

The last classification of non-Hodgkin's lymphoma was published in *Blood* in 2016, by Swerdlow and colleagues, and that's the last classification, 2016, where we know now we have over 60, six-zero, types of non-Hodgkin's lymphoma. Thirty years ago, we thought we had only ten.

So the improvement in classifications mirrors our better understanding of disease biology. We understand a little bit better about each disease.

And this classification actually does help us as clinicians, in terms of assisting prognosis and deciding on treatment.

When we look at causation and when we talk about occupational hazards and so forth, it is very difficult, nearly impossible, to look at that for every single subtype of 60 of them.

So when we look at causation, we look at non-Hodgkin's lymphoma as a big umbrella. That's how we view it, as clinicians. It's very difficult to say, oh, I want to know

exactly the cause of this particular type. Sometimes we can, and we have certain associations between infectious agents and certain viruses and particular rare subtypes of non-Hodgkin's lymphoma.

I mean, an example, *H. pylori* is associated with a form of non-Hodgkin's lymphoma called "MALToma." It's rare, but we know it's associated with it.

But for the most part, when we look at causation, we look at the entire disease.

Q. And in fairness to Monsanto, sometimes there's non-Hodgkin's lymphoma that's we just don't know the causes, right?

A. I have taken care of many patients --

Q. Sure.

A. -- with non-Hodgkin's lymphoma that we have no idea why they have it, and I'm not suggesting whatsoever that every non-Hodgkin's lymphoma is caused by glyphosate --

Q. Of course not.

A. -- at all. What I'm suggesting is that there's a subset of patients with non-Hodgkin's lymphoma that have developed the disease because of this exposure.

And I think identifying this risk would be very important now, and moving forward, to prevent future cases and to help some patient.

Q. Are they called modifiable risk factors?

A. Modifiable risk factors.

Q. And is that something that clinicians seek, to modify the behavior of the individual so that they would avoid the risk factor?

A. We do it every day in clinic and outside of clinic. There's a reason why we tell people to wear seat belts.

Q. Sure, or protective suits.

A. Right.

Q. Now, we've talked in this courtroom about latency, and as a non-Hodgkin's lymphoma expert, I'd like to hear your opinions in that regard.

A. So it really differs widely, and I think it's really -- and I have some examples just to illustrate my point.

It's very difficult to answer the question of what is the latency of non-Hodgkin's lymphoma, which is, from when you were exposed to an offending agent to the time of developing a advisable tumor. This varies widely. And I've said that previously.

Some cancers could develop in less than year of being exposed to a carcinogenic agent. Some could take much more time.

I put a quote here from the EPA, but if you move to the next slide on there, these are other quotes in terms of what the latency.

But I'll -- I want to show the two examples that -- there

are many examples I could bring in just to explain how the latency actually differs in patients.

There's an example that I -- well, before we go to the example, this is -- no, the next one, the World Trade Center. Yeah. So this is from the World Trade Center Health Program, and they state -- and I completely agree with the statement, because this is what we see in clinical practice. I mean, at the end of the day, we can look at numbers for weeks and weeks and weeks, but this is what happens in real life. This is what happens in real world.

It could be as early as 0.4 years, they said, based on low estimates, useful lifetime risk, and it could be much higher than that. And the two examples that I'm going to show you just illustrates this particular thing, because it's really what we see in practice.

So this is -- this is just an example. This is a paper that I actually helped with, although I'm not a co-author on it. So "PTLD" stands for post-transplant lymphoproliferative disorder. This is a form of lymphoma that occurs after solid organ transplantation.

So solid organ transplantation is the triggering event. Patients receive -- undergo solid organ transplantation, and then they are placed on immunosuppressant agents, so you won't reject the organ that you received. So the solid organ transplant and the immunosuppressants are the triggering event

that these patients have.

If you look at the arrows, this study showed that patients develop PTLD at a median time of 48 months. The range is one month to 216.

I have seen patients who get the solid organ transplant and a couple of months later, they develop this type of lymphoma. So they have had no risk factors prior to this trigger event. Their latency period was very short. They developed the disease. Others may take 216 months until they develop the disease.

Another example, in the following slide.

Q. Before we go to the next example, just to keep the record clear, they developed one within month up to 216 months PTLD, what is PTLD?

A. It's a form of non-Hodgkin's lymphoma.

Q. Okay.

A. But about five percent of PTLD could be Hodgkin. So PTLD stands for post-transplant lymphoproliferative disorder.

Q. Thank you.

A. So this is a form of lymphoma. Ninety-five percent are non-Hodgkin's, there's about 5 percent of these PTLD that are Hodgkin.

But the point I'm trying to make here is not the actual -- it's a lymphoid malignancy, and the latency is impossible to predict. In clinical practice, we don't even look at -- we

don't -- we stopped trying to predict.

JUDGE PETROU: So this is related to transplants and immunosuppressant drugs.

THE WITNESS: But that's a triggering event.

JUDGE PETROU: No, I understood. And I think I know the answer, but I want to be quite clear: You don't have a basis for determining a range of latency periods for non-Hodgkin's lymphoma based upon exposure to a pesticide, herbicide, something of that nature.

THE WITNESS: Yeah, my opinion is, it could vary. It could vary.

Again, you know, I view the chemicals or pesticides and so forth as triggering events, as an offender event, as a problem that this patient or this individual has.

So similar to this offending event, similar to this offending example, it could have short-term or long-term.

JUDGE PETROU: Based on a variety of factors.

THE WITNESS: Variety of factors.

JUDGE PETROU: Okay.

THE WITNESS: And the next example actually illustrates the exposure to chemotherapy. So the next example -- this is another example in terms of: When do patients develop treatment-related AML, which stands for "acute myeloid leukemia," or MDS -- myelodysplasia -- after bone marrow transplant? Bone marrow transplant, usually patients

receive high-dose chemotherapy, so they get chemicals, they get the chemotherapy.

And if you look at the arrow I have here, they developed this hematologic malignancy from four months to six years.

In heme malignancies, it is very difficult to say that a patient needs 20 years to develop something, or one year to develop something. We have seen it all over. And if you ask most hematologists and most folks who treat leukemia and lymphoma, they will tell you it could be very short; it could be very long.

And these are two examples. One of them -- both of them had a triggering event. That's why I brought them up. And there's not enough time to bring so many examples. More than happy to provide a lot of literature on this that shows you such a wide variation of latency.

BY MR. MILLER

Q. I think we're going to skip the explanations of the medical -- let's look at one or two, but let's see the next slide.

Real quickly, if we could move off of latency, and we're done now. Unless the Court has any questions, we're done with latency.

A. Sure. This is just, I guess, the explanation of the lymphatic system. You can keep moving.

This is the lymphatic system part of the -- again, it

helps -- B-cells and T-cells, like we talked about.

Next slide.

The B-cells usually produce antibodies that fight infections. The antibodies recognize prior offending pathogens that they may have been exposed to.

The T-cells usually do two things. They try to push -- they help the B-cells to do their job, and they also do their own job in fighting infections, as well as cancers.

In fact, a lot of the advances that you are hearing about in the news over the past couple years are working on the fact how can we manipulate the T-cells to do a better job in fighting cancer.

So non-Hodgkin's lymphoma, as we just talked about on the previous slide, could develop from T-cell or B-cell. And T-cell usually is worse than B-cells, in terms of prognosis and outcomes. The only way to differentiate between both of them is to do a biopsy. And there are about 60 types, as we talked about.

Next slide.

Again, there's not a whole lot here to say, except the fact that the lymphoma is part of the -- you know, when patients have lymphoma, it affects their immune system, so they are prone to the disease itself and to the infectious complications.

Next. Again. Next.

This leads to lots of organ dysfunction.

When I look at etiology of how certain offending agents may cause lymphoma, it's not -- I mean, again, it's always a matter of beautiful papers that are written in many peer-reviewed journals, but the reality is, nobody knows hundred percent what actually happens.

Oxidative stress is one proposed mechanism by which, you know, the cells are unable to fight the free radicals, and they are damaged. So this actually leads to the possibility of development of cancer in non-Hodgkin's lymphoma. There's good data that non-Hodgkin's lymphoma could develop from oxidative stress.

Q. This next slide, Progression to Tumor, can you talk about this in the context of what we call the two-hit theory of cancer?

A. Yeah. I mean, there's a lot to talk about this slide, so I'll try to simplify it.

And I think, you know, when you -- when you go -- when you see the word "chemical," and this could be -- think of it as any offending problem, offending agent. The example that I gave you for those two diseases were, one was bone marrow transplant, the chemicals, the chemotherapy one was the immunosuppression and support, but basically, an offending agents could cause an oxidative stress that damages the normal cells. The DNA damage could subsequently lead to having

additional mutations that you can't repair. The system is unable to repair the mutations that have evolved. And then, additional stressful events could occur that lead to the development of cancer.

So the type of offending agents -- or we're calling here "chemicals" just for simplicity -- could interfere in any part of this particular flow.

So you could have a chemical that is affecting the development or the evolution from normal cells to damaged cells, but as an additional triggering event that occurs after that, that might speed up developing a mutation, or speed up development of cancer.

It's a theoretical model. I think, as a clinician, my advice always to patients and families and people that we talk to is, at the end of the day, it may be very difficult to know when this particular thing happened, but this is what we can do to maybe prevent it from getting worse, and maybe what you can do to mitigate that problem in the future, and this is what you should do to move ahead and treat.

Q. All right, next slide, please.

All right, just a few comments on epidemiology we'll come back to if the Court wants to go through each study, but you've prepared this slide. Explain it to us.

A. Again, I'm not a an epidemiologist, but I did look at the epidemiology literature, because I think it's important to look

at. Ultimately, I think every epidemiologist will acknowledge that every study has its own merits, its own flaws. It's just the way it is. It's like every clinical trial.

Q. Have you seen that, as a peer reviewer?

A. Of course, the world is not perfect. It's just the way it is.

Q. Have you ever gotten a draft article from someone that wants to be in a peer-reviewed journal and you wrote on it "perfect study, absolutely flawless"?

A. I have never done that, and I think if I do this, the editor will call me and say, "What's wrong with you? There's a conflict of interest right there."

Q. Okay.

A. So it just doesn't happen, and that's why, anytime you look at peer-reviewed literature and you look at the footnotes you look at when the paper of received, and when the paper was revised and when the paper was accepted.

And I can tell you, every time I see that the time from received to revised very short, my eyebrows usually rise, because I'm thinking, okay, this was not given enough time to even look at, formally.

So again, some studies are good. Some studies -- no study is perfect, but as a clinician, you have to take the weight of evidence and make sense of it.

Q. Would a responsible clinician look solely at the epi- --

I mean, we've had some great questions, frankly, and one of them is: Does the epidemiology, all by itself, prove causality here? What's your opinion on that?

A. You can't just take epidemiology, right? I mean, I think you look at the epidemiology studies and then you try to link this with -- okay, epidemiology is very suggestive. Are there any reason to think there's some mechanistic evidence that this agent may cause problems, on the DNA level, on the cellular level? Then, is there any animal studies that may support some of this?

So then you need to look at all of this. And a lot of it -- from a clinician's view, we don't really sit down and re-analyze and re-perform a peer-review process for every single paper that has been published. It's already peer-reviewed. It's already published. It's done. My job as a clinician is not to peer-review the entire literature again.

Again, maybe look at other bodies and other experts who do this, and who do this such as the IARC, and I looked at the IARC very thoroughly, and I firmly believe in the conclusions of the IARC, and that actually makes a huge difference for us as clinicians.

Q. All right. I think you've now anticipated the next slide. Let's go to it, please.

A. So -- no, I think there's one before this, yeah.

Q. I'm sorry, go ahead.

A. Again, so from a clinician's view, we look at the totality of evidence. We do review epidemiology studies but we do consider the source. We try to look at this to the extent possible.

So looking at the evidence, when we look at the source and we look at a body such as the IARC, which was formed in 1965, has 25 member countries, meets three times a year, and the goal is just to assess the carcinogenicity of compounds, and then they've published these in *Lancet* and *Oncology*, I went back and I wanted to understand, well, what was the history of IARC? Why should I really believe what the IARC says?

Can we move to the next slide, please?

Q. Sure.

A. So here's the historical perspective. The IARC has assessed over 1,000 compounds so far. So 1,003 compounds, to be precise. International perspective and collaboration. Outside stakeholders are allowed to be there, and to observe.

And they don't take every agent that you tell them, okay, go take a look at this for carcinogenicity. No, they don't. You have to prove that there is enough human exposure to get the IARC's interest, and there's enough animal data and some studies to support that it's worth the time for the IARC to actually even look at these compounds.

And after all of this, very few agents the IARC would suggest that they are carcinogenic.

So from 1,003 compounds, only 120 were labeled as carcinogenic, 12 percent, and only 8 percent, 81, are probably carcinogenic.

So the totality, with all they've done, they came up with 20 percent of the 1,003 that either are carcinogenic and probably carcinogenic.

So the IARC is not out there to label everything as carcinogenic. In fact, 80 percent, they say they're not.

So as a clinician, I will look these epidemiology studies, then I look at bodies such as the IARC, I look at the history, and it's hard to argue, with all of the data that the IARC looked at and with the history, so I tend to obviously believe the data that came out of IARC.

Q. Sure. Go to the next slide.

We've heard a lot of discussion the Agricultural Health Study and the Agriculture Health Study updated report from Andreotti.

Do you want to weigh in on this? You have a slide.

A. Sure. So first, I think, you know, it's important to put into perspective that this study was actually looked at by the IARC, and it was actually taken into consideration by the IARC. So it was not necessarily ignored.

Q. The original study?

A. The original study.

Q. Sure.

A. So all of what this, to me -- again, I'm talking wearing my clinician's hat, and I think all of this is, is an updated analysis, in my mind, for an already flawed study.

The intent of the Agricultural Health Study was actually very good. The plan was very good. They actually wanted to figure out all of the these exposures and so forth.

But the study, by itself, has so many flaws, so it's great that we keep getting updates of flawed study, and I'm sure there will be additional updates in a few years, but it doesn't change the fact that there were so many flaws in this study, it's impossible to draw any conclusions.

You have 37 percent loss of follow up, and in the subsequent questionnaires, in Phase II and III, when you ask --

Q. Let me stop you right there. Did you go online and actually look at the questionnaire?

A. I -- I did, not all of them, because each one was 28 pages --

Q. Okay.

A. -- but I did look at a couple of the questions for Phase I and Phase II, yes.

Q. Okay, and -- well, did you have any concerns about that?

A. There are two major concerns. Just -- if I may.

The bullet point 4 is a very important part that I found -- it's intriguing, and it's actually written in the Methods section of the *JNCI* paper.

So participants that completed the questionnaire -- so in Phase II and Phase III -- they completed that answering only about their exposure for the one year immediately before they answer. So it wasn't for the duration of since the last time you actually answered. It was just for the one year immediately before.

So if you look at the Methods section of the *JNCI* paper, you will see that very well spelled out.

They say, you know, the respondents, they actually answered for the one year immediately before they answered the question. Well, that's only one year. And that's really an issue.

Q. Well -- I'm going to stop you there.

So in 1993, when they started, somebody fills out the questionnaire and they go, "Never used glyphosate." In '94, with the growth of the use of glyphosate, they used glyphosate, they use glyphosate in '95, they use glyphosate in '96, they use glyphosate in '97. They got non-Hodgkin's lymphoma. Are they listed as an exposed case or a non-exposed case?

A. Non-exposed, because they answered in 1992 that they were not. But not only this. I mean, this is one piece. But I'm going to even take you to the Phase II.

So on the Phase II questionnaire, as a respondent, you answer only for -- so if you're answering the question, you know, Phase II, let's say, 2003, right?

Q. Yes.

A. If you're answering the question in Phase II between 2003 and 2005, you are supposed to answer based on your exposure for the one year immediately before you are handed the questionnaire.

Q. And that's the questionnaire --

A. So you could be exposed in 1998, 1999 and 2000, but if you were not exposed in 2002 and you are answering in 2003, you are non-exposed.

Q. So you could have used six years' worth of glyphosate, but not the year before you filled out the second part --

A. Exactly.

Q. -- and you're constantly unexposed --

A. Exactly.

Q. -- even though you've had six years of exposure.

A. That's written in the Methods section of the *JNCI* paper.

Number two is, you already have significant dropout in terms of the -- you know, the folks who answered, on number 3 the control arm, the arm that was technically not supposed to get glyphosate, was -- had a high increased risk anyway. They were farmers. They were pesticide applicators. So they actually had higher risk of developing non-Hodgkin's lymphoma.

So when you choose the control group as a group that already has higher risk of non-Hodgkin's lymphoma, and you lose 37 percent of respondents, and a lot of folks are going to

answer non-exposed while they were exposed, and the glyphosate exposure is actually increased during the time period of the study, it is impossible to have to have a positive finding in the AHS. Of course it's going to be negative, because so many flaws.

Q. Let's go to your next slide, then, the real world implications of all of this.

A. Well, I mean, the real world implication is, at the end of day, you are faced with patients who have a disease, and again, if you have been with a friend or a family member or anybody, the first thing you ask is, why did I get this?

Unfortunately, in the majority of cases in lymphoma, our answer is, we don't know. That's the reality. We don't know why most patients get non-Hodgkin's lymphoma.

But there are situations that we do. There are situations that could be something linked to an occupation, something linked to a situation that you have, and that's when we tell a patient, I think this is why this occurred, and my advice to you is not to do this occupation or not do this function, because it may slow the progression of your disease, it may cause slowness of it, or it may prevent another type of lymphoma you have.

Q. And that's what we want from your real world opinions.

If you were with a patient tomorrow and they had symptoms of possibly having hematopoietic cancer and told you they were

applying Roundup®, would you tell them that's a modifiable risk factor?

A. Yes. I would.

Q. Okay.

A. Absolutely.

Q. All right. Finish looking at your slide here, if you would, sir.

A. Again, it says -- I think it's repeating some of the things that I've already mentioned in terms of the dose-response, in terms of trying to look at the totality of evidence.

We can move to the next slide.

Q. Okay.

A. This just has my view of how important it is to patients.

You know, we can talk a lot about p-values, and so forth, and I think it's really important to think that there's statistical significance and there's a clinical significance.

There's absolutely no magic in 0.05. This was an arbitrary number that was chosen, so you could level set when you look at clinical trials.

So there are many studies, in fact, in oncology that show drug A is better than drug B, with a statistical significance of 0.05, but it adds 10 days of life. Some of these papers were published in the *New England Journal of Medicine*.

How clinically significant is it? So again, it's a matter

of numbers. So clinicians care about the clinical significance of the data, not just of the p-value. Yes, we take p-value, yes, we look at all of this, but ultimately, what's clinically significant?

And I think there's enough evidence out there to suggest that the exposure to glyphosate have clinical significance in terms of causing and contributing to non-Hodgkin's lymphoma.

Q. I'm going to diverge from your PowerPoint for one second.

You did -- I'm going to just walk through and get it on the record if you reviewed these case-control studies, and if they formed a piece of the puzzle for your opinion.

The McDuffie study that we've talked about a lot here, 2001, did you review it, read it?

A. I have. I may not remember every single word, but I have.

Q. I understand, and it's got some issues that we've discussed, like all studies have, but did it form a piece of the puzzle for your opinion?

A. Yes.

Q. Okay, and Hardell 2002, was that a piece of the puzzle for your opinion, as well?

A. Yes.

Q. And it was not a perfect study either, was it?

A. There are no perfect studies.

Q. Okay, and De Roos '03, you reviewed that, and was that a piece of puzzle?

A. It was.

Q. Okay, and we've talked about AHS.

You did you review the Eriksson study 2008, and was that a piece of the puzzle for your opinion?

A. I did, and it was.

Q. Okay. You also reviewed the meta-analysis of Schinasi and Léon?

A. I have.

Q. And was that a piece of the puzzle for your opinions here?

A. Yes.

Q. And lastly, the meta-analysis of Chang and Delzell, you reviewed that, and was that a piece of the puzzle, formulating your opinions?

A. I have.

MR. MILLER: I don't know if the Court has any questions about the technicalities of these studies. I leave it to the Court.

Q. All right. Let's go, then, to your Conclusions slide.

A. So after systematic review of the literature, both epidemiological and other studies, applying the Bradford-Hill Criteria, holds an opinion that glyphosate exposure can and does cause non-Hodgkin's lymphoma in patients.

And again, this is just totality of evidence. It's very easy to poke a problem in every single study. I can do it myself. But at the end of the day, we have to look at the

totality of evidence, and that's what I did.

MR. MILLER: Thank you very much. Please answer the questions of the Court or counsel for Monsanto.

THE WITNESS: Thank you.

MR. MILLER: Thank you, your Honor.

THE COURT: How long do you plan on cross being? I wanted to see if now is a good time for a morning break.

MR. GRIFFIS: Twenty minutes or less, your Honor. We can certainly break, if you'd like.

THE COURT: You want to break? Yeah, let's break now, and we'll resume at half past.

THE CLERK: Court is in recess.

(Recess taken from 10:25 a.m. until 10:36 a.m.)

MR. GRIFFIS: I have some materials to hand out.

(Whereupon a document was tendered to the Court.)

MR. GRIFFIS: We have the binder for everyone we should, but do not yet have the three exhibits that we handed up copies of --

THE COURT: We got them.

MR. GRIFFIS: -- for your clerk. We just don't have quite enough yet. We'll resolve that later. I'm sorry.

CROSS-EXAMINATION

BY MR. GRIFFIS:

Q. Could we pull up first a copy of the slide 39 from the direct examination? Thanks.

A. Is this 39?

Q. Yeah, it's the same as 39 that was used in the previous examination, sir. This is our copy of it. Do you recognize that?

A. I do.

Q. Okay, and you see in front of you a document labeled, "Key Characteristics of Carcinogens as a Basis for Organizing Data On Mechanisms of Carcinogenesis," by Smith and others, sir?

A. Yes. It's a review article.

Q. It is, and do you see that author -- the second author and the last author Kathryn Guyton and Kurt Straif, do you recognize them as IARC executives?

A. I recognize Guyton and Straif.

Q. Okay. Do you see Christopher Portier at the end of the first line there?

A. I do.

Q. And do you know, sir, that this is one of the documents that IARC uses in assessing mechanism of cancer? This is the list of the 10 key characteristics of carcinogens when they're doing the mechanism analysis for IARC reviews these days; do you know that, sir?

A. I don't know if they use this. I did not know that. No.

Q. Okay. They do, and we will look at the monograph in a moment.

But take a look at the Discussion section. So that we can

see the list of the 10 key characteristics of cancer. This is the Discussion section.

A. Which page?

Q. In the abstract.

A. Okay.

Q. Okay. So we have labeled 1 through 10 the key characteristics of carcinogens that IARC looks at, and I'd like to point out that number 2 is genotoxic and number 5 is oxidative stress, and we all know that IARC found that there was strong evidence for those mechanisms, correct?

A. Yes, we do.

Q. Okay. Now, take a look, please, at number 3, "Alter DNA repair or cause genomic instability."

Chemicals that alter DNA repair or cause genomic instability, of course, can promote carcinogenesis by the mutagenic effect of those actions, right?

A. I don't think we know the exact mechanism of how this would occur after the genomic instability. Nobody really knows. All what we know sometimes is the genomic instability could occur upon exposure to something. What happens afterwards is really not well defined or discerned.

Q. On your chart, sir, "Altered DNA repair would have impact at the level of DNA repair," correct? It's on the slide in front of you.

A. I see that. This does not necessarily happen for every

carcinogen in that exact manner.

Q. Oh yeah, I understand.

A. Some causes one versus the other, and so forth.

Q. Yes, sir. I'm pointing out right now -- what we're pointing out right now is how various mechanisms of carcinogenesis, so that you'll understand, affect different parts of this process.

A. I understand.

Q. Obviously with other carcinogens, because IARC didn't find these mechanisms with regard to glyphosate, right?

A. Yeah, I understand. I just want to make sure to point out that there are -- we don't always know the mechanism of carcinogenesis of known carcinogens. So there were two important issues here. I want to make sure I go on the record of saying that.

Q. We don't know for glyphosate.

A. No, I didn't say for glyphosate. What I said is, we don't always know the exact mechanism of action of carcinogenesis for every carcinogen.

Q. And we don't know for glyphosate, right?

A. We sometimes have suggestive mechanism of action. We have evidence that this is how it may happen, how it may occur, but we don't always have an absolute, that this is the only way that carcinogenesis would occur, and no other way. We may find out in the future. I don't think anyone in this courtroom can

tell me how tobacco causes lung cancer.

Q. Sir --

A. We know it's a carcinogen.

Q. -- you don't claim that you know a mechanism by which glyphosate has causes cancer, right?

A. We have suggestive mechanisms through oxidative stress and genotoxicity. I said that we don't know if these are the only mechanisms by which glyphosate could cause cancer or non-Hodgkin's lymphoma. We may find other mechanisms the future that may be different than the current understanding.

Q. Number 7 is Immunosuppressive, right?

A. Yes.

Q. You have a section of your chart labeled, "Immune System, Chemical affecting the immune system." Immunosuppressive carcinogens would act in that section of the process, correct?

A. I see that, yes.

Q. And non-Hodgkin's lymphoma is fundamentally tied to the immune system, in that lymph cells are immune cells, right?

A. We would consider that correct, in terms of, it's somewhat of an immune system disease.

Q. And let's look quickly at number 9 and number 10. "Immortalization," which is a process by which cells that aren't supposed to be immortal become immortal and never die, which is real bad because we want our cells to eventually die once they stop being useful, right?

A. Yes. We would like to have a balance between cell survival and cell death.

Q. And then --

A. And whenever that balance goes towards survival of the bad cell, then there's a problem, pretty much in almost the majority of cancers. That's really how cancer develops.

Q. And 10, "alter cell proliferation, cell death or nutrient supply." So numbers 9 and 10 would act at the level of uncontrolled growth of mutated cells, that last box there, right?

A. Just the -- as it's stated, in terms of immortalization, affecting nutrient supply and cell death and proliferation.

Q. On your chart, that's where it would act, at the end, right?

A. It could be related to the -- any part, in terms of, you know, when the cells are mutated and then they develop into cancer, that's because there's no apoptosis, there is no cell death and the cells continue to proliferate.

So cancer, in general, just cancer, is overgrowth of cells, and that's literally why we have cancer that could occur in every body organ. It's a lack of balance between cell death and cell survival.

Whenever that scale tips towards cell survival of the malignant cell, these cells continue to proliferate, and eventually they become visible as tumors or as cancers on an

X-ray or clinically. So in every cancer, this is what you will see, this balance between cell survival and cell death.

Now what triggers this? What tips one way or the other? It's always up for debate, and sometimes it's well studied and well known. Sometimes it's not.

Q. In Exhibit 1030, sir, the IARC Monograph -- which I believe is in the record already -- would you turn to page 78.

A. That's a very abbreviated version of that IARC Monograph.

Q. It is, sir. In order to save trees, I left off the parts --

A. It's only three pages of a hundred-page document, so I hope I can answer the question.

Q. You can have my copy, with the full version --

A. I answer in context, that's what I mean.

Q. Okay. The context is section 5, where the results of the Working Group are given with regard to mechanism. Do you have Section 5.4 of the relevant data where mechanism is described?

A. 5.4, yes.

Q. Okay. On page 78, first line of the first full paragraph, do you see that the Working Group reported,

> "There is weak evidence that glyphosate or glyphosate-based formulations induce receptor-mediated effects"?

That's one of the key characteristics we didn't talk about. Do you see that?

A. I see that.

Q. And have you read the preamble before?

A. I -- I have not yesterday.

Q. Okay, and do you recall from your reading of the preamble "weak" is the lowest category for mechanism evidence, when there is any evidence?

A. Yeah. So let me just explain. It's a very important point, because that's why sometimes you say, mechanisms of action, and there are scenarios where a particular compound or a disease that you know how this disease developed or how this, or how A caused B, but it doesn't always happen across the board. So you don't have all mechanisms of the reason why cancer develops occur for every particular compound.

Q. Okay.

A. So some compounds may actually trigger cell survival. Some may prevent cell death.

Q. If it will help you, sir, I'm not trying to argue that any carcinogen has all 10 characteristics. So you don't need to counter me on that point.

A. I didn't review this particular evidence, but if the IARC says this particular aspect of the mechanism of action is weak, then it's weak.

Q. Okay, and cell proliferation or death is addressed in the next. "There is weak evidence" -- this is the top of the next paragraph -- "that glyphosate may affect cell proliferation or

death." Correct?

A. Yes, I see that.

Q. And the question I asked before, actually, I don't think you answered.

Do you remember, from when you read the preamble, that "weak" is the lowest category description that they have that they list for mechanism evidence?

A. I don't, but if you have it, I can look at it.

Q. I do have it, sir. It's in front of you. It's Exhibit 1049, page 21.

THE COURT: It's one of the loose documents.

THE WITNESS: Yeah, I just saw that.

BY MR. GRIFFIS

Q. Yeah, the last of the loose documents.

A. Which page?

Q. Page 21. They're describing their procedures under header C for Mechanistic and Other Relevant Data. At the top of the second paragraph, they describe the terminology, the strength of the evidence, that "any carcinogenic effect observed is due to a particular mechanism is evaluated using terms such as 'weak', 'moderate' or 'strong.'"

And obviously, the weakest term that they give there is "weak." Right?

A. Yes.

Q. Okay. Weak evidence is also in the monograph. Back to

page 78 of Exhibit 1030, in the next paragraph.

A. I'm sorry, are we...?

Q. We're back to the monograph, exhibit 1030, page 78.

A. Okay, mm-hm.

Q. And we're on to the next paragraph.

"There's weak evidence that glyphosate may affect the immune system, both the humoral and cellular response."

Correct?

A. Correct.

Q. And then finally, to wrap this up, the next paragraph.

"With regard to the other key characteristics of human carcinogens -- "

JUDGE PETROU: Counsel, you're reading really quickly.

BY MR. GRIFFIS

Q. (Reading:)

"With regard to the other key characteristics of human carcinogens, the Working Group considered that the data were too few for an evaluation to be made."

Right?

A. Yes, that's what it says.

Q. And like IARC, you aren't claiming evidence for mechanisms other than oxidative stress and genotoxicity, right?

A. I believe these are the suggestive mechanisms. I don't believe that anyone knows necessarily hundred percent the mechanism. And frankly, clinicians, as clinicians, we don't always necessarily -- it's nice to know, it's good to know. It provides an intellectual and intelligent conversation amongst colleagues and peers, but at the end of the day, the mechanism of action is not really that critical if you know something is causing a problem.

Q. It doesn't matter too much for a clinician, right?

A. I said, it matters. It doesn't matter that much if you're already convinced that there is a problem that occurs.

And I actually give you an example of tobacco association with lung cancer and bladder cancer. I think everybody in this room is convinced, hopefully -- if not, we have to talk outside the court -- that smoking and tobacco use does cause the majority of lung cancers, 95 percent, and the majority of bladder cancers.

We may not know how. We may not understand how. But just because I don't know how, I'm not going to call my patient and say, "Go ahead and smoke."

So I think it's very important to understand that we'd like to know the mechanism of action, we'd like to understand it, but clinicians care more about whether a problem has occurred and what to do about it.

Q. Take down the slide, please, Scott.

Dr. Nabhan, you can't say that glyphosate increases the risk of non-Hodgkin's lymphoma by 1 percent, or 15 percent, or what, right?

A. In some studies, it doubled the risk. In some studies, the odds ratio is 1.5. I think it increases the risk. I think studies are not always consistent in terms of how -- what is the incremental risk that we are talking about.

Q. I'm talking about the actual risk that you believe glyphosate actually increases in the real world.

A. And I think I just answered.

Q. We talked about that and you've said, "I can't say. It could be 1 percent, as far as I'm concerned." Right?

A. I actually didn't say it could be 1 percent. What I said is that it in some studies it has shown to have an odds ratio of 2 plus. In others, it was less than 2.

So the studies have shown increased risk of exposure to glyphosate with the development of non-Hodgkin's lymphoma.

To quantify that risk, there is a lot of controversy over this, and I'm not really sure that we know exactly what that quantification is, but it exists, and accordingly, it exists enough that we need to tell patients and people who actually use that agent about it, so we can prevent this from happening further.

Q. So is it true or false that it could be 1 percent, as far as you're concerned?

A. I don't know. I can't speculate. You're asking me to speculate, and I don't think I can do that.

Q. Okay. You've told me in the past it could be 1 percent, right?

THE WITNESS: Do I repeat the same answer, your Honor?

BY MR. GRIFFIS

Q. We can show you. Do you see, in tab 3 of your binders?

A. It could be a hundred percent. I see what you're saying. It could be 1 percent, it could be a hundred percent. My point is --

Q. You don't know?

A. -- I can't quantify the risk. In my mind, the risk is clinically significant enough that patients need to be aware of it. Now, you may think 1 percent is not clinically significant, somebody else may think clinically 1 percent is significant. Some people --

Q. Would you turn --

A. -- might say a hundred percent is not significant. To me, I think that's an individual thing, but the risk is not zero. It exists, and accordingly, we need to make sure we modify it to prevent this from happening to other patients.

Q. Would you are turn to your expert report, sir?

A. Sure. Where?

Q. It's in your binder. I don't have the same tabs that you

do. I think it's 3.

A. Tab 3, you say?

Q. I believe so. Is that right?

THE COURT: I think it's 1.

BY MR. GRIFFIS:

Q. 1, I'm sorry, tab 1, and turn to page 11 of it.

A. Page 11?

Q. Yes.

A. Sure.

Q. And do you see there under the large header, "Assessment of Carcinogenic Risk in humans," first header, sub-header "Epidemiological Studies," you started discussing the McDuffie study in the first paragraph?

A. I see that.

Q. Okay, and you said, in describing the McDuffie study, and this is about the middle of the paragraph,

> "Among major chemical classes of herbicides, the risk of NHL was statistically significantly increased among glyphosate-exposed individuals with an odds ratio 1.26, 95 percent confidence interval, 0.87 to 1.8,"

and we talked about that sentence when we had your deposition, right?

A. Yes.

Q. Okay. And you -- when you say, "statistically significant," what I learned, sir, is that when you say, "statistically significant," what you mean is an odds ratio of above 1.0, whether it's p-value of less than .05 or not, right?

A. I think -- and I just alluded to that earlier. There's -- the statistical significance is the p-value of 0.05, but there's nothing magic about the 0.05, and we have to always think of clinical significance as we look at many of these studies.

So if you continue to the second paragraph of this --

JUDGE PETROU: You know what, I need to take a five-minute break.

(Recess taken from 10:54 a.m. until 10:59 a.m.)

THE COURT: Everyone back?

BY MR. GRIFFIS

Q. Dr. Nabhan, you rely heavily on IARC for your opinion that glyphosate causes non-Hodgkin's lymphoma, correct?

A. I do.

Q. With regard to the -- you know what I'm talking about when I say the AHS 2018 study?

A. That's the *JNCI* paper?

Q. Yes.

A. Yes.

Q. You agree that the NIH funding that funded that paper and the project -- the whole AHS project -- means that high

standards and best practices were used in gathering and assessing the data, right?

A. No, I don't agree with that. I agree that it was well-intended when it first started, and obviously, it was a very important project to do. The intentions was very well conceived at the time, it was funded and so forth, but this does not mean that the way the trial actually took place necessarily was not flawed. There's a difference.

Q. Let me ask the question again.

Do you agree that the NIH funding means that high standards and best practices were used to ensure that the data was accurate?

A. I think I answered that. What I said is that the NIH funds studies that they believe are important to the public, and that was the intent, clearly.

But unfortunately, as the trial and as the study went on, there are so many flaws that took place that still, the NIH continued to fund it and has to report and so forth, but just because you fund a study, it means that you believe in the importance of the study, but you know, the NIH didn't intentionally say, we need to have 37 percent of people not answer questions. They would have liked for people to answer, but it happened.

So it doesn't mean that there are no flaws of the study just because the NIH funded it. I mean, that's saying that

anything that is funded by the NIH and the NCI, I cannot critique, which is not appropriate.

Q. Tab 4 is your January 15th, 2018 deposition. Why don't you turn there, sir, page 26.

And if we can have slide 35, please?

A. Page 26 of...?

Q. Tab 4 of your January 15th, 2018 deposition. I'm on page 26, lines 12 through 17. Do you recall this question and answer. My question is this, sir: "Do you agree that NIH funding, and perhaps you don't know -- "

A. You said page 24?

Q. Page 26, and it's 12 through 17. Are you there?

A. Page 24. It says, "And that's why -- "

THE COURT: Do you want to start reading from the middle of page 25, question, "Do you -- "

JUDGE PETROU: I think the problem is that the witness is looking at the numbers on the bottom of the page rather than the deposition page numbers.

MR. GRIFFIS: Oh, I see.

THE WITNESS: No, I can see the deposition numbers page 7, page 25?

THE COURT: Yeah, but I would start reading at page 25, line 14.

MR. GRIFFIS: Okay 25, line 14.

THE WITNESS: Please do.

BY MR. GRIFFIS

Q. Are you there, sir?

A. Yes, I'm here.

Q. (Reading:)

"QUESTION: Do you agree that National Institutes of Health funding means that high standards and best practices are used to ensure the data is accurate?

"ANSWER: Answer: It doesn't ensure the data is accurate. It just basically -- all that it does, it provides funding that the NIH views is important. You don't know what data you will generate for the funding, because when you fund a study, you don't really know what you are going to come up with a study. You just decide on funding a study -- "

Am I going too fast?

" -- you just decide on funding the study upon its inception, because you view it is important in the public domain, and that's what the NCI and the NIH did."

A. That's exactly what I just answered.

Q. (Reading:)

"They funded the study, and because of

interest, obviously, to the general public."

And then after a question about whether you had an NIH funding study before, at 8.

"QUESTION: I'm going to ask the question again, because I think you focused on the conclusions and whether the conclusions are accurate.

"ANSWER: Sure.

"QUESTION: My question is this, sir: Do you agree that NIH funding -- and perhaps you don't know, but do you agree that NIH funding means that high standards and best practices are used to ensure that the data is accurate?

"ANSWER: Yes.

A. At the time of inception, that's what they ensured, yes, but again, as you saw in my previous answer, which you weren't planning on reading, but it does say exactly that it doesn't ensure the data is accurate. It just basically says it provides funding for a study that's important.

So at the time you invest in a study, you realize it's very critical, it's important, I'm going to dedicate resources and money to fund it, and then you follow, and see what actually happens.

Some studies are great, and they maintain the integrity

and they're actually fine, and some are not.

So my point is, just because the NIH or the NCI funds a study, it doesn't mean that these studies are immune to criticism and they're not flawed.

Q. You would have approved --

A. In fact, the literature is full of studies that are funded by these agencies that are not accurate.

Q. You would have approved it for publication.

A. I would have approved it for publication, because I think it's important to be there. I would have accompanied it by a more critical editorial than the editorial that was written. I probably would have not accepted this paper in the *JNCI*. I would have definitely suggested a much lower impact journal.

Q. Now, despite this being a very major foul-up with a lot more data than the De Roos 2005 paper, you told me that this doesn't weaken your opinion about non-Hodgkin's lymphoma at all, right?

A. The follow-up of a flawed study would continue to show flawed results. If you follow it for 20 more years, it's going to still show flawed results.

Q. And when I asked you what kind of epidemiology study -- never mind the NCI *JNCI* 2018 study, but an ideal imaginary epidemiology study, what kind of epidemiology study would shake your conviction, you said, nothing would shake my conviction about non-Hodgkin's lymphoma and glyphosate, correct?

A. That's right, because you just look at the entire evidence. There is no -- and again, I think I said that earlier, there is no perfect epidemiology studies. You put any epidemiology study, and I promise you we both can find a lot of good things about it and bad things about it.

Q. At this point, nothing would you shake your conviction.

A. At this point, the IARC report is very convincing. It looked at the totality of evidence. It incorporated the AHS Study. The IARC only -- from 1,000 compounds that they reviewed over 40 years, only 20 percent they declared carcinogen.

I don't believe the IARC is out there to get compounds and just declare everything is carcinogen, no. They actually put a lot of thought into the data, a lot of thought into epidemiology.

And they're very critical even to accept to review a compound. They actually reject most of the proposed compounds, to decide whether they are carcinogens or not.

So it's very difficult to discard a body like the IARC, who put a lot of thought into all of this, and they conclude the conclusion that they have.

And then, in all honesty, I went back and I looked at some of these studies, and despite their flaws, there is convincing evidence that there is increased risk and causality, including the meta-analysis that was very interesting.

Q. Thank you, Doctor.

A. You're welcome.

THE COURT: Any redirect?

MR. MILLER: Very briefly.

REDIRECT EXAMINATION

BY MR. MILLER

Q. I just want to follow up on that last question.

What you told counsel was that if someone did a randomized clinically-controlled trial, that would have informed you and affected your opinion, wouldn't it?

A. It would be unethical to do.

Q. Well, that's the problem now, because it's a known carcinogen, it would be unethical to do a randomized clinical control trial.

A. Correct.

MR. MILLER: Thank you. I have no further questions.

THE COURT: Anything further?

MR. GRIFFIS: No.

THE COURT: Okay, thank you very much.

THE WITNESS: You're welcome. Thank you. Do I leave this here?

(Witness excused.)

THE COURT: All right, last witness?

You can hand it back to the lawyers. They can deal with it.

MR. LASKER: Your Honor, Monsanto calls Dr. Lorelei Mucci to the stand.

And just some prefatory comments before she gets to the stand. One, I'd like to introduce Alicia Shimada at counsel table, who's assisting me in this matter.

And second, I know your Honors have a lot of questions. I want to just lay out the order that I have sequenced things in, so if I've missed anything, you can let me know.

We're planning on first discussing, after her general opinions and some summary, the 2018 *JNCI* study and the arguments that have been raised by plaintiffs' experts about nondifferential exposure misclassification.

And then there are four issues that I have, I believe, your Honors are interested in, and that's why I've decided to prioritize, which is, confounding by other pesticides, the issue of latency, the issue of recall bias, and the issue of the proxies and proxy bias.

And obviously, if there are other issues that you want to cover, I'm sure you'll have ask a question, and if you let me know, I can try and guide Dr. Mucci to answer those questions, as well.

THE COURT: Great. Thank you.

LORELEI MUCCI,

called as a witness for the Defendant, having been duly sworn, testified as follows:

THE CLERK: Please be seated, speak clearly into the microphone, and spell your last name for the record.

THE WITNESS: My last name is Mucci. It's spelled M-U-C-C-I.

DIRECT EXAMINATION

BY MR. LASKER

Q. Good morning, Dr. Mucci.

A. Good morning.

Q. Can you please describe briefly for the Court where you work and what you do?

A. I am a cancer epidemiologist. Currently I am Associate Professor of Epidemiology at the Harvard School of Public Health, and I'm also leader of the Cancer Epidemiology Program at the Dana Farber Harvard Cancer Center.

Q. We've heard a lot of testimony over the course of this week about different types of scientific evidence, epidemiology animal toxicology, and mechanistic studies.

How does epidemiology fit in this body of science, in addressing the question of whether a particular substance can cause a particular type of cancer in humans?

A. Epidemiology is really an essential component in understanding causes of cancer, and the reason is that if we're interested in cancer in humans, the ideal model to study that is in humans.

Q. What type of evidence do epidemiologists need to see

before they can reach a conclusion that there's a causal association between an exposure and cancer?

A. It's important that epidemiologists not rely just on the findings of one study, but it's really important to evaluate the results that have been done in multiple studies, and preferably in multiple populations, to evaluate the consistency across studies.

Q. And within each individual study, what does an epidemiologist look for to determine whether there is a positive association between an exposure and an outcome that could inform causality?

A. So we're looking at all of the available epidemiological literature. When we're first evaluating each of these studies, we want to assess whether the observed association may be due to potentially bias, confounding or chance.

Q. Okay, we've heard a lot about that, so I'm not going to go through those issues, but Dr. Mucci, have you had an opportunity to review the glyphosate epidemiological literature?

A. Yes, I have.

Q. And have you prepared an exhibit that summarizes the findings of these studies?

A. Yes, I have.

Q. Okay. Let's put that up, slide 2. And if you could, explain for the Court what information is depicted on this

slide.

A. So there have been multiple publications that have evaluated glyphosate and NHL risk. However, those studies really can be summarized by these four main studies presented here.

The first study, which is called the NCI study, or Andreotti et al., is the only cohort study that has investigated glyphosate and NHL risk.

The lower three studies are case-controlled studies.

So the second study by Pahwa, et al. includes a pooled analysis of case-controlled studies from the United States and from Canada.

Orsi, et al. is a hospital-based study that was conducted in France.

And then finally, Eriksson was the case-controlled study that was conducted in Sweden.

Q. And there are a couple of other studies we've heard some discussions and brief discussion of in this case, a study by Hardell and a study by Cocco. Are those included in your table?

A. No. *A priori*, I decided to not discuss them here, and the reason is that the number of exposed cases in both of those studies was extremely low, so it was less than -- it was four cases in each that were exposed to glyphosate. So it really make inferences from those studies meaningless.

Q. Other than those two studies, do the -- does the data depicted on your forest plot encompass all of the data, epidemiological data that exists with respect to glyphosate and non-Hodgkin's lymphoma?

A. Yes, it does.

Q. And which of the odds ratios -- well, let me actually back up.

Can you explain for the Court what we're seeing here, with respect to the squares and the lines and the diagram?

A. So in this forest plot, for each of the studies, the square represents the estimated relative risk from each of the studies, and the line through it is the width of the 95 percent confidence intervals around each study, and then the actual size of the square refers to the overall size or power of the study, which is influenced not only by the overall size of the study, but especially the number of cases, particularly the number of exposed cases.

And so as you can see, Andreotti et al., because of not only the number of the cases but the number of exposed cases, is the most powerful of the studies.

Q. And what is the diamond on the bottom?

A. So I -- I undertook a -- I calculated what's called a meta-relative risk, which is a weighted relative risk that weights each of the four relative risks there by the size of the study, which comes up with a summary estimate.

Q. Okay, and before we get to that, I should have asked previously, which of the odds ratios in your forest plot or risk, or -- rate ratios adjusted for pesticides and which are not?

A. So the only one that is not adjusted is from Orsi, and that's because there were no multivariable adjusted odds ratios that were presented in that study. All of the others are adjusted for demographic factors, as well as for use of other pesticides.

THE COURT: Could I ask a follow-up question about that?

THE WITNESS: Yes, your Honor.

THE COURT: So, but you nonetheless included the Orsi study in your forest plot. Can you explain why?

THE WITNESS: Yeah, I think that's an important question. I included it because it does provide some data. However, really one of the challenges in doing meta-analyses is that the validity of the meta-analysis relies on the validity of each of these four studies.

So I present it more as a graphical depiction to show you the results of these studies, but I think we were going to walk through the studies, each of them, and discuss what the limitations are, and how those limitations might influence our results.

THE COURT: But -- and without going through all of

the detail right now, can you just kind of highlight for me or just flag for me what's the value that the Orsi study brings?

THE WITNESS: Honestly, I think there's very little in the Orsi Study. It -- even -- it was a hospital-based case-controlled study, which makes you concerned about the quality of the controls in that study. It's nothing founded, yes.

THE COURT: I'm trying to, again, without getting too much in the details --

THE WITNESS: Right.

THE COURT: -- maybe it's appropriate to tell me, "I'll get back to you on that" because I don't want to interrupt the presentation too much, I'm trying to distinguish in my mind, well, why did she include Orsi in the forest plot but not the other two that she said had so little -- so few cases that were useless?

THE WITNESS: Yeah, I think that's an excellent point. I think if I were performing -- I -- a true meta-analysis, what I would do is to, in that meta-analysis, actually discuss the quality of the studies, and I might limit and do a sub-relative risk estimate based on the data that I thought were the highest quality, and I think I would have excluded Orsi.

THE COURT: Okay.

BY MR. LASKER

Q. And I'm not going to ask you to calculate this on the stand, but given the weight of the various studies that incorporated in your meta-analysis, what role does the Orsi odds ratio play in your overall meta-analysis summary?

A. So in total, there were only 12 exposed cases in the Orsi, et al. study, and therefore, if we excluded that from the estimate of the summary relative risk, it would be virtually identical to what's estimated here.

So it's not having a lot of impact, but I think the points that you've raised, your Honor, are really important when we think about the quality of these studies.

Q. And if you could, just explain what that diamond, then, represents, in the summary.

A. So it's, as I mentioned, it's the summary relative risk, where we're waiting each of the studies, and coming up with a summary estimate.

The center of the diamond represents the relative risk estimate for the meta-analysis; and the width of the diamond gives you a sense of the width of the 95 percent confidence interval.

Q. And I think you've actually already answered this question in response to the Court's inquiry, but what is your view of the value of a meta-analysis, or meta-relative risk, in assessing of body of epidemiologic literature?

A. For me, I think it's-- it provides a graphical depiction for us to be able to compare results, across the studies.

However, I think if you really want to understand the results of each studies, and it's important to consider the strengths and limitations, and really to evaluate first whether the observed associations you see could be explained by bias, confounding or chance.

Q. Let's then start walking through the individual studies, and I'd like to start by discussing the Agricultural Health Study, which we've heard a lot about, but I don't know if we've had a summary of what that study is and how it was designed.

So if you could, explain to the Court what the study was.

A. So it's a cohort study of 54,000 licensed pesticide applicators from Iowa and North Carolina, and these individuals were selected specifically because there was interest in studying the health effects, both cancer and non-cancer health effects, of pesticides, and it was felt that pesticide applicators could provide high quality information about pesticide use.

The design was a cohort study. As such, it avoids the recall bias that we might be worried about in case-controlled studies. The questionnaire that's included in the Andreotti, et al. studies was based on two time points; first at baseline between 1993 and '97; and then again five years later, between 1999, and 2005.

The baseline questionnaire actually captured information not only about the current use of 50 different pesticides, but also collected information about past use of pesticides.

And the reason that's important particularly for glyphosate is that it allows us to look at potential latency effects of glyphosate, of more than 30 years of exposure information.

Also, another feature of the Agricultural Health Study, as you can see, 834 percent of the cohort were at some point exposed to glyphosate, and why that's important is that it allows us to also look at dose-response, and in particular, look at the potential associations with NHL for very high levels of glyphosate compared to no exposure to glyphosate.

THE COURT: Could I ask a clarification question about that?

THE WITNESS: Um-hum.

THE COURT: The 83 percent figure, is that from the baseline response?

THE WITNESS: No. I'm sorry, that was through the second questionnaire.

So the baseline questionnaire, I believe it was 75 percent of the population was exposed, at the baseline questionnaire, and then five years later, it was 83 percent.

THE COURT: Thanks.

THE WITNESS: So the cohort to follow up for cancer

incidence both in Iowa and North Carolina, there are high quality cancer state registries that were linked to the study, and so what's nice about that is it captures incident cases of cancer including non-Hodgkin's lymphoma; and through follow-up with 2013, there were 575 incident cases.

And as I mentioned --

BY MR. LASKER

Q. Let me just stop you there, because the court already understands that we haven't had any discussion about the cancer registries before. The court understands we can just move on but -- okay, good.

A. So there were, because of the prevalence of exposure, it's -- the Andreotti, et al. study actually has the highest proportion of exposed cases of any of the epidemiology studies, which is important when we think about both the statistical power of the studies, but also, as I mentioned, our ability to look at potential dose-response associations.

Q. Okay, I'm sorry, did you get to the last bullet?

A. Yeah. So there was detailed data that was collected through the questionnaires, on a range of demographic factors, lifestyle factors, as well as the use of a total of 50 pesticides, which allowed a detailed consideration of potential confounding factors in the analysis phase through multivariable models.

Q. What did the --

THE COURT: Could I -- sorry, could I ask a couple questions about the questionnaire?

So my recollection from Dr. Ritz's testimony was that this was, like, a 20- or 30-page questionnaire, something like that, and pesticide applicators were asked to fill it out when they were coming in to get their permit for applying pesticides.

And they were put in a room and given 20 minutes or a half an hour or something to fill out this questionnaire, sort of on the spot, without having any time to reflect on the amount of pesticide exposure they've had, and the various different pesticides they've used over the years.

That does seem kind of problematic in terms of reliability, and so I was wondering if you could comment on that.

THE WITNESS: Yeah, sure. So I think that's -- you know, I think with epidemiology questionnaires, we are always concerned about the potential for measurement error misclassification.

What's nice about the Agricultural Health Study was they evaluated the reliability of the responses.

I don't know if we want to pull up that.

MR. LASKER: We can jump to that part of it, if you want your Honor.

THE COURT: Sure.

MR. LASKER: We'll skip there, and we'll come back.

Q. Let's go to slide 6.

A. So there was, within the Agricultural Health Study, actually 4,000 of the participants came back one year later and filled out the same questionnaire, in the same sort of circumstances that they had filled out the questionnaire the first time.

What's nice about that is it allows us to compare the concordance of responses between the two questionnaires, and get a sense of the reliability of information that's presented by the participants.

And what that information showed us was that the quality of pesticide use, more generally, but also for glyphosate in particular, was quite reliable.

So the concordance for glyphosate between the two questionnaires was 82 percent. That's a value that is quite similar in epidemiology to other factors we look at, like tobacco use, for example. So that provided reassurance.

In addition, what was really important, I think, in this study was it showed, when looking at sort of the different dose-response levels, that the reliability of the responses for the levels of dose were 90 percent or more agreement.

And why that's important is that when you look at the dose-response associations that are presented in Andreotti, et al., it shows you that it's very unlikely that people in the very highest doses of glyphosate are potentially misclassified

and really had no exposure and vice-versa.

So it's possible that there's some potential misclassification at that lower range where people haven't used pesticides or haven't used glyphosate very often, but I think what this reliability showed was that the validity of the data for the higher doses is probably quite good.

JUDGE PETROU: So the 82 percent concordance rate relates to what?

THE WITNESS: Specifically comparing the answers on glyphosate use in the first and second questionnaires.

JUDGE PETROU: Specifically is that the yes, no, I've used, not used it, or the dosing?

THE WITNESS: Exactly. So it's the yes-no is 82 percent, but then when they looked at the level of dose, that's when they saw agreement of 90 percent, so that people who were categorized as moderate or high, if they were changing, it was really only one category. So you weren't getting people in the really higher categories being classified incorrectly in the lowest category.

JUDGE PETROU: So it's 82 percent concordance for yes-no, and then within the yeses, a 90 percent for the level of usage.

THE WITNESS: That is correct.

BY MR. LASKER

Q. Just to be clear, within the 90 percent you talk about one

level agreement or one category. What does that mean?

MR. MILLER: I'm sorry to interrupt. May I have the Exhibit number and a copy of that?

MR. LASKER: I wasn't -- actually, this is the Blair 2002. So it's Defense Exhibit 596.

Q. But you can explain it again, and talk about 90 percent --

MR. MILLER: I'm sorry.

MR. LASKER: I'm sorry.

MR. MILLER: 596?

MR. LASKER: I'm sorry. Thank you, my apologies.

(Whereupon a document was tendered to the Court.).

MR. LASKER: No, no, no (indicating) there.

THE COURT: We're all friends here.

JUDGE PETROU: Which Exhibit number in your binder is it, counsel?

MR. LASKER: It is tab 5 in our binder.

Q. And if you could, actually, take us to the tables in this study. So if you could actually walk the Court through this, this is in the outline -- I apologize that we weren't prepared -- and show the Court first where the 81 or 83 percent, whatever it is, for exact, for ever/never uses, and then what your point was about, within one level of -- I can't remember exactly what the term was.

A. So the ever/never comparison is presented in Table 1, which is on page 95 of this study, and glyphosate is near the

top, and you can see the exact agreement or concordance is 82 percent for the --

JUDGE PETROU: I need to ask a point of clarification, because I thought you were talking about, when you were giving us the 90 percent or 82 percent, I thought you were referring to the 4,000 individuals who filled out the same document or questionnaire one year later.

THE WITNESS: Yes. Yes, exactly.

JUDGE PETROU: Okay, and this Table 1, when it says between first and second questionnaire, it's referring to that one year?

THE WITNESS: Yes, exactly. Right, sorry, it's confusing. It's not referring to that follow-up questionnaire within the larger study. It's really referring to one year later.

MR. LASKER: And your Honor, this publication was before the second phase questionnaire. It's 2002.

THE WITNESS: And so then in the -- in the text -- and I think we -- can we call it up here?

MR. LASKER: Sure.

THE WITNESS: In the text, it talks specifically about the agreement.

MR. LASKER: It's going to be on the next page.

THE WITNESS: Is it on the -- it's in the discussion? Sorry. I'm can't recall specifically where it is.

JUDGE PETROU: I'm seeing where it says, 90 percent gave responses within one category of agreement?

THE WITNESS: Yes, exactly. Thank you.

JUDGE PETROU: It's -- yeah, it's the second page. It's page 9, the column on the left, and the first full paragraph.

MR. LASKER: There you go.

THE WITNESS: Yes, 90 percent exactly. Yes.

JUDGE PETROU: And what does it mean when it says, within one category?

THE WITNESS: So they were looking specifically at the lifetime-days categories; and there were multiple categories. I can't recall, I think there were a total of six or seven different categories.

BY MR. LASKER:

Q. I think it's footnoted on the table -- actually, no. Go back to the next table, go back to where you were.

A. To Table 1.

Q. No, I'm sorry, I'm talking to her.

Sorry go to Table 2, please.

A. No, it's not. It's not presented. I think it's only, unfortunately, presented in the text -- the discussion. But then we looked in the actual study specifically, where they have the different categories.

Q. I have a footnote in this table that has it, as well. If

you go down to the bottom of the table -- I'm sorry.

JUDGE PETROU: No, actually.

THE WITNESS: You're right, you're correct, in the legend, right here. So you can see these are the different categories for days of years per use.

And so essentially what was happening was that 90 percent -- if the exact -- the actual reporting on the first baseline was 5 to 9, the 90 percent of people were within one category of each other. So the likelihood that somebody who reported 5 to 9 would then report in the category of 60 to 150 was.

JUDGE PETROU: Okay, so if someone had originally reported 5 to 9 to be within one group, they would now have to report somewhere between less than 5, and 10 to 19.

THE WITNESS: Correct.

BY MR. LASKER

Q. And if you could, go back to your testimony previously where talked about -- and I think, your Honors, you've already had those quartiles of exposure in this study where the top dose was over a hundred-something days.

How does the fact that we have the different dose levels -- and we have a measure of risk at that highest dose group of over 109 days exposure to compare to people with no exposure -- how does this data -- what does this data suggest with respect to possibly misclassification bias between that

highest exposure group and non-exposed?

A. So this -- the results from this study would suggest that misclassification of people at the extremes, so highest versus lowest, or none, is very little, based on this reliability study.

Q. And just to refresh the Court's recollection, although I think the Court will recall it anyway, what were the rate ratios reported in the NCI 2018 study, comparing that highest-exposure group with over a hundred and some-odd days of cumulative exposure to glyphosate, with individuals who reported no exposure?

A. So there was no association at all between comparing those with the highest versus no exposure.

MR. LASKER: Your Honor, does that answer your question? Okay, great. I'll go back.

Q. Yes. So we were talking about --

THE COURT: Sorry, could I just ask one more very quick and probably dumb question?

The 4,000 -- roughly 4,000 people who filled out the questionnaire the following year, was that specifically for the purpose of testing this?

THE WITNESS: No. So they -- actually, it was sort of -- it was sort of a -- it was lucky, in a way. They had to come back specifically because they had to renew their pesticide applications, and so they would -- sort of, it was

lucky that they came back in, and so they -- the investigators took the chance to look at the reliability of information, because they were coming in anyway.

So they didn't design it specifically that way, but because the 4,000 people were already coming back, they gave them the questionnaire the second time to look at the reliability.

THE COURT: Do we know anything about that population and why they needed to come back and renew their applications?

THE WITNESS: Yeah, so it was specifically people who were from Iowa, and they had to, I believe, renew their licenses, and I think that was why they came back in. There was something about the renewal of their license that was required for them to come back in.

THE COURT: But we don't know what that is, what distinguished them from the other 52,000 people that required them to come back in, to renew their licenses?

THE WITNESS: That is correct.

THE COURT: Okay.

BY MR. LASKER

Q. Dr. Mucci, you had previously discussed some of the characteristics of the AHS cohort analysis. Can you briefly explain for the Court what the investigators reported out as results of their study in the 2018 *JNCI* article?

A. So, what were the results specifically?

Q. Yeah.

A. So there were a number of analyses that were evaluated within the Andreotti, et al. study.

First, there was no evidence of ever an association between ever exposure to glyphosate and risk of NHL.

There were two different estimates of dose-response that were evaluated, one looking at lifetime-days of use, and the other was lifetime-days of use that was also weighted by the intensity of exposure.

In neither of those dose-response associate relationships was there any association -- there was no association between the highest exposure to glyphosate and risk of NHL.

Because of the long-term follow up of information on glyphosate, the investigators were able to look at different potential latency of effects. So they were able to look at shorter effects of 5 years, 10 years, and the longer effects of 15 and 20 years or more of exposure; and in none of these analyses was there any evidence of an association between exposure to glyphosate and NHL risk.

Q. Now, plaintiffs' experts have criticized the 2018 *JNCI* study based upon something called nondifferential exposure misclassification. Have you reviewed this criticism?

A. Yes, I have.

Q. And is that criticism, in your opinion, valid?

A. So I think it's appropriate, and as I've mentioned, it's

appropriate whenever you're reading through an epidemiology study to first consider whether the observed findings are potentially due to confounding bias or chance.

However, after reviewing all of the analyses that the investigators did, including some sensitivity analyses that we'll talk about, as well as the validation studies, I don't think you can -- I don't think that makes sense.

There's also three specific reasons why it doesn't make sense. I've talked about the validation studies. I've talked about the sensitivity analyses. The first point actually is really that it doesn't make sense mathematically.

Q. Okay. Well, we're going to go back to each of these, but let's talk about mathematically why.

And I think we've had some discussion previously about how nondifferential misclassification biases towards the null, but if you could, again explain to the Court what -- how that would work.

A. So what happens with nondifferential misclassification is it's diluting an effect. And so if -- if the true association were positive, let's say 1.4, and there was differential misclassification, it would dilute the effect and make it look closer, the relative risk closer to 1.

If there was complete random error in the data, then you're -- the relative risk actually would be 1.

However, it's not mathematically possible for

nondifferential misclassification to make a positive association cross 1, and that's what would have to happen, given what the actual observed relative risk is for glyphosate exposure in the AHS cohort.

MR. LASKER: Do your Honors understand that?

THE COURT: Not fully.

MR. LASKER: Okay.

THE COURT: Maybe not at all. But I guess my math skills are de minimis.

But if you -- I guess what I don't understand is, let's say you have -- there is, in fact, a significant association between a chemical and a disease, and let's say, if you did the study properly, you would see -- you know you'd come out at a 2.0 odds ratio with, you know, with a small confidence interval.

THE WITNESS: Mm-hm.

THE COURT: And -- but let's say there's a bunch of misclassification error, and what you come out with is .99.

What you seem to be saying is if that misclassification did not occur, it could never go -- if you corrected it, it could never go above 1.

Or to put it another way, it seems like what you're saying is that if you had the perfect study, and it came out at 2, then it would be mathematically impossible for misclassification to bring it down to .99.

And if that's what you're saying, I don't understand that; and if it's not what you're saying, explain it to me again what you're saying.

THE WITNESS: Right. So it, in fact, it is what I'm saying. And so the reason is, in a cohort study -- and one of the examples that you have -- so if you have an exposed group here, and they're truly exposed, meaning that we're actually perfectly -- we perfectly classified exposed people as exposed, and let's say the incidence in that population is 10 in a hundred, and then you have the unexposed group, and they're perfectly classified as unexposed, and their true incidence rate is 5 in a hundred.

So then the relative risk would be 10 in a hundred divided by 5 in a hundred, which would be a relative risk of 2.

So what happens with nondifferential misclassification is you have some of the exposed people coming down in the unexposed group, and the issue there is that because it's not related to the incidence, you're basically bringing that higher incidence rate into the unexposed group.

So the denominator's going to be a little bit bigger than it, was; and then vice-versa, you're bringing some of that -- you could have it either way. There could be one direction of misclassification or both, and then you're bringing the -- so if you bring it just down, the exposed people are wrongly classified as unexposed, then it's going to dilute the effect,

because your denominator, or your -- sorry, yeah, your denominator is higher than what it should be.

Vice-versa, if you have some unexposed people who are wrongly classified as exposed, now they're bringing that same incidence rate that they have into their numerator. That's also going down. So again, the relative risk is also less. It's attenuated than what it was.

So if you basically make the groups -- even if you completely measure completely with error, the worst that you can do is make the two groups have the exact same incidence rate. There's no mathematical way for -- because it's nondifferential, because it's not related --

JUDGE PETROU: That's not really the point. You're talking about nondifferential classification, and it's your opinion there's no basis to believe that with this study there was differential classification --

THE WITNESS: That is correct.

JUDGE PETROU: -- that would impact the numbers in a way that's troubling.

THE WITNESS: That is correct. Because it's the cohort study, because there's no way that the cancer development influenced how they reported on their exposure because the cancer happened after they reported, it's nondifferential. So that's -- that's exactly right.

THE COURT: But couldn't it -- couldn't the errors

cause the result of the study to be somewhere below zero in a non-statistically significant way, still?

MR. LASKER: You mean below 1, your Honor?

THE COURT: Yeah.

MR. LASKER: You said, below zero.

THE COURT: Oh, sorry.

THE WITNESS: So in part, by chance, you could have something like that. However, there was actually -- and I can't recall the specific study that actually was -- Dr. Blair was one of the co-authors on this study, where they did different simulations where they made different assumptions about how much misclassification there had to be, as well as how the sample size and the number of cases would influence that.

And so with the larger the study you have, or the larger number of cases you have, the role that chance -- that chance finding of having a negative finding really diminishes.

So if we had a much smaller study, and we had a much smaller number of cases, then you might worry, just by chance, 1 in 20 times you might end up with this potentially small inverse association, but here, because the study is so large, because the number of cases is so large, that likelihood of a chance of the mis- -- nondifferential misclassification leading to a relative risk that's below 1 is very, very, very small.

JUDGE PETROU: So you'd mentioned that with the

first, the one -- I hesitate to say the second questionnaire, because we've been using that for the follow-up questionnaire -- but the 4,000 that did that second questionnaire a year later, where there was a 90 percent rate on the ever/never question.

(Simultaneous colloquy.)

THE REPORTER: I'm sorry, please speak one at a time.

JUDGE PETROU: Between the questionnaires, the original questionnaire and the follow-up questionnaire one year later that approximately 4,000 people completed, with the percentage in the low 80s consistency between ever and never, do you know whether that reflects a pretty even number going one way or the other, or whether the bulk of those went from ever to never versus never to ever?

THE WITNESS: I'm going to just look at the tables to see if we have some information about that or not.

So unfortunately, what we have is just the number of percent agreement. So -- and I don't remember reading in the discussion about the directionality.

JUDGE PETROU: Okay.

MR. LASKER: Your Honor?

THE COURT: Continue.

BY MR. LASKER

Q. Great. So I think we've now addressed the mathematical issue here.

And just to be clear, again, the issue of nondifferential misclassification in a mathematical issue, given the results of the study, also would be one that would have to see as between the very highest-exposure group and no exposure, in order to impact the results of the study, correct?

A. Right.

Q. So the second thing you mentioned was validation studies, or the second thing on your list, and can you explain what a validation study is?

A. A validation study is where we compare the information that's collected for example from a questionnaire, with some sort of what we think might be a gold standard, and that provides us some assessment of the validity of the findings.

Q. Okay. We've already talked about, I think, the main validity study, which is the Blair 2002 study.

So unless your Honors have any further questions about that 4,000 questionnaires, let's move on to the next part of the album.

A. There was --

BY MR. LASKER

Q. I think there's -- I think, actually, we should be on the next slide, on the different types of validation studies.

So we have the validation of the questionnaire responses we've already discussed about.

The next item on your list is validation of intensity

algorithm.

Your Honors are familiar with the intensity algorithm. Do we need to do anything further?

THE COURT: I could benefit from another explanation of it.

BY MR. LASKER

Q. Can you, Dr. Mucci, explain what the intensity algorithm was in the AHS study was, and what the purpose of it was?

A. So one of the dose-response measures that was used integrated not only the lifetime days of use, but also tried to estimate the actual dose of that exposure by integrating information that was reported on whether or not the individual, for example, personally mixed a substance, and therefore, might be have greater exposure; whether that person was using protective gear, as well as potentially the method in which they applied different pesticides.

And so the idea was to use an algorithm that had been developed to get a better dose of exposure to pesticides, and that's what the intensity --

JUDGE PETROU: Doctor, in regards to the protective gear, which seems like an important question to me in determining how much exposure there actually is, the questionnaire did not differentiate, if I remember correctly, between this list of pesticides and herbicides, is that correct?

THE WITNESS: That is correct, right. So it was asked just more broadly about the use of protective gear, and so I think that's a critical issue and one that the validation study, the intensity algorithm, can help us address whether the quality of the way that question was asked still holds up for whether it's valid in glyphosate.

BY MR. LASKER

Q. And just because, the next question in the outline, to clarify for the dose-response, there were -- I think you take it, two dose-response calculations, one that used intensity weighting and one that did not, is that correct?

A. Yes, that is correct. And also, just to say that none of the case-controlled studies integrated information on any of these measures of intensity in their assessment of dose-response.

MR. LASKER: Is your -- do you need any more information on the intensity algorithm?

Q. Okay, let's go to the validation study, and we've seen this study before. This is slide 7. It's the Acquavella 2006 table.

The table I have is Table 4. First of all, there's a variety of different numbers provided in this study, and we've talked about it -- we'll again talk about the ranking by intensity score, and urine levels of glyphosate.

But I first want to talk about the actual correlation

numbers that are also presented in this study, because plaintiffs' experts have pointed to the correlation of numbers -- I'm not sure if that's the exact terminology -- as being low, and that being an issue of concern with respect to how well this algorithm works for the epidemiologic study.

So if you could at least first address that issue, and then we'll go to this table.

A. Yeah, sure. So the correlation coefficients are estimated by comparing the actual intensity level with the actual level of the biomarker.

And so that what that means is that it's looking at to see whether the intensity algorithm can give us a really good estimate of the actual level of exposure, and a correlation of .23 isn't as high as we might want to see. However, what the goal of -- what this particular study shows and how the intensity algorithm ends up being used in the AHS cohort is instead categorizing individuals.

And so -- and why that's important is that I think the study by Acquavella actually shows that we can appropriately rank individuals on their exposure. We might be less likely to be able to say the exact dose of the exposure that they got, but we can more accurately classify individuals as having a very high level versus a very much lower level.

Q. And how, if at all, did the results of Table 4 inform that question?

A. Right. So what Table 4 does is to categorize individuals into -- if you look at the second shaded area of yellow, into four different intensity categories, based on the intensity algorithm; and then what we have -- the next two.

Q. Just for clarification, since there are two levels, if you can just explain what the two different measures are, why we have two of them?

A. Right. So the first actually calculated the intensity algorithm using field observers. The field observers were actually observing what the individual farmers were doing.

The second set of data is that data that's actually reported by the farmers. And so I think, in the sense the questionnaire and the Agricultural Health Study is based on self-reported data, that's why I was looking specifically at that one. But both of them, you know, show good ability of the algorithm to work.

And so what they compared, in terms of the biological marker, was to look at levels of glyphosate excreted in the urine, and then they're presented as either the mean or the median value.

And in this case, actually, if you could highlight on Figure 2, panel A --

Q. Just a second.

A. It's on page 72 of the manuscript, on the left side, and it's the first panel on the top of Figure 2. Oh, sorry that's

Table 2.

If we could have Figure 2 of panel A? Great.

So what this is showing us -- this is a scatterplot of the individuals, the 48 individuals that had urine levels of glyphosate.

This is what their distribution looked like this in those 48 individuals.

What's important to see is, you can see this sort of line of data at 0.5, and so essentially, anybody who was had a levels of glyphosate in the urine that were not detectable were there.

And so what happens is you have a lot of individuals at the zero level, which means your data are not normally distributed. So in that case, you should really rely on the median value, or the mean, because the data -- one of the assumptions of using a mean is that your data are normally distributed, which they are not.

Q. And just so the Court understands, and I can understand, am I correct, then, that what this is measuring is that there were these lines of individuals, including individuals at the highest intensity by algorithm, they weren't wearing protective gear or they were involved in mixing but used glyphosate, and nonetheless, didn't have any glyphosate detected in their system?

A. Well, we actually don't -- right, exactly. So you here,

right, exactly. That is correct, yes.

Q. Okay, and then --

JUDGE PETROU: I'm sorry, I should know but I don't. How are these intensity categories determined?

THE WITNESS: So these categories were based on the intensity algorithm, and then they divide the groups into three categories, which they -- I'm just trying to see how they divided these three groups.

JUDGE PETROU: And specifically, I'm curious if it's possible to know how that -- how those categories, which were mathematically determined, relate to actual exposure and use levels, because I've been curious throughout, as we've been looking at different studies, at how these various cutoff points are determined.

THE WITNESS: Right.

JUDGE PETROU: And I'd love to know if they in any way correlate with these intensity levels.

MR. LASKER: And just so I understand, is that with respect to the *JNCI* study, or --

JUDGE PETROU: There are a number of studies we've looked at.

THE WITNESS: Right, so I can definitely answer it for the *JNCI* study, how they made the cut points, they used quartiles --

JUDGE PETROU: No, I remember that.

THE WITNESS: But here -- yeah, so it looks like they're -- I think -- I don't know that they used tertiles, per se, but it looks like they tried to get three equal groupings of people, so they divide the 48 people into three groups, so that there would be a similar number of people. So it's essentially similar to -- to tertiles, dividing them equally.

But that's not the approach of the other case-control studies, as you mentioned, which is problematic; how did they arrive at these cut points.

Okay, so if we could go back to the figure or the table that we had up, Table 4.

So if we look at the median values for glyphosate comparing levels 1, 2, 3 and 4, what you can see is that the individuals who are ranked in the highest based on the intensity category are also have the highest median level of glyphosate in their urine.

And vice-versa; so you have a seven-fold difference between the highest and the lowest category of exposure.

BY MR. LASKER

Q. Okay. Can you, again, explain for us how this intensity algorithm then is used in that one -- the -- the dose-response analysis in the Andreotti study that incorporates intensity?

A. Oh, I'm sorry. Could you please ask that question again? Sorry.

Q. Sure. Can you explain how this intensity algorithm is

then used in the one dose-response analysis in Andreotti that incorporates intensity?

A. Right. So what they did was to take the lifetime-days or cumulative days of exposure, and then multiply that by this intensity algorithm to get the intensity dose, and then divided individuals into four equal quartiles of exposure.

MR. LASKER: And do you have any questions about this issue? Otherwise, I'll move to the third validation, which goes to imputation.

THE COURT: Yeah. Before we do that, why don't we take a lunch break.

MR. LASKER: Okay.

THE COURT: Why don't we return at resume 12:45, at 12:45.

(Recess taken from 11:57 a.m. until 12:45 p.m.)

THE COURT: Okay. You perhaps will not be surprised by this. I have another question, another math question for you. I wanted to follow up on your example.

Okay. So you gave me an example of, I think, 100 people unexposed, and a hundred people exposed. In the group of 100 people unexposed, 5 cases. In the group of the 100 people exposed, 10 cases.

THE WITNESS: Mm-hm.

THE COURT: Now, let me go from there, and give you an example. So let's say that misclassification error causes

four of the cases in the exposed group to move over to the unexposed group, and it causes two of the cases in the unexposed group to move over to the exposed group, at which point, I believe, we have seven cases in the unexposed group and eight cases in the exposed group.

Did I get those numbers right?

MR. LASKER: I'm sorry?

THE COURT: Let's try it again. Let's try it again. Okay?

MR. LASKER: I knew where you were going, but I didn't do the math, so I'm not sure.

THE COURT: All right. So we have 15 total, right?

THE WITNESS: Ten. I wonder if we could even somehow draw it.

THE COURT: Here, let's get a board.

MR. LASKER: Yeah we've got a board, we've got the chalkboard, maybe.

MR. MILLER: Your Honor can use the back of that board if you want, that large board and a marker. Do you have a marker? I knew this would come in handy somewhere.

Your Honor, may I stand over here? (indicating).

THE COURT: Sure.

(Court is writing on the board.)

MR. LASKER: This is a first.

JUDGE PETROU: Off the record for a moment.

(Discussion off the record.)

THE COURT: Okay. So we have -- in the unexposed group we have a hundred people, and we have five people with cases; and in the exposed group we have a hundred people, and we have 10 people with cases.

Let's take -- let's say that as a result of misclassification, four people move from -- four cases move from the exposed group to the unexposed group, so that makes nine. And that makes six. Right?

And let's say one -- here's where my -- this is where my math was off. Let's say one person from one case from the unexposed group moves over here (indicating). So that gives us seven, seven cases in the exposed group.

And leaves us with eight cases in the unexposed group.

Do I have that right? So we're still at 15. Okay?

THE WITNESS: (Witness nods affirmatively.)

THE COURT: So now, as a result of misclassification, we have a situation where we have more cases in the unexposed group than we do in the exposed group.

And so the odds ratio is going to be less than 1, right? What's the odd -- can it possible to do that calculation, roughly, what the Odds Ratio would be?

THE WITNESS: I -- I -- I'm not sure, but actually what you've shown is a very nice example of differential misclassification.

THE COURT: Why is it differential misclassification?

THE WITNESS: Because what we -- if it were nondifferential, then the -- a similar proportion of the exposed non-cases would also have been misclassified, as well.

Here, the exposure is a completely associated with the outcome. So therefore, it's differential. It's --

THE COURT: But why couldn't this have happened by chance as a result of misclassification error? Why couldn't -- why couldn't four people -- four cases have gotten over here from the exposed group, and one case have gone over here from the unexposed group.

THE WITNESS: Right. So I think that could be a scenario, but again, that would end up being differential because the misclassification of the exposure was different in -- at -- in the cases versus the non-cases.

So it's sort of -- it's --

THE COURT: So nondifferential just means that the errors occur from both sides, roughly equally? That's all that that means?

THE WITNESS: So both for -- so if there's mis- -- let's say that if, in fact, out of those 10 exposed cases, 4 of them were wrongly classified as unexposed, you'd have a similar proportion, you'd have 40 of the co- -- of the total cohort of exposed also misclassified, in order for it to be un- -- for the misclassification to be similar in the cases and the

non-cases.

THE COURT: You mean, so -- so what we would really have here is, like, 60 exposed people and 40 unexposed people, and what we'd really have is here is 40 exposed people and 60 unexposed people?

THE WITNESS: No. So, sorry. So out of the 10 exposed cases, you were saying that 4 of them were now unexposed.

THE COURT: Right.

THE WITNESS: So then 40 of those hundred would also go to the denominator there. So that's right.

But on the other side, you were just saying that there were -- how many cases were? Sorry, one?

MR. LASKER: One.

THE COURT: One.

THE WITNESS: Only one. So therefore, 10 of that hundred would have moved over. So it would be 60 plus --

THE COURT: But you're assuming -- I guess that's the confusion that I have, is -- and it's again, probably because my math skills are less than rudimentary, but you're assuming that if one -- if one case from the unexposed group goes over here, that means that a certain number of people from the unexposed group were actually exposed.

THE WITNESS: Exactly.

THE COURT: But does that have to be the case?

THE WITNESS: If it's nondifferential, then it, by definition, it does have to be the case. And because --

JUDGE PETROU: Hold on, hold on, because that is the question I asked you right before we took the lunch break, was, is it part of your opinion the assumption that the misclassification that occurred was nondifferential?

THE WITNESS: Correct.

JUDGE PETROU: And you said yes, the misclassification was nondifferential, and so there is that natural follow-up of, how do you know that, or why do you believe that?

THE WITNESS: Right, so the reason it's nondifferential in this cohort study is that there's no way that the development of cancer in the future in any way would have influenced how the people reported on what their exposure was.

There's -- there's not really -- you know, that's -- recall bias happens, and that's a differential bias --

JUDGE PETROU: Right, right.

THE WITNESS: -- because having -- being a case sometimes can influence how you report here --

JUDGE PETROU: So that's a recall bias issue.

THE WITNESS: Exactly, right. So that's a differential bias.

It's nondifferential because it's -- it's -- there are

similar amounts of misclassification in the people who ultimately become cases and those who remain cancer-free. That's why. That's the definition of nondifferential.

So the misclassification in the exposure is similar in the people who do develop cancer and those who don't; and so that's what we have in this situation, with a cohort study.

THE COURT: And so is another way of saying that, that -- that the -- using my example, forgetting for the moment about how many people go from the unexposed group to the exposed group and *vice versa*, is that a way of saying that my example of ending up with eight cases in the unexposed group and seven cases in the exposed group could never happen by chance?

THE WITNESS: Well, I think -- remember we were talking about that -- that issue, and Blair sort of investigated the effect of chance?

And if you have small numbers by chance, just as you were saying by chance you might have, even though it's nondifferential, just by chance you might have slightly more of the cases as you have going one direction than the other, in the -- in the situation -- even with a hundred, though, it seems sort of -- a hundred on each side starts to seem unlikely that you would have, by chance, a nondifferential misclassification that would lead to going through the value of one, and having a lower odds.

But especially in the case of the Agricultural Health Study, where you have 50,000 people 575 cases, because -- that the -- the role that chance would play, potentially, when nondifferential misclassification could lead to this type of result, is -- is very, very uncommon.

THE COURT: Okay, and if -- but in my scenario, is it correct to say that this is very, very uncommon, if everything else in the study went right?

Like, could other things in the study have gone wrong, to get us below one, an odds ratio of below one, such that the -- the -- the misclassification error could move us back above one?

THE WITNESS: It would be -- again, it would be -- it was highly unlikely.

And I think the way to think about the misclassification, let's say we have the hundred people who are exposed. We're really thinking about, well maybe 20 percent of them were misclassified. So you're moving 20 percent of the whole hundred, and then the question is: How many of that hundred were cases?

And then vice versa, with the unexposed group you have a hundred people. Let's say 10 percent of those people were misclassified as exposed. So by chance, how many of those are cases? And with a distribution of a hundred, and with 10 and 5 cases -- well, maybe 10 and five wasn't quite enough.

JUDGE PETROU: Right.

THE WITNESS: You could see more by chance that you might have this issue, but it's -- as you get larger numbers and as you get -- as you -- yeah, larger number sample size and larger number of cases, the role that chance could play in something like this is -- is quite rare.

And -- and with -- nondifferential sort of stands on its own. There may be other biases we want to talk about, but they're not going to have a multiplicative effect. They sort of act potentially independently.

THE COURT: Okay. Thanks. Sorry about that.

MR. LASKER: No, no problem.

JUDGE PETROU: Judge, I'll ask a follow up on that before we move into the next topic.

Yeah. So Doctor, your testimony was, and I quote, "the misclassification in the exposure are similar in the people who do develop cancer and those who don't."

That's the situation we have. And the last part wasn't an exact quote.

And one thing that you brought up was the whole recall bias issue and why that isn't an issue here. Fine, understood, get that.

What are the other main issues that you look at or are concerned about when thinking about misclassification in a case like this, and potentially differential misclassification?

THE WITNESS: It's in -- in the setting of a cohort study, it's -- it's -- I -- what the -- we're sort of reassured because situations of differential bias are just -- they don't arise in the way they do with case-controlled studies.

One type of differential bias that you could think about, which is not the case here, is if you have -- if you're following people for the incidence of non-Hodgkin's lymphoma, and you don't have complete knowledge of who develops non-Hodgkin's lymphoma or not --

JUDGE PETROU: Right.

THE WITNESS: -- and that's somehow maybe related to the exposure, you could have a bias here, but we're --

JUDGE PETROU: We've just talked about the registries and --

THE WITNESS: Right, exactly. So that's one type of bias that you could have that would be differential in a cohort study we could be worried about, but it's not a case here.

JUDGE PETROU: And I presume this is in your questions, but I'll flag it if it's not. I'd like to hear some of the same testimony relating to the follow-up data, the lack of people responding, how it was computed and why you think there's still nondifferential classification. Okay?

MR. LASKER: That's exactly where I'm going, your Honor.

THE COURT: But before you get there, one other

question about your testimony this morning.

You talked about, I think you gave a 90 percent figure for the response -- the responses for the second questionnaire, and I think you said that 90 percent of them landed within one classification of their response, in the question -- in the first questionnaire. Did I get that right?

THE WITNESS: Yeah, so in terms of the reliability study, the questionnaires that were one year apart, yeah. So 90 percent of those landed within one category in terms of the dose-response, yes.

THE COURT: And how many categories were there?

MR. LASKER: Could we put that back up? It's going to be the 2002 Blair Study.

THE WITNESS: It's Tab 5 and it's --

MR. LASKER: It is the footnote on Table --

THE WITNESS: Yes the footnote on Table 2. And so, for years of use --

MR. LASKER: Just one second.

THE WITNESS: Oh, sorry.

MR. LASKER: There you go. You got it.

THE WITNESS: All right. So for years of use there were six categories, and for days per year there were seven categories.

THE COURT: Okay, and do you know how many people hit their -- hit the same category that they responded on, in the

first questionnaire?

THE WITNESS: Yeah, that's a good question. Unfortunately they don't present that number here.

THE COURT: Okay, and so the range could be -- I mean, just using the Days Per Year category, the range could be anywhere from 20 to 150 days for those 90 people?

THE WITNESS: Mm-hm.

THE COURT: And -- and so we know that 10 -- those 90- percent of -- of respondents, and we know that 10 percent of the people who responded 40 to 59 days, responded with something higher than 150 days the next year, or something under -- under 20 days of the next year. Is that right?

THE WITNESS: Um, so I mean, I think -- I think so. If the true answer was between 40 and 59, and then, like you're saying, right. So 90 percent of them would have either been one category less or one category more.

And then -- yeah. It would be true that 10 percent of those individuals then would have ended up in the highest or in the lowest.

THE COURT: And so would it, in terms of numbers, roughly 90 percent of the people who first responded 40 to 59 days, all we know about them is that the following year they responded somewhere between 20 and 150 days a year.

And then the 10 percent -- for 10 percent of the people, roughly, who responded in the first questionnaire between --

that they used glyphosate between 40 and 59 days per year, they -- the second time, the following year they responded either with something more than 150 or something less than 20.

Is that -- did I get that right?

THE WITNESS: So between, I think, between 10 and 19, they would have landed in that category.

THE COURT: Couldn't they have also said --

THE WITNESS: Or that's right, yes --

THE COURT: -- less than five?

THE WITNESS: No, and so that is true.

And I -- but I think that when we think about misclassification and, as I mentioned earlier, that these types of reliability estimates are online with data such as for tobacco smoke, where we are able to show associations, and in different studies.

It's also in line with things like obesity, which again, we've studied with respect to cancer risk and validated multiple studies, and I think what's reassuring is that 90 percent people, if they were 40 to 59, are between 20 and that upper level, but they're not zero.

And so I think -- and again, what you could see also from the biomonitoring study and from the correlation coefficient being on the lower side is maybe you are not accurate in saying the exact level of intensity, but it seems like what we can do is appropriately rank people as high or low.

And I think -- I think that is one of the limitations with this approach, but I think you are able to rank people appropriately.

BY MR. LASKER

Q. And just to follow up on that, if we can pull up -- and I'm sorry it's the 2018 study, Supplementary Table 1.

And this goes back to a point that Judge Petrou was raising earlier about -- I don't have -- I'm sorry -- which I don't have my cheat sheet which tab is this for the --

MS. SHIMADA: Four, tab 4.

MR. LASKER: Tab 4.

Q. And if I could ask you to turn to Supplementary Table 1, which is Cumulative Days Exposure.

And as we looked at previously, there's a footnote on the bottom, on the second page of that table, at the bottom of the table, that talks about the quartiles of cumulative days of exposure, with the highest quartile being over 108.5 days, correct?

A. Yes, that is correct.

Q. And then if we look at the dose-response for non-Hodgkin's lymphoma, which is at the top of that same page, just based on cumulative days, in that highest Quartile 4, with greater than 108 days, the rate ratio is 0.8 compared to people who report absolutely no exposure. Correct?

A. Correct.

Q. Okay, and so again, what does that discussion you were just having with the Court about the levels of agreement between questionnaire responses indicate, when you have that 0.8 between the very highest exposure and no exposure?

A. Right. So it seems unlikely, based on the results of these validation studies, that -- that you have only, at most, minimal misclassification, and people who are in the highest quartile compared to those who were unexposed, so that amount of misclassification, you feel much better about at the extremes based on the validation studies.

MR. LASKER: Okay. So now, Judge Petrou, we'll move to the validation studies of the -- of the multiple mutation.

THE WITNESS: So that would be Tab 8.

BY MR. LASKER:

Q. Yes. Well, let's -- so first of all --

A. Sorry, sorry.

Q. Let me just ask the prefatory questions, and then that will get us there.

So first of all, Dr. Mucci, is multiple imputation a standard methodology in epidemiology?

A. Yes, it is. It's a standard approach that we use to deal with missing data in our studies.

Q. And there's been discussion of the nonresponders, the rate of nonresponders, which I believe is 37 percent. Have you been involved with cohorts studies where multiple imputation has

been used with that level of missing data?

A. Yes. One example is a cohort called the Swedish Mammography Cohort. It's a cohort of similar size, 50,000 women, who completed a baseline questionnaire, actually around the same time frame as the AHS filled out their baseline questionnaire.

There was a follow-up questionnaire where 30 percent of the women did not complete that follow-up questionnaire, and the study investigators have used multiple imputation to impute that data, and that imputation has been used in multiple complications.

JUDGE PETROU: What was the purpose of that study?

THE WITNESS: The main interest of that study was looking at risk factors for breast cancer as well as other cancers. It collected -- it was created by women who were first coming to mammography screenings in Sweden. They were given a baseline questionnaire, and the main hypotheses were around different lifestyle factors for breast cancer research and other cancers.

BY MR. LASKER

Q. And Dr. Mucci, had there been, prior to the 2018 *JNCI* study, other peer-reviewed publications that have come out of the AHS cohort that have used the multiple imputation methodology?

A. Yes. To date, there have been eight other studies that

have used multiple imputation.

Q. And did any of these other peer-reviewed publications look at glyphosate for other cancers?

A. Yes, three of those did.

Q. Okay, could we put up slide 8, which will be a slide that tries to explain how multiple imputation works?

And could we just, Dr. Mucci, explain what we're seeing on the screen?

A. Sure. So just to give a little background on multiple imputation, it works because there are known patterns of co-exposure to different factors in the data.

So you might have a person of a certain age who also smokes and tends to have a certain weight, et cetera, and the multiple imputation approach then uses people who have complete data, and say, who do -- for the people that are missing data, who do they look like that are closest to, and they use that information to impute.

So the variables that were used in the imputation included a range of demographic variables, lifestyle factors, medical history, as well as farming-related and pesticide use.

And so from this figure, there were three different pieces of questionnaire responses that were used to impute the data for the 19,000 individuals who did not come complete the Phase II questionnaire.

So first, there was information that was from the baseline

questionnaire for those people who have missing data; and then there was information -- and the people were matched to those who were -- the remaining 34,000 who completed both questionnaires using their baseline information.

And then again, there's information that was using the questionnaire responses for the Phase II survey, for those people who completed both.

And all three levels of that data were used in the imputation process.

Q. Okay, now, the plaintiffs' experts have argued that multiple imputation cannot account for an increase in use of glyphosate from the period of Phase I to the period of Phase II. Is that consistent with your understanding?

A. No. It's not. And the reason is that, as you can see from this diagram, there's -- there's information that's captured for the 34,000 individuals during that follow-up time to collect data that might be changing.

And because of the way the multiple -- and an advantage of this multiple imputation approach, in fact, is that it's able to capture those trends over time, and match people based on the correlation of data within individuals.

JUDGE PETROU: I'm sorry, I missed something completely. What data was gathered on the -- who did you say data was gathered on?

THE WITNESS: So in terms of --

JUDGE PETROU: In the follow-up.

THE WITNESS: In the follow up, so it was for the 34,000 individuals who filled out both questionnaires.

MR. LASKER: I'm going to go to the validation study, but I want to make sure your Honors --

JUDGE PETROU: Those were my questions to make it easier --

MR. LASKER: Okay, okay.

Q. Now, Judge Petrou raised the issue of whether or not there are differences -- there might be differences between individuals who responded to the questionnaire and individuals who did not respond to the questionnaire, that could raise concerns about potential bias.

Were there any validation studies that were conducted to look into that question?

A. There were, and I just want to comment also that we should be, as epidemiologists, concerned with the fact that there is 37 percent missing data. We do want to rule out that there are not biases that are systematic as a result of this missing data.

I think what's really nice, though, about the Agricultural Health Study is a number of validation studies as well as sensitivity analyses we're going to talk about.

So I think that the first strategy that the investigators did was in the manuscript by Montgomery, *et al.* -- no sorry.

MR. LASKER: I'll put that up. Its slide 9. It's Tab 7 in your binders, your Honors.

THE WITNESS: And so the first question they wanted to know: What were -- did the baseline characteristics differ for people who did and did not participate in the follow-up questionnaire?

And the reason that is important is that if -- if there are differences and those differences are in some way associated with the outcome we are interested in -- so cancer and non-Hodgkin's lymphoma -- that could induce what's called selection bias.

And so if -- if there were very limited differences between those who did and didn't participate, your concern about selection bias is reduced.

So in this study, what Montgomery did was to compare the characteristics of those individuals on lifestyle demographic factors. They also compared cancer incidence rates overall. They didn't look specifically at non-Hodgkin's lymphoma incidence rates, but they did look at cancer incidence overall. And what they showed was that overall, the differences between their participants and non-participants was actually fairly small.

And when we looked specifically at cancer incidence in the population, there was virtually no difference between those who did and did not complete the questionnaire.

They also in this study tested whether there was selection bias for three specific exposure and disease associations. They were not looking at non-Hodgkin's lymphoma, but they did look at smoking and lung cancer risk, as well as the association between smoking and non-cancer lung conditions.

And all of these data supported the likelihood that there was no selection bias induced by the fact that there was missing data, and it's really probably because the characteristics of those who did and did not participate were generally similar.

BY MR. LASKER

Q. And we also had some testimony about another validation study by Heltshe that pulled out some portion of the population to test the imputation method.

So if we can -- this is Tab 8 in your binders, Your Honor. It's slide 10 for those in the courtroom.

And this is described -- here's a graphic illustration of what was done in the Heltshe study, which is at Tab 8.

So if you could, explain to the Court what is depicted in this slide.

A. So what Heltshe, et al. did was another approach to assessing the quality of the imputation method.

And so what they did here was they had 34,000 individuals who completed both a baseline questionnaire and the follow-up questionnaire.

So out of these 34,000 individuals, they actually withheld 20 percent of them, which turned out to be about 6800 people.

So they took those people and put them aside, and then they used the same imputation method, and for the 80 percent of the remaining people or 27,000 individuals, they then imputed the data for that 20 percent holdout set.

And so what's nice about doing it in this way is they could directly compare the results of what the data looked like for the imputed values for these exposures compared to what the people actually responded to, and do that direct comparison and test how the imputation method worked.

MR. LASKER: Okay, and before I move on, do your Honors have any further questions about how this study was conducted?

JUDGE PETROU: Not right now.

MR. LASKER: Okay, so if we can just pull up slide 11.

Q. This is the overall conclusions of the Heltshe paper. There was also specific conclusions or specific data provided with respect to each of the, I think, 40 or so individual pesticides that they looked at.

And can you first just provide your opinion as to what this study showed and what it indicated with respect to the imputation both generally and for glyphosate?

A. So for overall use of any pesticides, the -- based on the

self-reported data, the prevalence of using any pesticide was 85.7 percent, and imputed prevalence was 85.3 percent. So they were actually fairly similar.

And similarly, the distribution for days of years per use as well as prevalence for specific pesticides was fairly similar for a variety of pesticides.

And we can actually look specifically to see how glyphosate did, comparing the imputed value versus what was observed in this holdout dataset.

Q. Okay, and why don't -- first of all, if you could direct the Court, because I don't have it in front of me -- there's figure number, but I'm not sure what page it is.

A. Right, so it's Figure 2 on page 414.

Q. Thank you.

A. So this is plotting the relative error in the imputed prevalence compared to the observed prevalence.

And it can be thought of, if you take one minus, it can be thought of similarly to the reliability study. It's the sort of concordance between the imputed and observed reported information on glyphosate use.

Q. Okay, let me just go back and take that back a step because I'm not sure if that was clear.

Could you repeat how you compared that to the Blair 2002 study on the reliability of the first questionnaire?

A. Right. So just to clarify, so what's plotted here are

relative errors for each of the pesticides. You can see there's a relative error of zero, which would mean they were perfectly concordant with each other.

The ones to the left, where it's negative, suggest that the imputed value was lower than it was for the observed value.

Then on the right-hand side, you have those where the imputed value was higher than the reported value for the pesticide.

And so the relative error, you can calculate the relative error, but to calculate the concordance, you can take one minus the relative error to give you a proportion of concordance between imputed and the observed data.

And when we do that, you can see glyphosate -- the relative error was 17 percent, which means that the concordance was 83 percent, which actually is fairly similar, in terms of number, where it was the concordance for the reliability between the baseline questionnaire and the one year follow-up for those 4,000 people that filled out those two, to look at the reliability. So fairly similar, in terms of a classification.

Q. And just to further clarify, this measure would be an ever/never measure, correct?

A. Yes, correct.

Q. And in this case, given the data that we have for the highest exposure group, we actually would need to be seeing

misclassification from the non-exposed to people at the very, very highest exposure, correct?

A. Exactly, correct.

Q. And there has been testimony in this case -- you can keep that up there, I'm sorry -- that the imputation methodology, while it may have been perfectly fine for other pesticides, was uniquely unsuited and did not work for glyphosate.

Is that consistent with the data that's reported in this validation study?

A. So actually, if you -- if -- if we could draw a line through the relative error for glyphosate, and draw a similar line on the right side, because again, some of them, the imputed value was less than the observed, and for some it was greater, but you really want to take the absolute difference, what you can see is that glyphosate ends up sort of being in the middle range.

You have a number of pesticides on both sides either over-imputed or under-imputed, which are -- have more error than glyphosate does.

Does that make sense?

Q. It does.

I don't know if your Honors are going to get there, but if your Honors understand, we can just move on.

A. Okay, right. So glyphosate, while not perfect, it certainly suggests it does quite well in relation to the other

pesticides that are presented here.

MR. LASKER: Okay, unless your Honors have questions, I'm going to move off the validation studies now into sensitivity analyses.

JUDGE PETROU: This is not exactly on topic, a related question. Does it concern you at all that the follow-up questionnaire only asked about usage in the prior year?

THE WITNESS: I understand the comments have been made about concerns, what that is. I'll say why I'm not concerned, and why it doesn't, I don't think, have really any impact on the results.

So if you read through the Agricultural Health Study, you can see that the baseline questionnaire was filled out between '93 and '97, and then the follow-up questionnaire was sent to individuals five years later.

MR. LASKER: If we can bring up, actually, so that we can all be looking at it, or your Honors can look at -- I don't know the Exhibit number. What was Andreotti again, what tab?

MS. SHIMADA: Tab 4.

MR. LASKER: And page 2, the method Study Design. And if we could just pull up that other....

THE WITNESS: All right. So if you go on the left column under Methods, under Study Design, that first paragraph discusses that the -- the follow-up interview questionnaire was

given five years -- approximately five years after enrollment.

And so what that means, then, since it was asking information about the questionnaire just prior -- I mean, sorry -- the year just prior to that follow-up, when that follow-up questionnaire was given, then really we're talking about a four-year period.

And so for me to be concerned about any substantial change, it would mean that there were people who were unexposed at baseline somehow started using glyphosate in those four years and then stopped, and then were not using it at the follow-up questionnaire.

That's the only -- those are the only people I would be worried about, about being misclassified, because they wouldn't be captured as using glyphosate in either the baseline or follow-up questionnaire.

It -- it seems like that proportion of people is probably fairly small. So the influence on --

JUDGE PETROU: So when you're doing -- and I should know this, but I don't. As I sit here, I can't figure out what the answer is. When they're doing the calculations, let's say we have someone who responded to both, okay? So we're not trying to impute data to that person. And on the first go-round he -- I think he said it was 96 percent indicated that there was no usage, and then at the five-year mark indicated heavy usage.

What is the presumption for those years in between?

THE WITNESS: Right, so that's a great question.

So they -- the way -- and this is how we do our epidemiology study --

JUDGE PETROU: Mm-hm.

THE WITNESS: -- was for the four years from when they were not using until when they started heavily using, they'd still be classified as not using, and then they would start heavy use. And so --

JUDGE PETROU: That's exactly what I was wondering about because I was wondering, what happens during that time --

THE WITNESS: In those four years.

JUDGE PETROU: -- because the presumption is that whatever the answer is on day one is the answer that is in place from day one through the next four years, regardless, and then what the answer is at the year five-mark goes backwards one year.

THE WITNESS: Right, and then it goes forward again with them, and so -- right, so you do raise an issue, are you concerned about misclassification.

But we know those -- those people were very likely unex- -- basically, the question is, how much would they change in that ranking if you knew for sure that all of them who were classified as unexposed actually were heavily exposed for those four years, and the question is whether or not they would they

change the ranking so dramatically.

I don't think so, because it's such a short amount of follow-up time. From the follow-up questionnaire until when the end of follow-up was is another between 8 and 14 additional years.

So you actually have more time of follow up from the baseline questionnaire than you do from that four-year time period.

So it -- it could introduce some error, but it's-- again, it's unlikely to be a substantial amount of misclassification.

THE COURT: Let me ask a follow-up question on that.

So is maybe another way to say that, that at least for purposes of ever versus never exposed, it's only going to be a problem -- that category of person is only going to be a problem if they're diagnosed with non-Hodgkin's lymphoma in that four-year interim?

THE WITNESS: So actually, if they're diagnosed -- right. Well, that's a good question.

It's -- if we're -- it would -- you might be worried about it if you're not -- that you're doing reserves without any consideration of latency.

So if you really think that is an extremely short latency, then maybe that would be a concern, but if you think that really the latency is at minimum 5, perhaps at minimum 10 years, then if those cases were diagnosed in that period, then

I'm actually not as worried anymore, because you have all of that information.

When the cancer probably was starting to develop, we're correctly capturing them as unexposed, so I think it's really an issue when we have shorter latency periods.

BY MR. LASKER

Q. Okay. Let's move onto the sensitivity analyses, your Honors.

And first of all, can you explain what a sensitivity analysis is?

A. Sensitivity analyses are analyses we do to test certain assumptions that we've made in our main analysis.

Q. Okay, and did the AHS investigators conduct any sensitivity analyses of the findings in their study?

A. Yes, there were three main sensitivity analyses that were done.

MR. LASKER: Okay, let's put up slide 12.

Q. And if you can, explain what was done in this sensitivity analysis.

A. Right. So the first two sensitivity analyses were, again, the investigators being concerned that the imputation might have led to some sort of bias, and so what they did here was to only use the complete data that they had from the baseline questionnaire. So they didn't integrate the follow-up questionnaire at all, so imputation was not an issue.

And so what -- when they did this analysis, you can see here that the relative risk estimate compares individuals in the highest exposure quartile to those who are unexposed, and the relative risk estimate there is virtually identical to what it was in the main analysis; so suggesting at least this testing of the sensitivity to the imputation seems to suggest it was not a problem. So --

Q. Let's put on slide 2?

A. Oh, so then another way -- and again, I think what's really nice about the approach that the Agricultural Health Study investigators took was they really wanted to test this issue of the imputation from multiple angles.

So the second strategy they used was to only use the complete data on the 34,000 individuals who answered both questionnaires, and then look at the association with cancer outcomes.

So again, this is the relative universe comparing the highest quartile to those non-exposed, and what you can see here is that the relative risk estimate is virtually identical to the main analysis, as well as the other sensitivity analysis, so again giving us reassurance that the imputation approach did not introduce significant bias.

Q. Okay. Before we move to a third sensitivity analysis, there was also a lagged analysis in this study. Can you explain how, if at all, that provided further, sort of,

sensitivity analysis of the results?

A. Right. So as I mentioned, there were four different lagged analyses that the investigators considered. They looked at latency periods of 5, 10, 15, and 20 years.

So since we in this study have follow-up up to 2013, the latency analysis from 15 and 20 years actually only relies on the baseline questionnaire, which was included for everybody.

So those results are sort of not influenced in any way by the imputation, and again, those relative risk estimates for the 15- and 20-year latency analysis were virtually identical to the main analysis.

Q. Let's go to the third sensitivity analysis.

A. So the third sensitivity analysis was addressing the question of whether the potential increase in glyphosate use in the AHS participants could have led to some sort of bias.

So that the fact that there wasn't data integrated on the third questionnaire into this study, that there might have been changing increasing use, might have led to -- might have influenced the results in some way.

So what they did here was they used the baseline questionnaire as well as the follow-up questionnaire, including the imputed data, but then they ended the follow up at 2005. So they're sort of ignoring, potentially or -- they're not ignoring, their testing the assumption about whether the change in glyphosate between 2005 and 2013 could have influenced the

results in some way.

And so what they showed here, again, was that there -- when you compare the highest exposure quartile to unexposed, there's no association between glyphosate and NHL risk.

Q. Dr. Mucci, given the findings of these validation studies and the sensitivity analyses that we've been discussing, is there any basis in the data to conclude that the findings of the 2018 NCI study were biased due to nondifferential misclassification?

A. No. Given the results of the sensitivity analysis and the validation studies, I -- I feel confident that we can include significant nondifferential misclassification. If there exists, it would be a very small of nondifferential misclassification.

Q. And we've talked, and a number of the experts have talked about sort of the nature of epidemiologists to critically review studies and raise criticisms of possible issues that could arise.

Is it standard epidemiological methodology, however, to ignore the findings of validation studies and sensitivity analyses when you're making those criticisms?

A. No, and the reason is that, as I mentioned earlier, as an epidemiologist, when you review a particular study or a body of studies, and you want -- you look first at the results. You want to try to understand whether those observed associations

could be due to bias, confounding or chance.

So it's really critical to take in all of the available information that helps you evaluate whether these bias or confounding might exist in your data. So it's really critical to take all of that information together.

Q. And given the results of the sensitivity analyses and the validation studies you've just walked through, what is your opinion as to the robustness of the findings -- the reliability of the findings that are reported in the 2018 *JNCI* study?

A. I think, you know, we haven't talked yet about some of the other issues, such as their approach to confounding, which again, I think their approach to confounding was extremely reliable.

So I think, taking into account that analysis approach that they use for dealing with confounding, as well as their concerns around various issues around misclassification, all taken together, I think these data are extremely robust.

MR. LASKER: Okay, I was actually going to move to confounding now, but that will take me largely out of the AHS study, so I want to make sure your Honors have had your questions answered with respect to that study, because the next discussion will be more statistical, for this.

THE COURT: Let me just glance at my notes real quick.

MR. LASKER: Okay.

THE COURT: Could I ask -- you touched on this already, and I apologize if you already directly answered the question, but how many people remained under-exposed after Phase II in the -- in the AHS cohort?

THE WITNESS: So there were 83 percent of the individuals who, by the end of the study, had reported prior exposure to glyphosate. So 17 percent of those remained unexposed.

THE COURT: And how did that compare to the Phase I response?

THE WITNESS: In the Phase I, I believe the -- the prevalence was 75 percent. So about 80 percent of individuals started using glyphosate between the baseline and follow-up questionnaire.

THE COURT: Okay. So one of Dr. Ritz's criticisms of the study that I think may be you have not addressed yet -- unless I missed it, which is entirely possible -- is the fact that way too many members of the cohort are exposed for the study to be useful.

Could you address that?

THE WITNESS: Yeah. Sure. So it's not correct, actually, and, in fact, it's a real strength that 83 percent of the cohort is exposed, because we can look at a whole range of exposure. We have people, as you can see --

MR. LASKER: Do you want to pull up the

dose-response?

THE WITNESS: Yeah, sure, if you could, put up the categories for the quartiles of the dose-response.

BY MR. LASKER:

Q. So now, is that the table -- supplementary table with the days of use?

A. Yes, correct. So what that allows us to do is to look at a whole range of exposure --

Q. No, no, no, the footnote on the end of this, at the end of the table.

A. The footnote there. Um. So we have 17 percent of 50,000 individuals. So it quite a large number who remained unexposed.

And then what it allows us to do is to look at low levels of exposure, all the way up to more than 108 lifetime-days of exposure. And if we think about the case-control studies, the upper end is -- I think the highest in one of the studies was 10. So we really can look -- because there's so much exposure, we can really look at high and low levels of exposure.

Another way to think about it is the prevalence of cigarette smoking in epidemiology studies right now is probably around 17 percent. Again, if you have to put that in a visual, 17 percent of 50,000 is quite high, and we can look at relatively small associations between cigarettes --

THE COURT: You say the percentage of people smoking

or the percentage of people not smoking?

THE WITNESS: So the percentage of people smoking is 17 percent. So 83 percent of individuals are not smoking in the study, so it's-- again, I think what -- you know, 17 percent, if there were only a hundred people in our cohort, it would be concerned about power.

Here, where we have 17 percent of 50,000 individuals, that's a lot of individuals who are unexposed who remain under-exposed.

Plus the advantage of having 83 percent have some sort of exposure is that we're able to test in this dataset whether very high levels of glyphosate where you might expect the -- you know, if this were -- if something were to be associated with cancer, what you'd expect is a lot more exposure to it would be associated with even stronger risk.

JUDGE PETROU: Finish your answer, before I ask.

THE WITNESS: So just I think here what we can do is we're able to look at doses of exposure that are 10 times greater than what the case-control studies are, in that upper quartile, but again, we don't see any association there. So it provides some reassurance.

Yes, your Honor.

JUDGE PETROU: Going back to an earlier answer, I believe you said, in response to Judge Chhabria's question, that you are weren't so concerned about the lack of data

between years 1 to 4, because -- am I understanding you correctly that you do not believe this is a disease with a short latency period?

THE WITNESS: Yes, for this particular exposure, correct. Yes.

JUDGE PETROU: Okay, so does it concern you at all, if my notes are correct, my notes indicate that the median years of use for the people in this study, over half of them have less than eight and a half years of exposure? Is that correct?

THE WITNESS: At -- that's a good question.

So the median, yeah, the median lifetime years of use was 8.5 years, yes. Correct.

JUDGE PETROU: So does that concern you at all, if it's your view that this is a disease with this kind of exposure requires a long latency period, does this indicate to you in some way that this is maybe more of an interim-level study rather than a more conclusive, final study?

THE WITNESS: So I think -- it's an interesting question, but the amount of years of use is a little bit different than the amount of follow-up time we have on those individuals. So --

JUDGE PETROU: So explain that to me. How is that different?

THE WITNESS: Right, so --

MR. LASKER: Maybe we could move to the slide on latency. Let me see if you could put up on the screen slide 17.

JUDGE PETROU: I do want to stick with this study for now, before you respond to it.

MR. LASKER: This study is in here. It's the top bar, just in responding to your question.

JUDGE PETROU: No, I see that.

THE WITNESS: So with the 8.5 years of use, you know, we don't know when exactly in time they were using that. They could have been using it in the 1980s, 1990s, 2000s.

But what we do know is the start of when they were exposed; but then we also have this huge amount of follow-up time.

So it's a different -- the different question that we have is, you know, how much follow-up time do we have from people when they potentially first could have been exposed, which was in 1975, and then all the way through 2013. So we actually have more than 30 years of latency.

So some of those 8.5 years were in the individuals who were using it very early on, and then stopped.

JUDGE PETROU: And then stopped.

THE WITNESS: And then some of them might have been more recent.

So I actually -- I feel quite confident here that there is

sufficient latency, given the distribution, and since the median was 8.5 years, if you look at the inter-quartile range --

JUDGE PETROU: Mm-hm.

THE WITNESS: -- which the upper range would be the 75th percentile, so 25 percent were using it at least for 14 years or more.

JUDGE PETROU: Isn't that -- just based on your earlier testimony, are you confident in the data relating to people who used it who were in the bottom three quartiles? The top quartile, you said, is how many years or more? Fourteen?

THE WITNESS: Years of use, yes.

JUDGE PETROU: Okay, so let's kick out that quartile. Is this data that you feel you can rely on if it's a total use of less than 14 years, for everyone?

THE WITNESS: Yeah so I -- I am. Again, because I think the question, this is really what happened to these people, so the question is, given that amount of exposure, is that enough to lead to cancer occurrence?

But so, you know, again they may have gotten -- let's say it's even only five years of exposure and let's say it happened here. You then have 10, 15, 20 years of follow-up, even from when that last happened.

You know, so with cancer, you -- let's say the analogy was cigarette smoking. So someone could smoke for 10 years and

then quit smoking. They actually unfortunately remain at elevated risk even 10, 15, 20 years after they stopped smoking. And so -- and you can pick that up in the data.

So I think it's an analogous thing where if there were an association, if a pesticide were able to cause cancer, if they were using it for five years and then stopped, that elevation would still be present 15, 20 years later.

JUDGE PETROU: Similar to the smoker, if the smoker kept smoking, that would be even worse.

THE WITNESS: And that would be even worse, exactly, right.

THE COURT: Could I ask one more question before we turn from the AHS Study? One more question about the high percentage of people being exposed.

Another thing sort of seared in to my brain from Dr. Ritz's testimony was this map that she put up, showing how much exposure has increased in Iowa compared to North Carolina, and I believe she said that the AHS data suggested that a lower percentage of people remained exposed in Iowa compared to North Carolina, and she really questioned that, given the -- how much glyphosate was used in Iowa.

I mean, I got the impression that everybody takes a shower in glyphosate every day in Iowa.

So do you have any comments on that?

THE WITNESS: I -- so I -- I know there was a piece

of data that looked at when farmers were starting to use glyphosate and pesticide applicators, and actually, like, on soybeans being one of the major crops that's being used with glyphosate, and that uptake already sort of started leveling off in the -- you know, I think it was around 2000 or so.

So, you know, I think this is a population who may have already been starting to use glyphosate, already; and so that the trends may be different than what you're seeing in the whole State of Iowa, where they might be using glyphosate more frequently and more recently in the home.

And I think there was some data -- and I'm not recalling the name of the particular article -- that looked at these -- these trends in use of glyphosate in different acreages of farms, but it's -- soybean was one of the major crops, and glyphosate use was already starting to come up in the late 1990s, early 2000s.

THE COURT: Okay.

BY MR. LASKER

Q. Okay. Since we're on the issue of latency, if we can go back to the slide that we had on the screen, and talk about what this slide indicates with respect to the potential issues of latency, with the various studies that have been discussed in litigation?

A. Right.

THE COURT: Sorry, before you -- Angie was just

showing the clock. You have, like, a minute left or something.

So how much -- assuming that we don't constantly interrupt, how much --

JUDGE PETROU: Big assumption.

THE COURT: -- how much do you think you have left.

MR. LASKER: I think we could probably finish in about 15 or 20 minutes.

THE COURT: Okay.

BY MR. LASKER

Q. Okay, so with respect to, then, the latency issue --

A. Right.

Q. -- what does this graphic illustrate on the question of latency periods between the different studies?

A. Sure, and as if I took -- actually, I just thought of an additional comment to the question that you had earlier about, sort of, you know, let's say that there -- you know, one of the questions is, has there, since that last second questionnaire, a dramatic uptake, and now everybody in the cohort is using glyphosate?

The AHS investigators in the sensitivity analysis actually tested that in their third sensitivity analysis, where they truncated follow-up to 2005, so they were only looking at cases that occurred up until 2005. So any exposure that happened in the future, so they sort of test that directly.

Q. So Dr. Mucci, can you just explain what is depicted in

this chart?

A. Yeah. So this chart shows the -- when cases were diagnosed in the various different studies.

So the Agricultural Health Study represents -- the first line of data you can see there include cases between 1993, which is the first incident case, all the way up through 2013, so it really has the longest potential latency.

You can see some of the these other studies, I put -- here I'm presenting the publications, not the summary studies that I mentioned.

So, for example, the NAPP study, which was Pahwa, et al. study, included both, you know, the Cantor, De Roos, as well as McDuffie studies; and what you can see there is some of the U.S. studies that were included in the North American Pooled Project have very short latencies.

So that in 1975, that's when the arrow shows glyphosate was approved for agricultural use in the United States.

And then at the very bottom, the gray arrow to the right represents a time frame when cases would have had the potential for a 10-year latency since glyphosate was first introduced.

And so what you can see here is that the -- the Cantor study, which was one of the first U.S. case-control studies, would not -- none the cases would have had 10 years of latency; and as a result, the analysis of the pooled project, also the majority -- the case-controlled study that contributed the most

cases was from Cantor et al., so therefore, this also has issues of latency.

MR. LASKER: I know you said you weren't going to ask any questions, but do you have any questions about this chart?

Okay, let's go to the issue of confounding?

THE COURT: Well, I didn't say we weren't going to ask questions.

MR. LASKER: I was going to do it during their time, that's why.

THE COURT: I have a very hypothetical question.

MR. LASKER: I'm sorry, your Honor that seemed unlikely.

Q. If we can go to the issue of confounding, based upon your review of the glyphosate epidemiology, do you believe it is appropriate to rely upon odds ratios that have not been adjusted for other pesticide exposures when that data is available?

A. No, I don't. I think it was a concern that many of the studies showed that individuals who were using glyphosate were more likely to be using other pesticides, and also use of some of those other pesticides were independently associated with NHL. So therefore, that meets the definition of confounders.

So it was important to at least investigate whether confounding due to other pesticides might be an issue.

Q. Okay, and there's been a question that's been raised at

various points in this proceeding about whether a confounder has to be causally associated with a disease for it to be -- for it to act as a confounder and for adjustments to be necessary. What is your opinion on that issue?

A. So that's actually not correct. The standard modern epidemiology approach to confounding is simply that the confounder should be associated in some way with the outcome.

I think an example of this is what we think about in -- as age. In our analyses for cancer incidence, we almost always adjust for age. It isn't age *per se* that causes cancer. There's something basically going on about age. But age captures as a proxy for something else.

So even though it's not causally related to the outcome, it's correlated with something else, and so therefore, it's appropriate to adjust for it, and by adjusting for something that's correlated with something else, for example, with pesticides, it may not be those specific pesticides, could be something else about farming, but we're able to capture the bias that's introduced by the confounding factor.

Q. Okay, and if we can put up slide 16, and we saw this slide previously. This is from the manuscript for the NAPP, and it discussed the approach they took for identifying the three pesticides that they adjusted for in their analysis.

And first of all, do you believe that this -- is this the proper analysis to identify confounders that should be adjusted

for in epidemiologic studies?

A. Yes, this is the appropriate approach to take. What they did was to identify factors or pesticides that were correlated with the exposure, and then they used the literature to look at pesticides that had been previously associated with NHL risk.

It doesn't matter if they're causally related, just that they were previously associated, because if that is the case, that meets the definition of a confounder that can introduce bias, and this was actually the similar strategy that the Agricultural Health Study took in their efforts to accounting for confounding other pesticides.

Q. And Dr. Mucci, in light of the fact that the NAPP investigators identified these three pesticides using this standard methodology as confounders, would it be methodologically appropriate to rely upon odds ratios from the NAPP that were not adjusted for these three pesticides?

A. No, it would not, because -- and what was shown in the slide deck that Dr. Pahwa presented, you can see the effect due to confounding by these three pesticides in the data.

When you look at the analysis, the odds ratios that were concretely (phonetic) adjusted, those were somewhat elevated, and those relative, er -- odds ratios were attenuated when you adjusted for confounding due to those other three pesticides.

Q. And with respect to -- also with respect to the Eriksson study, and just so the record is clear, because we've

not really sort of summarized, the Eriksson study is from the same research group that published the earlier Hardell study.

A. Yes, that is correct.

Q. Okay. This is a later study, looking at the Swedish population, correct?

A. Correct.

Q. In the Eriksson study, was there any evidence in the manuscript or in the paper that indicated that there was confounders -- other pesticides that would act as confounders for the glyphosate?

A. Yes, and so actually, the Eriksson group took a strange approach, actually, to defining the unexposed group. So in all of the other studies, individuals who were in the unexposed group were unexposed to glyphosate, and that's what we want to do. We want to compare what the risk is of NHL is in a group where the only difference is the exposure. Instead, what Eriksson did was to have in the unexposed group those who were unexposed to any pesticide.

So essentially, they threw out from the whole analysis people who were exposed -- well, unexposed to glyphosate, but exposed to other pesticides, and they eliminated those completely from -- from the analysis. And what resulted was that everybody who was using glyphosate by definition was also using another pesticide.

So it was almost as if they had introduced intractable

confounding by the way they defined the unexposed group, and that issue of confounding you can actually see in the multivariable analysis that they performed in Table 7 of the manuscript.

Q. And we've seen that table before, but could the multi-

THE COURT: That was the one with --

MR. LASKER: Yeah, that's the one with arsenic.

THE COURT: Arsenic, okay, thank you. I assume you're going to get to the arsenic.

MR. LASKER: Yeah, the arsenic. I can't go without the arsenic.

Actually, let's pull Table 7 up, so we can talk about that.

Q. This is in the Eriksson Study.

It's Tab 3, your Honors. There's Table 7.

And first of all, before we get to arsenic, although I know we will get there, does this multivariate analysis, given the design of the study, how they classified unexposed -- can multivariate analysis actually adjust for all potential confounding that might be in the study?

A. It's impossible to know, but it's-- it's concerning, because the definition, as I mentioned, of the unexposed group really leads to this intractable confounding.

So we didn't -- we don't have enough information to know what other pesticides, because of the definition, were highly

correlated with glyphosate use. So we can't really tell from the approach that they took.

And there's, you know, normally what we would have in a manuscript is some information about the association between the observation exposure and other exposures, so that potential confounders -- so we could look at the degree of confounding that was introduced. We don't have that here.

But one concern potentially here with Eriksson is the fact that we see so many elevated relative risk estimates.

Q. We're going to get to that.

A. Okay.

Q. That's the next thing we're going to be dealing with, but there was also indication in this manuscript -- and we've talked about it earlier -- about MCPA and the correlation between MCPA use and glyphosate.

Given that, and given the odds ratios that we said are reported in Eriksson for MCPA, does that pesticide -- at least we have enough information about that pesticide to determine whether or not it would be a confounder?

A. Yes, correct. Yeah. So from the manuscript, we know that people who are previously using MCPA were subsequently using glyphosate. So there was probably a strong correlation between the confounder and the exposure there.

And the univariate level, you can see that it's independently associated with the outcome. So therefore, it

meets the definition of a confounder.

MR. LASKER: And I'm now going to ask Judge Chhabria's question, which is: Is there a way, from the data that's been presented in this table, to remove arsenic out of the analysis and re-run the multivariate analysis to determine what the odds ratios would be?

THE WITNESS: No, it would not be possible to do at that. One thing to note, while -- the reason to not put a variable into a multivariable model, so a reason not to put a covariate in as a potential confounder if it is not a confounder, is it can sometimes influence the standard error or the 95 percent confidence interval and lead to a wider confidence interval.

Another important thing to remember with epidemiology is that if you have a confounded odds ratio, your -- by definition, your confidence interval is going to be biased. So you can't calculate the confidence interval unless you have an unbiased odds ratio.

So whether arsenic should or should not have been in the model, I couldn't say. We can't say because we don't have enough information in this manuscript.

You know, is it -- is arsenic standing in for some other potential confounder? Again I can't tell you. Could it have maybe affected the odds Ratio? Again, I can't tell you.

But what I can tell you is that it's okay if it's in there

and it's not a confounder, because all it would have -- it wouldn't impact the odds ratio. It would only affect, potentially, the standard error, or the 95 percent confidence interval.

Q. And so, to put a point on it, for glyphosate we have an odds ratio of 1.51 in multivariate, and confidence interval of .77 to 2.94. What would be a potential impact if arsenic was not a proper confounder --

THE REPORTER: I'm so sorry, could you kindly slow down and start your question again?

BY MR. LASKER

Q. Looking at the odds ratios for glyphosate, and the confidence interval for glyphosate in the multivariate analysis, if arsenic was not a proper confounder but still was put into that multivariate analysis, how would that have potentially impacted the multivariate odds ratio for glyphosate?

A. So it would have no effect on the odds ratio. It might increase the width of the 95 percent confidence interval by a small amount.

Q. And if we can move to the issue of recall bias, and there was -- first of all, what are the factors that can impact whether there's recall bias?

A. So recall bias in the study can occur for a number of reasons.

First, if -- there may be in the public domain some information about a potential cause of cancer. So once an individual has cancer, it's a stressful time, and you can ruminate about the potential causes of your cancer, and if you've heard, for example, that pesticides might underlie risk of non-Hodgkin's lymphoma, you may be actually sort of not realizing that you're doing this, but you may be over-reporting use of certain pesticides. So that's one way that recall bias can impact a study.

A second way which can impact a study is that the way in which cases -- the information from cases is collected differs from the way the controls information is collected. And that can be shown. So I know --

Q. Let me just move on to the next question, because I'm over my clock, and they want us to move it along.

A. Okay.

Q. Would it -- is recall bias something that happens just in general, or is it going to be specific to each individual study whether recall bias exists?

A. It's specific to each study.

Q. Okay, and we heard some testimony with respect to Dr. Ritz where a case-control study reports out odds ratios that are for all of the exposures or almost all of the exposures, above 1.0.

Is that, in your opinion, an indication of a potential recall bias problem?

A. When I see a case-control study and I see a number of the exposures have positive associations, I'm worried about some sort of systematic bias.

With a case-controlled study, the first bias you might think about is recall bias.

MR. LASKER: Okay. And if your Honors, we don't need to go through this in much detail, but in the Eriksson study, Tab 3 in your binder, I would refer the Court to Tables 2 and Table 4. We've already looked at those previously in Dr. Ritz's testimony, and those were -- they are what they are, and you can look at them.

Also, I would direct the Courts' attention to the McDuffie study, which is Tab 2 in the binder, and Table 2, 3, and 8.

And the McDuffie study present the odds ratios for all of the different exposures that are looked at in that study, and you can see where they are relative to 1.0. And we also have the Hardell study, which is Tab 15, and this study is actually a pooled analysis. It actually includes NHL, and then also hairy cell leukemia, they pooled two small studies into that one. And if you look -- that's at Tab 15, and you can look at all of the reported odds ratios. I don't have --

THE COURT: Could I just get a clarification --

MR. LASKER: Sure.

THE COURT: -- of your testimony, Mr. Lasker?

MR. LASKER: I'm sorry about that.

THE COURT: If you want a couple minutes to go through this with her, you can, but one thing I missed was whether you're talking about studies reporting out high odds ratios for other pesticides, or the concept of reporting out high odds ratios for other kinds of cancers.

MR. LASKER: Okay, so in this point of the --

THE COURT: Why don't you explore that with the witness.

MR. LASKER: Okay.

Q. So with respect to other studies, if there are other studies that are looking at other pesticides or other outcomes where there's not elevated odds ratios, what, if anything, does that tell you with respect to recall bias in an independent study, either looking at the same compounds or different compounds and the same diseases and different diseases?

A. So it may not tell us, really, anything, and the reason is that recall bias is really study-dependent. It's both the disease itself, as I mentioned, what's known about the association with the disease in the public domain, and then how cases and controls were queried.

I think, for example, with McDuffie there was an initial questionnaire, and then there was a follow-up interview for individuals who reported using pesticides; and what was shown was that the cases were interviewed more so than the controls,

and that -- those kind of things make you worry.

And there was another. There was a paper by Dr. Blair and Dr. Zahm that actually showed that the way in which individuals were probed about information, whether it was sort of an open-ended response or whether it was more probing through an interview, you're getting a different reporting of exposure; a higher prevalence in the interview.

So if more of your cases are getting interviewed than your controls, and by definition, because of that, they're just more likely to report on different pesticides, you're almost inducing a recall bias just because you're interviewing the cases differently than you're interviewing the controls.

THE COURT: So the way you see concern in McDuffie and Eriksson and Hardell is that when you look at the numbers, the red flag for you is that there's a higher than 1 odds ratio, not just for glyphosate and NHL, but for a variety of other pesticides and NHL.

THE WITNESS: Yes, that is correct.

THE COURT: Okay.

THE WITNESS: And that just makes me worry that there's some sort of systematic bias, and you sort of go through and think what biases might there be.

I think with Eriksson, another potential bias that we've already talked about is the confounding that was due to the way that the exposure -- the unexposed group was defined. But you

know, with any case-control study, we do want to rule out that recall bias might not lead to kind of spurious associations.

THE COURT: One thing that everybody agrees on is that farmers have had higher incidence of non-Hodgkin's lymphoma before the introduction of glyphosate.

THE WITNESS: Yes.

THE COURT: And on one level, that's perhaps helpful to Monsanto's case, but on another level, perhaps that diminishes the concern about recall bias stemming from the elevated odds ratios for the other pesticides, because -- I mean, just sort of stepping back and using logic, seems like -- it seems like it would not be an unreasonable assumption to say, well, they're probably -- regardless of glyphosate's effect, other pesticides -- there's probably an association between the use of those other pesticides and non-Hodgkin's lymphoma.

So in this context, might that actually diminish the concern about recall bias?

THE WITNESS: It potentially could, but it seems like, you know, in the case, I think, of Eriksson, for example, it's more like -- it's more likely to be due to the confounding. There probably aren't --

THE COURT: Well, Eriksson --

THE WITNESS: Right.

THE COURT: Well, maybe let's forget about

Eriksson --

THE WITNESS: Okay, right.

THE COURT: -- and talk about, you know, McDuffie or.

THE WITNESS: Mm-hm.

THE COURT: -- or -- I don't know. We haven't talked about De Roos 2003 yet --

MR. LASKER: Right.

THE COURT: -- but -- and I assume you were going to get to that. But if those studies show elevated odds ratios for other pesticides, is it as much of a red flag as it would be in a different context, I guess, is my question.

THE WITNESS: Well, I guess, I mean it's -- it's not -- for -- you're not definitively saying that there's bias, it just raises concern.

I guess the question is, then, are all of these pesticides that farmers are exposed to leading to NHL? That seems unlikely to be the case.

THE COURT: Why?

THE WITNESS: I think -- you know, it's interesting. Yeah, it's a good question, right. I couldn't say -- I haven't done a review of the epidemiology of these other pesticides. So you're -- it is possible. I couldn't exclude that, that's true --

THE COURT: Okay. Sorry, go ahead.

THE WITNESS: No, I was just going to say that

there's other issues, I think, with Cantor and the studies that are included in De Roos, that we haven't talked about, which are the bias that we do know about, which is for sure proxy bias, and that we see, though, when we adjust for the proxy bias, our results are attenuated towards the null value.

THE COURT: And there's the lag issue with those studies.

THE WITNESS: Exactly, yes.

THE COURT: But on this issue of recall bias, you know, flipping through the IARC Monograph, you know, they also talk about -- they explore the link between glyphosate exposure and other cancers.

THE WITNESS: Mm-hm.

THE COURT: Right? And it seems like -- I -- correct me if I'm wrong, but it seems like with respect to just about every other cancer these case-control studies have not shown elevated Odds -- or significantly elevated Odds Ratios. Right?

THE WITNESS: Right I.

THE COURT: And so doesn't -- if -- if these -- if with these kinds of populations, farmers and whatnot, who are pesticide applicators, if we -- if there was, you know, a recall-bias concern, wouldn't we be much more likely to see elevated Odds Ratios in these case-controlled studies of other cancers also?

THE WITNESS: So the -- it -- you know, the thing

about recall bias -- I actually am not as concerned about recall bias explaining the study findings that we have.

And again, if you think about the four epidemiology studies that I presented on that first slide, they really don't show any evidence of any positive association. I'm not quite as worried about recall bias in the context of this body of literature.

I am a little bit concerned with the McDuffie Study, because of this issue of the fact that the cases were more likely to be interviewed than the controls were.

And there was a prior study by Blair and Zahm that showed, you know, doing more in-depth probing, more likely to get people to report on not just glyphosate, but a variety of pesticides. So I think it's almost like it wasn't the classic way we think about recall bias, necessarily; but again, I'm not as worried about recall bias.

What I am worried about is confounding, because a lot of the estimates initially were not adjusted. I'm concerned about the proxies in the U.S. studies, and the bias that was clear from the analysis that Dr. Pahwa and colleagues did in the NAPP that showed, when you took away the data that was presented by proxies, that attenuated the Odds Ratio to the null value.

So again, those are the ones that -- the ones that I'm more worried about; are confounding and the proxies bias.

THE COURT: Why don't we turn to those?

MR. LASKER: Yes. Okay. Just one follow-up question.

Q. If all of the other pesticides were actually associated with non-Hodgkin's lymphoma, what does the impact of that have on the importance of adjusting for the confounding effect of other pesticides?

A. Right. That would be really critical. Then it supports the hypothesis or importance of adjusting for confounders.

Q. Okay. So let's go to the proxy bias issue, which -- we can just put up Slide 20. We've seen this before. This is from the De Roos 2003 Study. It's Tab 1, Defense Exhibit 720.

And what can you tell us with respect to the numbers of proxies or the percentage of proxy respondents in the cases and in the controls in this study?

A. So as you can see from this figure, 31 percent of cases data came from proxies; but actually a much higher proportion -- almost 40 percent of the controls -- had their data from proxies.

Q. Okay. And if we can just go now to Slide 21, which we've also seen previously during Dr. Neugut's testimony, this is a call-out of the glyphosate data from that table, but it is at Plaintiff's Exhibit 303.

THE COURT: Could you go back to that last slide just for one second?

MR. LASKER: Sure. Yeah.

THE COURT: Thanks.

MR. LASKER: Okay. If we can go to Slide 21. And, as I said, this is Tab 13. It was introduced as Plaintiff's Exhibit 303. This is a pull-out of the glyphosate data from that table.

Q. What does this data indicate, and how does that potentially impact the findings in the De Roos 2003 Study?

A. So this particular table looks at what the frequency specifically of glyphosate was, based on the data that came from the direct interviews with the respondent versus the proxies. And what you can see, actually, was there was a huge underreporting of glyphosate exposure by the proxies compared to the self-reported data. So it's --

Q. If we can go back to the De Roos 2003 table then. What impact would that have, then? Given the relative percentage of proxy respondents in the case and controls, what impact would that have on the reported Odds Ratio out of the De Roos Study for glyphosate?

A. So the -- the Odds Ratio in a case-control study is calculated as the odds of exposure in the cases divided by the odds of exposure in the controls.

Since you have a higher proportion of proxies who are underreporting the exposure in the controls, your denominator is getting smaller, which then means that your Odds Ratio is going to be overestimated away from the one -- null value.

Q. And if you'd turn to Slide 22, this is from the NAPP slide deck. And can you just explain for the Court what is reflected here, and how it relates to your prior testimony?

A. So what you can see -- and this -- and these are the estimates that are adjusted for confounders; the three pesticides that were potential confounders.

And what you can see here is the Odds Ratio, when you included both the proxy and self-respondents, was 1.13; but when you look at just the data for the self-respondents only, the relatively risk for ever exposure goes down to 0.95, suggesting there's a bias.

And also you can see when you look at -- it's also the case with duration, as well as the -- really, the most meaningful measure of dose-response in this table is the lifetime-days analysis. Again, there not much of a change, actually; but still slightly attenuated.

There was -- just to note, there was no difference in the frequency, but I don't think that's really a meaningful estimate of dose-response, just looking at the number of the days per year.

Q. And just to -- well, I think we're going to end it now, Your Honor, with my final questions on this.

Dr. Mucci, based upon your review of the the glyphosate epidemiological literature, have you reached an opinion as to whether there is evidence of an association between

glyphosate-based herbicides and non-Hodgkin's lymphoma?

A. Yes, I have.

Q. And what is that opinion?

A. So my opinion first is based on reviewing all of the evidence, and taking the estimates that are the most potentially unbiased estimates there are; so those that were adjusted for confounding, as well as for the U.S. studies accounting for the potential of proxy bias.

And when you look at the body of epidemiological literature on this topic, there's no evidence of a positive association between glyphosate and NHL risk. There's no evidence of dose-response of associations for glyphosate and NHL risk.

Q. And is it standard epidemiologic methodology to look at studies that report out null findings, and, through criticisms -- methodological criticisms of those studies, reach an affirmative opinion that there is causation?

A. No, it is not.

Q. And why is that?

A. Because you can't -- you can't -- you can't observe what the true relative risk is, if -- even if you're concerned about bias, there's no way to be sure what the true estimate is. You have the data that you have. You can't assess causation based on a null study, even if you are concerned about potential bias.

Q. And, given the body of epidemiologic literature with respect to glyphosate-based herbicide and non-Hodgkin's lymphoma, do you believe, following reliable methodology, an epidemiologist could conclude that there is a causal association between glyphosate-based herbicides and non-Hodgkin's lymphoma?

A. No. As we've discussed today, based on following a standard methodology and evaluating all of the studies, there's no way to come to a causal conclusion about glyphosate and NHL risk.

MR. LASKER: Thank you.

Your Honor, I don't have any further questions.

THE COURT: Why don't we take a ten-minute break? And then I'm assuming we're pretty close to wrapping up.

(Recess taken from 2:25 p.m. until 2:38 p.m.)

THE COURT: Okay. Have at it.

MR. MILLER: Thank you, Your Honor.

CROSS-EXAMINATION

BY MR. MILLER

Q. Good afternoon.

A. Good afternoon.

Q. How have you been, Dr. Mucci?

A. Fine, thank you.

Q. Very good. All right. I promise we have to talk slow. It's late Friday.

Let's define some areas of expertise. Then we'll move into some opinions. We can get through this, I think, fairly quick. You are an epidemiologist?

A. Yes, I am.

Q. Yes, ma'am. You're not a medical doctor?

A. No, I'm not.

Q. Or -- so you're not an oncologist or hematologist?

A. No, I'm not.

Q. You don't hold yourself out as an expert in those areas. Fair?

A. Correct.

Q. Okay. And we heard about occupational epidemiology from Dr. Ritz. You're not an occupational epidemiologist. That's fair?

A. My expertise is as a cancer epidemiologist. However, I am well versed in understanding the methodologic issue in all forms of epidemiology.

Q. You are absolutely an epidemiologist. I am not suggesting otherwise. Okay. All right. And you're at the Harvard T. H. Chan School of Public Health?

A. Yes.

Q. Yes, ma'am. And they have a website there. Right?

A. Yes.

Q. Yeah. And this is the first time that you've been an expert. Right?

A. Yes.

Q. Okay. And you don't want to leave your real-world opinions about these issues at the courthouse door. Right? You're -- you're not going to tell us something here that you don't practice every day in your practice? Is that a fair?

A. I'm sorry. I don't understand specifically your question.

Q. Well, I mean, people -- let's ask it a different question.

Is it fair for people to go to your website at your school, and rely on the information that they see on your website?

A. Which website specifically are you referring to? There are several websites of School of Public Health.

Q. Harvard University School of Public Health, T. H. Chan. Is it reasonable?

A. I'm sorry. I don't know which website you're referring to. Do you mean the main school website? My own personal website? I just wasn't sure which website you were referring

to.

Q. Would it matter?

A. Why don't you ask your question? Sorry.

Q. Can we rely on all of the websites at Harvard, or only a few of them?

A. Well, it's hard to make a blanket statement, since I'm not sure specifically what website. The information that -- any information that I provided, I feel very confident in relying on.

Q. Well, let's take a look. We looked at the website last night. And let's look at --

We've got a copy for you, ma'am, and a copy for the Court --

(Whereupon a document was tendered to the Court.)

MR. MILLER: -- and for defendants.

Q. These are some of the exhibits we intend to use as we explore these issues.

MR. WOOL: The first one's a PowerPoint.

BY MR. MILLER

Q. Let's put up exhibit -- Exhibit 111, which is tab in your binder. We're on to that one now.

MR. WOOL: It's Tab 9.

MR. MILLER: Thank you. Tab 9, so everyone knows.

Q. And this -- this is Harvard T. H. Chan. That's where you are a professor?

A. Yes, I am.

Q. School of Public Health? Ma'am, you have to answer verbally.

A. Yes, I am. Yes.

Q. All right. Thank you, ma'am. It says in pertinent part here -- and I just want to ask if you agree. We saw this last evening -- *IARC is a World Health Organization body that has among its activities to produce independent scientific consensus reports on the causes of cancer.*

That's true; isn't it?

A. Yes, it is.

Q. Yes, ma'am. All right. Let's go, then, to the next page in our book. And this is Tab 14 -- excuse me -- also off your website, ma'am. And what it says is that in March 2015, 17 experts from 11 countries assessed the carcinogenicity of 5 pesticides, including glyphosate, at the IARC. A summary of the final evaluations was published in *Lancet Oncology*.

This is from your website; isn't it, ma'am?

A. It -- just to clarify: Our school's website. It's not my own personal website.

Q. Yes, ma'am. I appreciate that clarification.

A. Yes.

Q. So at Harvard, at your School of Public Health, they put up -- it was an important piece of medical and scientific information; the fact that IARC had declared glyphosate a

probable human carcinogen?

A. I -- they're reporting on this publication and, yes, providing some context for the IARC panel. Yes.

Q. Sure. So if I were to go to the Harvard website to learn about glyphosate, I would see this -- right? -- as I did last night?

A. Yes.

Q. And it would tell me that glyphosate was classified as probably carcinogenic to humans, Group 2A. And it says, *indicating there was limited evidence for carcinogenicity in humans, and sufficient evidence of carcinogenicity in animals.*

Do you see that, ma'am?

A. Yes, I do.

Q. And, in fairness, you said to Counsel just before he sat down that you looked at the totality of the evidence. Do you remember that?

A. Yes.

Q. To be clear, you did not look at the mechanistic evidence, the toxicology, or the animal data. Fair?

A. What I was commenting on specifically was regarding the epidemiology studies, which -- I did look at all of the available epidemiology studies on glyphosate and NHL risk.

Q. Yes, ma'am, but you did not look at the toxic data. Right?

A. I was evaluating the validity of the epidemiological

findings specifically. And that's what I commented on in my discussion.

Q. Okay. You're entitled to explain, but I just want to be clear.

Answer: No, I did not look at the toxicological data. Right?

A. No, I did not look at the toxicological data.

Q. Yeah. All right. And, Dr. Mucci, you looked at -- you did not look at the animal data. True?

A. I did not look at the animal data.

Q. All right. Yes, ma'am. Thank you.

And you did not do the Bradford Hill analysis. True?

A. I did not do a formal Bradford Hill analysis in my report?

I do comment on some of the Bradford-Hill Criteria, and how those relate specifically to the epidemiology study, but I did not do a formal Bradford Hill analysis.

Q. And while you have told us that you do not rely upon or believe that we should rely upon the case-control studies here --

That's generally what you have told us. Right, Dr. Mucci?

A. That is not specifically what I've said. What -- I raised --

Q. Okay.

A. -- concerns about some of the methodologic issues for both the cohort study and the case-control study, and went through

some of those issues; but I didn't say we should not rely on the case-control studies.

Q. Yes, ma'am. I understand. Thank you for that correction, Dr. Mucci, because the Harvard website here says, quote, "Specifically, increased risk of non-Hodgkin's lymphoma was consistent across case-controlled studies of occupational exposure in the United States, Canada, and Sweden."

That's true; isn't it?

A. That is -- I think what -- the job here is to do a summary of what the IARC report said. And this is, in fact, what the IARC report said. So I think they're restating what IARC said.

I don't think they, in this website, were doing a formal evaluation of the epidemiology studies of glyphosate.

Q. And you and I, Dr. Mucci, had a chance to look at this when I had the opportunity to take your deposition up in Boston, I think, in October last year. Right?

A. Yes.

Q. And you have made no effort to ask the school of Harvard to pull this down because it's unreliable? Is it -- that's fair. Right?

A. I'm -- actually, I'm not concerned that it's unreliable. What I'm actually just saying is this is what was written about the IARC report. This was -- it actually all seems like valid information.

That the classification was two-way -- so that seems

valid.

That there was limited evidence of carcinogenicity in humans -- that seems valid.

So I think what they've done here is they're simply highlighting the announcement that came out from the IARC report here. So I don't think they're making any real consensus statement about their -- the state of evidence, themselves. They're really just reporting on what IARC reported on.

Q. They go on, on the Harvard website, if you would, please, to the next page. And I'm not going to read the whole thing, but they tell us about the potential mechanisms for cancer. And they articulate the two pathways that are referenced in *The Lancet* report and the IARC report. Right?

A. They do list also with respect to the IARC report here, yes. This is a summary of what was stated in IARC.

Q. Sure. And let's turn, now, to the report that you think is very significant: The Agricultural Health Study. Right?

Now, you have to answer verbally.

A. Oh, sorry. I Agricultural Health Study is one of the important epidemiology studies on this topic.

Q. Yes, ma'am. And when I took your deposition --

I'll tell you what. Let me just ask the question.

Fair that when I took your deposition, you did not know that the cohort was among licensed applicators; people who were

applying for a license to be pesticide applicators? Do you remember that?

A. I don't remember that. No.

Q. Take a look at it. And you have a copy there. And I'm not trying to --

MR. WOOL: It was Tab 19.

BY MR. MILLER

Q. All right. Tab 19, if you would. And I think you'll find that at page 39, line 18 to 22. Let me read it. And if there's anything else you or counsel want me to read, I'd be happy to. My question to you, ma'am, was, *Do you understand that they were applying for licensed commercial pesticide applicator licenses?*

Your answer was, *I was not aware one way or the other if they were.*

A. I think the context in which I was responding to was I wasn't aware one way or the other that they were actually in the process of applying for the application at the time they completed their questionnaire. I was definitely aware that these were the study was based on licensed applicators, themselves; but I'm not sure I was aware at the time that they filled out the questionnaire that they were actually applying for the license.

Q. When studies are being prepared and they're going to be performed, oftentimes the authors will put their methodology in

a publication, so other scientists can review that methodology. Is that fair?

A. It can be. It can be what they do. Yes.

Q. Yeah. I'm not saying it's done all of the time, but that's often done. That's fair; isn't it?

A. Yes.

Q. Okay. And ironically, the Agricultural Health Study was -- that methodology was available before the results came back. You're aware of that?

A. Could you provide the publication that you're referring to? I'm not sure which one you're referring to.

Q. Sure, sure. Harvard critiqued the Agriculture Health Study. You're aware of that; aren't you?

A. That is not correct. There were authors that were on faculty at Harvard. There were also authors on that study from many other institutions. It was -- so I would not refer to it as a "Harvard study."

Q. Okay. What's the tab on the Gray Study?

MR. WOOL: Tab 1.

MR. MILLER: Okay. Tab 1.

Q. And will you at least agree with me, Dr. Mucci, that this is, in fact, the federal government's "Agriculture Health Study: A Critical Review with Suggested Improvements"? Right? You have to answer verbally.

A. Yes. This is -- the title of this is what you've said,

yes.

Q. And Dr. Gray was the first author. Is that fair?

A. Dr. Gray was the first author. Yes.

Q. And where was Dr. Gray a professor at the time?

A. Dr. Gray at the time was at the Harvard School of Public Health.

Q. Okay. And as I go back -- and I want to go back a little bit. I apologize. But prior to your request to be involved in this by the Hollingsworth firm, you had done no studies about glyphosate. Right?

A. No, I had not.

Q. Okay. And you had done no critique or observation of the Agricultural Health Study. Right?

A. No, I have not.

Q. And you didn't -- weren't aware that, in fact, Dr. Gray, at Harvard, with others, had done a critique of the Agricultural Health Study when I first took your deposition. Fair?

A. At the time I took the deposition, I'm not sure if -- I don't think I was aware at that time of the deposition that this had been done, back in 2000.

Q. And it's important to note, so we put this in perspective, Year 2000, the first questionnaires had already been completed, because, as you and I know, they were completed in what years?

A. They were completed between 1997 and 2003.

Q. I think it was '93 and '97, Dr. Mucci.

A. I'm sorry. '93 and '97. Yes. Sorry.

Q. Okay. So they'd already been completed. And now we have Dr. Gray and about 10 or 12 doctors writing a critical assessment about what kind of information we might get out of the Agricultural Health Study. That's fair; isn't it?

A. So, yes. In fact, that is absolutely fair. And they raised a number of important concerns that -- as an epidemiologist, that I would be concerned about, as well. And what's really wonderful about what the Agricultural Health Study investigators have done, as we've talked about earlier today, is to perform a number of Sensitivity Analyses, validation studies that address these points that are raised in this particular publication since then.

Q. Let's take a look at what Dr. Gray and these other scientists said before the results came out. Okay? They said there were important limitations of the Agricultural Health Study. I'm sorry. I'm reading at --

MR. WOOL: Page 48.

BY MR. MILLER

Q. It's on the screen. Do you see it there, Doctor?

A. Yes.

Q. *Important limitations include low and variable rates of subject response to administered survey.* Do you see that?

A. Yes.

Q. You've told us that 50,000 people responded, about, to the first survey? Is that fair?

A. 54,000 individuals completed the questionnaire.

Q. How many licensed pesticide applicators were in during -- filed for an application during that process in North Carolina and Iowa?

A. I'm not really sure.

Q. It was over 90,000; wasn't it?

A. I'm not sure how many there were. No. I'll take that --

And actually, you know, that's fairly standard with the recruitment to cancer epidemiology studies. The Nurses Health Study is a study that I've been involved in where we had 120,000 nurses. We had actually sent out invitations to four times as many nurses in order to get that 100,000.

That type of low participation rate in the interim study doesn't lead to any bias. It's not really something to be worried about, actually. It is a comment, but it's not something to worry about.

Q. And I understand you're not worried about it here today, but I want to see what Dr. Gray had to say about it then. Okay? He said that, *Low and variable rates of subject response to administered surveys, concerns about the validity of some self-reported non-cancer health outcomes, limited understanding of reliability and validity of self-reporting of chemical use, and an insufficient program of biological monitoring to*

validate the exposure of surrogates employed in the AHS questionnaires, possible confounding by unmeasured non-chemical risk factors for disease, and the absence of detailed plans for data analysis and interpretation that include explicit a priori hypothesis --

Tell the Court what an *a priori* hypothesis is.

A. It's a hypothesis that a set the investigators will set out to test prior to doing any specific analyses.

Q. And to be clear, there was -- and that makes -- a study is more respected within the field of epidemiology is if it has an *a priori* hypothesis. That's fair; isn't it?

A. You know, I'm not sure the context in which they're saying this, in particular, because I think there were a broad set of *a priori* hypotheses that the AHS investigators were interested in specifically to look at the health effects of pesticides on cancer and non-cancer endpoints. So it's quite a broad set of hypotheses; but with a cohort study as rich as AHS is, I think it's a reasonable approach. So I'm not exactly sure the context in which they're saying there were not *a priori* hypotheses.

Q. Well, to be more specific, Dr. Mucci, I think you and I can agree it was not an *a priori* hypothesis prior to the questionnaires as to whether glyphosate increased the risk of non-Hodgkin's lymphoma. That's fair; isn't it?

A. I'm not sure. It may not have been. It might have been.

I'm not sure.

Q. What they warned in 2000 was -- if we go to the next page. And that's on page 52, Counsel.

MR. LASKER: Thank you.

BY MR. MILLER

Q. In the first box -- and again, this is from Dr. Gray, at Harvard, and others. *The low and variable response rates to the supplemental questionnaires seriously affect the quality of the Agricultural Health Study.*

That's what Dr. Gray said. Right?

A. That is what Dr. Gray said. It is what he said.

JUDGE PETROU: Just so I'm clear, those supplemental questionnaires -- I know there were a number of them. That refers primarily to the questionnaires completed by spouses. Is that correct? If you look at the prior page, it talks about it.

THE WITNESS: Oh, okay. Yeah, I haven't read through this since the deposition. So, yeah. So that may be what they're referring to, then, I guess.

JUDGE PETROU: I mean, I'm not going to testify.

THE COURT: Everybody else has.

JUDGE PETROU: So I would suggest, though, if we're going to answer questions about the supplemental questionnaires, to be clear what questionnaires we're talking about.

THE WITNESS: Right. So can we just say specifically what -- the questionnaires you're referring to?

THE COURT: And you can take your time to glance through for context, you know, before you answer questions about these quotations.

THE WITNESS: All right. Could you just point to me -- I'm sorry -- where specifically you're commenting on page 52?

MR. MILLER: I'm on page 52 of Dr. Gray's critique of what this study might provide. And let's look, now, at the third box down. It's -- we're still on page 52.

THE COURT: No. Let's keep looking at the first box. She can answer that question.

MR. MILLER: Okay. All right.

Q. So the question is: Did Dr. Gray and others say, quote, "The low and variable response rates to the supplemental questionnaire seriously affect the quality of the AHS?"

And I think the question we all want to know is: What is your response to that? And what supplemental questionnaires do you think we're talking about?

A. So in reading through on the second paragraph of page 51, they talk about the participation rates by the applicators to enroll into the study. So you have 82 percent private of applicators, and 42 percent of commercial applicators.

As I mentioned -- and I think, given what we actually are

taught at Harvard in terms of how the proportion of people who are invited to enroll actually do enroll doesn't affect the quality of data -- I'm not sure if that's what they're referring to.

It does seem, however, there were three supplemental questionnaires that were given to the applicator, to the spouse, and to the female family health which were being used to enroll the spouses and other family members for the Agricultural Health Study that we're looking by Andreotti, *et al*. That's really focused not on the other family members, but the applicators, themselves.

So while it may be concern about how these supplemental questionnaires are going to be using -- that particular point doesn't seem to be relevant to the topic of glyphosate and NHL in the Andreotti Study.

JUDGE PETROU: It's not relevant, even if part of the information that's being gathered from the spouse has to do specifically with pesticide exposure?

THE WITNESS: I don't think any information from the spouse was integrated into the intensity algorithm for the estimate of dose-response. I think there was a comment to me Andreotti's Study that said there was no proxy respondent information used in the data on glyphosate use, so I don't think that would -- the information on spouse was integrated into the intensity algorithm.

JUDGE PETROU: I just don't know. I'm just noting that on page 51, last full last paragraph, it starts by saying the supplemental questionnaires are intended to gather more detailed information from the applicator and his or her spouse about pesticide use.

So I -- I would like to know if you can answer the question about whether that additional information about pesticide use somehow, some way, made it either into the data that was used, or any of the reliability tests that were run on it.

THE WITNESS: Right. So in reading through the Methods section for the Andreotti Study as well as the earlier publication from De Roos, 2005, they only referred to the main study questionnaires. They don't mention, at all, using any supplemental questionnaires to estimate glyphosate exposure in any of the dose-response. So -- and if there was a specific comment about no proxy data was used. So -- which shouldn't -- yeah. So --

JUDGE PETROU: I understand that.

Also, one of the supplemental questionnaires is for the applicator, him or herself. So when you say, "No proxy data," that does not say to me that supplemental questionnaires prepared by the individuals applying the glyphosate or other chemicals was not used.

THE WITNESS: Right. And so I guess my -- what I

was -- when you read through 51, the comment is the AHS uses the supplemental questionnaires to enroll spouses and other family members.

So my thought in reading that was that perhaps -- well, it's just not clear to me what specifically the questionnaires are that are being used, or how they're being used; but the way, at least, it was described in the Methods section for the Andreotti Study doesn't describe any of these enrollment questionnaires. It doesn't -- you know, because I think that you would be concerned about missing data, potentially; but that isn't described, at all, in the Methods section for Andreotti, *et al*.

BY MR. MILLER

Q. Let's, if we could, because the Court's -- thank you.

THE COURT: Are you switching topics?

MR. MILLER: No. It's reasonably related to this topic, I think.

JUDGE PETROU: I like "reasonably related."

THE COURT: Well, I have a follow-up the question.

MR. MILLER: Yes, Your Honor.

THE COURT: Go ahead. You may be asking the question, so go ahead. I'll interrupt you if you --

MR. MILLER: That's all right, Your Honor.

I'm going to ask about the follow-up questionnaire, so if the Court wants to stick with the original questionnaire, then

I should --

THE COURT: When you say "the follow-up questionnaire," you mean Phase 2?

MR. MILLER: Yes, Your Honor.

THE COURT: Okay. Before you get to that, let me -- this discussion reminds me of another criticism that Dr. Ritz had. It's a little different from the one I was describing earlier when I was asking you about this. She talked about how the respondents to this questionnaire, in contrast to the Nurses Study that I guess you are involved in, just don't really care about it. They don't care, or there's a concern that they don't really care about the answers that they're giving, and they don't really care about how accurate they are.

Again, these are people who go in to get their pesticide license. And this is, like, something they need to get out of the way before they fill out their -- before they get their pesticide license. They may even view it as a precondition, or something.

And one piece of evidence that she cites for that is that they sent these people home with supplemental questionnaires, and very few people sent them in. So she cited that as evidence that these people don't -- these subjects -- these cohort people who are in the cohort don't really care. And that raises concerns about the quality of the answers they gave in the questionnaire when they were in to get their pesticide

license. And so I was wondering if you could respond to that.

THE WITNESS: Sure. I mean, I guess one comment would be these people -- if they were coming in at the time that they were, you know, getting their pesticide applications, they felt it was important enough to complete these questionnaires, at baseline, anyway. The questionnaires were fairly lengthy, and so they could have just said, *No. I'm sorry. I'm not really interested.*

So I guess my question would be: What evidence might she have that the quality of the data --

Because I think the question is if you're not -- if they don't really care one way or the other about what they respond to, there's going to be a lot of nondifferential misclassification. And then actually, what we saw through the reliability studies and through the biomonitoring study of the -- of the intensity algorithm was there was actually fairly good reliability, and fairly good estimate of dose-response in intensity algorithm.

So to me, that suggests that the quality of data they provided was fairly good; but again, you know, if -- if these individuals didn't really care, I guess the question is: Why would they go through the trouble of sitting there and filling out a questionnaire that might have taken them 45 minutes to do, when they could have just come in, gotten their application, and left?

THE COURT: Okay.

THE WITNESS: Again, I'm sorry. I don't know what their state of mind was when they filled it out.

BY MR. MILLER

Q. And out of the 90,000 people that were applying for the pesticide application, 40,000, approximately, of them did just that. They didn't fill out the supplemental questionnaire. Is that fair?

A. Yeah. So it looks like about 44 percent of the applicators completed and returned the additional questionnaire. I think that is what it says. Yes.

Q. Yes?

A. And I guess the question is -- and it's not clear to me, again, from Andreotti at all if, at all, this supplemental questionnaire was used in the study of glyphosate and NHL risk. So I'm not sure if that is meaningful or not meaningful.

Q. Well, let's go back and look what Dr. Gray cautions, if we could go to the third box on page 52. *If low response rates occur with the follow-up questionnaires.*

That happened; didn't it?

MR. LASKER: I'm sorry. Where are you?

MR. MILLER: I'm sorry. I'm on page 52. It's on the screen on page 52.

THE COURT: In it middle of the second paragraph.

MR. LASKER: All right. Thank you. Go ahead.

BY MR. MILLER

Q. *If low response rates occur with the follow-up questionnaires* --

That happened; didn't it, Dr. Mucci?

A. Yes. As we discussed, 37 percent of the participants did not come and fill out the second follow-up questionnaire.

Q. And what Dr. Gray tells us if that happens, as it did, quote, *The potential for bias will increase partly* --

-- from what, ma'am?

A. So the potential for bias will increase partly from misclassification of subjects, and partly from residual confounding.

Q. And you had told the Court earlier -- and if we can go -- and I'm going to come back to this, but you had told the Court earlier -- well, let me back up.

First of all, you and I agree that in that first period from '93 to '97, a person could fill out the response -- that questionnaire -- and say, "No use glyphosate," because they're not using glyphosate, and then start using glyphosate the next year?

A. Yes. That's correct.

Q. And if they were to get non-Hodgkin's lymphoma, they're classified as a non-user. Right?

A. Yes. And that is true. And as we discussed also, that seems to really be unlikely to cause substantial

nondifferential misclassification, because of the issue of -- that would be a very short latency period in what we're -- so it seems like unlikely to really lead to much of a misclassification.

Q. I never take good-enough notes when a witness is on the stand, but I did write this down. You said the latency problem wasn't that much of a concern for you -- correct me if I'm wrong -- because it was only four years between the first questionnaire and the second questionnaire.

Is that, generally speaking, what you said?

A. What I -- what I -- yeah. That is -- what I was -- yes, exactly. So any sort of measurement error that might have occurred during that time -- it's unlikely that the exposure that's happening in those four years is going to lead to -- immediately to the development of NHL, if there's a causal association.

Q. Right. And you, of course, have never treated anyone for NHL. Right?

A. Yes. That is -- well, that is true.

I think what I -- what many of the experts, including experts of your own, have stated is that with cancer, and with specifically non-Hodgkin's lymphoma, we're looking at latency periods of years; not one year or two years.

Q. You were here today when Dr. Nabhan, a board-certified hematologist/oncologist who has treated thousands of people for

non-Hodgkin's lymphoma, told us there were studies that, as early as four months after the insult, they have diagnosed non-Hodgkin's lymphoma. Are you aware of those studies?

A. So just to clarify, I came in at the end, so I didn't hear him say that specifically.

Q. I apologize.

A. But there are certainly types of exposures when the latency period can be quite short. But actually, you know, the AHS investigators were able to look at relatively short latency periods.

And again, when they looked at just the data on the longer latency, where you'd still capture that kind of exposure information from the baseline questionnaire, there was no association.

So it's -- they were able to look at shorter latencies and longer latency periods in that study.

Q. And you told the Court that it was only four years, but I'm going to suggest to you -- and I think you'll agree, once I do -- that it actually could be eight years between the first questionnaire and the second questionnaire.

A. That -- the way -- as they described in the Andreotti, *et al.*, Study, you know, the individuals were given the second questionnaire five years after the first questionnaire. And so the individuals who completed their first questionnaire in '93 were given that questionnaire. Then five years later the

people who were given their questionnaire in '97, again, were five years later. So the Andreotti Study actually specifically says that questionnaire was given five years after the first questionnaire.

Q. Not four, but five. Okay? Is that right?

A. Five years. And so why I said four years was that follow-up questionnaire asked about exposure information in the year prior.

Q. What year were the -- and it was actually a phone interview for the second questionnaire. Are you aware of that?

A. Yes. That is correct. Our CATI interview.

(Reporter requests clarification.)

THE WITNESS: CATI. CATI interview.

BY MR. MILLER

Q. And those --

A. Computer-Assisted Telephone Interview.

Q. And those phone interviews continued until when?

A. So the phone interviews were conducted -- can we --

Q. It's in the Methods section in the Andreotti.

A. I just can't recall. It's been a long morning, Counselor. I can't remember the specific details, but --

Q. It's 2005, ma'am?

A. If you can tell me what tab it is.

Q. Yes, ma'am. It's Tab 4 of the defense binder. Andreotti Study. On the Methods section, which is page 2 of 8, it says

phone interviews were completed in 2005.

A. Ah, I'm sorry. Tab 4?

Q. Yes, ma'am.

A. Tab 4, for me, is Exponent.

THE COURT: I think you should be in the black binder. That's the binder, I think, that plaintiffs --

THE WITNESS: Sorry. Sorry. Yes. Tab 4. Yes.

BY MR. MILLER

Q. If I say "ma'am" instead of "doctor", I mean no disrespect. Sometimes I just do that. And I apologize right now.

Dr. Mucci, if you'll look there, it shows that the phone interviews went on until 2005. Is that accurate, ma'am -- or Doctor?

A. Yes, it does say that. Yes.

Q. And so the first questionnaires were all completed by 1997. Right?

A. That's what it says. Yes.

Q. So we'd agree, then, now that it can be up to eight years between the first data collection and the second data collection. Right?

A. So then it actually would be seven years, if you want to take away --

Q. Sure. That's why I'm a political science --

A. Yeah, but given that the --

I think, on average, it was five years, as described in the Methods. And so they are really -- the majority of cases, then, would have been a four-year gap.

Q. Small matter, but from '97 to '05 would be eight years?

A. I'm sorry?

Q. Eight years; wouldn't it?

A. Yeah. I'm saying, though, it was eight years; but then because they collected information about the past year of exposure, yes.

Q. Sure, okay. All right. So eight years?

A. Yes.

Q. All right. Let's go back to our PowerPoint. And we're looking at, so we all continue our point of reference, the Gray Study; Dr. Gray from Harvard critiquing what might be found in -- the validity of what might be found in the AHS materials. And I'm at page 56, 57, if we could.

A. I'm sorry. What tab?

Q. I'm sorry?

A. What tab are we at?

MR. MILLER: What tab is that?

THE COURT: One.

MR. WOOL: Tab 1.

BY MR. MILLER

Q. All right. Tab 1. It's on your screen, ma'am, page 55 of 57.

THE COURT: 56 through 57.

BY MR. MILLER

Q. I'm sorry. 56. Excuse me. 56.

Okay. And I just want to ask you about this concept in epidemiology. It says, quote, *In large prospective follow-up studies of relatively common exposures and diseases, exposure misclassification tends to be nondifferential with regard to disease status.*

Right?

A. Yes.

Q. Okay. And you would call non-Hodgkin's lymphoma a relatively common disease, or rare? And I know you're not a medical doctor, but you have an opinion on that, and I'd like to hear it.

A. I'm sorry. Where are you talking -- I'm sorry.

Q. I'm just asking --

MR. LASKER: I'm having trouble.

THE COURT: I'm also having trouble finding it on page 56.

MR. MILLER: Oh, I apologize.

THE COURT: You're reading from page 56. Where on the page is it?

MR. MILLER: Where is it?

MR. WOOL: 57.

MR. MILLER: It's on 57 at the bottom right of the

page, Your Honor. And I'll wait until everyone finds it.

THE COURT: You said bottom right the page?

MR. LASKER: Got it.

MR. MILLER: Well, the bottom of the page. Excuse me.

THE COURT: Okay.

BY MR. MILLER

Q. Okay. So the first question is: Do you consider non-Hodgkin's lymphoma a rare or common disease?

A. In -- I -- in the -- in general, it is, on an annual basis, a -- it's more rare than it would be considered common.

In the context of this particular question where we have 575 incident cases of non-Hodgkin's lymphoma, we would consider that to be a large number of cases.

Q. But would you consider --

If one of your students at Harvard asked you, "Is non-Hodgkin's lymphoma a rare or common disease?" what would you tell them?

A. I would say it's more rare than it is common, but it's not an uncommon cancer.

Q. Now I want to read the next sentence, if I can, and ask you about it. You believe that the exposure misclassification in AHS and Andreotti is nondifferential, I believe you told us. Right?

A. Yes.

Q. Okay. This tells us, from Dr. Gray at Harvard, quote, *Nondifferential exposure misclassification will produce bias toward the null if exposure is classified dichotomously, exposed versus unexposed, high versus low exposure.*

A. Yes.

Q. That's true; isn't it?

A. Yes, it is.

Q. All right. Last sentence, and then we'll move on, but it says here in Dr. Gray's paper, quote, *There is no guarantee that exposure misclassification will be nondifferential, even if objective exposure assessment procedures are used.*

Is that true?

A. I'm sorry. Where are you reading?

Q. Yes, ma'am. At the bottom of the page 57, the last sentence. Do you see that?

A. Yes. And so actually, if you read the sentence before that, it provides the context for that second sentence. And the first sentence reads, *In small studies or studies in which exposure is rare or disease rates low, the impact of misclassification, again, is unpredictable.*

And it was sort of along the lines of what we discussed earlier, that, with nondifferential misclassification, in smaller studies, the role of chance can occasionally lead to crossing; but as we've sort of discussed, that is not the context here of the Agricultural Health Study, where we have

575 cases in 50,000 individuals, and a common exposure prevalence.

Q. All right. Last quote I want to ask you about Dr. Gray --

THE COURT: Hold on. Could I ask a follow-up question about that sentence?

MR. MILLER: Yes, Your Honor.

THE COURT: What the sentence does say is "in small" -- the sentence that you flagged for us -- "in small studies," which this is not, or "studies in which exposure is rare," which this is not --

THE WITNESS: Mm-hm.

THE COURT: -- or "disease rates are low," which this is?

THE WITNESS: I would say it's not; but you know, on an annual basis the incidence of non-Hodgkin's lymphoma is fairly low; but if we look at, with this long follow-up, the fact that we have 575 cases, I would -- I would not classify that as low.

THE COURT: Oh, see, I took -- when -- when they say disease rates are low, I didn't take that to be referencing total number of cases. I took that to be referencing --

THE WITNESS: The per-annual disease rate?

THE COURT: Yeah.

THE WITNESS: I think it's poorly written, I think, the way it's written.

However, what they're referring to is really the impact of small numbers of cases, which we don't really have here.

THE COURT: Okay. And so to the extent that -- to the extent they are trying to say -- may or may not be trying to say it. If they were trying to say that whenever the disease rate is low, the impact of misclassification is going to be unpredictable, you disagree with that?

THE WITNESS: I think -- I think if, in the discussion we had earlier, Your Honor, where we talked about when you have nondifferential misclassification in a small study, you can by chance end up having a bias that might be unpredictable, I wouldn't -- the way they've written it here, it makes it sound like it's more likely than not to be unpredictable. I think that the issue with nondifferential misclassification that chance may play a role if you have a small study with a low prevalence of exposure and a low rate of disease; but in the context of a larger -- and we've discussed that issue together. And I think there can be a role of chance, but I wouldn't classify it as unpredictable in small studies.

Still, for the most part, it's going to tend to bias to the null. Chance may be playing more of a role in the result; but when our study's much larger and the number of the cases is much larger and exposure is common, the role that chance might be playing in terms of how nondifferential misclassification

may act is -- it's pretty predictable, actually, there.

BY MR. MILLER

Q. Last quote on Dr. Gray and his study on AHS. And I'm on page 59, last full paragraph of full pesticide use. Do you see where we are?

A. The last paragraph on 59. Yes.

Q. In it middle of the paragraph. He says -- he and his colleagues -- quote, *The information that USEPA plans to collect* --

A. I'm sorry.

Q. Page 59.

A. That's not the bottom paragraph. That -- it's -- I'm sorry. Where?

Q. Page 59.

A. Yes.

Q. The last paragraph before --

A. Oh, before pesticide use.

Q. Yes. Yes, Doctor. Quote, *The information that USEPA plans to collect may be useful in its own right, but for the reasons stated above, it is not likely to be as useful as it could be for use in the epidemiologic analysis to be -- to be performed in the AHS.*

That was Dr. Gray's concern in Year 2000, before results were known. Right?

A. Yes. And -- and that was a concern that was actually

investigated by the AHS investigators using the biomonitoring studies to examine the extent to which their estimates of dose-response and using an intensity algorithm could appropriately rank individuals based on their biological exposure to pesticides like glyphosate. And so I think it's a reasonable concern to have about whether the questionnaire can accurately capture the actual exposure to the pesticides, but what was nice about the Agricultural Health Study is that they did, indeed, perform these biomonitoring studies to investigate how well the questionnaire data did in predicting the actual dose of exposure.

Q. Dr. Mucci, I apologize, but I was in too big a hurry. I do have one last quote I'd be in trouble if I didn't ask your opinion on. This is Dr. Gray, page 58, top of the page. He forewarned us in Year 2000, quote, *Misclassification will reduce the power of the study to detect any genuine cause/effect relationships, and will reduce the validity of the findings.*

That's what he was concerned about before the results were known. Right?

A. Yes. This was a concern that he raised.

Q. He went on to caution, *Reductions in power are serious issues, because they will undermine the ability of government and industry to regulate harmful exposures, and to reassure farmers with 'negative results.'*

That was his caution in Year 2000; right, Doctor?

A. Yes. And misclassification is a concern on the effect that it could have on reducing power; but for many of other reasons we've discussed earlier today, it is unlikely that there's substantial misclassification of glyphosate exposure in this study. We see this through the number of validation studies that were done.

Therefore, what we'd really be worried about is substantial misclassification. And again, the other part of it is that mathematically, when we look at what the estimated ever-versus-never exposure to glyphosate is on NHL risk mathematically, I don't think misclassification -- nondifferential misclassification could even have occurred to the extent to which -- that it would have an impact on statistical power.

Q. Well, your friend and colleague, Elizabeth Chang -- you know who she is. Right?

A. I don't know an Elizabeth Chang.

Q. Dr. Chang. I apparently got her first name wrong.

A. Dr. Ellen Chang.

Q. Excuse me. I apologize. Dr. Chang is a colleague of yours?

A. She was a colleague. She -- we were students together.

Q. Yeah. And Dr. Chang, in January of 2016, wrote a critique on this issue you've reviewed before: The Exponent --

A. Yes. We discussed it together in the context of the deposition.

Q. Yes, Dr. Mucci, I think we did. I just want to ask you one or two questions about it now, and then we'll just move on from it, as well.

MR. LASKER: What tab?

MR. MILLER: It's at Tab 4.

Right? Is that the right tab?

MR. WOOL: Yeah.

BY MR. MILLER

Q. So you're on Tab 4, Doctor? All right. And I just want to go -- you've talked about selection bias here today, and I want to look at what Dr. Chang had to say about that issue.

THE COURT: What page are you on?

MR. MILLER: I am on page 19, Your Honor.

MR. LASKER: 19?

MR. MILLER: Yes.

Q. See where it says "Selection Bias"? Let me know when you're there, Dr. Mucci, on page 19. She says, quote -- she and others that wrote the Exponent report -- *Over 80 percent of eligible pesticide applicators and 75 percent of spouses -- of married private applicators enrolled in the AHS Study during the initial recruitment phase, which took place at licensing facilities for application of restricted-use pesticides.*

And she references AHS 1996. Right? That's the methods

paper. Right?

A. Yes.

Q. Okay. *However, only 44 percent of enrolled pesticide applicators completed the detailed, take-home questionnaire shortly after enrollment.*

That's true; isn't it, Doctor?

A. As we discussed earlier, yes.

Q. And participation in follow-up questionnaires was also highly incomplete: 64 percent of private applicators, 59 percent of commercial applicators, and 74 percent of spouses in Phase 2. That's generally your understanding of the lost-follow-up issue that we have. Right?

A. So that the -- the -- as we discussed earlier, that is the proportion of people who did not complete these supplemental questionnaires.

Q. And Dr. Chang's conclusion was, *Thus* -- and I'm quoting. *Thus, considerable selection bias could have occurred if nonparticipation was related to exposure and health status.* Right?

A. Yes. That's what it says.

Q. She says as of January 2016, when this was written, quote, *A formal analysis of bias due to study-dropout rates does not appear to have been conducted.*

A. Ah, yes. That may be correct.

I guess my comment would be if -- if it doesn't seem that

these supplemental questionnaires were integrated into the Andreotti, *et al.*, Study, it's not -- it's appropriate to be concerned if we're going to be using these questionnaires in some other way, but since they don't seem to be an issue in the Andreotti, *et al.* Study --

JUDGE PETROU: I need to go back to that point, because I was skimming the Andreotti Study as you were testifying, and I just don't see that one way or the other in there.

THE WITNESS: Right.

JUDGE PETROU: So what is your, essentially, best evidence for the supplemental questionnaires, including the supplemental questionnaire prepared by the individuals actually applying these products were not -- that they were not used in the data?

THE WITNESS: So what's my evidence for this?

JUDGE PETROU: Right.

THE WITNESS: I feel like it's a really good question. And I couldn't -- I can't really speculate if it -- if they did use it and didn't mention it; but I guess my comment is that both the Andreotti Study describes in detail so much about its methods, about --

JUDGE PETROU: Well --

THE WITNESS: -- participation rates, and things like that. So I guess the question is: Why wouldn't they have

commented on that -- the use of the supplemental questionnaire and the issues with missing data if -- if they had used it? So I guess that's where I sort of come out, but I am not --

JUDGE PETROU: It seems pretty silent to me, as I read it, either way. That's why I'm kind of trying to push you a little bit on it, to see if there's some more information out there, or if we're just missing the key sentences in the Andreotti Report, which I may very well be doing.

THE WITNESS: You know, I guess, again, you know, it isn't clear that they have, or it isn't clear that they haven't. They just don't describe it in any way; but you know, my sense is that in the discussion Andreotti, *et al.*, really questioned and tried to, as we do with epidemiology, look at the observed associations and say, you know, *What -- to what extent could bias have led to the findings we have?*

And they discuss nondifferential misclassification. They consider the imputation approach, and the missing data there.

So I guess the question is: If they had missing data from the supplemental questionnaire, why didn't they describe that as a potential issue here?

JUDGE PETROU: Right.

THE WITNESS: So to me, that's why I think they didn't integrate it.

JUDGE PETROU: Conversely, why doesn't the author of the paper we're looking at right now care about this, if the

data wasn't considered?

THE WITNESS: I think that's a good question. So I guess the question is --

BY MR. MILLER

Q. While you're looking for that, this is Exponent, prepared for CropLife. I said Dr. Chang. I don't know that it was Dr. Chang that actually wrote it.

A. Right. So this particular Exponent publication isn't focused specifically on glyphosate, so it's not specifically focused on the Andreotti Study. It's more generally talking about the Agricultural Health Study in its totality. So I think perhaps they're commenting specifically on studies that might be integrating these follow-up questions or supplemental questionnaires; that they might potentially have concerns about selection bias and even, you know, I think -- you know, this --

And the reason, again, I'm thinking it's not an issue here in the Andreotti Study is they -- the Andreotti colleagues refer to the Montgomery piece, which compared the characteristics of the participants and nonparticipants in the follow-up questionnaire where we had so much missing data. So I feel like they think about -- they were thinking about these things. They were thinking about the concerns about missing data and its role, and sort of have commented on that potential in the data.

So that's why I think, although it is a concern more

broadly, potentially, in the Agricultural Health Study, it's not necessarily specific to the Andreotti the analysis of glyphosate.

Q. Last quote is on the screen from this Exponent critique. It's -- just to be precise, it's called "Design of Epidemiologic Studies for Human Health Risk Assessment of Pesticide Exposure." And here's the last quote that we want to ask about. It's on page 19. There conclusion was --

MR. LASKER: Where on page 19?

MR. MILLER: Page 19, last sentence, first paragraph. Selection bias.

MR. LASKER: Okay.

THE WITNESS: Last sentence of the first paragraph.

BY MR. MILLER

Q. Yes, Doctor. Quote, *Thus an analysis reliant on follow-up questionnaires or reliant on covariates with a high degree of missing data, selection bias is a major concern in the agriculture health study.* True?

A. So that is what the Exponent people have said. And it is, as I discussed earlier, a valid concern to have when you do have missing data. As I had mentioned previously, we when we have missing data like this, we are concerned potentially about selection bias.

However, what we've seen through Sensitivity Analyses, what we've seen through the validation of the imputation

algorithm, is actually that there didn't seem to be any bias introduced by the missing data.

Generally, the characteristics of the participants who filled out this second follow-up questionnaire and those who did not fill it out were quite similar. So there was some study analysis looking at potential for selection bias there. Didn't seem to have bias. And again, there were a number of validation studies of the algorithm, and also the Sensitivity Analyses.

So again, I think it is valid to have this concern. And it's a concern we should all have as epidemiologists. Was there an issue? So it's really nice that we can answer that question in the Agricultural Health Study because of the Sensitivity Analyses and because of the validation studies.

Q. We looked earlier, when we started our question and answer, at the website for Harvard School. Remember that general line of questions?

A. Yes.

Q. And I said or read to you what your website -- your school's website said about the importance of IARC. You generally remember that question?

A. Yes.

Q. And you said to me that was your school's website; not necessarily your opinion; something to that effect. Is that fair?

A. No. What I was clarifying -- you kept calling it my website. And I was just clarifying that that wasn't my website; that it was our school's website.

Q. But you do not dispute that those items are significant enough to be on your university's website. Is that fair?

A. I think it's important, as public health -- as a public-health institution, that we report when reports come out like this, to let the public know about recent findings. So I think it's completely valid for them to have commented on this IARC report --

Q. Sure.

A. -- and also to describe what the findings were.

And one of the points on the website also mentions that the epidemiology evidence of these was actually limited. I think that's what we've been talking about today. And I actually agree that there's limited evidence from the epidemiology studies.

And, in fact, now, since the IARC report, we have two additional pieces of data that add to this. One is this recent report of the Andreotti, *et al.*, Study, which is the largest number of exposed cases of glyphosate. And secondly, we have the analyses by Dr. Pahwa and colleagues in the NAPP, where they address the issue of residual confounding that existed, as well as the bias introduced by the proxies in -- in the North American studies.

So those were -- those data have come out since IARC was published; but even still with the data that IARC had, as you could see from our website, the evidence for the human data is felt to be limited.

Q. The Andreotti Study is not on the Harvard website. That's true; isn't it, Dr. Mucci?

A. The Andreotti Study was just published recently. It was published after that particular announcement came out.

I'm not sure who put the IARC findings on. I'm not sure that they're necessarily following this topic of glyphosate, but I think it is an important addition to add to the website, so that readers can have a bigger picture of what the epidemiology is. But I think, you know, as I said, the comment about IARC on our website does note that the epidemiology evidence on glyphosate and NHL risk is limited.

Q. And "limited," you know, in IARC, means "credible"?

A. I think it means that it's -- it's limited, which is what it says on the website. And so I think --

Q. What's this?

A. This is actually our textbook of cancer epidemiology that came out earlier this year.

Q. And you're one of the editors?

A. Yes, I am.

Q. And you cite IARC as authority for causes of various cancers in this book. That's true; isn't it, Dr. Mucci?

A. We discuss IARC in the context of assessing causation for cancer as one -- one scientific consensus panel, as we do on the website, as well.

Q. And this book is available in searchable format; isn't it?

A. I'm not sure what you mean.

Q. You can download it and search it; the whole book?

A. I wasn't aware of that, actually.

Q. Oh, really?

A. Yeah.

Q. Do you know how many times your book references IARC?

A. I do not.

Q. We have searched it, and I'll represent to you it's 475 times. You and I can agree IARC's a very reliable authority; can't we?

A. IARC is -- you know, I'm actually not sure how many publications in total are included in this book. I think IARC, as I mentioned, is one piece of evidence to consider in the evaluation of risk factors for cancer. And so I'm not -- I've never seen that IARC is not a good scientific consensus panel.

Q. But Hollingsworth Law firm didn't want you to comment on the totality of the evidence. They just wanted you to look at the epidemiology. Right?

A. Actually, they've -- no one at Hollingsworth ever told me not to look at other evidence. I'm trained as an epidemiologist. My expertise is in the area of cancer

epidemiology. Therefore, my expertise is being able to critically review the epidemiology evidence, which I have done for this for today, and for all of the information that I've provided in my Expert Reports.

Q. In your textbook, you rely on IARC for formaldehyde and embalming fluid, and voluntary smoking and lung cancer, among other areas. Right? You rely on IARC to be what you think is important enough to put in a textbook for people to look at causality?

A. So again, you're highlighting specifically what we've commented on in reference to IARC, but we also referenced a number of other articles. So, for example, if you look at the relationship between passive smoking and lung cancer, not only do we refer to IARC; you can see the next slide is we refer to the Surgeon General's report.

Q. Sure.

A. We also commented on individual epidemiology studies. And again, I think IARC is a piece of evidence to evaluate in looking at different risk factors and a summarizing evidence, but it's not the only piece of evidence.

Q. Nor was I suggesting it should be. A true scientist should weigh all of the evidence. Right? That's what you'd want your students --

A. In --

Q. I'm sorry. I didn't mean to interrupt. But that's what

you'd want all of your students to do, really?

A. In assessing whether, in epidemiology studies, there's an association between a risk factors and cancer, it would be important to evaluate all of the epidemiology evidence to assess whether there's an association between a factor and a disease.

Q. You've had some criticisms of the analysis of the epidemiologists that have testified for plaintiffs in this case. Generally, you remember that, in your direct examination?

A. What I've commented on is sometimes the inconsistencies that seem to come from some of the experts, you know, for example, you know, around latency. Sometimes there's a comment that we might think there are shorter latencies. Sometimes there are longer latencies. I think I've commented and critiqued the fact that sometimes the plaintiffs' expert witnesses have commented that you should use the highly adjusted estimates, and then other times they'll say, *Oh, you should really use the crude estimate*. So that's the comments I've critiqued.

Q. In your book -- we've Googled it up -- I'll represent to you, you cited Dr. Neugut seven times as an authority in cancer. Are you aware of that?

A. I -- again, so let's look at the specific studies. It looks like there were seven studies on which he was a coauthor,

and which we cited as part of our epidemiology studies. So I think those were probably very relevant to do.

Q. You know Dr. Neugut to be a man that uses reliable scientific methodology, in his 40 years of being at Columbia? Isn't that fair?

A. Actually, I don't know Dr. Neugut. I haven't followed his work. I'm not sure that I worked on these specific chapters. As you can see, different authors were assigned to different chapters. So I actually don't know anything about Dr. Neugut.

All I do know about are the comments -- some the comments that he made, some of which I did not agree with, as I wrote in my Expert Report.

Q. You cited Dr. Weisenburger eight times in your textbook. Are you aware of that?

A. No, I was not aware of that.

Q. Let's go to page 129 of your textbook. You lay out the determinations that IARC can make about whether an agent is carcinogenic. Right?

MR. LASKER: Mr. Miller, do you have a copy of the textbook so I can sort of read the context?

JUDGE PETROU: Exhibit 5.

MR. WOOL: Tab 5. Tab 5.

MR. MILLER: It's at Tab 5?

MR. WOOL: We copied the pages. And they're in sequential order, but the PowerPoint page -- pages numbers.

MR. LASKER: Okay. So what page are we on?

MR. ESFANDIARY: Move along.

MR. LASKER: Oh, I'm sorry. Okay.

MR. MILLER: Page 129, I think, of the textbook. Right?

Q. You know that is what you have in your textbook right.

A. So, yes, these are the established criteria that IARC uses. And, as we know, glyphosate received a classification of Group 2A.

Q. And you don't take issue with that. You haven't looked at the whole body of evidence. Right? You're not here to do that.

A. Exactly. I have provided my expert opinion regarding the epidemiology studies, which -- and again, important comment is that not only did I look at the epidemiology studies that IARC looked at, but now there's a lot more evidence that we have, including the updated analysis and the Agricultural Health Study, as well as the updated analysis within the North American Pooled Project.

Q. Dr. Mucci, in a 700-page textbook that just came out in 2018, where you've referenced IARC over 400 times, not one time do you or any of your coauthors say IARC got it wrong?

A. I'm sorry. That's -- I'm not sure the context in which you're saying this. We use IARC as a reference when we're describing relationships between risk factors and cancer risk.

I'm not sure specifically what you're saying. IARC got it --

Q. Wrong?

A. -- wrong. I'm not sure.

Actually, there is one example where IARC originally had a classification for coffee that -- I think they've since downgraded coffee's carcinogenicity in its most recent findings. So that's one example where IARC did get it wrong.

But I think IARC is -- as I've mentioned, it's one of the scientific consensus panels. It's what we've stated on our website. It's one source of information that we look at.

But again, you know, IARC -- what I'm commenting on today -- what I've commented on today specifically is on the body of epidemiology studies, which include studies that have come out since the IARC report.

Q. And those studies that have come out since the IARC report -- they've downgraded coffee, but they have not downgraded glyphosate-based products. They are still a 2A. That is true; isn't it, Dr. Mucci?

A. According to IARC's classification, the classification is 2A. However, my comments today and in my reports have specifically commented on the epidemiology studies.

And I think, in looking at the epidemiology evidence, there's no evidence of a positive association between glyphosate and NHL risk. Again, I haven't commented on other aspects that IARC has commented on.

Q. And you've mention four criteria that you were going to talk about at the beginning of your direct examination: Confounding, latency, recall, and proxy bias. Those were four topics that you discussed. Right?

A. Those are four topics they we discussed. Yes.

Q. And there are epidemiologists on the IARC panel that concluded that glyphosate was a probable human carcinogen. Right?

A. Well, that was the classification that was used. As I mentioned earlier, the -- the -- and if you pull up the website, again, the epidemiology was considered to be limited evidence.

And now we have even more evidence from the epidemiology studies, from a well-designed cohort study with a large number of cases. Again, the evidence of the association between whether or not glyphosate is classified in a certain way by IARC -- what we do know, what I've commented on specifically, is around the epidemiology studies. And based on those studies, there's no association between glyphosate and NHS.

Q. I know that's your opinion, Dr. Mucci. My question was very targeted. Can we at least agree there are epidemiologists on the panel that reviewed glyphosate?

A. Yes, there were epidemiologists that reviewed glyphosate.

(Reporter requests clarification.)

THE WITNESS: -- on the IARC panel.

BY MR. MILLER

Q. Isn't it fair to assume that the epidemiologists on the IARC panel knew about the concept of confounding?

A. Not only did they know about the concept of confounding, but they actually commented on confounding in the IARC panel.

Q. And still --

THE COURT: Mr. Miller, this line of questioning is not helpful to anybody.

MR. MILLER: Yes, Your Honor.

THE COURT: We know that the epidemiologists at IARC know about confounding.

MR. MILLER: Thank you.

Q. Let's move on, Doctor. It is late in the day. I just want to look at one other area with you. Let's turn to urinary bladder cancer, out of your textbook. You concluded --

THE COURT: By the way, Mr. Miller, I'll let you know that you have under six minutes left on your clock.

MR. MILLER: Thank you, Your Honor. I will use it accordingly. I appreciate that.

Q. All right. Well, I just want to look at that real quick, because I think it's very instructive. You mention --

THE COURT: Doesn't matter what you think. Just ask her questions --

MR. MILLER: Sorry, Your Honor.

THE COURT: -- in your remaining five and a half

minutes.

MR. MILLER: I won't let it happen again, Your Honor.

Q. Let's turn to page 562 of your textbook.

A. Is it in my binder. I don't have the textbook here.

Q. I'll give you a copy.

A. No. I mean, that's fine just.

THE COURT: Yeah. It's in the binder in Tab 5.

JUDGE PETROU: 562.

THE COURT: Well, if you look at Chapter 22, Urinary Bladder Cancer, I think that's what he's trying to get to.

THE WITNESS: Okay. Thank you, Your Honor.

MR. MILLER: If you want this, Doctor, I can hand you the whole book.

JUDGE PETROU: Counsel, what page are we looking at within this chapter?

MR. MILLER: Your Honor, page 562.

JUDGE PETROU: That's what I don't see.

THE COURT: Yeah. I don't see that, either.

THE WITNESS: Yeah. There's no 562 included.

BY MR. MILLER

Q. Are you familiar with the inter Actos issue, at all; pioglitazone issue, at all?

A. I'm sorry. I couldn't hear what you just said.

Q. Are you familiar with the Actos issue with bladder cancer that's reported in your book, or is this something you don't

recall? I just want to ask. That's all.

A. I'm sorry. I don't understand what you're saying.

Q. Actos.

A. Actos.

Q. Pioglitazone. Are you familiar with that?

A. Yes, I am. Thank you. Sorry. I couldn't hear what you were saying.

Q. We're both doing the best we can.

And my point is just this. You list the IARC finding. And in that situation, there were case-control studies that showed the association; a large cohort that did not show the association. Yet in your book you reach or report that it's a risk factor -- pioglitazone -- for bladder cancer.

A. I'm sorry.

Q. Do you see the point?

A. You pulled it away so quickly, I can't find it.

MR. WISNER: I can't see anything with this thing.

THE COURT: I think if you want to ask her questions about this, you should put the book in front of her. Perhaps you should have bought multiple copies of the book. Maybe you didn't want to support Dr. Mucci, but --

MR. MILLER: May I approach, Your Honor?

THE COURT: You may.

MR. MILLER: Here, Doctor. Sorry.

THE WITNESS: So actually what I'd like to comment

on, because I think what's more important is really what --

THE COURT: Well --

THE WITNESS: Yeah. Okay.

THE COURT: But first go ahead and answer his questions.

THE WITNESS: Okay. Sure.

THE COURT: And then if you need to --

THE WITNESS: Okay. Sure.

THE COURT: -- provide context to it, you can.

THE WITNESS: Sure. Sorry.

THE COURT: So I think what he was asking was, whatever that chemical or substance is called, he was saying you stated that there was risk associated with it, even though there was a negative cohort study and positive case-control studies relating to it. I think that was the question.

THE WITNESS: Right. So I think it's critical in any -- in evaluating the association of any exposure and any disease to critically evaluate the individual epidemiology studies. Just because it's a cohort study doesn't mean it's always going to be better than a case-controlled study.

However, in the context of glyphosate what's really important to remember is that when you use the most highly adjusted relative-risk estimates, and take away the bias that was present because of the proxies, the case-control studies actually are in line with the data from the cohort studies

supporting no association.

So in that case, actually -- in the case of glyphosate -- there doesn't seem to be a distinction between the evidence from the case-control cohort studies. They're all supporting no association.

But again here, you know, each -- just because -- just because a cohort study doesn't find something doesn't -- doesn't mean that it's -- you know -- do you know what I mean? Like, it's -- the cohort study doesn't always have to be right.

What's nice about a cohort study is it's free from some of the biases we're concerned about in case-control studies, but we always want to look critically at all of the epidemiology evidence to look at the results, and assess whether bias or confounding or chance might have influenced our study results.

MR. MILLER: Okay. This is my last question. I'm wrapping it up. What's the exhibit number of the book?

MR. WOOL: 301. It's a loose document. It's a loose PowerPoint.

THE WITNESS: "Towards a Cancer-Free Workplace"?

MR. MILLER: Yes. Yes. Is that it?

MR. WOOL: Yeah.

MR. MILLER: It should look like this on the front, Doctor.

MR. WOOL: I flipped it over.

MR. MILLER: There you go. Thank you.

Q. Doctor, you've seen this before. Right?

A. Yes, I have.

Q. And this is a presentation in Ontario, in June, of what we've called "NAPP data." Right?

A. Yes.

Q. Okay. And I just want to show you this, and walk through it with you, and then I'll sit down. Let's go, if we could, please, to this page. "Frequency. Number of Days Per Year of Glyphosate Handling and Non-Hodgkin's Lymphoma Risk."

Do you see that, Doctor?

A. Yes, I see it.

Q. Okay. Now, you did not go over this with defense counsel during your direction examination. Right?

A. No, I did not.

Q. Okay. And it says at the bottom that these results are adjusted for --

Could you let us know what they're adjusted for?

A. Yes. These are adjusted for age, sex, date, cancer in a first-degree relative, use of proxies, use of personal equipment, and the use of three potential pesticide confounders.

Q. They're also adjusted for proxy respondents; aren't they?

A. Yes, they put proxy respondents in the model. However, that's not an appropriate way to adjust for the bias due to

proxy respondents. Since it's a misclassification, you don't want to adjust for it like it's a confounder. You want to eliminate the bias by restricting your analysis to only self-respondents.

Q. After these scientists -- Dr. Pahwa, and others -- adjusted for use of a 2,4-D, use of dicamba, use of malathion, and use of proxy respondents for greater than two days' use, they had a statistically significant increased risk overall. Is that true?

A. Yes. While that is what is presented here in a June 3rd presentation, there's actually a presentation that was actually the one that was presented at the scientific conference on -- in August where the results are actually a little bit different; more attenuated. Those same results are the ones that are being highlighted in Dr. Pahwa's manuscripts, so we think they're the most updated results.

And then finally -- so that's an issue. So I think these data are a little bit old. They are adjusted for proxy bias.

But finally, when we're thinking about dose-response, this categorization of looking at number of days of the year is not really a meaningful estimate. When you look at the lifetime-days of use in this same analysis, and you adjust for the confounding, you can see the effect of the confounders on the association.

And there's -- in that analysis, there's no evidence of

dose-response relationship. This isn't really a meaningful estimate of dose-response, because what we're talking about is two days per year. You don't know if somebody's used it only one year or ten years, and so it's not really meaningful estimate of dose.

It's -- what you really want to be looking at is the lifetime years of exposure, which, again, in the Pahwa analysis, when you account for confounding, account for the proxy bias, shows no association.

Q. Last question, Dr. Mucci. Are you aware that now in the State of California glyphosate is listed as a known cause of cancer?

A. I was not aware one way or the other.

MR. MILLER: Thank you for your time, Doctor.

THE WITNESS: Thank you.

THE COURT: Okay. I would like everyone to give a round of applause to our court reporter. She had the hardest job in the room this week.

You can step down. Thank you.

THE WITNESS: Thank you.

(Witness excused.)

THE COURT: And I assume there's nothing further for user us to discuss right now. We'll just see you on Wednesday at 10:00 o'clock.

MR. LASKER: 10:00 o'clock? I didn't know. It's

10:00 o'clock in the morning?

THE COURT: I thought that's what we decided.

MR. LASKER: I have not tracked all of the e-mails.

THE COURT: We had a conversation about whether Judge Petrou may want to listen in. Does that work?

JUDGE PETROU: I should be able to finish my earlier hearing by then.

THE COURT: Well, so we'll plan on 10:00 o'clock. We'll let you know. It won't be earlier than that. The only chance is that it might be later; 10:30, or something like that.

MR. LASKER: Okay, or 2:00 p.m. Thank you, Your Honor.

THE COURT: If they're late, will you -- like, do I need to give them an excuse or something? Thank you.

(At 4:01 p.m. the proceedings were adjourned.)

I certify that the foregoing is a correct transcript from the record of proceedings in the above-entitled matter.

Lydia Zinn

March 10, 2018

Signature of Court Reporter/Transcriber Date

Lydia Zinn