Pages 596 - 770

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
Thursday, March 8, 2018

TRANSCRIPT OF PROCEEDINGS

APPEARANCES:

For Plaintiffs:

The Miller Firm LLC
108 Railroad Avenue
Orange, VA 22960
(540) 672-4224
(540) 672-3055 (fax)
BY: MICHAEL J. MILLER

For Plaintiffs:

Andrus Wagstaff PC
7171 West Alaska Drive
Lakewood, CO 80226
(720) 255-7623
BY: VANCE R. ANDRUS
AIMEE H. WAGSTAFF
DAVID JACKSON WOOL

For Plaintiffs:

Andrus Wagstaff PC
6315 Ascot Drive
Oakland, CA 94611
(720) 255-7623
BY: KATHRYN MILLER FORGIE

Reported By: Lydia Zinn, CSR No. 9223, FCRR, Official Reporter

APPEARANCES:

For Plaintiffs:
Weitz & Luxenberg PC
700 Broadway
New York, NY 10003
(213) 558-5802
BY: ROBIN L. GREENWALD
PEARL A. ROBERTSON

For Plaintiffs:
Baum Hedlund Aristei and Goldman, P.C.
12100 Wilshire Boulevard, Suite 950
Los Angeles, CA 90024
(310) 207-3233
BY: MICHAEL L. BAUM
ROBERT BRENT WISNER

For Plaintiffs:
Lundy Lundy Soileau & South LLP
501 Broad Street
P.O. Box 3010
Lake Charles, LA 70601
(337) 439-0707
BY: RUDIE RAY SOILEAU, JR.

For Plaintiffs:
Andrus Anderson LLP
155 Montgomery Street, Suite 900
San Francisco, CA 94104
(415) 986-1400
(415) 976-1474 (fax)
BY: LORI E. ANDRUS

For Plaintiff Sioum Gebeyehou:
Law Offices of Tesfaye Tsadik
1736 Franklin Street, 10th Floor
Oakland, CA 94612
(510) 839-3922
(510) 444-1704 (fax)
BY: TESFAYE WOLDE TSADIK

APPEARANCES:

For Plaintiff Wanda Clarke:
Sill Law Group
14005 N. Eastern Avenue
Edmond, OK 73013
(405) 509-6300
(415) 509-6268 (fax)
BY: TARA TABATABAIE

For Defendant Monsanto Corporation:
Hollingsworth LLP
1350 I Street, NW
Washington, DC 20005
(202) 898-5800
BY: KIRBY T. GRIFFIS
JOE G. HOLLINGSWORTH
JOHN M. KALAS
ERIC GORDON LASKER
HEATHER ANN PIGMAN
STEPHANIE SALEK
ERICA T. KLENICKI

Also Present: The Honorable Ioana Petrou
Leonora Lynham
Scott Duval

INDEX

Thursday, March 8, 2018 - Volume 4

Thursday - March 8, 2018 **8:05 a.m.**

P R O C E E D I N G S

---000---

THE COURT: All right. Ready to resume?

MS. GREENWALD: Yeah.

THE COURT: Oh, argument. You all asked about argument. I could have argument. I would not want to do it unless it's -- I want to do it -- I would like to have argument, I would like to have it when it's fresh, and the time that I could have it next week would be Wednesday morning. So, like, Wednesday morning at 10:00 o'clock.

MR. LASKER: And, your Honor, we had looked at that because actually, Judge Petrou is having something on Tuesday and there was a logic to that. Unfortunately, we have some medical issues on our side that week, and we were hoping to be able to do it the week after, on Wednesday.

THE COURT: I don't think so, because I'm going to be in trial.

MR. LASKER: Ah, okay.

THE COURT: So we need to do it next week, and I think Wednesday is the only time I can do it.

MR. LASKER: Well, that makes it easy, then.

THE COURT: So who were you planning on having for argument?

MR. LASKER: I'll be arguing.

THE COURT: Okay.

JUDGE PETROU: So counsel, if it's at all helpful, I could move our Tuesday to sometime on Wednesday, if you were trying to do it all in one day. That would work fine for me.

MR. LASKER: That would be great from me. I'm coming from the East Coast and we'll just have to figure out the timing of the two. How much time are you anticipating you'd like for argument?

THE COURT: I don't know. Five or six hours.

MS. WAGSTAFF: Each, right?

MR. LASKER: Test like, though. Right?

THE COURT: You know, an hour or two.

MR. LASKER: Okay.

THE COURT: And for me, it could be -- it could be in the morning or the afternoon. Doesn't matter, I don't think.

Is that right, Kristen?

THE CLERK: Yeah, I think that's fine.

THE COURT: Because we moved that other -- we moved the pretrial conference to Thursday afternoon, is that right?

MR. LASKER: I have been told that morning would be better on Wednesday, if we can do that.

THE COURT: Okay.

MR. LASKER: Then will we do the pretrial in the afternoon? Does that make sense?

JUDGE PETROU: I think I can make that work.

MR. LASKER: Okay.

THE COURT: And then I assume Judge Petrou will have her own argument at the appropriate time for her cases.

MR. LASKER: Just so I'm clear, will you be attending the argument?

JUDGE PETROU: I don't know.

MR. LASKER: That's fine, your Honor. Thank you.

THE COURT: I was assuming, I mean, anybody is welcome to come watch, but I assume that because this is argument in these cases, it should just be me presiding over that part.

MR. LASKER: Of course. That makes sense to me, your Honor.

MS. GREENWALD: That works with us, Your Honor.

MR. WISNER: And your Honor, for the JCCP proceeding what time?

JUDGE PETROU: Let's tentatively say 2:00 o'clock next Wednesday.

MR. WISNER: Okay, should I give notice?

THE COURT: Yes.

MR. WISNER: Okay.

THE COURT: Okay. Ready to proceed?

MS. GREENWALD: Yes, thank you, Your Honor.

CHRISTOPHER PORTIER,

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

DIRECT EXAMINATION (resumed)

BY MS. GREENWALD:

Q. Dr. Portier, yesterday afternoon -- if you could put up slide 26, please -- yesterday afternoon we were talking about slide 26, and we looked at the appropriate transcript last night, because it appears that you testified that the studies were 24- and 26-week studies. Did you mean to say 24- and 26-month studies?

A. Yes, 24- and 26-month studies.

Q. Okay, great. Thank you.

Okay, so if we could turn to slide 31, please.

Yesterday, at the end of the day, we talked to Dr. Portier about roaming data, and that was slides 4 through 30, correct?

A. Correct.

Q. Using slides 31 through 33, can you please explain to the Court the methodology that scientists employ for determining whether the tumors found in animals arose by chance?

A. Okay. So once you see all of these tumors in this case, you have to be worried that there are so many animals, so many pathology evaluations going on, that maybe they just arose by chance, and so you can actually address that.

Here's the methodology, in simple terms. Suppose you have

an evaluation that requires 20 Cochran-Armitage tests. For each test, you determine if the p-value is less than .05. So you've got significance or not significance. Because it's 20 tests and because the false-positive rate is five percent, by chance, you would expect to get one positive finding.

Suppose there are three significant findings. Then you can actually calculate the probability of seeing three or more significant findings. Using simple first-year statistics and probability in this case, with 3 for 20, the probability is .076. That means there's roughly a 1 in 13 chance all three significant findings are due to chance.

So that's the methodology I'm going to employ for all of these tumors.

Next slide, please.

Q. If you can go to the next slide, please.

A. So this is the tumors in the rats. And I'm not going to walk you through this huge table. I'll do just one, the one that matters.

If you look at male Sprague-Dawley rats, the first line, there were 86 evaluations done. That means you expect 4.3, because 86 times .05. We observed 7, and the probability of that is .139.

I also looked at .01, we expected .9. That's 86 times .01. We observed three, and the probability of that is .056.

So roughly it's a 1 in 18, 1 in 20 chance that all three

highly significant tumors in male Sprague-Dawley rats arose by chance. In my opinion, this is an unlikely finding.

Next slide.

This is the CD-1 mice. Again, I'll just do the first one, the males. We expected 2.1. We observed 8 for .05. The probability of that is virtually zero, one in a thousand. The same thing for .01, it's roughly one in a thousand.

These tumors cannot have arisen by chance. It's just an extremely rare event, if that were the case.

Q. Next slide.

Dr. Portier, given these data, how do scientists determine whether a chemical induces cancer in rodents?

A. So the best place to go for this would be to look at the definitions that EPA and others have for what constitutes sufficient evidence of carcinogenicity in animals.

This is EPA's, and I'll read it,

> "An agent that has tested positive in animal experiments in more than one species, sex, strain, site, or exposure route."

That's the -- that's the limit of the detection. You have to see two or more.

Next slide.

THE COURT: Can you adjust your mike a little bit closer? I'm told that you're not coming through on the video.

Sorry, I know yesterday I told you to move it away from you, so I apologize.

MS. GREENWALD: That was my fault, your Honor. I asked him to please move it away, also.

Q. Dr. Portier why don't we stay on this slide. Does the data here support a finding of sufficient evidence under the EPA definition?

A. Absolutely.

Q. And can you explain how?

A. There were at least five very strong tumor findings in these data. They didn't arise by chance. There's biological reason to believe that they're real. I'll show that in a minute. To me, it's so obvious that this is a positive study practice.

Q. Okay, if you can turn to slide 35, please.

Is the definition for EChA and IARC virtually the same as that for EPA, even though there are a lot more words on the page?

A. Yes they're effectively the same. And I will point out that EChA and IARC use exactly the same definition. EChA took IARC's definition into their guidance documents.

Q. Okay. By the way, I want to ask you -- I want to go off point for a minute.

In your deposition, do you recall that counsel for Monsanto criticized you for failing to disclose work on this

case, in connection with a letter to the -- a letter, Archives of Toxicology, a publication, in which your letter to the editor was published? Do you recall that?

A. Yes, I do.

THE COURT: I didn't understand that question.

MS. GREENWALD: I'm sorry.

THE COURT: Can you ask it again?

MS. GREENWALD: Of course.

Q. In your deposition, counsel for Monsanto criticized you for failing to disclose a letter to the editor that you sent to Archives of Toxicology, the editor of that publication, in which you did not identify that you were working on this case; do you recall that?

A. Yes, I do.

Q. And that letter related to your criticism of the European -- European Food Safety Authority's flawed methodology in analyzing the data in this case, correct?

A. Correct.

Q. And did you do anything about that disclosure following the deposition?

A. Yes. We wrote a letter to the editor, and they've since added a conflict-of-interest statement.

Q. Okay, and your publication, so to speak, what they published was actually your letter to the editor, correct?

A. Yes, correct.

Q. Okay. If you can go back, please, to slide -- if you could go to slide 36, please.

Is statistical significance all that one -- all that a scientist needs in order to decide that there are positive findings in rodent studies?

A. No. You look at other issues, as well. They're sort of in the little one paragraph I read from EPA, and these are some of the other issues.

Q. And what is the biological significance of these rodent study findings?

A. Well, you -- you have tumors in multiple studies, multiple species, multiple strains, and multiple sexes, and I've listed them here for you to take a look at. That's one the things you'd like to see if you really want to call this a positive study or positive studies.

You want to see regression from preneoplastic to benign to malignant. Not seeing it doesn't take it away, but seeing it adds strength to the evidence, and we have three cases where that occurs.

Next slide.

Rare tumor types really raise the biological significance of a finding. We have two rare tumor types in these studies.

If you see tumors at multiple sites in a single study, that also strengthens the evidence you've got a positive finding, and we have three cases where that is the case.

And finally, if you have tumors that are similar in laboratory animals and humans. That strengthens the case.

Malignant lymphomas in mice -- so when doctors want to develop a therapy, researchers want to a develop a therapy for NHL, they use a mouse that produces malignant lymphomas, and they test the therapy in the mouse.

So the malignant lymphomas in the mouse are the closest thing to NHL in humans. There is no NHL in mice.

Q. Okay. If you can go back to slide 25, please. Yesterday we jumped over this slide, it was late in the afternoon, and so I'd like to go over this now, Dr. Portier.

Can you please explain how tumors other than lymphomas are relevant to the analysis here; and how they fit in to the question of NHL in humans?

A. Okay. So historically, if you look at the evidence, there's a dozen papers on this.

People have taken all of the known human chemical carcinogens from IARC's list or from the Report on Carcinogens list and they've looked to see if these occur in laboratory animals.

And so all known human carcinogens are carcinogens in laboratory animals. There's not a single one that was missed. Arsenic was missed for a while, but some very clever colleague of mine figured how to find the right mechanism that worked.

Rats and mice generally do not get the same tumors when

both species are given the same chemical in the same experiments at the same time. So seeing the same site in humans and rodents will strengthen the biological plausibility of causality mediums, but it won't necessarily detract from it if you don't find that.

And that's how it's used in these types of overall evaluations. That's the standard procedure for looking at this.

Q. Okay. Slide 38, please.

Based on the results of the studies that you've testified about here today and that are set forth in your expert report in greater detail, what conclusions have you reached about whether glyphosate can cause cancer in humans?

A. In laboratory animals.

Q. In laboratory animals, I'm sorry.

A. Glyphosate can clearly cause tumors in laboratory animals; malignant lymphomas in male mice and angiosarcomas in male mice, hemangiomas in female mice, kidney tumors in male rats, and mice, and skin tumors in male rats.

Q. Okay. If you can go to the next slide, please.

Now, we looked at this slide yesterday, but it didn't have the bottom part on it, and I'd like you to talk about this slide now in connection with the mechanism of action of glyphosate as it applies to human cancer.

A. Sure. So this slide is simply to illustrate how chemicals

can interact with the cancer process.

So you've heard about genotoxicity, up to this point. The chemical can go directly in to the cell and damage DNA, and that would be genotoxicity.

The chemical can create oxidative stress in the cells, so that you have free oxygen radicals. All of the cells have lots of oxygen and they produce free oxygen radicals that are cleared up. But if you start producing too many, these free oxygen radicals can bind to DNA and other things, causing the DNA damage. So you can get genotoxicity through a secondary pathway.

The chemical can affect DNA repair. That's not as common, but it clearly can. Chemicals can affect cellular replication, and when they do that, it can be selective. So a mutated cell will grow even faster with the chemical there. That's called a promotional effect. And there is some evidence that glyphosate has a promotional effect, as well, but it's just one study.

And finally, the chemical can affect the immune system. Once you start getting tumors in the body, the immune system tries to get rid of them because they're odd things to have in the body, and if you affect the immune system, you can block that action, and then spontaneously occurring tumors will become faster, they'll appear faster.

Q. If you can move to slide -- past slide 40, and you can go to slide 41, please.

What considerations do scientists use to evaluate mechanism?

A. Well, there's -- there's many different types of studies when you start looking at mechanisms.

You have *in vivo* observations. These are studies done in living organisms, mammals usually, but not always; humans, laboratory animals and wildlife. And then you have *in vitro* observations. These are done in cells, in some sort of laboratory container. There are various types, and you have human cells or animal cells.

When you look will at the data, you give more -- if -- assuming all of the studies are of equal quality, because that's not always the case, but let's assume they are -- you give the greatest weight to the human *in vivo* observations, then the laboratory *in vivo* observations, then the human cells, then the animal cells, then the wildlife. That would be my own personal metric, but I think that was pretty much shared scientifically by most others.

Finally, again saying the same thing I had said about the same tumors in humans, seeing a plausible mechanism strengthens causality. Failure to see a mechanism does not negate other positive findings, because we don't know how cancer is caused in every single case; and so you're left wondering about it, but that doesn't -- it shouldn't pull away from causality.

Q. Next slide, please.

What methodology did you follow to reach your opinion in this case that glyphosate is gene toxic?

A. This is different than what I did with the animal studies. First, I did the same thing. I evaluated the quality of all of the studies. That you have to do. And there, you're looking at the duration of the studies, the timing of the exposure versus when you take an observation.

If there's cell killing in the *in vitro* studies, because cell killing can cause all kinds of things, like DNA damage and oxidative stress, independent of the mechanism we're looking at for the chemical.

The type of assay used. Some assays are better than others, et cetera.

I didn't do data analysis here, because I don't have access to the raw a data in any way, shape, or form. I've got some of it, but not all of it. So instead, what I did was take what the authors of the papers had done, in terms of giving me p-values and evaluations and things like that, and I evaluated their analysis and their conclusions presented by the author.

One thing I will say. Many of these authors did pairwise comparisons. They didn't do trend tests. So they're not using the strongest statistical methodology they could be using. There's nothing I can do about that. I gave greater weight to what I will call challenge assays.

So suppose you have a compound like glyphosate which is

inducing oxidative stress, and you see that. You can put antioxidants in, and it goes away. And that's -- that's stronger evidence because now you've blocked the effect, the effect itself.

And then I did in-depth scientific exploration of the findings by reading other materials and looking at other stuff.

Q. Okay, you can go to the next slide, please.

Just very briefly, are these the studies that you looked at, about DNA damage in humans?

A. Yes. We've seen these already. These are the three studies on DNA damage in humans that were done in Central and South America. Two of them are clearly positive. One of them is -- arguably may be positive; maybe not.

But that's -- that's the evidence in humans directly.

Q. So unless the Court has questions about those, I'd like to go to the forest plot, which is the next slide, and have you explain what this forest plot is, in connection with the genotoxicity of glyphosate.

A. Yes. So you've seen that analyses for epi data. You've seen forest plots for the epi data.

What Ghisi did here, what they did here was they extracted all of the data on micronucleus frequency. So that's a type of assay that's done, and it's one of the more common assays. It's generally provided by the company to the regulatory authority, to seek approval for the -- for the chemical.

So here, what you see is all of it plotted out for you to look at it. And what I'm pointing out here, with the little red arrows, is what the results of the meta-analysis are. So this is just a forest plot.

If you look at only the regulatory studies, the finding is statistically significant. If you look at all of the studies with pure glyphosate, the finding is statistically significant. If you look at all of the peer-reviewed studies, it's significant. If you only look at mammals, it's significant, and if you look at all of them together, it's significant.

So this is one way of quickly giving you a feel for what all of this data could look like. I didn't have to do this. They did it for me.

Q. If you go to the next slide, please, I think you've already covered this generally, about the *in vitro* mechanism studies. Is there anything you want to add to what you've already testified about?

A. No.

Q. Okay. So Dr. Portier, what do you conclude about the genotoxicity of glyphosate, based on the evidence in this case?

A. Glyphosate is genotoxic. It causes DNA damage, it's clear, in several different assays and several different species of several different types.

The glyphosate formulations also are genotoxic. They do the same thing. And I didn't show it to you, but glyphosate

can also cause oxidative stress. That's in my Expert Report.

Q. Okay. Lastly, Dr. Portier did you apply Bradford-Hill considerations in reaching your opinions in this case?

A. Yes, I did.

Q. So, good. So can you please explain, briefly, how you applied Bradford Hill and your conclusions based on Bradford Hill?

A. I wrote the entire expert report around Bradford-Hill. So I looked at consistency. It's strong. This is the epi data alone. Using multiple studies, most are positive. There's a positive meta-analysis, and the new Agricultural Health Study has such low power, it's fatally flawed.

Looking at the strength of the evidence, I recall it's strong. You have six of seven studies with a modest increase, but a meta-analysis that's positive.

Q. Can you slow down just a little bit, please?

A. Yes. Biological plausibility, I would rate that very strong. You have multiple cancers in multiple species; it's not due to chance. There's rare tumors, and you've got gene toxicity and you've got oxidative stress.

Gradient deals with dose-response. In humans, there's some evidence there. In the animals, it's perfectly clear there is dose-response. I gave that moderate.

Temporality is satisfied. The dose comes before the disease.

Specificity was not needed. NHL has additional causes.

And finally, coherence is strong. This stuff is absorbed. The strong relationship between NHL and malignant lymphomas in the mice gives a strong similarity.

So overall, that would be my evaluation by those considerations.

Q. Thank you, Dr. Portier. Last question: What is your -- next slide, please. I'm sorry.

What is your opinion in this case about whether glyphosate and glyphosate-based formulations cause cancer in humans?

A. To a reasonable degree of scientific certainty, given the human, animal, mechanistic evidence, glyphosate probably causes NHL, and the probability that glyphosate causes NHL is high.

MS. GREENWALD: Okay, thank you.

I have no further questions. Thank you, your Honors.

THE COURT: All right. So Mr. Lasker.

MR. LASKER: Your Honors, I apologize for the size of the binders you're about to receive. Dr. Portier has done a number of analyses and has a number of expert reports with attachments, and I'm going to try and go slowly, so that you guys are always with me through the binders. So if you're not there, I trust you will let me know.

And Dr. Portier, also if you're not finding where I am in to the binders -- and counsel, also, you have the binders, as well. Okay, great.

(Whereupon a document was tendered to the Court.)

CROSS-EXAMINATION

BY MR. LASKER

Q. Good morning, Dr. Portier.

A. Good morning.

Q. Dr. Portier, you reached your opinion that glyphosate can cause NHL during your time as a special advisor at that IARC Working Group meeting in March of 2015. Correct?

A. I've since strengthened it, but I did agree with the IARC finding.

Q. Right, and prior to your work on that working group, you had never looked at the science regarding glyphosate, correct?

A. That's correct.

Q. And you agreed with the IARC Working Group conclusion then -- and, I believe, as you testified yesterday afternoon -- you agree still today that the epidemiological evidence regarding glyphosate and NHL was at the time of the IARC meeting limited and not sufficient by itself to demonstrate causality, correct?

A. At an IARC meeting, you would never say it's sufficient by itself. You would -- you would say the human evidence is sufficient, but you're still going to look at the animal evidence and everything else.

But in this case it's limited evidence, that's correct.

Q. Right, and thank you for the clarification. IARC has a

classification for human evidence of "sufficient," and they have a classification below that for "limited," and in this case, the IARC Working Group decided, based upon the epidemiology that existed, that it was aware of, that the evidence in humans was limited, and you agree with that, correct?

A. Correct.

Q. And you still agree with that today?

A. Yes.

Q. And the IARC Working Group also reached a conclusion with respect to the animal cancer bioassays, and in that area of the -- of the lit- -- of the science, they concluded that the information was sufficient, or, the evidence was sufficient that glyphosate can cause tumors in animals, correct?

A. Correct.

Q. Up until the final day of the Working Group meeting, though, through the work that had happened beforehand in the first, I guess, six days of the meeting, the IARC Animals Sub-group was recommending that IARC conclude that there was only limited evidence of carcinogenicity in rodents, correct?

A. There was -- I don't know. There was a meeting on the fourth day or fifth day, where that is what they said they were thinking of doing; and there was great debate on that.

Q. We discussed this during your deposition, but there was, in fact, a meeting that was scheduled for March 9th, among the

Mechanisms subgroup.

And we can go to this, if you want, to refresh your recollection; but I believe we discussed that as of March 9th, which was the day before the Working Group meeting ended --

A. Okay.

Q. -- the subgroup was recommending that the full Working Group classified that evidence as limited.

Does that refresh your recollection, or not?

A. It does. I do remember the meeting. I thought it was Friday, not on Monday, but yes.

Q. Okay, and you were at the Working Group as a special advisor, so you had a sort of different role. You didn't vote, for example, correct?

A. Correct.

Q. But one of the things that you did do during that meeting was provide some assistance to some of the other Working Group members in statistical analysis that they conducted, correct?

A. No. In evaluating analyses, yes.

Q. Okay. I'm sorry, I misspoke. So they -- I think at one point you said they asked you if you knew where they'd look to find a certain type of statistical test, which is a Cochran-Armitage Trend Test, correct?

A. Correct.

Q. And then afterwards, you checked over their math to see if you agreed with how they did the analysis, is that correct?

A. Well, I didn't have the program myself, so I just looked at what came out, and it seemed appropriate.

Q. Okay, and that -- if we can go to the IARC Monograph.

And this is at Tab 7, your Honors, and it will be -- it's in Volume 1, Tab 7, of the Portier papers. So the -- the monograph, you've all seen this before, and if I could -- I don't know if Judge Petrou has, but the rest of us are familiar.

Turning to page 33, I guess it starts on 32, and then goes to page 33. And this is discussing the Knezevich mouse study the 1983 mouse study that Monsanto conducted, correct?

A. Oh, its always difficult, because --

Q. It might help you, if you go on page 33, you'll see some of the tumor counts, if you'd get familiar with those. So on page 33, you'll see these tumor counts that we've talked about for renal tumors, right?

A. This is Knezevich and Hogan.

Q. Okay, and this analysis on page 33, in that first column on the left, about two-thirds of the way down, which is the renal tubule tumor data, with the P trend's here reported as statistically significant, that is the Cochran-Armitage Trend Test that we were just talking about that the Working Group conducted during that meeting, correct?

A. It's the -- it's the same test, but the p-value is calculated at by an approximation method, based on the normal

distribution grid and the EXACT method.

Q. Correct, and that's the point I was getting at, that you sort of anticipated.

After the meeting, some other biostatisticians pointed out -- and you agreed -- that there were flaws in this analysis, and using the P-trend test, and that the EXACT trend test would have been actually the correct measure to use here, correct?

A. That is correct.

Q. And you'd been using the EXACT trend test in your presentation here today, correct?

A. That's correct.

Q. And under the EXACT trend test, this trend actually is not statistically significant, correct?

A. But there's more in this paragraph that you missed.

Q. I understand that.

A. Okay.

Q. But I am correct that using the EXACT trend test, this is no longer a statistically significant finding, correct?

A. It's a marginally significant finding, by my definition. It's .068.

Q. Okay, and if I could, also, just on that same page, there were two mouse studies that the IARC Working Group considered in reaching their conclusions.

The second is what we've been talking about. It's the

Atkinson Study. It's on the second column of page 33. It's that last paragraph.

And I think, again, looking at hemangiosarcoma numbers, that may help you sort of place that study in the mind. It's that 24-month CD-1 Mouse study, the second paragraph on the right column, final paragraph on the right column.

A. Yes.

Q. Okay, so this is the Atkinson Study, and the IARC Working Group is reporting on hemangiosarcomas in that study.

Now, in your testimony here today and in your report, you also provide the data from that study for renal tumors, correct?

A. Yes. Every time I saw tumors in one CD-1 mice, I did it in the other CD-1 mice.

Q. And in this Atkinson Study, the findings for renal tumors were two tumors in the control, two tumors in the low-dose, zero tumors in their mid-dose, and zero tumors in their high-dose, which you calculated as a significant -- statistically significant inverse trend, correct?

A. I'd have to look at my p-values to make sure.

Q. Okay. Well, let's do that.

This is Tab 22. So this is in the second volume. And when you get to Tab 22, it's going to be page 11, I believe, is where you present -- or, I'm sorry. Hold on, a second.

A. Page 34.

Q. Page 34?

A. Yeah.

Q. Thank you. I tried.

A. Yes. It is a significant negative trend.

Q. All right. So just so the record is clear, this is the same mouse study that IARC looked at, and for the kidney adenomas and carcinomas combined, as you note in your expert report, there was two in the control, two in the low dose, zero in the mid-dose, and zero in the high dose, which is an inverse -- statistically significant inverse trend of less tumors with greater dose of glyphosate; correct?

A. That is correct, but I will point out that the IARC Monograph group did not have the Atkinson kidney tumor data. At least that was -- it was not apparent that they had the kidney tumor data.

And the historical controls, which I point out, for the kidney tumors were very, very low, making those three tumors at the high dose very biologically significant.

So the decision was not just the p-value, it was also the historical controls.

Q. I understand that, and I think you mentioned at that point you'd talked about the fact that, of any study anywhere that you had seen in CD-1 Mouse, you had never seen more than two control animals with this type of tumor.

Was that your testimony?

A. I -- I think it was something along those lines. I can't be certain. Where was I testifying?

Q. That was yesterday, here.

A. I don't recall saying exactly that. That's the best I can say.

Q. But in any event, was it the -- was it the Atkinson Study, which is the second study in the monograph, that one situation where you've ever seen two tumors in a control group?

A. No. I was referring to the historical control databases that I looked at after the IARC Monograph meeting. I looked at several, and in those, there were -- there was one case with two animals in a control population.

Q. Okay, and then --

A. I don't know if it was the Atkinson Study. It might have been.

Q. And then for IARC, they looked at two total mouse studies, and it just happened that one of them had two tumors in the control group. The other --

A. Yes, except IARC didn't see that.

Q. Okay. Now, you signed up --

THE COURT: Sorry, could I ask a follow-up? You said, "Except IARC didn't see that." Why didn't IARC see that?

THE WITNESS: They didn't have that study. That data was not available. IARC was, or -- the Atkinson Study, they were using the write-up on that study from JNPR, the Joint

Meeting on Pesticide Residues of WHO; and so they were unable to know what the counts were, because JNPR only put the positive findings in their report.

BY MR. LASKER

Q. And just to complete the loop on that, I guess, for the Knezevich Study -- and we're still on page 33 in the monograph -- the IARC group did not have the data on hemangiosarcomas from that study either, correct?

A. As far as I remember, yes, that's correct.

Q. And, in fact, in the Knezevich Study there were no hemangiosarcomas found in any of the treated animals, correct?

A. That is correct.

Q. And the IARC Working Group just didn't know that when it did -- when it did their analysis.

A. It probably did not change their analysis.

Q. Well, I'm not -- we can all speculate on what that would have done or would not have done, but the IARC Working Group just didn't know that, correct?

A. Correct.

Q. Okay. So you signed on, or -- you signed an agreement to serve as an expert with plaintiffs in this litigation on March 29th, 2015, correct?

A. Going to be close to that date. Again, I'd have to look to check, but it's very close.

Q. Two to three weeks after you came back from the Working

Group, correct?

A. Yep, something in that range.

Q. And since that time, you've also been involved not only in working as a plaintiffs' expert, but in presenting your opinions in various regulatory proceedings and before various regulatory agencies about your views about glyphosate and non-Hodgkin's lymphoma and cancer, correct?

A. No. Mostly I am presenting my views about the analyses they'd done, and the faults with their analyses, not my argument or view that says glyphosate causes cancer.

Q. Okay. Well, we have -- if we can go to -- and I apologize -- tab 13, which was your original expert report in this case, and -- sorry, I'll wait until you get there. Sorry. That's Volume 2.

A. Um-hum.

Q. It's got Tabs A. B.

A. There it is. It's the first one.

Q. Whatever, yeah. So that's why it gets a little confusing.

And I actually want to go to these tabs. These tabs are appendices that you attached to your initial expert report, and it includes various submissions that you made, I think, either to the European regulators or to the U.S. EPA, if I have that correct. But correct me if I'm wrong.

A. Some of them are.

Q. Okay, and if we can look, for example, at tab B, this is a

submission that you provided to the U.S. EPA, and this was in connection with EPA's and the OPP's analysis -- that was hard, sorry -- office of Pesticide Programs, I believe.

A. Yes.

Q. Okay, and so this is a submission that you made to EPA in connection with their review of the OPP report on glyphosate, correct?

A. That is correct.

Q. And the EPA OPP has subsequently finalized its review, and that was just, well, more recently, in, I believe, the end of 2017, correct?

A. No, EPA's current report is out for public comment for the next 60 days, and then they will finalize it.

Q. Thank you, I stand corrected.

And you submitted -- this was a guess -- a year and a half after you had been retained as a plaintiffs' expert in this litigation, correct? That was October 4th, 2016?

A. Yes.

Q. But as you state in your disclaimer here, you were submitting this report on your own behalf. You were not submitting it as a plaintiffs' expert. Correct?

A. That is correct.

Q. Okay. and so the EPA had the benefit of your analysis as an independent scientist and your review of this data, correct?

A. That's correct.

Q. And over the course of your work -- and we're going to go through some of these different analyses that you provided at different times -- you have provided a variety of different pools of -- pooling of data?

JUDGE PETROU: I just want to interrupt for one second. You mentioned that the EPA report is currently out for public comment, is that correct?

THE WITNESS: Correct.

JUDGE PETROU: When do you expect there to be a final EPA report?

THE WITNESS: That's a --

JUDGE PETROU: Best guess --

MR. LASKER: Now we'll test your expertise.

THE WITNESS: My guess is it will probably be out there in the summer.

THE COURT: Wanna bet?

BY MR. LASKER

Q. So, Dr. Portier, in the various submissions -- and we can walk through some of these -- and, in fact, we can start with the same tab. We're on tab B.

If you go to page, I think -- let me see one second, here -- for example, tab -- page 19 in that same document we're looking at, initial Expert Report.

You provide here a pooled analysis of male hemangiosarcomas. Do you see that Table 7 on top of that page?

A. Yes, I do.

Q. Now the pooling methodology that you used in this submission is not the pooling methodology that you -- well, it was presented to the Court in this case, correct?

A. No. The -- the pooled analysis with all of the four CD-1 mice, that is the simple pooling. This is the same for that first column, for the first number and P trend. The P for that was also approximated, because I didn't have an EXACT program for doing an EXACT, I since have, but that is the same analysis. The rest are somewhat different.

Q. Hm. So one of the things that you did in -- at one point in your pooling is -- and I think you talked earlier a little bit about the Poly-3 Test, which is trying to adjust for different lengths of survival in individual animals, correct?

A. Correct.

Q. And at one point in your analysis, in your submissions to various regulatory agencies, you attempted to use that Poly-3 Test to equalize the length of the 18-month and 24-month studies, and pool them using that Poly-3 analysis that you came up with, right?

A. That is correct, but I was criticized for that, and I looked at it and I said, well, I don't really need to do this. I can do this analysis without having to do that adjustment. And so I just got rid of it.

Q. Okay, and another thing that you did is you did pooling,

and then you dropped any findings where the dose was greater than a thousand milligrams per kilogram, and that's -- you have that listed in your Table 7-2, correct?

A. Yes, that is because EPA was saying that there was no positive trend below a thousand mg/kd/day, and I simply demonstrated for them that there was.

Q. And I also, I believe -- and I was trying to follow this as it was going on, kind of complicated, but you also combined doses to do pooling based not on sort of simple, just put them all in and pretend it's one test, but to categorize doses in various categories.

And I think you had zero being a control, which is obvious, and then zero to 10 mg/kg -- milligrams per kilogram, 10 milligrams per kilogram to 1500 milligrams per kilogram, and then anything above 1500 milligrams per kilograms.

And you grouped the studies that way, and did pooling analysis using that approach, correct?

A. That approach was used more for graphical purposes, so that I could put the plots that generally showed the trend. I did the analysis just for completeness. But I didn't really use that.

Q. Okay, but we have -- and maybe you can go to tab C, because this is a little bit clearer. I don't know which submission this was, to which agency, but this is a different -- a different one. Maybe this is a different -- a

presentation.

Do you remember where this was -- where you were using this PowerPoint? I don't know that it matters.

If you go to -- and if your Honors are with me, Figures -- the last two pages in this tab 3 PowerPoint, Figures 7 and Figures 8.

This is sort of that graphical demonstration that I was talking about. You have a Poly-3 adjustment, which is, now you're trying put these 18-month and 24-month studies together with the Poly-3 adjustment --

THE COURT: Wait, I'm not sure I'm with you.

MR. LASKER: Okay.

THE COURT: So you're talking about tab C to his initial expert report?

MR. LASKER: Yes. It's the second volume.

THE COURT: Okay.

MR. LASKER: And tab 13, and tab C.

THE COURT: Okay, and then what?

MR. LASKER: It's the last two pages. They're not numbered. And it kind of -- oh, maybe I have it. No mine's probably wrong, because I have Table 9 and Figure 7, but it's the Figure 7 which says hemangiosarcomas in male CD-1 Mice.

Do you have that?

THE COURT: Yeah.

BY MR. LASKER:

Q. So that page, and then the next page, are your depictions of your methodology then which included that Poly-3 adjustment at the time, and also was grouping them into different dose groups.

And then I think the Figure 8 shows, again, you combining them in to those dose groups, correct?

A. So first of all, this was not an appendix of my expert report, which is what you started with. This was a slide I sent you when you asked for copies of everything, but I don't recall having this as an appendix of my expert report.

Q. Well, I'll just represent, and I don't know if you were aware of this or not, this was submitted to us as your expert report, with all of these documents attached. This was document 3 to your expert report.

A. I didn't know that. I don't have a problem with it. This is not showing my analysis. This is just showing the data.

And the second one, as I mentioned, is simply a graphical tool to let you see the trend better. It's hard to see the trend in Figure 7, but you can clearly see it in Figure 8.

The p-values from the statistical analyses are the ones from Figure 7, and it's highly statistically significant. I didn't think anyone could see that from this plot. Hence, I did the second plot.

Q. Okay, and then if we go to tab E, there's another

attachment. Again, I'm not sure when this was presented, or where.

But if Your Honors are with me...?

JUDGE PETROU: Where on tab E?

MR. LASKER: I was waiting to get to tab E.

Q. So this, now, is Table 7, and here you have, again, a variety of different pooling approaches that you used, and one thing you were doing here was you were also pooling the studies for the CD-1 mice and the Swiss mouse, which is that fifth mouse study, and you also did analysis where you pooled that data together, correct?

A. That is correct.

Q. And that's not the methodology, either, that you wrote the pooling analysis you presented to this court, correct?

A. That's correct. I've since then changed my mind and decided that I was not going to pool different strains of rats and mice.

Q. Okay, and one other thing that you've done -- which I think is another tab, unfortunately, if you don't recall -- but you also at one point were doing your P trend analysis using -- I think you still are -- using the EXACT test, but then you also did some P trends using the asymptotic test, you started doing that if there was more than 10 tumors, I think, in the finding. Is that -- does that refresh your recollection?

A. It's -- it might have been 10 or 15 --

Q. Okay.

A. -- but the asymptotic converges the p-value for the EXACT, once you get that high, and running more than 10 takes a tremendous amount of time on my computer.

Q. Okay.

A. These analyses were not done for the expert report.

Q. No, I understand that. I understand that.

A. The expert report was asking me to do something else than what I was doing in my response to EPA.

Q. I understand. I understand.

A. Okay.

Q. I'm not quibbling with you on that. And you have -- and to be fair to you, I think, there's no standard methodology for doing what you're doing in this case, correct, the way of pooling animal studies?

There's lots of different ways you can do this, and you've tried out a lot of different ways of doing this over the last, um, two and a half years, correct?

A. There -- there are certainly ways to pool information and do an analysis. It has never been done for -- well, that's not true. It has been done for animal cancer studies that I'm aware of in two cases, where they used the simple pooling I used as well. But it's not typical to have this many animal studies, so I had to do something to try to bring that together.

Q. Okay.

A. But it's a standard procedure that I've used.

Q. Okay, and I think the two times that you talked about where you found, other than your pooling in this case, where there's been pooling of animal studies, that was by Dr. Dourson, is that correct?

A. That's correct.

Q. And what he did, what is actually different than what you're doing also, is he pooled the male and the female rodents within an individual study, correct?

A. He had two papers. I think one was a cross-study and one was within an individual study.

Q. And he was pooling the male and the female rodents, correct?

A. I think with the cross-study, he pooled males and males and males and females.

Q. So that's another approach that one person took in these two papers.

A. Yes.

Q. Okay, and all of these submissions -- I don't know that I've captured all of them, because I know that you've continued to present to various regulatory agencies.

Have you -- well, first of all, all of these presentations that we've talked about and the different pooling approaches that you used in other submissions were presented and given to

the EPA, for example, correct?

A. You -- you have my submission to EPA.

Q. Okay, and you also submitted your -- those pooling analyses or those prior pooling analyses to the European regulators, correct?

A. I submitted -- I didn't submit to them the pooling information. I gave a presentation before the European Chemical Agency Risk Assessment Review Group, and in that presentation, I discussed pooling.

Q. Okay, and was that the same pooling methodologies or one of the pooling methodologies we've looked at, or was that the methodology that you were presenting in this case, or was that is different methodology?

A. It may have been one of these slide sets. It's the same basic methodology.

Q. Okay, and the EPA and the European regulators have seen your -- at least they have some of your pooling approaches, and they've considered that in their analyses, but they concluded, contrary to you, that glyphosate did not cause cancer in those animals, correct?

A. That is not correct.

Q. The EPA in its OPP report has -- which the Court has and has read -- concluded that the evidence did not show that glyphosate caused cancer in animals, correct?

A. That is correct. Your previous statement included them

doing pooling, which was not correct.

Q. Right, and I understand, in fact, you're the only one anywhere, despite all of the folks -- and there have been lots of folks who have been looking at this data over the years, around the world -- you're the only one anywhere who's done a pooling analysis, correct?

A. So first of all, EPA's Science Advisory Panel told them to do a pooled analysis of the glyphosate data. That is in their report from the review they did of glyphosate. They highlighted my pooling to suggest this is something EPA wants to do.

So in answer to your question, I might be the only one who's done it, but it has been recommended by others.

Q. To be fair -- and we're not going to be able to get into the SAP, that's the Science Advisory Panel. I was there, lots of folks were there. There were a number of people on that panel. There were a number of biostatisticians. I think your brother actually, as it happens, was on that panel.

The biostatisticians on the panel did not recommend that EPA use your pooling approach, did they?

A. I'd have to look at the report. They recommended EPA use a pooling approach. They didn't say --

Q. Well --

A. -- it should be mine.

Q. Well, we'll have to just leave it at that, because that's

another tab in another binder. I'm not going to be able to do that here today.

But I believe you testified this morning, based upon your pooling analyses, that, "to me, it is so obvious that glyphosate causes cancer, in animals" -- I think that was your testimony earlier, correct?

A. No.

Q. Okay. Maybe I misunderstood it.

A. Again --

Q. It's not obvious to you?

A. You're arguing -- your arguing two things there. One is that I reached the decision based upon pooling; that is incorrect. And the second is my decision; that is correct.

Q. Okay. So is it, then, your testimony that from your pooling analysis, it is not obvious that glyphosate causes tumors in animals?

A. The evaluation of animal carcinogenicity data goes beyond statistical p-values, and so my conclusion on glyphosate is due to all of the information that's available for me to look at. The pooling analysis is part of making that decision.

Q. I understand that, but I was just trying to parse it out a bit.

Is it your opinion, based -- it was only the pooling analysis, wouldn't you think, based only on the pooling analysis, that that shows that glyphosate causes tumors in

animals?
A. I can't do that. You're asking me to separate all of my knowledge that I've used in evaluating this, and just go to one little piece of it, and I'm not going to do that.
Q. Okay. So the pooling analysis, then, is just one little piece of your opinion?
A. It's part of the analysis and evaluation of the data, yes.
Q. And if that was all you had, you would not be able to opine even that glyphosate causes cancer in rodents, is that fair?
A. This -- if that was all I had, then I wouldn't be analyzing or evaluating these data, because then I wouldn't know about all of the quality issues of the studies, and that -- the fact that you've got matches across various sexes and species of the different types of tumors. That all plays a role.
Q. Okay, I understand that, and I respect you have all of these other things that you're talking about, but if somebody else was looking at this, another scientist was looking at this, and let's say you were that other scientist and all you were presented was this pooling analysis, am I correct in my understanding that that would not be enough for you to reach a conclusion that glyphosate can cause cancer in rodents?
A. Not me, no.
Q. Okay. To be clear, so it would not be enough for you; is

that correct?

A. If all someone gave me were a bunch of tumor names and some pooled p-values, and nothing else, that would definitely not be enough for me to say glyphosate causes cancer.

Q. Okay. The -- you also mentioned in your testimony the fact -- I think this was yesterday afternoon -- that the data that you had to look at on the animal studies was incomplete because you did not have the full reports, except for the three studies by Monsanto.

There are, I think, 12 -- no -- of the -- I guess there would be nine other rodent studies that were conducted by other companies. And you don't have those full reports, correct?

A. That is correct.

Q. And you explained how that was -- that made it difficult for you to do your analysis, correct?

A. It makes it difficult for me to judge the quality of the study. It makes it difficult for me to verify that the regulatory agencies, with regard to things like survival, and stuff, got that right. It's very difficult to judge that, and it makes it impossible for me to do a survival-adjusted test.

Q. Now, the regulators at EPA and the regulators in Europe, the regulators in other countries in the world that have looked at this data, they actually have those full reports, those full animal study reports for all 12 of the studies you've been talking about, correct?

A. I assume they do. I can't be certain of that.

Q. Okay. So in their analysis, they have the ability to be able to do the type of thorough review of the animal data that you just are not in a position to do, correct?

A. That's not correct. They did not analyze the data. The European Food Safety....

I can walk you through the way in which they do their evaluation, Your Honor, if you'd like to know; but they don't analyze the data.

Q. Okay. Well, I don't want to get into a debate about your view of what they did or they didn't do. My question was --

A. No, it's not my view -- I'm sorry, it's not my view. They state it in their document, that they did not re-analyze the data. It's not my view.

Q. Dr. Portier, they had in their possession the full study reports and all of the data that you did not have. They had that in their possession, correct?

A. I assume they did.

Q. And the scientists at those agencies had the opportunity to review those data, correct?

A. They had the opportunity to look at it.

Q. And you were in Europe during your conversations with various -- and you've also -- I think you talked with some of the European Union ministers at various points in time, is that correct?

A. I spoke with the Minister of Health of the European Union.
Q. Okay, and there was a point in time -- and I'm not sure if you're that aware of it or not -- where there was a Reading Room created in Europe. Are you familiar with that?
A. Yes, I am.
Q. Okay, and they put into that Reading Room the full -- or, not the full, but -- additional information about these animal studies, correct?
A. I -- I don't know. I didn't go.
Q. Okay, but it was available for anyone?
A. That's what they claimed.
Q. Okay, it was available for anyone to go. If you wanted to go, you could have.
A. No. There were rules associated with going into that room. You had to be invited, so you had to petition to go in. There were a whole set of rules I'd looked at it, and I decided that the rules made it impossible to use it appropriately.
Q. Okay. So it's your understanding -- was it your understanding that you can't do anything more than just ask if you could go and sign your name and go?
A. You had to ask every day. If -- if you'd like to get the rules, then I'll be happy to comment on why I did not take them up on that.
Q. Okay. No, that's fine.
A. But just to be clear -- okay? -- we're looking -- if I'm

looking at individual animal data from these studies, I'm looking at 50,000 pieces of information; and being able to go in to a reading room four hours a day and try to extract that information would have been a ridiculous task for -- with 50,000 data points.

Q. There's a lot of data regulators have, isn't there?

A. There's a lot of data that the regulators have not looked at.

Q. Again, I'll just -- I have no way to argue with you about what other people did, so I won't try to do that.

The -- and so what we have -- just to recap, you had reached your opinion that glyphosate caused cancer in March of 2015, when you were at that Working Group meeting, correct?

A. I agreed with the IARC decision.

Q. Okay, and since that time, you've done a whole variety of different analyses that have changed over time, and ultimately, you have an opinion analysis that you presented in this case to support that -- that finding that you have, that glyphosate causes cancer, correct?

A. There's too many things in that question for me to be able to answer it.

Q. I'm happy to try and reword it, then.

You reached your opinion in March of 2015 that glyphosate can cause cancer, correct?

A. I agree with the IARC decision.

Q. And since that -- well, maybe that's -- maybe that's what's holding us up. Was IARC's decision that glyphosate can cause cancer -- maybe I'm wording that incorrectly. Let me rephrase that.

Did you reach an opinion in March of 2015 that glyphosate can cause cancer in humans?

A. I've said it before. I agreed with the IARC decision, which was, it's a probable human carcinogen, by their definition.

Q. Okay so that you're making a distinction. Maybe it's a distinction with a meaning, maybe it's not. I don't understand.

Is it your understanding that IARC reached a conclusion that glyphosate can cause cancer in humans?

A. IARC reached the conclusion that glyphosate is a probable human carcinogen.

THE COURT: So I'd be curious -- it sounds like you think there's a difference between those two things, and I'd be very curious to hear your explanation of that.

THE WITNESS: So first of all, for the IARC meeting, I didn't have to reach a decision, because I was not allowed to reach a decision.

So I made my decision in March of that year, and that I'm now carrying through here is not a fair characterization; and I'm trying to make that distinction, but the IARC has very

clear classification criteria, and those -- they stick to it very carefully.

I didn't use their classification criteria here. I used straightforward Bradford Hill.

So I don't want to convolute the two, if -- if I have to, because they're not the same.

THE COURT: So that's what I would be interested in hearing more from you about.

Mr. Lasker was asking you about the issue of whether glyphosate can cause cancer in humans, and then you seemed to draw a distinction between that concept and IARC's conclusion that it's a probable carcinogen.

And so what I'm interested in hearing from you is: What distinction do you draw between those two formulations, if you will?

THE WITNESS: So when IARC reviewed it, they didn't have all of the M.R. data, and I spent a lot of time, for a year and a half, at my own expense, analyzing all of that animal data that was there, that was becoming available for people to look at.

So my opinion was changing over time, as I looked at more and more of these studies. And so -- and in essence, it's --

THE COURT: I get that, I get that, but what I'm asking is probably a more simplistic question than you think I'm asking.

THE WITNESS: Okay.

THE COURT: You seem to draw a distinction between the statement glyphosate can cause cancer in humans, or glyphosate can cause NHL in humans on the one hand, and glyphosate is a probable carcinogen on the other hand.

You seem to be either drawing a distinction between those two things, or at least resisting conflating those two things, and I want to hear from you, just conceptually, why -- why that is.

THE WITNESS: So the wording, "Glyphosate can cause cancer" is inaccurate. There are three categories at IARC that potentially could say the same thing: A known human carcinogen, that means it can cause cancer; a probable human carcinogen cause cancer, a possible human carcinogen can cause cancer.

So I don't like the wording with regard to an opinion on causality that was reached by IARC that I'm agreeing to. It's not that it can cause cancer. It is that it is a probable human carcinogen with a specific classification. It's not known, and it's not possible.

That's the distinction. Maybe I'm being too picky, but --

THE COURT: Well, no. So what you're saying is not that it -- that the IARC conclusion is that it probably can cause cancer. Is that right?

THE WITNESS: Correct.

THE COURT: Is that what you're saying?

So you're -- you want to -- your concern is that you don't want to overstate the IARC's conclusion? Is that it?

THE WITNESS: Or understate it, that is correct.

THE COURT: Okay, I appreciate that. Thanks.

BY MR. LASKER

Q. And just so I'm clear, maybe I don't understand the distinction, you mentioned that you have done a lot of analyses since March 2015, at your own expense, of all of this data.

And you obviously have also been doing this for plaintiffs' counsel, and you've been retained and paid money starting in March of 2015, and throughout. We have your invoices from plaintiffs' counsel also for analyses of that data.

Is it that sometimes you did work and you didn't bill the plaintiffs' counsel, and sometimes you did work and you did bill the plaintiffs' counsel?

A. Absolutely not. The plaintiffs' counsel asked me to serve as an expert witness in January of last year. At that point, I re-analyzed all of the data as carefully as I possibly could. Before, I was just commenting on regulatory responses.

So the consequences of me making a slight error are -- or a missed calculation is completely different than this setting.

So until that point, they had not asked me to analyze any data. They had simply been using me as for -- for expert

comment.

Q. Well, and I hadn't intended on going through this, although I do have one slide I guess I could go back to, but you did -- and we talked about this in your deposition -- bill the plaintiffs' counsel I think about $8,500 in June of 2016 for reviewing the EPA's Cancer Assessment Review Committee report, correct?

A. That's correct.

Q. Okay, and so there are some things you were doing during that period and that you were doing on behalf of the plaintiffs' counsel, and you were billing for; and then there are other things you were doing that you viewed as being independent of your work for plaintiffs' counsel that you were not billing for; is that fair?

A. You -- your question was about analysis of data, and that's not what I did with the CARC document. It was simply, provide an expert opinion, and I am answering to the analysis of data business. They did not pay me to analyze data until January of last year.

Q. Okay, and although you were retained in March of 2015, did you understand at any point in time that the analyses that you were doing would be part of what you were doing in this case, or did you view that as entirely separate?

A. I viewed it as entirely separate.

Q. Okay. Trying to get back to where I was in my outline,

here.

So I want to try to go through what you're doing in this case now with your pooling analysis, and I know you provided some slides, and I had a little bit of an advantage because I've been looking at these for a long period of time, but I was trying to come up with a different way, also, to look at these.

And so I'd like to walk you through, if we can, and first of all, with respect to your opinions in this case, as late as December of -- I think it was -- let me make sure I have this correct -- I think it was December of 2016, yes -- you were of the opinion that glyphosate was not positive for carcinogenicity in the rats. Correct?

A. I'm sorry, say that again.

Q. As late as December of 2016 -- and I think this was, now, 21 months or so after you signed on as a plaintiffs' expert, and after the IARC Monograph -- it was your view that the animal studies did not know that glyphosate caused tumors in rats, correct?

A. No. I don't recall that. It was my opinion that less than positive findings in individual rat studies.

Q. Okay. Let's go to -- we were there. It's tab 13, which is, again, is your original Expert Report. And now we are at tab I. We haven't gotten to tab I yet, have we?

And, your Honors, let me know when you're there.

THE COURT: We're there.

MR. LASKER: Okay.

Q. And these are some major points you were making in response to some criticisms I think you mentioned that you received from your first submission to EPA.

And in paragraph 2, you're talking about analysis across the studies, and this is --

THE COURT: Is this -- sorry, is this paragraph 2 under Major Points or Minor Points?

MR. LASKER: Yes, starting Dr. Haseman's analysis of p-values.

THE COURT: Okay.

BY MR. LASKER

Q. And this is -- and we'll get to this a bit later on. This is that sort of analysis of multiple comparisons that you presented this morning about looking at what you'd expect and what you'd observed when you look at all of the data and try to figure out, given that there are hundreds of different studies here, and you have a 1 in 20 chance of a hit, this is talking about that type of analysis, correct?

THE COURT: I didn't really understand that question.

MR. LASKER: Yeah, I know.

THE COURT: Why don't we take a short break.

MR. LASKER: Okay.

THE COURT: Why don't we take our morning break and resume again at 9:30.

MR. LASKER: I'm trying, your Honor.

(Recess taken from 9:20 a..m. until 9:30 a.m.)

THE COURT: Mr. Lasker, can I have a very quick sidebar with you?

MR. LASKER: Sure.

(Sidebar conference heard but not reported.)

THE COURT: It was just a follow-up question for Mr. Lasker about the medical issue that he raised earlier with his team.

BY MR. LASKER

Q. Doctor -- sorry. Dr. Portier, over the break, did you have an opportunity to review -- and I guess I'll make sure everybody's back where we were.

We were at Exhibit 9 to your Expert Report, so tab -- at least I'll get myself back to where we were -- tab 13, and Exhibit 9, otherwise known as I, document 9. And we were at that second paragraph, under Major points.

And have you had a chance over the break to review that?

A. Yes, I have.

Q. Okay, and so at that time -- and this is the last sentence of that paragraph. You stated in your comments that were submitted to EPA, if you ask the question, is glyphosate positive in mice, the answer is yes, whereas the answer in rats is probably no. Correct?

A. That's what I says. That's sloppy language on my part,

because that's not what I was talking about. I don't believe that. That is clearly an incorrect statement.

That whole evaluation was talking about whether all of the tumors seen in the rats occurred by chance, and whether all of the tumors seen in the mice occurred by chance, and what I should have said was, the chance -- the probability that all of the tumors occurred in mice is virtually zero, and it's possible, at that time, that all of the results in the rats could have disappeared, but since that time, your expert found six additional tumors in the rat studies, and that changed that probability.

Q. Okay. Well, first of all, I want to take that in parts. If you could, turn to tab 14 in your binder. It's the very next tab. And this -- this is -- it's somewhat earlier.

This was at least some e-mail that I assume you didn't send to yourself, but you sent to somebody. This is talking about that Horizons -- that article, or that pro/con piece that you were talking about that you submitted with respect to your views of the EFSA, regulatory -- EFSA regulatory decision that glyphosate does not cause cancer, you were on the yes side; and then Jose Tarson was on the no side, correct?

A. Correct, we did pro/con.

Q. And on your statement on pro, if I could direct you to the second column, and about midway through right above the -- sort of the call-out, there is the line that you wrote then, with --

I guess it's five lines up from the call-out, "With the exception....."

Are your Honors with me?

THE COURT: Yeah.

THE WITNESS: Yes, I'm seeing it.

BY MR. LASKER:

Q. "With the exception of growth in a few non-malignant tumors, none of the rat studies showed any effect," correct?

A. That's based on the IARC Monograph. This whole discussion is based upon what was seen in the IARC Monograph, in which they only had two non-malignant rat tumors.

Q. And you, at this time, again had been -- I guess now it's only about a year in, since you had signed on as a -- with a law firm that's an expert in solvents in this case, correct? This --

A. I don't know what the date of this --

Q. Well, I'm judging by the e-mail. The e-mail says March 2016.

A. Yeah, I don't know when the Horizons piece was done and taken out, but I would probably say yeah, I probably was.

Q. Okay, and if we can -- and I apologize. You have slide 32, which was in your presentation, and let's put that on the screen?

MS. ROBERTSON: Sure, he's working on it. He'll have it open.

MS. GREENWALD: If you want any of those slides, just tell us.

MR. LASKER: I just did.

Q. So slide 32 is your current understanding of the findings in rats; and we may talk a little bit more about this table later, but when you did all of these analyses of the different tumors, and when you look at them -- first of all, when you look at all rats, of both sexes, for that p-value of .05, which is the p-value that most people have been talking about the most at this time during this proceeding, you did not find any statistically significant difference between what you'd expect to see by chance, and what, in fact, was observed for rats in all of these studies, correct?

A. Not correct.

Q. Oh, well, I'm sorry. I'm looking at your table, here, and maybe I'm misreading it, for all rats, both sexes, male and female, you have 291 sites; 14.5 expected, because that's one of 20, right? That's the math? That seems to be the correct math, right? And then 16 observed, and your probability is .385, correct?

A. Where?

Q. I'm sorry, the bottom row.

A. Oh, for the P .05.

Q. Yes.

A. Yes.

Q. So for all rats, both sexes, all of the studies looking at all of the tumors that you found up until this point in time, you would expect by chance to see 14.5. You saw 16, and that's clearly not a statistically significant difference, correct?

A. That's for P .05.

Q. Okay, so you've also done a p-value of .01, I understand that, and when you did that analysis, you found a more a little bit of a difference.

And you report that as .074, but again at least as we've been understanding from the other experts who have testified, that is not a statistically significant difference, either.

A. You're confusing a probability calculation with a statistical test. This is not a statistical test. This is a probability calculation. What is the probability that I would see six positive tumors in this dataset? And that probability is .074.

That means -- what that actually means is it's a -- it's a 1 in 18 chance that all -- in the last line -- all six observations arose by chance, and in my opinion, that's not a statistical test, and in my opinion that's very unlikely.

Q. Okay, and just to be fair, obviously, there are lots of different probabilities with different counts, and some of them are higher and some of them are lower, and that's all reflected in the various numbers that you have on this table, correct?

A. Correct, but my conclusion only dealt with male

Sprague-Dawley rats.

Q. Okay, that's fine. So let's -- I want to try and -- and you can take that down. Thank you very much. I want to try, if we can, to -- well, yeah. I want to try, if we can, to walk through some of the pooling you presented in this case. And I'm trying to come up with a way -- and hopefully I have -- of sort of walking that with you.

And I'd like to talk about the Sprague-Dawley rats.

A. I didn't hear you.

Q. I'm sorry, I'm going to try and go through the Sprague-Dawley rats from your pooling.

And if I can put up slide 161, please. Or if you could. Thank you. And we'll wait until we're in range.

Okay, and these are the four different Sprague-Dawley rats studies that you considered. There's the Lankas study, the Atkinson study, the Stout and Ruecker study, and the Enemoto study, and I Just want to walk through some of your analyses here that you presented in your expert report.

So let's start with tab 22, your Honors, and it's in binder two.

And this is Dr. Portier's rebuttal report, and in particular, what we talk about what's on page 6, which is -- and the first full paragraph, which starts,

"Returning to Table 2, after pooling all the data for adrenal cortical

carcinomas for female Sprague-Dawley rats."

Do you see that?

A. Yes.

MR. LASKER: Your Honors are with me?

THE WITNESS: Yes.

BY MR. LASKER

Q. So when you -- as I'm reading this, when you did your logistic regression analysis pooling all four of these studies together, you got a p-value of .984, and the way that works -- that is -- is statistically significant in the inverse direction, correct?

A. That's correct.

Q. Okay. So if we just put that up. Pooling all four of these slides together, you'd actually have a protective effect, although nobody actually would submit that to any regulators as proof that glyphosate is protective against adrenal cortical tumors, correct?

A. Correct.

Q. Okay, but what you did -- and you describe this in, again, on page 6, and you talked a little bit about that in your direct -- is you decided to take out the Lankas study because that's a 26-month study, correct?

A. That's correct.

Q. Okay.

A. And that's, in fact, what's driving the negative trend,

because the Lankas study is 26 months. It's control response. It's untreated animal responses so much higher than the 24 months, and when you group them together, it looks like it's going to drop.

If you remember, the Lankas study has very low doses, and so it's got all of these responses way up here (indicating) near the controls, and the others have much lower response because they're 24-month.

So the trend you see at 24 months disappears, because of the big number in Lankas at 26 months.

Q. Okay. I thought I understood that. So just, we'll go to the next slide, and what you did is you dropped Lankas and you pooled the other three studies, and that is what you present in your expert report as the significant trend for adrenal cortical adenomas that cannot be easily discarded, and suggest a potential for glyphosate to affect the adrenal cortical, tumors, correct?

A. I don't know, you've moved in and out of the microphone, I missed some of your question.

Q. I've got too many papers here.

THE COURT: You were also talking pretty fast.

MR. LASKER: I will slow down when I read. Sometimes I stop realizing that. I'm sorry, your Honor.

Q. But it is this analysis that you then rely upon for your conclusion in your expert report, that this -- the significant

trend seen for adrenal cortical adenomas cannot be easily discarded, and suggests a potential for glyphosate to also affect adrenal cortical tumors, correct?

A. That -- the -- that statement is talking about the individual animal data, the individual study data, and the pooling.

Q. Okay.

A. And everything about it that you asked.

Q. Okay. So let's move to kidney adenomas, and unfortunately, we have to go to another tab in our binders, tab 4. This is your amended expert report.

And when your Honors are there, let me know.

JUDGE PETROU: Page...?

MR. LASKER: Page 35 and 36 is where it will start.

BY MR. LASKER

Q. Unfortunately, we will stay with this tab for a while.

And at the bottom of page 35, again, on your -- I think its your amended expert report, we were talking, the final line, the fact that tumor in Sprague-Dawley rats showing a strong significant trend in kidney adenomas in males.

So that's what we're talking about now, kidney adenomas in males, and that sort of screens our next row.

And as you describe in this paragraph in your expert report, when you pooled all four of the studies together, you did not find a statistically significant trend, correct?

A. That is correct.

Q. Okay, so let's put that up on our display. Actually, it's all four of them.

Do we have the next slide? Yes.

So of all four of those together, there was no trend, but again, you described this earlier, because the Lankas study -- you decided, based upon your analysis, to remove that. You did -- you removed Lankas, and then you report a statistically significant trend. Correct?

A. In -- in the pooling --

Q. Yes.

A. -- that is correct.

Q. Right.

A. But again, it's the same thing. Would you like me to explain why you would expect this with a 26-month study versus 24? Okay.

THE COURT: I remember that from yesterday's testimony.

BY MR. LASKER

Q. So let's move on to the next two tumor types, and that's thyroid C-cell tumors and interstitial testicular tumors.

And if we can start with the testicular tumors, that is at page 35, in the same report we were looking at.

So if you just turn back to page 35, and the paragraph here starts,

"Another significant trend seen in Sprague-Dawley rats is the finding of testes interstitial cell tumors from Lankas 1981."

Correct? Are you with me?

A. I'm sorry?

Q. Page 35?

A. Yes.

Q. The full paragraph under the table starts, "Another significant trend seen in Sprague-Dawley rats -- "

A. Correct.

Q. " -- is the finding of testes interstitial cell tumors from Lankas 1981," correct?

A. Correct.

Q. And then you pooled all of the data together; and you did not find an effect, correct?

A. That's correct.

Q. So let's put that up. I think it's, the next one would be all four of them. No effect. Thank you.

Then you state, though,

"However, as noted above, the Lankas study was for 26 months, and the other two were for 24 months. The tumors could be a result of a longer exposure period, even though the dose is substantially lower in

this study, compared to the other three tumors."

Correct?

A. Correct.

Q. So for this tumor type, you are suggesting -- we go to the next slide -- that the Lankas study might be the informative study, because it may have allowed for sufficient time to pass for these tumors to develop, correct?

A. No, I don't know what you mean by, "the informative study."

Q. Well, okay. You were presenting the possibility in your expert report, or you were presenting the suggestion in your expert report that the Lankas study may have identified these tumors because there was sufficient time for them to develop, correct?

A. The Lankas study had a positive finding for testicular interstitial cell tumors. That's non-arguable. Clearly did.

My discussion here was, again, because it's 26 months, it's possible this finding could have occurred in the other studies, if they'd gone 26 months.

So I can't really rule it out totally, but the wording here is very weak.

Q. I understand. I'm just trying --

A. Okay.

Q. I'm just trying to look through this, and I think this is

similar with thyroid C-cell tumors in females. That's at page 34, which is just a page right before where we were.

And it's your second paragraph.

> "In Sprague-Dawley rats, there were four studies that were acceptable for inclusion in evaluation of causality, with one yielding strong positive responses for thyroid C-cell tumors in females, and testicular interstitial tumors and hepatocellular tumors in males, hepatocellular adenomas in males, and another."

And then you turn to the Lankas study again, and its finding for thyroid C-cell carcinoma in female rats, which was a significant finding.

A. I'm not finding this -- the female paragraph.

Q. I'm sorry, it's the first full paragraph on page 34. It starts, "In Sprague-Dawley rats there were four studies...."

A. Yes. Okay.

Q. All right, and if you go five lines into that paragraph it says, "Lankas 1981," in bold?

A. Yes.

Q. "...saw a significant increase in thyroid C-cell carcinomas in female rats." Do you see that?

A. Yes, I saw that.

Q. Okay, and that was statistically significant, for the Lankas study, correct?

A. Yes. That is correct.

Q. Okay, and then going down a few more lines, when you pooled all four of the studies together, you did not find any statistically significant trend?

A. That is correct.

Q. And then you have that same discussion that you had for testes, interstitial testicular tumors, that it may be that because the Lankas study is 26 months, there has been additional time for these tumors to develop, and if those other studies had been for 26 months, they would have seen those tumors as well, correct?

A. Might have seen those tumors, and the last sentence clearly shows you what I thought of this finding.

Q. So it was weak evidence, but it was some.

A. It was weak evidence.

Q. In your opinion.

A. Its weak evidence. That's what it is.

Q. Okay, and then, just to finish with thyroid C-cell tumors, in males -- that's the next paragraph down -- and I'd have to go to a another tab to do this, but the bottom line is that for this tumor, you ended up pooling all four of the studies together in order to reach a statistically significant finding, correct?

A. No. That's a -- that's a -- first of all, I don't pool them to reach a statistically significant finding.

Q. Oh, I didn't mean to say that.

A. I pooled the data to evaluate what will happen with the data. This is a mistake. I should have put both sets of pooling.

Q. Okay, but --

A. That's clearly a mistake, and we can look at my slide and see what happens with both sets of pooling, but here, that's a mistake. I should have put the other pooling.

Q. I'm sorry, what's the other pooling? I'm lost now.

A. Removed Lankas.

Q. Oh, remove Lankas.

A. And pool the remaining three.

Q. For this one you, at least in your expert report, you pooled all four of them, and,

> "From these data, I conclude that there's evidence that glyphosate causes thyroid C-cell tumors in male Sprague-Dawley rats."

A. That's what it says, but I'm telling you, it's a mistake. I should have put the over pooling there, as well. I think I'd still have the same conclusion with the other -- with the three, but I'd have to look.

Q. Okay that's fair enough. And I'm not going to do -- I

have one of these for Wistar rats, but I'm not going to go through that one.

I want to switch, though, to the mice, because we haven't talked about mice yet. And first of all, with respect to the mice studies, you mentioned there were, for the CD-1s, there were those 24-month studies, and then the 18-month studies, correct?

A. Correct.

Q. And when you pooled the data for all of the tumors you looked at, for the 24-month studies, you didn't find actually any statistically significant trends for any of the tumors you looked at, just looking at the 24-month studies, correct?

A. I'm sorry, say that again.

Q. Sure. When you pooled the results from the 24-month studies, you did not find any statistically significant increased trend under your methodology, correct?

A. I'd have to look at my slide to make sure, or -- or somewhere in this.

Q. Well, let me -- I think if we have either -- well, my colleague may be -- let me --

So this is, again, your rebuttal report. What tab is that? Tab 22, thank you.

A. Yep.

Q. Whoops. So if -- if you can go to tab 22 -- are you there?

A. Yeah.

Q. Okay, great, and this is your rebuttal report, and it is at page 11, which is Table 3, sort of summarizes your various pooled analyses for the mice.

And are you with me?

A. I'm with you.

Q. Okay, so you have the pool in the Atkinson and Knezevich studies, as we've discussed. Those are the 24-month mouse studies, correct?

A. That's correct.

Q. And for those mouse studies, when you pooled the 24-month mouse studies, you did not have any statistically significant increased trend for any of the tumors you looked at, correct?

A. I have one marginal increase, and the rest are much bigger.

Q. Okay, and I want to talk about that marginal increase. That is the renal tumors that we were talking about before when we were discussing the IARC Monograph, correct?

A. That is correct.

Q. Okay, and so -- I'd like to sort of -- if we can put up slide -- well, let me set the foundation first. I'm sorry. I want to again put up those numbers before I talked about them, but -- and if you recall, maybe this can shorten this a little bit, those were the two studies. One, the Knezevich study, had one renal tumor in the control, zero in the low dose, one in

the medium dose, and three in the high dose, correct?

A. I believe that's correct.

Q. And the Atkinson Study, as we talked about, had two renal tumors in the control, two in the low dose, zero in the mid-dose, and zero in the high dose, correct?

A. That is correct, but of course, they're different doses.

Q. I understand.

A. All right.

Q. So let me just see if we can put up the slide. I just want to make sure we had that foundation.

So these are the two 24-month studies, and we have this distribution, and I believe, from your calculation, you talked about -- we talked about this previously -- Knezevich was about .065, marginally significant increased trend, and Atkinson was, I think, something like .981, which is a negative -- an inverse trend, statistically significant. Correct?

A. Correct.

Q. Okay, and then through your pooling methodology, you pooled these findings together, and so it's -- you're treating it like it's one study, as I understand it.

So you have two control groups, with one or two tumors in them, and then you have low dose, I think that's the third and fourth block, and two and zero are low dose.

The next two, zero and one, is the mid-dose, and the final zero and three are the high-dose. I understand they're

different doses in the studies, but those are how those tumors distribute among the two studies, correct?

A. No, I mean, the doses are tremendously different.

Q. Oh?

A. The high dose in the Knezevich and Hogan study is more than four times larger than the high dose in the Atkinson Study, and the high dose in the Atkinson study matches the mid-dose in the Knezevich and Hogan study. So you've completely mixed these up, in a different way than they should have been.

Q. Okay, so just so I understand, it is that the high dose, then, in that Knezevich study, 4,840 milligrams per kilogram, is way higher than any of the doses you used in any of the animal studies -- I think, than -- than on that whole dataset we have, correct?

A. It's -- I think it's the biggest, but it's not far from one of the rat study numbers.

Q. And we have had some testimony earlier today -- and I think you also, earlier today, because you referenced it -- as referenced yesterday in Dr. Jameson's testimony, about EPA stating that for its guidelines, 1,000 milligrams per kilogram was the highest dose that they look for in their studies, correct?

A. I don't know what you're asking me to say is correct. That you discussed it?

Q. Well, that's a good point. You are familiar with the fact that -- or, am I correct that EPA, in its guidance documents, states that 1,000 milligrams per kilogram is an appropriate high dose for these types of studies?

A. You're incorrect. That is not what their guidance says.

Q. Okay, and their guidance talks about 1,000 milligrams per kilogram as acceptable high dose?

A. No, their guidance doesn't talk about 1,000-milligram per kilogram. EPA referred to the OECD guidelines, but the OEC guidelines have two problems with them in regard to this particular issue. Number one, those guidelines were issued in 2009, and that's when they came to it from 5 percent in diet to 1,000 milligrams per kilogram per day. The previous guidelines were 5 percent in diet. Every one of these is less than 5 percent in diet. So they all matched the previous OECD Guidelines.

Secondly, EPA's cancer guidelines for doing cancer risk assessment clearly state 5 percent in diet.

Q. Okay, thank you.

A. I will finish by saying the OECD guideline doesn't put it as a strict thousand. They're saying that people who submit to the agency don't have to go higher than a thousand. They're not saying, never go higher than a thousand.

Q. Okay, fair enough. And just to finish up this discussion, through your pooling methodology, when you pooled the

Knezevich study, which was a moderate, or -- it wasn't statistically significant, but it was -- I'm sorry, what's your terminology for this?

A. Marginally significant, by itself --

Q. By itself --

A. -- historical controls.

Q. And the Atkinson study, which is a statistically significant inverse negative study, when you combined those together, you ended up with what you opine in this case is a marginally significant increased trend, correct?

A. Yes.

Q. Okay. I just want to -- so -- and that's how you're pooling analysis works in this case, correct, to be able to provide this sort of data?

A. That's what occurs after the pooling.

Q. Okay, and there is another analysis that you -- that you did, and this is for hemangiosarcomas in male mice, and this is again -- I'm sorry -- tab 4, and it's going to be -- I'm sorry -- on page 48.

And here, you're looking at a hemangiosarcomas. This is the first full paragraph on page 48. It starts, "For hemangiosarcomas in males...." Do you see that?

A. Yes I see it.

Q. And you're talking in the second line there about pooling the 24-month studies, and again you find, as we've just

discussed, there's no trend at all. It's basically flat. Correct?

A. That -- I don't know if it's basically flat.

Q. Well the P trend is about .49. That's almost as close to flat as you can get, right?

A. Yeah, but -- that's fine.

Q. Yeah?

A. There's nothing there.

Q. Okay, and then you point out, though, that the main difference between these two findings is that, again, in that very, very high-dose group in the Knezevich study, there were no tumors found; zero of 50 response in animals exposed at 4,841 milligrams per kilogram per day in the study by Knezevich and Hogan. Correct?

A. That's correct.

Q. And so what you did -- and again, one of your Sensitivity Analyses -- is you just -- you looked to see what would happen if you removed that high-dose group from the Knezevich study. Removing this one exposure group in the pooled 24-month analysis yields a P trend of .001, which is then a positive trend for this tumor, correct?

A. Correct, but I didn't use that in my overall decision. It was -- it was a matter of noticing that this was the case and validating that yes, it was the case.

And this is a very -- this finding is very sensitive to a

single response in a single-dose group.

Q. And that, in fact, also explains how you -- what happened when you did that analysis for the renal tumors, where you combined 1013 and 2200 to get a marginally significant increased tend, is because it was very, very sensitive to those three tumors in that very high-dose group, correct?

A. That -- that finding would probably disappear -- in fact, it would definitely disappear -- because of the high-dose group.

Q. Okay, and we talked a bit about malignant lymphomas in mice, and I'm correct, I believe -- and we have this data, again, we were -- I thought I have Exhibit -- which tab is this Exhibit 1335, the rebuttal report?

MR. KALAS: Tab 22.

MR. LASKER: Tab 22.

Q. You can refresh your recollection, but when you looked at malignant lymphoma in the 24-month mouse studies and you pooled those together, you did not find any statistically significant increased trend for malignant lymphomas in the 24-month studies, correct?

A. That is correct.

Q. And when you pooled all four of the studies together, you got what I think you've defined as a marginally significant finding, correct, for malignant lymphomas? It's on the same table.

A. I don't see -- oh, the pool of all four, down at the bottom. Yeah, marginally significant.

Q. And then, but if you do just the 18-month studies, then you can -- then you are able to get your -- or then you were able to calculate a statistically significant increased trend.

A. When you pool the 18-month study, there is a statistically significant trend. I didn't try to get it. That's what it is, and 18-month and 24-month studies, as I explained yesterday, as -- there's a big difference in time. As the number of animals in the control group go up, it gets noisier, and you cannot find a statistically significant increase like you could at 18 months.

In fact, the argument put forth by industry when they convinced OECD that they could do 18-month mouse studies was that the 24-month mouse studies were too noisy, and the 18-month mouse study would have less in the control, and so the ability to see an increase is enhanced.

That's why they did the 18-month studies as the two most recent studies, and 24-months before, is because OECD changed the guidelines to allow it.

Q. And just on this issue of malignant lymphomas, you cannot cite any source document or any published document that suggests that CD-1 or Swiss albino mice are appropriate mouse models for assessing the potential for a substance to cause non-Hodgkin's lymphoma in humans, correct?

A. Say that again, please.

Q. Sure. You cannot cite any source document, any published document, that suggests that CD-1 or Swiss albino mice are appropriate mouse models for assessing the potential for a substance to cause non-Hodgkin's lymphoma in humans, right?

A. I can cite dozens.

Q. Okay. Well, let's put this up. I'm sorry, slide -- and this is your deposition.

A. Can I -- can I -- I mean, I think --

THE COURT: Hold on a second. Let him do his thing, and then you're free to --

THE WITNESS: Thank you.

THE COURT: -- you're free to respond to his thing.

MR. LASKER: Let me do my thing.

THE COURT: But as you do your thing, the first thing that you need to do is cite the page and line numbers.

BY MR. LASKER:

Q. Here's the full transcript. That's where I'm taking him. So it's Tab 1 in your report. It's your deposition.

A. Okay.

Q. And page 171, line 21 through page 172, line 3.

A. 171.

Q. Are you with me?

A. Yes, I am.

Q. Okay, and I asked you the question at line 21, and you can

read all the way through to the end.

I say,

"QUESTION: No. That's not really a problem with the question. Can you cite to any source document, any published document that suggests that CD-1 or Swiss albino mice are appropriate mouse models for assessing the potential for a substance to cause NHL in humans?"

There was an objection, and then I'll read your full answer.

"ANSWER: No, probably not. I'm hesitating because the problem is OECD says these mice, CD-1 mice, are good mice for studying chemicals for producing cancer, hence that document, in essence, is recommending if you are going to look for cancer -- NHL is a cancer -- then that's the right model. That's why I'm hesitating. That's not what he's talking with about here, but that's why I was hesitating, sorry."

And then I repeat the question. And -- I can continue reading through this for context, if you want.

A. Oh, no, that would be fine.

Q. And if you read through 174, you disagree with me, I keep

asking you, and you state again on line 9, page 173, "I cannot cite a single publication."

Have I been reading that correctly?

A. You have been reading it correctly, and it still holds. I wasn't paying as close attention to your question as I should have been, but it's still the same answer.

NHL is a cancer. CD-1 mice are recommended to use in cancer bioassays to detect cancers.

We've talked about the fact that there is -- that any cancer seen in an animal flags the probability of getting cancer in humans. You want to know about specifically for NHL. And as I was saying earlier, that's not generally something that happens.

Q. Okay. That's fair.

THE COURT: Could I -- you had an exchange with Mr. Lasker a little bit about ago about the OECD guidance. Did I get the acronym right.

THE WITNESS: Yes.

THE COURT: OECD guidelines, and I believe what you said is that people are told they don't have to test at higher than a thousand milligrams per kilogram.

THE WITNESS: That is correct.

THE COURT: Is that right? And we had some discussion with Dr. Jameson about this yesterday, but I wanted to hear from you why it is, if you know, why it is that that is

the guideline, and what is the significance of that for this case?

THE WITNESS: So the reason that OECD chose to do that guideline was because they put -- they put another guideline in place, and then the mouse model guidelines no longer made sense.

They were trying to find a way to save money to reduce the amount of animals that are used, et cetera, and so they put a line in that says, If you can show that this does no harm to an animal at a thousand milligrams per kilogram per day, any compound, then you don't necessarily have to do a bioassay.

Once they put that in, they said, well, why should we then let the bioassay go to the maximum tolerated dose if it's bigger than a thousand milligrams per kilogram per day? So we'll cut that off too, and so you don't have to go above that.

From a scientific perspective, I still prefer using the maximum tolerated dose, but OECD and everyone in it has decided that you don't have to go any higher than that. It's unusual for the maximum tolerated dose to exceed the, a thousand milligrams per kilogram per day. In essence, for most bioassays, that that has no bearing whatsoever. For this one, it has bearing, because they have exceeded 1,000 milligrams per kilogram per day.

THE COURT: Okay.

BY MR. LASKER

Q. Dr. Portier, I'd like to switch now a bit to your discussion about multiple comparisons, and how that impacts statistical analysis.

And I think you explained how -- what happens with p-value .05 is if you do 20 tests, you're going to have one that pops out as gradient .0 -- well, less than .05, just by chance, correct?

A. No. You -- you might have one pop out, by chance at .05. You don't necessarily -- you might have two.

Q. Right, it's chance. I understand.

A. You don't know what chance really is.

Q. Okay, and while you were discussing that in the context of individual tumor findings, that same logic would apply with respect to any analysis that was pooling data for individual tumor types, given the size of our dataset, correct?

A. I think it would be misleading if I brought the pooled analysis into that calculation.

Q. I wasn't suggesting that. I had a simpler point.

There is, in any individual study, maybe 30 or 40 tumor sites that are looked at by the pathologist, correct?

A. I have a table with that in my Rebuttal Report. It's not 20 or 30. Well, the pathologist might look at them, but you wouldn't analyze them.

Q. Well, the pathologist would analyze them.

A. No, a statistician would analyze them.

Q. The pathologist would look to see if there were tumors, and then if they found tumors, then the statisticians would analyze them, right?

A. Yes.

Q. And so you'd have maybe 30 or 40 sites, and that's for males and for females, so that as in any one study, you're going to have 60 to 80 sites, correct?

A. You have 30 to 40 sites in males and females.

Q. So 30 to 40 in males, 30 to 40 in females, and you pooled separately for males and females in your analysis.

A. I pooled what?

Q. Separately for males and females in your analysis?

A. Oh, yes. Okay.

Q. And then we have mice and rats so we have 12 different studies we're looking at, correct?

A. Twelve studies in mice and rats, that's correct.

Q. So that is, you'd have to multiply that 12, by the 60 to 80, to figure out the total sites that the pathologist looked at. It's a lot of sites, correct?

A. It's a lot of tissues that they looked at, that is correct.

Q. And so out of all of those tumors, because there are so -- those sites, because there are so many, again, you have this multiple comparison problem if you just start looking at one

tumor site or another tumor site.

You would expect, given how many tumor sites you're looking at, however you do an analysis, by chance you might have some that looked like a positive trend, correct?

A. It's -- you -- I -- you're -- it's a very confusing statement you made. So I think you'll have to repeat it for me. I'm sorry.

Q. Okay. There are maybe a thousand -- I don't know -- there are hundreds, at least, or a thousand different tissue sites that have been examined, individual tissue sites that have been examined by pathologists in this large dataset.

A. Most of them -- most of them with no tumors at all.

Q. I understand that.

A. Correct.

Q. And given they have all these different tumors sites, if you were to do trend analyses, some of them would be zero because there's no tumors, and some have tumors, and will have findings one way or the other.

And by chance, the way statistics work, some of them are going to appear statistically significant. That's just statistics, right?

A. In any statistical analysis, you have a type one area, you have a false-positive rate. And yes, so for any one test, a false-positive rate applies.

Q. Okay, and I just want to talk a little bit about the

different tests that you did on multiple comparisons in which you were looking at individual tumors and not the pooled analysis, and you presented some of these slides, we looked at the one you just did for rats a moment ago.

I just want to talk a little bit about the genesis of that table, because you presented a table very much like the table you presented to this Court in your initial expert report.

Do you recall that?

A. Yes.

Q. Okay, and in your initial expert report, you actually had the numbers -- they were different in two ways, that I'd like to sort of discuss with you.

Again, you're comparing the total sites that were analyzed, and then the observed tumors, and you're seeing whether or not they are greater or less than chance. Correct?

A. That's correct.

Q. And in your initial expert report, you actually had a higher number of total sites than you have in your current report, correct?

A. For some, yes.

Q. Okay, and you decreased that number of total sites not based upon actually going through and counting up total sites, but based upon your judgment that actually, the -- or your estimation that the number of total sites that you had probably should be lower, correct?

A. No. I -- that's not correct. So the original numbers came from Joe Haseman in his comments to the USEPA. Joe Haseman was the Chief Statistician for the National Toxicology Program for 25 years, and those were his numbers. He created -- he created those numbers by reading two of the rat studies and two of the mouse studies and counting up, and then, to that, adding what is a reasonable number of these pooled analyses, and adenomas and carcinomas.

I went back and counted all of the studies, put those counts for what's one, two, less than equal to three, into my analysis, and used those numbers in the -- in the rebuttal, and still, the same number of pooled analyses that I had with Dr. Haseman, but I counted them all.

Q. Well, let's just take this in steps. First of all, Dr. Haseman, when he did his analysis along lines that he did, reported to EPA or submitted to EPA his findings, which was that the number of tumor findings in the study were what you'd expect to see by chance, correct?

A. You have my tab on that with my comment back to him.

Q. I understand that you don't agree with him. I'm just making clear for the record his conclusion, when he did this analysis, was that the number of individual tumor sites identified in these rodents was exactly what you'd expect to see by chance, correct? That was his conclusion?

A. That was his conclusion.

Q. All right.

A. But he concluded it based on only half of the tumors from the available data, because EPA didn't report half of the tumors.

Q. I understand you disagree with him. I just want to make clear what his analysis was, and I want to turn now to your adjustment of your total tumor site.

And if you can go back to your deposition, at tab 1, and this is page 316:23. Are you with me?

A. Yes, I am.

THE COURT: Are you raising something that from the deposition testimony that you believe is contrary to something that he just said?

MR. LASKER: Yes. At least, I hope so.

THE COURT: Okay.

BY MR. LASKER

Q. So we're discussing this same Table 15 here, and I asked you, at line 23, page 316,

"QUESTION: Have you gone through the exercise of adding up the sites that you think should be combined, so you actually have the total number of sites with adenomas with carcinomas, and adenomas and carcinomas combined, where you believe that's appropriate?"

And you stated,

"ANSWER: You can't do that evaluation sort of in isolation. So, no, I have not done that."

Did I read that correctly?

A. The question you just asked, and the previous one, had a slight difference in answer. I was talking about the tumors from the Greim supplements and sitting down and adding them all up, and Greim supplements don't have adenomas and carcinomas combined. So I can't count that one by myself unless I add it myself.

But if you remember, I'm relying on the -- some of my tumor counts come from the regulatory agencies. I can't be sure how many analyses the regulatory agencies did to give me those numbers. So I don't know what the true denominator is from where I got my data sources, and hence, I can't do that, but I did count every tumor in the Greim supplement.

Q. Oh, I appreciate the clarification, and just so the record's complete, and I didn't ask you this, but it's also on page 318, lines 7 through 17, just in further clarification of your answer, if you could agree -- and tell me if this is correct. I asked,

"QUESTION: I'm not asking about the number of analyses that were done. I'm asking you about the number of analyses that could be

done, because that's what you're Total Site column is, correct?"

And you state:

"**ANSWER:** No, the Total Site column should be an estimate of the number of sites that were done. That is what it's attempting to give you."

Correct?

A. That is correct.

Q. Okay, and your estimate of the total sites that you could look at went down from your first expert report to your current expert report, correct?

A. In some of the groups, yes.

Q. And you also -- and you talked about this a couple of times -- increased the number of sites where you observed tumors, and a lot of that was based upon the work that Dr. Corcoran did, where he found some tumors you hadn't found, and you added that to your observed sites, correct?

A. That is correct.

Q. And so that's what you used as your comparison to do your multiple comparison analysis, correct?

A. That is correct.

Q. And I believe you testified that Dr. Corcoran was not qualified to actually identify tumor sites, but for this purpose, you used his -- the tumor sites he identified,

correct?

A. That was not what I testified to. The question was whether or not he was qualified to evaluate the carcinogenicity of these studies, and my answer didn't deal with his statistical qualifications. It dealt with his qualifications in understanding what a bioassay is.

Q. I appreciate that clarification, but Dr. Corcoran actually also has a total number of sites that he looked at to identify all of those tumors, correct?

A. He actually has two.

Q. Okay, and he did just, like Dr. Haseman, he did an analysis, just like you did -- and we'll hear from him later today or maybe tomorrow -- and he did not -- his conclusion, like Dr. Haseman, was that the number of sites found with these P trends less than .05 was what you'd expect to see purely by chance, correct?

A. But he made lots of errors in the sites that he looked at, as well as analyzing sites with less than three tumors total, at the sites.

Q. I understand you disagree with him, and I understand you disagree with Dr. Haseman --

A. No, I agree with Dr. Haseman. I'm sorry, that's putting words in my mouth.

Q. I'm sorry, maybe I misunderstood. Dr. Haseman concluded that the number of sites identified is what you'd expect to see

by chance. Do you agree with that?

A. I was answering the question about the number of how you calculate the number of sites. I agree with Dr. Haseman on how you calculate the number of sites, and I disagree with Dr. Corcoran.

Q. Okay. I understand.

Let's switch over to your opinions with regard to genotoxicity, and you -- you talked about a little bit about oxidative stress. Do you recall that?

A. Yes.

Q. And just so people understand what that is, oxidative stress is part of the energy system that drives our ability to move, correct?

A. That is correct.

Q. And exercise causes oxidative stress, correct?

A. Exercise causes free oxygen radicals that are used up during the exercise and afterwards, but yes.

Q. Okay. Just so I'm clear, exercise causes oxidative stress, correct?

A. It increases the number of free oxygen radicals because the body needs them at that point. But yes, it -- it's not -- I don't know if you would call it oxidative stress. That's my problem with the terminology. It clearly increases the amount of free oxygen radicals in the cell.

Q. Okay. If I could ask you to turn to tab 1 again, that's

your deposition.

A. Yep.

Q. At page 353.

And are your Honors with me?

JUDGE PETROU: Mm-hm.

BY MR. LASKER

Q. Starting at line 3, we have the question we just talked about, and, "You agree that oxidative stress," I asked you, "is happening in our body all ever the time correct?"

And you answer, "It's part of the energy system that drives our ability to move."

My next question, "So exercise causes oxidative stress, correct?"

And your answer was, "Of course."

A. I'm correcting the answer, because I don't know if the definition of "oxygen stress" means free oxygen that's not needed versus free oxygen that is needed.

We are agreeing on the same thing, that there are oxygen radicals; they get much higher during exercise, in the cells.

Q. Okay, and you would agree -- I'm not sure I understand the qualification, but you agree, or at least -- well, I've got to ask the question first.

Do you agree that having a cold causes oxidative stress?

A. Probably.

Q. Okay, and that was the answer you gave, not quite

qualified, but that was the answer you gave in your deposition, so we're doing good.

THE COURT: You don't need to be testifying.

MR. LASKER: I'm sorry, I wasn't actually meaning to imply anything.

THE COURT: Well, you were.

MR. LASKER: I was just talking.

Q. And you would agree that it is fair to say that the fact that a chemical causes oxidative stress does not mean that it causes cancer, correct?

A. That is a fair statement, that is correct.

Q. Okay, and we talked about genotoxicity. You would also agree that even if a chemical is genotoxic, that does not mean that it causes cancer, correct?

A. Let me talk about general scientists first, and then about myself, if that's okay.

Q. Sure.

A. There are scientists who believe that genotoxicity is equivalent to cancer. It's getting smaller as a group over time, but there are some who still believe that genotoxicity should be equivalent to cancer, and most genotoxic compound companies don't even create them if they can avoid it because it creates such a controversy.

In my reading of that literature, I would say that just having a genotoxic finding does not lead to cancer.

Q. All right, and in fact, a human cells routinely experience DNA damage in the ordinary course of cell replication, without any chemical exposure, correct?

A. That's correct.

Q. And the human body has repair mechanisms that respond to DNA damage so that it doesn't cause further damage, correct?

A. That is correct.

Q. And for -- I think you actually have -- you had a slide that you presented that sort of shows showed this progression for a chemical to cause cancer through genotoxicity. The genetic change has to progress to a mutation.

A. Through genotoxicity, yes, that would be correct.

Q. And just because a chemical can cause DNA damage, but doesn't mean that it will cause mutations. Correct?

A. That is correct.

Q. And you also agree that the scientific evidence is insufficient to classify glyphosate as a mutagen or capable of causing mutations, correct?

A. Let me think about that one for a minute. I have to run through all of the assays that I looked at in my head.

I would have to conclude that that is correct. It's genotoxicity, it's not mutations.

I will point out that for most evaluations of the genetic toxicity of chemicals, they don't sequence DNA and look for mutations.

Q. Okay.

A. So it would be rather unusual to have data that would allow me to say, yep, it's a mutation.

Q. Okay. Well, in fact, both glyphosate and glyphosate-based herbicides have repeatedly tested negative for mutagenicity in the AIMS test, correct?

A. That's reverse mutagenicity in the AIMS test. It's a specific gene for a specific case. That doesn't mean it isn't causing mutations, because the genome's a little bit longer than what you see in the Salmonella.

So it's a -- its a clearly -- it clearly is negative in the reverse mutation assay in Salmonella.

Q. So just so the record is clear, both glyphosate and glyphosate-based herbicides are clearly negative in the AIMS test for mutagenicity, correct?

A. I don't, right off the top of my head, I don't recall if I looked at the AIMS assay results for the formulations. I'd have to go back and look at my report to be able to answer that. I did look at the glyphosate ones, that's I'm certain of.

Q. And they were negative?

A. There were one or two positives in there, but there were predominately 23, 24 negatives, one would have to conclude that that was negative.

Q. Just to perhaps refresh your recollection, if you could go

back to your deposition, tab 1, at page 347, line 10 --

A. Yeah.

Q. -- and it's line 10 through line 20.

A. Yes.

Q. And the question on line 10,

> **"QUESTION:** And you do agree, though, that both glyphosate and glyphosate formulations have consistently tested negative in the aims mutagenicity test? Correct?"

And your answer?

> **"ANSWER:** They have consistently, with the exception, I believe, of four studies, but there were a lot of studies -- consistently tested negative for the reverse mutation assays of a specific gene in Salmonella."

A. Different, no.

Q. So yes, the AIMS test --

A. Just say Salmonella.

Q. Yeah, okay. Does this refresh your recollection that glyphosate-based herbicides, likewise, at least from your review as of the time of your deposition, tested negative for mutagenicity in the AIMS test?

A. The glyphosate formulations. I'm really uncomfortable with that. I know I said this, but today, I'm uncomfortable saying I really did look at the formulations. I really would

have to go back and look.

Q. That's fair.

A. But I'm willing to say this. My vague recollection is that it's predominantly negative for the formulations.

I hesitate because there are so many different formulations, I'd want to go carefully look through it and see if the different formulations had something different in them, so that the few positives they had might have come from a very specific formulation. But that's my recollection at this moment.

Q. I'd like to turn to the three human *in vivo* studies you mentioned. I think you stated in your direct testimony that you gave the greatest weight to human *in vivo* evidence for genotoxicity, as I recall, correct?

A. What I said was, given all else equal and of equal quality studies, I would rate the human *in vivo* evidence the highest.

Q. Okay, and there were three studies that you cited to. I think you said two were clearly positive, and one was possibly positive. Correct?

A. Yeah. It was -- one could interpret it as positive, one could interpret it as negative. It's a fair call to go either way with that study.

Q. Okay, and the first the first study is Paz-y-Miño 2007.

And this is, I believe, Defense Exhibit 1289. I'm sorry, it wasn't in our binders so I have copies for your Honors.

(Whereupon a document was tendered to the Court.)

THE COURT: Mr. Lasker, can I ask you roughly how much longer you have with this witness?

MR. LASKER: Five minutes.

THE COURT: Okay. We can take a little short break after that.

BY MR. LASKER

Q. And this Defense Exhibit 1289 is the Paz-y-Miño 2007 study, correct?

A. That is correct.

Q. And this is actually dealing with a planned Colombian spraying in Ecuador, which for other reasons I know about, and this was the first test that you identified as a positive test for genotoxicity, correct?

A. That is correct.

Q. And if I could direct -- ask you to look to the last paragraph of this publication, where the investigators are summarizing their conclusions, from this paper?

A. Very last paragraph.

Q. And the investigators state "Our findings suggest...."

Are your Honors with me? Okay.

> "Our findings suggest the existence of a genotoxic risk for glyphosate exposure in the formulations used during the aerial sprayings, and indicate the need for

further studies on individuals exposed to glyphosate to determine its possible influence on genetic materials."

Correct?

A. That's what it says.

Q. And as you mentioned, there were two more studies. There was Bolognesi 2009 and there was Paz-y-Miño 2011. They did an additional study, correct?

A. Yes, I believe so.

Q. And the Bolognesi study is at tab 25 in your binder; your second binder. And if we go to those investigators' conclusions, at the end -- are you with me?

A. I'm trying to get to the end.

Q. Okay.

A. Okay.

Q. Page 985, the second column. Those investigators, and they're -- this is the first full paragraph -- state that, third line down, they're talking about Bradford Hill, which we've heard some testimony about in this case,

"Based on the applicable Bradford Hill guidelines, it is not possible to assign causality to the increases in frequency of BNMN."

And that was their measure of genetic damage, right?

A. That is correct.

Q. "...observed in our study," correct?

A. That's what he says.

Q. And you disagree with that, I take it?

A. I don't -- I didn't apply Bradford Hill to that one study. So I can't agree or disagree with it. Do I believe there are positive findings in this paper? Yes, I do.

Q. The investigators -- well, let's take a look, then, at the final paper in this series, and that's Paz-y-Miño 2011, that was the third in this series, correct?

A. That's correct.

Q. And that was at -- that's at tab 26. And if we can go to the conclusion again, which is at page 50 -- are you with me?

A. I'm on 50, yeah.

Q. Okay, so the bottom of the first column on the left, the final paragraph in their conclusion states,

> "Several research studies related to glyphosate exposure have been conducted in Colombia by Bolognesi...,"

and that's the study we were just talking about. You can see by the reference, correct?

A. Yes.

Q. (Reading)

> "...Sanin, *et al.*, and Solomon, *et al.*, which state that the study populations have low genotoxic risk associated with

glyphosate."

Correct?

A. That's what it says.

Q. And then they continue, "Regarding our study," so this is now their 2011 study, "we obtained results showing no chromosomal alterations in the analyzed individuals."

Do you see that?

A. That's what it says, yes.

Q. And do you agree that that was their finding?

A. No. Table 2 says that's not their argument. That's not their finding.

Q. Okay. So you disagree with Paz-y-Miño and you disagree with Bolognesi as to their conclusions, but -- based upon your analysis of the data?

A. I don't disagree with Bolognesi's conclusions.

Q. Oh, I'm sorry.

A. His abstract conclusion is very clear. He says there is genotoxic risk from exposure to glyphosate. That's his conclusion. I agree with that, from his paper.

Q. Okay, and his conclusion that causality cannot be determined, or -- we can go back and quote the Bradford Hill analysis -- his conclusion that there was not causality, do you agree with that, or not agree with that?

A. I don't know what he did. All he said is one sentence that says, we tried to apply it. There's no description of why

it didn't work. I think it didn't work because they didn't have enough data to be able to do it, not because it didn't work. I mean, not because it goes the opposite direction, but I don't know because there's nothing in there.

All I can do is refer to the last sentence in his abstract, which very clearly states, we saw significant effects.

MR. LASKER: I have no further questions, your Honors.

THE COURT: The last sentence in the abstract -- I'm looking at the last sentence in the abstract.

THE WITNESS: For Paz-y-Miño or Bolognesi? I'm sorry.

THE COURT: I'm looking at the last one, Paz-y-Miño, that --

THE WITNESS: Oh, yeah, that one -- that one, they're clear.

THE COURT: Is that what you were pointing to just now?

THE WITNESS: No, I was going back to this other Paz-y-Miño paper. The last sentence reads,

> "These results suggest that in the formulations used during aerial spraying, glyphosate had a genotoxic effect on the exposed individuals."

THE COURT: Okay. Thank you.

Any redirect?

MS. GREENWALD: Can we take a short break? Then I'll be really quick, if at all.

THE COURT: Absolutely. Why don't we return at 11:00 o'clock, and then with lunch today, hard stop at 12:00 o'clock. We'll have lunch right at 12:00.

(Recess taken from 10:48 a.m. until 11:02 a.m.)

THE COURT: When do we get to watch the movie?

MS. GREENWALD: We didn't bring popcorn, though we could go get some quickly.

Your Honor, we don't have any further questions of Dr. Portier, and I just wanted to say at this point, other than Dr. Nabhan, who is obviously not coming until Friday, the plaintiffs -- that's the end of our presentation. The movie now is our counter-designation to Monsanto's designations. They're not our affirmative designations.

So thank you, and thank you, Dr. Portier.

THE COURT: Sorry to keep you waiting during the break.

THE WITNESS: That's okay. I needed a break.

THE COURT: All right.

MR. LASKER: Thank you, your Honors.

We will be presenting the video of Dr. Blair first, and then Dr. Ross maybe after lunch.

I do want to make one clarification based on a question Your Honor asked earlier.

Dr. Blair provided some testimony with respect to the NAPP. He was looking at the June 2015 data that he was looking at numbers from that slide deck. Most of the testimony in this case relates to a later slide deck, a later analysis, which was in August of 2015.

And so the discussion we've had acknowledges that have been focused upon the data from that later slide deck that later analysis is slightly different. So if you hear numbers that are slightly different, I just wanted you to understand why that was.

THE COURT: Okay, and so, if I remember correctly, the August -- the August was the Brazil presentation, and June was Canada? Is that right?

MR. LASKER: That's correct.

THE COURT: Okay. Whenever you're ready.

(Videotape was played but not reported.)

MR. LASKER: That was amazingly timely, Your Honor.

THE COURT: It was. And Mr. Lasker, I kept -- I kept feeling tempted to say -- to ask you to slow down. But I have a feeling you would have, just like in real life, you wouldn't have listened to me.

MR. LASKER: I do what I do, Your Honor.

THE COURT: So we'll resume at 1:00 o'clock.

THE CLERK: Court is in recess.

(Recess taken from 11:58 a.m. until 1:07 p.m.)

THE COURT: All right. You going to try to slow down in the next deposition?

MR. LASKER: Actually, it's Mr. Griffis you're going to be hearing, so that's going to be fine.

THE COURT: Excellent.

MR. LASKER: We'll now be playing excerpts from the deposition of Dr. Ross. Dr. Ross was a member of the mechanistic subgroup for the working group.

(Videotape was played but not reported.)

THE COURT: Quick question.

Are the documents that you all asked them about -- are they going to be in the record?

MR. LASKER: Yes, Your Honor, the parties have been talking about that and submit them at the end of the day.

THE COURT: Okay. Great.

JUDGE PETROU: Can someone tell us now what article it was that he was the author number 68?

MR. WISNER: It's the consensus statement about the IARC's reliability issued in response to the glyphosate manuscript.

MS. WAGSTAFF: Would you like us to print you out a copy of that now?

JUDGE PETROU: That's fine.

MS. WAGSTAFF: Oh.

THE COURT: All right. What's next?

MS. PIGMAN: Monsanto calls Dr. Thomas Rosol.

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

THOMAS ROSOL,

called as a witness for the Defendant, 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 it's directly in front of you. And for the record, please state your first and last name, and spell both of them.

THE WITNESS: Thomas Rosol. T-h-o-m-a-s R-o-s-o-l.

THE CLERK: Thank you.

DIRECT EXAMINATION

BY MS. PIGMAN

Q. Dr. Rosol, please tell the Court what your profession is.

A. I'm a veterinary pathologist, with expertise in toxicologic pathology. I was a Professor at Ohio State University for 30 years, and retired. And now I am a professor at Ohio University College of Osteopathic Medicine, and Chairperson of the Department of Biomedical Sciences.

Q. What role does a veterinary pathologist play in the analysis of animal toxicology data?

A. Well, the first thing the veterinary pathologist does -- and typically, it's a board-certified veterinary pathologist, because that's required by the regulators -- generates all the data. All the histopathology slides are reviewed. And if the animals, during their necropsy or autopsy, have gross lesions, then a pathologist will look at those gross lesions also. Then the data is evaluated by data analyst, and sometimes statisticians. And then the data comes back to the veterinary pathologist to interpret the stats and the data.

Q. And you mentioned board certified -- board certification. Are you board-certified veterinary pathologist?

A. I am.

Q. And is veterinary pathology is a medical specialty?

A. Absolutely. So first of all, I'm a veterinarian. I went to veterinary school, and practiced veterinary medicine. I was trained to diagnose and treat animal diseases; everything from rats and mice, to dogs, to elephants. A very exciting profession.

And then the other thing veterinarians routinely do in their work is they compare everything they do to humans. We translate what we do to human medicine, because we learn from human medicine, and human medicine learns from us. It's interesting from a medical-school perspective, which I am now gaining, it doesn't work backwards like it does in veterinary medicine. So "translational science" is a very common term

used now: To translate findings in animals to people.

Q. And I want to be clear on this from the outset, Dr. Rosol. Does rodent bioassay data predict cancer in humans?

A. No, it does not.

Q. What does it predict?

A. Rodent bioassay data demonstrates whether a chemical is carcinogenic in either a rat or a mouse.

Q. And are there chemicals that are carcinogenic in rodents that have been proven not to be carcinogenic in humans?

A. Absolutely. In fact, most of the drugs we take and many of the chemicals we use every day are carcinogenic in rodents, and have been shown not to be carcinogenic in humans.

Q. How many rodent bioassay data reviews have you been involved in, in your career?

A. Intensive reviews, probably in the range of a hundred.

And then many, many other ones with subset data or incidence data.

Q. And have you used your expertise in the field to evaluate the glyphosate rodent bioassay data?

A. Yes, I have.

Q. How many rodent bioassays did you look at?

A. I examined 12 rodent bioassays: Five mouse, and seven rat.

Q. If you could tell us, what is your opinion, Dr. Rosol?

A. So my overall opinion that -- to the best of my ability

and scientific rigor, I found glyphosate to not be a carcinogen in rats and mice.

Q. And are you offering that opinion to a reasonable degree of scientific certainty?

A. Yes, I am.

Q. And can you explain the slide we're looking at for us, and how that led you to your opinion?

A. Okay. So initially I looked at each bioassay individually and examined all the data, read the pathology reports, and made my opinions of carcinogenicity on an individual basis. And I found as individual studies, none of them demonstrated to me evidence of carcinogenicity in rats or mice.

Then I looked at them in toto, because we had -- had some false-positive data that I interpreted. And looking at them in toto and looking at repeatability between the bioassays, it helped confirm my original conclusion that none of the bioassays demonstrate carcinogenicity. So my overall opinion after looking at all 12 bioassays is that glyphosate is not a rodent carcinogen.

Q. And in terms of those findings, how does the glyphosate rodent dataset compare to other bioassay data that you've reviewed?

A. That's a great question. So, as we've heard from -- from others, this is an enormous dataset. It's unprecedented. I have not been involved in a study where I've looked at 12

bioassays for the same chemicals. So from that aspect, it was very, very interesting to me. And there was excellent repeatability across the studies, between the 12 studies.

Q. So is it one of the cleaner sets you've ever reviewed?

A. That's exactly correct. So it's very important to put this dataset into perspective. That I don't think has been shared at this hearing up to this point in time. This is one of the cleanest sets of data I have ever evaluated in terms of carcinogenicity. And this is something I routinely do throughout my life. So from my perspective, this data is -- has no evidence of carcinogenicity. And -- if you use the proper methodology to interpret the data.

Q. We'll talk a little bit more about that methodology in a moment, but I want to ask a couple other questions before we get there. Over what period of time were the bioassays you reviewed conducted?

A. Over three to four decades.

Q. And were the bioassays conducted by different laboratories?

A. Absolutely. Multiple laboratories produced this data.

Q. Did those two facts have any influence on the strength of the opinion you're offering?

A. Yes, it did. And it -- it strengthened my opinion, because multiple laboratories were involved, and there was clear evidence of repeatability of the negative findings.

Q. The Court has already heard that bioassays contain different dose groups, so we won't go back over all of that, but I do want to ask you how the high dose groups in rodent bioassays you reviewed compare to anticipated human exposure.

A. So as we mentioned, most rodent bioassays use the maximum tolerated dose. And this is usually hundreds to thousands of times greater than the maximum human exposure. And the goal for this is to actually induce toxicity, and make sure there is some toxicity.

It was also mentioned that a thousand milligrams per kilogram per day is the maximum dose. And those are now the accepted OECD Guidelines.

However, there's one caveat to that that hasn't been mentioned. That is if the chemical or drug is expected to be exposed to humans at that high of a dose, then the dose can go higher. And in this case, the dose -- or the expected exposure in humans is much lower than that. So a thousand milligrams per kilogram per day would be the maximum amount, but we do have some studies --

THE COURT: I think this is probably a pretty dumb question, but is it -- is it a one-to-one translation? So a thousand milligrams per kilogram for the animal, compared to a thousand --

THE WITNESS: No, no. That's not correct.

THE COURT: -- for the --

THE WITNESS: That's not correct. So there are -- so dosage is given based on body area.

THE COURT: Mm-hm.

THE WITNESS: Okay? And so a human's body area -- we have a less area per mass than a mouse. So there are correctional factors for mice and rats.

So, for example, if a dosage in a human was -- correct dosage was -- you know, to treat a disease, for example, was 10 milligrams per kilogram per day, the dosage in a rat might be 50; and in a mouse it might be 70. So somewhere in the range of five to ten is a correct correction for that, for the different species?

THE COURT: Okay. And so when you're studying -- when you're doing a mouse or a rat study, you are making some assumption about how much humans are being exposed to this?

THE WITNESS: If you do it by body area; but now with standard testing it's actually done better than that. And what they do is they use the -- the pharmacokinetic data, where you actually look at the blood level of the chemical in the animal and in the person, and you get a curve.

You know. You give a drug. The blood level goes up, and then it goes down. And you measure the area under the curve; the AUC. And so you can very specifically say whether the animal's getting a similar AUC than the human. So it's much better than doing this correction for body area. So science

has advanced.

And then even with different sexes -- for example, the area under the curve might be different in male animals than female animals. That's why it's so important to have both male and female animals in the studies, is because males and females may metabolize the drug very differently, or absorb the drug very differently.

MS. PIGMAN: You're going to be told to slow down in about five seconds.

THE WITNESS: Okay.

THE COURT: And so part of what you're going to present to us to today, I assume, are assumptions about what kind of exposure humans are getting to glyphosate?

THE WITNESS: No. I deliberated over the animal carcinogenicity.

THE COURT: Okay, but those studies --

I mean, a decision about how much to dose the animal -- shouldn't be it based, in part, on how much exposure humans are getting?

THE WITNESS: Not necessarily. The decision is made -- so there's short-term toxicity studies. And then these are the long-term toxicity studies. And so you base your maximum dosage on what you find in the short-term studies. And in the short-term studies glyphosate is a very, very weak toxin. And you can give very, very high levels to animals.

So the studies went to the thousand milligrams per kilogram per day, or even higher in some earlier studies, because it's not very toxic. And so you want to maximize the ability for these assays to detect carcinogenicity in the chronic studies.

So most chemicals are much more toxic than glyphosate, and so the dosages are based on these AUCs.

THE COURT: Okay.

BY MS. PIGMAN

Q. Dr. Rosol, speaking of dose, were you in the courtroom when doctor -- and did you hear Dr. Portier testify that the only variable in a rodent bioassay is dose?

A. Yes, I was.

Q. Do you agree with that statement?

A. No, I don't. It's partially true. And I think what Dr. Portier meant to say was that the only dependent variable is the dose of the chemical compound.

What was -- what really needs to be discussed is the biologic variable. In animal studies the greatest cause of variability in the data is biologic variability, which we absolutely cannot control for. That's why there are 50 to 60 animals per group: Because animals differ. And even though we use inbred animals, which are animals that are like brother/sister matings for many generations to make the animals very similar, we still have a tremendous biologic variability.

Q. The next question if we could put up the next slide, please. What findings do you expect to see in any rodent bioassay?

A. So in a way, rodents are like people. Rodent bioassay is the -- is the approximate life span of the rat or mouse. And so rats and mice -- as they get older, they develop cancer. And about 30 to 40 percent of rodents will die of cancer if they're allowed to live for their lifespan, just like in people, just like in dogs, and just like in cats. So we expect cancer in these assays. All right?

Some tumors develop to a greater level than other neoplasms, but in these studies you can actually see neoplasms from any cell in the body -- literally hundreds of different kinds of tumors -- but some are more common than others.

Veterinary pathologists are used to this variability, and we take that variability into account. The terminology I use for this is a "natural history." Each type of tumor has a natural history. And this is how physicians and veterinarians use the knowledge to diagnose and treat disease.

A good example is a person might say, *Oh, I have cancer.* First thing I want to know is: Exactly what kind of cancer is that? Because the prognosis of the patient is going to be very different, depending on the cell type involved.

Now as so, every bioassay I looked at has cancer. We expect that. Okay? So we cannot assume that tumors observed

in the exposed groups are compound mediated, until we follow the process the veterinary pathologists do to interpret the data correctly. And, as I mentioned, the first step is to do statistics, and then follow the process to evaluate the data.

So assessment of whether tumors are observed, are compound mediated, requires consideration of a number of factors that we'll talk about shortly.

Q. And if we could go to the next slide, I'd like to ask you how many tissues. You mentioned a lot. How many tissues are you evaluating in a bioassay?

A. I don't expect you to actually read all of the words under every tissue. This is just for emphasis; that every tissue in the body is examined, from the nose, to every part of the gastrointestinal tract, to the brain, to all of the organs. And so, in general, 35 to 40 different tissues are examined from each animal. Okay?

So every animal in each group is examined. There are eight groups, because there are four groups of males, and four groups of females. And this is approximately 16,000 tissues that are -- that are evaluated by the veterinary pathologist. This takes approximately six months.

So when a pathologist does one of these studies, including all of the data analysis, interpretation, and report-writing, because the reports are between 1- and 2,000 pages, it takes about a year and a half for a pathologist to do a bioassay.

Q. And are statistical analyses performed at some point in these bioassays?

A. Yeah. So, as I mentioned, the veterinary pathologist is involved in the gross examination and the histologic examination. And this data is usually put into a computer program. And then the computer and the data is delivered to a statistician. A statistician then completes descriptive statistics and inferential statistics. The inferential statistics are the different tests and p-values that we've heard so much about. Then the data's returned to the veterinary pathologist. They take that data, and they determine biologic significance of the findings.

In terms of rodent bioassays, the biologic significance is whether there was a chemically mediated effect.

Now, keep in mind the pathologist is not just looking for tumors. These are old animals. And as people get old, we get many diseases. So the pathologist diagnoses all of the degenerative conditions, all of the inflammatory conditions, all of the preneoplastic conditions, and all of the cancer conditions. So each organ has many diagnoses.

Q. And you mentioned false-positive a moment ago. How many false-positives do you typically expect to see in a rodent bioassay?

A. So in general, a good rule of thumb is that you expect one false-positive for every 20 examinations. There are many

hypotheses that are tested for carcinogenicity in these studies, and so in my personal experience, I usually see two to five false-positive incidences of cancer in a typical rodent bioassay.

JUDGE PETROU: And does that number stay, whether you're talking about the control group or one of the treated groups?

THE WITNESS: This is a conclusion made by the statistician on a particular neoplasm that includes the control and dosage groups.

JUDGE PETROU: Mm-hm.

BY MS. PIGMAN

Q. Do false-positives typically occur in a specific tissue type?

A. No, they do not. They'll occur in a -- these are false-positives, so they're random.

Now, think about this unique dataset we have. When I usually am involved in deliberations over these kinds of data, I'm looking at one mouse study and one rat study. Okay? There might be two to five false-positives in the mice and in the rats.

Now we have 12. Okay? So the number of neoplasms that are false-positive are going to be very large. And you can see there's a number of different tumors in many different tissues that are under consideration for these bioassays. And I think

that absolutely reflects what I would have expected. There are very few carcinogens I have been familiar with that would affect so many different tissues.

Q. Dr. Rosol, if we could go to the next slide, please. Are there dangers in misinterpreting false-positive data?

A. Yes. And this is what the veterinary pathologist does. Once we get the deliberations back on the statistics, then we look at this data. We follow a process. And if he just look at the statistics, you will improperly assume that the statistical significance means a biological significance. I think that's what's happening in this case. That's why we have so much deliberation in this process.

It's scientifically invalid to ignore all of the other factors that we take into consideration when we interpret the data in a bioassay. And so this creates misleading interpretations of the data. And this is why it's very important to read the pathology report.

Q. And now mentioned this factor --

Oh, sorry.

JUDGE PETROU: So, Dr. Rosol, you said there were very few carcinogens that you have familiarity with that affect so many different tissue types. Is that correct?

THE WITNESS: That is correct.

JUDGE PETROU: But I didn't get the follow-up on that, which is that if you see it affecting so many different

tissue types, do you tend to say it's more likely or less likely a carcinogen?

THE WITNESS: If the effects are real or biologically significant, then that would mean it was a very severe carcinogen. And this is very uncommon.

And if you look at the toxicity data in the short-term studies, this is one of the safest compounds I've ever seen. So it just doesn't fit. They don't correlate.

BY MS. PIGMAN

Q. So moving on to the next slide, which is your methodology -- we're going to come back to this a little later in connection with the specific tumor type -- but if you could, just briefly highlight some of the factors that you look at as a veterinary pathologist.

A. Okay. Yes. And I generated this slide to give you a feel for how I do this. First I look at size and magnitude of effect. This is very important to me. The effects in these studies are very small.

Then I look for a dose-response, because the incidence should increase with dose.

I look for precursor lesions and lesion progression that we heard about in the earlier testimonies.

Historical controls are very important to me. And importantly, the variability in each historical control varies between tumors.

I also take into consideration if we expect a neoplasm. If you don't expect a neoplasm, it has been estimated that p-values of .05 overestimate effects by at least 90 percent. So this is an interesting statistical deliberation.

I look at the morbidity and survivability, which was not very important, except in the Swiss mouse experiment, because most of the animals survive until termination.

And what's really unique about this dataset is we can evaluate repeatability. I can look at seven rat assays that were very similar, and five mouse. This is unbelievable.

Q. Are you aware of Dr. Portier's testimony earlier about pooling data across these 12 bioassays?

A. Yes, I'm aware that he pooled his data.

Q. Is that a valid scientific practice in your area of expertise?

A. In evaluation of rodent bioassays by veterinary pathologists, I have never seen anyone pool data; and I think this is absolutely scientifically invalid. And I noticed that this was not referenced in any way. And I noticed that Dr. Portier does not publish in the peer-reviewed literature on pooling of data. So this is actually quite a surprise to me. And I -- I think it's invalid, but actually it didn't affect my decision-making in my interpretation of the data, either.

Q. And I do want to talk now move about to lymphoma specifically. Does lymphoma spontaneously occur in mice?

A. Yes. Lymphoma is -- is a high-incidence entity in mice, and it has a high degree of variability. This is in contrast to rats that have a very low incidence of lymphoma.

Q. Why is lymphoma so common in mice?

A. Great question. We really don't understand all of ramifications of that, but probably it relates to genetics of the animal. And mice are unique, in that there's a retrovirus that can cause lymphoma in mice that rats do not have, so I suspect that those are two of the major reasons.

Q. And does that high background rate make mice a poor model to test causation of lymphoma?

A. Okay. So we heard both sides of this a little bit. So it makes them a poor model for determination of carcinogenicity of lymphoma, because of the high background and the high variability.

It makes them actually an interesting model for studying treatment of lymphoma, because they have lymphoma, so you can actually treat it. And in my laboratory I have done experiments using human lymphoma in mice, which I find much more valid than looking at mouse lymphoma to make translation to human disease.

Q. And do experts in your field consider rats a better model to determine what causes lymphoma?

A. A better model? For carcinogenesis, if you see an increase in lymphoma in rats, this would be stronger evidence

of a carcinogenic effect.

Q. In the seven rat studies that you reviewed in the glyphosate dataset, did you see any evidence of lymphoma?

A. No, I don't.

Q. All right. If we could go to the next slide, Dr. Rosol, I believe this is a summary of your review the CD-1 Mouse study data. Is that right?

A. That is correct.

Q. Can you explain to us what we're looking at?

A. Yeah. So this is a rather complicated slide. And what the bars represent is the dose in the high-dose groups. Okay?

So we have two high-dose groups. And these are, again, in the four mouse studies with glyphosate. We have two high-dose groups that are 4900 and 4300; so very high doses. And then we have two groups 988, and 810. So close to a thousand. Okay?

Two of these studies are 24 months, and two are 18 months, but what I want you to do is look at those numbers at the bottom of the page. This is what I would get, as a pathologist. I'm looking at the incidence data for lymphoma in four different studies of CD-1 mice. And you can see this incidence. And when you look -- see, you never have the luxury of looking at this much data. 2542. Those numbers are the same. 2206. Also the same. 4216.

And so if you randomize these numbers, that's actually what's happened here. And if you just focus on the last count,

0125, this might look like a dose-response, when it absolutely isn't; because these aren't the numbers you need to diagnose a biologically significant effect of lymphoma in mice.

Me and my piers would look at this data and say, *This is an absolutely clean set of data.*

Q. And when you say the numbers are all the same, can you just explain a little more what you mean by that?

A. Yes. So in CD-1 mice, I would expect a number of incidence anywhere from zero to six. And probably I would accept zero to nine, based on the historical data I have seen in these datasets. So these numbers, zero to six, could be randomized in any group. And that's what we have here.

Q. And going back to an issue we talked about a moment ago -- and we can go the next slide -- how do the doses used in these studies compare to EPA estimate of potential human exposure?

A. So as I earlier mentioned, so the highest exposure estimate for occupational handlers is 7 milligrams per kilogram per day.

And what I find interesting -- something I learned from these deliberations was that -- was that there was a cutoff in the epidemiology data at two days per year of exposure.

Now, keep in mind these mice -- every bite of food they took, they were eating glyphosate. Okay? So they usually eat eight to twelve hours a day. And so they have this exposure 365 days a year, at ten to a thousand times fold; the dose

that's considered the maximum exposure. So a very different kind of experiment.

THE COURT: The could you repeat the part about the maximum exposure in humans, and where that comes from?

THE WITNESS: That -- that comes from the EPA report. I think that's a 2017 report from the EPA.

THE COURT: And what is it again?

THE WITNESS: It's 7 milligrams per kilogram per day.

THE COURT: Okay.

BY MS. PIGMAN

Q. And the Court has already heard a little bit about the Swiss mouse study. We can go through that one pretty quickly if we can have the next slide. Did you review that, as well?

A. I did review that.

Q. What was your ultimate conclusion?

A. My conclusion was that there was not evidence of a carcinogenic effect with a cause of lymphoma based on these data. Keep in mind the Swiss mice have a much higher background level than we expect in the CD-1.

Q. Stepping back from lymphoma for a moment, did you apply the same multifactorial methodology we've been discussing to your review of all of the incidence data in the glyphosate bioassay dataset?

A. I used my same methodology that all veterinary pathologists use for all of the data that were in the 12

datasets.

Q. And if we could go to the next slide, please. Tell us what you concluded after that review.

A. So I analyzed these eight factors in relation to the natural history for the neoplasms for the different species and different tissues. I found no compound mediated effect in any of the 12 studies.

Q. Are you aware of any other scientific groups that have applied the same methodology you did, and reached the same conclusion?

A. Absolutely. Every publication I read in *Toxicologic Pathology*. All of the pathologists I work with. This is the approach that's time honored. It's over 50 years old. Every study I read in *Toxicologic Pathology* uses this -- uses this analysis.

Q. And are you aware of any other groups or regulatory agencies that have applied this methodology specifically to glyphosate?

A. So as I was able to read the pathology reports, all of the pathologists for the 12 studies used this methodology. And they found no compound mediated effect.

The EPA used this methodology. EFSA used this methodology. So many other groups have used the same methodology. I think if any person or group or veterinary pathologists uses this methodology, they will come to the same

conclusion I and others have.

MS. PIGMAN: Okay. Unless there are further questions, we'll pass the witness at this time.

MS. WAGSTAFF: Dr. Rosol, I don't anticipate referencing it, but do you want a copy of your deposition transcript?

THE WITNESS: Sure, if you've got it.

MS. WAGSTAFF: And your Expert Report?

And if I use it, I'll give Your Honors a copy, unless you'd like one now.

THE COURT: Doesn't matter.

MS. WAGSTAFF: Okay.

CROSS-EXAMINATION

BY MS. WAGSTAFF

Q. All right. Dr. Rosol, my name's Aimee Wagstaff. We've never met before; have we?

A. I don't believe so.

Q. So you've been here for a few days. Right?

A. I arrived on Sunday.

Q. Okay. So you saw -- were you in the courtroom when Dr. Jameson testified?

A. I was in the courtroom on Tuesday and Wednesday.

Q. Okay.

A. So yes.

Q. Yes, you were. So did you hear Dr. Portier testify, as

well?

A. That is correct.

Q. Okay. Excellent. And in your report you referenced the 1983 Monsanto Mouse Study. Right?

A. That is correct.

Q. Okay. And you I think said in your deposition -- and I'm paraphrasing you, but you said that there was one specific control-group tumor that was interesting to you. Do you remember that?

A. I'm not sure what you're referring to.

Q. Okay. So did anything stand out to you about the 1983 control-group tumors in that study?

A. For which type of tumor are you referring to?

Q. Renal.

A. Yes, I do remember the data from that study.

Q. Okay. What do you remember about that renal tumor?

A. So there was quite a bit of deliberation over that neoplasm. So I remember that the original dataset was that there were no control tumors.

Q. Right.

A. There was one in low-dose. No. You know, I may be mistaken. Can I look in my --

Q. Sure, of course.

A. -- report? It was like zero one zero three, or zero zero, but I have to -- I'll find out. I don't know if I have that in

my report. There was either one tumor in the low-dose, or the mid-dose. I think it was in the mid-dose, but I'm not sure. If you could refresh my memory what this -- incidence level was.

Q. Well, let me just kind of step back. I think you mentioned to Ms. Pigman earlier that one of the things you do in your analysis is that you look at the slides. Right?

A. I looked at the slides?

Q. Yeah.

A. No. I looked at the data.

Q. Okay. So do you know if those slides exist in the 1983 --

A. I would assume they exist somewhere.

Q. Okay. Would you be surprised that I've actually seen them?

A. No, I wouldn't be surprised.

Q. Why haven't you seen them?

A. I don't need to see them.

Q. Okay. So even though there was great debate over them by both the EPA, there was a Pathology Working Group over them, we filed a motion to compel to see them, it didn't cross your mind that maybe you might want to look at them?

A. Not at all. So I've served on many Pathology Working Groups. This is an excellent process to reach consensus on a final diagnosis. I know some of the pathologists that were on that actual Pathology Working Group. I have complete

confidence in their interpretation of the neoplasms.

Q. But it wasn't important for you to actually lay your eyes on them?

A. No.

Q. Okay. Now let's go to something we probably agree on. You heard both Dr. Jameson and Dr. Portier testify. So you heard Dr. Jameson say that the toxicology is used to determine if a chemical is an animal carcinogen. Right?

A. I don't know exactly what process he uses. I can describe the process I use.

Q. Okay. Well, would you agree that toxicology is used to determine whether or not an agent is an animal carcinogen?

A. Toxicology is a science. And toxicologists design experiments --

Q. Mm-hm.

A. -- to assess carcinogenicity.

Q. In animals?

A. In animals.

Q. Okay. Excellent. And you heard Dr. Jameson testify to that. Correct? We can -- I mean, that's a pretty basic toxicology principle. Right?

A. Yes.

Q. Okay. And you -- you also heard Dr. Jameson testify that you then used the epidemiology to determine the tumor site in humans. Right?

A. I believe I heard that.
Q. Okay. And didn't look at the epidemiology literature in this?
A. I'm a veterinary pathologist. I focused on what I am an expert in.
Q. You didn't look at the epidemiology in this case. Right?
A. I only read some of the general knowledge and read the IARC report. So I read some information, but I do not proffer an opinion on epidemiology.
Q. Okay. So you didn't rely on epidemiology in your opinion. Correct?
A. Absolutely not. I only evaluated the data from the 12 bioassays, and made my opinion on carcinogenicity.
Q. Okay. Excellent. And you mentioned earlier that there were chemicals that are carcinogenic in rodents, but not in humans. Do you remember testifying to that --
A. Yes.
Q. -- a few moments ago? Just -- what's an example of one?
A. Oh, sure. There are many examples. So I don't know. Are you familiar with GLP-1 agonists?
Q. No. I mean, I'm going to take your word for whatever you say.
A. Well, GLP-1 agonists are a brand new drug.
Q. I just need to know the name of one.
A. GLP-1 agonist, parathyroid hormone are two examples I've

been very recently involved in. And the GLP-1 --

(Reporter requests clarification.)

THE WITNESS: And this is -- these are new drugs for diabetes. And when these drugs were being developed by multiple pharmaceutical companies, they found that they induced cancer in rats in the thyroid glands. And then another company developed a very similar drug, and it induced thyroid cancer. So it was very clear that this class of drugs induces cancer in had both rats and mice. So obviously the FDA is very concerned.

And once we recognize a carcinogen in a rodent, then you have to determine the mode of action before you can determine human relevance. To determine the mode of action requires experiments over five years or more. So all of the pharmaceutical companies got together and figured out the mode of action.

And to make a short story -- make a story short, they found that this was due to binding of the drug to certain cells in the thyroid gland. This only happens in rats and mice. Doesn't happen in dogs, doesn't happen in primates, and doesn't happen in people.

Now all these drugs are on the market, and helping diabetic patients.

Q. Okay. And I'd actually didn't write down the name of that. What was it?

A. GLP-1 agonist.

Q. Okay. And what does the epidemiology data say for GLP-1 agonist?

A. So it's interesting. So since it does cause cancer in rodents in the thyroid gland, the FDA still requires that post -- post registration of that drug, they're checking the patients for thyroid tumors. And they do that with a biomarker.

To the best of my knowledge, they actually haven't found any tumors induced by those drugs, but they're looking for it. Now, what's interesting is in the process of looking for these tumors, they've actually identified patients that spontaneously developed thyroid tumors. The thyroid tumors were removed, and they were cured. So it's just an amazing story.

Q. There's really no epidemiology data for that one?

A. I don't -- I am not knowledgeable on epidemiology. Yeah.

Q. Okay. Excellent. All right. And you know we're not challenging your qualifications here. I'm sure you're a very fine veterinary pathologist to render this opinion. We're actually not really even challenging your conclusions or your methodology too much.

What we're most concerned -- I wouldn't say "concerned" is the right word -- just curious about is the time you spent in Brussels. So if we could talk a little bit about that --

A. Sure.

Q. You went over to a Reading Room. Correct?

A. That's what it was called.

Q. Orbing. And this Reading Room houses the data for all these 12 cases that we've been talking about. Right?

A. Well, the data from the 12 bioassays --

Q. Mm-hm.

A. -- were present electronically on individual computers in the Reading Room. This was available to anyone who wanted to go. I chose to go. And it was very easy to go. You basically just signed up online. You could sign up for up to four half days. I signed up for four half days. And I looked at this data. And this was some of the data that I used in my deliberations.

But what's very interesting is -- is once I examined all the incidence data that was available, I actually didn't need to go to the Reading Room, but I'm still glad I went. And the information weighed in on my decision.

Q. And it would probably be easy to go -- you're right -- if -- if it wasn't just open for six weeks, and not publicly known to people. I mean, how did you find out that it was even open?

A. I don't remember.

Q. You don't remember if you were researching or --

A. I probably -- I probably was informed by Hollingsworth counsel.

Q. Okay. And it was open from August 24th, 2016, to Halloween of that year; so about six weeks. Is that right?

A. I don't recollect the opening hours.

Q. And that was right around the time when you were drafting your Expert Report. Right?

A. I completed my Expert Report July 31st.

Q. Okay. And so you spent -- I think you testified -- around 12 hours --

A. Correct.

Q. -- ish. I mean, I'm not going to hold you to that, but around 12 hours. Right?

And you looked at the data for all 12 rodent cases?

A. Well, let me clarify this. So first of all, this was a room with a long table that had approximately 10 computers on this table. Okay? All of the data was on the computers. Okay? So I was monitored. When I was in the room, usually there was only one or two other persons in the room that were examining the data. And these were the slowest computers you can imagine. Okay? And you can look at one screen at a time.

Q. Okay. So --

A. And so if each report is 1,500 pages, you can imagine how much data I actually got to examine in these two days. Not very much.

Q. Right. So how many --

A. I actually wrote this all down in my notes, so you can

actually see all of the data that I examined.

Q. Sure. So how many pages do you think -- do you think you actually went through?

A. Well, the most important thing that I wanted to read that actually wasn't necessary for my conclusion is I wanted to read my peers -- other veterinary pathologists -- how they interpreted the data, and how they reached these conclusions.

So the first thing I did was to read the pathology reports, which was approximately 30 pages for each study. This was something I could easily accomplish in the first day.

Then I selectively I went through some of the data in the other studies -- I mean in the 12 studies.

Q. Okay. So I was just -- I just went and got my calculator. Sorry. You said that you did 30 times 12. Right? So that's 360 pages of pathology reports. Is that right?

A. Mm-hm.

Q. And then how many other pages do you think you reviewed?

A. Oh, I don't know. I looked at summary data. So -- and when I looked at the summary data, I actually wrote it down. So this is -- was a very slow process. Right?

Q. Sure.

A. And so I took approximately 50 handwritten pages of notes. And I would guess I looked at 10 to 20 pages of summary data for each study.

Q. Okay. So that's another 150 pages or 200 pages, so

around -- you've looked at around 600 pages. Right?

A. Yes, but actually that summary wasn't very useful to me. Why? Because -- because I could only write down some of the data, but I wanted to have samples of the data I looked at.

So all of this data that I looked at, except for pathology reports, is present in Greim in the supplementary data. So I actually came back and relied more intensely on Greim to finish my deliberations, because the data I actually wrote down in the Reading Room was not sufficient for me to complete my interpretation.

Q. Okay. Do you feel like your opinion is more credible than Dr. Jameson, and/or Dr. Portier because you visited this private Reading Room?

A. No, absolutely not. My opinion is more credible because I used the proper evaluation of the data to reach my conclusions. The Reading Room -- the Reading Room pathology reports did not influence my interpretation, but it is nice to see that all of the other pathologists on all 12 studies agreed with my interpretation.

Q. Okay. So would it be fair that around -- you reviewed around 600? I don't want to put words in your mouth.

A. I really couldn't tell you how many pages.

Q. Okay, but we would agree that there are -- I mean, I think in just the 1983 study, alone, there are around 4,000 pages. Isn't that right?

A. Right. And keep in mind that this -- these were old computers with monochrome screens. And you hit the arrow, and you'd get the next page. And you'd hit -- I mean, it was excruciating.

And actually, the computers went down on the first day. So for an hour and a half I couldn't even look at the data. So, like I said, this was not important for me to make my conclusions.

Q. But -- so at most, I mean, you probably reviewed 1 percent or something of what was over there. Right?

A. I reviewed a small percentage of the data.

Q. Okay. And it wasn't important for you to stay and review more? I mean, you had this data no one else has access to. You didn't want to review it all?

A. No. I was ready to leave after two days. I had what I needed.

THE COURT: Jeez. In your Expert Report you made it sound so fun. It was like -- it was as if you were vacationing in Tahiti.

THE WITNESS: I had a couple nice dinners.

BY MS. WAGSTAFF

Q. So have you reviewed any slides in your -- in your -- the preparation of your Expert Report?

A. No, I haven't. In this kind of work I rarely look at slides. I do look at slides when there are disagreements in

diagnoses. And I participate routinely in Pathology Working Groups.

MS. WAGSTAFF: Okay. And there was -- well, actually, strike that. No further questions.

THE COURT: Anything further?

MS. PIGMAN: Nothing.

THE COURT: Thank you.

We were thinking maybe we'll take a break, and then go until 3:00 or 3:15; something like that. So why don't we take -- why don't we resume at 20 after?

MR. GRIFFIS: Thank you, Your Honor.

THE CLERK: Court is in recess.

(Recess taken from 2:13 p.m. until 2:26 p.m.)

THE COURT: All right. What's next?

MR. GRIFFIS: Monsanto calls Dr. Chris Corcoran.

THE CLERK: Please raise your right hand.

CHRISTOPHER CORCORAN,

called as a witness for the Defendant, 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: Sure. It's Christopher. C-h-r-i-s-t-o-p-h-e-r. And the last name is Corcoran. It's

C-o-r-c-o-r-a-n.

THE CLERK: Thank you.

MR. GRIFFIS: Slide please.

DIRECT EXAMINATION

BY MR. GRIFFIS

Q. Good afternoon, Dr. Corcoran.

A. Good afternoon.

Q. You have a doctorate in biostatistics from Harvard University. Right?

A. Yes.

Q. Could you show us on the map which is Slide 2 where it is that you work, sir?

A. I'm sorry. I just noticed that when Dr. Neugut was here, that Utah actually appeared on that map, so I was kind of excited about it.

THE COURT: That doesn't seem like where Utah actually is.

THE WITNESS: No. I said the same thing. Apparently Utah is south --

MR. GRIFFIS: It's someone's mental map, I guess.

THE WITNESS: There you go.

BY MR. GRIFFIS

Q. Sir, we've heard some attacks on you over the last few days. So I'd like to spend just a minute on why it is that people should listen to you about the opinions that you've

given in your Expert Report. Could we have your qualifications slide, please? I hope this is showing up in a more centered way on other monitors.

A. Mine is a little off center.

Q. We're good.

A. We're good. Well --

Q. Go ahead, sir.

A. I'm sorry. Should I go ahead?

Q. Absolutely.

A. Well, I was kind of relieved this morning because when Dr. Portier was testifying, he acknowledged that he thinks I am qualified from a statistical standpoint, so that was a relief; but I guess one thing I want to point out is that I'm here to evaluate the statistical evidence from the rodent carcinogenicity studies.

All of the charts that Dr. Portier showed with -- that were filled with p-values for, you know, his logistic regression models for his trend test -- that's actually my dissertation was about. So my dissertation -- my doctoral dissertation at Harvard was about trend tests for these kinds of dose-response experiments; and specifically, with specific focus on what to do when you're analyzing small samples, and what to do when you're analyzing samples that come from different sources, like, say, in this case, from different studies. So that's my area. That's one of my areas of

research expertise.

Q. Have you been involved, sir, in creating industry standards for analyzing samples when events are rare?

A. Well, yeah. For example, one of the trend tests that I created as a part of my doctoral dissertation almost 20 years ago that was published had to do with this exact setting, you know: What to do when you have rare outcomes or uncommon events you're looking at, like some of the tumor types we're talking about here for glyphosate, for these glyphosate experiments. But what to do when you have to compute a trend test when the samples sizes are small, and you have this kind of -- this kind of within-study -- these within-study differences that we have heard about throughout the testimony over the past few days. How to handle them.

And before my -- before I solved this problem with my advisor, there was no option for this. And so this area of small-sample inference statistical analysis is basically in a trend test is something that I have a lot of expertise and experience in.

Q. And have you had NIH -- National Institute of Health -- grants to develop tests for regression with small samples and rare outcomes, sir?

A. Yeah. I've -- well, this total really represents the sum total of all NIH-funded grants. I've worked on a lot of collaborative projects having to do with risk for Alzheimer's

disease, cognition in aging, hip fracture among the elderly, autism, cancer, and other chronic diseases. So I've worked on these large, complex, interdisciplinary projects that have been funded by the NIH.

But two major NIH grants that I've had over the past, you know, I'd say decade -- actually, I guess you could argue three, but at least two grants have to do specifically with this methodology -- logistic regression -- and doing trend tests, basically, when you have outcomes that are relatively uncommon.

Q. Okay. Let's apply your expertise, sir. And would you -- I'm not going to recapitulate your whole Expert Report, of course, but would you please summarize your critique of Dr. Portier, please?

A. Sure. My independent evaluation, after having read his Expert Report along with the material that was in the appendices of his Expert Report -- you know, we've been in the weeds a lot the last few days, so I want to try to kind of categorize these problems in a way that helps us to kind of identify what the broad problems are.

And so, you know, consistent, I think, kind of with my Expert Report, which has more detail, I think I'd classify these problems in three categories. I mean, one is just the inconsistency from, you know, throughout his evolving analyses; that he hasn't used a consistent approach. He's responded and

reacted to other criticisms, but it's been kind of a -- you know -- a moving-goal-post kind of endeavor. His analyses have evolved.

I think the second, which is a really serious problem, is this pooled approach that he's using, which is completely flawed. And -- and, you know -- and I think it has -- has kind of a big bearing on his conclusions.

And the last, which I think is the overarching problem and the most serious problem, is what in statistics we call a "multiple testing problem" or "multiplicity problem" that -- we've heard that talked about on and off for the past few days, as well.

But you know, the problem is: What do you do when you compute hypothesis tests for, in this case, hundreds, perhaps even thousands, of outcomes? How do you handle that?

And there are some conventional statistical approaches that are used and that we teach, you know, in universities and so on, that I teach to my students when I teach courses in categorical data analysis; but there are conventional approaches that are used; are widely accepted, you know, in research circles. And those adjustments were not applied here, which is of major concern, because of the -- you know, there's a lot of other people to talk about because the possibility of having these spurious associations that have nothing to do with glyphosate-related effects.

Q. Okay. Dr. Corcoran, lots of people in this room know that peer review is one of the things that Judges consider when they're deciding whether scientific evidence is reliable or not. And I don't expect you to comment on the legal standard, but is it the case that Dr. Portier's method has gone -- method with regard to glyphosate has gone through a sort of peer review?

A. Yeah. Well, I think that's one of the things here that's interesting, is that, you know, as far as the statistical analysis goes for these toxicology studies, there has been no peer review to this point. I mean that's, I think, more or less what this is kind of about.

Q. Some of his piers have been commenting, though. Right?

A. Right. I mean, there hasn't --

I'm sorry. Let me rephrase that. There hasn't been a peer review of the sort that I would expect if I sent a paper to a journal with the results that -- you know, that he has or that I have. So that formal process hasn't happened.

But it's happening kind of, I guess you'd say, on an ongoing basis, as his analyses have evolved, you know, beginning -- beginning with his work with the IARC Working Group, and continuing through these Expert Reports that he's produced.

So, you know, it's -- I guess what I want to emphasize -- it's not just me. You know, I've done my own independent

evaluation of his work, but as I've examined his Expert Report, and especially the material that came with the Appendix, there have been other -- there have been other researchers in the field who, you know, even have, perhaps you'd argue, more direct experience than I have with toxicology directly, like Dr. Tarone and Dr. Haseman. And their conclusions have been negative.

Q. Okay. Without getting into the weeds about the biostatistics critiques of Dr. Tarone and Dr. Haseman and the responses and so on, would you just acquaint us briefly with what it is that Dr. Tarone said?

A. Right. Dr. Tarone -- and again, this was part of my review of Dr. Portier's Expert Report, because this was in the Appendix. Dr. Tarone -- you know, Dr. Tarone responded. I mean, I think he published a paper about the IARC results, but this was just some brief correspondence of his. And he criticized the use of the approximate trend test, which, you know, we don't need to get into too much technical detail, because I've outlined, you know, the rationale for the approximate versus the exact test in my Expert Report.

Q. Dr. Tarone said that an exact test should have been used by Dr. Portier instead of an approximate test?

A. Right. That's right. And he had, you know, a couple of other criticisms. One is that he was wondering why negative affects were ignored, for example; why we're only looking just

in one direction, when there are -- there are a bunch of incidence -- I guess tumors where there was decreasing incidence across dose groups.

Dr. Haseman -- he had -- he shared a couple of those criticisms, but he also -- he also referred to the pooled analyses that Dr. Portier was doing as fatally flawed -- is the way he put it. And he also said that historical control approach that he was using was flawed.

And again, I don't want to go onto the -- some of the technical reasons for that, because they're all contained in my Expert Report, but my independent conclusions --

Oh, and I guess another criticism Dr. Haseman had was the multiple testing comparisons; that there wasn't really a good accounting for that. In fact, it was that criticism, I think, that led to Dr. Portier's inclusion of his Table 15, you know, in his -- in his report that we've -- there's been a little bit of discussion about today.

Q. Dr. Portier keeps adjusting to respond to these criticisms?

A. Right. Kind of -- his approach is moving along and evolving, but the bottom line is that there hasn't been kind of -- there it wasn't an *a priori*, you know, strategy or a consistent approach to any of these analyses. They've just kind of evolved as time has passed.

Q. Okay, sir. Let's go to Slide 6, and talk about some

examples of inconsistent methodology that you identified in your Expert Report.

A. Well, yeah. I reviewed some of these in my Expert Report, but, for example, you know, toward the beginning he was using the approximate trend test. Now, you know, he acknowledged the exact trend test was useful, and he started using it in some of his subsequent analyses, but it's still a problem, I mean, for two reasons.

One is Dr. Jameson. You know, in his results I was interested to see yesterday that he's still using the approximate test, even though, you know, Haseman, Tarone, several other people that we've had -- you know, other people who have testified -- have talked about how it's important to use the exact.

Q. That last slide of Dr. Jameson's where he was showing: These are the --

A. Right.

Q. -- the ones that I consider to be statistically significant p-values? Those were from the approximate; not the exact test?

A. He was using an approximate p-value, which, as I pointed out in my Expert Report, and as Haseman pointed out, and Tarone pointed out, that can vastly underestimate the actual p-value. And so it can lead to a large excess of spurious associations. So it's still a problem now.

It's also a problem for -- you know, in terms of Dr. Portier's Rebuttal Report, because he used -- you know, he responded to my critique. And he used a logistic regression. He described that during his testimony yesterday; but again, he's noted using exact logistic regression there.

So he was right that if you use logistic regression in the right way, it can allow you to do a trend test or accomplish the same purpose as a trend test, but he used the approximate version of the logistic regression model, so we're kind of back at square one. In other words, we still have this exact-versus-approximate problem.

Q. Okay. What's next, sir?

JUDGE PETROU: Wait. Before we go to what's next, I just want to understand, because you're complaining about him using inconsistent methodology; saying, *Then it was an approximate trend test. Now* -- I'm not quite sure when then and now are; but in any event, now states that context. But if I understand your testimony correctly, you think it's a good thing that he's how using the exact trend test?

THE WITNESS: Yeah, but it's still problematic for two reasons. One is that it's still is a problem now, because he's still using approximate version of the trend test with those logistic regression results that he showed the other day. So he wasn't using exact logistic regression, which, again, is another thing for the -- that was a focus of my, you know,

dissertation. So I -- that's something I know quite a bit about.

But the second issue is just a kind of a history of inconsistent --

JUDGE PETROU: No. I heard that.

THE WITNESS: Yeah -- methodology. So that's the reason.

Yes, I'm happy when somebody's using that, but it's still not being used uniformly now.

BY MR. GRIFFIS

Q. What's the next example, sir?

A. Well, you know, the IARC Monograph. I mean, you know, I have to admit I'm a little bit confused by this, because I -- you know, what I heard -- what I've heard testimony over the past few days is that -- and I think this may have been Dr. Jameson -- that they had the Greim data, or they had the data from the 12 studies available during the Working Group meeting, but they -- he said that for one reason or another, they didn't use all of the data.

Well, my reading of the IARC report is that they dismissed, you know, all of the rat studies and some of the mouse studies, saying that they were not usable, for their own reasons.

But -- but in other words, then rat studies were not admissible; now they can be used.

And so now we seem to have settled on this canon of these 12 studies, but that hasn't always been the case.

So, you know, it's a little bit confusing to me as an external reviewer. You know, those issues are a little bit confusing in terms of why we -- why they were not admissible, but now they are.

Q. Yes, sir. What else?

A. Well, this has to do with the pooled analyses. You know, I think Dr. Portier -- and there have been others who have testified over the past few days that, in spite of your best efforts to control these bioassay experiments, you can't control everything. So there are these underlying differences, like environmental or genetics differences, that arise from study to study, that have to be accounted for. And that's -- those were not important, because, you know, Dr. Portier said he was just going to kind of lump data together across studies, which, of course, was, you know, criticized by Joe Haseman and myself.

But now, again, he says that they're important, because he fit logistic regression models that he said accounted for that, although his models didn't completely. But at any rate, the study difference were not important. Now they are important. That's why he applied the logistic regression models. So again, this kind of strikes at consistency. There has not been a consistent approach.

Q. Could we have the next slide, please?

A. Sure. I pointed out some of these examples in my Expert Report, so I don't want to belabor this, because I believe Mr. Lasker kind of went over this in his cross-examination, but this is especially striking to me. And there were a few examples of that that I outlined in my Expert Report.

You know, Dr. Portier talked today during his cross-examination about how, you know, in the case of adrenal cortical tumors among females in these Sprague-Dawley rat studies -- these four studies. He excluded Lankas, because he eyeballed the -- you know, the kind of the spontaneous tumor rate among controls, and he decided that it was not consistent with the other studies, and so he eliminated Lankas from his computations. And he computed his trend test p-value based on an incorrect but a pooled analysis with these other three.

And he did a similar thing for kidney adenomas.

Oh, sorry. Let me go back.

But with thyroid C-cell tumors and interstitial testicular tumors, he, you know, just focused on Lankas, at the expense of the other three. And finally with thyroid C-cell tumors, he included all four.

I mean, this is -- I know that, you know, Dr. Portier said that, *Well, I've got a lot of experience, you know, in -- in this field, so I feel like I can navigate these using my own judgment*; but there are statistical approaches for making this

kind of assessment without just making an executive decision about what to include or exclude just based on your own personal judgment.

And those approaches were not used. He didn't do -- you know, this is a statistical issue. You know. Are the Lankas rats in this case -- are they different from the others? Are they different enough for me to eliminate? That's a statistical issue, and that wasn't really accounted for.

THE COURT: Can you show me where in his report he relied on the thyroid C-cell tumors conclusion there in the third line, where only Lankas is used?

THE WITNESS: Yeah, I think I can, if you just give me a second. Do I have his report or no?

THE COURT: Take your time.

MR. GRIFFIS: Yes.

THE WITNESS: What tab is it?

MR. GRIFFIS: His main Expert Report is Tab 2.

THE WITNESS: Well, that's my -- oh.

MR. GRIFFIS: I'm sorry three. Three.

THE WITNESS: Oh. Three.

THE COURT: Tab 3.

MR. GRIFFIS: Tab 3. Yes.

THE WITNESS: So at page 34 of his report.

THE COURT: Okay.

THE WITNESS: He says that he says that -- at the

bottom he focuses on the Lankas study. However, the Lankas study was for 26 months, and the other three were for 24.

The C-cell carcinomas could be a result of the longer exposure period, even though the dose was substantially lower than the --

THE COURT: Right, but then in the next sentence he says, *From these data I conclude that the evidence is weak that glyphosate causes thyroid and C-cell tumors in female Sprague-Dawley rats.*

THE WITNESS: But he does -- but he does include this in his -- I guess you'd say, his patchwork of evidence.

In other words, if you look at the Table 8 --

THE COURT: Okay.

THE WITNESS: -- you'll notice that for thyroid C-cell tumors there's a plus sign. He's been testifying that --

THE COURT: Sorry. Where? Can you give me a second to --

THE WITNESS: Oh, I'm sorry. Right in the middle of the table there's a plus sign.

So in other words, he's counting that as what he has been calling "marginally significant," which is a p-value for him between 5 and 10 percent. What I'm pointing out is that --

THE COURT: And this is for -- that plus sign is for female rats?

THE WITNESS: That's right.

THE COURT: And how can I tell from looking at that table that that's for female rats?

THE WITNESS: I think under -- on the top, the column header "Thyroid C-cell Tumors -- Females."

THE COURT: Oh, okay. Right. Thank you.

THE WITNESS: So, you know, as he did with his slides during his -- during his testimony, where he color coded the slides to show, you know, if you kind of squinted your eyes and crossed them slightly, you could kind of see where the significance was. That's kind of what he's doing with this table, is that he's using plus signs to indicate something approaching significant or something highly significant, so that the impression one gets in looking at this table is that, well, we see a pattern of significant -- ordinarily significant results. And so that's how he's using these kinds of results to support his conclusion.

BY MR. GRIFFIS

Q. And it's part of your criticism -- the inconsistency from tumor type to tumor type, and what is clustered together to reach these conclusions?

A. That's right. Yeah.

Q. Could we have the next slide, please? The whole thing?

A. Sure. Again, I don't want to belabor this one, either, because I think that -- I think that Mr. Lasker already

questioned him about this; but from a statistical point of view, what I want to point out here is that in -- and I'm trying to review this based on his own citations that he uses to support his pooling, but the idea here is that in one group, the Knezevich Study, you have what at least you observe as a higher incidence in the highest dose group compared to the lowest.

So it looks like -- you know, we know we haven't done a formal statistical test, but it looks like at least there's higher incidence than there is in the low-dose group.

And the Atkinson Study is -- again, as Mr. Lasker already reviewed today, combining these kidney tumors in the way that he did, he got, you know, 2200, which actually turns out to result in a p-value less than .05 that there is decreasing incidence of tumor with glyphosate.

Well, again, from a statistical standpoint, one would not ever just throw these data into the same pot and analyze them, because, as we'll see, using his own citations, an important step is to decide whether these affects are even, you know, significantly different before you combine them.

So in other words, an important step in any kind of analysis where you're using data from more than one study is to decide whether the effects are consistent.

Q. Let's go there and look at that, sir.

A. What's that?

Q. Let's go there and look at that. And let me ask you a couple prefatory questions.

A. Sure.

Q. There are a couple of citations that Dr. Portier made in his Expert Report to articles that he said he followed in the pooling analysis. Right?

A. Yeah. I was interested in these articles because of the way that he pooled. He said that these articles supported his approach, which is basically just to lump datasets together, as though they came from the same experiment. And so I think --

Q. These are the Friedenreich and --

A. Friedenreich and Blettner, yeah, studies. I mean, these are the ones that I took a look at. Now --

JUDGE PETROU: Are those in the exhibits?

MR. GRIFFIS: Well, yeah. They're not in a tab. They're in the back pocket of the binders. And let me give you the references. This is reference 91 and 92 in Dr. Portier's Expert Report. And I'm going to be asking some questions about the Friedenreich.

JUDGE PETROU: So I see that the methods for pooled analyses by Friedenreich is labeled as Exhibit 911 there.

MR. GRIFFIS: That's right.

JUDGE PETROU: And is it Exhibit 598 for the other one?

MR. GRIFFIS: I believe that's right. Is that right?

JUDGE PETROU: For the *Traditional Reviews, Meta-Analyses, and Pooled Analyses in Epidemiology* by Blettner, *et al?*

BY MR. GRIFFIS

Q. 598. I have some questions for you from Exhibit 911.

(Reporter requests clarification.)

BY MR. GRIFFIS

Q. The one I just did? You've looked at both of these. Right?

A. Yes.

Q. And are they about pooling animal studies, or are they about pooling epidemiology studies?

A. No. They're both in epidemiological journals. You know, the principles that -- the principles that they outline for combining datasets for different sources are basically correct. I don't -- I just heard -- I just heard the previous testimony about, you know, how these datasets may or may not be pooled by people in the toxicology community. And so I don't really have anything to say about that; but you know, Dr. Portier included this. This was his justification. And so this is what I would kind of expect to see in his analysis, in other words.

Q. It's okay. So on the subject that you were raising before I brought this up, so that we could look at a reference while you spoke, sir, you said that when -- before you do a pooling --

A. Yeah.

Q. -- if you're even allowed to do it for animal studies in the first place, you would look at whether there's heterogeneity of results. Right?

A. Right. And --

Q. So could -- I'm sorry. Could you bring up, Scott, Step 6 from Friedenreich? That's on page 298, left-hand column.

A. Right. There are several steps that are outlined in both of these papers. This one -- I don't know -- has seven or eight. The other one has something like 12. But they both -- you know, they both basically say very similar things.

Q. It says -- I'm reading the second sentence, last -- also the last sentence of that first paragraph.

A. Right.

Q. *If, on the other hand, statistical and methodologic heterogeneity of effect is found across the studies, it would be more appropriate to use a random or mixed effects model to estimate the summary effects.* Right?

A. That's right.

Q. Did he do so?

A. No.

Q. Step 7 is on the next column. Explaining any heterogeneity between studies. And I'd actually like to look at the second paragraph here; the second paragraph under that column. Yes.

And -- but I have a real -- actually, a broader question; a more lay question. When you explain heterogeneity between studies, does "explaining" mean sitting down and giving a reason why it's okay to put studies together?

A. No. It doesn't mean that you, just off the top of your head, explain away the reasons for the heterogeneity, or explain away why it is that you don't have to take care of it.

This is a statistical issue. And so the correct statistical model, which, you know, Dr. Portier, I think, made kind of an attempt at after my -- after my own Expert Report was filed -- in his Rebuttal Report he said, *Well, I'm using logistic regression*, but this is a really crucial step.

With respect to that Knezevich and -- sorry -- Atkinson?

Q. Atkinson, yes.

A. -- the Knezevich and Atkinson example has a showing.

In other words, what this step has to do with is that you need to check to see formally whether or not those dose-response effects in these studies are the same, before you just throw them into the same bunch.

And I gave an example in my own Expert Report where I stepped through that very carefully for one of the combined analyses that Dr. Portier did. He didn't say anything about that specifically. I think he mentioned it briefly in his testimony yesterday, but he didn't really say too much about that in his Expert Report.

What I did is I said, *Look. If you're going to combine the Brammer, Suresh, and Wood studies*, which was another example I showed you in my Expert Report, *you need to assess whether or not the dose-response effects are what we would call "homogeneous,"* or whether they're similar.

And when I did, I saw that they were not.

And so, you know, I demonstrated how you would step through that kind of analysis to make sure that your pooling, you know, was -- was correct.

Q. So this isn't a matter of biology judgment. It's a matter of biostatistics?

A. No. It's a statistical approach. You know. We're just talking about the correct statistical approach.

And again, it's the same issue that was raised by, you know -- by Joe Haseman, as well, in the appendix material in his Expert Report.

Q. You told us a little earlier, sir, that the biggest issue that you identified with Dr. Portier's methodology was a multiple testing --

A. Right.

Q. -- problem. Would you --

A. Before we actually advance to that, could I just say one more thing about the pooling?

Q. Absolutely.

A. Statistically speaking, since we've been talking here a

lot about p-values and how to interpret them, and, you know -- and how especially to interpret results when we've computed hundreds or hundreds -- or thousands, this is -- this pooling issue is really crucial. This is not just a minor technicality, because, as I again explained in my Expert Report, if you don't handle that heterogeneity correctly, then the consequence is that you end up, in some sense, overstating your sample size.

So in other words, what that does is it leads to an even greater increase in potential spurious associations due to chance if you don't make sure that you soak up, you know, those differences between studies.

And so, you know, yes, the way that you handle it might seem, you know -- to a non-biostatistician it may seem like a technical issue, but it has enormous practical consequences. And that's why Joe Haseman was so adamant about it. And that's why I pointed it out, as well. So anyway, sorry.

Q. Okay. Thank you. Multiple testing -- that's another thing that Joe Haseman and you both raised. Correct?

A. Yes.

Q. Would you please explain it the way that you explain it to people who aren't, themselves, biostatisticians already?

A. Right. When I'm trying to explain this problem, you know, again, I think it's been described by -- within other testimony over the past few days, so I'll be brief.

But when I'm trying to explain this problem to my students I teach, I sometimes just refer to it as "the green jelly bean problem," because I use this comic strip.

Is it coming up?

Q. I don't think so. Slide 11, please.

A. This is XKCD.com. It's a kind of a comic for geeks and nerds, but this is kind of what we're talking about. So here are a couple of researchers who want to find out whether or not a jelly beans cause acne. So they gather some data. They look at people who are eating more jelly beans. They compare their acne rates to people who are eating less -- fewer jelly beans. And they get a p-value that's greater than point .05, so they decide, well, there's no evidence that acne causes jelly beans.

But then as all of us -- you know, because it's human nature, as all of us are prone to do, and especially in the research community, when we have a lots of data to play with, we start doing, you know, subset analyses, basically. We start dividing the data. We start slicing and dicing the data, and looking at different subgroups to see whether or not, you know, we can find any subgroup for which there's an association. And so we start computing lots of p-values.

And so here, you know, we're computing it for purple, and then brown, and pink. And I don't know if this monitor has great color resolution, so I hope I'm describing those correctly.

Q. You don't need to name all those colors.

A. Cyan and salmon. I don't know. There are a lot of colors here, but -- and then finally bingo! For the green jelly bean down there, we see a p less than .05, which is the 1 out of 20, as Dr. Portier said, on average that we'd expect to see. And so that's the thing that we advertise. You know, that's the sexy result.

And when I'm -- you know, for somebody like me, especially in academia, where I'm trying to make a career out of, you know, publishing positive results, this leads to a serious excess of spurious associations where we're just looking for p-values less than .05.

Q. Can you just tell us in a nutshell what the difference is between the first experiment, where they looked at jelly beans overall, and said, *No significant result*; and the second one, where they looked at each subset of colors, and found one, and then made a report about it?

A. Yeah. I mean, sure. The first experience -- the first experiment is a planned, you know, experiment that has to do with a single hypothesis about jelly beans and acne. And so that's the whole point of the experiment.

The rest of it is data dredging. I mean, it's data mining. It's looking at as many subgroups as we can to, you know, find associations. And, you know, when we use the p less than point .05 rule, we'd expect for about 5 percent of those

to come up by chance.

Q. So if you look at enough jelly bean colors, you'll find one just by chance, alone?

A. And, in fact, if we reran that experiment, chances are the next go-around, we might see zero color jelly beans; specific colors that come up with p's less than .05. We may see 2. We may see 3. On average, we'll see 1. And the next time you run that jelly beans don't cause acne, it'll be a different color.

(Reporter requests clarification.)

THE WITNESS: Yellow or red might be the one that comes up positive on the next go-around.

THE COURT: I think what he said is that, you know, the next time you run it, you might see zero, or you might see 1, you might see 2, or you might see 3.

BY MR. GRIFFIS

Q. So does Dr. Portier's work have a green-jelly-bean problem?

A. Yes, it does. As I describe in my Expert Report, we're talking about, you know, hundreds -- perhaps, you know, even you could argue, many more than that -- potential p-values based on this approach the kidney computed. And there's no adjustment for that multiplicity.

Q. When you say there's no adjustment, do you mean he made none; or there's no remedy in the field of biostatistics for this?

A. There is a remedy. And it's pretty straightforward. And it's recommended within our own profession that you do something like that. He just didn't apply it.

Q. What is it called?

A. Generically, it's called a "multiple testing adjustment," or "MTP" for short.

Q. Which one did you apply in your Expert Report?

A. Well, the one that I applied is what's referred to as the "false discovery rate approach," which -- it's grown a lot more. Its use has become a lot more widespread. And it's really generally kind of accepted now that -- it's very good. It performs very well in situations like these, where you have dozens or hundreds or thousands. I work on genetic experiments, where we do millions of hypothesis tests.

And what the false discovery rate approach does that, you know, multiple testing adjustments have not done historically is it avoids -- for lack of a better phrase, it avoids throwing the baby out with the bathwater because, you know, people recognize couple of decades ago, as we -- as we, you know, accumulated more and more data, and as it became possible to do so many more statistical procedures, they realized that, well, we don't want to place too high a penalty on this multiple test adjustment, because we may throw out -- I guess what you would say true-positives. We would throw out actual effects. And we want to avoid doing that.

And so this false discovery rate approach was developed specifically to make sure that you minimize the number of true effects that you discard or that you reject, at the expense of making sure that you keep that 5 percent type error rate.

Q. Could we have slide, 14 please? 14. Yes.

What does your field -- what are the standards of your field with regard to how to deal with this sort of problem?

A. Well, as Dr. Portier talked about yesterday, the American Statistical Association is the oldest professional organization of its kind. It's, you know, the body that most all of us -- you know, Dr. Portier and myself, people like us, statisticians, biostatisticians -- it's the body that we belong to. It's our professional society.

They actually came out with a very -- they took a very unusual step a few years ago, because p-values are so overused and so abused. You know, in my Expert Report I pointed out that there's actually been a lot of attention paid to them in the popular press, not to mention the scientific press, because so many results are not reproducible. We just see the green jelly bean thing advertised, and then nobody can every reproduce it. And we see lots of episodes like that.

So the ASA convened a panel OF very highly regarded statisticians in our field. And they met together, and they came out with this statement on p-values to kind of give the -- you know, the profession some guidelines. And they suggest a

few simple steps that are easy to apply in situations like this, where you have, you know, many, many p-values. One is full reporting of all p-values, full transparency; so, in other words, report about everything that you did everything that you tried.

Q. Is that an issue with Dr. Portier's report?

A. Yeah. I don't -- I mean, we have kind of some selective results, especially when it comes to the pooling; but we don't -- I mean, I was interested when I actually saw his deposition that, you know, one of the Hollingsworth attorneys asked him, you know, *How many how many p-values did you compute?* And he couldn't really answer -- because I was curious about that, too.

Q. Why does it matter if he didn't know how many; couldn't say how many p-values he computed?

A. Because that really undermines your ability to report, to be completely transparent about everything that he did.

Q. Is it possible to do accurate false discovery rate or other corrections, if you don't know how many p-values you calculated?

A. No, absolutely not. I mean, that's the baseline. You have to know how many p-values you computed, before you make an adjustment. So that's at a minimum.

Q. Okay. Would you briefly discuss the next bullet, sir? We're a little short on time.

A. Right. And I think -- the second bullet point -- some other testimony has alluded to this. You know, P-values -- they do tend to be overused sometimes and abused on there.

So one -- and a second thing that the ASA suggests is -- is actually looking at treatment effects; so dose-response effects instead of just p-values.

And finally, you know -- and I guess very importantly -- adjusting p-values for the number of tests using, for example, false discovery rate, which is the most highly recommended approach in this kind of case, where you have, you know, so many p-values that you're evaluating, and that you want to make sure that you don't throw out, you know, the true positives along with the, you know, the false positives. So the FDR approach is the recommended standard in situations like this, or it's recognized as the standard.

Q. I know you talked about it at length in your Expert Report, and I don't want to recapitulate all of that now -- we haven't the time -- but would you please just tell us when you did the false discovery rate analysis with regard to Dr. Portier's data, to the extent you could understand it, what did you find?

A. I applied the false discovery rate adjustment, I think, in my Expert Report some of the summary results; at least, for any -- any tumor types that could have been statistically significant. Those are all contained in Appendices C and D,

and so we don't need to put those up here; they're in the Appendix.

But what I found in the end was that there was none. Once you actually adjusted for the multiple tests, there was no evidence of any glyphosate-related effect.

And, by the way, that was looking either for increasing risk of tumor -- increasing incidence of tumor -- or decreasing.

MR. GRIFFIS: Thank you, sir.

THE WITNESS: Thanks.

THE COURT: Cross?

MS. ROBERTSON: Your Honor, plaintiffs do have cross. We're asking if we can break for the day so we can try and clean up some of the questions to make them as concise as possible.

THE COURT: Okay. The only thing I'm concerned about is, you know, getting through tomorrow.

MS. ROBERTSON: Understood, Your Honor. I mean, concise as possible -- given the testimony of Dr. Corcoran, I'm going to need to readjust my questions. I've been allotted 12 minutes by my side. And I just definitely need to make sure my 12 minutes --

THE COURT: Are used properly?

MS. ROBERTSON: Yes, please.

THE COURT: All right. Fair enough.

So, you know, we have about four and a half hours of air time left. And I assume -- I can't remember. Who's Monsanto's next witness after this?

MS. WAGSTAFF: Dr. Goodman?

MR. LASKER: Dr. Goodman is scheduled, Your Honor.

THE COURT: You may not call Goodman. You may go straight to Mucci?

(Reporter requests clarification.)

MR. LASKER: We have to look at our timing, as well, with all of our witnesses at that are remaining. We have Dr. Nabhan also. So I just don't know when he's going to be going on, and what his time will be.

MS. WAGSTAFF: Your Honor, we told you that Dr. Nabhan needs to come out of time. So we could probably finish up Dr. Corcoran tomorrow morning. And then put Dr. Nabhan on after that, if that would work for everybody.

MR. LASKER: Yeah. That's what we were anticipating.

MS. WAGSTAFF: Okay. And then we would be done.

THE COURT: Okay.

THE CLERK: I think you'll have time.

(Discussion off the record.)

THE COURT: I mean, I guess if we start at 10:00, I mean, my -- the issue I'm concerned about is my hijacking too much of Mucci's time, so I want to make sure I have enough time.

MR. LASKER: That's part of our calculation. We anticipated that, Your Honor.

THE COURT: But I guess we should be okay. I mean, if we start at 10:00, and we --

I think what I would like to do is sort of tweak our calendar tomorrow, if that's okay with people. Start at 9:00, and plan on ending at around 3:00.

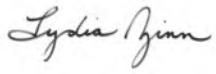
MS. ROBERTSON: Yes, Your Honor.

THE COURT: That way, if we really need to go past 3:00, that gives us a little room. I'm not sure we'll -- I mean, with four and a half hours left. And, you know, that -- that's about 9:00 to 2:30, or something like that, if you include lunch breaks and whatnot. I think that would be fine, but I want to give us a little bit of cushion. So why don't we start at 9:00 tomorrow?

MS. ROBERTSON: Yes, Your Honor.

(At 3:12 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.



March 9, 2018

Signature of Court Reporter/Transcriber Date

Lydia Zinn