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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
Wednesday, March 7, 2018

TRANSCRIPT OF PROCEEDINGS

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Also Present: The Honorable Ioana Petrou
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I N D E X

Wednesday, March 7, 2018 - Volume 3

Wednesday - March 7, 2018 **10:01 a.m.**

P R O C E E D I N G S

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THE COURT: Okay. Good morning. A couple quick things.

One, I have received and e-mail from some citizen about this case and the issues we're discussing this week, sort of a lengthy e-mail. I have not read it, but I'm going to hand it -- I'm going to let Kristen hand a copy to each side.

I have not read it, I'm not planning on reading it; but since somebody tried to communicate with me, I thought I'd give it to you.

And then I understand the plaintiffs filed a letter asking for more time. I haven't read the letter, but I have been thinking on my own that it probably would be fair to give the plaintiffs more time. We -- mostly I -- have been interrupting the plaintiffs' experts quite a bit. I anticipate I will have to do that less of the defendants' experts, because I have developing a better understanding of the lay of the land; and the basics of these. And so I think it would be fair to give you some more time.

What I'd propose to do now is add 60 minutes to your clock, and with the idea that I -- you asked for 90, right?

MS. WAGSTAFF: Correct.

THE COURT: -- with the idea that if you -- you know,

if you continue -- you've also been operating in a pretty efficient manner, I think. And so if you -- assuming that continues, and it really is necessary to add another, you know, some a little bit of additional time, I can entertain that, but for now we'll add 60 minutes to your clock.

MS. WAGSTAFF: Thank you.

THE COURT: And no, I'm not adding 60 minutes to Monsanto's clock as of now.

MR. LASKER: That was not my question, actually.

THE COURT: Okay.

MR. LASKER: My question's a little about bit different, because we actually have both time on the clock; and actual real time before this hearing is over.

And the original chess clock was set up based upon how much time we were going to have in court. If plaintiffs have an extra hour, or what happens at the end is that we have problems getting our witnesses on, even if we have time left, because the time is allocated such that we would end at the end of the day on Friday.

THE COURT: Yeah, I don't think that will be a problem. I mean, I think even adding another hour to the -- to the plaintiffs' clock, we probably could end easily finish by 4:00 o'clock, or before 4:00 o'clock on Friday.

But I also would think we may be able to go past -- we'll probably be able to go past 2:00 o'clock tomorrow.

I mean, originally we had a hard stop of 2:00 o'clock because we were in the ceremonial courtroom, and there was an induction for a new magistrate judge taking place there, at 4:00 o'clock, and so we had to clear out by 2:00.

But now that we're here, we don't -- I don't believe we have any reason to have a hard stop at 2:00 o'clock, so that would the way we would probably do it, but I'll get back to you on that.

MR. LASKER: Thank you, your Honor.

THE COURT: Sure.

MS. WAGSTAFF: Okay, and your Honor, plaintiffs are prepared with the witnesses we anticipate being on at 4:00 o'clock today to go past 4:00 o'clock, if the Court wants to entertain that, as well.

THE COURT: Okay, great. So let's -- why don't we go ahead and resume with Dr. Neugut.

MR. MILLER: Dr. Neugut.

ALFRED I. NEUGUT,

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

CROSS-EXAMINATION (resumed)

CROSS-EXAMINATION

BY MR. LASKER

Q. Good morning, Dr. Neugut.

A. Good morning, Mr. Lasker.

Q. I want to focus on issues that were raised by the Court during your testimony earlier today, and see if we can answer some of the Court's questions.

I believe you were having conversation with Judge Chhabria about proxy respondents and the potential concern of differential bias, if there were different percentages of proxies among the cases as compared to the controls.

Do I have that -- do I understand that correctly?

A. Yes.

Q. And, in fact, that is what happened in the U.S.-based case-control studies, correct?

A. Yes.

Q. Okay, if we can put up slide 93, and this is from De Roos 2003, which is Defense Exhibit 720.

And this is -- there are two columns. One is the overall pooled study, but the second column is the data that was included in the analysis of multiple pesticides; and what we have highlighted here is the fact that there was 40 percent proxy respondents among controls, compared to 31 percent proxy respondents among the cases. Correct?

A. Yes.

Q. And the concern that you would have, if I understand you correctly, for differential bias, is that if proxies would have less recall of pesticides -- if they just didn't remember, because they were not actually leaving the individuals

exposed -- then you would have a lower response rate for a given pesticide for proxies, because of that fact; they just don't know. Correct?

A. I didn't say lower response for glyphosate, or for herbicides; I said that I would think it would be more erroneous, that there would be -- I would be -- I would have less faith or less confidence in the responses given by -- by proxy respondents.

Q. I understand. I'm just trying to explore some of the possible biases that coexist.

So theoretically, if it were the case that proxies just didn't know, and therefore, did not provide information on pesticides, so that the rate of pesticide usage reported by proxies was lower than the respondents themselves, that would create a potential bias in this situation, correct?

A. It could.

Q. And what would happen in that circumstance is that for the controls, the rate of glyphosate usage would be artificially pulled down, right?

A. I mean, these are things I sit in my office and ponder for -- for a long time, and you're asking me to speculate on the stand and, you know, in a matter of a few moments.

It's not an easy question to --

Q. Well let me --

A. -- to think through.

Q. Let me make it concrete. If proxies were to only remember a pesticide use 5 percent of the time, and the self-respondents would remember it 20 percent of the time, then because you have more proxies than controls, you'll have a lower incidence of pesticide use, because of that proxy bias, correct?

A. Theoretically, or possibly. I don't know.

Q. Well, mathematically. I mean, that's just a calculation you can make. If you have more proxies than controls, and they are providing you with a lower response rate for pesticide usage, that means you're going to bring down the reported percentage of pesticide use among the controls compared to the cases, correct?

A. Again, I don't know that proxies are going to give you a lower rate, and I --

Q. I understand that.

A. -- erroneous.

Q. This is a hypothetical question, I understand that.

A. Right.

Q. But hypothetically, if the proxies gave a lower number than self-respondents, in this situation, that would create a bias; it would pull the percentage of pesticide use among controls down, and it would result in a bias upward in the odds ratio, correct?

A. Ah, what happened to the proxies in the cases?

Q. Well, that's the issue with a differential, correct? You

have fewer proxies in the cases.

So because you have more proxies in the controls, if they have a lower reporting rate, you are going to bias your findings, and the odds ratio will be pushed up, correct?

A. So theoretically, that would bias the odds ratio up. Is that what you're saying?

Q. Yes. Is that correct?

A. If -- if the circumstances that you're describing occurred, that's correct.

Q. Okay, and, in fact, we know that that is what occurred in this case, don't we?

Let's put up slide 97, and this is from plaintiffs' Exhibit 303. Dr. Weisenburger put this data up, or put this study up yesterday; but they pointed to a different part of the study.

This was the issue of recall bias, but they had a different calculation in that study that also looked at the issue of proxy or surrogate respondents versus actual respondents, the actual farmers, and what they found and what they reported in that study was that the proxies actually didn't remember this information; and only 1 percent of them identified glyphosate as compared to 13 percent of the actual respondents.

So that's exactly the situation we just talked about, given the different response rate in the De Roos 2003 Study,

that created a bias that pushed the odds ratio up, correct?

A. Can I see the paper?

Q. Sure. It's Plaintiffs' Exhibit 303, and it is at page 59.

And there's also -- sorry if your Honors don't have this, but I think we pulled it up.

MR. MILLER: Excuse me, counsel. May I have a copy?

MR. LASKER: It's Exhibit 303.

THE WITNESS: You need to show Table 7 from somewhere. It appears Table 7, which was an entirely different Table 7 --

THE COURT: Hold on a sec, Dr. Neugut. Let them get straightened out.

Can you get a copy to the --

MR. LASKER: I just handed it to them.

THE COURT: Great.

BY MR. LASKER

Q. We're going to have to wait for this out-of-range to drop out, but the table has a variety of different pesticides, you pull out the glyphosate data, we're pulling it up on the screen, you'll be able to see it as the appears in the paper, and glyphosate is towards the bottom there. There we go.

And as we're discussing, the response rate for proxies for glyphosate was 1 percent versus 13 percent for the self-respondents, the farmers. Correct?

A. Give me a moment. Well, again, I'm working this out,

sitting here on a dime, is difficult for me. I mean, this is based on two interviews, in the control group.

Q. This is based on all the data presented on respondents from this same case, which is a U.S.-based case-control.

This is the data that Dr. Weisenburger presented to explain why there was no recall bias in the study. It's the same paper.

A. And the conclusion that you're asking me to draw?

Q. Based upon this, and what you just testified about the differential rate of proxies in the De Roos study, because of the fact that the proxies have a much lower response rate for glyphosate, that created a proxy bias that moved the odds ratio in De Roos 2003 for glyphosate and non-Hodgkin's lymphoma upward, correct?

A. How many proxies were there in the study?

Q. Thirty-nine -- 40 percent versus 31 percent. We just looked at that data.

A. Mm-hm.

THE COURT: And Dr. Neugut, you should feel free to take whatever time you need to review this. This is a study that you are relying on in support of your opinion, and so if you -- to the extent you need to refresh your memory on the details of the study, feel free to do so.

And Mr. Lasker, while Dr. Neugut is reviewing it, what -- this is -- the document that you are using right now is the

actual De Roos 2003?

MR. LASKER: This is -- no, this is Plaintiff's Exhibit 303. This is an article by Blair that was presented to the Court, and put in to evidence by the plaintiffs on the issue of recall bias.

And this was a study that they were explaining showed that there was not recall bias, and they were doing that based on the percentage of respondents both on the case and controls that provided information on pesticide use.

THE COURT: Okay, and this -- so would this be in Weisenburger's binder?

MR. LASKER: It should be. It was presented on the second day it came back.

THE COURT: Oh, I have it. I see it. Yes.

BY MR. LASKER

Q. And if it helps you, I believe the page right before the table has a section on surrogate respondents or surrogate interviews; and talks about the fact that I think more than twice of them, as compared to farmers -- that I don't remember -- and said that surrogate farmers in general had less recall, or recalled fewer pesticides, reported fewer pesticides, et cetera.

I think -- since you don't have a copy.

A. Well, I haven't previously read this paper, I don't think, or I don't have a recollection of this particular paper.

That's why I'm having more difficulty with it.

THE COURT: So Dr. Neugut, is the answer basically that you don't know the effect of surrogate responses on the reliability of the De Roos study?

THE WITNESS: So I'm going to have to pass on that, and I'll have to say that at least -- I don't think it would be fair for me, under these circumstances, to make an assessment just this quickly.

BY MR. LASKER

Q. I understand, and we've already discussed the fact -- although we did look at this in your deposition, you are aware that in the NAPP, they did an analysis that would have a sensitivity analysis to remove this proxy bias if it exists, and we had prior testimony that that moved the odds ratio from 1.13 to .95. We did discuss that during your deposition. Do you recall that?

A. I don't recall discussing it during the deposition, but again, I've sort of not been discussing the NAPP in general.

Q. Well, let's move on, then.

Dr. Neugut, the -- if we can talk about the 2018 NCI study, and there's been some discussion about the follow-up about how much latency period was available there.

You agree that the 2018 study had nearly 40 years of follow-up after the introduction of glyphosate onto the market, correct?

A. I'm sorry, I didn't hear what you said.

Q. The 2018 *JNCI* study had nearly 40 years of follow-up after the AHS -- of the AHS cohort after glyphosate was introduced to the market, correct?

A. Possibly. I don't know for sure, but it had a lot of follow-up.

Q. Slide 39. And that was my question, your answer at the deposition. Do you recall that?

A. I don't recall it, but if I said it, then I said it.

Q. And Judge Petrou asked some questions about how many days of use there were in this study, and there is an analysis in the 2018 *JNCI* study of cumulative days, without any intensity measure. Do you recall that?

A. There is an analysis of --

Q. The duration, number of cumulative days of exposure of the cohort members in that study.

A. I mean, I think that's what the main analyses are based on, aren't they?

Q. Well, there are two metrics, but let's just focus on the cumulative days.

And if we can, put up slide 94, and this is from Defense Exhibit 544, which is the Andreotti study we've all been looking at.

I mean, there's a supplemental table at the back of that study, and it has at the footer at the bottom of the table,

quartiles, tertiles and medians, that talk about the number of cumulative days of exposure for the individuals that were placed in the different dose groups.

And what this means -- and correct me if I'm -- if I'm wrong -- but am I correct that, for example, the highest quartile of cumulative days exposure in the Andreotti study, those individuals had, on average, over 108 days of exposure to glyphosate?

A. Yes.

Q. Now, when we were talking -- when I was talking to Dr. Ritz -- and we can put up slide 98 quickly -- we went through this discussion about hypothetical limitations, and that those should not be sufficient to discount a study findings, and what we really want -- and what we should really demand is data, not opinions.

And you agree with that, correct?

A. I think opinions are sometimes useful, but -- and opinions are -- should be buttressed by data.

Q. Okay, and while you've raised a number of limitations about the 2018 study, you cannot point to any data that would suggest that if you -- if biases you believe exist did exist, the .85 rate ratio (sic) that's reported in the NCI study would actually be a statistically significant positive association; can you?

A. .85 was what? I'm sorry if I've having trouble hearing

you.

Q. I'm sorry. The 2018 NCI study, for its overall finding -- and we can put up slide 40, because we discussed this in your deposition -- was approximately a 0.85 risk ratio for non-Hodgkin's lymphoma and glyphosate, correct?

A. Yes.

Q. And you cannot point to any data that would show that the biases you believe existed did exist; the actual rate ratio (sic) of that study would be statistically significant, above 1.

And bring up, perhaps, slide 45, if that helps.

And I asked you this exact question in your deposition; and you agreed that you could not -- couldn't identify any data to support that opinion, correct?

A. I mean, in general, when you discuss biases, you're being critical of what's put in front of you. It's rare that one can really have the opportunity to be able to analyze the data and to be able to show that -- that it really has the effect that one suggests.

Q. And you don't have the data in this case, correct?

A. No.

Q. Okay, and you -- you talked about nondifferential misclassification bias, and you talked a little bit about the 2005 study, and the questionnaire in that study.

In response, you said 90 percent -- or 10 percent error, I

think you identified in that first questionnaire?
A. Mm-hm.
Q. But you do not believe that the null finding in the dose-response analysis in the 2005 AHS Study was caused by nondifferential misclassification, right?
A. Hm.
Q. Let's put slide 46 up.
A. No, I'm going to be untrue. I would not be certain as to it. I mean, the numbers are small, so it's difficult to know why that was a null finding, but a misclassification of 10 percent, again, with a risk ratio of 1.3 or 1.4, could have caused that to be a negative -- a null finding, as well.
Q. Well, Dr. Neugut, I'm correct that at your deposition, when I asked you this question, you agreed that you do not have a criticism of that finding --
(simultaneous colloquy)
A. Could I see the context of the deposition, and how this was put before and after?
THE COURT: Two things, Dr. Neugut. One, you absolutely can see the context of the deposition. So if you want to ask them to give you the full deposition transcript, you can. But number two, you can't interrupt.
THE WITNESS: I'm sorry.
THE COURT: When he's asking you a question, you have to let him finish his question.

THE WITNESS: Okay. I'm sorry.

MR. LASKER: And your Honor, I'm happy to give Dr. Neugut the full transcript.

I would ask that if we're going to continue along this way, we get extra time on the defense clock.

THE COURT: We'll deal with that later.

MR. LASKER: Okay. Thank you, your Honor.

(Discussion off the record.)

THE WITNESS: That's correct.

MR. LASKER: Thank you.

Q. And with respect to the 63 percent of the cohort that responded to the second questionnaire in the 2018 study, you also do not have any concerns about exposure misclassification, correct? We can put that up, if you want. And this is slide 47.

A. You mean, aside from the 10 percent initial misclassification?

Q. Yeah, aside from the misclassification in the 2005 study we just talked about, you do not have any concerns about exposure misclassification among the 63 percent of the cohort that responded to the second questionnaire on the 2018 study, correct?

A. Not that I would -- no, we're not -- know whether or not they answered correctly, or how much misclassification error there was on the second questionnaire, as well.

Q. But Dr. Neugut, when I asked you this in your deposition, you did agree that, except for that questionnaire that was part of the 2005 study, we just heard your testimony on that, you agreed that you didn't have concern about exposure misclassification with respect to that 63 percent of the cohort in the 2018 study, correct?

A. Then I was mistaken then, and I'm correcting my answer now.

Q. Okay, and you were aware that in the 2018 study, when they looked at those 63 percent separately and just looked at the association among those individuals, there was no association between glyphosate and non-Hodgkin's lymphoma, correct?

A. I'm aware of that, but then again, we're again talking about the same misclassification errors and the same moderate association, and the potential for attenuation towards the null, which we've talked about previously.

I mean, in addition, we're talking about a selected --

Q. Dr. Neugut, there's no -- the question's been....

He's answered the question, your Honor, if I may?

THE COURT: You can let him finish his response.

THE WITNESS: So we're talking about an answer in a very selected cohort.

BY MR. LASKER

Q. And Dr. Neugut, outside of this litigation, you were not aware of anyone who's argued in any forum that the use of the

imputation methodology makes the findings of the AHS cohort studies unreliable?

THE REPORTER: Unreliable...?

BY MR. LASKER:

Q. Outside of this litigation -- I'm going to put this up, it's slide 57. Outside of this litigation, you were not aware of anyone who's argued in any forum that the use of this imputation methodology makes the findings of these agricultural health cohort studies unreliable; that's correct, right?

A. I don't understand the question.

Q. Well, that is what you asked --

A. Are you talking about in general, or are you talking about with regard to the glyphosate and NHL specifically?

Q. With respect to glyphosate and NHL specifically, you agreed -- and let me bring up slide 54 -- that glyphosate in the imputation methodology did about as well -- it was sort of in the middle of the pack with respect to all of the different pesticides looked at in the AHS, correct?

A. Yes.

Q. And again I'll ask you: And what you've testified in your deposition, you're not aware outside of this litigation of anyone who's argued in any forum that the use of the imputation methodology makes the findings of these AHS studies unreliable.

A. I don't read the fora where anyone would do it.

Q. Let's move on, to the Eriksson Study, and you would

agree -- and this is Defense Exhibit 877. This is the Swedish study that -- and we talk about this with Dr. Ritz -- that because of the way that they defined "unexposed individuals" as being unexposed to all pesticides, there was a methodological flaw in the Eriksson Study design, correct?

A. Talking about univariate analysis.

Q. We're talking about slide 57 for a second. Okay, I'm sorry. I was asking, with respect to the Eriksson Study, you agree that there was a methodological flaw in the study, correct? Because they defined "unexposed" as unexposed to all pesticides, correct?

A. Which table are you referring to?

Q. Well, it is the entire study, but I will bring up slide 72, and your testimony in response to my question in the deposition,

> **"QUESTION:** If, in fact the Swedish case-control studies defined "unexposed" so that there was no exposure to any pesticide, and allowed exposures to other pesticides to occur -- that would be a methodological flaw in the study, correct?"
>
> **THE REPORTER:** I'm so sorry, Mr. Lasker, I lost you.
>
> **"QUESTION:** -- that would be a methodological flaw in the study, correct?

And your answer, "Probably, yes."

Do you agree with that, Dr. Neugut? Right?

A. Yes.

Q. And you also agree that this methodological flaw would make it impossible to actually adjust for the potential impact of other confounders, correct?

A. So --

Q. Slide 73? And I can give you the context, if you want, but it's actually the very next. It's right after the question and answer I just gave you.

THE COURT: Mr. Lasker, while he's reviewing the material, let me just make a comment.

I think you're pulling up his deposition testimony too quickly.

MR. LASKER: Okay.

THE COURT: You're asking him a question, and you're giving him half a second to think about the answer, and then you're pulling up his deposition testimony.

MR. LASKER: Right.

THE COURT: Why don't you let him think about the answer to the question, answer it, and then, if you need to, pull up the deposition testimony.

MR. LASKER: I understand, your Honor.

THE COURT: Okay.

THE WITNESS: So subsequent to our deposition I went back and looked at the paper again; and looked at it again now,

and what it says that it excluded control -- it only used controls who were unexposed to herbicides. That was only, as I read the paper, was only in the univariate analyses.

BY MR. LASKER

Q. Dr. Neugut, at your deposition, you agreed that given the systematic bias in Eriksson, it was impossible to reach a conclusion with respect to any individual pesticide exposure reported in the study, correct?

A. I just said that I'm -- at the time I misread the way the study was conducted, and that the exclusion of the herbicides or the exposure to herbicides for controls was only in the univariate analyses.

I don't believe that that was the case in the context of the multivariate analyses paragraph.

Q. And the multivariate analysis is Table 7, where the odds ratio for glyphosate went down to 1.5 and was not statistically significant, correct?

A. Correct.

Q. And just, in the final answer to my question, you did testify at your deposition that given the systematic bias in Eriksson, at least as you understood it at that point in time, you believed it was impossible to reach a conclusion with respect --

(Simultaneous colloquy.)

THE COURT: Hold on, you've got to let him finish his

question.

BY MR. LASKER:

Q. -- with respect -- during your deposition, you testified that given the systematic bias in Eriksson, it was impossible to reach a conclusion with respect to any individual pesticides exposure reported in the Eriksson Study.

That was your testimony, correct?

A. You've got me. That's what I said at the deposition. Thank you.

But as I say now, at the time I misread the paper, and understood that the -- when they said in the -- it's a poorly written method section, and when they excluded the herbicide exposures from the controls, they were referring to the univariate analyses, not to the multivariate analyses.

So if you want to say that my conclusion and my answer to your deposition question is for the univariate analyses, you're correct, but for the multivariate analyses, that's not true.

MR. LASKER: Okay. Thank you. No further questions.

THE WITNESS: Thank you.

THE COURT: Any redirect?

MR. MILLER: Very brief, your Honor.

REDIRECT EXAMINATION

BY MR. MILLER

Q. Dr. Neugut, I won't be long. I know you have a flight.

I wanted to go first to Exhibit 303, which is a 1993

article shown to you by the defense counsel, written by Dr. Blair.

Now, you did not put this originally in your reliance materials, right?

A. I'm sorry, what paper are you referring to?

Q. It's an article. I believe he handed you a copy. "Patterns of pesticides use among farmers, implications for epidemiologic research."

Remember when counsel was talking to you about, he thought there was a bias?

A. Yes, sir, this paper?

Q. Yes, sir, because of proxy responders versus... Yeah, yeah, I see the problem. Thank you.

So I want to show you the conclusion that they drew in this paper that counsel didn't show you -- I've highlighted it -- and ask you about it. Excuse me, I keep moving around.

They conclude, "Comparison of reporting by cases -- "

THE COURT: Sorry, what page are you on?

MR. MILLER: I am on page 1, Your Honor --

THE COURT: Sorry?

MR. MILLER: -- of Exhibit 303, on the top right-hand column.

THE COURT: Thank you.

BY MR. MILLER

Q. (Reading:)

"Comparison of reporting by cases and controls provided no evidence of case response (differential bias), thus inaccurate recall of pesticide use by subjects or surrogates would tend to diminish the risk estimates -- "

A. Yes.

Q. " -- and dilute exposure response gradients."

Has that been your experience --

A. In general, yes.

Q. -- with this? So I think counsel was suggesting it raised the risk, but in fact, these authors concluded it reduced the actual risk odds ratio, right, sir?

A. Yes.

Q. All right, sir, we'll move on. You've talked about, when we talked about confounding, how malathion and di- -- I think it's diazinon -- I hope I'm pronouncing that right -- are known by the scientific community to be causes also of non-Hodgkin's lymphoma. Is that a fair understanding of what you said?

A. I don't know if I said, it but they are.

Q. Well, and I wanted to you ask you, in the AHS study....

Excuse me, is it on?

MR. WISNER: You want it on?

MR. MILLER: Yes.

Q. In the AHS Study -- you prepared this PowerPoint, the

slide that I forgot to show you yesterday.

A. Yes.

Q. In the AHS study, when they studied malathion and diazinon with their database, were they able to find the positive association with non-Hodgkin's lymphoma, that the scientific community now accepts?

A. So this is a slide which lists several herbicides and pesticides which IARC has reviewed, and listed as either Type 1 or Type 2 -- Type 2A carcinogens. So -- and these were all evaluated in the AHS Study.

So I put this slide together. It was in my supplemental report to the court.

And just to illustrate that, the AHS Study, when it found no association with glyphosate, which IARC had found to be a probable carcinogen, which I would reiterate from yesterday, again, I think the scientific community would consider that to have a probability of 70 to 90 percent or so of being a carcinogen. So it also missed malathion and diazinon. I have no idea how you say it, but diazinon.

It missed two other proven, or -- or two other carcinogens which IARC has also defined as being 2A.

So -- so the sensitivity of the AHS Study -- or the ability of the AHS Study to identify potential carcinogens, one really has to have some question, some skepticism about how good a study it is for identifying carcinogens from the

herbicide group.

And I would suspect it's probably because, as well, they also don't have powerful risk ratios, or there were other reasons why it would have missed it. But the point is, glyphosate is not the only carcinogen which it's missed. It also misses others. So the AHS Study has missed others, as well.

Q. I only have two other questions. One, I just wanted to mark the exhibit.

You said that you initially began your scientific inquiry on this issue of glyphosate and non-Hodgkin's lymphoma by reviewing the monologue (sic) prepared by IARC. If we could turn on the overhead, I just want to confirm we have this. This is the right document? You have a copy of the monologue?

MS. WAGSTAFF: Monograph.

MR. MILLER: Monograph, monologue, excuse me. I'm sorry.

Q. This is a 91-page document prepared by IARC. This is what you initially reviewed?

A. Yes.

MR. MILLER: Yeah, and we'll move -- we'll talk about admissibility later.

Q. And finally, counsel talked with you about the issue of whether Andreotti or the AHS follow-up would change IARC's or the community's -- scientific community's opinion of whether

glyphosate causes non-Hodgkin's lymphoma, and I just want to go back to Exhibit 149, which we looked at with you yesterday, which are the briefing notes that IARC scientific and Governing Council members received, prepared by the IARC director.

And they talk about this issue. If I can, I'll ask you, on page 4, they state, quote,

> "The lengthy court testimony given by Dr. Blair does not support any change in the classification of glyphosate consequent to the latest AH publication."

Now, is that also your opinion, that the latest paper does not change the classification of --

A. That's precisely what we've been talking about for the last couple of hours in the testimony, both direct and on cross-exam.

MR. MILLER: Okay, thank you, Doctor. I have no further questions.

THE COURT: Anything further, Mr. Lasker?

MR. LASKER: No, your Honor.

THE COURT: Okay, thank you.

THE WITNESS: Nothing further? Thank you for having me.

THE COURT: Thank you for coming. Better check to make sure your flight didn't get canceled.

THE WITNESS: Thank you.

THE COURT: Because I guess the storm is really bad on the East Coast.

THE WITNESS: It's one of the beauties of California.

THE COURT: Welcome to stick around, if you like.

MR. MILLER: Thank you, Doctor.

MS. WAGSTAFF: Your Honor, we have books for the next witness.

THE COURT: Thank you.

(Whereupon a document was tendered to the Court.)

THE COURT: All right, ready for your next witness?

MS. WAGSTAFF: Yes. Plaintiffs call Dr. Jameson. And while he is walking up to the stand, I would like to take a moment to thank you for joining us, in this proceeding.

JUDGE PETROU: My pleasure.

MS. WAGSTAFF: I know you're very busy in Oakland.

JUDGE PETROU: I will see some of you next week.

THE CLERK: Please remain standing, and raise your right hand.

CHARLES W. JAMESON,

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

THE WITNESS: I do.

THE CLERK: Thank you. Please be seated. Go ahead and adjust your microphone so that it's directly in front of

you, and please state your first and last name for the record and spell both of them.

THE WITNESS: My names is Charles W. Jameson. C-h-a-r-l-e-s, J-a-m-e-s-o-n, but I go by "Bill."

DIRECT EXAMINATION

BY MS. WAGSTAFF

Q. All right, thank you. Dr. Jameson, this is your first time appearing as an expert witness in litigation, is it not?

A. That's correct.

Q. All right, and this is your first time giving testimony in court?

A. That's correct.

Q. All right. So first just take a moment and tell the judges a little bit about yourself.

A. Okay. Good morning, your Honors.

THE COURT: Good morning.

THE WITNESS: I'm Bill Jameson. I have 40-plus years of toxicology experience, working first for the National Cancer Institute, which is part of the National Institutes of Health; and then later at the National Institute of Environmental Health Sciences, which is also part of the National Institutes of Health.

In my tenure at the National Institutes of Environmental Health Sciences, I served as the Director of the Report on Carcinogens. Report on Carcinogens is a document required by

the Public Health Service Act of 1969 that requires that the Secretary of Health and Human Services submit a report to Congress that lists all the chemicals that are either known or reasonably anticipated to be human carcinogens to which a population of United States are exposed, and my responsibility was to prepare the whole report for the Secretary.

I've also been a member of 14 IARC Monograph Working Groups. It was also including IARC Monograph 112 Working Group, where glyphosate was discussed, where I served as Chairman of the Experimental Animal Subgroup for that Working Group.

BY MS. WAGSTAFF

Q. Okay, excellent. So to summarize, you've been a governmental toxicologist for about four decades, is that right?

A. Yes, ma'am.

Q. Okay, and you're since retired, correct?

A. Yes, I retired in 2008.

Q. Okay, and as well as a toxicology opinion, you're also giving an opinion on epidemiology, is that correct?

A. That's correct.

Q. Okay, and in support of your epidemiological opinion, you have tendered a list of all of your epidemiological qualifications, training, experience, right?

A. That's correct. I just put together a list of -- of all

the -- all my past dealings with evaluating epidemiology data.

Q. Okay, and you've been evaluating epidemiological data for four decades, is that right?

A. That's correct.

MS. WAGSTAFF: And for your Honors, you have a list that he just discussed in your notebook. It's Exhibit 321. And we'll move it in as an exhibit later.

If you could move to the next slide, please.

Q. And so Mr., er -- Dr. Jameson, can you please discuss your conclusions in this case?

A. Okay. As the slide indicates, in my expert report, I concluded to a reasonable degree of scientific certainty that glyphosate and glyphosate-based formulations are probably human carcinogens; and also concluded to a reasonable degree of scientific certainty that glyphosate and glyphosate-based formulation caused non-Hodgkin's lymphoma.

In response to some of the questions that your Honors raised over the past couple of days, I also have on this slide my opinion that exposure to glyphosate not only can cause non-Hodgkin's lymphoma, but it is currently doing so, at current exposure levels today.

And I also feel --

MR. HOLLINGSWORTH: Your Honor, we object to that opinion. It's not in his expert report. We've never discussed that with him.

THE COURT: Overruled.

THE WITNESS: And the epidemiologic data demonstrates credible evidence that exposure to glyphosate and glyphosate-based formulations cause non-Hodgkin's lymphoma in humans.

BY MS. WAGSTAFF:

Q. Okay, excellent. And when did you form this opinion?

A. I first formed this opinion as a result of my participation in the IARC Monograph 112 review of glyphosate, in March of 2015.

Q. Okay, and so that was before or after you began work in this litigation?

A. Oh, that was at least a year before I was retained as an expert witness.

Q. Okay, excellent.

If you could, turn to the next slide, please.

All right, I'd like to spend a few moments talking about your methodology, how you came to reach those conclusions.

A. Sure.

Q. Can you please tell the Court about that?

A. The methodology I used to reach my conclusions is the same scientific method that I used, using the intellectual rigor that I have been using all my professional life when reviewing data, to determine if this material causes cancer in humans.

I performed literature searches. When asked to give my

opinion, my first step was to do a thorough literature search of all of the publicly peer-reviewed literature on glyphosate as it relates to its carcinogenic potential.

I also was provided with reports from the EPA, during my review at the IARC Monograph; and also I was able to get some of the actual laboratory reports of the animal studies that I reviewed, from counsel.

I looked at all of the available epidemiology data that had been published on glyphosate and applied the Bradford Hill criteria, which has been discussed previously, in coming to my conclusions.

In toxicology, I evaluated all of the available toxicology data I could find, and it showed that glyphosate is an animal carcinogen, and that is the premise that is widely accepted in the toxicology -- the scientific community, that if something is shown to be an animal carcinogen, then it is probably also a human carcinogen; and it's biologically plausible that it is an animal -- that it is a human carcinogen.

And then I also looked at the mechanistic data that is available for glyphosate, and glyphosate-based formulations, and this data shows that glyphosate is gene toxic in humans, and also causes oxidative stress in humans, and oxidative -- that's an important observation, because oxidative stress has been linked to the formation of non-Hodgkin's lymphoma in humans.

Q. Okay, and that's the same methodology you used while you were a government employee, or -- in government toxicology for four decades, correct?

A. That's the same methodology I used for when I participated in the IARC Monograph, and it is also the methodology I used while at the National Institute of Environmental Health Sciences National Toxicology Program for the report on carcinogens.

Q. Okay, excellent. And if you could turn to the next slide, please.

All right, and I know that Judge Chhabria had some questions about the hazard assessment for Dr. Neugut yesterday, and you heard that testimony; did you not?

A. Correct.

Q. Okay, so let's just spend a couple of minutes.

Why don't you let the Court know if you did hazard assessment, and what that means.

A. Well, I performed a hazard assessment in reviewing all of the available data on glyphosate and glyphosate formulations, and the basic question when you do a hazard assessment is, can glyphosate cause cancer in real world exposure levels?

MR. HOLLINGSWORTH: Objection, your Honor. That's outside the confines of his report, that opinion specifically.

THE COURT: I understand that, and I'll let him testify about it here today, and we can talk about the validity

of the opinion at a later time.

MR. HOLLINGSWORTH: Thank you.

THE WITNESS: And the answer to the question is yes, glyphosate can cause cancer in real world exposures levels.

And another question that -- that came up in some of the discussions over the past couple of days is, does hazard assessment consider chemicals in the abstract?

The purpose of doing a hazard assessment to determine if something is a carcinogen is -- is to get data on a chemical, to see if it could potentially be a human carcinogen.

The best way to do that is to do an animal bioassay. You use the animals to test the chemical, to see if it can cause cancer in the animals; and if it does cause cancer in the animals, then it's very -- it's biologically plausible that it very likely will cause cancer in humans.

So the chemicals are selected for doing these hazard assessments because there is some concern that there's human exposures to these, and trying to determine if there is a cancer hazard associated with that particular exposure.

When doing a risk assessment, you take the information from the hazard assessment that it is a carcinogen, and then apply it to individuals to see if the material -- in this case glyphosate -- if it causes -- if it can cause cancer to an individual, at the -- at the dose levels that they're being exposed to.

BY MS. WAGSTAFF

Q. Okay, and I'm not quite sure you answered your own question, but does a hazard assessment consider chemicals in the abstract?

A. No, it's not in the abstract. Most -- at least in my experience in the National Toxicology Program -- I worked in the rodent bio- -- before I became involved with the Report on Carcinogens I was involved in the NTP rodent bioassay program, and I worked for many years in identifying chemicals to study for that.

And basically, there we identified chemicals that have some possibility of human exposure; and if it is human exposure to the chemical, and there's nothing known about the cancer of it, then we would want to investigate it to see if it potentially could be a human carcinogen.

Q. Okay, excellent. And you conducted hazard assessments at IARC, correct?

A. That's correct.

Q. And you conducted hazard assessments when you were at the national NTTP, correct?

A. Correct.

Q. And is it a generally accepted method for determining whether an agent is an animal carcinogen conducting a hazard assessment?

A. That is absolutely correct. Not only do we do it in

the -- did we do it in the National Toxicology Program and does IARC do it, but regulatory agencies, such as the Environmental Protection Agency, the Food and Drug Administration, require animal bioassays. They -- you know, studies to be submitted to them for registration of pesticide, or a drug, or what have you. And so it is the standard for identifying human carcinogen.

THE COURT: Before we get too deep into the animal bioassays, could I ask a couple of follow-up questions about hazard assessment?

THE WITNESS: Yes, sir.

THE COURT: So I'm looking at your expert report.

THE WITNESS: Mm-hm.

THE COURT: Page 5. Do you have your expert report in front of you?

THE WITNESS: No, sir, I don't.

THE COURT: Do you want to give him a copy of his report?

THE WITNESS: Okay.

THE COURT: Okay, so I'm looking at page 5, and the -- the top paragraph, the carryover paragraph --

THE WITNESS: Mm-hm.

THE COURT: -- which discusses the difference between hazard and risk.

THE WITNESS: Okay.

THE COURT: Hazard assessment and risk assessment. And this is taken -- this language from your report is taken directly from the IARC preamble, right?

THE WITNESS: That's correct.

THE COURT: And so you're describing both the assessment that IARC conducted and the assessment that you are conducting in this report, is that correct?

THE WITNESS: That's correct.

THE COURT: And what you've -- the assessment that you conduct in your report is co-extensive with the assessment that IARC conducts?

THE WITNESS: Correct.

THE COURT: Okay, and it says in that paragraph the distinction between hazard and risk is important, and the monographs identify cancer hazards even when risks are very low, at current exposure levels, because new uses or unforeseen exposures could engender risks that are significantly higher. In other words, hazard assessment determines whether an agent can cause cancer.

So when I read that in your report and in the IARC preamble, I took that to mean that the conclusion reached by IARC that something is a probable carcinogen, or even a known carcinogen, kind of doesn't get you all the way to the conclusion that you identified in the -- in that first slide that was shown about your opinions that a -- a carcinogen is

currently causing cancer in human beings at the exposure levels they are currently experiencing.

Am I misinterpreting the sentence --

THE WITNESS: Well --

THE COURT: -- in your report?

THE WITNESS: -- yes, in a way, you are.

The caveat is put in there because for so many -- for a large number of the chemicals that IARC has reviewed -- and this is also true for a number of the chemicals that are listed in the Report on Carcinogens as carcinogens, and this is usually in the category 2A, and 2B -- when a material is identified as an animal carcinogen, and therefore biologically plausible to be a human carcinogen for a large majority of the cases, there is no human epidemiology data to go along with that.

Since there is no human epidemiology data available, you can only say that it is either possibly or probably a human carcinogen because animal data points to it, and there may be some strong mechanistic data that was actually conducted in human cells that show that it was potentially -- you know, that it causes gene mutations, and is a -- a mechanism that one would conclude could lead to cancer in humans. So -- but we have no human data.

The human data -- the epidemiology data that you review is the data that -- that shows you in the real world what people

are really exposed to when they use it as a farmer, or as -- in a factory, or a drug that an individual is taking for a particular disease. The epidemiology data is what shows you that, under real world exposure situations, this is what happens.

And so that description is there for those chemicals, basically, for which there is no epidemiology data. Now, when we did do the hazard assessment reviews --

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

THE WITNESS: Sure.

THE COURT: And I want you to finish your thought, but just a quick clarification question.

My understanding from reading the IARC Monograph, including the preamble, is that when the Working Group classifies something as a probable carcinogen, it's usually when they do have some epidemiological evidence.

THE WITNESS: That's correct.

THE COURT: Okay. So when something is classified as a 2B, it might commonly be because we have no meaningful epidemiological evidence.

THE WITNESS: Correct.

THE COURT: And when we classify something as a 2A -- that is, a probable carcinogen -- it means we have -- there is some amount of epidemiological evidence, but the IARC describes

it as "limited" evidence. Is that right?

THE WITNESS: Well, that could be the case, but there are also instances --

THE COURT: But isn't that how IARC describes it, and isn't that how you describe it in your report?

THE WITNESS: Um, well, if --

THE COURT: In your report, don't you say that there is limited evidence --

THE WITNESS: Yes, there's limited evidence --

THE COURT: Okay.

THE WITNESS: -- and the reason -- the reason why I say there's limited evidence is because I -- I established criteria for evaluating the data, and I describe in there what is meant by -- by "limited" data.

And so I'm sticking to my criteria when I say, you know, based on the -- based on the fact that for the epidemiology, an association is very credible, but confounding factors cannot absolutely be explained away. I mean, it's close, but they -- they can't absolutely be explained away. So therefore, by the definition of my criteria, that's limited.

That's -- that's my mindset, because for the Report on Carcinogens, I actually wrote the criteria for the Report on Carcinogens, and that's the wording that I used, and it's very similar to what is in IARC, which it's been doing. So that's where that's coming from.

To get back to the -- to the previous question -- I've lost my train of thought, sorry.

THE COURT: Oh, that's okay. Let me ask you the question a different way. It might bring you back to what you were thinking about.

THE WITNESS: Okay.

THE COURT: So looking at this Conclusions slide, the one that is up there now --

THE WITNESS: Okay.

THE COURT: -- I'm trying to -- the questions I'm asking you are trying to get at, what are the IARC's opinions.

THE WITNESS: Mm-hm.

THE COURT: What did the Working Group conclude? And what are you concluding that the Working Group did not conclude? Okay?

So looking at the first bullet --

THE WITNESS: Okay.

THE COURT: -- you say,

> "I conclude, to a reasonable degree of scientific certainty, that glyphosate and glyphosate-based formulations are probable human carcinogens."

I take it that that is coextensive with the IARC's conclusion, is that right?

THE WITNESS: That's correct.

THE COURT: Okay. Now the second sentence:

"I also conclude, to a reasonable degree of scientific certainty, that glyphosate and glyphosate-based formulations cause NHL in humans."

The IARC did not reach that conclusion; is that correct?

THE WITNESS: That -- I think if you -- if you read the monograph and look at the epidemiology section, they did say that, that exposure to glyphosate formulations was associated with non-Hodgkin's lymphoma. I think that's the word -- similarly wording to what is in the monograph in the epidemiology section.

THE COURT: Right, the monograph says that there's limited evidence of carcinogenicity in humans, and identifies the studies that -- where -- that suggest an association.

THE WITNESS: An association with non-Hodgkin's lymphoma.

THE COURT: With non-Hodgkin's lymphoma.

THE WITNESS: Right.

THE COURT: But there is not a conclusion.

THE WITNESS: -- that it --

THE COURT: -- by IARC. If we could go back to the Conclusions slide.

There is not a conclusion in the IARC Monograph that glyphosate and glyphosate-based formulations cause NHL in

humans, is there?

THE WITNESS: It is not an absolute statement to that effect, that's correct.

THE COURT: So to the extent you're providing an opinion on that, that is your opinion.

THE WITNESS: Absolutely.

THE COURT: Not the -- not the IARC's opinion.

THE WITNESS: Not the stated IARC's opinion, but I -- but I --

THE COURT: And you draw from that --

THE WITNESS: Absolutely.

THE COURT: -- from the monograph, to reach that conclusion. I understand that.

THE WITNESS: Yeah.

THE COURT: But I -- and you'll get to talk more about this with the lawyers, but I just want to have this sort of delineate these basic boundaries --

THE WITNESS: Sure, sure.

THE COURT: -- between the IARC's Working Group's conclusions and yours.

THE WITNESS: Right, right.

THE COURT: So you draw from their work --

THE WITNESS: Right.

THE COURT: -- to reach this conclusion that glyphosate and glyphosate-based formulations cause NHL in

humans, but they did not reach that conclusion or articulate that conclusion.

THE WITNESS: They did not articulate that conclusion.

THE COURT: Okay.

THE WITNESS: I had to learn -- being a member of the IARC Working Group, I had the luxury of participating in the discussions during the IARC Working Group meeting, and discussed the data with all of the epidemiologists.

THE COURT: Can you go back to the Conclusions slide again?

MS. WAGSTAFF: Sure, sure.

THE WITNESS: To discuss all the, you know, the data with all of the epidemiologists, the formally trained epidemiologists that were present at the meeting, and -- and I can say there were -- there were a couple of epidemiologists at the meeting, at least when the meeting began, that were saying they really felt that there was sufficient evidence in humans that glyphosate caused non-Hodgkin's lymphoma.

But in -- but as the process for the IARC Monograph, the whole Working Group sits down and evaluates all of the data, not only the epi, but the toxicology and mechanistic data, and we have a rather, you know, detailed discussion of what all of the data is saying.

And so that's how the -- the ultimate decision of the

Working Group is made. And I would point out that the -- that the monograph, and the conclusions in the monograph, are that of that monograph Working Group.

And so it's everybody in the Working Group participated in the discussion, and voted on the various -- listings that are in the monograph, so --

THE COURT: And so you mentioned that were that there were some scientists who believed that there was sort of stronger proof, stronger epidemiological proof, of a link between glyphosate --

THE WITNESS: And non-Hodgkin's lymphoma.

THE COURT: -- and non-Hodgkin's lymphoma than what was articulated.

THE WITNESS: In the --

THE COURT: In the monograph.

THE WITNESS: In the monograph.

THE COURT: Okay, and were there any dissenters?

THE WITNESS: Yes.

THE COURT: Were there people who said that it -- you know, there's not -- who argued that there is not enough evidence to support the Working Group's conclusion that there is limited evidence of carcinogenicity in -- of glyphosate.

THE WITNESS: Yes, sir, I was just about to say that, that, you know, I've always said if you -- if you get three epidemiologists in the room, and you ask them their opinion,

you get four opinions. So --

(Laughter.)

THE COURT: So far, it seems like, to me, the epidemiologists have nine opinions.

THE WITNESS: So there were people that came in there and said, oh, this is a -- excuse me -- a flaming carcinogen, human carcinogen, there's non-Hodgkin's lymphoma everywhere. And then there are others that say, no, no, no, the data's just not there; there's maybe an indication it's not there, it's not statistically significant; even though it is a significant finding it's not statistically significant.

And so that's all part of the review process of the IARC and there's a similar thing when I did the Report on Carcinogens, you know, all of the scientists get together, we all discuss the data, and -- and then, you know, after everybody has had an opportunity to discuss their side and their opinion of what the data says, then you come to a general consensus of, okay, we have to look at the criteria that we're given to use when we do an IARC Monograph. We have to use their criteria and use their wording that is in the preamble when we ultimately make a final decision.

So that's where a lot of the wording comes from, because we're limited, if you will, by what the preamble says we have to use.

THE COURT: Okay, and then going to the second bullet

on your Conclusions slide, just as --

THE WITNESS: Okay.

THE COURT: -- again, just in terms of delineating between what's IARC's conclusion and what's your opinion here.

THE WITNESS: Right.

THE COURT: The first part of the bullet, "Exposure to glyphosate can cause NHL."

THE WITNESS: Right.

THE COURT: That is coextensive is the IARC's conclusion, yes?

THE WITNESS: Yes, but it's my --

THE COURT: And you're -- and then the second part of this bullet is, "is currently doing so at exposures levels of today," that's not an IARC conclusion.

THE WITNESS: That's mine.

THE COURT: Okay.

THE WITNESS: But I mean, it just logically finds -- follows that --

THE COURT: And you'll have time to get into detail about it, but I just -- just for -- in terms of establishing a framework for your testimony --

THE WITNESS: Sure.

THE COURT: -- I just wanted to sort of get those basic points out.

THE WITNESS: Sure.

THE COURT: And then the third bullet point, I take it, is pretty similar to the IARC's --

THE WITNESS: Right.

THE COURT: -- conclusion. The way the IARC puts it is, there's limited evidence of carcinogenicity in humans, and they note that -- that the epidemiological studies have shown -- some of the epidemiological studies have shown an association between glyphosate and NHL, and your conclusion is that there's credible evidence that exposure to glyphosate causes NHL in humans. Correct?

THE WITNESS: Correct. And if I may, the bullet you're referring to there is basically trying to answer a question you asked the other -- defendant's other experts.

Taken alone, what does the epidemiology data tell you? In exclusion to the toxicology or mechanistic data, what does the epidemiology alone tell you?

THE COURT: Okay. Could I -- just one more follow-up question, at least for now, on this concept of hazard identification --

THE WITNESS: Mm-hm.

THE COURT: -- and how it is distinguished from risk assessment.

I'm now looking at this briefing note for IARC Scientific and Governing Council members prepared by the IARC Director, January 2018.

THE WITNESS: Yes.

MS. WAGSTAFF: (indicating).

THE WITNESS: Thank you.

THE COURT: And I'm looking at page 10.

THE WITNESS: Okay.

THE COURT: I'm looking at the fourth bullet --

THE WITNESS: Okay.

THE COURT: -- on page 10, which reads "In contrast...."

MR. HOLLINGSWORTH: Your Honor, can we get a copy of that, please?

THE COURT: Sure. You should have it from yesterday, no?

MR. HOLLINGSWORTH: Okay.

MS. WAGSTAFF: It's Exhibit 149. I have a copy, if you'd like me to give you one.

MR. HOLLINGSWORTH: Sorry, your Honor. Thank you.

THE COURT: I'm looking at the fourth bullet, which says,

> "In contrast to hazard identification, the specific exercise of risk assessment typically involves extrapolation beyond the observed data, employs a variety of statistical models, and is based on anticipated levels of exposure and

background cancer incidence rates that are often specific to a population or region."

So again, when I read that, I took that to mean -- kind of hazard identification is a bit closer to simply inquiring whether the substance is capable of causing cancer; and risk assessment is something closer to inquiring whether people are getting cancer from the substance at current exposure levels.

And so again, let me just ask: Am I misinterpreting that bullet point, from IARC?

THE WITNESS: No, that's absolutely correct. I mean, very simply, hazard identification is asking the question: Can the material cause cancer, yes or no?

And so you do the studies. You test the animals at as high a level as they can tolerate, and see if it causes cancer. If it does, then it's biologically plausible and accepted in the scientific community that it's probably a human carcinogen, as well.

Then -- then the risk assessment takes that information, hey, this chemical has been shown, let's see what the people are -- are exposed to, and then do the calculations that they're talking about, that, okay, based on the -- you know, some of the -- you could take some of the information gleaned from the toxicology data about dose, what doses cause the cancer, and then try to extrapolate it to the human situation, and do your calculations and what have you and say, okay, the

dose is so low that there's not a possibility, or the dose is very close, or when need to do more studies, that type of thing.

THE COURT: Okay, or, you know, we don't know if the dose is too low or close, and so we are going to -- we're going to proactively impose restrictions --

THE WITNESS: Sure.

THE COURT: -- on the use of the chemical --

THE WITNESS: Right.

THE COURT: -- to make sure that people aren't getting hurt by it.

THE WITNESS: To err on the side of safety is absolutely what people -- what I think that the regulatory agencies are trying to do, is to make sure that it's safe, people are safe.

THE COURT: Okay, great. Thank you. Sorry for the detour.

MS. WAGSTAFF: Okay, no problem, and I just have a follow-up question from that.

THE WITNESS: Okay.

BY MS. WAGSTAFF

Q. Instead of talking about hazard assessment sort of in the abstract, or -- I think you said that the preamble has a definition of a hazard assessment, that it's supposed to capture whatever data you have on any chemical.

Let's talk about what happened actually in the hazard assessment for glyphosate.

A. Okay.

Q. The Working Group 112 actually considered the epidemiology, correct?

A. Correct.

Q. And that is the real world exposure, right?

A. Correct.

Q. Working -- Working Group 112 actually had an exposure group, right?

A. Absolutely, yes.

Q. And in that exposure group, they considered real world exposure, right?

A. That is a very important piece of data that is used by the Working Group especially for the epidemiologists, so they know what people are exposed to, and at what levels.

Q. Okay, so whether or not hazard assessments are used to determine whether they can cause cancer or at what level, it is true that Monograph Working Group 112 considered real world exposure levels, right?

A. Absolutely.

Q. Okay, and did you consider that in your hazard assessment for this case?

A. Yes, absolutely.

Q. Okay, and one last thing, if you could pull up Exhibit 57,

which is the glyphosate monograph.

Do you guys have a copy, or do you need one? Okay.

Page 75, if you could blow up that last page, please 75. Yep, on the right, starting with, "In summary."

So Judge Chhabria was asking you questions on the position that the Working Group took with respect to NHL, and I didn't know if you wanted to refresh your memory as to what the Working Group determined with respect to NHL.

A. Right. Well, this is just summarizing the epidemiology data, and basically what the monograph is saying is that in summary, the case-control studies in the U.S., Canada and Sweden reported increased risks of -- for national -- for non-Hodgkin's lymphoma associated with exposure to glyphosate. The increased risk persisted in the studies that adjusted for exposure to other pesticides. However, the AHS -- the AHS cohort did not show an excess of NHL.

So the Working Group noted that there was excesses reported for multiple myeloma, in three studies. But that's not part of what we're talking about here.

Q. Okay, excellent.

And then one last question on this. The definition of "limited" as set forth by IARC includes the finding of credible evidence, correct?

A. Right. It says a credible -- that exposure to the material -- an association between exposure to the material and

cancer in humans is credible, but that all the confounders could not absolutely be explained away.

Q. Okay, excellent. So let's go back to your PowerPoint now, and why don't you tell the Court a little bill about what toxicology is.

A. Okay. As I've indicated earlier, toxicology is used to determine whether the agent is an animal carcinogen. That's -- that is done to see, A, if it causes cancer in laboratory animals, and B, if it does, is it biologically plausible that it is a human carcinogen.

This is a premise that is generally accepted in the scientific community, that if an agent causes an cancer in animals, that it's biologically plausible to be a human carcinogen.

And while the Bradford Hill has been discussed quite a bit over the past couple of days, and I'll admit that the Bradford Hill initially was published and used in the epidemiology community, but here, the toxicologists have picked up on the Bradford Hill criteria and looked at it, and it was very applicable to the toxicology studies that we do. And so we -- we follow the Bradford-Hill criteria when we do toxicology studies, as well.

And so -- the bottom line is, the toxic- -- the animal bioassay studies or the animal toxicology data is very applicable to humans, because of a general acceptance that you

can apply the results from the animal bioassays to predict that an agent is a human carcinogen.

Q. Okay, excellent. You keep talking about a "carcinogen." What does that mean?

A. A carcinogen is a material that causes unregulated cell growth in -- in -- in an organ, in animal. It's unregulated cell growth that basically causes the tumor formation in the animal.

Q. Okay, so the cancer is -- you're defining the cancer as sort of unregulated cell growth or cell division?

A. Correct.

Q. Okay, and is it generally accepted by peer-reviewed literature that you can apply what you learned from toxicology to predict cancer in humans?

A. Yes.

Q. Okay. Can we go to the next slide, please?

And Monsanto has made a lot of hay in the papers about your use of rodent models as a predictor of cancer in humans.

So in this particular toxicology set, there were four types of rodents used, CD-1 mice, Swiss albino mice, Wistar rats and Sprague-Dawley rats. Are those generally accepted rodent models in toxicology?

A. Yes, those are widely accepted and widely used in animal bioassay studies. In fact, those are the species that were used by Monsanto and other industry people in -- in doing the

bioassays and submitting the data for registration of their materials.

Q. All right. Now, let's focus on your second bullet point. You have a phrase in there called "tumor site"?

A. Mm-hm.

Q. Can you tell the judges what that means?

A. When you refer to a tumor site, basically that just means the organ within the animal where you observe the -- the tumor, the place where the unregulated cell growth happened.

Q. Okay, and in this -- in this body of toxicology we have lung tumor sites, right?

A. Specifically glyphosate?

Q. Yes.

A. Yes.

Q. We also show renal tumor sites?

A. Correct.

Q. We also show pancreatic tumor sites?

A. Correct.

Q. And we show malignant lymphoma, correct?

A. Correct.

Q. And then NHL is a tumor site, right?

A. NHL is a tumor site.

Q. So Monsanto has claimed that you have to have matching tumor sites in the animal and in the human. Can you speak to that little bit? And I think you sort of articulate it in your

second bullet point.

A. Yeah. In toxicology, and in at least my vast experience and familiarity with the literature, it's very rare to have an animal model for a specific tumor site in humans. It just -- they just don't exist. There may be one or two, but it's very, very rare to have that.

The purpose of the toxicology studies is to see, A, does -- is basically just to define if the material causes cancer in animals; therefore, it is probably -- it is very likely to be a human carcinogen.

So the animal bioassay data is used to say, yes, it is a carcinogen, and then you use the epidemiology, you go and look at a population that is exposed to a particular material to identify where in humans the tumor site could be.

Q. All right. So let's just try to make this as simple as possible. You used the animal data to figure out if the chemical causes unregulated cell division in the animal, regardless of where, correct?

A. Correct.

Q. Okay, and then once you know that the chemical causes unregulated cell division in the animal, you use the epidemiology to figure out where that will happen in the human, right?

A. That's correct.

Q. Okay. So the toxicology gets you so far, and then you

couple it with the epidemiology to figure out where specifically it occurs in the human. Is that correct?

A. Correct.

Q. Okay, and that's -- that's typically how toxicology is used, correct?

A. That's very typical of how the -- how it works.

Q. Okay.

A. And --

Q. And is there a specific rodent model for an NHL tumor site?

A. No, not to my knowledge. There is -- there is no specific tumor or animal model for the NHL, although I will admit that -- that the -- in the mice, the data in mice, we have a number of studies where malignant lymphoma was found in mice; and malignant lymphoma is a tumor of the lymphatic system in mice. NHL is the lymphatic system in the rodents.

Humans have B-cells and T-cells, which are the affected cells in non-Hodgkin's lymphoma. The rodents in this case, the mice, also have B-cells and T-cells in the lymphatic system that are effected by glyphosate. And so there you have very good correlation, if you will, which you very -- you don't always have, that glyphosate causes a tumor in a mouse at a similar site to where you see it in humans.

Q. Okay, excellent. And if you could pull up slide 327, please, you were asked this exact thing -- can you blow up the

entire thing? -- in your deposition. You've been deposed three times in there litigation, right? You've had the most depositions. You're very lucky.

A. That's correct.

Q. And do you remember being asked by Mr. Hollingsworth, quote,

> **"QUESTION:** My question is whether the hypotheses that mouse renal tumors are predictive of non-Hodgkin's lymphoma specifically in humans has ever been tested."

Do you remember him asking you that?

A. I remember being asked that many times yes.

Q. Okay, and throughout the course of your eight-hour deposition, you were asked that about every single tumor site, right?

A. That's correct.

Q. And you gave an answer, and what's highlighted is the answer that Monsanto put in your -- in their brief, but I just wanted to show your entire answer, which is consistent with what you've said today, right?

A. Yes. You know, they -- this -- this is my -- my entire answer to that question.

I came back and said, again, this, you know, is the purpose of the bioassays, to see if a chemical causes cancer in animals as a predictive tool for what it causes in humans.

Now, I mean, the fact that something causes a kidney tumor in a mouse, I don't know what that means about causing non-Hodgkin's lymphoma in humans --

THE REPORTER: I'm so sorry, I lost you. I lost you. Something causes kidney tumor in a mouse --

THE WITNESS: Oh, the fact that something causes a kidney tumor in a mouse, I don't know what that says about causing non-Hodgkin's lymphoma in humans. I don't know that that's been investigated.

BY MS. WAGSTAFF:

Q. Okay. So let me just stop you right there, and what you were talking about is what we just discussed --

A. Correct.

Q. -- is that the animal data tells you whether or not the chemical causes unregulated cell division, correct?

A. Right.

Q. And then what you say at the end of your answer is, the purpose of doing the study in a mouse is to see if it causes cancer, and that's used as a predictive tool to see if it causes cancer in humans.

A. Correct.

Q. And that's what we just discussed, is that you use the epidemiology to figure out the human tumor site, correct?

A. That's correct.

Q. And Monsanto didn't give the court your full answer,

correct?

A. That's what it appears, yes. I didn't see the briefs, so I don't know.

Q. Okay, excellent.

And this is Exhibit 327, and it's in your -- the judges' notebook, and we'll move that in to evidence as well.

If you can go back to the slide, please, Mr. Wisner. Okay, excellent.

And the last bullet point, you sort of touched on this a little bit. NHL is a cancer of the lymphatic system, right?

A. Correct.

Q. Okay, and is it important in any way that the rodents in the model have a different lymphatic system and/or immune system than humans? Is that important, and how did you put that in your analysis?

A. Well, I mean, the fact of the matter is, physiologically they're different. The lymphatic system in the mouse is physiologically different than the lymphatic system in humans, but there are also similarities. Like I said, like I indicated before, there are B-cells and T-cells in the mouse, and there are B-cells and T-cells in the human lymphatic system, and those seem to be the cells that are affected by glyphosate that causes cancer.

Q. Okay. So it would be a more appropriate question that the similarities we should look at that are relevant here rather

than the differences, is that correct?

A. Correct.

Q. Okay. If we can go to the next slide please?

So we're finally getting to the studies you that you reviewed.

A. Okay.

Q. Looks like you reviewed 12 rodent studies.

A. Correct.

Q. And those were the mice and the rats that we discussed earlier.

A. Correct.

Q. Okay, and why don't you tell the Court a little bit about what information you reviewed in making your opinion and whether or not that body of information is generally relied upon in the toxicology community.

A. Okay, kind of -- and I indicated before, I performed a peer-reviewed literature search to find all peer-reviewed literature available for glyphosate and cancer.

I've looked at tumor tables for individual animals. These were tumor tables that were provided in some peer-reviewed publications, or were provided from the actual studies that were performed on the animals.

And for some, but not all, I had the actual pathology reports from the study laboratory to review, that I also had narrative summaries from the some of the studies, and in fact,

for some of those studies, I also had the entire lab report, testing laboratory report of that bioassay.

And this is the type of information that is typically that I -- that I have routinely used in -- in doing cancer hazard identifications throughout my 40-year career. I've been looking at all of the data to -- to come to an evaluation of the potential carcinogenicity of the substance.

Q. Okay, excellent.

Mr. Wisner, if you could, pull up Exhibit 324. All right, and I have copies. I think these are in your book. If you could, blow it up so that it fits the screen. Yeah, just right there, yep.

And so this is a table that you made, correct?

A. It's a table, it's a cheat sheet, if you will, that I put together to remind me what -- what I found in the various studies, and --

Q. This is tab 8.

A. And I use the -- basically, I referred to the Greim publication in this table as a means of just keeping straight which studies I was looking at.

The first column is identified -- identifies the study where the study -- who the principal investigators were and the year that the study was done.

The second column identifies which strain of animal --

Q. Hang on, real quick, when it says Study 10, just so the

judges know when they look at this later --

A. That refers to the Greim paper, study 10 in the Greim paper.

Q. Okay, and that's really of no significance other than that?

A. That's the only --

Q. Okay.

A. Like I said, I just use that as a means to --

Q. Organization.

A. -- to organize my thoughts, if you will.

Second column is Strain, which identifies what strain of mouse was used, and if it was a male and females, or females.

The third column identifies the dose levels that were used in the studies, and for what duration the study was.

The next -- the fourth column identifies the tumors that were observed that were significant, and the incidence.

The 1 of 49 means that there was one tumor in 49 animals; and it goes from control low, medium, and high dose. That that's the order of the material -- of the numbers in there. Those are referred to as a tumor incidence.

The next column identifies the statistical significance of the tumors that were listed.

And then the last column is an evaluation, is basically my comments on the -- on the particular study. And again, I put this together for my -- on my own purpose, just to remind me of

what each study -- I found in each study.

Q. Okay, excellent, and I'm sure Monsanto's counsel will ask you about these cases in detail on your cross-examination, but I wanted to explain to the Court what these were.

If you look on the upper left-hand side of it, you'll see that this is for the mice. This is for the mouse?

A. Yes.

Q. In your book, you also have one that you made for the rats, right?

A. Correct.

Q. And also, you have a chart that you made similar to this for the epidemiological case-control, right?

A. Correct.

Q. You also made one for the meta-analyses, right?

A. Correct.

Q. Okay, and did you make one for the cohort study?

A. I did not make one for the cohort study, the AHS study, because there was only one study, and that found null association, and plus I have some concerns about the study itself. So I didn't make a table for that.

Q. But you made an entire expert report, and you submitted for a deposition just on that specific study, correct?

A. I did, yes.

Q. Okay, and that expert report is also in your book.

So those are Exhibits 322, 323, 324, and 325, and we'll

move those in to evidence, as well.

(Exhibits 322, 323, 324, and 325 entered into evidence.)

MS. WAGSTAFF: Our next slide, please. Yep, dosing.

Q. I'd like to talk a little bit about dosing. One of the complaints that Monsanto has about the toxicology is that these animals are just given insane levels of glyphosate that would be irrelevant to any analysis we have to do today.

So could you please talk a little bit about dosing within the toxicology field?

A. Sure, I'd be happy to. As I indicated before, the purpose of an animal bioassay is to determine if, given the dose -- if an animal is given a dose that it can tolerate for its lifetime, does it cause cancer in that animal? So this is done by using what's referred to as a maximum tolerated dose.

The maximum tolerated dose is defined as a dose which you can give to the animal over their lifetime which does -- which causes up to -- which causes up to 10 percent decrease, causes no more -- I'm sorry -- that can cause no more than a 10 percent decrease in body weight over the study, or a 10 percent increase in mortality. In other words, you can have 10 percent of -- less than 10 percent of animals die over the course of the lifetime.

Now, the animal bioassay was -- was started, if you will, back in the late '50s, early '60s, and rodents or mice and rats were selected as the test species of choice, because of their

relatively short lifetime. You can do a lifetime study in a mouse and a rat in two years, or a little over two years.

And so the bioassay is -- that was developed to study the animals do a lifetime study in the animals at the maximum tolerated dose, a dose that they can tolerate without seeing these 10 percent decrements in body weight or mortality, and to see if, given as much material as the animals can tolerate, does it cause cancer in the animals.

And if it does cause cancer in the animals, then it's biologically plausible that it causes cancer in humans.

Q. Okay, thank you. And the MTD is a generally accepted standard for dosing rodents in toxicology, correct?

A. That's correct. The National Toxicology Program's rodent bioassay, which is a preëminent study of the government -- the government is part of the National Institutes of Health and so it's a government program -- is the gold standard, if you will, and every protocol for an animal bioassay is performed at the maximum tolerated dose.

I can go in to a discussion of, if -- and reaching the maximum tolerated dose is an important concept in evaluating the adequacy of an animal bioassay, because if you test -- do a test at a level that does not reach the maximum tolerated dose, and the study is completed and you don't see a 10 percent decrease in body weight or mortality over the course of the study, then you say the maximum tolerated dose wasn't reached.

So if you don't see an effect in that study, then it's an invalid study for carcinogenicity, because the animals could have tolerated more -- more material.

But kind of on the flip side of that, you can run a study at less than the maximum tolerated dose; in other words, a study where the animals could have tolerated more material, but if you see an effect in that study, it's a valid study, because you can evaluate that effect.

In the animals, even though they could have tolerated more, you just say that, well, if you had given them more, you would have seen more tumors than you did see, but you could see a statistically significant increase in tumors even though you didn't reach the MTD.

Q. All right, so that's actually two very important concepts I just want to try to summarize in laymen's terms, if I can.

So you have this concept of MTD, right?

A. Yes.

Q. And toxicologists all over the world use that dosing concept, correct?

A. Correct.

Q. Okay, and it's not -- it's not a hard line, right?

A. It's something you have to determine in the course of doing your studies. You usually do preliminary, what are called prechronic studies for up to 13 weeks, where you test different doses to see what the animals can tolerate over that

time period, and then you set your maximum tolerated dose based on those results.

Q. Okay, excellent. And you just mentioned two concepts that I'd like to discuss. One is, even if you don't reach the MTD of the animal, if the animal shows some effects, that information is still important and valid and should be considered. Is that --

A. Absolutely.

Q. -- what I heard you say?

A. Absolutely.

Q. Okay, and the second one is, even if you reach what you would consider to be MTD, there are other considerations that you take in to account, like body weight or things like that, that would suggest to you, in your experience of 40 years as a toxicologist, that in fact, MTD was not reached, is that correct?

A. You look at the data, the body weight data and the survival data, and if you don't see any effect compared to the controls that's more than 10 percent, then it -- they could have tolerated a higher dose.

Q. Okay, and those are scientific judgment calls that come with the experience of being a toxicologist, right?

A. Correct, that's what comes with toxicologists, and that is the rule, if you will, that is applied by all toxicologists when they review an animal bioassay study. In my experience

with IARC and also in reviewing the data for the Report on Carcinogens, that's part of the evaluation. You look at the study, you look at the survival and the body weight, and to see if the animals were tested at the MTD or if they could have tolerated higher levels.

Q. Okay, and so you use these principles that you had learned in your 40-plus years as a government toxicologist when you did your analysis on MTD in this toxicology dataset, right?

A. Right. That makes me feel like an old man, 40 years.

Q. Okay, sorry. It's a good thing.

All right. Next slide, please?

THE COURT: Is now a good time for the old man to take a lunch break?

MS. WAGSTAFF: I actually only have about 10 more minutes, if we want to finish.

THE COURT: Okay.

MS. WAGSTAFF: I could probably be, unless you have a lot of questions for him. Okay.

THE COURT: Go ahead.

MS. WAGSTAFF: Unless you want to stop.

THE WITNESS: No, that's fine.

BY MS. WAGSTAFF

Q. Okay, so next I want to talk about concurrent and historical controls.

A. Okay.

Q. Please tell the judges what those are, and how you factored them into your analysis today.

A. Okay. Concurrent control are the control animals that are -- that you have that are run concurrent with the -- with the study that you're performing. Those are animals that are -- that are the same strain, same genetic background. They're handled exactly the same way as the treated animals. They only difference is, they are not exposed to the material you're studying. In this case, it would be the glyphosate. Those are the concurrent controls.

Those are the most appropriate controls to use when you're evaluating the study, to see what the -- what the tumor incidence or the increase in tumor incidence was in the treated animal versus what it was with the animals that got no material.

Another piece of information that is -- that toxicologists routinely look at is what we refer to as the historical controls, and a historical control are the control or animals that are not been treated with a chemical, in studies that were performed at -- at other facilities, or in the reported literature, where you get a -- this -- the historical controls are used for people to get a feel for what the spontaneous incidence of a tumor in is an animal. It gives you a larger population, if you will, of animals that were -- (whereupon a document was tendered to the Court) -- were not controlled, but

were treated in a similar manner; not the exact manner but, you know, you look at historical controls of all the feeding studies that you can look at, or all of the drinking water studies, or all of inhalation studies that you're looking at.

You use that historical data to see, what's the spontaneous incidence of this? And you use that to say, well, the control group in my study has the same number of tumors as has been seen in the past in similar studies; or the control group has fewer tumors than you would see in the past; or has more tumors. But it's just a piece of information that you use in the evaluation.

You always use the concurrent controls as the most appropriate control, and you use that -- that gives you more information than looking at the historical controls, but the historical control is a piece of information you need to evaluate the validity of your study.

BY MS. WAGSTAFF:

Q. And is your view on the importance of concurrent and historical controls shared by the toxicology community?

A. Yes. In fact, I've published on this.

Q. Just handing out your article.

A. (Laughs.)

Q. I hope this doesn't make you feel old. It's from 1988.

If you could, pull up Exhibit 295, please. The front page, just make it a little bigger. Highlight his name as an

author. Well, you guys can probably all see it.

Yeah, and then let's move to page 7, and let's look at your views on historical and concurrent controls back from 1988.

There were some suggestions by Monsanto that your views have changed since you became part of this litigation. So I just -- this was 30 years ago, so I want to make sure that this is still what you believe today.

Could you take a moment to look at it?

A. Sure. What we stated in our paper was that although concurrent control groups are always the first and most appropriate control group used for comparison, the treating control groups, historical control groups, can be helpful in overall assessment of tumor incidence.

Consequently control tumor incidence from NTP historical control database are included in -- are included from particular laboratory and from the overall program for the tumors appearing in these associated -- appearing to be associated with chemical exposure.

Q. Okay. So back in 1988, you were saying the same thing. Both are pieces of information to consider, concurrent is more important.

A. Absolutely.

Q. All right, let's just move down to the next paragraph, just because we have this page up, and I just am curious about

your opinions on p-values from 1988, and this is the article that you wrote, right?

A. Right.

Q. And in this article, you're saying that if you just look at the first....

If you could blow up, you know, the first couple sentences -- just keep going down, keep going down, go down. Yeah, that's probably enough. Is there any way to highlight that or something? Yeah, there you go.

A. Yeah, and in this, we were just saying that p-values are objective facts, but unless a p-value is extreme, proper use of it to decide whether or not the chemical is carcinogenic involves subjective and scientific judgment.

Although the p-values may be helpful in deciding whether or not a substance is carcinogenic, they -- but they must not be used inflexibly or given undue weight.

Q. Okay, excellent. And that was -- that was obviously peer-reviewed -- that opinion was peer-reviewed in 1988.

A. Yes.

Q. Okay, and let's -- you can pull that down. Let's turn to the next slide, where we talk a little bit about replication.

Please tell the Court what replication is, and how you used it in your opinion.

A. For the purpose of toxicology, I mean, very simply, replication means you see the same effect in two different

studies, or in multiple studies. It's just another piece of evidence that you use in evaluating the overall strength of the data.

I would point out that -- that usually you don't have the luxury of having a lot of studies in animal bioassays. For the glyphosate situation, it's -- it's very -- it's extraordinary to have these many animal studies to evaluate, or -- animal carcinogenicity studies to evaluate. Usually, at most, you'll have two, because of the expense, because of the time and expense used that is necessary to do animal bioassay.

So it's very rare that you have several studies to compare to see if you have replication, but it's just another piece of the information. And if you do have replication across studies, that just strengthens the evidence that this is an animal carcinogen and this is the tumor site for that particular study.

Q. All right, excellent. And over your course of your career, did you ever determine that something was an animal carcinogen when there was no replication?

A. Oh, yes, there was -- that, as I said, you don't usually have the luxury of more than one study, and if the results from a single animal bioassay study is very strong, I mean, then it makes it easy to determine, but you -- you look at the strength of the study, if it's well conducted, done on GOP guidelines, and you look at the data generated from the study and make your

evaluation, but you can definitely make an evaluation from one study.

Q. Okay, excellent. And you can have replication across species, right?

A. You can have replication across species, you can have replication across sex.

Q. Strain?

A. Strain.

Q. And laboratories or authors?

A. Right.

Q. Okay.

A. Right. I mean --

Q. So was there replication in this toxicology data set?

A. Yes, and for glyphosate, there was replication of several tumor sites.

Q. Okay.

A. In fact --

Q. And in fact, you've made a replication chart.

A. I made a chart.

Q. And it's number 10 in your notebook. And why don't you tell the Court, while they look for this, explain to them what this is.

A. Basically, I've -- I just use this as a method to highlight replication in the studies. We had replication in male CD mice, for angiosarcoma --

THE REPORTER: I'm sorry, in male CB mice?

THE WITNESS: In male CD-1 mice. I'll slow down, I'm sorry. We had replication -- we observed liver tumors in Wistar rats and Sprague-Dawley rats, although the incidence of the liver tumors in the Wistar rat were not significant.

We had replication of malignant lymphoma in mice. We had replication in males and females in the Swiss mice. We had replication in male CD-1 mice in two separate studies. We had replication of malignant lymphoma in CD-1 mice and in Swiss mice. So we had a lot of replication for the malignant lymphomas in the mouse.

Pancreatic islet cell adenoma, we had replication in the rat in males; and for the renal tubular adenomas, we had replication in two studies, in CD-1 mice; and we had replication across species in the CD-1 and the Swiss mouse.

Q. Okay, excellent. And is it fair to say this is a lot of replication?

A. Yes, it is. It's -- I mean, that just shows that in the course of the study, there were -- there were similar tumors being -- the same tumor was being observed in different studies done at different laboratories at different times. So that just strengthens the evidence that it's an animal carcinogen.

Q. Okay, excellent. And was it significant to you -- and you touched on this earlier -- that the malignant lymphoma, which is the closest tumor site to NHL, was replicated four times?

A. That's correct.

Q. Okay, but you testified in your deposition that there's a high spontaneous rate of malignant lymphoma in Swiss mice. First of all, why don't you tell the Court what a high spontaneous rate means, and secondly, how you that factored that in to your analysis.

A. High spontaneous rate just means background rate, just means that -- that the incidence of a particular tumor seen in the historical controls, from a lot of studies, is -- is, you know, relatively high, 10, 20, in fact, some are even up to 30 percent of the animals get tumors before they die, spontaneously.

And in my deposition, it came up that the malignant lymphoma had a high historical rate, and in fact, that's true in the Swiss mice especially. In the Swiss mice, the background -- historical background rate is very high.

But when I did my evaluation and looked at these lymphomas in the CD-1 and the Swiss mice, I went to the literature to see what the background rate was, and the incidence rate in all four of these studies were higher than the historical incidence rate. Even though you have a high incidence rate in the controls, it was the treated animals had a higher rate than seen in the historical controls.

Q. Okay, and just for purposes of a hypothetical question, if you remove those four malignant lymphoma brown lines from your

chart, that would still be a lot of replication, right?
A. From the other tumor sites, yes.
Q. Right, and what's the significance of the -- well, strike that.
Is a renal -- a renal tubular adenoma, is that a rare tumor site?
A. It's a rare tumor in the mouse, yes. The historical rate is very low among those.
And again, I looked at the historical rates in the literature and compared to the historical rates that are reported. The incidence of these tumors in these studies were higher, you know, almost by a factor of two in some of the studies, than the historical rates.
Q. And is it true that when you see rare tumors in these toxicology studies, it just strengthens your opinion that an agent is carcinogenic?
A. Yes, absolutely. That's one of the criteria, that if you see a significant increase in a rare tumor in the animals, that strengthens the evidence that it's an animal carcinogen.
Q. Okay, and the renal tubular adenoma was actually replicated three times, twice? Three times --
A. It was replicated in three different studies --
Q. Okay.
A. -- and in two different species.
Q. Okay. That's what -- you said it more eloquently than me.

If we can go to our last slide.

All right, and so we've already talked about sort of your IARC experience at the beginning, but why don't you just....

You stated that you were the Chairman of the Experimental Animal Subgroup, is that right?

A. Correct.

Q. And is that the definition of "sufficient" that IARC found?

A. Yes. A causal relationship was established between the agent and the increased incidence of the malignant neoplasms.

Q. Okay, great, and I'll just ask two sort of concluding questions. The first one is the Greim review article. Let's just put this to bed once and for all. Did IARC consider the Greim review article?

A. Absolutely. We reviewed the Greim article, and as this slide shows, it's discussed in section 313 and section 323 of the IARC Monograph.

Q. Okay, and the Greim review article came to you in the form of a peer-reviewed review article?

A. It was a peer-reviewed review article. The article -- that article came to us at IARC. It indicated that it had additional information, raw data, which were the individual animal tumor tables. It was available on the website, but we could never get the website to work properly while we were at the IARC meeting, although a hard copy was provided to us

during the meeting.

Q. Okay, and you have since reviewed those -- that data, correct?

A. In reaching my opinion, I had the time to go through and review all of -- all of that data that was a supplement to the Greim Paper, as well as the data from the actual study laboratories.

Q. And what effect did that review have on your opinion? Did it strengthen, weaken, or have no --

A. Oh, that strengthened my opinion, absolutely, because I determined that there were a number of tumors were present in the studies, as the chart showed before; that there were significant increase in multiple tumors in multiple studies.

Q. Okay, and I'm just going to hand to you a chart that you have made that shows the Greim paper.

Again, let me hand it to you guys.

(Whereupon a document was tendered to the Court.)

If you could pull up 328.

And I will -- I will let Monsanto's counsel ask you specific details about this on their cross, but just for the Court's own edification, this is a chart you made where you, once again, on the left-hand column, identified the studies as they are identified in the Greim Paper, just for organizational purposes, right?

A. Right.

Q. Okay, and then you list in the middle what -- the findings from IARC, right?

A. The -- on -- the middle the middle column says "IARC," and those were the tumor sites that -- the studies and the tumor sites that were identified in the IARC monograph are highlighted in the orange-yellow.

And then in the others -- the final column, under the CWJ, those are the additional tumor sites I identified after I went through and evaluated all of the data that was in the supplemental tables and the study reports that I was able to get.

Q. Okay, excellent. And you are CWJ, Charles William Jameson?

A. I am CWJ.

Q. Okay.

A. And as I look at this, it looks like I made a mistake. The orange says, tumor sites identified by, it should just say "IARC," and then the blue is the ones that I identified by me and IARC.

Q. Oh, so you flipped --

A. I'm sorry, that's right. I've identified the same sites as --

Q. This is correct isn't it?

A. That's correct. I'm sorry.

Q. All right, okay. So you can put back up our PowerPoint,

please. And that's Exhibit 328, that we will also move in to evidence.

(Exhibit 328 entered into evidence.)

BY MS. WAGSTAFF:

Q. And one last question. The IARC Working Group 112 considered the null finding of the AHS when they made their determin- -- when they made it's determination, is that correct?

A. Yes. The Agricultural Health Study was discussed extensively during the IARC Monograph, and we had the preliminary De Roos Study that had been published concerning the AHS Study, and it turns out that the -- that we -- during IARC Monograph 112, we looked at, I think, a total of four pesticides that had been evaluated in the AHS.

And so it was decided that a very detailed description of the Agricultural Health Study would be included in the malathion monograph from -- from Monograph 112, and all of the other monographs, including glyphosate, would refer the reader to the extensive description of the AHS study in the malathion monograph for more details about the evaluation of the AHS.

So this slide just says -- gives the pages in the malathion monograph where the AHS Study is discussed, and just an excerpt taken from the malathion monograph, which also applies to all of the other chemicals, including glyphosate, that,

"Nondifferential exposure misclassification bias relative risk estimates towards the null in the AHS, and tends to decrease the study precision. This was something that was observed at the IARC meeting. The Working Group considered the AHS to be a highly informative study."

So I mean, it was reviewed, felt to be very informative, but even at that time, they were concerned about misclassification.

Q. And at the time, again, just to hammer this point home, the IARC Working Group knew that it was a null finding, is that correct?

A. Yes.

MS. WAGSTAFF: Okay, and the malathion IARC Monograph is in your book, and it's Exhibit 329. And we can move that in.

(Exhibit 329 entered into evidence.)

And also, I don't know if I did before, but Exhibit 53 is the -- or 57, I'm sorry, is the IARC Monograph.

So unless the Court has any other questions for you, I'll pass the witness?

THE COURT: Okay, great. Why don't we take our lunch break and return at 1:00 o'clock. Thank you.

(Recess taken from 12:05 p.m. until 1:00 p.m.)

CROSS-EXAMINATION

BY MR. HOLLINGSWORTH

Q. Sir, in your evaluation of the glyphosate rodent bioassay data, you did a hazard assessment, right?

A. Yes, sir.

Q. And, in fact, at your deposition you told me about 18 different times that you had done a hazard assessment, isn't that right?

A. I don't know the number of times, but I was asked a lot of times.

(Whereupon a document was tendered to the Court.)

Q. In your report for this court, your expert report, sir, you said that there's an important distinction between the term "hazard" and the term "risk," right?

A. That's correct.

Q. And you said that, quote,

> Risk is defined as the probability that exposure to a hazard will lead to a negative consequence."

True?

A. In general terms, that's accurate.

Q. And the IARC preamble also defines the distinction between hazard and risk, doesn't it?

A. Yes, sir.

Q. The preamble states that a cancer hazard is an agent that

can cause cancer under some circumstances, while a cancer risk is an estimate of the carcinogenic effects expected from exposure to a cancer hazard; isn't that right?

A. That sounds right. I don't know if that's the exact wording. I'd have to look at the preamble to see if that was the exact wording.

Q. Well, you quoted that at page 5 of your report in this litigation, didn't you?

A. I did quote the IARC preamble, yes.

Q. Did I misread that?

A. I don't know. I'd have to have it in front of me to see if you did or not.

Q. The preamble to the -- to the IARC methodology also states that a cancer hazard is an agent that can cause cancer under some circumstances. True?

A. Sorry, could you repeat that?

Q. The preamble, the IARC preamble states that, quote, "A cancer hazard is an agent that can cause cancer under some circumstances." Isn't that right?

A. That sounds right.

Q. That's in your report, isn't it?

A. But again, I'd have to see the preamble to make sure that was the accurate wording.

Q. Didn't you state that in your report, sir?

A. I quoted the preamble in my report, but I'd have to have

it in front of me to make sure it was the accurate reading.

Q. The IARC preamble also states that a cancer risk is an estimate of the carcinogenic effects expected from exposure to a cancer hazard, right?

A. I'm sorry, if I may --

THE COURT: Why don't you just put it in front of him.

THE WITNESS: Yeah, if you could provide me with the preamble, I could verify what you're saying exactly.

THE COURT: Rather that leaving everyone to wonder if you're reading it exactly correctly or not.

MR. HOLLINGSWORTH: I'm reading from the same page that I think your Honor was reading from.

THE COURT: Why don't you put it in front of him, if you want to pursue this line of questioning.

THE WITNESS: Thank you.

MR. HOLLINGSWORTH: Sure.

THE WITNESS: So where in here is the preamble?

BY MR. HOLLINGSWORTH

Q. It's -- it's referred to in your report at page 5, which is Exhibit 883.

A. But in the documents that you just provided to me, where is it located?

MS. KLENICKI: It's under tab 883.

MS. WAGSTAFF: It's in Volume 2.

THE WITNESS: I got that now. And what page is it on, please?

MS. KLENICKI: Five.

THE WITNESS: Okay. Now, where exactly in this were you referring? I'm sorry.

BY MR. HOLLINGSWORTH

Q. I'm referring to the first incomplete paragraph where you state,

> "The IARC preamble states that a cancer hazard is an agent that can cause cancer under some circumstances."

Do you see that?

A. "...that can cause cancer under some circumstances," yes.

Q. Yeah, you wrote that in your report in this case, right?

A. I was quoting from the preamble, that's correct.

Q. Okay, and it also says that,

> "A cancer risk is an estimate of the carcinogenic effects expected from exposure to a cancer hazard."

Do you see that? Did I read that correctly?

A. "A cancer risk is an estimate of the carcinogenic effects expected from exposure to a cancer hazard," yes.

Q. You wrote that, right?

A. Yes.

Q. Okay.

A. Quoting from the IARC preamble.

Q. Okay, and then your next sentence is that,

"The monographs are an exercise in evaluating cancer hazards, despite the historical presence of the word 'risks' in the title."

Did you write that?

A. I wrote that, and that was -- I was told by the people at IARC that the main reason this is included in the preamble IARC Monograph preamble is because they wanted to make sure that people don't look at the monograph as a risk assessment. It is not a risk assessment document. It is a hazard identification document. And that was the reason this sentence was put in the preamble.

Q. And your report is an exercise in hazard identification or hazard assessment, isn't it?

A. That's correct, as I state in my report, it's a hazard assessment.

Q. Now, if you look at the next sentence, sir, on page 5 of your report, the one that follows from the one that we were just discussing, you state, quote, "The distinction between hazard and risk is important."

Do you see that?

A. That's what it says.

Q. See that? And then, your report goes on to state that,

"The monographs identify cancer hazards, even when risks are very low at current exposure levels."

Do you see that?

A. Yes. It says that, even though risks are very low, but doesn't say that they don't exist.

Q. Sir, did you write that?

A. I wrote -- I wrote that the distinction between the hazard and risk is important, and the monographs identify cancer hazards even when risks are very low, at current exposure levels.

Q. Did you -- did you tell me in your deposition that hazard assessments do not establish the exposure conditions that would pose cancer risks to individuals in their daily lives?

A. In my deposition I said what, again? I'm sorry.

Q. Did you tell me that hazard assessments, quote,

"...do not establish the exposure conditions that would pose cancer risks to individuals in their daily lives"?

THE COURT: Why don't you ask him if he believes that now, what's his opinion now.

MR. HOLLINGSWORTH: Okay, is it -- is it --

THE COURT: Hold on a sec. If he says something that you believe is contrary to what he said in his deposition, then you can bring up his deposition testimony. That's normally how

we do it.

MR. HOLLINGSWORTH: Sure.

Q. Is it fair to state that hazard assessments do not establish the exposure conditions that would pose cancer risks to individuals -- to individuals in their daily lives, sir?

A. No.

Q. Is it fair to state that risk assessments are different from hazard assessments?

A. Yes.

Q. Isn't it true that the determination of what would pose cancer risks to individuals in their daily lives is a formal risk assessment?

A. I'm sorry, could you repeat that again?

Q. Isn't it true that the determination of what would pose cancer risk to individuals in their daily lives is a formal risk assessment, according to your report to Congress?

A. It -- it could be, but hazard assessment also could be that.

Q. Do you remember when I asked you a question at your deposition and you gave the following answer to the following question?

"QUESTION: The determination of what would pose cancer risks to individuals in their daily lives is a formal risk assessment, according to your report to Congress, right?

"**ANSWER:** That's correct."

Do you remember that?

A. I'd like to see the deposition -- what the deposition says, I'm sorry.

Q. No, my question is: Do you recall that?

A. Sitting here right now, no, I don't.

Q. Mm-hm.

A. And just -- I've been -- I've had three depositions, and I've been misquoted and things have been taken out of context about what I said so many times, I'm hesitant to confirm that without seeing what my deposition actually said and the context in which it was said.

Q. Is it fair to state that the determination of what would pose cancer risks to individuals in their daily lives is a formal risk assessment, according to your report to Congress?

A. I'd have to look at the -- now are you referring to the Report on Carcinogens?

Q. Yes.

A. I'd have to look at the section of the Report on Carcinogens to make sure that's what it actually says.

Q. Okay.

A. I don't have it rote to memory.

Q. Do you recall getting -- do you recall giving me the following answer to this question at your deposition?

"**QUESTION:** The determination of what would

pose cancer risks to individuals in their daily lives is a formal risk assessment, according to your report to Congress, right?

"ANSWER: That's correct."

A. Again, I'd like to see the deposition -- well, you know, see my deposition, to see if that's actually reflecting what I said, and also in what context it was said.

Q. Sir, EPA performed a risk assessment on glyphosate, didn't they?

A. They have done it many times, yes.

Q. And EFSA, which is the European Food Safety Agency -- the European health food -- food health administration called EFSA performed a risk assessment on glyphosate, didn't they?

A. They have performed a risk assessment, yes.

Q. And you have not done a risk assessment for glyphosate, have you?

A. I have not been asked to do one yet, no.

Q. Okay. Sir, you reviewed a total of five dose feed bioassays of glyphosate in mice, and seven dose feed bioassays on glyphosate in rats, true?

A. Correct.

Q. And you agree that the dataset of bioassays in rodent -- long-term rodent chronic bioassays is more than you usually see for a particular compound, true?

A. The dataset for glyphosate is very large, yes.

Q. In fact, you said it's an unusually large body of toxicology.

A. That's true. You usually don't have the luxury of having that many studies to review for one chemical.

Q. You described the amount of toxicology data from animal carcinogenicity bioassays as extraordinary, didn't you, in its size?

A. I -- I might have used that term, yes.

Q. You didn't cite -- you didn't cite anything in your report that says that the mouse system, experimental mouse system, is a good model for determining or predicting human non-Hodgkin's lymphoma, did you?

A. That's because the studies that I reviewed were all animal bioassay studies to determine if glyphosate causes cancer. They weren't designed to see if it was relevant to non-Hodgkin's lymphoma in humans. That wasn't the purpose of any of the studies.

Q. You didn't cite anything in your report that states that the experimental mouse system is a valid model for predicting human non-Hodgkin's lymphoma, did you, sir?

A. That's really an inappropriate question, because that's not what the bioassay studies are -- are performed for. They are performed to determine if the chemical can cause cancer in laboratory animals.

Q. Well, sir, that's not my question. My question is: Do

you remember when you were deposed in this case, and you gave this answer to the following question?

"QUESTION: You didn't cite anything in your report in this case, sir, in which you relied on any publication that states that the experimental mouse system is a valid model for predicting non-Hodgkin's lymphoma in humans, did you?

"ANSWER: No, I did not use any reference to that effect, no."

Do you remember giving that answer to that question?

A. That is my deposition in here? Can I see what my deposition says?

MR. HOLLINGSWORTH: Can you pull up slide 2, please?

THE COURT: If you want to ask questions about prior deposition testimony in the way that you're asking them, then you need to give him the full transcript of the deposition, sir.

MR. HOLLINGSWORTH: He has the full transcript, sir.

THE COURT: Okay. So why don't you direct him to the page that you're -- that you're asking him about, so that he can take a look at it in context.

MR. HOLLINGSWORTH: I have the page on the screen, sir.

THE COURT: Tell him what the page is in the

transcript, so that he can look at it in context.

MR. HOLLINGSWORTH: I believe it's at page 27, lines 18 to 24.

JUDGE PETROU: And what Exhibit number is it in the binders?

MR. HOLLINGSWORTH: Exhibit 737.

MS. WAGSTAFF: And which of the three depositions was that?

MR. HOLLINGSWORTH: This is the deposition taken on September 21st, which is the deposition about his expert witness report.

JUDGE PETROU: Okay, I lost the page. It's Exhibit 737, what page?

MR. HOLLINGSWORTH: Page 27, at lines 18 to 24, is what I said. I hope that's right.

Q. Sir, do you see the question that begins, "You didn't cite anything in your report in this case..."?

A. Yes. That's line 18?

Q. Yes.

A. Okay.

Q. Did you read that question and answer? Sir, do you have my question in mind?

A. Yes, I see that, but if you read on in my deposition, you ask again,

"QUESTION: Isn't it current -- isn't the

current literature in the case that the mouse system is not a good -- is not a good predictor of lymphoma in humans?"

And then my answer to that is:

"ANSWER: There may be, or may have -- there may have -- may be some publications in the literature to that effect. But again, the purpose of doing these studies is, most, the studies -- the purpose of doing an animal bioassay study is to determine if the chemical can cause cancer in experimental animals, and it is not -- not looking to investigate, does it form a specific kind of tumor that is the same found in humans. At least routinely, that is not the case.

"Now, sometimes I think -- the state of the art is that you can develop genetically modified test species, transplant human genes into the animals or something like that, and do some studies that may give you some more information. As to the formation of a cancer in humans based on the special animals, but I'm not familiar with what the -- that research, and I can't speak to that right now, but I know the type of research is being

done. I have no idea if there's anything being done with non-Hodgkin's lymphoma, I haven't looked at that."

Q. Thank you. Thank you, that's very good. Thank you.

You claim that glyphosate causes kidney tumors in male CD-1 mice in the 1983 Knezevich study, which has also been referred to as the 1983 Monsanto mouse study, right?

A. That's correct.

Q. And the fact that something causes a kidney tumor in a mouse doesn't really tell you anything about whether it would cause non-Hodgkin's lymphoma in humans, isn't that right?

A. Again, the design of an animal bioassay is not to look -- if it causes -- if it's similar to non-Hodgkin's lymphoma in humans.

The purpose of an animal bioassay is to study if the chemical can cause cancer in laboratory animals, and if so, then it's biologically plausible that it's a human carcinogen. That's the purpose of why these studies are run. It's not to investigate non-Hodgkin's lymphoma in humans.

So that's really an inappropriate question.

Q. You told me that the fact that something causes a kidney tumor in a mouse doesn't really tell you anything about whether it cause -- whether that relates up to causing non-Hodgkin's lymphoma in humans, right?

A. I told you that is really not an appropriate question.

Q. Okay. The fact that -- that something causes a kidney tumor in a mouse, and its relationship to non-Hodgkin's lymphoma in humans, really has not been investigated, has it?
A. I'm not aware that anybody has done any studies to that effect. And to be honest with you, I don't think anybody would -- would try to do that kind of a study, because it's -- it's -- it's -- it's not what the data is telling us from the animal bioassay. Its just telling us that it causes kidney tumors in the CD-1 mouse.
Q. You're not aware of any publications or research on whether mouse renal tumors are actually predictive of non-Hodgkin's lymphoma in humans, are you?
A. I'm not aware of any studies, no, but....
Q. You've never published a paper addressing the issue of the relationship of kidney tumors in mice to non-Hodgkin's lymphoma in humans, right?
A. No, I have not.
Q. And by the way, before IARC, you had never published a study saying that glyphosate causes non-Hodgkin's lymphoma in humans, yourself, had you?
A. Prior to IARC, that is correct.
Q. And you don't know of any literature, published medical literature in the entire world literature of medical and science activity, that stated before IARC that glyphosate can cause non-Hodgkin's lymphoma in humans, do you?

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

Q. You don't know of any literature in the worldwide science and medical literature that states that glyphosate can cause non-Hodgkin's lymphoma in humans, do you?

A. There's a lot of literature that says glyphosate causes non-Hodgkin's lymphoma in humans.

Q. You don't know of any study that's been done on whether there's a mechanism that causes kidney tumors in the mouse that is similar to a known mechanism that leads to non-Hodgkin's lymphoma in humans, do you?

A. No, but these are all -- you know, they're misleading and irrelevant questions, and they -- they really -- that's not how toxicology works, as far as animal bioassay is concerned.

As I indicated before, you do the animal bioassay to see if it causes cancer in animals to say that if it does, then it's biologically plausible that it causes cancer in humans.

You then take that data and you look at the humans that are exposed to the chemical, or the formulations, in real world situation and real world doses, and see if you see tumor formation in humans.

Q. You're not --

A. So that's how -- that's how it works.

Q. You're not aware of any data or published studies that record what the error rate would be in predicting non-Hodgkin's lymphoma in humans, based on the finding of kidney tumors in a

mouse, are you?

A. That is really not -- that's not really -- I hate to say, that's a ridiculous question, but it's really not an appropriate question to ask, based on the animal bioassay data that you get. That's not the purpose of an animal bioassay.

The animal bioassay is performed just to see if a chemical causes cancer in animals, as it leads to the biological plausibility of a human carcinogen, and that's why those types of studies are required by the EPA, by the FDA. That's why the -- the National Toxicology Program spends tens of millions of dollars a year to do animal bioassay studies.

They don't do animal bioassay studies to say, oh, we're studying Compound X in mice and rats, so we can say it causes non-Hodgkin's lymphoma in humans.

We've run an animal bioassay study to say Compound X causes cancer in animals, therefore, it's probably a human carcinogen. So we need to get busy and look at the populations out there in the world that are exposed to real world -- real world levels, real world concentrations, of Compound X, in the real world situation, if it causes cancer in humans, and if so, where.

Q. Sir, you've never attended a lecture where there was a discussion of whether or not mouse renal tumors are predictive of non-Hodgkin's lymphoma in humans, have you?

A. No.

Q. You don't recall that the investigators in the Monsanto 1983 study on mice were investigating any type of association between the possible formation of kidney tumors in mice and non-Hodgkin's lymphoma, do you?

A. No, the purpose of their study was to determine if glyphosate caused cancer in those animals; only if it caused cancer, not a particular kind of cancer or if it was related to any kind of cancer in humans. The purpose of that study was to determine if it caused cancer in humans.

Q. You don't think that --

A. I mean, in animals, excuse me, in animals.

Q. You don't think that any experimental pathologists have ever looked in to the issue of whether or not mouse renal tumors are associated with non-Hodgkin's lymphoma specifically in humans, do you?

A. I don't know -- knowing the veterinary pathologists that reviewed the slides, I don't know that anybody would be interested in trying to do anything like that at all.

Q. Now, going back to the Knezevich and Hogan study, which is a 1983 mouse study, again, that's the Monsanto study from 1983, and you have actually read that report, have you, sir?

A. Yes.

Q. You've read the report of the original investigators who were Knezevich, which I'll spell for you at some point, and Hogan. Right?

A. Yes.

Q. And if you could, sir, and you've -- I already asked you whether you had read the pathology report. You told me in your deposition that you have. And what I'd like to do is read to you from the conclusion of that report, and ask you if -- if you are familiar with this.

And I'll put this on the screen. It should be slide 6.

My question is whether you recall reading this in the report, sir, at the conclusion part of the Path report, quote,

> "Neoplastic findings were of the type commonly encountered in mice. Bronchiolar alveolar tumors of the lungs, hepatocellular neoplasms and tumors of the lymphoreticular system accounted for the majority of those encountered. There were no suspected test substance associated trends in the incidence of these tumors or any of the other spontaneously occurring neoplasms."

Did you read that when you did your work in preparing your expert report in this case?

MS. WAGSTAFF: Counsel, can I have a copy of that document?

MS. KLENICKI: It's in your binder at 1524.

MS. WAGSTAFF: Okay, so it's at 1524? Thank you.

BY MR. HOLLINGSWORTH

Q. You read that, right, sir?

A. It sounds familiar; but it's been a while since I read that report. So I don't know if it -- if that is accurate or not.

Q. You didn't read that report in preparation for your testimony today?

A. I read so many things, I don't know that I went back and read that report.

Q. So your -- your sense is that what is written on the screen here, that I represented as the conclusion from the study --

A. It sounds -- it sounds familiar, yes.

Q. Okay. There's also another conclusion from that slide 7, which addresses the issue of the renal tumors. And I'll put that on the screen.

I'd like to ask you if this sounds familiar. It is,

> "The only other neoplasms that occurred" -- that's neoplasms, excuse me -- "with any frequency in treated mice were renal tubular adenomas which occurred in males."

Are you looking at the screen, sir?

A. I'm sorry?

Q. (Reading:)

"There were present" -- excuse me -- "three were present at the high dose and one at the mid-dose level. The distribution of these benign tumors was considered spurious and unrelated to treatment, due to the absence of other renal lesions suggestive of or supportive of an effect on the urinary system."

Do you see that?

A. Yes, that's what this statement says.

Q. Did you read that in connection with the preparation of your report, sir?

A. If it was -- if that is what was in the study report, it is.

Q. So the original investigation -- investigators in this study, who were Dr. Knezevich and Dr. Hogan, made this conclusion after they reviewed all the -- all the tissue slides in this case, right?

A. That was their conclusion.

Q. And they were veterinary pathologists, who actually looked under the microscope at tissues. That's what they did for a living, true?

A. Being veterinary, I assume. I don't know their background. I don't know them personally, but --

Q. Did you look at their signatures on this report?

A. I did.
Q. They're signed "D.V.M." aren't they? Doesn't that stand for Doctor of Veterinary Medicine?
A. That doesn't necessarily mean they're pathologists.
Q. Okay, but anyway, the people who had reviewed this study and prepared this report are the people who signed the report and made that conclusion, and they had reviewed all of the slides from this report, and you didn't review any of the slides, right?
A. I didn't have access to any slides, no.
Q. You wouldn't be qualified to review the slides, would you?
A. Probably not.
Q. You didn't look under the microscope at any slide in connection with preparing your expert report here, did you?
A. No, I did not.
Q. And you disagree with the conclusion of these authors, true?
A. That there were adenomas, three adenomas in the high dose? Could I have the slide up here again, please?
Q. Well, you disagree with their conclusion that there were no substance-related lesions or tumors, in the opinion of the authors of this report? You disagree with that, true?
A. Well, I disagree with that, and -- and I would say the initial EPA review of this data, that was submitted for registration of glyphosate, also disagreed with that. It was

from the EPA report when I --

Q. Well, we'll get to it?

A. -- when I was reviewing the data that I picked up that these renal tumors were -- were at least in the -- in the first of the review of EPA were -- were significant, and because of the rarity of these tumors in the CD-1 mouse. So that's what raised a red flag for me to take a harder look at the incidences.

I don't know if you want me to go into the -- the rest of the history that I know about these, but eventually --

Q. I'd like to ask the questions, if you don't mind.

A. I wasn't answering a question. I was going to tell you about the study.

Q. Well, let me -- let me ask you about -- let me ask -- ask you some additional questions about the study first, and then we'll discuss the history and your understanding of it, okay?

A. Okay.

Q. You said that these renal tumors that you referred to in your report that were -- you say were caused by glyphosate, in the Knezevich and Hogan study, are rare?

A. Yes.

Q. And you cited to a report called Chandra & Frith (1994) for that proposition, didn't you?

A. Mm-hm.

Q. And Chandra & Frith is the same -- is the same study that

IARC relied on in its report, true?

A. It was used in the IARC Monograph, that's correct.

Q. And that's because Chandra & Frith only had one incidence of renal tumors in their entire historical database, right?

A. Well, no. Basically, I think it's in the IARC Monograph because it was the only peer-reviewed publication we could find that addressed spontaneous tumors incidence in CD-1 mice.

Q. You remember seeing in the materials you read, though, that there were three renal tubular lesions that had occurred spontaneously in the Biodynamics database, right?

Biodynamics is the laboratory that conducted this study, and that's who Knezevich and Hogan worked for, true?

A. I don't recall. How many studies were there in there?

Q. I don't know, but you told me in your deposition that you recalled that from some material that you had read, didn't you?

A. Yeah, but I'd need to see that information again. I don't recall, and I need to know how many different and how many historical animals I've seen. I mean, three -- just saying three -- that could be three out of 10; three out of 20, three out of 500, three out a thousand. I don't know what that number means.

Q. Do you remember that there was another laboratory that EPA was reviewing at the time called "Hazelton" that had a 7.1 incidence of renal tubular lesions in their spontaneous database?

A. That sounds about right.
Q. Would you agree that historical control data from the lab that -- lab that actually conducted the study is more reliable as a comparator than historical data from multiple different laboratories?
A. It -- it would be if -- if it was the same species -- same strain of mouse, you know; and contemporary time, when this study was done.
Q. Now, the high-dose animals -- there were three dose groups, a low dose, mid-dose, and high-dose, and a fourth group was a control dose, which received glyphosate. True?
A. I'm sorry, say that again?
Q. The study typically has four study groups: A control group at zero glyphosate, a low dose, mid-dose, and high-dose group, and that's how the studies are set up, and there are usually 50 or 60 animals in each of those groups. True?
A. That's correct. That's what was in this study.
Q. And the high-dose group in this study -- the Knezevich study or the Monsanto '83 study -- received 4,841 mgs per kg per day of glyphosate, true?
A. Yeah, 30,000 parts per million into the feed, right.
Q. That's milligrams per kilogram per day, right?
A. That's, yeah, 30,000 parts per feed based --
THE REPORTER: I'm sorry, could you kindly repeat your answer? I lost it. 3,000 parts per...?

MR. HOLLINGSWORTH: No, I think he said, 4,841 mgs per kg per day.

THE REPORTER: Thank you. Sorry, gentlemen.

BY MR. HOLLINGSWORTH

Q. Sir, the high-dose group received 4,000, roughly, 4,841 milligrams per kilogram per day, right?

A. I think that's what it equated to.

Q. And the EPA guidelines for carcinogenicity testing state that the highest dose tested need not exceed 1,000 milligrams per kilogram per day; isn't that right?

A. Those are the EPA Guidelines, but that -- that is not what you need for an animal bioassay to determine carcinogenicity.

They -- I don't know how they came up with that 1,000 milligrams per kilogram body weight per day, value, but as in my experience with doing cancer hazard assessments for the National Toxicology Program Report on Carcinogens and IARC, that's -- that number is rather low.

Q. So you disagree with EPA, and you also disagree with the OECD, which is the international governing body, which also says that 1,000 milligrams per kilogram per day is the absolute upper-limit dose for animal bioassay; isn't that right?

A. You have to understand that these agencies are regulatory agencies.

Q. Well, can you answer my question, sir? My question is: You disagree with EPA, and the international regulatory body

OECD on this issue, true?

A. I'm not disagreeing with what they are recommending. It's the reason why they're recommending it. They are recommending that because their responsibility is risk assessment, and by setting a level of a thousand milligrams per kilogram per day, their saying that in the real world situation for risk assessment, you shouldn't go over that, because that wouldn't mimic what you see in a real world situation of human exposure.

What we're doing is trying to do a -- in animal bioassay we're trying to determine, can it cause cancer? We're not doing risk assessment, we're doing hazard assessment. So in order to do hazard assessment, you test it at the maximum tolerated dose, which I've discussed earlier.

So that's why I disagree, because it doesn't tell you anything about, is it an animal carcinogen, testing it at a thousand milligrams per kilogram per day, that you need to do it at a higher level, because the animals are able to tolerate a higher dose.

That's where the difference comes in. It's two different thing. One is doing a risk assessment, one is doing a hazard assessment, and the hazard assessment is important in this particular issue because we're identifying something as an animal carcinogen, and therefore, biologically plausible to be a human carcinogen.

And that's the question: Is it -- could it be a human

carcinogen? Yes. All right, go to the real world situation. Look at the real world exposures, the people that use the material and are exposed to it in a real world situation, and look to see if there's any cancers in those individuals.

And for the purpose of glyphosate formulations, do you see non-Hodgkin's lymphoma?

Q. And when you say you see non-Hodgkin's lymphoma, you're basing your opinion on what IARC said, true?

A. I'm basing my opinion on the peer-review literature for the epidemiology studies of glyphosate formulations.

Q. Okay. Let's go back to these renal tubules, and the mouse study from 1983. You also looked at another study involving the CD-1 mouse, which was Atkinson, and you talk about Atkinson in your report, don't you?

A. Correct.

Q. Are you aware that the incidence of renal tubules reported in the male mice in that study was 2200? That is, two in the controls, two in the low-dose group, zero in the mid-dose group, and zero in the high-dose group?

A. I recall seeing something to that effect. Yes.

Q. Did you consider that in your report?

A. I considered that incidence, but that was -- that was a negative finding, because the incidence in the concurrent control animals was the same level as that of the treated animals in the low dose. So that really was not an effective

to glyphosate.

Q. Why didn't you consider that negative finding overall when you evaluated the effect on renal -- the renal cells that you said you saw in the 1983 study?

A. It was negative -- it was a negative effect. So it didn't -- I didn't include it because I -- in my report, I only addressed the positive effects that were seen in the animal bioassay studies.

Q. All right. Sticking with Atkinson for a moment, that's a 1993 study, right?

A. Right.

Q. And that's done by a sponsor different than Monsanto; a different sponsor, true?

A. Okay.

Q. And you have stated in your report that the Atkinson study shows that glyphosate causes hemangiosarcomas in male mice, true?

A. That's correct. There was a statistically significant positive trend in the formation of the hemangiosarcomas. The incidence in the high-dose animals was 9 percent versus zero percent in the controls. So it didn't quite reach statistical significance, but that's a pretty good increase.

And the historical incidence for this, in this strain of mouse -- of mouse, is around 1 percent.

Q. Now you're reading from what you called your cheat sheet

at the deposition right?

A. Right.

Q. Uh-huh. Now, to your knowledge, no one has done an investigation to see if there's a correlation between the formation of hemangiosarcomas in laboratory animals and non-Hodgkin's lymphoma in humans, true?

A. Well, again, that's an inappropriate question to ask. That wasn't the purpose of the study. The purpose of the study was to see if it caused cancer in laboratory animals as a predictor of cancer in humans, and it wasn't designed to investigate the correlation of hemangiosarcomas in male CD-1 mice to non-Hodgkin's lymphoma in humans. So that's not a -- that's not an appropriate question to ask.

Q. Now, as a toxicologist, you're familiar with Hayes' Principles of Toxicology, right?

A. Okay, yes.

Q. Hayes says that the hemangiosarcomas are common background neoplasm in mice, doesn't he?

A. I'll take your word for it.

Q. Now, EPA concluded that these hemangiosarcomas in the Atkinson study were not treatment-related, didn't they?

A. The -- I'm sorry, could you repeat that?

Q. EPA concluded that the increase in hemangiosarcomas in the Atkinson study from 1993 in CD-1 mice were not treatment-related; isn't that right?

A. That's what they concluded, but they did indicate in their report that it was statistically significant for an increase in the trend of formation of these hemangiosarcomas.

Q. And did you -- did you look at the consideration that EPA gave to the background incidence of hemangiosarcomas in CD-1 mice, sir?

A. Yeah. I think what they said was the incidence in the high-dose males is above the historical upper limit of 8 percent for this tumor at the performing laboratory.

Q. And -- and JNPR concluded that the hemangiosarcomas were not considered to be caused by the administration of glyphosate. Isn't that right?

A. I -- I recall them saying that. Yes.

Q. What is JNPR?

A. What is JNPR?

Q. Yes.

A. It's a European regulatory agency, I believe.

Q. The authors of the Atkinson Study also concluded that there were no compound-related neoplastic lesions from that study in CD-1 mice. True?

A. That's what their conclusions said, yes.

Q. So you disagree with EPA the European JNPR and the original study investigators. Right?

A. Well, I was asked to look at the data, evaluate the data, as I -- as I do and have done in the the past, and give my

opinion. And in my opinion, based on the data, the increased trend in formation of hemangiosarcomas is statistically significant, and therefore a real effect.

And therefore, glyphosate caused these tumors in the CD-1 male mice in this study.

Q. By the way, there was no increased incidence of hemangiosarcoma in the high-dose males in the Knezevich Study; was there?

A. It wasn't any reported, no. There may have been one or two -- I don't know -- but it wasn't significant.

Q. Knezevich and Atkinson are both 24-month long-term mouse bioassays. And they're in the same strain of mouse: The CD-1 Mouse. Right?

A. That's correct.

Q. You know that the high-dose group in Knezevich received over four times the dose of glyphosate as the high-dose group in Atkinson. Right?

A. That's correct.

Q. Now, you claim that glyphosate caused lung cars no -- I should say lung adeno -- a-d-e-n-o -- carcinoma in male CD-1 mice in the Wood Study. Right? Are you looking at your cheat sheet?

A. I'm looking at my cheat sheet.

Q. Okay. The Wood Study was a 2009 study. Right?

A. That's correct.

Q. And that was from -- that was by a different sponsor than Monsanto, of course.

A. Okay.

Q. And, now, you agree that no one has designed a study to determine whether an increased incidence of adenocarcinoma in a mouse has any relationship to the formation of non-Hodgkin's lymphoma in people. Right?

A. Again, that's not an appropriate question.

Q. There's --

A. That's not the purpose of the study.

Q. You're not -- you're not aware of any published papers investigating the association between lung adenocarcinoma in the CD-1 Mouse, and non-Hodgkin's lymphoma in people?

A. I'm not aware that anybody has ever looked at that. No.

Q. You know that EPA concluded that adenocarcenoma -- adenocarcinomas in this study were not related to glyphosate treatment. True?

A. No, but the EPA report did state that there was a statistically significant increase in the trend of the formation of these tumors in the animal. They made that observation in their report.

Q. You've testified before that Dr. Portier is your long-time friend and colleague. Right?

A. I -- in my professional career at NIHS, I worked with Chris for almost 30 years, yes.

Q. And in your deposition, you told me that you defer to Dr. Portier on his use of statistics and biostatistics. Right?
A. I -- I would do that because he is a biostatistician, so he is more adept at doing this statistics than I am.
Q. You know that Dr. Portier, in his report, says that he cannot attribute the increase of lung adenocarcinomas in this Wood Study to anything other than chance?
A. I skimmed through Chris' report. I really don't know what he did and how he came to that conclusion; but again, I --
Q. You know that he came to the conclusion, though. Right?
A. Pardon me?
Q. You know that he came to that conclusion?
A. To which conclusion is that?
Q. The one I just stated; that he could not attribute the increased in lung adenocarcinomas in the Wood Study to anything other than chance?
A. To be honest with you, I don't know if -- if he -- if that's stated in his report or not. Like I said, I skimmed through the report, and I didn't commit it to memory; but it's not unusual for a toxicologist to come to -- you know, to have different evaluations looking at the data. I was asked to look at the data and come to my conclusion. I'm sure Chris was asked to look at the data and come to his conclusion. And our conclusions are in the report.
MR. HOLLINGSWORTH: Can you pull up Slide 21, please?

Thanks, Scott.

MS. WAGSTAFF: What tab is this in, in our book?

MR. HOLLINGSWORTH: This is Exhibit 737.

MS. KLENICKI: That's incorrect. Hold on.

MS. WAGSTAFF: Is it in these books you gave us?

MS. KLENICKI: It is in the volumes.

MR. HOLLINGSWORTH: I don't know.

Q. Do you see this statement from Dr. Portier's report?

MS. WAGSTAFF: Hang on. Let us -- can you tell us where?

MS. KLENICKI: 885.

JUDGE PETROU: You said Exhibit 737. That's the deposition transcript, instead of the report.

MS. KLENICKI: It's 885.

MR. LASKER: It's 532.

JUDGE PETROU: I'm not opening it yet. Are we sure?

MS. WAGSTAFF: It's the beginning of Volume 1.

JUDGE PETROU: It's good exercise with the binders, but --

MR. GRIFFIS: 532.

BY MR. HOLLINGSWORTH

Q. You're familiar with Dr. Portier's report on this issue of lung adenocarcinomas in male mice in the Wood Study. True?

A. Like I said, I skimmed through it. I didn't read it in great detail, and I didn't commit it to memory, no.

Q. Have you considered his statement that, *In summary, the moderate findings in one 24-month study and the negative finding when any studies are pooled suggests that the linkage between glyphosate and lung adenocarcinomas in male CD-1 mice is due to chance*?

A. Well, I mean, that's Chris' opinion, in his looking at the data.

Q. Yeah.

A. But my opinion in looking at the data, and the fact that it gave a statistically significant positive increase in the trend of the formation of these tumors in the CD-1 mice, led me to believe that that was an effect that was caused by glyphosate.

Q. So you disagree with Chris, and you disagree with EPA, and you disagree with the study -- original study investigators, and you disagree with EFSA. True?

A. I guess I'm not a very agreeable person.

Q. Okay. These lung adenocarcinomas were not replicated in any other mouse or rat study; were they?

A. The lung tumors? That's correct.

Q. And -- but you agree that it would strengthen the data to replicate the results of a study in other experiments. True?

A. It would -- it would add a -- to the -- it would add to the data. And, yes, it would strengthen the data if you could have a replication of this effect in different studies.

Q. Now, in your direct testimony here in the court today you talked a lot about malignant lymphoma in mice, and how powerful you thought those findings were. Do you recall that?

A. Yes, sir.

Q. You claim that glyphosate caused lymphoma in three of the five mouse studies that you reviewed. Right?

A. That's correct.

Q. And you agreed that there is a high background incidence of lymphoma in experimental mice. True?

A. Depends on the strain.

Q. In CD-1 mice, you told me that there's a fairly high incidence. True?

A. It's fairly high.

Q. And I told you that the papers show 50 percent incidence of spontaneous tumors in CD-1 mice that is lymphoma. And you said, yeah, it could go that high.

A. Well, subsequent to that, I -- after the deposition, I went back and looked for myself what I could find in the literature. And the incidence of the CD-1 mice is not that high.

Q. What is it?

A. Not 50 percent.

What I could find in the published literature was at 4 percent.

Q. Was what?

A. 4 percent in the CD-1 Mouse.

Q. Okay. You know Jerry Ward very well. Right?

A. I'm very -- I'm familiar with Jerry Ward.

Q. He's an experimental pathologist, and you've published with him?

A. Yes.

Q. And you believe him to be very well known and respected in his field of experimental pathology, which is the study of mice and rats?

A. Yes.

Q. And you agree with him that lymphomas are among the most common tumors in many strains and stocks of mice, especially those used in safety assessment. Right?

A. Would you repeat that again, please?

Q. You would agree with Jerry Ward that lymphomas are among the most common tumors in many strains and stocks of mice, especially those used in safety assessment?

A. They -- they are common.

Q. You're aware of scientific literature which states that the mouse is not a good model for looking at whether a chemical causes lymphoma, because of the high background incidence or spontaneous incidence of lymphoma in experimental mice. True?

A. I don't know that I'm familiar with that literature or not, no.

Q. It's true that no increased incidence in lymphoma was

observed in any of the seven rat studies that you reviewed. True?

A. No, there were no lymphomas observed in the rats; but there were lymphomas observed in three different studies in two different strains, and in males and females.

Q. You reported no increased incidence of lymphoma in the mouse study by Knezevich, which is the 1983 mouse study. Right?

A. Correct.

Q. And you reported no increased incidence of lymphoma in the Atkinson Study, which you've referred to in connection with other lesions that you say are caused by glyphosate. Right?

A. Correct.

Q. And you agree --

A. It's not that -- I'm sorry. That's not to say there weren't lymphomas in those studies. They just weren't significant.

Q. You agree that the CD-1, as a strain, has a high spontaneous incidence of lymphoma. True?

A. The CD-1?

Q. Yes.

A. Yeah. Like I said, my search of the literature found that it was around 4 percent.

Q. Sir, in fact, lymphoma is one of the highest spontaneous tumors observed in CD-1 mice. Isn't that right?

A. Okay, but in what context are you saying that?
Q. I'm just quoting you from your deposition, sir, in which you said, *I know it's one of the highest ones*.
A. Yeah. It can be one of the highest ones, but that might mean it's only, you know, 2 or 3 percent.
Q. Well, that's because --
A. That doesn't mean that it's 99 percent or 80 percent. It just means relative to other tumors that are spontaneously formed in the animals, it's high.
Q. Well, you're just referring to the known variability of lymphoma in the CD-1 Mouse; aren't you? It varies. It comes across in all kinds of different rates, from -- depending on laboratory and what-have-you. Isn't that right?
A. The spontaneous rate?
Q. Yeah.
A. Well, I mean, you get -- you get different rates from different laboratory --
Q. You have variability?
A. Oh, you have variability. Yes.
Q. Yeah. According to your assessment methodology, sir, just because something occurs because of a spontaneous rate is no reason to discount it from being an effect. Right?
A. Just because it has a high background level, there's no reason to discount it? Is that what you're saying?
Q. Yeah. Didn't you tell me, quote, "Just because

something" --

THE COURT: Before you get in to his deposition testimony, let him provide his actual testimony.

MR. HOLLINGSWORTH: Sorry.

THE COURT: You can wait and see if there is -- if you perceive a conflict between the two, in which case we can get into his deposition testimony.

MR. HOLLINGSWORTH: Okay. There's a rule on that. I'm trying to follow it, but I slip up sometimes.

THE COURT: You're not.

You want to ask the question again?

MR. HOLLINGSWORTH: Yes.

Q. According to your hazard assessment methodology, sir, just because something occurs because of a spontaneous rate is no reason to discount it from being an effect?

A. That's correct. What I was meaning by that is: Just because an animal has a high spontaneous rate of a particular tumor, if you see a significant increase in that particular type of tumor in your study, and that increase is well above the historical rate, then it's an effect of the chemical, and it's not a reason to discount the study just because there's a high historical incidence of that particular tumor. What the study is telling you is that the chemical is causing an increase in the number of spontaneous tumors that the animal sees, so it is causing additional cancer in the animal.

Q. There's no literature anywhere on the planet that says, quote, "Just about because something occurs because of a spontaneous rate is no reason to discount it from being an effect," is there?

A. I don't know that I understand the question.

Q. Can you point me to any literature anywhere on the planet that says what you say, which is, quote, "Just because something occurs because of a spontaneous rate is no reason to discount it from being an effect"?

A. Okay. Well, then, again, I feel like I'm being taken out of context, because what I was saying was just what I said: Just because an animal -- the animals you are looking at have a high spontaneous rate of a particular tumor, and you see a significant increase in the incidence of that tumor when you treat it with a particular chemical, there's no reason to discount it because it has a high -- because it -- because it has a high spontaneous rate, because that significant increase in that tumor is due to the treatment with the chemical.

Q. EPA and EFSA and the original investigators in the CD-1 Mouse study had all concluded that there was no effect from treatment with glyphosate in connection with those lymphomas. True?

A. That's what they said in their reports.

Q. Let me ask you about the Sugimoto -- S-u-g-i-m-o-t-o -- Sugimoto 1997 mouse study which was done by Arysta Chemical,

A-r-y-s-t-a. That's not Monsanto. That's a different sponsor, called "Arysta." Do you have that in mind, sir?

A. Yes.

Q. You claim that glyphosate caused lymphoma in the CD-1 mice in that study, too. Right?

A. That's correct.

Q. And the Sugimoto Study investigators concluded that there were no compound-related neoplastic or oncogenic -- o-n-c-o-g-e-n-i-c -- oncogenic affects from the administration of glyphosate in this study. True?

A. I'm sorry. I was reading something when you -- could you repeat the question?

Q. Sure. The original Sugimoto Study investigator -- those are the guys who are actually experimental pathologists, who look under the microscopes at all of these tissues. Right? Right?

A. I --

Q. Those are the original investigators?

A. I have no idea what their background is or what they do.

Q. Did you read their report?

A. I read their report.

Q. Did you see what the authors said about the report from the path. study in the report?

A. Yes.

Q. They concluded that there were no compound-related

neoplastic or oncogenic affects from the administration of glyphosate in the study. Right?

A. That's what they said in their report.

Q. And there were no conclusions from EFSA or EPA that were any different than the original authors' conclusions about the Sugimoto Study. Right?

A. To the best of my recollection, that's accurate.

Q. Did you consider the EPA's evaluation of Sugimoto when you did your opinion in this case?

A. Yes, I read their report.

Q. So you disagree with EPA, and you also disagree with the European health/safety agency known as "EFSA," E-F-S-A. Right?

A. Evidently.

Q. Now, EFSA reported an historical control incidence for this laboratory that conducted the Sugimoto Study as between 4 and 19 percent. True?

A. What tumor are you referring toe?

Q. I'm referring to the Sugimoto Study.

A. Yeah, but what particular tumor site are you referring to?

Q. I'm referring to the -- to the lymphomas.

A. Oh, to the lymphomas. Okay.

Q. Yeah. Remember, I asked you this in your deposition.

A. I don't remember being asked that in deposition, but okay.

Q. Okay. All right.

A. I had three depositions, so it's hard to remember which --

Q. You think that the historical controls from a particular laboratory that has conducted or evaluated a study are very important considerations when you evaluate the results of any bioassay study. True?

A. That's correct.

Q. Historical controls aid in the evaluation of the data, in your view. True?

A. It aids in evaluation, yes, but the concurrent controls are the most appropriate ones to use for comparison.

Q. Okay. Let me go back to the Wood Study again. That's the Nufarm Study, N-u-f-a-r-m. Nufarm was the sponsor of this study in 2009. Do you have that in mind, sir?

A. Yes, sir.

Q. Have you got it on your cheat sheet there?

A. Yes, sir.

Q. You claim that glyphosate induced lymphoma in the Wood CD-1 Mouse study. Right?

A. Yes, sir.

Q. But you said that you did not have access to the full study of the investigators?

A. For this particular one, I do not believe I have the full study report.

Q. And in this study you relied heavily on Greim. True?

A. I relied on Greim, and I also relied on EPA evaluation of the study.

Q. Now, the original investigators -- the experimental pathologists who put together this report -- said that there was no compound-related effect, whatsoever, in this study with respect to oncogenic or neoplastic affects. True?

A. That's -- as I recall, that's what -- the information that I got from the study. That's what they said.

Q. And EPA and EFSA specifically considered the lymphoma findings in the male mice in this study, and they did not consider them to be treatment-related because of the high background incidence of lymphoma generally in this mouse strain. True?

A. I know they did not -- they discounted these tumors, but I don't remember that they specifically said it was because of the high background incidence, but I just don't recall.

Q. Do you disagree with the EPA and EFSA in that case?

A. Evidently I do, yes; but if you look at the incidence of the malignant lymphoma, it was zero in the controls. That's the interesting thing about these lymphomas in the CD-1 mice.

In the Wood Study, there were -- if it has a high spontaneous incidence, then why, in the control animals, don't we see some lymphomas? And you don't.

And then, well, in the Sugimoto Study there were two in the -- in the control --

Q. Sir, I discussed with you --

A. -- but --

Q. -- that the background incidence or spontaneous rate of malignant lymphoma in the CD-1 mice historically at the Wood Laboratory was 12 percent in males. True?

A. I don't recall -- no -- seeing that number.

Q. Did you -- you don't recall seeing that number?

A. No. Like I said, I went to the published, peer-reviewed literature to look at what was reported in there for the spontaneous incidence of malignant lymphoma in CD-1 -- male CD-1 mice, and --

Q. You came back with 3 percent? Is that what you said?

A. Came back to find was 4.

THE COURT: Don't interrupt the witness.

MR. HOLLINGSWORTH: Sorry.

THE WITNESS: 4 percent is what I saw.

BY MR. HOLLINGSWORTH

Q. 4 percent?

Did you read the EFSA report on the Wood Study, in which they said the incidence of spontaneous lymphoma raged from zero to 30 percent?

A. Was that for the CD-1 Mouse.

Q. For the CD-1 Mouse?

A. I don't know that. I don't remember that, at all. No. That sounds very high for the CD-1 Mouse.

Q. Okay.

A. If you say Swiss Mouse, I would agree, maybe; but not the

CD-1 Mouse.

Q. Okay. Is it fair to state that there's a high variability of lymphoma -- spontaneous lymphoma -- in CD-1 mice generally?

A. A high variability? I -- I -- that's possible. I don't know that I know that for a fact.

And like I said, I relied on what was published in the literature, and that said that the average was around 4 percent.

Q. Did you read it study by -- or the review article by your friend, Jerry Ward, on the issue of lymphoma -- lymphomas in mice?

A. I probably did, but I don't remember. Sorry.

Q. Let's turn to rats. You made a claim in your Expert Report that glyphosate causes pancreatic islet cell -- that's i-s-l-e-t -- cell tumors in Sprague, S-p-r-a-g-u-e, Dawley, D-a-w-l-e-y, rats. Sprague-Dawley rats. True?

A. Which study are you referring to?

Q. I'm referring to the -- sorry. I'm referring to the Stout and Ruecker Study.

A. Okay.

Q. I believe that's 1990. And the sponsor was Monsanto. Do you have in mind?

A. Yes, sir.

Q. Now, you're not aware of anyone doing any research about the connection between pancreatic islet cell tumors in rats,

and non-Hodgkin's lymphoma in humans; are you?
A. Again, that's really not an appropriate question, because the purpose of the bioassay study is to see if it causes cancer in laboratory animals. And it wasn't designed to investigate if there was a relationship between the tumors you see in animals, and non-Hodgkin's lymphoma in humans. So that's really not an appropriate question to ask.
Q. You're not aware of anyone who's published papers that a Court could rely on, saying that pancreatic islet cell tumors in rats are predictive of non-Hodgkin's lymphoma in humans?
A. I'm not aware of any -- anybody investigating that or publishing on that. No.
Q. Now, you also said that there was no statistically significant trend in the incidence of pancreatic islet tumors in this 1990 rat study by Monsanto. True?
A. I also reported what? I'm sorry.
Q. That there was no statistically significant trend in the incidence of these tumors that you claim were caused by glyphosate. True?
A. No, there was no statistically increase in trends; but there was a statistically significant increase in the incidence in the logos animals.
(Reporter requests clarification.)
THE WITNESS: Low. Yeah. L-o-w. Low-dose animals. I'm speaking too fast.

What I will say: That for the Stout Study in my investigation -- in my review of the EPA report, the EPA performed an additional analysis on the -- on the animals where they excluded the animals that died or were killed before Week 54 or 55. And when they did that analysis, the islet-cell adenomas were statistically significant in the low-dose and the high-dose. So when the EPA did their analysis, they found statistically significant increase in both low-dose and high-dose animals.

And I'll also point out that the incidence of the islet-cell adenoma in the low-dose and the high-dose was almost twice that seen in historical controls.

Q. Sir, didn't you report in your report that there's no statistically significant trend in the incidence of these pancreatic islet-cell tumors in rats?

A. There's no significant increase in the trend; but there's a statistically significant increase in the low-dose and the high-dose animals in here, and that's a very significant finding.

Q. You also concede that there was no apparent progression to carcinoma, either. Right?

A. Well, that's -- that's an observation I made, yeah, that they -- they didn't see any carcinomas in there; that they were all adenomas; but it's not --

Q. Well, that's not --

A. Adenomas progress -- you know, eventually could progress to the malignant.

Q. That's not even correct, either, sir; is it?

A. What's that?

Q. There was a carcinoma in the control group.

A. But that's what they found; that what -- ha -- but that's in the control group. I was talking about the treated animals.

Q. Yeah. Okay.

A. I was talking -- I mean, you've got to look at how you evaluate the data. You compare. You're looking at the formation of the adenomas in the treated animals, and if the adenomas in the treated animals then progress to a carcinoma.

Q. An adenoma's a benign tumor. Right?

A. It's a nonmalignant tumor. That's right.

Q. And there was a carcinoma in the control group in this study?

JUDGE PETROU: I'm having a very hard time following, because you're constantly speaking over.

MR. HOLLINGSWORTH: Okay.

THE WITNESS: Sorry.

THE COURT: It's his fault.

THE WITNESS: Yeah.

THE COURT: You want to try to ask your question again?

BY MR. HOLLINGSWORTH

Q. There was a carcinoma in the control group in this -- in this particular study; wasn't there?

A. One carcinoma. Yes.

Q. Yeah. You didn't report that in your report; did you?

A. I'd have to look at my report. I may have. I may not have. I don't know. But it was -- you know, it was -- it was a -- I reported the adenomas that were found. And it could be that since there was only one carcinoma in the control group, I didn't -- I didn't put it down.

Q. Okay.

A. But that didn't have an effect on my evaluation.

Q. You also said in your deposition that there's no dose-response in the incidence of pancreatic-islet-cell tumors in the 1990 study. True?

A. No dose-response. Did I say no dose-response, or did I say there was no trend in -- in dose? I'd have to look at my report to see exactly what I said.

Q. Do you remember when I asked you this question --

Question:

-- and you gave the following answer?

Question: There was also no -- no dose-response that you could observe in these pancreatic-islet-cell adenomas that you saw in the treated groups. True?

Answer: No. It's not a true dose-response.

Do you remember that?

MS. WAGSTAFF: Counsel, can I get the cite for that?

MR. HOLLINGSWORTH: Sure 198. 198:3-19.

MS. WAGSTAFF: Which deposition?

MR. HOLLINGSWORTH: Sorry. It's the expert deposition. It's the one that was taken in September.

Q. Sir, let me ask you this. EPA did not consider the pancreatic-islet-cell tumors to be a true carcinogenic effect; did they?

A. That's -- in their report, that's what they state.

Q. And neither did EFSA; the European regulatory agency?

A. That's accurate.

Q. So you disagree with EFSA, you disagree with EPA, and you disagree with the original authors of this study, who were Stout and Ruecker. Ruecker's spelled R-u-e-c-k-e-r. Right?

A. I guess that that's accurate.

MR. HOLLINGSWORTH: Are we okay to keep going, or should we take a break?

JUDGE PETROU: How much more do you have?

MR. HOLLINGSWORTH: I have a little more.

JUDGE PETROU: Sounds like it's time to take a break.

MR. HOLLINGSWORTH: I'd say a half an hour.

THE COURT: Okay. Let's take a break. We'll be back at 2:30.

THE CLERK: Court is in recess.

(Recess taken from 2:17 p.m. until 2:33 p.m.)

THE COURT: All right. Ready to resume?

MR. HOLLINGSWORTH: Yes, Your Honor.

BY MR. HOLLINGSWORTH

Q. Dr. Jameson, do you have in front of you in the tabbed binder Exhibit 873?

A. Yes, sir.

Q. This is the revised glyphosate-issue paper, *Valuation of Carcinogenic Potential*, by the Office of Pesticide Programs at EPA, December 12th, 2017. And this is about glyphosate. Do you have that? Do you see that?

A. Yes, sir.

Q. If you looked at page 88, EPA is discussing the same Wood Study that you and I were discussing before the break. That's the Wood Study that was conducted in 2009 by a different registrant than Monsanto. Do you recall our discussion about Wood?

A. Yes.

Q. And our discussion about malignant lymphoma?

A. Yes.

Q. And the background incidence of malignant lymphoma?

A. Yes.

Q. Do you see the last two sentences -- sorry -- the last three sentences on this page, which is page 88 of 216 in Exhibit 873?

A. Okay.

Q. Where it states as follows: *Historical control data have been submitted from the same testing laboratory for 10 studies of similar duration?* Do you see that?

A. I'm sorry. Where does it say about --

Q. I'm looking at this paragraph titled "malignant Lymphoma."

A. Okay.

Q. The last three sentences of that paragraph start out with the --

THE COURT: I think you're referring to the last four sentences of the paragraph, which is why he's confused.

MR. HOLLINGSWORTH: Oh, excuse me. Sorry.

THE WITNESS: Okay. I see.

MR. HOLLINGSWORTH: Yeah. The last four sentences. Thank you, Your Honor.

Q. The first one says, *Historical control data have been submitted from the same testing laboratory for 10 studies of similar duration*. Do you see that?

A. Okay.

Q. And it goes on and says, *These data were generated within approximately five years of the Wood Study that we're -- we have been referring to*.

Do you see that sentence?

A. Okay. Mm-hm.

Q. And the historical control rate -- range EPA reports was

zero to 32 percent. Do you see that?

A. I see that.

Q. And the last sentence is, *All observed incidences of this tumor type were within the historical control range*. Do you see that?

A. Yes, I see that.

Q. And that last sentence refers to EPA's evaluation of the Wood 2009 study, in which you claim that lymphomas were caused by glyphosate. True?

A. Okay.

Q. So you disagree with EPA?

A. Well, in this paragraph I'm -- I mean, just a quick read through, but I didn't see. Are they referring to CD-1 Mouse here? Mice here? I don't see that they refer to it specifically for CD-1 mice.

MS. KLENICKI: It's at the top of the page.

BY MR. HOLLINGSWORTH

Q. *In a feeding study, CD-1 mice* --

Do you see that; the first sentence?

A. Well, yeah, they said, *In a feeding study, CD-1 mice received glyphosate*, in the first paragraph; but talking about the malignant lymphomas, they were just saying that the data were -- historical and control data were submitted from the same testing laboratory for 10 studies of similar duration, but it doesn't say that it was specific for the CD-1 Mouse, so --

Q. Well, the whole study is about CD-1 Mouse. And the whole section of this report is about CD-1 Mouse.

Are you suggesting that they're talking about a different strain of mice than CD-1 Mouse?

A. They didn't say specifically when they're referring to the historic controls for malignant lymphomas that it's for CD-1 mice.

Q. The historical control range of malignant lymphoma they refer to is a range of zero to 32 percent. Do you see that?

A. For malignant lymphoma in those 10 laboratories.

Q. Yeah.

A. But it doesn't say that it's for the CD-1 Mouse.

Q. No, it doesn't. Okay.

A. And all -- and what I'm saying is I went to the peer-reviewed literature; found the peer-reviewed article. And in that article specifically on spontaneous tumors in CD-1 mice, it says 4 percent is the historical rate. So that's where I got my figure from.

Q. Sir, do you remember when we were -- when we were deposing you about the Supplemental Report that you had, and I asked you some questions about the malathion section of the IARC Monograph that you worked on involving --

THE COURT: Why don't you ask him a question? And then if his question is inconsistent with his deposition testimony, you can ask him about his deposition testimony.

Okay?

MR. HOLLINGSWORTH: Sure.

Q. Dr. Jameson, I'd like to turn to the mouse -- the malathion section of the Monograph 112. Do you have that in mind?

A. Yes, sir.

Q. Do you remember when we --

JUDGE PETROU: I'm sorry. What's the exhibit number?

MS. KLENICKI: 1030.

THE WITNESS: It's in this book. Where in this book is it?

JUDGE PETROU: It's Volume 2, sort of halfway through Tab 1030.

THE WITNESS: 1030? Thank you.

BY MR. HOLLINGSWORTH

Q. Now, this is a discussion of the Agricultural Health Study.

A. Okay.

Q. And I believe you referred to this in your direct testimony here today. True?

A. I'd refer to sections of this. Are you referring to a particular page in this?

Q. No, I'm not yet.

A. Okay.

Q. This -- this is -- this is the malathion subsection of

Monograph 112. That included --

A. Yeah. That's what it looks like. Yes.

Q. And it included three or four other subsections on different chemicals, one of which was glyphosate. Right?

A. In Monograph 112 there were --

Q. Yeah.

A. -- there was a monograph written on glyphosate. That's correct.

Q. And the glyphosate section of that monograph refers the readers to the section on malathion for a discussion of the Agricultural Health Study?

A. That's correct. And I think, as I mentioned earlier today, the reason for doing that is the Monograph Working Group wanted to make sure there was a thorough and complete description of the AHS Study available to the reader; but it was so long, they didn't want to put it in every monograph.

And since there were three or four chemicals that we reviewed at that time that were also included in the AHS, they wrote the detailed description in the malathion monograph, and then in the other monographs, including the glyphosate monograph, and the epi section. When they discussed the AHS results, they referred to the malathion monograph for a detailed description of what the AHS Study was.

Q. And the -- the group -- the IARC group was -- what? -- 16 people?

A. I -- I don't remember the exact number, but it's usually around 16 or 17 individuals that are actual Working Group members, yes.

Q. And you all voted to approve this section on the Agricultural Health Study from the malathion portion of the monograph?

A. That's correct. Yes.

Q. And you intended that what you said about the Agricultural Health Study in the malathion section of the monograph should apply with equal weight to glyphosate. True?

A. In the description of the AHS Study, not -- but I mean, the results for glyphosate and the AHS Study are contained in the glyphosate monograph.

Q. So the general comments made about the AHS Study in this portion of the malathion monograph are -- you intended to be applicable equally to glyphosate?

A. That's correct.

Q. And the group said that it considered the AHS Study to be highly informative. Right?

A. Page, please?

Q. Page 21 of the malathion monograph?

JUDGE PETROU: Before you get to that question, Doctor, could you turn to page 9 of this Exhibit?

THE WITNESS: Okay.

JUDGE PETROU: And that's where it begins talking

about the Agricultural Health Study. Correct?

THE WITNESS: That's correct.

JUDGE PETROU: And it keeps going toward page 10, and then to page 11. So my question is: On page 11, about halfway through the column on the left, there's a paragraph in brackets. And also in the right-hand column, halfway through, there's another paragraph in brackets. It says in "Conclusion."

My question is simply: What do these bracketed paragraphs mean? Were these part of the Final Report, or --

THE WITNESS: These -- these are when a bracketed comment is included in an IARC Monograph, those are -- are meant to note that those are the conclusions or the observations of the Working Group, and not part of the publication or the paper that they were describing at the time.

So this conclusion that's on the right-hand column of page 11 that's in brackets, "Conclusion of the Working Group," noted that the exposure assessment methods used in the mouse studies were relatively crude. That is the Working Group saying that.

JUDGE PETROU: Commenting.

THE WITNESS: So that's the purpose of bracketed.

And if you look at the at all of the monographs, there are bracketed statements all through it. Those are to designate this is what the Working Group was saying, and not what was

contained in the actual paper.

JUDGE PETROU: That's helpful. Thank you.

THE WITNESS: Okay.

BY MR. HOLLINGSWORTH

Q. If you go to -- if you stay on page 9, I'm -- I don't have time to go through this whole thing, but I want to ask you about a couple of things the Working Group said that I'm looking at the first full paragraph in the right column. Quote, *Great efforts were made in the Agricultural Health Study to assess exposure among agricultural pesticide applicators and their spouses.* Do you see that sentence?

A. Yes, sir.

Q. Did I read that correctly?

A. Yes, sir.

Q. And in the next sentence says, *These questionnaires and algorithms have been extensively described and have undergone several tests for reliability and accuracy that have provided considerable insight into the quality of this exposure assessment.* Do you see that?

A. Yes, sir.

Q. And if you look at page 11, there is a section that says, at the bottom on the left-hand column, in which it's stated, *Almost all of the studies* --

Do you see that sentence?

A. Yes.

Q. *Almost all of the studies relied on self-reported data, which, as discussed above, is reasonably reliable and valid when applicators are reporting their own use*. Do you see that?

A. Yes.

Q. And then it goes on to say, *But may not be suitable for spouses or other farmworkers, particularly those exposed by re-entry*. Do you see that?

A. Yes.

Q. And the next sentence says, *Proxy respondents are unlikely to know the details of use of specific pesticides by next of kin*. Do you see that?

A. Yes.

Q. Did you vote to approve that?

A. To -- to -- yes. I voted for the wording of this section of the monograph. Yes.

Q. Do you see the sentence that -- it's -- that -- where IARC says, *Apart from the AHS*, which is the first full paragraph in the right-hand column on page 11?

A. Yes.

Q. *Apart from the AHS, few of the studies included expert review of the data, or performed validity or reliability studies*. Do you see that?

A. Okay.

Q. That paragraph is suggesting that the other studies -- the case-control studies, unlike the AHS -- did not include,

necessarily, expert review of the data, nor did they perform validity or reliability studies, such as AHS had done. True?

A. I don't know that that's what it's referring to, or not.

Q. Okay.

A. It doesn't specifically say the case-control studies. It just says few of the studies included expert review.

Q. Okay.

A. And to be honest with you, I think it's referring to some of the studies in -- that have been published as a result of the AHS Study.

And I would also point out that the bracketed comments that are included here, which are the exact -- are actually the comments from the Working Group. I read it previously, in response to Your Honor's question.

In conclusion -- and this is the statement of the Working Group. *In conclusion, the Working Group noted that the exposure assessment methods used in most studies were relatively crude*.

So, I mean -- and as I recall, in the discussions we had about the AHS Study at IARC, there was a lot of concern over exposure assessment and misclassification, and the weakness that that imparted to the study. And there were a lot of people that were concerned about that adequacy of the study, even at this point.

Q. Well, that sentence you just read doesn't refer to the

AHS; does it?

A. Well, it's in the AHS section. I mean, it's in the section discussing the AHS Study.

Q. It refers to "most studies." It doesn't say it -- that the AHS specifically was crude; does it?

A. No. I think it's referring to the AHS Study there.

Q. Okay. If you'll turn to page 15, in the right-hand column at the top of the page, I think it's the second sentence.

THE COURT: Could I ask a follow-up on your last question before you move on?

I'm just looking at page 9, and 10 and 11 --

THE WITNESS: Mm-hm.

THE COURT: -- of the monograph; the section on Malathion.

On page 9 begins a section in which you discuss the Agricultural Health Study. Page 11 begins a section in which you discuss other epidemiological studies.

THE WITNESS: Correct.

THE COURT: So I assume that the --

THE WITNESS: Oh, oh, oh. I'm so sorry. Yes.

THE COURT: -- I assume that the "In conclusion" sentence is about the other epidemiological study.

THE WITNESS: I stand corrected. I'm so sorry. Yes, I misread that. I'm sorry. Absolutely right. Thank you for catching that. I didn't mean to mislead.

BY MR. HOLLINGSWORTH

Q. If you'll go back to page 15, sir, I was referring to the right-hand column at the top of the page. I was interested in this sentence, which is, *The AHS being a cohort study* --

Do you see that?

A. Yes.

Q. -- *avoids recall bias*.

Do you see that?

A. Yes.

Q. Did I read that correctly?

A. Yes.

Q. *Since exposure was obtained before the onset of cancer*.

Do you see that?

A. Yes.

Q. And it goes on to say, *Misclassification of pesticide exposure in the AHS cannot, however, be excluded, because exposure was retrospective and self-reported (as is as is typical for most case-control studies*).

Do you see that?

A. Yes.

Q. *But the error would be nondifferential, and in most scenarios would not inflate risk estimates*.

Do you see that?

A. Yes.

Q. Did you vote to approve that?

A. Yes. I think the beginning sentence that you read, *The AHS, being the cohort study, avoids recall bias.*

Since exposure is obtained before the onset of cancer, it precludes recall bias of -- of people saying that -- people that have a disease when they're first recruited recalling that they were exposed to a pesticide, as opposed to, in a cohort study, you're recruiting people who have no disease; and so therefore, their recall wouldn't be biased by the fact that they already have the disease.

Q. Now, if you look at page 21, sir, I'm not going to ask many more questions about this, but I want to ask about page 21, please, the bottom of the left-hand column.

A. Okay.

Q. And if you look at the sentence that starts, *For individuals in the AHS who did not complete a Phase 2 re-interview*.

A. I'm sorry. On the left-hand column?

Q. Did I say "right"? Excuse me.

A. No. I -- I misheard you. I'm sorry. So we're -- talking about the left-hand column?

Q. Yeah. And sentence that starts, "For individuals." Do you see that?

A. I'm trying to find it. Where is it in the --

Q. It's -- it's about nine lines up from the bottom of the left-hand column on page 21, sir.

A. Oh, okay. "For individuals." Yes. I'm sorry. Yes.

Q. Okay. I'm going to read that. *For individuals in the AHS who did not complete a Phase 2 re-interview five years after enrollment*. Do you see that?

A. Yes.

Q. And then it goes on and says, *An imputation method was used*. Do you have that?

A. Yes.

Q. *That permitted inclusion of all participants in Phase 2 analyses*. Did I read that correctly?

A. Yes.

Q. And then it says, *The imputation method was based on their baseline data, even if portions of subsequent data were missing*. Did I read that correctly?

A. Yes.

Q. *Which led to the observation that neither missing data nor imputation had major impacts on the main results for many of the pesticides*. Did I read that correctly?

A. Yes.

Q. Did you vote on that?

A. Including parathion, diazinon, and malathion; but it doesn't say anything about glyphosate.

Q. Did you read the Heltshe Study?

A. Did I read the Heltshe Study?

Q. It was a reference to your Supplemental Report, sir.

A. Oh, to the -- yeah -- imputation? Describing imputation methods? Yes.

Q. Yes. Heltshe includes glyphosate in her list of pesticides that were covered by this methodology; doesn't she?

A. Yes.

Q. There's a table that includes glyphosate in the Heltshe Report that I asked you about in your deposition. True?

A. True, but as I stated in my deposition, the imputation for glyphosate, I feel, is flawed, because they're basing the imputation on data from the original exposure assessments from the questionnaire. And the -- that data was -- was asking for recall of what they were exposed to 10, 20 years before. And so there was a lot of recall bias in that. And so the initial data was flawed.

So if you're going to use flawed data and the imputation method, then you're going to get even more flawed data. So that's one of the main criticisms, I understand, of the AHS Study now, because -- because of the method of exposure assessment at the very beginning.

And can I make an observation of my own?

THE COURT: Go ahead.

THE WITNESS: That as far as the AHS Study, and the most recent Andreotti Paper that came out in 2018, and the question about, *Has there been publications criticizing that study or criticizing the results?* -- well, the paper just came

out in January of 2018. It's just a month or so ago. And it takes a while for peer-reviewed publications to come through the mill.

So the fact that there aren't any doesn't mean that there -- there aren't opinions to that effect, and that there won't be papers coming out in the peer-reviewed literature probably in the very near future. I'm not aware of any that are being done, but that's just my opinion.

BY MR. HOLLINGSWORTH

Q. At the time that the -- this IARC Monograph was done in March of 2015, did the Working Group know that the AHS had used imputation methodology for glyphosate?

A. At the time of the --

Q. At the time that this IARC Monograph was done, did the -- did the Working Group know that -- that AHS had used the imputation method for glyphosate, in particular?

A. Well, I mean, it's in here. Yes. It's in the monograph.

Q. Now, Dr. Jameson, you don't consider yourself to be an epidemiologist; do you?

A. I am not a formally trained epidemiologist, but I have over 30 years of experience in doing assessments -- cancer assessments -- where I have evaluated and reviewed countless epidemiology studies, and given opinions of what the epidemiology data is saying.

In my work at the NIHS for Report on Carcinogens, that was

part of my everyday work: To evaluate epidemiology data, along with the toxicology and mechanistic data.

In my participation in IARC, I'm asked to review the epidemiology data, and vote on the relevancy and the adequacy of the data, and what it means.

So, while I'm not formally trained in epidemiology, I feel like I am an expert in epidemiology, because of all of my past experience and work in that area.

Q. Do you remember when I asked you the following question, and you gave the following answer at your deposition in September? Or more --

THE COURT: Hold on a second.

What is page number and the line number, so that opposing counsel can look at it, as you are proposing to read it? And, of course, opposing counsel can also propose that you read additional lines, if it's necessary for context.

MR. HOLLINGSWORTH: Sure. At 44, lines 1-3. This is the supplemental deposition.

JUDGE PETROU: So what exhibit number is it?

MS. KLENICKI: 738.

MR. HOLLINGSWORTH: This is Exhibit 738. It's a supplemental expert deposition. It's at page 44, lines 1-3.

And my question is: Do you remember giving the following answer to this question?

Are you an epidemiologist?

Answer: I am -- I consider myself a toxicologist. I do not consider myself an epidemiologist.

MS. WAGSTAFF: And I would suggest you read pages starting at 113, please, as well.

THE COURT: Page 113?

MS. WAGSTAFF: Yes.

THE WITNESS: 113?

MS. WAGSTAFF: Right, but I'm saying to put it in context.

THE WITNESS: Okay.

MR. HOLLINGSWORTH: Well, Your Honor, I have a question pending.

THE COURT: Read it.

THE WITNESS: Where is it --

THE COURT: Mr. Hollingsworth, go ahead and read --

MR. HOLLINGSWORTH: My question: Do you recall giving the following --

THE COURT: Hold on a second. Page 113. I assume starting at line 13?

MR. HOLLINGSWORTH: It's page 44. Page 44.

THE COURT: Mr. Wagstaff, what were you --

MS. WAGSTAFF: 113, page or line 8.

THE COURT: Okay. You go ahead and read that.

MR. HOLLINGSWORTH: This is at page 44, Your Honor.

THE COURT: You're trying to impeach him with his

prior deposition testimony.

MR. HOLLINGSWORTH: Right.

THE COURT: And opposing counsel wants to have other deposition testimony read, to put in context your impeachment. I agree that you should have to read that, so can you go ahead and read that?

MR. HOLLINGSWORTH: Well, I haven't asked -- I haven't gotten an answer to my question yet.

THE COURT: Read the whole thing, and then ask him the question.

MR. HOLLINGSWORTH: Okay. My question is, sir --

THE COURT: No. Read page 113, starting at line 8.

MR. HOLLINGSWORTH: Okay. That is --

(Pause in proceedings.)

MS. KLENICKI: (Indicating.)

THE COURT: Why don't you read all the way through page -- about the middle of page 115.

MR. HOLLINGSWORTH: This is a question by Ms. Wagstaff.

THE COURT: Yep.

MR. HOLLINGSWORTH: Okay. (Reading.)

"MS. WAGSTAFF: Do you recall when Mr. Hollingsworth asked you if you were an epidemiologist? And I believe you answered that you were a toxicologist. Is that correct?

"ANSWER: Correct.

"QUESTION: Okay. Can you explain how being a toxicologist relates to you being an epidemiologist, if at all?

"ANSWER: Well, I think I stated earlier that in doing your -- the work that I did and continue to do in cancer-hazard identification, the requirement is that you became an expert in a wide variety of different areas, one of which is toxicology, one of which is epidemiology, one of which is genotoxicity and mechanism of action. One is exposure.

"And based on the 40 years that I have been doing this work, I have gotten what you considered on-the-job training in all of these areas. My degree is in chemistry, but I have been -- I have done toxicology since I graduated from the University of Maryland. And on-the-job training is as good if not better than a college degree is, just -- in just about all areas.

"I have worked closely with the epidemiologists, helping them in their studies. I have been asked to review epidemiology studies and papers as part of my work with IARC, and I give my opinion as to what the epidemiology data is saying, and if it meets their criteria for evaluating epidemiology data, as far as

being a sufficient evidence or limited evidence in for causation of cancer.

"For the Report on Carcinogens, I also have worked with epidemiologists who help us evaluate the nominations for the Report on Carcinogens. As part of my responsibility, I wrote criteria for evaluating epidemiology data for the Report on Carcinogens. And those criteria are still used today in evaluating the data; the epidemiology data for the Report on Carcinogens.

"So while I profess to be a toxicologist, you can't say, *Well, I am a toxicologist, and an epidemiologist, and a mechanistic expert, and a genotoxicologist, and what-have-you*. I take on the moniker of 'toxicologist,' but you have to understand that in doing hazard identification, you have to become an expert in all of those areas in order to evaluate the data and give an opinion.

"And so, while I don't have the degree in epidemiology, I have the experience and training to consider myself an expert in epidemiology to evaluate this data."

THE COURT: Okay. Can you go ahead and ask him your question now?

BY MR. HOLLINGSWORTH

Q. My question is: Do you recall when I asked you the following question, and you gave the following question?

"Are you an epidemiologist?

"ANSWER: I am. I consider myself a toxicologist. I do not consider myself an epidemiologist."

A. That is what I said at that time; but as you read into the record, I do consider myself an expert in epidemiology because of my past experience and -- and working that I've done over the past 40-plus years.

Q. Are you board certified in epidemiology?

A. No, sir, I am not board certified in epidemiology.

Q. Are you board certified in toxicology?

A. No, sir, I am not.

Q. Sir, you did the Report on Carcinogens to -- that was made to Congress for about 11 years, you said?

A. Well, I was involved with it for about 18 years. I was the director for about 9 or 10 years, yes.

Q. During those 18 years, you never reported to Congress that glyphosate was a carcinogen, or that it could cause non-Hodgkin's lymphoma in humans; did you?

A. I never reported glyphosate because we never reviewed it. No.

MR. HOLLINGSWORTH: No further questions, Your Honor.

Thank you.

THE COURT: Thank you.

Do you have any redirect?

MS. WAGSTAFF: I do. Just a few moments.

REDIRECT EXAMINATION

BY MS. WAGSTAFF

Q. Okay. And the only exhibit I'm going to use is 149, if y'all want to get that handy, which is the briefing note for IARC Scientific and Governing Council members from January of '18.

So tell me when you're ready, Dr. Jameson. Do you have that in front of you?

A. Which is that, now?

Q. I don't know if yours is marked "149," but it's called, "The Briefing Note for IARC Scientific and Governing Council Members Prepared by the IARC Director." Do you need a copy?

A. I need a copy. I'm sorry.

THE COURT: Do you want to grab a copy for Judge Petrou, as well?

JUDGE PETROU: Sure.

(Whereupon a document was tendered to the Court.)

THE COURT: Thank you.

MS. WAGSTAFF: Mm-hm. All right. This one has little highlights on it, but --

THE WITNESS: Okay. That's fine.

BY MS. WAGSTAFF

Q. All right. The first question I would like to ask you, just -- just to make it clear for the Judges, is: You did review both the negative and positive data for glyphosate being a carcinogen. Correct?

A. That's correct.

Q. Okay. And if you could, pull up Exhibit 149. The only thing I really -- I'm afraid maybe I did a bad job of this on my direct, but the hazard assessment -- we're getting hung up on what it means, and the definition of what a hazard assessment is versus a risk assessment. And I think we can simplify this a lot. We can just sort of agree to disagree on what the definition means, by looking at what you guys actually did. Right?

A. Yes.

Q. And so whether we agree with Monsanto on what a hazard assessment means, can we agree that you considered in your analysis here the human data?

A. Yes.

Q. Okay. And you -- you considered all of the epidemiology. And you considered that in your analysis: The doses that humans receive. Correct?

A. Yes.

Q. Okay. And if you can, turn to page -- and I know you can't speak for all 17 or 18 members of IARC 112. Right?

A. Right.

Q. You can only speak for Dr. Jameson; but luckily the IARC director answered this question for us.

A. Right.

Q. So it came out in January of 2018, on Exhibit 149. If you turn to page 8, luckily, we know if IARC 112 considered real-world exposures. In fact, it's even in quotes. So can you look at that section, and read into the record those bullet points?

A. Okay. The document reads, *Monograph evaluation takes into account real-world exposure by evaluation of epidemiological studies. A charge leveled at the monographs is that evaluations are divorced from the real world; i.e., are named without taking into account realistic human exposures. However, epidemiological studies are a central part of monograph evaluations, and, by definition, deal with people exposed in daily life, including at work.*

The study frequently considers the gradient of risk observed with different levels of exposure. One part of the monograph evaluation is specifically dedicated to describing the circumstances under which human exposure occurs, and at what levels.

In addition, when considering scientific evidence of carcinogenicity, including by logical mechanisms, the Working Groups placed special emphasis on whether the observations are

relevant to humans.

In light of occurring 'real-world' human exposures, Working Groups synthesize evidence in humans, animals, and other model systems in reaching overall conclusions.

Q. All right. So we don't need to get any more on whether IARC considers real-world exposures. Right?

A. Correct.

Q. And this comes from the director of IARC, which is a pretty high-up person, I would guess, at IARC?

A. Within the World Health Organization, yes.

Q. And that summarizes sort of the analysis you did, as well, with respect to real-world analysis?

A. I absolutely considered real-world exposures in reviewing the epidemiology data.

Q. So it's okay if we have different definitions of what "hazard assessment" means. We can all agree that both IARC and Dr. Jameson considered real-world exposures. Right?

A. Absolutely.

MS. WAGSTAFF: All right. No further questions.

THE COURT: Anything further?

MR. HOLLINGSWORTH: No, sir.

THE WITNESS: Thank you for the honor, Your Honor. Thank you.

MS. GREENWALD: Plaintiffs call Dr. Christopher Portier.

THE CLERK: Please raise your right hand.

CHRISTOPHER PORTIER,

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

THE WITNESS: I do.

THE CLERK: Thank you. Please be seated. And for the record, please state your first and last name, and spell both of them.

THE WITNESS: Christopher Portier. C-h-r-i-s-t-o-p-h-e-r. P-o-r-t-i-e-r.

THE CLERK: Thank you.

DIRECT EXAMINATION

BY MS. GREENWALD

Q. Good afternoon, Dr. Portier. You have the slide also in front of you in the book, but you have a screen there, and we can go through it that way.

Your Honors, you have notebooks. Great. So the slide deck is Exhibit 1, Tab 1.

Dr. Portier, can you please describe your qualifications for the opinions you're providing in this case, focusing in particular on your work-related experience?

A. Certainly. I have a Ph.D. in biostatistics, with a minor in epidemiology. My thesis topic was the optimal design of --

(Reporter requests clarification.)

THE WITNESS: The optimal design of the two-year

rodent carcinogenicity study to assess cancer hazard of chemicals.

I spent over 30 years at the NIH; the National Institute of Environmental Health Sciences. During that entire time I was a Principal Investigator there, with my own laboratory, initially starting out in statistics, and ending up in molecular biology and toxicology, with my own wet labs.

For part of that time I was the -- I ran the U.S. National Toxicology Program, which is the world's largest tox. program.

I was director of CDC's National Center for Environmental Health, and the U.S. Government's Agency for Toxic Substances and Disease Registry. Both of these do risk evaluations.

ATS New York advises communities about what to do about toxic dumpsites, and works with EPA so the sites will be cleaned up.

I've done a lot of national and international science advisory boards. I was Chair of the President's National Science and Technology Consult Toxics and Risk Subcommittee. I've sat on EPA Science Advisory Panels for pesticides for five years. And I was the Chair of the IARC Advisory Group that rewrote the preamble in 2006.

And I will comment on, if you don't mind, a discussion you had regarding the preamble -- I believe it was yesterday -- and the use of the term "quantitative," and under "probably human carcinogen," I think the interpretation that was a little bit

wrong.

What IARC is saying that, when they say it's a probable human carcinogen, they don't want the public to think that means if you're exposed to glyphosate, you'll probably get cancer. That is not what it means.

It means that the literature is so strong, that we think it's probable that humans will get cancer at some level of exposures to glyphosate.

BY MS. GREENWALD

Q. Dr. Portier, what is biostatistics?

A. So biostatistics is the discipline of statistics, but applied to assays and experiments in the biological realm. Typically, biostatisticians work in epidemiology or in animal laboratory data.

Q. And why is biostatistics important to the opinions you're providing in this case?

A. Well, you have to -- you have to understand statistical significance of each individual experiment in order to move forward, but the -- the important thing about the "bio" in "biostatistics" is that you really want to know your experimental field. You spend time, you spend effort learning how these experiments are done, what are their limitations, et cetera, so that you get the right evaluation to answer the question that is actually being asked.

Q. Okay. You just mentioned "experimental field." Do you

have specialties within biostatistics?
A. Do I have a specialty?
Q. No. Are there specialties within biostatistics; and if so, do you have a subspecialty?
A. Yes. There are specialties in biostatistics. I guess my subspecialty would be environmental laboratory studies.
Q. Of animal bioassays?
A. Of animals, and cells, and molecular biology studies, and things along these lines, although I have some valid background in climate change, and other areas.
Q. Are you a fellow of American Statistical Association?
A. Yes, I am.
Q. And when did you become a fellow?
A. 1992, I believe.
Q. What does it mean to be a fellow?
A. It American Statistical Association elevates -- they vote, nominate, bring in one-third -- at the max, one-third of 1 percent of the statisticians who belong to the ASA get awarded to be fellows with the American Statistical Association. They do that percent every year, so it's probably about 3 to 4 percent, total. It's an honor.
Q. Have you read the Expert Report and deposition transcript of Dr. Corcoran?
A. Yes, I have.
Q. And is he one of the experts that Monsanto has proffered

in this case?

A. Yes, it is. He is, I believe.

Q. Based on your review of his report, his CV, and deposition testimony, do you have -- does he have, in your opinion, relevant experience in evaluating bio -- animal bioassays?

A. No.

Q. And why is that?

A. Well, because to evaluate the animal bioassay data to decide whether you're seeing a positive result or a negative result, you have to be able to not only run a statistical test on it, but you really have to understand the biology. A lot of other things go into deciding whether this is a positive finding or not, and I don't think he has experience in that area.

Q. Dr. Portier, have you ever been an expert witness in a lawsuit before this case?

A. No, I have not.

Q. And other than "Science Day," when you presented general science of toxicology to Judge Chhabria in this case, actually, is this the first time you've ever testified -- is this the next time you've ever testified in a courtroom?

A. Yes, it is.

Q. Okay. Slide 3, please.

A. And it makes me nervous.

Q. No one else. Just you.

What are the fields of expertise that underlie your opinions in this case?

A. I reviewed all of the epidemiology literature, all of the toxicology literature, all of the mechanisms-of-cancer literature, as well as my extensive experience in the field.

Q. Okay. So before we get into the details of your methodology and your conclusions, please tell the Court what opinions you have reached after reviewing the epidemiology, toxicology, and mechanisms of cancer.

A. It's right here on the screen. To a reasonable degree of scientific certainty, given the human, animal, and mechanistic evidence, glyphosate probably causes NHL, and the probability that glyphosate causes NHL is high.

Q. Okay. Now I'd like to get into the methodology that underlies that opinion. Slide 4, please.

What epidemiological review did you undertake? I mean, what conclusions did you reach based on that review?

A. So I reviewed all of the literature. There were six case-control studies showing similar modest increases of associations between glyphosate and NHL.

There was one cohort study -- the Agricultural Health Study -- with no apparent effect.

I will point out that there were dozens of ancillary studies. Some case-controls studies had special studies looking at their exposure metrics, and how well they were

working. The Agriculture Health Study has an extensive collection of ancillary studies, as well.

What I concluded is that causality is possible, but there's still the possibility of bias, chance, and confounding in these data. I believe it's not likely that these things would explain the entire association. So my conclusion is that the data supports an association of glyphosate with NHL.

Q. So when you say these things would not change your decision, you mean bias, chance, and confounding. Is that right? I just want to make sure that I understand.

A. Correct. I don't believe they're strong enough. I don't believe they're strong enough -- bias, chance, and confounding -- to completely explain the entire association.

Q. Understood. All right. Slide 5, please.

Can you please explain the phases of a two-year animal carcinogenicity study? I'll get that word wrong every time.

A. Can he we just say "cancer study"?

Q. I want to do "cancer study."

A. So a two-year cancer study is intended to cover the major portion of an animal's lifetime. The animals start on this study at six weeks. So six-week-old mouse, a six-week-old rat -- they have reached puberty.

These rodents are randomly placed into different dose groups, so that you avoid any chance of bias by putting all of the animals with one weight in one group, or something along

those lines. So you're very careful to make it as random as you possibly can. Everything is controlled in these experiments. So the animals get the same diet. The animals get light and dark cycles that are carefully controlled, et cetera.

The idea is that the only difference that would -- that would explain the cancers, if you see them increase in the animals in the dose groups, is the dose. So everything else is controlled.

So, unlike epidemiology, where you have lots of confounders you have to concern yourself with, there are no confounders in an animal cancer study. It's a completely controlled study.

Typically dosing goes for two years.

There's generally a control group -- we talked about that earlier -- and three different dose groups.

It's generally rats and mice; and males and females.

And it's 50 to 75 rodents in each sex-species group in these studies that we're looking at here.

Now, I'll say "sex-species group" quite often. That's jargon for toxicologists. It's simply the way you break it up in little, little boxes. There are two sexes, probably two species, and four dose groups. And so when I talk about that, it's looking at each of those.

At the end of the study -- again, usually two years -- any

rodents that are still alive get sacrificed. Any rodents that died earlier were, of course, kept. Every one of these animals gets a full pathology review on them, which means they typically remove up to 40 organs from the animals. They take slices through those organs; create histopathology slides. You probably saw them in high school. And those are then sent to a pathologist who reads them.

In the National Toxicology Program -- I can easily describe that -- that pathologist -- after they read it, another pathologist verifies that the first pathologist got it right.

Then any disagreements between those two pathologists -- there is a Pathology Working Group that comes in of independent pathologists who look at the disagreements, to make sure everybody gets to the same agreement, in terms of which tumors are which tumors.

After that is when the analysis starts. So once you've decided exactly which tumors are there, then come the statisticians and the toxicologists, looking at the results, and finding after about a year after the end of the study, a year and a half, results are reported.

Q. Okay. Slide 6, please.

Can you please summarize the guidelines that apply to the analysis of animal cancer data among the various agencies that review such data?

A. Yes. There's guidelines all over the place. Now, there are guidelines on design of the studies. There's guidelines on how to analyze the studies. And there are guidelines on how to interpret these studies.

EPA has Guidelines for the interpretation and analysis of the studies. The NTP has guidelines for all three aspects of it. IARC has guidelines for the evaluation. The European Chemicals Agency doesn't have the independent guidelines for design and analysis -- in fact, they use the guidelines by the OECD; the Organization for Economic Cooperation and Development -- but they do have guidelines for review.

We talked about the European Food Safety Authority earlier. The European Food Safety Authority uses EChA's guidelines -- the European Chemicals Agency -- to do their evaluations. And that's because legally, EChA owns the guidance. And EFSA -- they let EFSA do it whenever they feel like it.

OECD has guidelines for all three, and the National Academy of Sciences has spoken about all three. I will make one other comment that somebody had discussed earlier, again, if you don't mind. There was a statement that said EFSA did a risk assessment for glyphosate. That is incorrect. By European law, if a compound is a pesticide and it's carcinogenic, it is banned. You don't do a risk assessment.

There is a little bit in the law that says if the human

exposure is absolutely minuscule, then maybe we'll let you put it in there; but if it's a pesticide -- so they don't do a risk assessment. All they have to do is identify it as a carcinogen, and then it would be banned.

The USEPA didn't do a risk assessment, either. The USEPA decided it was not carcinogenic. And once they do that decision, they don't go and calculate risk. So they only do a hazard assessment. So all of these are hazard assessments.

Q. So, Dr. Portier, are most of the guidelines of these various agencies that you have on Slide Number 6 -- do they have similar guidelines on how to evaluate, analyze, interpret data of animals; cancer data, studies?

(Reporter requests clarification.)

BY MS. GREENWALD

Q. Do they all have similar guidelines for how to evaluate and analyze animal data?

A. Yes, they do. I -- I would give you one example. All of them say that if you see a positive Armitage linear trend test or a positive Fisher Exact Test in an animal cancer study, these should be considered positive findings in the statistical means; not the biological means.

Q. Did you follow these guidelines in your analysis of this case?

A. Yes, I did.

Q. Okay. Slide 7, please.

Can you please explain the statistical methodology used in toxicology to evaluate rodent cancer studies, and how to interpret those evaluations? I'm staying with "cancer."

A. Yes. Originally, in the -- in the past, most people did a Fisher Exact Test. Fisher Exact Test compares tumor response in one dose group to the control group. So in a typical study you'd have three Fisher Exact Test p-values.

But the correct way to do it is the Cochran-Armitage Trend Test, which is the way most people do it. All of the regulatory reviews have Cochran-Armitage tests in them. The benefit of the Cochran-Armitage Test is that it simultaneously analyzes all of the data, and looks for a trend in the data with increasing dose. Now, these studies are designed to have increase in dose; the idea being that as the dose increases, the probability of getting cancer is increasing. So therefore you want to analyze it that way, which is what the Cochran-Armitage Trend Test does.

If you have all of the information -- so if I'm the National Toxicology Program, and I know what happened to every one of my rats and mice in my study, then I'm not going to use either of these two. I would use a survival-adjusted test. That's because of some of the animals die early, and you want to account for that difference in survival between different groups that might make a difference on the p-value.

The NTP uses the Poly-3 Test, which is a test I invented.

Q. You didn't use the Poly-3 Test here; did you?

A. No. That's because I don't have the individual data for the individual animals.

Q. Had you -- sorry. Had you --

A. And I don't know when an animal died, and whether it had a tumor or not, except for three of the studies that -- I decided that if I'm going to compare studies and look at cancer across all the of the studies, I wanted to use the same methodology, so I stuck to the Cochran-Armitage Trend Test.

Q. Can we go to the next slide, please: Slide 8?

Can you please describe the Cochran-Armitage Trend Test using this diagram?

A. Yeah. This diagram is intended to show you what would typically see an animal bioassay. This is the one you were talking about just now; the Wood Study. Malignant lymphomas in male CD-1 mice.

The big black dots -- those are the response signal to each of the doses. The dose is the x-axis. The proportional tumor is the y-axis. The confidence bounds around the dots are just typical 95 percent confidence amounts. Fisher's Exact Test for each one of these. You can see I put the p-value for that.

And then the Cochran-Armitage Test, which is making this trend right through the middle, the p-values there -- what the Cochran-Armitage Test really does is calculates the slope of

that line, and looks to see if the slope of that line is different from zero.

(Reporter requests clarification.)

THE WITNESS: Different from zero. I'm sorry.

If it's significantly different from zero, that's what the p-value is.

BY MS. GREENWALD

Q. So, Dr. Portier, I'm going to ask you if we can just slow it down a little bit. The court reporter has been going all day. And you know this material very well, but it's hard to take it all down. So if we can just slow it down a little bit, I know she would appreciate it.

A. I'll try.

Q. I know. It's all we can ask.

If you can go to the next slide, please.

Can you please explain p-values, which have been a lot of -- subject to a lot of discussion and writing in this case, why they are methodologically necessary for scientists, and what p-values inform us about the hazards of glyphosate exposure?

A. Certainly. I'd be happy to. So statistical tests are built around what's called a "null hypothesis" and an "alternative hypothesis." In animal cancer studies, the null hypothesis is that the chemical does not increase the cancer risk when given to the animals. The alternative hypothesis is

they can increase the tumor response, as a function of dose.

Now, statistical tests aren't as simple as we sometimes want them to be. Statistical tests depend upon a complex set of assumptions embodied in a statistical model. And so you have to realize when interpreting this statistical test, you're doing it under the assumption that that model is correct. And sometimes that model's not correct, or you're really not certain.

Anyway, the p-value is the probability of observing the data that you saw under the null hypothesis that there is no effect. So you're calculating the probability that these data are so different than what the model would say under the null effect, that I think it's -- it's -- it can't possibly be from that null-effect model.

Traditionally, p-values less than 0.05 or 0.01 are used to reject a null hypothesis in favor of the alternative hypothesis. So that's how p-values are used in this confection.

Q. Dr. Portier, you have a reference on your slides here to Greenland. Is that an article about statistical tests?

A. Yes. The Greenland article talks about the complexity of statistical tests, as well as how to use p-values. We had the discussion yesterday about -- and the day before -- p-values in the epidemiology literature, and whether it's a bold line or not. Greenwald does a good job of discussing that.

MS. GREENWALD: Your Honor, that's Tab 2 in your book.

Okay. If you can, keep it slow.

THE WITNESS: I'm really trying.

BY MS. GREENWALD

Q. Okay. If you can go to the next slide, please.

How do scientists determine which tumors to analyze in an animal cancer study, and why?

A. That's something that's always debated at least a little bit. So you do these 40 organs. You take the slides. You look at all primary tumors -- so a primary tumor's something like a liver carcinoma or a liver adenoma -- but you don't look at every single possible, because there are limitations to what statistics can find for you.

And so usually the rule of thumb is if you have three tumors across all of the dose groups -- so maybe one control, one low-dose, one mid-dose. That would be three tumors -- then you include that as a primary tumor that you evaluated for the -- from this study. That's because less than three tumors can't be found statistically significant.

You don't do metastatic tumors. So when a tumor forms in the body, as it gets older and older, it begins to bleed off cells. And these cells get picked up in the blood; transported to other parts of the body. And those are metastatic tumors.

Common metastatic tumors occur in the lung from -- from a

cancer in the liver. These metastatic tumors are interesting, but they're not related to the causing of the cancer. They're consequence of the cancer. So you might analyze them, but they're not included in the discussion of causality in the animals.

If there are rare tumors that you think are increased, where you have less than three tumors, then you would use historical controls. I will point out that rare tumors are defined to be less than 1 percent historically in the control animals.

You would combine benign and malignant tumors when there are at least three total tumors. So we talked about adenomas and carcinomas before. That's a combination you would do. So you do the primaries, as well as those combinations.

And finally you would combine systemic tumors that occurred in multiple organs when there are at least three total tumors. The example here is the malignant lymphomas. They occur in the spleen. They occur in the uterus. They occur in various parts of the body. And you collect all of that information, and do it as one lymphoma or not.

JUDGE PETROU: So I have a question. The second bullet point was that if it was a rare tumor, less than 1 percent historically, then you look at the historic data. Correct?

THE WITNESS: Correct.

JUDGE PETROU: So presumably the converse is also true: If it's not a rare tumor, you don't look at the historic data -- or not?

THE WITNESS: You could -- I like looking at the historic data all of the time, just to see what informs me about the study that I'm looking at; but Rule One in cancer bioassays is that the current control is the best control for doing your analysis. And the reason for that is quite simple. Even though you try to control everything in the laboratory, you can't do it from one study to the next; but the controls that are fed and housed at the same time as the treated animals are most like those treated animals. So you use that.

But in a case of a rare tumor, sometimes the historical controls that -- you only see two. Let's take the kidney tumors we're talking about here. You see three at the highest dose. So you can do a p-value on that, but its p-value's .06, so it's not statistically significant at the 5 percent level; but in my historical controls for these kidney tumors, it's very low. The highest we ever saw was 2 in any dose in any control animal. And so that makes this a biologically important finding.

And you can actually do an analysis of those historical controls, and see if that's statistically significant.

BY MS. GREENWALD

Q. Dr. Portier, what's the basis for requiring three or more

tumors?

A. You require three or more tumors because you can't find a statistically significant finding without three of them. And the question that you would ask that was driven by that point is: Are these tumors arising due to random chance? And I will get to that in a minute.

Q. Okay. Do you know whether Dr. Corcoran followed the three-or-more-tumor guidance in his analysis?

A. He mentioned it.

Q. Did he follow it in his analysis?

A. Oh, he mentioned it. He talked about it, but when he came to his false discovery rate at the table toward the end of his report, he used all of the -- all of the tumors. So he analyzed somewhere around -- I guess it's about 600 or 650 sites that had less than three tumors; one or two tumors.

Q. Thank you. And did Dr. Corcoran count both primary and secondary tumors in his analysis?

A. Yes. He did metastatic tumors in the analysis, as well.

Q. In your opinion, is that methodologically flawed?

A. It doesn't speak to the question of causing cancer in the animals, if you're talking about metastatic tumors. It doesn't speak to the question at hand.

Q. So for the issue at hand in this case, would that be methodologically flawed to count both primary and secondary tumors?

A. Yes.

Q. Next, Slide 11.

Can you please state the type of data that was available to you for your review of glyphosate animal studies?

A. Sure. A little background. When you do an animal study, you write a full technical report from the animal study. Even though it's not going to be published in the open literature for these type of regulatory studies, they still write an entire report which talks about what materials were used, what methods were used, how the animals were housed, what feed they got. It gives you have the statistical analysis done by the laboratory, and the final conclusions done by the laboratory.

I want to make it clear I have none of those full study reports. It's not available to me for almost all of these. I have study reports for three of the studies from Monsanto. They didn't -- to me, to my eyes, having looked at cancer studies for a long number years, they didn't like look like a full study report. I didn't see the statistical analysis I expected to see, and things like that. So I was a little lost.

They did have individual animal pathology data, but it was pretty poorly documented. It was hard for me to figure out exactly what was done there.

The data by Greim, *et al.*, 2015, they have supplements at the end of their documents. I think you have them there.

MS. GREENWALD: Yes. It's Tabs 3 and 4, Your Honor.

Q. So Tab 3 is the Greim Study, and Tab 4 is the supplements to the Greim study?

A. And if you just look at Tab 4, I want to simply show you what this type of data looks like, in terms of what you have to pull to try to figure it -- what to do with it. It's interesting that it isn't electronically available. The National Toxicology Program makes all of their data electronically available to anybody; even the pathology slides. And so none that of that is available in this case.

But I did use some of the data from Greim to answer some of the questions I've done. He doesn't provide individual animal data, so I couldn't do survival adjustment. He does not provide combined malignant tumors. That, I had to work on on my own in some other way. Some of the systemic tumors in his table are not available, but the regulatory authorities -- he has done those, so I could use their results to get the same number.

So as a result, using only Greim, I wanted to miss [sic] important tumor findings. So you have to use a combination of things.

(Reporter requests clarification.)

THE WITNESS: If you only used Greim's, you would miss important tumor findings.

BY MS. GREENWALD

Q. All right. So we'll slow down again.

A. Yes.

Q. I'm just going to remind you every other slide to slow down.

A. Every slide.

Q. Okay. So let's go to Slide 12, please.

Did you follow generally accepted methodology when evaluating the animal data for glyphosate?

A. Yes. I followed the methodology used by virtually every regulatory agency and IARC --

Q. Can you explain that, please?

A. -- except for the -- except for the fact that I was not able to really look at the reports from the individual studies.

I evaluate the study quality. That's the first thing you have to do.

I used a full study reports, where possible. Otherwise, I had no choice but to rely on summaries by the regulatory authorities. EFSA had some fairly decent summaries of these studies that I could work from.

Quality issues that I reviewed included survival -- how well did the animals survive? -- weight gain; diet; the substrain used. These were all issues you look at to decide: Is this the right type of study? And is it a quality study?

The regulatory agencies did different types of analyses of the data. And I wanted to be very consistent across all the studies, so I re-analyzed all of the tumors, myself, flagged by

any regulatory authority, such as EPA, EFSA, IARC, or EChA. And in addition to what was flagged by them, I included seven tumor sites that were identified by Dr. Corcoran, but not identified by regulatory authorities. For each case, I present the Fisher's Test p-values, but that's for informational and discussion purposes. I am using the Cochran-Armitage Trend Test for causality.

Once I did that, I analyzed all these same tumor sites in all of the studies, using the same sex-species strain. So if the Wood Study saw malignant lymphomas in CD-1 mice, I went back and looked at malignant lymphomas in all of the other CD-1 Mouse studies, so I could make a direct comparison of what the various studies were telling me.

I used historical data for rare tumors. And I used a pooled analysis to evaluate all studies for a particular tumor site. I performed Sensitivity Analysis, in case study designs are different, or in cases where highly different control responses exist. And I also did sensitivity to the pooling exercise. Since they're different statistical methods, I used two different methods for pooling. So that's a sensitivity there, as well, to see if the pooling method makes a difference.

Q. Okay. Slide 13, please.

You just mentioned historical controls.

A. Yeah.

Q. What is a historical control range, and how does that fit into your methodology?

A. So as identify pointed out before, the concurrent control is the appropriate group to use in almost all analyses of animal cancer data. And everybody agrees on that: All of the regulatory authorities; all of the toxicologists. "Historical controls" refer to multiple controls that unexposed groups from the same sex-species strain, usually from the same laboratory, and usually from the same time period. They are typically used in only two situations. And this is one of my big complaints about the regulatory authorities and how they did glyphosate; but these are the two really acceptable scientific methods -- places for using historical controls.

Rare tumors -- as I've pointed out before, it's hard to pick up a rare tumor, because you get few of them, and you have to be worried about it. I know an example from the NTP for fluoride where we had two osteosarcomas in a mouse strain from exposure to fluoride. And what was usual was the osteosarcoma wasn't in the bone; it was in the muscle mass, which we've never seen. And so we thought that a positive finding, because having two animals with that was unheard of. We've never seen it since. So clearly, something due to the fluoride.

If you see unusual patterns -- and the most obvious one is the one I've drawn here for you: A flat dose-response. Here's a case. If you look on the right, you see where it says

"historical controls"? So that's the range of historical controls.

Now, what you have here is your three dose groups give the same flat response. It's right in the middle of the historical control range. And the control group is way down toward the bottom of the historical control range. This is probably a statistical -- just occurred by chance. And this would usually be discarded, but here you're looking at historical controls to guide you on whether to discard that finding or not.

Q. Dr. Portier, if scientists do not use historical controls with rare tumors, how would that impact their historical analysis?

(Reporter requests clarification.)

BY MS. GREENWALD

Q. If scientists do not use historical controls with rare tumors, how would that impact their statistical analyses?

A. They would -- they would not see the tumor. The p-value would be less. It would be greater than .05. And they would claim it is not a statistically significant finding. That's why you have to use historical controls.

Q. And you say they would not see the tumor. What does that mean: To not see the tumor?

A. So if I see a response that is, let's say, 0002 -- so there's two tumors in the highest-exposure group -- that cannot be statistically significant by any test that we're looking at

here if it's out of 50, which is the typical size.

But if my historical control group, say, is like it is for hemangiosarcomas in CD-1 mice gone for 18 months -- zeroes; completely zeroes on 26 studies -- then those two animals are highly statistically significant when you compare the inside dataset.

Q. Thank you. Next slide, please.

Can you please false-positive rates, and power, and how they apply to the methodology that you employed to your analysis of the data here?

A. Absolutely. The false-positive rate is the probability of finding a chemical that causes cancer when, in fact, it is not carcinogenic. So this is that 5 percent/1 percent number that you're talking about. You're willing to -- you're willing to take the risk that the 5 percent is strong enough that you're really seeing a cancer finding. That's what the false-positive rate is.

Statistical power is the probability of finding a true carcinogenic effect.

(Reporter requests clarification.)

THE WITNESS: Cancer effect. The probability of finding a true cancer effect.

This means that if truth is that this is really a carcinogen, then what's my probability of picking it out in this type of study using this test? That's what statistical

power is.

It's dependent upon the study design.it's dependent upon the magnitude of the effect, so it's going to vary all over the place; but the Cochran-Armitage Trend Test is the most powerful test for linear alternatives when looking at binomial data. So it is the right test, by statistical terms. That's what this means.

BY MS. GREENWALD

Q. Can you go to the next slide, please? Can you explain what the --

THE COURT: Hold on a sec before we do that. Should we -- I'm trying to think how long we should go today, and what -- if we're going to go a little bit longer, whether we should take a little break right now.

MS. GREENWALD: We'll do whatever works for Your Honor. So shall we -- and we can take a break now, if you'd like. If you're willing to go a little longer, I leave that up to -- where --

THE COURT: So why don't we take a ten-minute break? And we'll go until around 4:30, 4:40, something like that.

MS. GREENWALD: Sure. Thank you.

THE COURT: Okay. Thank you.

(Recess taken from 3:52 p.m. until 4:03 p.m.)

THE COURT: Okay. You can resume.

MR. GRIFFIS: We need a moment to get our team back,

Your Honor.

(Discussion off the record.)

THE COURT: Go ahead.

BY MS. GREENWALD

Q. Dr. Portier, right before the break I think you were about to explain how the false-positive rate and power fit into your methodology.

A. Can I have my slide back?

Q. Yeah. 15. Slide -- I think they're just putting it up. Yep. There you go.

A. Ah, yes. Here. So this is one way to evaluate the power of statistical tests using a simple simulation exercise. On the computer here what you've got is just a graphic showing you what a null effect looks like versus what a positive effect looks like.

The table below it, the N fold is this thing on the side that says how big the positive effect is. So by using zero the high dose that's at 4 percent, just like a controls -- I can then run 10,000 animal studies on my computer; make them up randomly. And you get a false-positive error rate of 4.4 percent, which is right near the target of 5 percent.

If it doubles from 4 percent to 8 percent at the high dose, then you have a power of 23 percent. If it triples, you have a power of 52 percent, and it goes up to 16 percent. So it's four times more than a 4 percent. It's 75 percent

statistical power.

75 percent is a very good statistical power. 23 percent is not so great. So, as I've pointed out, it's a function of how strong the carcinogenic effect can be.

Q. Next slide, please.

You testified before about combining adenomas and carcinomas because of the progression of cells to tumors. Will you please explain that progression, using the chart on page 16?

A. Yes. We seem to have lost a line. Between normal cells and damaged cells, there should be a little arrow there.

Cancer is believed to be a multistage process. So you have a bunch of cells that are normal doing the function they're supposed to do. And the thought is you get a damage to DNA in that cell. Cells get damaged. DNA in cells gets damaged all of the time. And there are processes within the cells that take that damage, and repair it.

One example is you have two strands of DNA. And one of them is damaged. The other one is not. The machinery reads through, and fixes the one damaged cell. And it has ways of figuring out which way that's supposed to go. And there are lots of different types of DNA repair processes in the cells.

But if the damage is still on the cell -- on the DNA -- and the cell replicates, then that damage goes with that DNA. It's duplicated. And now you have a cell that doesn't know

it's got damage, that's a mutated cell. And that's sort of the start of cancer; but for the most cancers that happens multiple times, different types of mutations, before you really start seeing the adenomas and the carcinomas down the line. So one of the things you look at when you're thinking about a cancer study is this concept of progression of the tumor.

I'll take a moment, again, if you don't mind, to address a question you were addressing yesterday or the day before on lag time, because I'm not --

Q. Do you mean latency? Lag time is latency?

A. Latency. I'm not sure anyone defined it, and I suspect that everyone had a different idea of what latency is. So there are three definitions that I can think of right away for latency. The first definition is in this model that I have up here. The first mutation of the first cell -- from there to the point where we have an observable tumor, that is a latency period. And so it's clear mechanism of cancer. Latency period. I suspect that's what most people were thinking about.

But there's a second latency period, because I get exposed to a chemical like glyphosate. And it has a probability of causing that mutation. And that mutation can be reversed. So it takes a while before you even get that first mutation from exposure to chemical. So the time from first exposure of the chemical to the time of tumor is a different latency period. Okay?

Then there's a third latency period. That is I've got 5,000 people in my cohort study. And I have to collect enough people with the tumor to be able to detect it in the exposed group. So not only do I have to expose people for long periods of time, but I also have the latency, because I have to wait to find a large enough number of people to see the cancer.

When we try to measure latency period in an epi study, it's inexact. It's certainly not measuring the first latency period that I gave you -- the mechanistic one -- but there are some things we can say.

Glyphosate. Dr. Weisenburger did a --

THE COURT: Sorry could I interrupt for a clarification question?

THE WITNESS: Yeah.

THE COURT: You said there were three definitions. I got the first two. I didn't quite understand the third. You said there were three potential definitions of latency?

THE WITNESS: So, yeah. The third one is: In order for me to -- in an epi study, in order for me to be able to -- first I have to be able to tell you the causes the cancer. And that requires having enough people with a positive response -- so I'm not just looking at one person -- and following them over time. I have a group of people.

JUDGE PETROU: So just to interrupt, so that I understand, as well -- so, for example, when we were told it

took 10 years in that study before we could see, is that the third example that you were giving?

THE WITNESS: Yes. That's not the latency in terms of the --

JUDGE PETROU: Right.

THE WITNESS: It's latency in terms of from start of study, to when we could possibly see something.

Now, Dr. Weisenburger did a number of nice papers on lag times for NHL. And in one of the papers -- I believe it was an exposure to radiation -- the lag time from exposure to radiation to the tumor was one year. That's fast. That's a very fast period of time of time; but the radiation probably caused a mutation the minute it was given to them.

And so that would argue that the mechanism lag time is probably maybe on the order of a year, or maybe on the order of two years, but it's something in that range. Theoretically it could be in that range.

So when we think about lag time, and whether that -- those early case-control studies make any sense, it's very complicated to just be able to say, "No, they don't," or "Yes, they do," because this whole idea of latency is very, very complicated.

BY MS. GREENWALD

Q. Okay. Any other questions? Any other comments on latency or this Chart 16?

A. No.

Q. Okay. Slide 17, please.

What are some of the challenges that scientists face?

JUDGE PETROU: I'm sorry. Can we go back? Because you put that slide up, and started your conversation about why do you combine adenomas and carcinomas. And so I was hoping you could finish the answer to that. You started to explain.

THE WITNESS: That's the next slide.

MS. GREENWALD: That's coming with the next slide. So this is the two slides together. I wish we had a split screen. So Slide 17 talks about --

JUDGE PETROU: Okay.

MS. GREENWALD: -- how Dr. Portier and other scientists actually combine the adenomas and carcinomas. And we can go back to the other slide, if you'd like, once he gets to 17.

THE WITNESS: Next slide.

BY MS. GREENWALD

Q. Do we need one more slide? I think --

A. Right there. So if you see tumor progression in a study -- so I see adenomas, and I see carcinomas -- it strengthens the finding that this chemical is causing that particular set of cancers.

Problem is: It's difficult to observe tumor progression.

This is -- in statistics, we call this type of experiment

"destructive sampling." Once I look at the animal's liver, the animal is dead. So I can't see that the animal had an adenoma, and then later had a carcinoma. All I can do is count adenomas and carcinomas in dead animals. That creates a series of problems for the combined. Benign agents are not always reported. These adenomas are not always reported in some of the studies. Small, benign lesions can be easily missed.

Let's take an example. The liver of a mouse is, I believe, about 3 centimeters, 4 centimeters. So I think of it as a ball. Maybe that's too big. That would be too big. Maybe 1 or 2 centimeters -- as a ball.

But the NTP takes two slices through those livers for pathology. Each slice of the tissue is .002 inches thick. It's thinner than paper. So the actual sampling of the liver looking for tumors is .1 percent of the liver. It's very little tissue.

Now, when you do the liver, you palpate it first. You feel for bumps and lumps. And so you always cut the bumps and lumps; but in terms of trying to find small benign lesions, you're going to miss them, almost certainly.

Finally, as you go from these adenomas to carcinomas -- so let's take a theoretical case. A single adenoma is growing. And there's a second mutation which brings in a carcinoma. That carcinoma eats that adenoma, basically. As those cells replicate, they replicate faster than the adenoma. They push

the adenoma cells to the edge. And those -- those just get -- cytotoxicity takes it away.

And so you seldom see a carcinoma with pieces of the adenoma around the edge of it. So it's very hard to observe that progression. As such, then most cancer biologists would say that observing progression from benign to malignant is not required from a cancer bioassay. Seeing it strengthens the finding. Not seeing it should not remove the finding. So if I just see carcinomas and I don't see adenomas, I think that's still a valid finding.

JUDGE PETROU: So the last bullet point on this slide is missing the word "observing" -- right? -- because it's observing the progression is not required?

THE WITNESS: Correct.

JUDGE PETROU: And in regards to going from adenomas to carcinomas -- and I don't know whether you can answer this question -- is the likelihood of an adenoma turning into or evolving into a carcinoma -- does that vary tremendously, depending on the type of tumor we're talking about?

THE WITNESS: Yeah. Certain tumors don't even have those progressions. Malignant lymphomas -- the only premalignant state is swollen lymph glands. And you get swollen lymph glands with so many different things, that it's unlikely you would look for that or see it --

JUDGE PETROU: Mm-hm.

THE WITNESS: -- in these studies, but that's my understanding of the pathology of malignant lymphomas.

BY MS. GREENWALD

Q. Can we go to the next slide, please?

Now there, we talked earlier about animal studies that you evaluated in this case. You didn't evaluate every single study. Correct?

A. I evaluated every single study.

Q. I should say you didn't accept all of the studies.

A. I evaluated --

People have talked about the 12 animal studies. There are actually 21 animal studies available for review for this for glyphosate; 13 in rats. But of those 13 in the rats, 6 of them are really not acceptable for an evaluation of this sort, for a variety of reasons. They don't describe the glyphosate properly, so you don't even know what they've tested. They used 10 animals per group; that's just not big enough. So there are reasons you would discard those.

In the mice there were eight studies. Only three were acceptable for use. And that gives you the 12 that you were talking about earlier.

Q. Now, are the studies that you rejected -- have they been universally rejected by every scientist that's been looking at this data?

A. Yeah. Of the reviews that include them, they have all

excluded those same studies that just were poor quality.

THE COURT: I just want to correct the record on one thing. You said only -- I think you said only three acceptable mice studies; and your slide says five. I assume you meant to say five?

THE WITNESS: I meant to say five. I'm sorry. That was a mistake.

MS. GREENWALD: Thank you, Your Honor. I missed that, also. I appreciate that.

Q. So Slide 19, please. If you can, use Slide 19 to explain to the Court what evaluation you undertook, using the example in male Wistar rats -- male Wistar rats. And I believe that was talked about, actually, with Dr. Jameson, as well.

A. Yes. So this is one set of results from a series of three bioassays in male Wistar rats. The first study is -- I think this is about adenomas. This is liver tumors. The first study is the Suresh Study from 1996. You can see the counts there. And the p-value is .374. It's not statistically significant.

Brammer is statistically significant, with a p-value of .008.

And Wood is not statistically significant.

So the question in looking at something like that one asks is, *I've got one positive, two negatives. What does that mean?* How do I turn that into a question of, yes, the positive is real; or no, the positive's not real, and the other two are

correct?

So scientists face that problem. And there is a way to deal with it.

Next slide.

Q. Next slide, please.

A. But there's a second problem here that you might have missed on this table, and that is that the Suresh Wistar rats have a control response of almost 50 percent, and the rest of the Wistar rats have a control response of zero.

The Wood and the Brammer study -- if you look at the little blue dots and green dots here, they line up very nicely.

You look at those red dots. That Suresh Study is way out of line.

So there's a second question scientists have to ask. How do you handle the very high control response in the Suresh Study?

So the answer to both of these -- next slide --

Q. Next slide, please.

A. Thank you.

The answer to both of these is to use pooling, and some degree of Sensitivity Analysis. So the first thing you do when you see something like the Suresh Study with the high background is you look for a scientific explanation. So in this case I went back to the original reviews done by EFSA, and I looked at the diets; that they all had three different diets.

So then I went and looked at the components of the diets: How much carbohydrates; how much protein from fish; things like this. They're all pretty much identical. So I don't think it was the diet that made the difference.

Maybe it's the substrain. They're CD-1 mice, but there are substrains of CD-1 mice. There are all three different substrains, so there's no guarantee that there would be any difference there.

So I went to all of that and looked at it. I could not find an explanation.

Now, when you take Wistar rats and grow them in one lab through multiple generations, and you grow them in another lab through multiple generations, they drift apart from each other. And so that's a known phenomenon. So this might be some sort of genetic drift in the two different colonies over time; but I can't prove that, because I don't have the genetics of the individual animals checked out.

JUDGE PETROU: Do you look at all -- I'm just thinking back to what you were saying earlier regarding the historic data. When you have a group like in the Suresh study that has a such a high rate of disease in the control group, are you also then trying to compare it to the historic data, to see if it's in line?

THE WITNESS: Yeah, but I couldn't find a good historical control dataset for Wistar rats. So -- at least,

not one that I believed would allow me to answer that question. So, no, I didn't.

So the solution is to analyze the data together, and do some Sensitivity Analysis. Now, in my Expert Report I used simple pooling concept. It's very easy. These studies are supposed to be replicates of each other. And so instead of analyzing them separately, just throw them all together. Treat them as one big bioassay. They keep their doses. Treat them as one big bioassay, and just analyze it using the Cochran-Armitage Trend Test. And then you test the sensitivity to the inclusion of Suresh by doing the analysis with them in there, and with this study out of there; and look to see how much of an impact that has.

Dr. Corcoran, in reading my Expert Report, criticized my use of simple pooling, and suggested I use a General Linear Model approach.

Cochran-Armitage Trend Test is a General Linear Model. It falls in that class and GLMs can be used to evaluate the impacts of variables beyond dose analysis, so it is a reasonable way to approach the data, as well.

I decided to, in addition to simple pooling, use logistical regression for doing the analysis of the pooled data. So you'll see two different poolings, and that allows me to look at the sensitivity of the analysis method to the final result. And sometimes you'll see two p-values, one of which is

Suresh in and Suresh out, so that we could look at how sensitive all of these significant findings are to these differences between the studies.

Next slide.

Q. Well, not yet.

A. Oh.

Q. Do scientists conduct pooling here to reach a particular result?

A. Oh, no.

Q. Okay.

A. You're doing -- I should have said this earlier. P-values -- I don't believe they're straight lines. I don't believe a 5 percent is: Yes, it's significant/no, it's not. I want to look at these p-values.

This pooling is giving me an idea of how sensitive these p-values are to changes in the data, but it's also telling me whether the trend is consistent across the multiple studies. So even though I get a .3 p-value in one study, and a .008 in another, that .3 may be going up ever so slightly, and the .008 is going up a lot more. And you put them together, it's still going up, the statistics come back and says, *Yeah, you still have a significant finding*. So it allows me to address that question in an objective fashion.

Q. So, Dr. Portier, Monsanto, as you know, has criticized you for conducting pooling here to reach a particular result. Do

you agree with that?
A. No, I don't agree with that. I am using pooling for a particular result. I want to understand these data, and find out what they're actually telling us about carcinogenicity for glyphosate.
Q. So I should have said you didn't do it for a particular outcome. Correct?
A. That's correct.
Q. Is the pooling you conducted here the type of analysis you would have performed in the 30-plus years you worked for the federal government designing, evaluating, and investigating animal bioassays?
A. Yes.
Q. Interpreting animal bioassays?
A. Yes.
Q. I want to make sure the testimony's clear just now, because I think at one point you interspersed CD-1 mice. All of this testimony is about the Wistar rat. Right?
A. Yes.
Q. I just want to make sure that's clear.
A. Up to that point right now, yes.
Q. Correct. That's what I meant.
A. Sorry.
Q. That's okay. And do scientists perform Sensitivity Analyses to reach a particular outcome?

A. No. Scientists perform Sensitivity Analyses to -- in these types of situations to see how sensitive the results are to important characteristics in the data that you're looking at.

Q. And again, Monsanto has suggested that you conducted a Sensitivity Analysis here to reach a particular outcome. That isn't true; is it?

A. That's not true.

Q. Okay. And is the Sensitivity Analysis that you conducted here the type of analysis you would have performed in the 30-plus years you worked for the federal government, designing and evaluating the animal bioassays?

A. Absolutely.

Q. Okay. Did Dr. Corcoran conduct a pooling analysis or Sensitivity Analysis of the data, to your knowledge?

A. No, he did not. I think he did one example, but I don't think he analyzed all of the data that way.

Q. Okay. Next slide, please. Now you get your next slide.

A. Okay.

Q. Please explain the Sensitivity Analysis that you performed in the studies identified in this slide, and how it works.

A. There are three major concerns I see in these studies that I want to look at the sensitivity of. The Lankas 1981 Study is a 26-month study.

(Reporter requests clarification.)

THE WITNESS: Lankas. L-a-n-k-a-s.

Lankas is a 26-month study. The other three studies are 24 months. That doesn't seem like a lot, but you're going from a moderately old animal to a very aged animal in these two months, and so I want to make sure that Lankas is not driving the results one way or the other.

The second is the Wistar rats with Suresh. I showed you the response for adenomas. Suresh's study had a lot of odd control response to it, and so I'm going to check it for everything, and look at it very carefully.

And finally the four studies in CD-1 mice. Two of those studies are 18 months; the other two are 24 months. I probably shouldn't combine all four of them, but I will. But I'm going to look at the sensitivity with those combinations to how many months they were evaluated.

BY MS. GREENWALD

Q. Okay. So if you'd -- all right. Next slide, please.

You have a legend here. What's the purpose of this legend, and how are you go going to use that legend to explain some of the data here?

A. Yeah. I was trying to figure out how to rapidly, essentially, show you what I see in the data. And so I'm going to show you tables after this point. And the tables will have gray squares, red squares, and different colors of the red squares.

Highly significant findings are the dark red. Significant findings have this kind of pinkish color. And largely significant, which is .1 -- .05 to .1 will have this much lighter color.

And so what you'll be able to see in the table is where the action is, sort of, and how important some of these tumors are.

Q. Okay. So if you'll look at Slides 4 and then 25 --

MS. GREENWALD: Should we maybe -- Your Honors, maybe we can do these -- well, I'll leave it up to you. We have a number of slides to sort of go through the findings, and explain how the Sensitivity Analyses and pooling worked in this case. That would probably take --

THE WITNESS: Thirty minutes.

MS. GREENWALD: -- fifteen minutes. You want me to go now and do this?

THE COURT: It's probably a good time to --

MS. GREENWALD: It's up to you.

THE COURT: I don't really care, either. Why don't we -- just to make sure -- maybe just to make sure we're not pinched for time, we should --

MS. GREENWALD: Okay. We'll do it quickly.

THE COURT: -- plow ahead now.

(Discussion off the record.)

BY MS. GREENWALD

Q. So I think maybe the best thing, since there are 11 numbers on this chart, let's not have any testimony too much about numbers. And we can just explain the charts to the Judges, so we don't have a burden on the court reporter with numbers. Okay?

A. Okay.

Q. So why don't we just go through? I'm going to let you walk through Slides 4 through 30, not talking fast, but move through them quickly so that you can explain basically how you do your pooling and your Sensitivity Analysis with the data you have here in this case.

A. Okay.

Q. But you'll need to tell Pedram how you want him -- when you want him to move the slides.

A. So this is -- this type of data will be appearing from now on. You have the three -- the tumors on the left side. And the middle is the study. And these are the three studies in Wistar rats. Then the -- you have the p-value underneath each of those studies. And then you have the pooled analysis. You have the pooled analysis using a General Linear Model, and the pooled analysis using the simple model.

So let's look at the hepatocellular adenomas we were looking at before. The bracketed number under "GLM" is when I excluded from the pooling. And the first number above that is

when it's in the pooling.

What do we see in this slide here?

We see that it doesn't matter how you pool the data. When I pool the data, it's statistically significant.

So the pooling on the hepatocellular adenomas suggests that the increase you see in Brammer holds across all of the studies when you put them together.

THE COURT: Pull your microphone a little tiny bit away from you. It's making a popping noise.

THE WITNESS: I'm sorry. Thanks.

So in this case, it really doesn't matter how you pool. It's a significant finding.

BY MS. GREENWALD

Q. When you say it doesn't matter how you pool, you mean whether you use GLM or simple?

A. Correct, but you have to pool to answer the question.

Mammary adenomas and carcinomas is quite different. As you can see here, if I include the Suresh Study, I have a non-significant finding. And if I exclude it, I have a significant finding; again, regardless of which pooled analysis I'm going.

So now I have a dilemma. I have to decide which is which.

So I went back and looked at the data for mammary gland adenomas and carcinomas. There's actually a statistically significant decrease, as the defenses counsel told me during my

debriefing -- my deposition. There is a statistically significant decrease for mammary-gland adenomas and carcinomas in the Suresh Study, and an increase in the Brammer and Wood Study combined; again, pointing to the fact that the Suresh Study appears to be not quite the same Wistar rat as the other two studies.

And here, excluding it might -- in fact, in all of these, excluding it might make much -- make more sense.

Skin keratoacanthoma. I'm going to spell that for you. K-e-r-a-t-o-c-a-n-t-h-o-m-a. You can see here, again, no matter how I pool it, it doesn't matter. It's pretty much a positive finding.

Pituitary adenoma show the opposite. So it's positive in the Wood Study; but no matter how I pool it, it disappears. There is no statistical significance there.

And finding pituitary adenomas in females -- pooling does matter in this case. I would argue after looking at these data that we pooled them all together. The simple analysis is not working. The GLM was doing a better job. But when you exclude the Suresh Study, you can see that it becomes highly statistically significant. So again, I have to look at this, and decide what I'm going to say about that one tumor.

I think we can -- next slide, please.

Q. All right. So let's go to Slide 25.

A. Okay. There. Can we come back to this one tomorrow?

This is one we talked about already --

Q. Yes, right.

A. -- about: Why are tumors other than lymphomas relevant, and how do they fit? And I think --

Q. Go through the data first. We'll start with this tomorrow. We'll go back to 25 tomorrow.

A. That will work. That will work.

Q. So now we're on 26.

A. Okay. This is the tumor finding and Sprague-Dawley rats. I'm not going to go through every single one of these. I'll point out a few.

This is the case where the Lankas Study is 26 weeks, and the other studies are 24 weeks. So again, the bracketed number is the p-value without Lankas, and the p-value with Lankas. What you see here is pretty much positive findings in everything except for the adrenal cortical carcinomas in the females. And I haven't decided exactly what I'm going to say about that, but it's a weaker finding than some of the others, so I don't really need it. You'll see that at the end, when I address the findings from here.

Next slide.

Q. Next slide.

A. This is the opposite. Here, these are also Sprague-Dawley rats. This is the rest of the tumors in the Sprague-Dawley rats. And these are all effectively negative from the pooling,

even though you see some positive findings in the individual studies. The pancreas islet cell tumors here are in here -- you talked about that earlier -- but they're in here because the regulatory agencies sought significant values for the Fisher's Test; significant p-values. And so they mentioned it.

And since I said I was going to look at all of the tumors that the regulatory agencies looked at, I also included this tumor, even though the trend test is not statistically significant.

Q. Next slide, please.

A. CD-1 mice. They hemangiosarcomas in male CD-1 mice. You can see that the Atkinson and Knezevich & Hogan study are 24 months; Sugimoto and Wood are 18 months. So you actually have three pools of analyses here. You have the 18 months by themselves; the 24 months by themselves. And they're all five of them together.

What you see here for the hemangiosarcomas is pretty much a positive finding. The Wood Study had no hemangiosarcomas at all, so it was zero across the board. The Sugimoto Study had a small increase in tumors. But for my historical control database that I used, I had 26 studies for 28 months in CD-1 mice with hemangiosarcomas, and not one of those studies had a hemangiosarcoma in it.

And when I compared that to the historical controls, it had a very significant finding. Atkinson and Knezevich & Hogan

were, again, the same; but Atkinson was significant by itself. I didn't really have to go to a historical control dataset to get that answer, but I put the historical control number here for you to see, as well. I would call this a positive finding in looking at the pooling, especially in the 18-month studies.

Now, you might ask, *Well, why don't the 24-month studies have a positive finding, too*?

Well, the control response at 24 months is much higher than the control response at 18 months. And so if you see just a small increase with a high control response, statistically you can't pick it up; but if you see it with a very low control response, you can pick it up. And I believe that's what's happening here. The 18-month studies are in a very low control/response place, and you're able to see the trend. The 24-month study's not as strong.

Q. Can you go to the malignant lymphoma? Let's jump down to the malignant lymphoma. And then maybe the rest the slides can be self-explanatory for the Court.

A. That would be -- that would be great. The malignant lymphomas --

Q. I saw a big smile.

So just let's go to the malignant lymphomas, since obviously that's what we're talking about in this case. And you can tell us whether there's any significance to those, beyond what the numbers are on this piece of paper.

A. Sure. The malignant lymphomas -- you see the numbers here. 18-month studies are all highly positive for malignant lymphomas. The 24-month studies are not positive for malignant lymphomas. Overall, it's a marginal finding if I throw them all together.

The malignant lymphoma historical control rate from the Ward Paper that you were talking about before is 4 percent, exactly the same as the control rate that Bill was talking about, but that's for 24 months; that's not for 18 months. For 18 months, that number's much smaller. I don't have a good -- I do have historical database for that, but I don't remember what it was. I can't tell you what it is here.

Anyway, I didn't need it, because I saw a statistically significant finding against the concurrent control, which is always the better control. So I don't have to go look at the historical controls. And, in my opinion, this is the positive finding in the 18-month mice.

Next slide is all negative, I think.

Q. Right. So I think we're going to not go through anymore of the individual data slides. The Court has them.

Your Honors, would you want to call it a day now, and then we'll pick up tomorrow morning? And we should only have 15, 20 minutes left. And there won't be anymore charts. Well, a couple.

THE COURT: Use whatever charts you want.

You can step down.

THE WITNESS: Thank you very much.

(Witness excused subject to recall.)

THE COURT: So let's talk about what we have left real quick. What do we have left from plaintiffs?

MS. GREENWALD: For the plaintiffs we have Dr. Nabhan on Friday. He's not arriving until tomorrow night. And then we have the deposition segments from Dr. Ross and Dr. Blair. And then we rest. That will be the end of our presentation.

THE COURT: And then what did you say? How much time did you say you planned to take with the deposition excerpts from Blair and --

What was the other person's name?

MS. GREENWALD: Dr. Ross.

THE COURT: Ross. Sorry.

MS. WAGSTAFF: Well, actually --

MS. GREENWALD: I think we're trying to shave it down a little bit.

MS. WAGSTAFF: Yeah. Plaintiffs didn't make any affirmative designations. They're just in response to Monsanto's. So if they cut theirs down, we would cut ours down. I think we're about --

MS. GREENWALD: We're at 40 now.

THE COURT: You mean 40, total; what both sides want to put in from that?

MS. GREENWALD: No, no. So, as Aimee said -- as Ms. Wagstaff said, we didn't designate anything. And we got a designation from Monsanto. And to make the record full, so we had full responses to what they cut, we need to put in around 40 minutes on either side.

THE COURT: Okay. We're going to hear all of that together.

MS. GREENWALD: Correct. Correct. I don't know how much. I don't know what their time is.

MR. LASKER: Ours is a little bit under 30 minutes. I don't know exactly, but I guess we'll be playing something for about an hour and 10 minutes, unless there's further cutting options.

THE COURT: All right. So that's -- so -- and then Monsanto is just -- are you just calling the four witnesses, or are you calling --

MR. LASKER: Yes, Your Honor.

THE COURT: Just those four witnesses. Okay.

MR. LASKER: Yeah.

THE COURT: And it looks like the plaintiffs have a little under four hours left. And the defendants have -- what? -- about five and a half hours left?

MR. LASKER: I think we have more, but I don't --

THE CLERK: Exact numbers: Plaintiff has 3 hours, 49 minutes, 27 seconds.

MR. LASKER: That's exact.

THE CLERK: Defense has 5 hours, 48 minutes, 15 seconds.

THE COURT: Shall we round up?

MR. LASKER: We don't appreciate that. Talk to her.

THE COURT: I just meant by seconds, not --

JUDGE PETROU: I have the same question. Would that -- remaining time include the additional 60 minutes that we're going to --

THE CLERK: Yes.

THE COURT: Yeah. So it looks like we'll -- you know, we can go past 2:00 o'clock tomorrow if we need to; but I think that we should be finishing well before 4:00 o'clock on Friday, especially if we go --

What's that?

-- especially if we go past 2:00 o'clock tomorrow.

MS. GREENWALD: Your Honor, is this a good time? Sometime this week can we talk about when oral argument will be? Doesn't have to be today. I know it's late in the day. We all were wondering when Your Honor might schedule a date.

THE COURT: Yeah. I was thinking about that. And my guess is that it probably would be useful to have. It wasn't clear to me that it would be useful to have further argument, but I think it probably would be. I would want to do it sooner rather than later, while all of this stuff is fresh. So let's

all talk about that a little bit tomorrow.

MS. GREENWALD: That's very helpful. Thank you very much.

THE COURT: Thank you.

THE CLERK: Court is adjourned.

(At 4:44 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 8, 2018

Signature of Court Reporter/Transcriber Date

Lydia Zinn