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EXHIBIT 15

FILED UNDER SEAL

Page 1421

IN THE CIRCUIT COURT
TWENTIETH JUDICIAL CIRCUIT
ST. CLAIR COUNTY, ILLINOIS
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DIANA HOFFMANN, individually and as Independent Administrator) of the Estate of THOMAS R. HOFFMANN, Deceased, et al.,)
Plaintiffs,)
vs.) No. 17-L-517
SYNGENTA CROP PROTECTION, LLC, et al.,)
Defendants.)

VIDEO-RECORDED VIDEOCONFERENCE
DEPOSITION OF
PHILIP BOTHAM, Ph.D.
Volume 6 (Pages 1421-1683)

January 5, 2021

(Beginning at 4:39 a.m.)

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(The original exhibits were provided to the court reporter electronically to be attached to the original and copies of the transcript.)

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IN THE CIRCUIT COURT
TWENTIETH JUDICIAL CIRCUIT
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DIANA HOFFMANN, individually and as Independent Administrator) of the Estate of THOMAS R. HOFFMANN, Deceased, et al.,
Plaintiffs,
vs.) No. 17-L-517
SYNGENTA CROP PROTECTION, LLC, et al.,
Defendants.

–oOo–

VIDEO-RECORDED VIDEOCONFERENCE DEPOSITION OF PHILIP BOTHAM, Ph.D., produced, sworn, and examined on Tuesday, January 5, 2021, taken on behalf of the Plaintiffs, with the witness appearing from Jealott's Hill, England, before RENEE COMBS QUINBY, a Certified Court Reporter (MO) #1291, Certified Shorthand Reporter (IL) #084-004867, Certified Shorthand Reporter (CA) #11867, Registered Diplomate Reporter, and a Certified Realtime Reporter.

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IT IS HEREBY STIPULATED AND AGREED by and between counsel for the Plaintiffs and counsel for the Defendants that this deposition may be taken in machine shorthand by RENEE COMBS QUINBY, a Certified Court Reporter and Notary Public, and afterwards transcribed into typewriting and the signature not waived by agreement of counsel and consent of the witness.

--oOo--

PROCEEDINGS 4:39 a.m.

THE VIDEOGRAPHER: We are on the record. Today's date is January 5th, 2021, and the time is 4:39 a.m. This is the video-recorded deposition of Philip Botham, Volume 6, in the matter of Diana Hoffmann, et al., versus Syngenta Crop Protection, LLC, et al., Case Number 17-L-517 in the Circuit Court, 20th Judicial Circuit, St. Clair County, Illinois.

This deposition is being held at remote locations. The reporter's name is Renee Quinby. My name is Shaun Steele. I'm the certified legal videographer. We are with Alaris Litigation Services.

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Would the attorneys present please introduce themselves and the parties they represent.

MR. TILLERY: For the plaintiffs, Steve Tillery of the law firm of Korein Tillery.

MR. NARESH: For Syngenta, Ragan Naresh, Kirkland & Ellis.

MR. ORLET: For Chevron, Joe Orlet.

MR. HOPP: For Growmark, Tony Hopp.

THE VIDEOGRAPHER: Would the court reporter please --

MR. ZACHER: Wilbur Ellis Company, Gerhardt Zacher.

THE VIDEOGRAPHER: Anyone else? Would the court reporter please read the stipulation and swear in the witness.

THE REPORTER: This is Renee Quinby. I am a Certified Court Reporter. This deposition is being taken remotely, and those participating in these proceedings today are attending via videoconference with the witness appearing from England.

Counsel acknowledge their understanding that I am not physically present with the witness and that I will be reporting this proceeding

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remotely. Counsel further acknowledge that I will not be administering the oath in person but am doing so remotely.

The parties and counsel consent to this arrangement and waive any objections to this manner of proceeding.

Counsel, please indicate your agreement verbally on the record by stating your name and that you stipulate to these terms, after which I will swear in the witness and we may begin.

MR. TILLERY: This is Steve Tillery on behalf of plaintiffs. We stipulate and agree to these terms.

MR. NARESH: Ragan Naresh for Syngenta. We also agree to the terms.

MR. ORLET: Joe Orlet for Chevron. So stipulated.

MR. HOPP: Tony Hopp for Growmark. So stipulated.

MR. ZACHER: Gerhardt Zacher, Wilbur Ellis Company, agreed.

PHILIP BOTHAM, PH.D.,

of lawful age, having been first duly sworn to testify to the truth, the whole truth, and nothing

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but the truth in the case aforesaid, deposes and says in reply to oral interrogatories propounded as follows, to-wit:

--o0o--

EXAMINATION

BY MR. TILLERY:

Q. Dr. Botham, you're giving this deposition, your end of it, from what location, sir?

A. I'm in Charles Hill in England.

Q. Okay. And I'm in St. Louis, and we'll be taking this remotely. You understand the rules that we've discussed previously apply here as well. Okay?

A. (Nods head.)

Q. And now –

A. Okay.

Q. Yeah. Do you have information available to you or the ability to pull documents up on eDepoze for this deposition?

A. Yes. I've eDepoze -- I have eDepoze open and live and available.

Q. All right. This, as you understand, is the continuation of your prior deposition, right?

A. I understand that, yes.

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Q. All right. So this is actually another volume of the deposition and a continuation starting on page 1421 of your dep, and also we start here with the sequential numbering of your exhibits. So the first exhibit we use will be called 134. Okay?

A. (Nods head.)

Q. Do you have any questions about the procedure?

(Reporter clarification.)

(Off the record discussion.)

BY MR. TILLERY:

Q. So do you have any questions about the procedures?

A. No. I have no questions at this stage.

Q. And then my next question to you was since June of 2020, what additional work have you undertaken in connection with this case to prepare yourself for this deposition?

A. Yes. I've been provided with copies of a number of expert reports, which I have read; also some transcripts of depositions of experts, which I've also read through. I've reminded myself of my previous input to this process.

So I've reread my own deposition

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transcripts and, of course, continued to keep up to date with the literature on the subject of paraquat and Parkinson's disease.

Q. What literature have you seen that's come out since June that relates to any of the issues we've discussed? Not necessarily in detail but just the topic of the literature.

A. Well, we -- we always have done it through regular monitoring of the literature, and it continues to be quite a big body of literature.

There have been a few important papers, including a new epidemiology paper which I've particularly focused on. But it's been a pretty broad reading of -- to make sure that I'm as up to date as possible.

Q. And the regular monitoring you've talked to me about in the past, is there a formalized method at Syngenta for monitoring this, or is it done by area of interest by the scientists?

A. We do have a formal process. So we engage an external company to look at the literature to provide us with monthly reports of literature, which is – which relates to the relationship between paraquat and Parkinson's disease and

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actually paraquat toxicity more broadly. And I and some colleagues review those monthly lists and look up some specific papers as to when we feel it's appropriate.

Q. How long have you been working with the monitoring company, the external company in place to assist you in monitoring worldwide literature?

A. I think the external contract has certainly been in place for at least five years.

Q. And prior to that how did you do this?

A. It was done through our own internal resources.

Q. Did you have an assigned scientist or person involved to monitor this?

A. It was less formal than it is now, and we tended to do that within a team. So a number of individuals would do that.

Q. So how many people would, for example, monitor studies concerning the neurotoxicity of paraquat?

A. At the moment we have four people who specifically look at that including myself.

Q. Who are those four?

A. So that's myself. It would be

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Dr. Andy Cook. It would be Dr. Dan Minnema, and Dr. Haitian Lu, who has joined the team fairly recently.

Q. And where did he join from?

A. He joined the company from another organization, another company, around about a year ago, I think.

Q. Okay. Have you read -- strike that. Which depositions have you read?

A. I've read the depositions of the Syngenta experts that were -- that provided reports.

Q. Okay. Were there any, to your knowledge, that were omitted, or did you try at least to read every deposition of every witness taken by the plaintiffs in the case?

A. I read those depositions which were particularly relevant to the issues of safety, and I read those in more detail, certainly. So I didn't read absolutely every one in detail.

Q. Do you have a list of the ones you read?

A. I would have to -- to check my notes to give you the exact list.

Q. Okay.

A. But, again, I can do that at some

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point.
Q. Okay. You have the notes with you, though, right?
A. I have notes here in the office with me, yes.
Q. Did you read, for example, the deposition of Dr. Smeyne?
A. No. Dr. Smeyne? I've not read that one.
Q. Okay. All right. Okay. What else have you done besides reading depositions and the plaintiffs' reports?
A. And keeping up to date with the literature, as I said.
Q. Going forward.
A. Well, I've continued to lead the paraquat health science team, which we've talked about in my previous depositions.
We have regular monthly conference calls where we have been finalizing some of the research work that we have been doing, including some final publications, and also discussing some of the literature findings that we've been talking about a few minutes ago.

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Q. Has your –
(Reporter clarification.)
BY MR. TILLERY:
Q. Strike that.
Has your pharmacokinetic study been published?
A. It has been accepted for publication subject to some modifications, which we have now made.
Q. Okay. And where is that? What publication?
A. I would just need to go back and double-check. I believe it's Regulatory Toxicology & Pharmacology, but I would just like to double-check that that's where it's finally landed.
Q. Okay. Your health science team, paraquat health science team, are those meetings where minutes were taken?
A. No. At the moment, we -- the health science team doesn't attempt to capture minutes, formal minutes.
Andy Cook will, however, capture actions, and we'll put those into an email. And so there is a record of the activities that we're

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engaged in.
Q. And how long has that process been in place?
A. Well, the health science team as it's now constituted really started back in 2008, and it has evolved over time. There are now fewer people who are involved in the first instance. So it's been going in -- really in one form or another for 12 years now.
Q. And who is on the health science team today?
A. So it's myself, Andy Cook, Dan Minnema --
Q. Haitian Lu. Are there –
A. Haitian Lu, yes.
Q. Aren't there other people?
A. Yes. And one other person, Alex Stevens. And he has been the – one of the lead scientists on the pharmacokinetic papers. So he's been called up to the team in the last year or so.
Q. And do you meet monthly?
A. Approximately monthly we'll have a conference call.

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Q. How long do these meetings last?
A. Between one to two hours.
Q. Okay. And are you the chairman or head of that group?
A. Yes. I'm the chairman, and I still lead the health science team.
Q. Okay. All right. Our very first exhibit we're going to talk about today is Exhibit 134. Okay?
(Exhibit 134 was identified for the record.)
BY MR. TILLERY:
Q. And I want you to take a look at this exhibit, make sure that your eDepoze is working, and that you can look at this.
And just for the record, this is the Paraquat Subchronic Neurotoxicity Study in the Rat. It's an EPA guideline study of June 2006, 90 days in food.
Do you remember that study?
A. I do.
Q. Okay. Let's see if we can pull that out and let you look at it.
Throughout the deposition, please, if

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you need to spend time with a document or exhibit and make sure that you've read it adequately to satisfy yourself that you can answer my questions, just ask for additional time to do so.

A. Okay. The eDepoze is working so I can see the report.

Q. All right. And why don't you just take a second to familiarize yourself with that. And some of it, it's – we'll refer to this as the "Chivers Report, 2006 Guideline Study."

A. Okay. I've refamiliarized myself with the first part of that including the summary. Honestly, it's a very big report; so I suggest we try to focus where you would like to.

Q. Right. I don't think that it will be necessary for you to get into the details based upon my questions. Okay?

A. Fine.

Q. So Exhibit 134, for the record, is a study entitled "Paraquat Subchronic Neurotoxicity Study in the Rat," correct?

A. Correct.

Q. And this is a subchronic neurotoxicity study that the EPA required Syngenta to perform,

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right?

A. That is correct.

Q. In terms of specific neurotoxicity studies, not studies where, you know, clinical signs might have been evaluated but a specific neurotox study, to your knowledge, was this the very first neurotox study undertaken by Syngenta for the EPA at their direction?

A. This was certainly the first neurotoxicity study done in accordance with the EPA guidelines on neurotoxicity studies.

Q. In other words, this was the first time that you'd been asked to do a study that the EPA focused specifically on neurotoxicity, correct?

A. That is correct.

Q. All right. "Subchronic" means it was a 90-day study, right?

A. That is right.

Q. A long-term study would be one that was four months or longer; is that right?

A. Long-term studies are generally of 18 months to two-year duration.

Q. Is there an interval period of time for a study?

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A. Sorry. Would you repeat that question?

Q. Yes. Is there something in between? How long is a chronic study?

A. A chronic study would generally – in the rodent, a chronic study would generally be 18 months to two years. In a nonrodent, the chronic study would be 12 months.

Q. Has Syngenta ever performed a long-term paraquat neurotoxicity study to your knowledge?

A. No. The long-term chronic studies that we've conducted have been the guideline studies in rodents and nonrodents, which include an element of assessing neurotoxicity but not to the extent that is required in the specific neurotoxicity study we're talking about now.

Q. And just so we're clear for the record, then – excuse me. I'm sorry – Syngenta has never undertaken any neurotoxicity studies longer than 90 days for the observation of specific neurotoxicity end points; is that correct?

A. That's correct, yes.

Q. All right. Now, let's put this study in perspective time-wise in terms of the deposition and those who look at and hear your deposition later.

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This guideline study that we've marked as Plaintiffs' Deposition Exhibit Number 134 actually took place fairly soon, within a year or so, of Dr. Louise Marks doing her C57 black mouse studies, correct?

A. Yes, that is correct.

Q. As a matter of fact, even though she had completed her studies and had her study results, her studies had not yet been written up into study reports until June of 2007, correct?

A. That is correct, yes.

Q. But she had actually done the studies on the C57 black mouse starting in 2003 or 2004 and finishing in 2005, right?

A. Yes. That is my – my understanding.

Q. All right. So by June of 2006, Syngenta already knew the results of three paraquat neurotoxicity studies performed by Dr. Louise Marks; is that right?

A. Yes.

Q. Now, we've previously discussed in great detail the scientific studies and the results that Louise Marks obtained, right?

A. We have.

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Q. All right. Those are the ones that we discussed where she had one result from her first study, and then once she trained in Dr. Dino DiMonte's laboratory and started using automated stereology equipment instead of manual equipment, she found in each of the three follow-up studies that paraquat caused a statistically significant loss of dopaminergic neurons in the substantia nigra, correct?

A. That is correct.

Q. And, again, I think we've spoken of this earlier in this deposition, but the loss of dopaminergic neurons is one of the hallmark pathologic signs of Parkinson's disease, right?

A. It is.

Q. Now, if we can go -- if you'd pull up Exhibit 135, please, which is the next one.

(Exhibit 135 was identified for the record.)

BY MR. TILLERY:

Q. We're going to come back to this study that's up now, Dr. Botham, but I want to ask you some questions about some guidelines.

A. Okay.

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Q. If you could just familiarize yourself with this particular document, Exhibit 135 is entitled "Guidelines for Neurotoxicity Risk Assessment," isn't it?

A. I'm just opening this now. And, yes, I can confirm that.

Q. And it was published on May 14th, 1998, in the Federal Register, right?

A. Yes, that's correct.

Q. And I'm sure that Syngenta knew all about this -- provisions of this neurotoxicity risk assessment document at the time it came out, right?

MR. NARESH: Objection as to foundation.

THE WITNESS: Yes. We would have known that.

BY MR. TILLERY:

Q. All right. Now, if you'd go to page -- I believe it's -- is it 17?

If you'd go to page 17 of the document, the lower left-hand corner has a page reference. And if you'd just skip to 17 and specifically paragraph 4.

A. Okay.

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Q. Could you -- could you slowly and clearly read that into the record, that section, paragraph 4?

I don't think this is being captured; so we have to take our time today and make sure that we document what is appearing on the eDepoze screen. Okay?

A. So on the page 17 that I've got in front of me, paragraph -- paragraph 4 starts, "It is also assumed that..."

Q. Yes. That's the -- that's the provision, please.

A. Okay. So I'll read on.

"It is also assumed that, in the absence of data to the contrary, the most sensitive species is used to estimate human risk. This is based on the assumption that humans are as sensitive as the most sensitive animal species tested. This provides a conservative estimate of sensitivity for added protection to the public. As with other noncancer end points, it is assumed that there is a nonlinear dose response relationship for neurotoxicants. Although there may be a threshold for neurotoxic effects, these are often difficult to

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determine empirically. Therefore, a nonlinear relationship is assumed to exist for neurotoxicants."

Q. This provision had been published for eight years from the time Syngenta did its 2006 guideline studies with the rat, correct?

A. Correct.

Q. And at that time Syngenta knew from the Dr. Marks studies that the C57 black mouse was sensitive to paraquat exposure and consistently showed evidence of dopaminergic cell loss in the midbrain following exposure.

Is that a fair statement?

A. Yes. I -- that is fair.

Q. Okay. And despite this knowledge, Syngenta never told the EPA and other regulators or the general scientific community of Dr. Marks' findings in 2006, correct?

A. That's not quite correct. I think, as we've discussed before, we did discuss that -- the work of Dr. Marks, for example, with Professor DiMonte.

Q. Right. He was a consultant with you, right?

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A. He was, yes. But we did speak to him at a time prior to him being a consultant.

Q. So -- but did you, for example, send these Marks studies to the EPA until last December?

A. No. We did not send those to the EPA.

Q. Okay. And did you publish those in the public literature where scientists from around the world could view them, read them, the same way you read studies every month?

A. Again, as we've said before, the initial work of Dr. Marks was presented at the scientific meeting.

Q. Right. That one was because it was negative. Remember?

A. The reason why it was presented was not because it was negative. It was presented because that was the information we had at the time, and we wanted to discuss with others why we may have got a negative result compared to the positive result that other researchers had found.

Q. Okay. And you actually did a presentation at a neurotoxicity seminar or a presentation group, right?

A. That's correct.

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Q. And when her studies were corrected and she came back and found that she had been using a piece of equipment that wasn't sensitive enough, the manual technique, and started using an automated technique, she got three studies in a row with the same type of findings, didn't she?

A. She did.

Q. And did you go back to that same neurological groups and seminars in the following years and present those three studies?

A. No, we did not.

Q. Okay. And did you call the EPA and send it to them?

A. No, we did not.

Q. Did you publish them in general -- in the general literature?

A. No, we did not.

Q. Okay. After the rat guidelines study was done that we've pulled up here as Exhibit 134, did it occur to you that you should follow this section and tell the EPA about the Marks black mouse studies?

A. No. That was not a consideration that I was certainly involved in, in considering, no.

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Q. Okay. Who was involved in considering that?

A. If anybody would have been involved, it would have perhaps been our regulatory colleagues in the United States, but I am not aware if that -- if that indeed did occur.

Q. But you are aware that the people at Jealott's Hill and other laboratories for Syngenta around the world were aware of this provision of the EPA's guidelines for neurotoxicity risk assessment dated May 14th, 1998, correct?

A. Correct.

Q. Okay. So they knew you were supposed to use the most sensitive laboratory animal that you could find to the -- to the chemical, the study, correct?

MR. NARESH: Mischaracterizes the document.

THE WITNESS: Correct.

BY MR. TILLERY:

Q. Okay. So after the rat study was done by Dr. -- by Chivers and the results published and the results were made aware of, no one from Syngenta, including the test author Chivers, ever indicated

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that you had discovered at Syngenta a more sensitive laboratory animal in terms of paraquat exposure, correct?

A. That, I think, is not quite how I would put it in terms of whether indeed you could say that the mouse was more sensitive in terms of the end points, which are required in this guideline neurotoxicity study.

Q. Did anyone call the EPA and say, "You know, even though we didn't get the same results in the rat study, we had just finished some C57 mouse studies and three in a row showed neurotoxicity"? Did you do that?

A. No, we did not do that.

Q. All right. Did that ever come up as a topic? Was it ever discussed?

A. As I said a few minutes ago, I'm not aware that such a discussion did take place. I certainly don't recall me getting involved in such a discussion.

Q. Okay. Let's go to Exhibit 136.

(Exhibit 136 was identified for the record.)

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BY MR. TILLERY:
Q. So she's pulling up on eDepoze another exhibit for us to look at, and if you'd open this. And for the record, this is Exhibit 136. Okay?
And take a look at this document as well, Dr. Botham.
MR. NARESH: Stephen, for the record, is this the same as a previously introduced version of the Marks study?
MR. TILLERY: I don't think so. I don't believe this one is. This is a rat study that she did in 2006.
THE WITNESS: Okay. I can see this. I'm just reading the first part of it.
BY MR. TILLERY:
Q. Yeah. If you can just familiarize yourself with it so – where you remember the study.
A. Okay. I've read the summary; so I think that probably would be fine for now.
Q. All right. So in – strike that.
In 2006 Dr. Louise Marks performed another study, and this one involved rats, correct?
A. That's correct.
Q. And I think we discussed this back in

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February that she, in fact, had done this study, but we didn't spend much time on it.
Do you remember that?
A. Yes. We didn't focus on this one.
Q. Right. If you would turn to page 21 of that document, and let's look at the conclusion of Dr. Marks' rat study.
A. Yes. I've done that.
Q. And would you mind just reading in the last three sentences – well, we may as well read the four – the whole conclusion of the paper under 6.0 on that page, all six lines of that paragraph.
Could you read those into the record slowly and clearly, please?
A. "10 milligrams per kilogram paraquat dichloride when administered IP, intraperitoneally, twice weekly for four weeks to male Sprague Dawley rats did not result in nigrostriatal toxicity as determined by the assessment of dopaminergic cell number in the substantia nigra pars compacta and astrocytic and microglial expression in the substantia nigra. It would therefore appear that the 20 to 25 percent cell loss observed in the C57 black mouse in three previous CTL studies" – and

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the numbers are given – "is not reproducible in the rat. This finding suggests the effects observed may be species and/or strain specific."
Q. Now, if we kind of break this down to make sure that what you read is fully understood by the people who look at your deposition later, this was the reference to the Sprague Dawley rat studies, the same kind of animals done in the guideline studies, correct?
A. Yes.
Q. Okay. So the guideline studies were undertaken using exactly the same test animal as Dr. Louise Marks used when she tried to follow up from her C57 mouse studies, correct?
A. That's right.
Q. All right. And here it references a – three separate studies: One is XM7258. One is XM7371, and one is XM7480. Those are the research reports that we have previously marked and admitted as exhibits in this deposition, correct?
A. Correct.
Q. Those are the ones that showed a 20 to 25 percent loss of dopaminergic cells in the brains, the substantia nigra portion of the brain, of the C57

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black mouse, correct?
A. Correct.
Q. So what Dr. Marks is saying here is that the 25 – 20 to 25 percent cell loss observed in the C57 mouse in her three studies were not reproduced in the rat and that the suggestion may that – may be that the result is species or strain specific, correct?
A. Correct.
Q. Given the results of Dr. Marks' black mouse studies, why did Syngenta decide to do this EPA guideline study with the rat instead of the black mouse when it knew the C57 black mouse would show evidence of neurotoxicity?
A. Well, one very important reason is that when you are conducting guideline studies and particularly actually this neurotoxicity guideline study which was relatively new and – you really have to make sure that you understand the significance of any changes that you might see in such a study. So you need to actually understand some of the background to the model that you're using so that you can interpret the changes fully.
We would have not been able to have had

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that background for all the different parameters that you have to assess in a guideline toxicity study in the mouse because we had no experience of using the mouse in the guideline studies.

Q. But you did. You did have experience using the C57 mouse in the studies that Dr. Marks had just completed, right?

A. Indeed with a very specific focus on the pathology in the brain and not more widely with respect to how you might assess neurotoxicity.

Q. But actually didn't you use basically the same study parameters as she used in the C57 mouse when you did the 2006 guideline study from the EPA with the rat?

A. The guideline study requires you to look much more broadly at the potential effects on the nervous system, so looking at pathology, neuropathology, not just in the substantia nigra but other parts of the brain, the peripheral nervous system, and also particularly focusing on whether there are any clinical expressions of neurotoxicity in the behavior of the rat.

Q. But you can also assess clinical observations in a mouse as well, can't you?

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A. You can. But understanding the variability, the natural variability, does require you to do a lot of – of work before doing a full -- a full guideline study. And we had not done any such work using the mouse.

We had focused on the rat because that is the -- the normal species that the EPA would expect to be tested.

Q. But didn't you know at the time she completed her rat studies in the work she'd done that, if you repeated the same test, you were likely to get a same result, right?

A. The test that we're talking about, I mean, they -- I can't give you an exact chronology. But the -- the rat study that Dr. Marks did and the guideline study that Dr. Chivers did were at approximately the same time, and I'm not quite sure precisely when they were done relative to each other.

Q. But you did -- C57 black mouse study, didn't you?

(Reporter clarification.)

BY MR. TILLERY:

Q. Are you –

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MR. NARESH: Hold on.

MR. TILLERY: We're getting a lot of feedback.

THE VIDEOGRAPHER: Everybody hang on a second. I think that's what Renee was getting ready to say. I'm not sure whose end it's coming from. I can't really tell.

(Discussion off the record.)

BY MR. TILLERY:

Q. Whether or not you had done the specific study prior to the initiation of Chivers, you had completed the C57 mouse studies by Dr. Marks, hadn't you?

A. Yes.

Q. And you knew what those results were likely to be. She had repeated the first positive finding in two subsequent tests changing her test parameters but using paraquat and ended up with generally the same confirmatory results, didn't she?

A. Yes.

Q. And you told me you found nothing technologically wrong with any of her studies; isn't that correct?

A. That is correct.

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Q. All right. So it wasn't due to some error committed by her. You knew that these study animals, the C57 black mice, would show the same results if you did the same neurotox studies again, right?

A. Yes, that's correct.

Q. And replicability is very important in science, isn't it, sir?

A. It is.

Q. So if different laboratories at different times for different mice come back with the same results, that sort of establishes the premise of the study, doesn't it?

A. It does.

Q. All right. The EPA was requiring Syngenta to conduct the 2006 guideline study because there had been an association in the literature between paraquat and Parkinson's disease, correct?

A. I don't believe that that is necessarily correct. The EPA were requiring registrants to conduct adult neurotoxicity studies, guideline toxicity studies, very broadly, so not just on paraquat.

So my understanding is that this study

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was not conducted specifically because of the allegations of Parkinson's disease.

Q. Were those allegations included in that series of reasons for why they wanted the studies?

MR. NARESH: Objection. Foundation.

THE WITNESS: I don't know.

BY MR. TILLERY:

Q. Okay. Syngenta, however, never told the EPA or the public scientific community that Dr. Marks' studies replicated the scientific literature and proved that paraquat exposure in the C57 black mouse would cause strong evidence of neurotoxicity of paraquat at that time, did they?

MR. NARESH: Objection. Asked and answered. Calls for a legal conclusion.

THE WITNESS: We did not inform the EPA at that time. That is correct.

BY MR. TILLERY:

Q. And you didn't inform the public health community at – in a general way through publication means the same way you're informed monthly when you read studies, correct?

MR. NARESH: Same objections.

THE WITNESS: Not entirely correct. As

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I said earlier, we did share that with the scientific community at the neurotoxicity scientific meeting.

BY MR. TILLERY:

Q. You showed one study, and that study had negative results. That's the one you shared, right?

A. We did. But then we went on to do -- to discuss our subsequent studies, the ones that did show a positive effect, with scientists outside of the company, including Professor DiMonte.

Q. Who else did you share the results with besides Dr. DiMonte who had become a consultant with your company?

A. Other external experts who were included in paraquat health science team meetings at that time.

Q. Right. Yeah. So who were those people who were not in some way a paid consultant and under an obligation to maintain the confidentiality of the scientific disclosures?

A. Well, there were quite a significant number of people who were involved in our discussions between the period of circa 2007 to 2009 to 2010. I wouldn't want to give a complete list.

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I agree some of them were at some point consultants, but a number of scientists that we spoke to in that period were not consultants. They were coming in to talk to us about Parkinson's disease and about the potential of chemicals to cause Parkinson's disease. And at no point did we ask them to sign confidentiality agreements to not talk about our research.

Q. Actually, you did exactly that with Dr. DiMonte, didn't you?

A. Well --

Q. You're aware that counsel representing you has produced to us a nondisclosure agreement for Dr. DiMonte with Syngenta. You're aware of that, right?

A. I -- as I said, I was making the distinction between consultants and other experts. And my point was that we were not trying to say to every expert that they needed to maintain confidentiality.

Q. But we can agree the best way to get the word out around the world – scientists who speak multiple languages, different people in different schools, universities, cities throughout the world –

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is to publish the results, correct?

MR. NARESH: Objection. Asked and answered multiple times.

THE WITNESS: The -- the important point here is that we were not denying the results of other research in the public domain which we were at that time confirming in the Marks studies.

And, actually, to get published that simple replication of results which are also in the public domain is not necessarily that easy. Journals will not always accept studies which simply say what is already known.

BY MR. TILLERY:

Q. So your statement you're making -- strike that.

Did you --

MR. TILLERY: Renee, did we get a lot of feedback here still?

THE REPORTER: Yes.

MR. TILLERY: Okay. Well, let's go off the record.

THE VIDEOGRAPHER: We're going off the record. The time is 5:26. This ends Media Unit Number 1.

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(Recess taken.)
THE VIDEOGRAPHER: We're going back on the record. The time is 5:38. This begins Media Unit Number 2.
BY MR. TILLERY:
Q. Dr. Botham, you acknowledge that -- excuse me. Strike that.
Dr. Botham, you acknowledge that Dr. Dino DiMonte was the subject of a nondisclosure agreement with Syngenta.
Who else did Syngenta have such nondisclosure agreements with?
A. I can't comment in terms of a comprehensive list; so -- because I was never involved in setting those agreements up myself. So I wouldn't want to give a list which was not accurate.
Q. Well, in terms of the people who were consulting with Syngenta about issues relating to the potential neurotoxicity of paraquat, you know who those people were, right?
A. Yes, indeed.
Q. All right. Who were they?
A. So that would be people --

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MR. NARESH: Dr. Botham, I'm -- I'm sorry to interrupt.
Could you make that time frame a little bit more clear, Steve, in your question? We've been switching back and forth between present and past.
BY MR. TILLERY:
Q. Okay. So in terms of the consultants you were using in the 2006 to 2011 time frame, that era, who were those people?
A. So some of the principal people who were acting as consultants included Sir Colin Berry. We would also at that time have been consulting with Jack Mandel and Pierluigi Nicotera and Professor DiMonte, as we've said. So those were probably the principal people.
Q. But Dr. Colin Berry had been one of your consultants for years and years, correct?
A. Yes. Sir Colin had been a consultant since the early 2000s.
Q. All right. And Jack Mandel had worked with you on many other projects, including atrazine, hadn't he?
A. That's correct.
Q. All right. And Nicotera, who was

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running the program -- running the program that Dr. DiMonte went to, correct, in Germany?
A. That's right.
Q. All right. Was also consultant to Syngenta, right?
A. For a shorter period, yes.
Q. Okay. So why don't you tell me the scientists who were not consultants because all three of these people were from your own records.
Tell me the ones who were not consultants who you were using in your analysis of the potential neurotoxicity effects of paraquat from, say, the 2006 to 2011 time frame besides these people?
A. Well, that's where I would need to refer back to, for example, the minutes of our health science team meetings because the record there would show that there are a number of invited guests that came to talk to us about their own research.
I mean, an example -- one example, Professor Joan Abbott from London. I don't believe that she was a consultant. She was invited because of her work and her understanding of the blood-brain

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barrier.
Q. Right. She couldn't -- let me start over because we got a lot of feedback on that.
She came to you initially in June of 2009, didn't she? June or July?
A. I don't -- I don't have that particular date in mind.
Q. And then was retained as a consultant to do evaluation work for Syngenta and made a lengthy presentation of her work in the fall of that same year, correct?
A. I don't have that detail of exactly what status she had. I know that initially she was not a consultant.
Q. And so tell me where anyone else who was not part of this group called in to Syngenta and paid like she was -- she was paid to appear there. You knew that, right?
MR. NARESH: Objection. Foundation. Assumes facts not in evidence.
THE WITNESS: I don't -- as I said, I was never involved in these agreements; so I can't confirm whether she was paid or not.

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BY MR. TILLERY:

Q. And we went over the – the Joan Abbott blood-brain barrier presentation in this dep before, didn't we?

A. We did.

Q. All right. And that was the presentation you're talking about when she was an invited guest the first time, right?

A. That's right.

Q. And she was paid an honorarium for appearing, right?

A. Again, I can't confirm that.

Q. All right. Now, tell me of all these people you say that you invited in and told, which one of them ever published any of the three studies that Dr. Louise Marks did which confirmed neurotoxicity of paraquat in the C57 black mouse?

A. I don't really understand why any of them would have published work which was not their own.

Q. Well, you're thinking of publication in terms of formal publication in a journal.

I'm saying did any of them cite to it in any of their own published works to your

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knowledge?

A. I can't comment on that. I'm not aware of whether they did or they did not.

Q. Well, let me ask you this: In all of the years you've been doing these assessments of scientific literature, have you ever seen any of these three Marks studies confirming the neurotoxicity of – of paraquat in the C57 mouse referenced in any journal – scientific journal articles?

A. No. And it would be very unlikely that that would be the case because those – as you have pointed out, those Marks studies were not published. And the – nor were they speaking – a journal would only allow you to cite published work.

Q. So I move to strike your answer as unresponsive. Let's start over.

In all the years that you've been doing these assessments of scientific literature, have you ever seen any of these three Marks studies confirming the neurotoxicity of paraquat in the C57 mouse referenced in any journal – any scientific journal article?

MR. NARESH: Object to the question as

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assuming facts not in evidence and containing lawyer argument.

THE WITNESS: No, I don't recall having seen them.

BY MR. TILLERY:

Q. All right. Let's go back if you can. There's a back button on your eDepoze. We're going to go back to number 134, which is the exhibit we started with, your first one.

A. Yes. Excuse me. I'm – I've just seen – only just noticed, I'm sorry, that I've been thrown out of eDepoze. So you just need to give me a few minutes to get back into it.

Q. Okay. That's fine. Do you want to go off the record to do this?

MR. TILLERY: Let's go off the record while he does that.

THE VIDEOGRAPHER: We're going off the record. The time is 5:47. This ends Media Unit Number 2.

(Discussion off the record.)

THE VIDEOGRAPHER: We're going back on the record. The time is 5:47. This begins Media Unit Number 3.

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BY MR. TILLERY:

Q. And you have identified in your eDepoze Plaintiffs' Deposition Exhibit 134 once more, right, sir?

A. I have, yes.

Q. All right. Now, let me direct your attention to the "Executive Summary" ending, I think, on – let's see. It's -- ours is – the Bates number is 762. It's the justification for test selection. If you go through this, I'm trying to direct you to the "Executive Summary" of the study. Actually, it's page 11 of the study.

A. Yes, I'm there.

Q. Okay. So we're clear on what this study did, paraquat was fed to rats in their diet for at least 90 consecutive days, right?

A. That's correct.

Q. Okay. And the -- the administration of paraquat to the animals was not by IP injection. It was by food, right?

A. That's correct.

Q. So let's talk about this. You and I in an earlier discussion in this deposition talked about routes of exposure.

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Do you remember that?
A. I do.
Q. All right. Now, when you have a route of exposure of ingestion, do you find that to be as efficient in terms of the percentage of the chemical that enters the bloodstream as administration through other means, for example, IP injection?
A. I wouldn't use the word "efficient," as you always find different routes of administration will produce different blood levels of -- of any chemicals that you administer to animals.
Q. Okay. Well, how does the administration through dietary intake in a rat compare to IP injection of a rat?
A. Well, the kinetics are very different because you'll – you have to go through the absorption of paraquat from the gastrointestinal tract in order for the substance to get into the bloodstream intraperitoneally. Then there is a tendency for substances like paraquat to get to the bloodstream more quickly.
Q. And in higher levels, right?
A. And that can result in higher levels.
(Reporter clarification.)

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BY MR. TILLERY:
Q. We're having more trouble with this. All right. So the question – let me start over if I can.
We were in the middle of discussing the issue of the routes of exposure for the rats in the study. This was a dietary study, right?
A. That's correct.
Q. And an IP injection study would be the use of a hypodermic needle injecting a very specific amount into the peritoneum of the test animal, right?
A. That's correct.
Q. All right. And when you did that, as you said, you would have – I use the word "efficient." What word would you use in terms of getting a level into the bloodstream from the amount dosed? Let's just say – let's make sure we're on the same page.
If you take the same amount of chemical and put it into an available food source for the rat, and it's paraquat we're testing, you take that same exact amount and inject it into the rat, into the peritoneum. Now, tell me in your opinion how the amounts differ in terms of what enters the

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bloodstream?
A. Well, if it were technically feasible to put exactly the same amount of paraquat into the diet as compared to an intraperitoneal injection, that's another question. But if you were, then it is more likely that you would see, at least for a time, higher levels of paraquat in the bloodstream from an intraperitoneal injection.
Q. Now, let's -- for purposes of this discussion, let's go through and find out why in your view you think that the ingestion of this results in less uptake in the bloodstream.
Why – what is the physiology of mammalian species that causes less of it to enter the bloodstream from ingestion?
A. Well, first of all, it's put into the diet; so the paraquat will be mixed with the different dietary constituents that you feed to the rats. So that in itself may mean that some of the paraquat doesn't get absorbed. It will simply come out, excreted. That which is able to be absorbed has to cross from the stomach into the blood supply, and then the blood supply will take the paraquat around the various tissues of the body.

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Intraperitoneal ingestion bypasses some of that, including the effective diet. And so that's the reason why there's a greater potential for a higher concentration in the bloodstream for a time.
Q. And in terms of the differences in percentage that would reach the bloodstream when you're mixing it in a food source for dietary intake versus IP, does Syngenta have a working hypothesis of the percentage comparison between the two routes of exposure?
A. Well, we've certainly done kinetic studies comparing the -- how much paraquat gets into the bloodstream from the two different routes of exposure that you're describing, and we've published that work.
Q. Okay. Do you happen to remember what the difference is?
A. No. I'd have to go back and look at the publications to give you the real numbers.
Q. Who was the principal investigator on those studies?
A. Well, the intraperitoneal ingestion route was the kinetics that were included in our

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2013 Breckenridge paper, and the dietary study was published under Minnema, et al., I think, in 2014.

Q. Are those the two studies that you think answer these questions?

A. They are, yes.

Q. Okay. Are there any others you can think of?

A. Those are – those are the principal ones where we did the most thorough analysis of the -- of the kinetics.

Q. Okay. Now, the doses used in the subchronic neurotoxicity study in the rat in 2006, the so-called Chivers study, were 15, 50, or 150 parts per million, correct?

A. Correct.

Q. The study detailed clinical observations, including quantitative assessments of landing foot splay, sensory perception, and muscle weakness, correct?

A. Correct.

Q. Those would be considered neurobehavioral effects, right?

A. If there were changes, yes.

Q. They would be considered some evidence

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of neurotoxicity if there were changes, right?

A. That's correct.

Q. Body weights and food consumption were measured weekly, right?

A. Yes.

Q. The brain was weighed, right?

A. Yes.

Q. Nervous system tissues were removed and analyzed microscopically as well, right?

A. Yes.

Q. The study found neurobehavioral tests and neuropathological examination of the central and peripheral nervous system showed no effects from the paraquat exposure, correct?

A. That's correct.

Q. But in the study, Syngenta did not measure the loss of dopaminergic neurons in the substantia nigra of the rat, did they?

A. That is correct.

Q. Syngenta did not measure the levels of dopamine in the striatum, did they?

A. That is correct because in both cases those were not required according to the guideline published by the EPA.

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Q. Move to strike your answer as unresponsive.

Syngenta did not measure the levels of dopamine in the striatum, did they?

MR. NARESH: Objection. Asked and answered.

THE WITNESS: Correct.

BY MR. TILLERY:

Q. Okay. Syngenta did not measure levels of dopamine metabolites in the striatum, did they?

A. We did not.

Q. Syngenta did not investigate whether there was an upregulation of alpha-synuclein in the test animals, did they?

A. We did not and, again, for the same reason I indicated a few minutes ago.

Q. But my question is did you or did you not investigate whether there was an upregulation of alpha-synuclein in that study?

A. We did not.

Q. Okay. You didn't test for the parameters that might have shown a positive result, right?

MR. NARESH: Objection to that.

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THE WITNESS: That's not fully accurate. The – the parameters that are required in this test, as you just read out, include some important clinical observations where, if there was pathologically significant neurotoxicity, you would expect to see changes in those behaviors.

BY MR. TILLERY:

Q. Okay. But you didn't do an analysis of the upregulation of alpha-synuclein. You didn't measure levels of dopamine metabolites. You didn't measure dopamine in the striatum. You didn't measure loss of dopaminergic neurons.

There was nothing preventing the people who conducted the Chivers study from doing that in the rat to complete the study, was there?

MR. NARESH: Objection. Compound.

THE WITNESS: Other than that they were not a guideline requirement and actually could have resulted in the study being rejected by the EPA.

BY MR. TILLERY:

Q. So this – EPA wouldn't want more information, they'd want less. Is that what you're saying?

A. Well, EPA, if we had done additional

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measurements of that sort, would have wanted to be assured that we had the -- the expertise, the background, the understanding of those parameters in this model, in the rat model. And so they may well have questioned the study on that basis.

Q. Has -- has the EPA ever questioned Syngenta's ability, scientific ability, to conduct a test of a laboratory animal?

MR. NARESH: Objection. Scope.

THE WITNESS: Now, are you referring specifically to neurotoxicity studies?

BY MR. TILLERY:

Q. Yes.

A. No. Because we have conducted them according to the guideline.

Q. So I move to strike your answer as unresponsive.

Has the EPA ever questioned Syngenta's ability to conduct a neurotoxicity laboratory animal study?

A. Not that I'm aware of.

Q. Okay. You had a trained stereologist available in your laboratory in the person of Dr. Louise Marks at the time the study was done,

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didn't you?

A. We did, yes.

Q. Was she asked to do any stereology work in the Chivers study?

A. I don't know whether that question was asked. I suspect not, but I wouldn't have definitive evidence of that.

Q. Is there any evidence in anything you've ever read that anybody suggested that maybe you want to look at the rats for your own personal analysis at Syngenta?

A. I wasn't directly involved in those -- in that study; so I'm not aware personally of any such conversation.

Q. Okay. Now, let's go to paragraph 2.3. It's page 12, the very next page.

A. Okay.

Q. And the heading of that is "Justification for Test Selection."

Do you see that?

A. I do.

Q. And it says, "The rat was used because it is the species generally recommended for the assessment of neurotoxicity." Right?

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A. Correct.

Q. Who would have made that decision to include that language?

A. That would be the study director.

Q. And who was that?

A. Dr. Chivers.

Q. Okay. So Dr. Chivers made the determination to use this species based upon the fact that it was the generally recommended test animal for the assessment of neurotoxicity, right?

A. Not just that. I think the second sentence is also important. The rat was used -- the strain of rat that we used because I think, as I said in previous questions this morning, because of the background data, our understanding of that model, and being able to interpret any findings.

Q. But you already knew at that time that if you did this study for the EPA guideline and used the C57 mouse, you were going to have to report that it caused death to dopaminergic neurons in the substantia nigra portion of the mouse, right? You knew that?

A. If we had used the mouse and we'd seen that effect, of course.

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Q. Well, is there any reason to believe that after Dr. Marks had been trained on the correct use of the equipment and got three consistent results in the C57 mouse, is there any question in your scientific mind and analysis that you would have gotten exactly the same result again?

A. Well, you have to also bear in mind that this guideline says that, under normal circumstances, you will -- you would use the oral or dietary route of exposure, not intraperitoneal injection. So had we used the mouse with dietary exposure, we may not have seen the effect.

Q. Okay. So you're saying the same result would work conversely with the rat?

You think if you would have used something other than dietary in -- introduction of paraquat that you might have gotten a positive result as well?

A. Was your question would we have got a positive result had we used a different -- an ingestion route in the rat?

Q. Yes.

A. That was always possible.

Q. Well, then did you think about maybe

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taking a couple of the rats and giving them IP injections of paraquat instead of the dietary and just see if it made a difference? Did you do that?

A. No. Because this test was being done in accordance with EPA guidelines for whom the risk assessment was critical. And as we've just read, the -- the relevance of the route to possible human exposure is important; hence, the use of the oral dietary route.

Q. Is there any reason that you can't conduct any study you want to conduct? I mean, Dr. Marks' work was not required by any regulatory body, was it?

MR. NARESH: Objection. Compound.

THE WITNESS: No, it wasn't. That's because we were trying to understand the -- the -- certain findings in the public research.

BY MR. TILLERY:

Q. Right. So there's no reason you couldn't have done a rat study by IP injection, right? There's no prohibition on Syngenta doing such studies. You could have done it if you had wanted to, correct?

A. Well, we could have done it if we had

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wanted to, but as I said, the expectation of the EPA for this type of guideline study is that you should use a relevant exposure route for humans.

Q. Right. What I'm asking you, if you would answer me clearly, please, sir, is had Syngenta wanted to conduct their own studies irrespective of the requirements of any regulatory body worldwide, they could have gone into the laboratories, ordered up the animals, and done the study and checked for results, correct?

A. Well, we did do research studies in the rat. You've pointed to the study by Marks earlier on, for example.

Q. Okay. So you clearly could have done that had you wanted to?

A. Technically speaking, of course.

Q. Yes. Now, tell me the circumstances where humans would -- strike that.

Tell me the circumstances where the usual applicator of paraquat as you understand that application to take place. And I'm thinking about the United States, okay, and how this is sprayed onto farm fields and other locations in the usual ordinary manner. Okay? Tell me how humans would be

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exposed to paraquat through oral ingestion.

MR. NARESH: Object as compound.

Go ahead.

THE WITNESS: Under normal circumstances you wouldn't expect an applicator to be exposed to paraquat using -- through the oral route unless they were contaminated around their mouth. But, no, normally speaking, that would not be relevant for an operator.

BY MR. TILLERY:

Q. All right. And the relevant exposure would be what?

A. Either dermal or sometimes by inhalation.

Q. And "inhalation," by that you mean where the people are breathing. When they're applying it, there's mist in the air. They breathe this in. Or when they're mixing or loading it, they breathe it in through their nose. It goes down there -- into their lungs and goes through the alveolar structures into their bloodstream, right?

MR. NARESH: Objection to form. Compound.

THE WITNESS: Yes.

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MR. NARESH: And assumes facts not in evidence.

THE WITNESS: That -- that can -- that is a potential exposure route.

BY MR. TILLERY:

Q. All right. And that, of course, is a completely different route than the oral ingestion route, right?

A. It is.

Q. Applicators of paraquat would be those people who would have the most direct exposure in the usual sense in the use of this chemical, correct?

A. That is correct.

Q. And I think you've told me before in the same deposition that, in your view, the most likely route of exposure is -- to applicators is inhalation, correct?

A. I don't know if I said that because I know, for example, also dermal exposure is also likely.

Q. Okay. So "dermal exposure" meaning mixing it, getting it on their hands, splashes, that sort of thing?

A. That's right, yes.

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Q. Okay. But in this study, the route of exposure was an oral ingestion, right?
A. That's right.
Q. And when Marks did her rat study in 2006, what was the means by which she got paraquat into the rat? Did she use ingestion?
A. You'll just need to -- to quickly remind me. You showed that in a previous exhibit, the Marks 2006 study.
Q. Right. The rat --
MR. NARESH: Dr. Botham, if you feel like you need to look at the exhibit --
THE WITNESS: Yes. I do, yes.
BY MR. TILLERY:
Q. Why don't you do that, sir.
A. Yes. I'll need to do that, I think.
Q. Why don't you confirm what Syngenta used -- chose to use as the means by which paraquat was introduced into the lab animals in her rat study.
A. Yes. I'm just going to that now.
MR. NARESH: I'll object to the characterization of the question.
But it's Exhibit 136, Dr. Botham, if you'd like to take a look.

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THE WITNESS: Yep. Thank you.
Yes. So this was intraperitoneal ingestion.
BY MR. TILLERY:
Q. They didn't use -- she -- strike that.
She did not use dietary intake, did she?
A. No, not in this study.
Q. She used IP ingestion, right?
A. Correct.
Q. Did she ever use dietary intake on any of her paraquat toxicity studies?
A. I don't believe so, no.
Q. She always used IP ingestion, right?
A. Yes. Because, again, we were trying to see whether we could replicate or understand the public research which had used that route of administration.
Q. Did anybody at that time voice any opinion about the legitimacy of using IP ingestion as the means of introduction -- introducing the chemical into the laboratory animal?
A. There was a constant discussion about the relevance of the IP injection route because it

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isn't one that would normally be used in order to understand actual risk to exposed humans.
Q. Did you raise that objection yourself?
A. It wasn't an objection as such. It was because we were faced with the reality that the public research had used that mode of applicator -- of administration. And so we didn't think it was necessarily relevant, but it was important nevertheless in order for us to get a better understanding of what was happening.
Q. Now, if you'd turn to page 14 under Section 3.4.1 of the exhibit -- the last exhibit which is 134.
MR. NARESH: We're back to Chevers -- Chivers?
MR. TILLERY: Yes.
THE WITNESS: Okay. Tell me again which page you want me to go to?
BY MR. TILLERY:
Q. Page 14.
A. My eDepoze has temporarily lost the ability to give me page numbers but -- okay. Now it's come back up again.
Yes. Page 14. I'm there. Thank you.

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Q. The rats in this -- strike that.
The rats in the study were 42 days old at the start of the study, right?
A. That's correct.
Q. Approximately what age in humans does that correspond with?
A. Well, the life span of a rat is between two to three years, so 700-plus days. So, you know, a quick mental calculation, that would be obviously a young -- a child to young adult.
Q. It would be probably a preteen human, wouldn't it?
A. Yeah. At the start of dosing, that's true.
Q. All right. And the study lasted 90 days, right?
A. Correct.
Q. So on the very last day of the study, the rats were approximately 132 days old, right?
A. That's right, yes.
Q. About four and a half months old, right?
A. That's right.
Q. And if you wouldn't mind doing your quick mental math, tell me the approximate age that

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would be in correspondence to humans.
A. Well, it would be around about 20s, mid-20s, mid-to-late 20s.
Q. Okay. Now, in terms of onset of Parkinson's disease in humans, what is your understanding of the average age of onset of the disease?
A. My understanding is that's around about 65 years of age.
Q. Okay. And yet in your animals at the latest period of time, they would have been in the mid-20s -- right? – in a corresponding age?
A. Yes. That's correct.
Q. Okay. How many people with Parkinson's disease onset that's not genetically related have you ever heard of who have developed Parkinson's disease by age 20?
A. It would not generally happen, be expected to happen.
Q. It just simply wouldn't happen, would it?
A. No, it would not.
Q. And why is that?
A. Well, because Parkinson's disease is a

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disease of age, and loss of cells in the substantia nigra is something that happens in everybody to an extent as you grow old.
Q. And when you add neurotoxin, which takes other dopaminergic cells out of the functioning range, you end up with the onset of one of the hallmark symptoms of Parkinson's disease. And that's the absence of motor control, correct?
A. Yes. Indeed, some toxins we know do that.
Q. But you don't see that in 20-year-olds, do you?
A. No, we don't.
Q. Have you ever read any piece of literature anywhere which showed from exposure to a chemical that any person had the onset of Parkinson's disease in their 20s?
A. No.
Q. Okay. Nothing would prohibit you at Syngenta from using older animals as test subjects, would it?
A. Other than, again, the guideline here of toxicity studies require you to use young animals because, remember, these guideline neurotoxicity

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studies are not focusing on the potential for Parkinson's pathology. They're looking for neurotoxicity much more broadly.
Q. Okay. But other than the guideline studies and other than anything that you were told to follow by the EPA, anything else?
If you were doing your own studies, there's nothing that would prohibit or prevent Syngenta from using older test animals, correct?
A. There are no practical reasons why that couldn't be done, certainly.
Q. Right. Now, in this study that we're -- we have as Exhibit 134 up for view, if you go to Section 4.9.3, it says, "There were no treatment-related" –
MR. NARESH: Hang on. That's quite a bit ahead. Can you give us a page number?
MR. TILLERY: Yeah.
THE WITNESS: I'm getting there.
MR. TILLERY: It's page 23.
THE WITNESS: Yes. I'm there.
BY MR. TILLERY:
Q. It says, "There were no treatment-related microscopic findings," and it

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references Table 16, right?
A. It does.
Q. The incidence of demyelination or nerve fiber degeneration in the control and high-dose groups were considered spontaneous and not related to treatment, right?
A. That's right.
Q. And that's because you had roughly the same number of demyelination findings in the control group as you had in the test group, right?
A. That's right.
Q. So you couldn't draw any conclusion from the demyelination either way because it appeared in your test – in your control animals, right?
A. Well, you could fairly conclusively imagine that that showed that it was, as it says here, a spontaneous finding not related to treatment.
Q. Right. Okay. Now, if you'd turn to Table 16. I think that's page 104. If you can go there. Tell me when you're there, sir.
A. Yep. Just getting there. I don't know if there's a quicker way of doing this rather than clicking --

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Q. There actually is. In the lower corner, it says "Pages." If you click on that and then just type in the page number.
A. Oh, right.
Q. It will take you directly to that page.
A. I will do that. Which page number, please?
Q. It would be page 104.
A. Thank you.
Q. Take a look at that table, please. It's entitled "The Intergroup Comparison of Microscopic Findings."
A. Okay. Yes, I'm there.
Q. And if you look at the zero PPM column, those are the control animals, aren't they?
A. That's correct.
Q. Okay. And then there's another column, 15 PPM, right?
A. That's right.
Q. How many animals were in that category?
A. Twelve.
Q. And then there's a 50 PPM dosing group, right?
A. Correct.

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Q. And there were 12 animals in that group?
A. That's right.
Q. Okay. And then there's a 150, right?
A. That's right.
Q. Okay. Now, do you see? If you can, look at those numbers. And do you see the findings under the 15 and 30 PPM dosing groups?
A. No. I think you mean 50, not 30.
Q. Fifty. That's exactly right. Fifteen and 50. Do you see that?
A. I do.
Q. Why were there no findings in those columns?
A. Well, it's an interesting observation.
The – you might have expected that you would see such findings in those animals also, but this is – this is biology. Sometimes you do see this.
Q. Okay. So you see nothing untoward with your test at all, right?
A. Well, no, because the – the ones – the animals that did not receive tests – also did not receive PPM gave exactly the same incidences of these findings as the 150.

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Q. Okay. So you had in the control group – you see the findings that were made in the control group? They received no paraquat, right?
A. Correct.
Q. And then if you skip all the way over to the 150 PPM range, you see that level, right? In all these categories – distal tibial nerve, eye, proximal sciatic nerve, proximal tibial nerve. Do you see those?
A. Yes.
Q. They show – they show findings. And those – comparing those to the 150 range, right?
A. Yes.
Q. And then in the middle – 15 and 50 – zero findings. And you're saying that's due to biology? When the control group roughly parallels the 150 group, you're saying that's biology?
A. Well, that's one explanation. I would – I would need to just double-check by reading the report in full, which I don't have – have time to do, as to whether those were – were actually – those observations were made in the – in the 15 and 50 PPM.
I think this indicates that they were

Page 1500

looked for, but we'd need some time – you didn't necessarily always look at all the dose groups. So that would need to be double-checked.
Q. So one explanation could be that they simply – that they didn't even look for them, right?
A. That's – that's possible. But I -- but the fact that it says naught would suggest otherwise, but that is something that would require a thorough reading of the report.
Q. And as you sit here today for your deposition, you're unable to tell me why the control group has numbers which correspond very closely to the 150 PPM group but that the intermediate or the intervals of 15 and 50 parts per million show absolutely zeros in every category, right?
A. Other than the potential explanation I've just given.
Q. And you don't know whether that's correct or not, do you?
A. No. But I would be able to check that if I read the – this – this report in detail.
Q. And the only explanation would be that no observation was made, right?
A. Unless it really is just a biological

Page 1501

phenomenon and that it just by happenchance that was the case.

Q. Well, why don't you explain that biological phenomenon to the court and jury how the control group with no exposure has roughly the same as a 150 parts per million dietary disclosure – exposure and yet the 15 and 50 part per million has zeros, all zeros. Explain that to me.

A. I think it would be only wise for me to give a detailed explanation of that after I've had a chance to read the report in full.

Q. Okay. So right now that's not an explanation you're able to give. Would that be a fair statement?

A. I think that's – that's -- that's right. And I think it would be important to – to do a proper analysis of that.

Q. Okay. Let's go to the next exhibit, which is 137.

(Exhibit 137 was identified for the record.)

BY MR. TILLERY:

Q. And if you would look at this document for the attorneys on this deposition, this is

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Syngenta PQ-00224355. I direct your attention to page 1. It's a 542-page document, and this is entitled "Paraquat Technical paraquat tech – Acute Neurotoxicity Study in Rats." The reference number is AR7536. It's a regulatory report. It's dated June 8th, 2006, and the author was Mrs. A. Brammer.

A. Correct.

Q. Do you know Mrs. Brammer?

A. I do.

Q. And is she a Ph.D.?

A. No, she's not.

Q. What about Chivers? Is Chivers a Ph.D.?

A. Yes. Dr. Chivers was a Ph.D.

Q. Okay. Now, what was the purpose of this study? Not in terms of who asked for it, but what was – what were you testing?

A. So this is to assess the potential for neurotoxicity with a -- an acute dose rather than the 90-day dosing that we talked about before; so normally that would mean a single dose.

Q. Okay. It's an acute neurotoxicity study of paraquat technical, again, using Sprague Dawley rats, right?

A. Correct.

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Q. It's a guideline study, right?

A. It is another guideline study.

Q. Now, if you turn to the top of page 11 of this document.

A. Okay.

Q. There's a reference to "Study design," right?

A. Yes.

Q. The rats were administered oral doses of zero for control, right?

A. Yes.

Q. Twenty-five, 75, or 250 milligrams per kilogram of weight, paraquat technical. And they were observed for a period of 14 days, right?

A. Yes.

Q. If you continue on, on the – that same page 11, the report says, "There was no treatment-related clinical observations," right?

A. Yes.

Q. At page 11, the report says, "There were no effects on brain weight and no neuropathology at 250 milligrams per kilogram," right?

A. Yes.

Q. So there were no treatment-related

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effects at 25 milligrams paraquat technical either, right?

A. Yes.

Q. Syngenta in this study did not measure the loss of dopaminergic neurons in the substantia nigra in the rats, did they?

A. No, they did not.

Q. Syngenta didn't measure the levels of dopamine in the striatum of the brain of the rat, did it?

A. No.

Q. Syngenta didn't measure the levels of dopamine metabolites in the striatum, did it?

A. No.

Q. Syngenta scientists didn't investigate whether there was an upregulation of alpha-synuclein in the Sprague Dawley rats of this study, did they?

A. No. And, again, for all the reasons I mentioned earlier. It's -- these were not guideline requirements.

Q. But they didn't do that even on their own, did they?

A. That? No.

Q. Okay. So this was a 14-day study that

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doesn't tell us anything about the long-term effects of chronic low-dose exposure to paraquat.

Would you agree with that?

A. I would agree because that was not the purpose of the study.

Q. Okay.

MR. TILLERY: I am switching to a new topic; so let's take four- or five-minute break. Okay?

THE VIDEOGRAPHER: We're going off the record. The time is 6:29. This ends Media Unit Number 3.

(Recess taken.)

THE VIDEOGRAPHER: We're going back on the record. The time is 6:35. This begins Media Unit Number 4.

BY MR. TILLERY:

Q. So, Dr. Botham, you first learned of issues with possible falsification of some paraquat research by Dr. Thiruchelvam in July 2012, correct?

A. That date sounds about right, yes.

Q. Okay. And if we could go to Exhibit 138 at this time. Pull that up and look at it.

(Exhibit 138 was identified

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for the record.)

BY MR. TILLERY:

Q. This was a document that was produced to us by your counsel. It was marked as Syngenta PQ-31528525, and I'm looking at page 1 of that document.

Do you see that?

A. I do.

Q. Okay. And this is a document dated July 13, 2012, correct?

A. Correct.

Q. And this is a document where you first notified Syngenta's paraquat health science team of this fact in a memo, right?

A. That's correct.

Q. And to your knowledge was anyone at Syngenta ever aware of this issue with Dr. Thiruchelvam's scientific misconduct before July of 2012?

A. Then I believe that it -- as this document suggests, that it was the previous month, June, when the Office of Research Integrity published their findings. So I believe that would be the first time we were aware of it.

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Q. So it would be -- it would be -- June of 2012 would be the first -- earliest date that you or anybody else learned of this from -- from the -- any source?

A. I believe so, yes.

Q. Okay. And after an investigation, two studies and one scientific investigator were determined to be involved, correct?

A. That's right.

Q. The investigator was Dr. Mona Thiruchelvam, right?

A. That's correct.

Q. No other scientist was implicated in that research misconduct as far as you know, correct?

A. There was nobody -- no other scientist was mentioned in that ORI report.

Q. Okay. And would you agree that, although the findings of research misconduct did cast doubt on the work of Dr. Thiruchelvam, that does not remove the fact that other researchers made similar findings, including with respect to paraquat alone, right?

A. That's correct. Yes.

Q. Now I'm going to show you Exhibit

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Number 139.

(Exhibit 139 was identified

for the record.)

BY MR. TILLERY:

Q. And please take a look at that. This is a list of five studies.

A. Okay. Got it.

Q. These are studies you have looked at, read, or analyzed at some point in time in the past, correct?

MR. NARESH: I'll object to the foundation of this document.

Would you mind just explaining what this document is, Steve?

MR. TILLERY: It's taken directly out of one of your reports word for word of a Dr. John Whysner. It's the last page of his report.

THE WITNESS: Well, I'm not familiar with that particular report.

BY MR. TILLERY:

Q. Yes. I know that. But I'm talking about the studies.

And my question to you is this: To Syngenta's knowledge, has anyone anywhere discovered

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fraud of any kind with respect to any of these five studies that you know of?
MR. NARESH: I'll object to the scope.
THE WITNESS: No. I'm not aware that anybody would claim fraud for these studies.
BY MR. TILLERY:
Q. Whether fraud or any impropriety whatsoever?
MR. NARESH: Same objection.
THE WITNESS: Certainly, nothing that is in the public domain.
BY MR. TILLERY:
Q. Okay. Has any journal ever asked any of these studies be withdrawn or retracted –
MR. NARESH: Same objection.
BY MR. TILLERY:
Q. – to your knowledge?
A. I -- I don't know the answer to that question.
Q. Do you have any personal knowledge of any kind that any of these five studies were tainted in any way by any misconduct?
A. No. I've got no direct evidence for that.

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Q. Okay. And this is Exhibit 140, we're going to pull up next.
(Exhibit 140 was identified for the record.)
THE WITNESS: Nothing has come through, I'm afraid.
BY MR. TILLERY:
Q. For me either. There it is.
A. Okay. I can see that now.
Q. Okay. There we go.
All right. This document is entitled "Systemic" – strike that.
This document is entitled "Systematic Review of parkinsonian Syndromes in Short- and Long-Term Survivors of Paraquat Poisoning."
Do you see that?
A. I do.
Q. It's Exhibit 14. The authors are Jeffrey Brent, M.D., and Tammi L. Schaeffer, DO, right?
A. Yes.
Q. What is a DO?
A. I've got no idea, actually. I'm sorry.
Q. Okay. Does Syngenta rely on this study

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to show that paraquat is not associated with Parkinson's disease?
A. No. It doesn't rely on it, and indeed the title describes this was more focused on parkinsonism, parkinsonian syndromes, not specifically on Parkinson's disease. And the two are different.
Q. Right. It may short-circuit our analysis is why I'm asking.
To your knowledge, has Syngenta ever looked at this document or this study as any proof or evidence whatsoever that Parkinson's disease is not associated with exposure to paraquat?
MR. NARESH: I'll object to the extent it calls for an expert conclusion.
THE WITNESS: Well, as I've just indicated, because it's focusing on – particularly on parkinsonism, which is the effects seen with MPTP, this was more appropriate in terms of answering the question "Is paraquat potentially going to cause the same issues as MPTP does?" which is mostly rapid onset parkinsonism.
BY MR. TILLERY:
Q. So really the study was to determine

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whether parkinsonism, number one, would be caused by paraquat, right?
A. Right.
Q. And then the secondary component was not just parkinsonism, but would the method by which this occurred in terms of point in time be consistent with MPTP, right?
A. That's right. That's one major feature of this paper.
Q. All right. It wasn't, as you understood it, to make any kind of determination as to whether or not paraquat caused Parkinson's disease?
A. No. I believe that the authors were not trying to make any claims around Parkinson's disease. I think, as I've read this paper again myself recently, that it mostly talks about parkinsonism.
Q. Okay. Was Dr. Brent a paid consultant to Syngenta regarding the topic of the manuscript?
A. He may have been. That's a -- that's something, again, I would need to check.
Q. Well, why don't you go to the bottom of the front page, second paragraph after the line, and let's see if I'm reading this correctly – correctly,

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right?
"Dr. Brent has served as a paid consultant to Syngenta Corporation regarding the topic of this manuscript." Is that correct?
A. That's correct. So that's -- that's what I was looking for, yep.
Q. All right. So let's see if we can be consistent and clear that the objective of the study was to assess whether high-dose paraquat exposure was associated with the development of parkinsonism, not Parkinson's disease, right?
A. That was --
MR. NARESH: Objection.
THE WITNESS: That was -- I'm sorry.
Yes. That was the major focus. But obviously, as the paper says, then there was certainly reference to Parkinson's disease and whether this may also cast doubt on the relationship with Parkinson's disease, but the main focus was parkinsonism.
BY MR. TILLERY:
Q. Well, that's really where I'm going because to the extent that it does cast doubt on that relationship, I want you to answer some questions.

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Okay?
A. Okay.
Q. Do you think that this paper casts doubt on that association between Parkinson's disease and paraquat?
A. It's another -- just another part of the weight of evidence.
In and of itself, I think it would be difficult to conclude that this analysis rules out the possibility that paraquat could cause Parkinson's disease.
Q. And why is that?
A. Because the -- the way in which the data were assembled was looking at clinical signs in a relatively short period after acute poisoning.
Q. And you know that the onset oftentimes is many, many years later, right?
A. That's right.
Q. And as a result of that with delayed onset and with focusing on people who were evaluated within ten years of their exposure, you don't take into account the latency of the exposure in terms of the onset in an older person, correct?
A. That's correct.

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Q. All right.
MR. TILLERY: Would you like at this point to take a lunch break for you, sir? Would that be appropriate?
THE WITNESS: I think that would be very helpful. Thank you.
MR. TILLERY: All right. We'll do that. How long would you like? A half an hour?
THE WITNESS: That -- that should be fine. Thank you.
MR. TILLERY: All right. We'll come back at our time -- what time is it now? We'll come back at about 20 after the hour. Okay?
THE WITNESS: Very good.
MR. TILLERY: All right. Thank you.
THE VIDEOGRAPHER: We're going off the record. The time is 6:48. This ends Media Unit Number 4.
(Recess taken.)
THE VIDEOGRAPHER: We're going back on the record. The time is 7:23. This begins Media Unit Number 5.
BY MR. TILLERY:
Q. Dr. Botham, we were in the process of

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discussing Plaintiffs' Deposition Exhibit Number 140, and I'll refer to it simply as "the Brent study."
You'll know what that means, right?
A. I do.
Q. All right. Now, as we indicated, the objective of the study was to assess whether high-dose paraquat exposure was associated with the development of parkinsonism, correct?
A. That's correct.
Q. The study was not intended to tell us anything about chronic low-dose oxidative (audio difficulties).
(Discussion off the record.)
BY MR. TILLERY:
Q. Starting over. The study was not intended to tell us anything about chronic low-dose occupational exposure to paraquat, correct?
A. Correct.
Q. MPTP -- strike that. I'm getting a lot of feedback. I'm sorry.
MPTP is a known neurotoxicant that can be created while making synthetic heroin, correct?
A. Correct.
Q. A few days after use, MPTP's metabolite

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MPP+ causes parkinsonism in people, correct?
A. Yes. In some people who – who have injected themselves.
Q. And paraquat has a similar chemical structure to MPTP, correct?
A. It looks on paper to be similar; but, in fact, the chemical properties of MPTP and paraquat are very different.
Q. As a matter of fact, the way in which they react, the way in which they transfer across the blood-brain barrier, the way in which they have an immediate effect, the way the parts of the brain they affect are different, aren't they?
A. Yeah. MPTP certainly has a very different property in terms of its ability to cross membranes, for example, compared to paraquat. And, therefore, it may not be unexpected that it has different effects.
Q. Now, if you wouldn't mind, if you could go to the first page of Exhibit 140, and if you look at the second column.
Do you see that in the third paragraph?
A. Okay.
Q. And the author says there, "Given their

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very close structural similarity, if paraquat does cause PD, it would be expected that it would almost certainly do so in a manner similar to MPTP, and rapid onset parkinsonism should, therefore, occur following high-dose paraquat exposure."
Do you see that?
A. I do.
Q. The hypothesis tested in this study, therefore, is that high-dose paraquat exposure sufficient to cause significant systemic human toxicity would be associated with the emergence of features of parkinsonism.
Do you agree with that premise?
A. Well, to the extent that it does depend also on the fact that whilst there is similarities, as this says, that that is not necessarily similarity which extends to the properties, the actual toxicity or kinetics of the two. They could be different.
So I would say that this is broadly right, but it could be -- it could be put -- it could be modified to make it clearer.
Q. And so would you – just so we're clear: Would you endorse that statement without change?

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Would that be a premise or hypothesis that you would explore as it's framed?
A. Well, inasmuch as we know that MPTP is metabolized to MPP+, which is more similar to paraquat, it's not unreasonable as a hypothesis even though, as I say, you could have been a little bit clearer about the way in which that was written.
Q. Well, based upon the hypothesis that people exposed to a high dose of paraquat would develop parkinsonian symptoms like those who consume MPP+, Brent assessed acute paraquat poisoning cases, right?
A. He did.
Q. And I think in an earlier part of this deposition, you indicated that Syngenta supplied information from their database to assist in the process, correct?
A. Yes. We did, yes.
Q. And you did that from a database that you had of people who had ingested paraquat, right?
A. That's correct.
Q. And we're going to talk about those databases that you reference later. But the – the fact is, is that you've been keeping at Syngenta a

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database of exposures, right?
A. We've got a database of what we call "adverse health incidents" that have been reported through, for example, National Poison Centers.
Q. And how long has that been up – in process?
A. Well, in its current state, since around about 2003, although prior to that, we were -- we were collecting information in a similar but not -- not identical manner.
Q. As a matter of fact, information was being collected by Chevron itself, wasn't it, back in the 1960s and '70s?
MR. NARESH: Objection. Foundation.
THE WITNESS: Yeah. I mean, I don't know that for sure. I've seen a few indications that might have been the case, but I don't know exactly how Chevron was doing that.
BY MR. TILLERY:
Q. For how many years has Syngenta or a predecessor entity been collecting this data about adverse health effects from exposure and ingestion to paraquat?
A. Well, as I've just said, the current

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mechanism with the adverse health incident database goes back to 2003, and I know that information was being collected before then. I can't give you an exact date range for that, but certainly quite a few years prior to 2003, we would have been collecting information.

Q. Wouldn't you certainly have been collecting it in the United States after ICI started selling the product directly and distributing it?

A. In the United States, there was a system called Prosar, which was – It's very similar to the adverse health incident database that I've been describing where we, again, were reliant on doctors, poison centers, giving us information on acute toxicity -- toxicity or poisoning.

Q. What was Prosar?

A. Prosar was another database, essentially, similar to the adverse health incident database.

Q. Who housed or managed that database?

A. That would be -- I'm not quite sure exactly what their title was, but it was basically some product stewardship professionals in the U.S.-based team.

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Q. Were they working for Syngenta?

A. Yes, they were.

Q. And in what office?

A. They would be in the Greensboro office.

Q. Okay. Do you know who those people were?

A. I wouldn't be able to give you names off the top of my head right now, no. I would be guessing if I gave you names today.

Q. Okay. Well, would you check on that and give those names to me tomorrow, please? And I'll withhold any questions on the databases until tomorrow.

MR. NARESH: Steve, if there are other things you'd like him to look into, I understand you want to hold the substantive questions. But if there are other things you'd like him to look into on that issue, it's probably worth asking those questions now so he can try to arm himself with answers for tomorrow.

MR. TILLERY: Yeah. Actually, off the record for a second.

THE VIDEOGRAPHER: We're going off the record. The time is 7:33. This ends Media Unit Number 5.

MR. TILLERY: Actually --

THE VIDEOGRAPHER: One moment. Okay. Go ahead.

(Discussion off the record.)

THE VIDEOGRAPHER: We're going back on the record. The time is 7:34. This begins Media Unit Number 6.

BY MR. TILLERY:

Q. The two pathologic hallmarks of Parkinson's disease are loss of dopaminergic neurons in the substantia nigra and Lewy body deposits comprised primarily of a protein called "alpha-synuclein," correct?

MR. NARESH: Objection. Asked and answered.

THE WITNESS: Those are two of the hallmarks, yes.

BY MR. TILLERY:

Q. So this study proceeded on the assumption that MPTP and paraquat impact humans in basically the same way, correct?

A. With respect to parkin- -- parkinsonism, which is not the same as Parkinson's disease.

Q. Right. And if the assumption turned out to be wrong, the entire study would become irrelevant, right?

A. Well, it's not necessarily right to say irrelevant. I think, as I said before, this is all part of weight of evidence which is trying to be assembled to determine the likelihood that paraquat may be causing Parkinson's disease.

Q. Okay. Excuse me a second, sir.

Actually, if you go to page 4 of the exhibit. Tell me when you're there.

A. I'm on page 4, yes.

Q. All right. And if you would look over into the second column it would be the --

A. Yep. Okay.

Q. The sixth paragraph. When the authors say, "The paradigm upon which this experimental approach rests assumes that if paraquat were a cause of Parkinson's disease, it would act in a manner similar to that of MPTP. However, it is possible that paraquat works in a -- by a completely different mechanism. If that is the case, the model of acute high-dose exposures may not be relevant."

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Do you see that?
A. Yes.
Q. Do you agree with that from this study?
A. Yes. That's really what we've just been saying.
Q. All right. Paraquat and MPTP reproduce some features of Parkinson's disease in experimental animals. Would you agree?
A. Yes, that's correct.
Q. Scientists have document – documented that the toxic metabolite of MPTP and MPP+ is transported into dopamine neurons through the dopamine transporter, correct?
MR. NARESH: Object as calling for an expert opinion.
And, Steve, can I have a standing objection on this line of questioning, or shall I continue objecting?
MR. TILLERY: Yes. Yes, you can.
THE WITNESS: So the answer to the question is, yes, that's the way in which MPP+ is believed to transfer across membranes.
BY MR. TILLERY:
Q. Based upon its structural chemical

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similarity to MPP+, it's been proposed that paraquat exerts selective dopaminergic toxicity through the transport by the dopamine transporter and subsequent inhibition of mitochondrial complex 1, correct?
A. That's how MPP+ works.
Q. Right. And --
A. That's not how paraquat works.
Q. And you say it works differently, right?
A. I do.
Q. Okay. Have you ever seen a scientific study finding that paraquat is either a substrate or an inhibitor of the dopamine transport?
A. We believe that paraquat is not a substrate for the dopamine receptor.
Q. Have you – strike that.
Have you or anyone else at Syngenta published any research which has found that paraquat is either a substrate or an inhibitor of DAT?
A. No. We -- we have worked -- for example, we've collaborated, as we said earlier, with Professor Joan Abbott, who, I believe, has actually done some experiments to show that MPP+ and paraquat differ in terms of their transporter receptor binding.

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Q. So not only have you not done any such research, you would disagree with that notion, correct?
A. The evidence would suggest that it's not. The two -- the two behave differently.
Q. And that is, just so we're clear on the record, paraquat is neither a substrate nor inhibitor of DAT, correct?
A. That's our understanding.
Q. Are you aware – I'm going to refer you to a particular chemical compound H dehydrorotenone.
Are you familiar with that?
A. I'm familiar with rotenone, yes.
Q. All right. Are you aware that in vivo exposure to MPTP but not paraquat inhibits binding of H dehydrorotenone in complex 1 in brain mitochondria?
A. I can't bring to mind the precise experiments where that has been shown.
Q. Do you know that MPP+ is an effective inhibitor of complex 1 activity in isolated brain mitochondria while paraquat exhibits weak inhibitory effects only at millimolar – millimolar concentrations?
MR. NARESH: I just want to say I'll

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object to this line of questioning on the scope grounds as well.
May I have that as a standing basis for this line?
MR. TILLERY: Yes. You -- yes, you can have it.
Q. Go ahead, sir.
A. Yes. I'm more aware of that, and that's why I was saying that MPP+ and paraquat may look more similar and act – and be more similar chemically, but they do not behave in the same way, for example, in terms of mitochondrial effect.
Q. And that undermines the entire premise of the Brent study, doesn't it?
A. No, not necessarily. I think the premise is still that if you argue that MPTP or MPP+ could nevertheless act in other ways similarly to paraquat that you -- such a study as Brent put together might have found that. But, you know, this is clearly why I use the term "weighted evidence" rather than "definitive proof."
Q. Well, the data indicate that, despite its apparent structural similarity to MPP+, paraquat exerts its effect on dopamine neurons in a manner

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that is different than MPTP, correct?
A. There's certainly evidence that shows that, yes.
Q. So what scientific studies, to your knowledge, was Brent relying on for the conclusion that if paraquat causes Parkinson's disease, it does so in a manner similar to that of MPTP?
A. Well, he was not starting his hypothesis from the level of detail of mechanistic similarities or differences. He was starting from what -- a significant body of literature which was making the claim that paraquat and MPTP may be -- may act similarly or be very similar in their properties.
Q. So the direct answer to my question is he wasn't relying on any study, was he?
A. He wasn't relying on a particular study to -- to do this analysis, no.
Q. Right. MPTP exposure gives parkinsonian symptoms but does not lead to the development of Lewy bodies, does it?
A. I believe that's true. And that may be because people have not been able to -- to look at that in more detail because that's maybe something

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that could occur long after exposure.
Q. In a latent period many years later?
A. Correct.
Q. So if paraquat acted in humans just like MPTP, one could only conclude that paraquat causes parkinsonian symptoms and not Parkinson's disease, right?
A. Yes. And that indeed is what I believe both Brent and myself are saying.
Q. Parkinson's disease can be clinically diagnosed only when about 60 to 75, 80 percent of the dopaminergic neurons in the brain have died or stopped producing dopamine. Would you agree?
A. Yes. In -- that's right.
Q. And that's when the motor symptoms become apparent, right? Motor symptoms of Parkinson's disease, right?
A. That's correct.
Q. So high-dose paraquat poisoning would have to kill 60 to 80 percent of the dopamine neurons quickly to cause Parkinson's motor symptoms, right?
A. Yes, probably.
Q. In this study, the authors evaluated paraquat poisoning cases as to whether they met a

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case definition including significant differences in the measures of toxicity, didn't they?
A. Right.
Q. And he references in his study a -- vague references to authors' extensive files on paraquat.
Do you know that? He references that. In fact, the files that he got came from Syngenta, didn't they?
A. You need to point me where -- to where that -- that is said.
Q. Well, actually, I think it's on page 2 of the study. And if you want to see where he says it, it's in the very first sentence of page 2. It carries over at the bottom of page 1. "Secondly, publications were retrieved from the authors' extensive files on paraquat."
Do you see that?
A. Yes, I can see that.
Q. And actually he got the files from you, didn't he?
MR. NARESH: Objection. Foundation.
THE WITNESS: Yes, I guess so. I'm not precisely sure what he means by "files" there,

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however.
BY MR. TILLERY:
Q. Yeah. But the information he got came from your database, right?
A. That would be my assumption.
Q. Right. Well, that's what you told me earlier in this deposition that after your meeting or as part of your meeting in Atlanta in 2009, it was decided to undertake the Brent study.
Do you remember that part of your testimony?
A. Yes. I do, yeah.
Q. All right. And what was designed was to use Syngenta's database to supply information to -- to Dr. Brent to do this study, right?
A. Indeed, which is why I'm supposing that "files" means access to that database.
Q. Right. So what he -- what he didn't say is that he got the information from Syngenta, right?
A. Unless it says it somewhere else.
Q. You don't see it there anywhere, do you?
MR. NARESH: And, Dr. Botham, if you need to, you know -- on a question like that, if you need to take review --

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BY MR. TILLERY:

Q. Absolutely. If you want to take your time, you can do it. If you can see it, direct me to it because I was never able to see where he got his information from Syngenta and Phil Botham.

A. Yeah. I'm just checking that.

No. I can't see any reference to that. I mean, he does acknowledge that Syngenta didn't have any relevant analysis, but by indication, you could say that that was saying that Syngenta did have a role in supplying him with information. But it's an implication.

Q. Okay. So where in – are you reading that it says Syngenta had a role in giving him information?

A. No. I'm sorry. I'm reading from the bottom of page 1, the footnote, where it said that Dr. Brent was a paid consultant. And it says, "The manuscript was solely written by the authors. Syngenta Corporation had no role in the data analysis presented herein or in the production of this manuscript."

Q. Okay. And that, to me, sounds like he's saying that Syngenta had nothing to do with this

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other than paying him?

A. I don't know that he's -- that's what he was meant -- he was meaning through this. I think he was much more meaning to say that we did not influence the conclusions of this study.

Q. So what it means is that you gave him the data, right?

A. Yeah. We don't -- we absolutely gave him the data.

Q. All right. And –

A. Some of -- let's say some of the data, not all of the data.

Q. Okay. And look at the bottom of page 1, second column, "Secondly, publications were retrieved from the authors' extensive files on paraquat," right?

A. Yes.

Q. That's what he said?

Okay. He doesn't say Syngenta, does he?

A. No.

Q. Okay. The publications found through the research were – were reviewed for clinical information on the paraquat poisoning patients from

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the database as far as you know, correct?

A. Correct.

Q. Publications were from 17 different languages, weren't they? That's what he says in the report?

A. That's right, yes.

Q. Okay. And these had to be translated into English, right?

A. Yes.

Q. He didn't say how that happened, right?

A. No, he did not.

Q. This study, as we've said, was one that was decided on in your meeting which was largely in defense of paraquat in 2009 in Atlanta, Georgia, correct?

A. Yes, that's my recollection.

Q. Now, let's go back to this exhibit.

Fully published cases in medical or scientific journals were included, he says, right?

A. Where are you now looking, please?

Q. It's actually in the – it's page 2 of the document.

A. Yeah. Under "Inclusion and exclusion criteria"?

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Q. That's correct.

A. Yeah. Okay. Yes, I can see that.

Q. All right. And clinical information was assessed for one of four cardinal features of parkinsonism, right?

A. Yes.

Q. And he used bradykinesia, postural stability, rigidity, and tremor, right?

A. Correct.

Q. And then he developed in Table 1, if you look there, a criteria for fulfilling the case definition of paraquat poisoning, right?

A. Yes, that's correct.

Q. And if you look, the cases included by the authors had to be neuroevaluable, a word I hadn't heard before. Neuroevaluable, meaning that descriptions had to be included which indicated that an assessment of neurological symptoms had been done either initially or at follow-up after recovery, right?

A. Yes. That's my understanding of what – how that term was used.

Q. Okay. Classifications were survive, live for at least 30 days for long-term survivors, or

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short-term lived between 15 and 30 days, right? Those were his categories? That's page 2.
A. Yes.
Q. So long-term survivors included people who died after 30 days, right?
A. Yes, that's right.
Q. And cases were assessed by physicians who were board-certified in toxicology, right?
A. Yeah. It mentions that before. So it actually says in the -- further up on page 2, "All articles were reviewed by physicians with board-certified status in medical toxicology."
Q. In toxicology?
A. Medical toxicology, yeah.
Q. And let me ask you something. How many toxicologists have you ever heard of treating Parkinson's patients?
A. Toxicologists would not be allowed to treat Parkinson's patients.
Q. They would not be able to legally treat a Parkinson's patient, would they?
A. No. That's right.
Q. And they could never diagnose them, legally, could they?

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A. Not legally in terms of treatment and so on, yes.
Q. As a matter of fact, neurologists and movement disorder specialists are the ones who diagnose and treat Parkinson's patients, correct?
A. Yes, that's correct.
Q. Have you ever in your life heard of a toxicologist treating a Parkinson's disease patient?
A. No, I've not heard of that.
Q. Now, 83 patients out of all the thousands looking through your database, it looks like there's in one of the databases I looked at yesterday -- we're going to talk about these at greater length tomorrow -- it looks like there are about 3,700 dead people from their ingestion of paraquat. And that only starts in the early 2000s and leaves out the preceding 35 years.
How many would you guess have died from this chemical from either intentionally or intently ingesting it?
MR. NARESH: Objection. Scope. Calls for speculation.
THE WITNESS: Yeah. You've asked me that before. And I have not -- no basis to make any

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kind of informed judgment on that, on that number.
BY MR. TILLERY:
Q. Would you -- would you at least believe it exceeds 10,000 people who have died from ingesting it?
MR. NARESH: Same objection. Asking for speculation.
THE WITNESS: Yes. It's speculation but not unreasonable to say it would be greater than 10,000.
BY MR. TILLERY:
Q. All right. Now, from your analysis of this study, did the authors report how long any of these so-called long-term survivors lived and how long after poison -- the poisoning event they were neurologically evaluated?
A. Well, my understanding is that that information was, as far as possible, collected. Obviously, they were reliant, however, on the information as it was available rather than necessarily interviewing the -- the individuals concerned.
Q. And the reason is, is because they didn't actually come in contact with the individuals

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concerned. They were relying upon somebody else's reports done over a course of many years, right?
A. Indeed, yes.
Q. Okay. So they never listed that information about how long any of these so-called long-term survivors live and how long after the poisoning event they were neurologically evaluated because they didn't have the information, correct?
A. If they didn't have the information, they couldn't do that, certainly.
Q. Right. Do you know how the authors confirmed whether all of these patients' health outcomes were reported by experts who were even able to recognize signs of parkinsonism?
A. Well, as I said, the paper indicates that a group of people who are medical toxicologists were involved in supporting Professor Brent and his coauthor with this. So they, I guess, would have sufficient knowledge of the normal symptoms of Parkinson's disease to -- or parkinsonism to look out for.
Q. But you're not going to suggest in this deposition under oath that a medical toxicologist has the level of understanding of Parkinson's disease or

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parkinsonism that's on the level of a movement disorder specialist who is a neurologist, are you, sir?

A. There was no attempt here to -- to say there was a definite diagnosis of -- of Parkinson's disease, certainly.

It was an attempt to look for some of the clinical signs that would be associated largely with parkinsonism.

Q. How did the authors even confirm whether neurologic exams had ever been conducted?

A. They, again, were reliant on the documentation for each case; so --

Q. Now, where is -- where is that documentation?

A. That would be in the databases that -- or the files that they had access to. And some of those were from Syngenta, as we've discussed. Others were from elsewhere as is indicated in the -- in the paper.

Q. And where are those files? Where were they? Where -- were they made available for review for others?

MR. NARESH: Objection. Foundation.

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THE WITNESS: I mean, again, the detail of how that information was made available to them, I can't comment on; but, yes, they would have been given physical paper files or access to other information as -- as needed.

BY MR. TILLERY:

Q. I -- your -- I think we're missing each other. You're talking about how they conducted the study initially.

What I'm saying is how does one who comes along behind them verify whether or not the analysis that they were relying upon was accurate? They don't list the studies. They don't list the data. It's not anywhere referenced for anybody later to see, is it?

A. No. That's a fair comment. I mean, they were entirely reliant on the information they had available.

Q. Okay. But nobody else behind them can verify their results because the data isn't available for them, right?

A. Well, the data exists; so it could be made available if it was requested.

Q. Okay. Would it be available to -- to

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Syngenta?

A. Some of that information was data from Syngenta, as we've been saying, and others were in the public domain so I understand it.

Q. Would you agree that no mention of parkinsonism symptoms in a published report may simply mean that no neurologic evaluations had been conducted as this review refers to neuroevaluable poisoning patients and not patients who actually were neurologically examined?

A. What this paper is able to show is that, within some of the limitations that we've been discussing, there were no clear or obvious signs of parkinsonism recorded no matter how that was done in the individuals that were included in this analysis.

And that's what neuro-analyzable meant -- that there was enough information for them to come to a judgment. Nobody was saying that was a definitive diagnosis.

Q. Yeah. I unfortunately have to move to strike that answer as not responsive to my question.

One more time, sir. Would you agree that no mention of parkinsonism symptoms in a published report may simply mean that no neurologic

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evaluations had been conducted as this refers to neuroevaluable poisoning patients and not patients who actually were neurologically examined?

A. The information that was available was sufficient for them to determine that there had been a neuro evaluation.

Q. Okay. So you're saying the fact that they were evaluable means they were evaluated?

A. They were evaluated as far as the information available allowed.

Q. Okay. These patients averaged 22 years of age, right?

A. Yes.

Q. Okay. And we've already been through this, but you've told me that the average onset of Parkinson's symptoms -- of Parkinson's disease is in the 60, perhaps mid-60s, correct?

A. That's correct. But, again, this was about parkinsonism, which can happen in younger people.

Q. The longest post-poisoning follow-up was ten years, right?

A. Yes.

Q. These authors expected that the

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parkinsonism would occur within a short time after poisoning, right?

A. Finality –

MR. NARESH: Objection. Foundation.

MR. TILLERY: Sorry?

MR. NARESH: Objection. Foundation. Go ahead.

THE WITNESS: Finality with MPTP, you would expect to see symptoms in short -- in a short time.

BY MR. TILLERY:

Q. Didn't they actually contradict this assumption in their discussion stating that paraquat neurotoxicity is distinct from that of MPTP and rotenone and then cite the Richardson, et al., paper? Have you looked at that?

A. Yeah. Let's just go back and look just where you're referring.

Q. It's in the "Discussion" section.

A. Uh-huh. So just point me to the words that you're looking at there, please.

Q. Okay. Let me see if I can find it.

Well, if we both start reading the "Discussion" section, we'll –

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A. Yeah. I'm doing that.

Q. We may have to come back to this later, sir.

A. Okay.

Q. Okay. Because I can't seem to put my finger on it.

Let's go to Exhibit 141.

(Exhibit 141 was identified for the record.)

BY MR. TILLERY:

Q. Who is Peter Hertl while this is being pulled up?

A. Peter Hertl used to be an employee of Syngenta. Laterally, he was the head of product safety and product registration globally. And before that, he held positions in -- in product safety.

Q. And his – his job or authority extended to all parts of Syngenta AG's affiliated companies worldwide, correct?

A. That's correct.

Q. And was he on the board?

A. No. No, he was not. He was a member of the R&D, research and development, leadership team laterally. And before that, product safety division team.

Q. Was he a member of the executive committee at any time?

A. No, never.

Q. Okay. Who did he report to, to your knowledge?

A. For most of the time, when he was head of safety and regulatory, to Gerardo Ramos.

Q. And who was Gerardo Ramos?

A. He was the head of R&D.

Q. For the whole company?

A. For the whole company, yes.

Q. All right. Let's look at this exhibit if we can. And here there's a reference to a person named Mirva, and the last name is spelled H-e-j-j-a-o-u-i. How do you pronounce that?

A. I think it's Hejjaoui.

Q. Hejjaoui. Do you know who she is?

A. I have forgotten who she was, actually.

Q. What was her job?

A. That, I can't remember. I'm sorry.

Q. Okay. Well, let's look through this. And he had – "he," Dr. Herti, had sent this paper,

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Brent; and he also sent the Breckenridge paper to this person, Mirva Hejjaoui. Okay? Is that right?

A. Yes. And I can see now where she fitted in. So yes.

Q. All right.

A. I'm following you.

Q. And who does he send that September 2013 email to? Dr. Herti?

A. To Charles Breckenridge and myself.

Q. He sent it to you. Okay. And he said, "I shared the Brent and Breck paper with Mirva. Her background is in PD research, ETH Lausanne."

What's that mean?

A. Well, PD research is Parkinson's disease research. And ETH Lausanne, if I remember correctly, is a research organization in Lausanne, which I think is in Switzerland.

Q. Right. And he – and he says to you in this email dated September 10th, 2013, you and Dr. Charles Breckenridge. He says, "She recently joined our seeds group as operational support person – a few steps down from my office."

By the way, before I go on. Would that be in Basel, Switzerland?

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A. Yes. That would be in Basel.
Q. Okay. "I was interested to know what critique points could be brought out by individuals familiar with the subject area; namely, Parkinson's disease research," right? That's what you took from that statement, correct?
A. Correct.
Q. "I followed these two up with the Widnes paper."
Do you see that?
A. Yes, I do.
Q. "I followed up with her on her critique points."
And then he said, "I don't need a reaction from your side." In other words, you don't need to send anything back. "Just FYI." Just for your information, correct?
A. Correct.
Q. And he says, "Signed, Peter," right?
A. Okay.
Q. Now, five days before, he had received a response from Mirva Hejjaoui, right?
A. Yes.
Q. And what does the "CHVS" mean behind her

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name under the -- on the email?
A. CHVS is the company way of designating location. CH being the two letters for Switzerland, right, and BS being Basel.
Q. So she was working at the headquarters of Syngenta AG in Basel, Switzerland, wasn't she?
A. She was.
Q. All right. And she said to him, "Dear Peter. Thank you for sending the paper. Please find my comments on the papers you have sent previously," right?
A. Yes.
Q. All right. And he was asking for her to give her assessments of this paper, right?
A. Yes.
Q. And she had some criticisms of this study, didn't she?
A. Indeed, yes, and that's some of those we've already been talking about.
Q. Right. Did you disagree, before we go through these, with any of her criticisms?
A. I think it's not so much a case of disagreeing, and I must say I'd need a little bit more time to really take onboard some of these

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things. But it's more to do with the -- the context of those questions and whether they are actually criticisms or actually observations which we are well aware of and have been taking into consideration.
Q. Well, let's go through them. Okay?
So she says in the very -- "The papers investigated were not cited," right?
A. In the Brent paper, yes. Yes.
Q. The papers weren't cited that they're relying on. That was her big first criticism.
Then she said, "No cases other than intoxication by oral ingestion were investigated," right?
A. Right.
Q. Then she says, "No possibility to assess Parkinson's disease symptoms (bradykinesia, tremor at rest, rigidity, postural instability) with those patients as they were in a coma state or unconscious."
Do you see that?
A. Yes. And that's true for those patients who were in that state; but, of course, not all --

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Q. So --
A. Not all the cases were in a coma --
Q. Yeah. But how many of those 83 were in that state?
A. I don't have that number immediately at hand.
Q. Can you look at that study and figure it out?
A. I don't know that I can. I would need time to look it up.
Q. Okay. So without studying it, you can't answer my question, right?
A. No, I can't.
Q. Okay. Without access to the papers investigated, how would any subsequent researcher verify if this study had been done honestly?
A. Well, they would need to get access to the same information which, as I said, if it were requested, I'm sure would be made available.
Q. Okay. So the answer to my question would be without access to the papers investigated that were not provided as support for this -- in support of documentation of the paper, a subsequent researcher would not be able to verify if the study

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had been done honestly, would they?
A. Yes. Of course, you would need access to that information.
Q. Right. Another criticism is that no cases other than intoxication by oral ingestion were investigated, right?
A. Yes.
Q. No – no possibility to assess Parkinson's disease symptoms. We talked about that because the condition of the patients.
And also --
A. Yes.
Q. – the authors did not want to consider any other hypothesis other than that paraquat and MPTP have the same mode of action, and they did not present arguments to back this up.
Is that what she says?
A. Yes. And that's the discussion we were having not too long ago this morning that paraquat and MPTP may indeed not have the same mode of action.
Q. And she puts another comment about the paper of – Brent paper, "Clear indication of PQ toxicity."

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What does that mean?
A. Well, again, this is one of the things that I would need to get more of an understanding of the context. So I'm not -- I can't – I can't really put words into her mouth as to what she meant by this.
Q. Well, when you got this email, did you call and ask what she meant?
A. I didn't do that. I don't know whether Dr. Hertl asked that.
Q. Did Dr. Breckenridge do that?
A. I don't know.
Q. Was there any follow-up discussion after these comments were made by an expert in Parkinson's disease research?
A. I honestly don't remember whether there was such a follow-up.
Q. That is you, Phil Botham, GBJH, right?
A. It is. But as Peter Hertl himself said, he wasn't looking for a reaction from our side, as it were. They -- it is conceivable that we took those comments as being helpful, but we didn't need to follow up. But, again, that would need to be checked.

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Q. Okay. And then she says, "It's not convincing to evaluate the results of other studies since there was no access to the raw data or follow-up. That wasn't possible."
Isn't that what she said?
A. Well, I think it's saying the same thing that, yes, you can't necessarily corroborate if you don't have access to the raw data, and also no significant longer term follow-up was done. That was not within the parameters of this study.
Q. So all this study tells us is that high doses of paraquat poisoning do not cause parkinsonism in the same way that MPTP does, right?
A. That is the most significant finding of this paper, correct.
Q. What other finding do you think it gives us besides that finding?
A. Well, it suggests that potentially paraquat and MPTP are not the same.
Q. Okay. Now, on that same exhibit if you look at the bottom, there's a reference to a paper by Breckenridge. Do you see that?
A. I do.
Q. So this same person, Mirva Hejjaoui,

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commented on a paper that had been done by Breckenridge, right?
A. That's right.
Q. And that paper was done in what year? 2012 or '13?
A. It was published in 2013.
Q. Okay. And apparently Peter Hertl sent the Breckenridge paper to Mirva Hejjaoui for her evaluation and consideration of it, right?
A. Yes.
Q. And you were coauthor of that Breckenridge paper, weren't you?
A. I was.
Q. And what did she say here? "Different protocols were used for paraquat and MPTP administration (different age of mice, different concentrations, and different injection frequency)."
Now, what did you understand the significance of those comments to mean with respect to the Breckenridge study?
A. Well, I think this is a good example of what I said earlier about context because I suspect that Mirva Hejjaoui didn't understand why we did different – used different protocols.

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This was not meant to be a comparison of paraquat with MPTP. MPTP was used in order to be able to show that the methodologies we used like the stereology which we've talked about frequently actually was able to detect a -- an effect with something which should have caused the effect; namely, MPTP.

Q. Okay. So you did that because you had knowledge of and accepted of -- acceptance of the fact that MPTP or MPP+ was a known neurotoxin, right?

A. Yes. In terms of substantia nigra pathology.

Q. In terms of substantia nigra pathology, you knew it was a given that that could be used as a control. That was the -- one of the bases for that 2013 Breckenridge study, right?

A. That's correct.

Q. All right. Now, if we go down the list, it says, "Paraquat was shown to cross the blood-brain barrier in a concentration twice as high as was found in the olfactory bulb. One of the first nonmotor symptoms of PD patients is olfactory dysfunction. It would have been interesting to check that and do behavioral studies on the mice."

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Do you see that comment?

A. Yes.

Q. Do you agree that one of the first nonmotor symptoms of Parkinson's disease is olfactory dysfunction?

A. Yes. It's -- it's frequently reported to be a premotor symptom.

Q. It's in the -- it's in the prodromal phase of the --

A. Yes.

Q. -- disease, correct?

A. Yes.

Q. Okay. And it says, "Paraquat was shown to cross the blood-brain barrier, and a concentration twice as high was found in the olfactory bulb."

Do you remember that in the Breckenridge study?

A. Well, I'd need to go back and look again at the fine detail in Breckenridge. I think, as I said earlier today, that Breckenridge publication did include kinetics as well as pathology. So we certainly looked at how -- how much paraquat got to where in the body.

Q. And then she says at the end, "Different results were observed from the literature concerning PT – PQ – paraquat-induced TH+ neuron reduction, but there's no elaboration on the possible causes of the discrepancy," right?

A. Yes.

Q. So in other words, she was saying that the public literature got different results than you reported, but there was no effort to explain why those different results were obtained, right?

A. Yes. And, again, context is important.

So at the time of publishing Breckenridge, we were still not entirely clear why there was that discrepancy, but we went -- we didn't allow the research period to stop at that point.

Q. Right.

A. We went off –

Q. -- study, right?

A. – did further work --

(Simultaneous speech interrupted by the court reporter.)

MR. TILLERY: Okay. Sorry. Let's take a -- it's been an hour. Let's take a three- or four-minute break, and then we'll come back. Okay?

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THE WITNESS: Okay.

MR. TILLERY: And we'll start the -- we'll start the Breckenridge study. Okay?

THE WITNESS: Okay.

THE VIDEOGRAPHER: We're going off the record. The time is 8:22. This ends Media Unit Number 6.

(Recess taken.)

THE VIDEOGRAPHER: We're going back on the record. The time is 8:35. This begins Media Unit Number 7.

BY MR. TILLERY:

Q. Before our last break, you mentioned the Smeyne study. You said, "Particularly the Smeyne study."

I was going to ask you to explain why that particular study in particular was important to you?

A. Yes. Well, in the Smeyne study, we were really trying to make even clearer what this mouse model was telling us and understanding at that time that there were a number of possible technical reasons why the preexisting public research suggested that paraquat could affect neuronal cells

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in the substantia nigra; whereas, we were unable to consistently find that effect with all the work we did.

So we looked at a number of those variables -- the mouse strain, the time of dosing, and lab housing conditions and so on. So that coupled with some of the reasons that we gave in the Breckenridge paper were -- we're trying to do what -- what was suggested in that letter from the Syngenta employee in Basel to understand why -- what might be going on to explain the differences.

Q. Okay. Well, let's look at Plaintiffs' Deposition Exhibit Number 142, please.

(Exhibit 142 was identified for the record.)

THE WITNESS: Okay. That's come through for me. Thank you.

BY MR. TILLERY:

Q. Can you identify this exhibit?

A. Yes. This is a copy of the Breckenridge publication that we've been discussing -- the publication in 2013 in the Journal NeuroToxicology.

Q. And it's called "Pharmacokinetic,

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Neurochemical, Stereological, and Neuropathological Studies on Potential Effects of Paraquat in the Substantia Nigra Pars Compacta and Striatum of Male C57BL/6J Mice," right?

A. That's correct.

Q. And we have as the principal investigator Charles Breckenridge, right?

A. That's correct.

Q. And then he is followed by, as the list goes on, Nicholas Sturgess.

He worked at Syngenta Limited Jealott's Hill at that time, right?

A. Yes, that's correct. And he was previously at CTL Syngenta.

Q. Okay. And then there's a Mark Butt, right?

A. Yes.

Q. And he worked at Tox Path Specialists, LLC, in Frederick, Maryland, right?

A. That's right.

Q. What did he do in this study?

A. He was one of the two pathologists -- external pathologists that were taking a lead on these investigations.

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Q. And then there's Jeffrey Wolf. And it says he was Experimental Pathology Laboratories, EPL Laboratories, in Virginia, right?

A. Yes.

Q. And what was his job?

A. He was the second principal pathologist that I was referring to.

Q. Okay. Then there's Dan Zadory, and he is listed at EPL Laboratories. What was his job?

A. Yeah. He worked for Jeff Wolf. So he was the person who did a lot of the detailed lab pathology.

Q. Okay. Did he do the stereology work in the case?

A. Correct.

Q. Okay. And he did the stereology in the Smeyne study, and he did the stereology in the Minnema study as well, right?

A. That's right.

Q. Okay. And then there's Melissa Beck. And what was her role?

A. She worked for WIL Research Labs. So we -- we obviously had people looking after the dosing and housing animals.

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Q. And James Mathews -- what was his job?

A. James -- now, I can't remember exactly what James did. He was at RTI International. So I'd have to double-check exactly what his role was.

Q. Okay. And there's Merrill Tisdel. She worked for Syngenta Crop Protection, correct?

A. Yes. It's a gentleman. And, yes, he was with Syngenta.

Q. And what did Merrill Tisdel do?

A. Merrill was one of the people in the product safety department in Greensboro. So he -- he was largely involved in what we call "study monitoring." So he went to visit WIL and -- WIL Laboratories particularly to make sure that everything was being done appropriately.

Q. And Daniel Minnema -- he also worked for Syngenta. And what did his job entail?

A. Yes. He is a neurotoxicology expert. So he was particularly involved in reviewing some of the data.

Q. And then there's Kim Travis, Andy Cook, Phil Botham, and Lewis Smith, all either employed by or formerly employed by Syngenta, right?

A. That's right.

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Q. Okay. This particular study -- the Breckenridge 2013 study, we can refer to it as -- examined the effects of paraquat dosing on the C57 black mouse by intraperitoneal injection, didn't it?

A. That's right.

Q. This is another of the studies that was decided on in the meeting in the lab, correct?

A. Yes, that's right.

Q. Okay. And one of the pathologic hallmarks of -- of PD is the loss of dopamine-producing neurons in the substantia nigra, right?

A. That's right.

MR. NARESH: Objection. Asked and answered.

Go ahead.

BY MR. TILLERY:

Q. The TH is tyrosine hydroxylase, right? That's what's referenced in this study? TH?

A. Yes. TH is tyrosine hydroxylase.

Q. That's an enzyme that controls the rate-limiting step in making dopamine, right?

A. That's correct.

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Q. So it is the key enzyme in the protection of dopamine from dopaminergic neurons, isn't it?

A. It is, yes.

Q. Without TH+, no dopamine is produced, is it?

MR. NARESH: I will object to this line of questioning as calling for expert testimony. If I may have a standing objection?

THE WITNESS: Yes. Tyrosine hydroxylase loss would compromise the ability to produce dopamine.

BY MR. TILLERY:

Q. So cells that produce dopamine have the TH enzyme in them, right?

A. Yes. And it's expressed as a subsurface marker, which was the -- actually, the main reason we were looking at it in the study.

Q. The SNpc refers to the substantia nigra pars compacta, right?

A. That's right.

Q. It is one part of the brain that produces dopamine, right?

A. Well, the part that produces dopamine is the striatum. So there is a nerve -- a nervous connection between the substantia nigra and the striatum. And that's -- that's -- dopamine is produced at the end of those -- those nervous connections.

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Q. Dopamine is the neurotransmitter that is responsible for controlling movement, correct?

A. It is.

Q. The loss of dopamine is what causes the onset of motor symptoms in PD patients, Parkinson's disease patients, right?

A. That's correct.

Q. Now, in this study, you were dosing the animals in the amount of 1, 10, 15, 25, 30, or 35 milligrams per kilogram per week, correct?

A. That's correct.

Q. And if you want to look at page 3 of 14, that will give you the dose administration if you want to verify my statement.

A. Yes. Thanks for that. And, yes, that is correct.

Q. Okay. Mice were injected intraperitoneally -- and we refer to that and you refer to that as an IP -- one, two, or three times with each injection separated by a week, correct?

A. That's correct.

Q. The study was done to show that paraquat does not cause the death of dopaminergic neurons in the substantia nigra, correct?

A. Not quite correct. It was to investigate whether paraquat might cause the loss of dopaminergic neurons.

Q. But at a dose of 15 milligrams per kilograms three times weekly in Study 4 of this study, you did find a statistically significant reduction of TH+ dopamine-producing neurons in the substantia nigra, correct?

A. We did, and we made that very clear. We were not trying to hide that effect.

Q. Well, but scientists don't try to hide things, do they?

A. No, absolutely not. Certainly, we don't.

Q. So like -- like the -- the three positive Louise Marks studies, right?

A. Correct.

Q. Okay. You wouldn't want to hide those, would we?

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A. No.
Q. No. Okay. So there was a reduction in that Test 4 of about 30 percent of the TH+ neurons, right?
And if you want to verify that, that's page 8, first column under "Stereology, Studies 4 and 5."
A. Yes. Okay. That's fine.
Q. All right. Now, if you go to page 8, again, there is a Figure 4. Okay?
A. I've got that.
Q. Okay. Do you see Figure 4?
A. I do.
Q. All right. So you replicated the findings of loss of dopaminergic neurons with 15 milligrams per kilogram similar to findings in the independent literature, correct?
A. Absolutely.
Q. And independent studies done in laboratories worldwide show that paraquat causes loss of TH+ neurons in the substantia nigra. Would you agree?
MR. NARESH: Object to -- let me just make -- would you just let me -- let me get my

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objections in if you would.
So I'll object to the question as phrased. I think it's incomplete. But if you feel like you can answer it, please go ahead.
BY MR. TILLERY:
Q. Go ahead, sir.
A. Now, just ask the question again, please.
Q. Okay. Independent laboratories and studies done -- strike that.
Independent studies done in independent laboratories worldwide have shown that paraquat causes loss of TH+ neurons in the substantia nigra. Would you agree?
A. Yes.
Q. Okay. And, again, I think we said the loss of TH+ dopaminergic neurons in the substantia nigra is one of the pathologic hallmarks of Parkinson's disease, right?
MR. NARESH: Objection. Asked and answered.
THE WITNESS: It is one of the hallmarks, correct.

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BY MR. TILLERY:
Q. And the dose of 15 milligrams per kilogram administered three times a week caused paraquat to kill more TH+ neurons than the MPTP did, correct?
A. In this study, that is -- that is the case.
Q. So paraquat was more toxic than your positive control of MPTP at that dose in Study 4, wasn't it?
A. Yes. But you have to be very careful about how you interpret the -- the results of the study.
So this study was looking at more than just the measurement of TH-positive cells. It was also looking to say if that cell death was real, then you would also see other pathological events which would, if you like, confirm that it was cell death. And that was where our study went further than the published research and was unable to show that.
Q. Yeah. I move to strike your answer as unresponsive.
My question is simple. So with respect

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to paraquat as used against the control MPTP in Study 4, paraquat was shown to be more toxic than the positive control of MPTP at least in that study, correct?
A. I think that isn't the right way to put it because, as I said in quite a few questions ago now, the purpose of MPTP was not there to do a comparison of the potency of -- between paraquat and MPTP. It was there as a methodological control.
So I don't think you can make conclusions about the effect of 15 milligrams per kilogram being greater than that with MPTP.
Q. Well, did you have more evidence of the death of TH+ neurons with the use of MPTP or with the use of paraquat in Study 4?
A. Well, if you look at the totality of the data in this paper, MPTP caused all the other pathological changes that we would have expected to see if there was a genuine loss or death of the neurons in the substantia nigra. So the other pathology confirms that that was the case with MPTP but not with paraquat.
Q. And I move to strike that as unresponsive.

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I'm asking you a specific question. And we're looking very specifically at a – on page 8, Figure 4, the column. And you're comparing the control versus paraquat, and you're looking very specifically at one study. Okay?

And all I'm asking you is using that one study, Study 4, if you compare there and you look at the 15 milligrams per kilogram administered three times per week, paraquat killed more TH+ neurons than MPTP did.

Is that a correct statement?

MR. NARESH: I'll object to the characterization of the study. I don't think that accurately characterizes Study 4.

THE WITNESS: No, it doesn't. I absolutely -- I agree.

This -- the Study 4 measured – did more than one type of measurement. It also measured the other pathology that I'm talking about. So you have to look at all the effects, not just the one that's in Figure 4.

BY MR. TILLERY:

Q. Okay. Let's look at the TH neurons with respect to Study 4 that were impacted by MPTP. What

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was the number?

Go to your – go to your Figure 4 if you wouldn't mind.

A. Which figure are you asking me for?

Q. I'm looking at page 8 of that study, and that's Study Number 4, experiment in Study Number 4.

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

Q. My question is I want you to compare the impact on TH neurons between paraquat and the control MPTP in Study 4. What were the raw numbers?

A. So you're asking me to look at the – the black line which is MPTP and the one immediately to the left which is the green hash 15 milligrams per kilogram?

Q. Right.

A. Yeah.

Q. What does that tell you? Is my answer correct – is the answer "Yes" to my question?

A. There was a difference in the number of measured neurons between those two groups.

Q. And which –

A. Yeah. And they were both different to the control.

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Q. And which one had sustained more loss of TH neurons? Is it paraquat?

A. Yeah. The paraquat 15 milligrams per kilogram, which, again, I say we were very open to discussing in this paper.

Q. So the answer is, yes, paraquat killed more TH+ neurons than MPTP at the level in Test 4 of 15 milligrams per kilogram administered three times a week; isn't that true?

A. No. It's not true. It says that that measurement suggested that there were fewer neurons measurable in the paraquat-treated animals compared to MPTP, both compared to controls.

It does not, however, when you look at the totality of the data in this paper, say that that necessarily leads to a conclusion that more cells were killed.

Q. Well, then what is that model – what is that table in that study for if it doesn't mean what it says? If a reader can't come along and look at your table, they have to give you a call to get your spin on whatever it really means. I mean, if one is reading this as a scientist, what does it tell them?

It tells them in Study 4 at the

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15 milligram per kilogram administered dose three times per week, paraquat killed more TH+ neurons than MPTP. That's what it says, doesn't it?

MR. NARESH: Objection. Compound and –

THE WITNESS: No.

MR. NARESH: Objection. Compound and argumentative.

You can answer.

THE WITNESS: No. It doesn't say that necessarily.

It says that the ability to detect neurons using this stereological method suggested that there was a difference. But what I'm saying is that you have to look at all the information in order to properly interpret that, and that was really the heart of this paper.

So the reader of this paper wouldn't be able to see that what we're saying is that, yes, using the stereological method, there was a suggestion that more cells were killed, more to your point. However, that was not backed up by other evidence which you would expect to see to confirm --

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BY MR. TILLERY:
Q. So the other – the other evidence would be Study 5, right?
A. It would be the other pathology that we looked at to look at microglia, astrocytes, and so on.
Q. And you did a Study 5 where you tried to replicate exactly the results of Study 4, right?
A. Right.
Q. And you did it the same way, didn't you?
A. I believe so, yes.
Q. And you used the same dosing regimen in Study 4 and 5, but you did not find the same result of loss of TH neurons with paraquat, did you?
A. That's correct, yes.
Q. Okay. So between the studies of 4 and 5 at 15 milligrams per kilogram, you could not replicate your own results, right?
A. That's correct. And that's – that was -- that was the continued picture that we were seeing here that this was a phenomenon that was difficult to replicate.
Q. And if you go to page 12 of the study, and I think it's line 10, you state, "The low-dose

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regimen used in these experiments was deliberately employed to determine if the stereological methods would be sensitive enough to direct relatively small changes in the number of TH+ neurons in the substantia nigra pars compacta," correct?
A. That's correct.
Q. Okay. So stereology is a method used to count neurons and preserve brain tissue, right?
A. That's right.
Q. And the purpose of this study was to develop a stereological cell-counting method that was sensitive enough to detect very small changes in the number of TH neurons that could have been affected by paraquat, right?
A. Absolutely. That's why we are using MPTP, as I've said before, to really make sure that our methodology was sensitive.
Q. So your positive control was MPTP, right?
A. Yes.
Q. And it's considered a chemical that causes parkinsonism symptoms in animal models, right?
A. In humans, certainly.
Q. It's a known neurotoxin, right?

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A. Yes. Yes.
Q. Causes a measurable loss in neuronal cells in the substantia nigra, right?
A. It does.
Q. In Study 4, you dose the mice four times in eight hours with 10 milligrams per kilogram of MPTP, didn't you?
A. Correct.
Q. You found a statistically significant loss of TH neurons with chromogenic stain, right?
A. That's correct.
Q. In Study 5, you dosed the mice four times in eight hours with 10 milligrams per kilogram of MPTP, right?
A. That's correct.
Q. But in Study 5, you did not find a statistically significant loss of TH+ neurons with chromogenic stain, did you?
A. No. But we did see it with a fluorescent stain.
Q. Move to strike your answer as unresponsive.
But in Study 5, you did not find a statistically significant loss of TH+ neurons with

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chromogenic stain, right?
A. We used two methods to be able -- so we could be really sure that we knew what we were measuring.
Q. Right. Actually, I'm going to ask about the other one. Can you answer my question?
Did you or did you not find a statistically significant loss of TH+ neurons with chromogenic stain in Study 5?
A. No. It was just below the level of statistical significance.
Q. So, again, you did not replicate your results, did you?
A. MPTP on that occasion didn't give the expected level of response.
Q. You're not able to replicate your results with paraquat at 3 milligrams -- actually, dosing three times a week at 15 milligrams per kilogram and – in studies 4 and 5 either, were you?
A. Yes. But we were much more frequently able to show a significant effect with MPTP.
So you've pointed out one experiment where that was just below significant level. But, generally speaking, MPTP did give the expected

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response.
Q. Is it important if you're just below significant levels like at .6 or .06 to consider the -- where the needle is pointing on those in terms of the importance of them?
A. I don't quite understand the question.
Q. I'm trying to say this: I mean, your statistic -- a confidence interval that you're looking at 95, you're going to look at anything less than .05 is – is – is going to be statistically significant generally, right?
A. Right.
Q. In a laboratory.
So if it's – if it's .06, do you look at that as you just said you did here and give consideration to it because of how close it is to an arbitrary level of statistical significance?
A. Yes. You could do. But we didn't rely on that because we also have the second method to detect a lot of TH neurons in terms of the fluorescent method.
Q. Now, if you go to Figure 4 again on page 8, using your stereological method, you found about a 25 percent loss with MPTP, right?

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A. Okay. Yeah.
Q. Is that right?
A. Yes.
Q. And you gave MPTP dose of 10 milligrams per kilogram every two hours for a maximum of four doses, right?
A. That's right.
Q. And that's a total of 40 milligrams per kilogram, right?
A. That's correct.
Q. You're familiar with the Brooks study. You cited it in one of these – the 1999 Brooks study. Are you familiar with that?
A. Yes. Indeed, yes.
Q. Okay. They administered 40 milligrams per kilogram, right?
A. I would need to go back and check that but --
Q. I'll represent to you that's what I saw in the Brooks study.
A. Okay.
Q. But they found a 50 percent loss. Did you know that?
A. Yes. I do -- I mean, I don't remember

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the exact numbers, but I do remember that they got a different level of response.
Q. So your method did not detect the same amount of loss that Brooks did, right?
A. That's true.
Q. Okay. You used mice in this study that were nine to ten weeks old when they were dosed with paraquat, right?
A. Yes. I think that's correct.
Q. And that equates to mid-teens to adults? I'm sorry – strike that.
That equates to mid-teens in -- in human beings, correct?
A. Yes. I think that was what we calculated this morning, wasn't it?
Q. Okay. When the experiments were complete, the mice were 12 to 15 weeks old, which is the threshold mature adult phase of their life. It's equivalent to late teens or early 20s for humans, correct?
A. That's about right, yes.
Q. Okay. Now, if you'd go to Figure 1, page 5. This is a reference to pharmacokinetic results.

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A. Yeah. Okay. Excuse me. I was just getting there. Yes. I'm with you now.
Q. Would you take a look at this and familiarize yourself with it, please.
A. Okay.
Q. Do the pharmacokinetics results show that paraquat cleared from the blood within hours but can be found in the brain and persist in the brain for days?
A. Yes. That's true.
Q. So you found clearly that paraquat does cross the blood-brain barrier, right?
A. It certainly gets into the brain, yes.
Q. And how long is the half life of paraquat in the brain?
A. I believe we calculated it around about 22, 23 days from memory.
Q. Okay. Could you in this study determine where in the brain the paraquat was located?
A. Well, this Figure 1 shows we -- we looked at various parts of the brain, and both those parts of the brain that were behind the blood-brain barrier and -- and also areas that were outside the blood-brain barrier.

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So we detected more, actually, in the olfactory bulb, as we were talking about earlier, which is outside the blood-brain barrier.

Q. Have you ever taken a look at your studies and compared them in terms of the age of the mice with the effects that the age has on the outcome of neurotoxicity studies of paraquat?

A. Yes. I mean, we looked at age of mice -- excuse me -- as one of the factors that may be important in the Smeyne study that we talked about was published a few years after this one.

Q. Okay. Now, let's move to Exhibit 143.

(Exhibit 143 was identified for the record.)

BY MR. TILLERY:

Q. And if you'd open up this exhibit, take a look at it and tell me if you can identify this.

A. Okay. So this is a follow-up -- one of the follow-up studies that we did where we looked at the administration of paraquat to mice but using a different route of administration. So this was in the diet.

Q. So let's look, if we can, at the -- if we go back to the prior study, I'll look at this and

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show the publication date.

The Breckenridge study was submitted -- received for publication August 14th, 2012; accepted March 12th, 2013; and put online March 21st.

Does that sound right?

A. That is correct, yes. I've actually got it -- I just had a -- looked at a copy I've got by the side of me, and that is correct.

Q. All right. And then if you look at this one, it says it was received -- "this one" being Exhibit 143, the so-called Minnema study. It says this one was received September 27th, 2013; available online January 3rd, 2014. Right?

A. Yes.

Q. Okay. Now, this group of authors is virtually identical to the prior study, right?

A. It is.

Q. Is there any difference in this group other than the fact that Dan Minnema is now listed as the primary or principal investigator?

A. No. I think it's identical.

Q. Okay. This one did not use intraperitoneal -- intraperitoneal injection, though, did it?

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A. No. This used diet.

Q. And, again, the stereology was done by Mr. Zadory?

A. That's correct.

Q. In this study for 13 weeks, you fed male and female C57BL/6J mice control zero, then 10, 50 milligrams per kilogram of paraquat, right?

A. That's correct.

Q. Neurochemical, neuropathological, and stereological measurements indicated no losses of dopamine or its metabolites in the brains of paraquat-treated mice, right?

A. That's correct.

Q. No loss of dopaminergic neurons were reported, right?

A. That's right.

Q. No activation or -- of astrocytes or microglia, right?

A. That's right. That's the initial pathology I was talking about in the previous study.

Q. And the mice you used were ten weeks old at the beginning of the study, right?

A. Just checking that. Yes. Applied at seven weeks of age.

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Q. And at the end of the study, they were 23 weeks old, right?

A. That would be about right, yes.

Q. Okay. So what does that equate to in the human population? Teenage?

A. I'm --

Q. Preteen? Something like that?

A. Yeah. I mean, it's similar to what -- the calculations we made before; so into their 20s.

Q. In maybe their 20s. At -- into a category where we've never in medical history seen a Parkinson's disease human victim, correct?

A. Yes, that's right.

Q. Okay. Now, if we could go to page 7.

A. Okay.

Q. Excuse me. That may be the wrong page. Okay. If we go to -- let me read this -- seven, yes.

Okay. In the bottom of the first column, do you see the paragraph that starts off "Several previous PQ studies"?

A. Yes. I'm -- I'm there.

Q. Okay. And it says, "Several previous paraquat studies have used C57BL/6J male mice eight

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to ten weeks of age and multiple, typically three, IP administrations of paraquat. The doses used were typically 10 milligrams."

Okay. "Using this animal model, a number of laboratories have observed a reduction in neuromal cell counts of dopaminergic neurons in the substantia nigra following dosing."

Do you see that?

A. Yes.

Q. And they reference Brooks, et al., 1999; Jiao, 2012; McCormack, 2002. Right?

A. Yes.

Q. Now, would you mind reading the next sentence into the record?

A. "Our IP," Intraperitoneal, "studies using neuropathology, stereology, and specific stains -- stains for glial activation have failed to replicate previously published findings even with doses of paraquat approaching the maximum tolerated dose, 25 milligrams per kilogram dose by the IP route."

Q. And you actually referenced Breckenridge there, didn't you?

A. We did.

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Q. So you looked at Breckenridge and said despite the findings in Study 4 in the Breckenridge study, you indicated that your studies using this -- all of these techniques did not find evidence of a problem, right?

A. That's right. That's what I was explaining before. We -- we went a number of steps further than those -- some of those previous studies. And so our overall conclusion is that there was no clear effect even at the 15 milligrams per kilogram when you looked at all of those parameters.

Q. Okay. But you didn't say a single word there about the fact that Louise Marks had done studies ten years before, three studies in a row, that directly contradicted what you published in that paper, correct?

MR. NARESH: Objection to form. Argumentative. Assumes facts not in evidence.

THE WITNESS: No, we didn't. And -- and we've recognized some of the reasons for that, that the Marks studies --

BY MR. TILLERY:

Q. I'm asking you if you did or you didn't.

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Did you put it in there?

A. Well, no, because the Marks studies were not published.

Q. All right. So does this say in here anything about published -- publishing?

You say here, "Our IP studies using neuropathology, stereology, and specific stains for glial activation have failed to replicate previously published findings." And that is --

A. Right.

Q. -- exactly opposite of what she found in her studies. She said in her conclusions that her studies did replicate what was in the public domain, didn't she?

A. Yeah. Both statements are correct.

Q. Okay. You just left it out, didn't you?

A. We -- we -- I mean, your insinuation is that we deliberately left it out, and that's not a reasonable comment to make because we fully recognized that the public research shows that there's an effect. That's where the whole research program was based, an assumption that that was correct.

Q. That statement is a lie, isn't it?

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That statement in that study that you all signed on behalf of Syngenta is an absolute bald-faced lie, isn't it?

MR. NARESH: Objection. Compound. Argumentative. You're already asked the question in nonargumentative terms.

THE WITNESS: It certainly is not a lie, no. If you're referring to the statement "Our IP studies," et cetera, that is not a lie.

BY MR. TILLERY:

Q. Okay. Was -- was Louise Marks' study an IP study?

A. It was.

Q. Did it involve C -- the same study -- same study mouse?

A. It did.

Q. Did it involve neuropathology, stereology?

A. It -- it just used stereology.

Q. Right. And did she find evidence of impact at statistically significant levels in three studies on the dopaminergic neurons in those C57 mice?

A. Yes. In the same way that Brooks and

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Jiao and McCormack did.

Q. So the reason you put that in there is because it – you chose not to publish her studies. Is that the reason?

A. No, not at all. Absolutely not.

Q. So you -- you -- did you forget to mention her?

A. No. There was no need to mention her – mention those studies.

Q. Was there a footnote to reference her?

MR. NARESH: Steve --

BY MR. TILLERY:

Q. Was there a footnote by the –

MR. NARESH: Steve, I know you're getting –

MR. TILLERY: Excuse me.

MR. NARESH: You keep cutting the witness off. No. Steve, you --

MR. TILLERY: Let me finish my question.

MR. NARESH: No, no, no, no, no. You keep cutting the witness off. I let it go three times. I know you're all heated but --

MR. TILLERY: I'm not heated.

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MR. NARESH: But I'd ask --

MR. TILLERY: I'm sleepy.

MR. NARESH: I'm going to ask –

MR. TILLERY: I'm sleepy. I'm not heated.

MR. NARESH: You've got to let the -- you've got to let the witness answer a question. You can't talk over him. The court reporter can't get it down.

BY MR. TILLERY:

Q. Let me just – let me withdraw the question.

Did you put anywhere in this study a footnote about Louise Marks having done these studies?

A. No, we did not. And there was no need to because we were very open that the public research says that what was also seen in those original Marks studies is the -- was the – was the working hypothesis that paraquat does have an effect. We were never denying that. We were never hiding it.

What we – these studies didn't replicate it, especially when we looked in the

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greater detail as we have here with the other pathological measurements.

Q. I move to strike your answer as unresponsive.

Did you put anywhere in this study any reference to Louise Marks, sir?

A. No.

Q. Okay. And you say you weren't trying to hide it.

Were you aware, sir, that it wasn't until I demanded in a letter that the Louise Marks studies be disclosed that they were in December of 2019? Were you aware of that?

MR. NARESH: Objection. Asked and answered ten minutes ago.

THE WITNESS: Yeah. Certainly, I was aware of the history of reporting those Marks studies to the EPA, yes.

BY MR. TILLERY:

Q. Okay. They weren't reported before I made that – sent that letter, were they?

MR. NARESH: Same objection.

THE WITNESS: No, they weren't.

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BY MR. TILLERY:

Q. Okay. So I am looking at this sentence again. And it says, "Our IP studies using neuropathology, stereology, and specific stains for glial activation have failed to replicate previously published findings even with doses of paraquat approaching the maximum tolerated dose."

And that's talking about IP route, correct? Is that what it says?

MR. NARESH: Objection. Objection. Asked and said. You read that statement verbatim earlier.

BY MR. TILLERY:

Q. Is that what it says?

A. Yes.

Q. And does – is there any portion of that which conditions your statement about your IP studies being published?

A. You're referring to the Marks studies again?

Q. I'm saying is there anything about that sentence that we just read that conditions your IP studies as only being published IP studies?

A. I'm not quite sure I yet understand

Page 1597

what –

Q. You're telling me – you just told the ladies and gentlemen of the jury and the judge that the reason you left her out of there and didn't put her in the study is because her – her results weren't published.

I'm asking you looking at that study, where does it condition your IP studies as being published?

MR. NARESH: Objection. Mischaracterizes prior testimony.

THE WITNESS: Yeah. I'm not saying that the reason you gave was the reason we didn't include it there. I think I've said again just now very recently that the reference to published data in Brooks, Jiao, and McCormack which Marks replicated was an adequate demonstration that we were well aware that other research groups with -- were -- believed that paraquat affected dopaminergic cells in this mouse model.

BY MR. TILLERY:

Q. Now, let's go back to the study again if we can, and let's go to page 8 of 9.

A. Okay.

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Q. You used the positive control of MPP – MPTP, correct?

A. We did.

Q. Again, it's known neurotoxins can be used to induce parkinsonian-like symptoms in laboratory animals at times, correct?

A. Yes.

Q. And you administered MPTP via IP injection, right?

A. We did.

Q. You didn't use the diet?

A. That's correct for the reasons I've discussed previously. This was a methodological positive control, not a comparison of the effects of MPTP with paraquat in the diet.

Q. I move to strike your answer as unresponsive.

You didn't use the diet for the administration of MPTP in your test animals, did you, sir?

A. For the reasons that – yes, that is correct for the reasons I just indicated.

Q. Okay. I will – we can get a court order on it. I'm not going to burn up any more time.

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I move to strike your answer as unresponsive. I'm not going to ask it again. I'll ask the court to order you to reappear.

So you were comparing paraquat that was given in the diet to MPTP that was administered through IP injection, right?

A. That's right.

Q. And that's not an apples-to-apples comparison? Whether it's part of your test design or not, it's not an apples-to-apples comparison, is it?

A. It's not, and it was not meant to be.

Q. You administered four doses of 10 milligrams per kilogram of MPTP about two hours apart, correct?

A. Yeah. I think that is correct.

Q. Do you want to verify that, sir?

A. Yeah.

Q. On page 2 and in the second column, last paragraph. If you can –

A. Yeah. Just let me double-check that.

Q. Go ahead.

A. Yeah. Okay. Go ahead.

Q. Okay. In the female dose, if you'd go to page 8 of 9 again.

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A. Okay.

Q. In the female-dosed mice, those dosed with MPTP, you only found a reduction in dopamine neurons of 5 percent, right?

A. That's right.

Q. And the P value was .11. So it's not statistically significant compared to the control, correct?

A. That's right.

Q. So that means that MPTP did not kill a statistically significant amount of dopamine neurons compared to the controls?

A. That's right.

Q. So your stereology method could not defect what should have been a large change from the controls, correct?

A. Well, you say "Should have been a large change." Again, this is where you do see inconsistency between labs; so -- and also differences between male and female mice. I mean, that, again, other people have found.

Q. What did you assume for this study that mice eat in terms of their body weight per day when you did the dietary calculations for paraquat?

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A. So just repeat your question. I'm not quite sure --

Q. Yeah. I mean, I want to know what assumptions you made in terms of the amount of food that was exposed to paraquat for administration, dietary administration, how much by way of percentage of body weight that the mice ate per day.

A. How much --

Q. Can you look up at that?

A. So what -- so what percentage of their body weight --

Q. Yes.

A. -- did they consume as diet?

Q. Right. In their -- what did you assume in the study? You were one of the coauthors.

A. I -- that -- I really can't answer that question without going back to the detail.

Q. Well, why don't you look at it. Take your time and look at it and tell me.

A. I'm not sure that this paper tells me that.

Q. Are you sure? You can't --

A. Well --

Q. -- find that information?

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A. Well, why don't you point me to where – where you think might be the answer?

Q. Here's what I – maybe we just do it this way: Do you believe that mice would eat 50 percent of their body weight per day?

A. Fifty percent of their body weight per day? I mean, I couldn't -- I couldn't answer that question off the top of my head.

Q. Okay. Do you know what the statistics and other studies show the average consumption by virtue of body weight of food is for a laboratory mouse?

A. I must admit it's a while since I was directly involved in these kind of studies; so I don't have that figure to mind.

Q. Well, if the study shows 50 percent and you calculate the amount in their system by virtue of what you assume they ate in terms of percentage of body weight and, in fact, the industry norm for a long time has been 17 percent of body weight per day, that would dramatically impact the results of your study, wouldn't it?

MR. NARESH: Object to the --

THE WITNESS: So -- .

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MR. NARESH: Objection to the improper hypothetical.

Go ahead and answer if you can.

THE WITNESS: So what you're trying to tell me is that in this study, the mice did eat 50 percent of their body weight compared to a norm of 17 percent? I can't confirm that one way or another, I'm afraid.

BY MR. TILLERY:

Q. Okay. So -- well, let's do it this way, then, so that we don't have to take the time for you to read the study, which you can do this evening if you want to.

Let's just assume that a study assumed for purposes of dietary intake that paraquat-laced food was consumed at 50 percent of the mouse's body weight per day. Let's just assume that –

A. Uh-huh.

Q. -- whether it's true or not. Okay? Are you with me?

A. Okay. Yeah.

Q. And then let's assume that, in fact, the mice consumed really only a third of that amount or 17 percent per day of their body weight. Would that

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impact the results of your study?

MR. NARESH: Same objection.

THE WITNESS: Well, I think this is a difficult -- an interesting comparison, but you do have to remember that in the study we also measured the internal kinetics. So we measured how much paraquat was actually absorbed, which is a much more appropriate measure of exposure to paraquat than how much was in their diet.

And, you know, in broad terms, the amount of paraquat that was absorbed in the study was not too dissimilar from intra – intraperitoneal dosing would.

BY MR. TILLERY:

Q. So from your standpoint there would be no difference whatsoever because you made a check and determined the amount from a pharmacokinetic standpoint that was actually in the circulating bloodstream of the mouse, right?

A. Right.

Q. Okay. So it didn't matter whether – the amount of food the mouse actually consumed because you were checking the amount that was in the circulating bloodstream. Is that your answer?

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A. Absolutely, yes.
Q. Okay. Okay. Do you know -- do you know Dr. Richard Smeyne?
A. I do.
Q. And how do you know him?
A. Because he – subsequent to the study we've just been discussing, he agreed to collaborate with us because he had – he was one of the people who published suggesting that paraquat does affect cells in the substantia nigra. And you mentioned the Jiao paper earlier. I believe that Dr. Smeyne was one of the coauthors of that paper.
Q. So you understand that Dr. Smeyne was retained by Syngenta to do a paraquat study using a mouse model, right?
A. He was.
Q. And you were a coauthor of the Smeyne study as well, weren't you?
A. I was.
Q. Okay. And the Smeyne study was submitted for publication over two years after the Minnema study was submitted, correct?
A. That's right.
Q. Okay. Were you aware at the time

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Dan Zadory did the stereology cell counting in the Minnema and Breckenridge studies, he was doing the cell counting incorrectly?
MR. NARESH: Objection. Assumes facts not in evidence.
THE WITNESS: Yes. What evidence have you got for that, please?
BY MR. TILLERY:
Q. I'm asking you a question, sir. Were you aware at the time that Dan Zadory did the stereology cell counting in Minnema and Breckenridge studies that he was doing the counting incorrectly?
MR. NARESH: Objection. Assumes facts not in evidence.
THE WITNESS: I would need to understand what he meant by "incorrectly."
BY MR. TILLERY:
Q. So you don't know – you know nothing about the fact that he was not performing stereology correctly?
MR. NARESH: Objection. Assumes facts not in evidence.
THE WITNESS: I would need to know more detail in order to be able to answer that question.

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BY MR. TILLERY:
Q. You would need somebody who was an expert in the field to tell you what he was doing wrong?
A. That would help.
Q. Is Dr. Smeyne an expert in the field of stereology?
A. His laboratory certainly conducted stereology, and Dr. Jiao is the person who did that.
Q. Dr. Jiao and Dr. Smeyne, right?
A. Right.
Q. And they're both well-respected stereologists, aren't they?
A. They certainly have done a lot of work with that technique, yes.
Q. And you understood that Dr. Smeyne is listed as a witness in this case, right, by Syngenta?
A. I did know that, yes.
Q. Okay. And just for the record, we're talking about Zadory's counting of dopaminergic cells in the substantia nigra of laboratory animals exposed to paraquat. Okay? Do you understand?
A. If you mean that's what you're talking about, then okay.

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Q. That's what I'm talking about. Okay. And -- and just so we're clear, Dan Zadory did the stereology of brain cell counting, and you've told me in the Minnema study, the Breckenridge study. And he did one part of it in the Smeyne study too, didn't he?
A. Yes. He was one of the people but not the only person who did that.
Q. Right. And you would agree that getting the cell counts right is absolutely fundamental and essential to the validity of the study, wouldn't you?
A. Yes, indeed.
Q. Because if the cell count is not accurate, too high, it will cause the study to underreport brain cell loss due to paraquat exposure, correct?
A. It would, yes.
Q. Okay. And that would render the study results inaccurate, wouldn't it?
A. Yes. It might, yes.
Q. You were aware that Dr. Smeyne was working with Dan -- Dan Zadory in his study. And did you know that Dan Zadory was getting his cell counts far too high because of the method he was using?

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A. Right. Okay. Now -- now I'm beginning to understand your -- your comments.

Yes. Absolutely, I was clear about -- I was well aware of that, that there were a lot of active discussions about the methodologies that were being used. And there were some differences because it's -- it's a complicated technique. It's not just a simple case of looking down a microscope.

Q. Well, were you aware that he was counting -- overcounting the substantia -- in the substantia nigra the dopaminergic neurons of a C57 mouse by more than two-to-one what they should have been?

A. Right. I'm -- now that you're getting down to that level of detail, which is what I was hoping for before, I certainly do remember a lot of discussions around why that might be. Whether one was right and the other was wrong, I think it's fair to say that nobody characterized one as being incorrect and one as being correct.

There -- there are different ways in which this technique is -- is used and not just by the two -- two people that you're -- you're talking -- talking about now.

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Q. Well -- well, given the fact that there's only a little over 8,000 dopaminergic neurons in a mouse's brain, can you explain how Dan Zadory counted 20,000?

A. Yeah. I mean, that -- that was -- that was one of the -- the discussions that we were having. And this is -- I think there's too much technical detail that would be required to -- to go into this, but it depends where you draw the margins and where you're looking. It depends on how deep you cut the sections. It depends on the -- on the resolution of the microscope you're using.

So there are a number of technical reasons why you would come up with a different number on total neurons.

Q. Well, have you ever looked at Dr. Smeyne's explanation of why Dan Zadory at the time he -- any of the times he was doing cell counting before 2016 was doing it incorrectly?

A. I mean, I think I do remember some of that. I wouldn't be -- I think it would be incorrect to say that I was involved in all the detailed discussions. I know that Charles Breckenridge was more involved in that.

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But I believe that Dr. Smeyne always said that whilst the absolute total number may differ depending on what technologies you've used, you're still looking at changes in those numbers in response to MPTP and paraquat. So measuring different numbers does not necessarily mean that your -- your experiments are invalidated.

Q. Well, let's see exactly what he meant. Let's go to Exhibit 144. And just so we're clear, this is from the deposition of Richard Smeyne taken in this case, page 321, line 18 through page 327, line 14.

(Exhibit 144 was marked for identification.)

BY MR. TILLERY:

Q. And if you would please watch this, and then I'll ask you some questions about it. Okay? Okay. Can you see that, sir?

A. I can see it now, yes.

Q. You can see it now? Okay. Give me a second.

MR. TILLERY: Can you get started or do I? Just take this.

MR. NARESH: And I'm sorry to

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interrupt. Are we supposed to be seeing something?

MR. TILLERY: You can't see anything?

THE WITNESS: No. It's just a free screen. Sorry. I thought you were still working on the technology.

MR. TILLERY: I'm sorry. Just -- they're not seeing anything. Sorry.

THE WITNESS: Are we -- I mean, can we -- can we press play on our end? Is that the way to do it?

BY MR. TILLERY:

Q. I think you should press play. Can you hear this, sir? Are you able to hear anything on your end, Dr. Botham?

A. Yes. I can hear it now.

Q. Okay. Did you hear that, Dr. Botham? Dr. Botham? Can anybody hear me?

MR. NARESH: I can hear you, Steve.

BY MR. TILLERY:

Q. Dr. Botham, can you hear me?

A. Yes, I can hear you.

Q. Did you hear what he said?

A. Yes, I can hear it.

Q. Did you hear what his -- are you still

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listening to it?
A. I'm still listening to it.
Q. All right. Sorry. Tell me when you're finished.
(Whereupon, a video was played.)
THE WITNESS: Okay. Yeah. I could hear that. Thank you.
BY MR. TILLERY:
Q. All right. And the video will – is marked as Plaintiffs' Deposition Exhibit 145 and the transcript of that video – can we offer that up? – is Exhibit 145.
(Exhibit 145 was identified for the record.)
BY MR. TILLERY:
Q. And I just want to show it to you so that you can verify it's the same document that you just listened to.
MR. NARESH: And, Steve, for rule completeness reasons, would you also mind showing him and/or playing for Dr. Botham 329, lines 2 through 11?
MR. TILLERY: 329. I don't know if I

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have 329. I don't have -- I stop at 327. You'll have to do that on your redirect.
MR. NARESH: Well, I'll object. I'll object on rule completeness grounds. I think he needs to see the whole – the whole testimony, not just a part of it, in order to answer your questions.
MR. TILLERY: Well, you're – you're able to do that on your – your clarification, not --
MR. NARESH: No. I disagree for the same reasons as you articulated on the Greenamyre issue here. I think that if you're going to play any of it, you've got to play the rest of it for completeness.
MR. TILLERY: I'm happy to do it. I don't have it here. I'm happy to play this at the – at the hearing, or you can show it to him at a break. That's up to you. But I don't have that here.
Q. It's – the clip that I showed you is the one, and I want to make sure you can at this point, sir, look at this exhibit and confirm that that's what you listened to. And that's page 321,

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line 18, through page 327, line 14, of the Richard Smeyne dep. And if you'd look at that and see if that looks like what you just listened to.
A. Yeah. I'm looking at it now just to let you know.
Yeah. Okay. I would agree the transcript looks to be a record of what I've just seen on the video.
Q. All right. Thank you. So this –
MR. NARESH: So wait. So, Steve, before -- I do object to asking questions about a partial playing of a deposition transcript that he's not reviewed. I -- I take you at your suggestion that why don't we take a break now.
MR. TILLERY: I don't have the transcript –
MR. NARESH: Yeah. That's fine. And so why don't we take a break now. I'll show him the part that I think that he should see for rule of completeness reasons, and then you can ask your questions after that.
MR. TILLERY: Well, I don't have but two questions. So I have just follow-up questions, and then you can -- and then I can finish this – I

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think that's actually it. No. I think I have just one or more questions that have no relevance to this, but let me -- let me follow up with this.
Q. So you would agree from the sworn testimony from Syngenta's retained stereology expert Dr. Smeyne that as of the time Dr. Smeyne met with Dan Zadory that Zadory was not using the correct procedure in counting dopaminergic brain cells until he was corrected by Dr. Smeyne. Would you agree with that statement?
MR. NARESH: I -- I object to the characterization. I also object on the rule of completeness reasons I previously articulated.
BY MR. TILLERY:
Q. Go ahead, sir.
A. Yeah. So the – there were certainly -- it's certainly true that the methodology that Dan Zadory used may have, as Dr. Smeyne has indicated, overestimated the total number of neurons.
However, two things are important: One is that, in spite of that, you would still expect even using that different methodology to have been able to detect an effect of paraquat had it actually

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happened; and, two, when we worked with Dr. Smeyne using Dr. Smeyne's approved stereology, again, there was no effect of paraquat seen.

So I think the implications of this -- of this methodological issue are not as profound as you might be trying to make out.

Q. I move to strike your answer as nonresponsive, and let's go back to my question.

Would you agree with me from the sworn testimony that you've just listened to from Syngenta's own retained stereology expert Dr. Richard Smeyne that at the time he saw and visited and watched Zadory conduct stereology technique in Zadory's own laboratory that Zadory was not using the correct procedure in counting dopaminergic brain cells in laboratory animals until he was corrected by Dr. Smeyne. Would you agree with that?

MR. NARESH: Same objections as before, and I'll also object on best evidence. Dr. Smeyne's testimony speaks for itself.

THE WITNESS: Yeah. That – that is certainly the technical view, but I think your -- nevertheless, you have to ask what would it actually

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matter in terms of interpretation of the studies?

BY MR. TILLERY:

Q. Well, let's say this: He was counting, according to Smeyne's sworn testimony, twice as many cells as actually existed, wasn't he?

A. The -- yes. It sounds like the calculation that the automated stereology uses was projecting twice the number, yes.

Q. And he was doing it because he was assuming that the number of cells was homogenous throughout the substantia nigra, correct?

MR. NARESH: I again object to this line of questioning on complete -- completeness grounds and best evidence grounds.

MR. TILLERY: I'll let you have that continuing objection.

Q. Can you answer me, sir?

A. That is the reason given. And, actually, it is a reason that I remember being explained to me at the time.

Q. And that – that accounted for the difference in the cell count numbers, correct?

A. It -- it was probable -- it was a probable explanation, yes.

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Q. And Zadory's errors in analysis could certainly explain the inconsistent results in the Breckenridge study as well, couldn't they?

A. By "inconsistent," you mean the total – total neurons in the Breckenridge?

Q. Yes.

A. Yes.

Q. And they could certainly explain negative results in the Minnema study too, couldn't they?

A. No. I think that this is a different question, which is what I was saying earlier.

Whether that methodological counting issue actually had an impact on the outcome of the studies, it's not all that likely because other methods were used to confirm whether or not cells had been lost as a consequence of pathology. We didn't rely just on the one stereological assessment.

Q. Well, to the extent that you did rely upon cell counts, you used this – you didn't use staining techniques when you used stereology, did you? In the Minnema study.

A. We used -- you mean we used a

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fluorescent method?

Q. What I'm asking is, is that when you – when you reference in your study the loss of dopaminergic neurons, were you referring to cell counts through stereology?

A. Yes. The effects included those that we measured with stereology, yes.

Q. All right. And if that stereology number was wrong because of a technique making the assumption of a homogenous number of dopaminergic neurons throughout the substantia nigra, an incorrect assumption, that could influence the counting, correct?

A. But you would expect that that would be evened out because both the controls and the test animals were subjected to the same counting methodology. So if there was an effect, you would see it regardless of what the total number was.

Q. Okay. Now, let's go back to the discussion section of the Minnema study. And this is Exhibit 143. Do you see that?

A. I'm just getting there. Yeah. Okay. I've got it.

Q. And do you see where it says, "Among the

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many studies in the literature that have examined the potential effects of paraquat in the substantia nigra pars compacta, relatively few studies have involved long-term continuing – continuous dosing."

Do you see that?

A. Yeah. Just getting there. Hold on.

Q. It's in the discussion.

A. Yeah. I think – yeah. Which page are you on? A page number, that would be helpful.

Q. Yeah. It's page 5.

A. Must be yours. I haven't got 5. Right. Okay. I'm with you. I'm with you now. Thank you.

Q. All right. If you take your time and under "Discussion," do you see the first line?

A. Yeah. I'm there. Thank you.

Q. It says, "Among the many studies in the literature that have examined the potential effects of paraquat on the substantia nigra pars compacta, relatively few studies have involved long-term continuous dosing," correct?

A. Correct.

Q. Now let's go to the last sentence, and it says, "The relevance of these dose levels, routes,

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and durations of exposure to human paraquat exposure scenarios and, therefore, to human risk assessment is difficult to assess."

Is that what you said?

A. Sorry. Where -- where are you now reading?

Q. The last sentence of that same paragraph.

A. Oh, the same paragraph. I'm sorry. Right.

Q. "The relevance of these dose levels, routes, and durations of exposure to human paraquat exposure scenarios and, therefore, to human risk assessment is difficult to assess."

Is that what you wrote? The –

A. Correct, yes.

Q. -- sentence?

A. Correct.

Q. Okay. So as of that time, assuming that this chemical had been on the market since the mid-'60s in the United States, what are we talking about now? Thirty-five plus 14 years – 49 years. Would that be fair?

A. 1965 to forty -- '15, yeah. Forty

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years.

Q. Forty, 45 years. Would that be right?

A. Yep.

Q. Forty-nine years. Forty-nine years, I guess.

So after 49 years of selling this product in the United States, Syngenta scientists were still saying they really didn't know how to do a human health risk assessment for paraquat, right?

MR. NARESH: Objection to the characterization.

THE WITNESS: No. I think that's not what we were saying at all here.

BY MR. TILLERY:

Q. Well, did you say these words? "The relevance of these dose levels, routes, and durations of exposure to human paraquat exposure scenarios and, therefore, to human risk assessment is difficult to assess"?

A. Right. But this was referring to the kind of studies that were involved – that included subcutaneous injection, intraperitoneal injection, et cetera.

Q. Did you ever ask Elizabeth Anderson for

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help in designing a human health risk assessment?

A. Not as I recall, no.

Q. Do you know her?

A. I know her. I don't know her, but I know the name.

Q. Okay. Did Syngenta ever reach out to her and say, "Can you help design a human health risk assessment? Help us understand how this chemical paraquat affects applicators and how it might make them sick by neurotoxicity."

Did you ever do that?

A. I'm not aware that we did.

Q. Okay. Was she ever consulted to do any kind of analysis or guidance, counseling, on human health risk assessment of paraquat?

A. I don't – I don't know. I don't think so, but I don't know.

Q. Okay. You never were told about it if she was, correct?

A. I'm pretty sure that's the case.

Q. Okay. Would it be accurate to say that in all the years of sales of paraquat, Syngenta has never conducted a long-term neurotoxicity study of paraquat?

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A. It depends how you define "neurotoxicity study." We've done a lot of studies on neurotoxicity, and some of those have been long -- long-term studies. But you've got to define what you mean.

Q. I'm talking about -- well, you said earlier in this deposition that long term was what? A year?

A. One to two years, yes.

Q. Okay. Have you ever done a one-year study where the end point was -- the study parameters were focused upon evaluating whether or not paraquat caused neurotoxicity?

A. The chronic studies that are guideline studies for 12 -- sorry -- for 18-month or two-year studies in the rodent and one year in the dog have included some assessments of neurotoxicity but not at the level of granularity or detail that might be appropriate in terms of Parkinson's disease.

Q. Well, let's put it this way: In those studies, did you evaluate cellular loss or damage in the substantia nigra of those test animals?

A. No, we didn't, which is one of the things that I was just referring to.

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Q. All right. So let me rephrase my question.

Would it be accurate to say, then, in all the years Syngenta has sold paraquat, Syngenta has never conducted a long-term neurotoxicity of paraquat where an evaluation of cellular loss in the substantia nigra of the test animal was made?

A. No, we haven't. But we've compensated for that, as is normal toxicological practice, by using extremely high-dose levels in shorter term test studies.

Q. Can you answer my question directly? Have you ever done such a study?

A. I said in the beginning of that, no, we haven't.

Q. Okay. Would it be accurate to say that in all the years of sales of paraquat, Syngenta has never conducted a study of the effects of paraquat on the upregulation of alpha-synuclein?

A. No. We have never looked at alpha-synuclein in that -- in any level of detail.

MR. TILLERY: Okay. Let's take a -- a 15-minute break at this point. Okay?

THE VIDEOGRAPHER: We're going off the record. The time is 10:04. This ends Media Unit Number 7.

(Recess taken.)

THE VIDEOGRAPHER: We're going back on the record. The time is 10:25. This begins Media Unit Number 8.

BY MR. TILLERY:

Q. When did -- strike that.

When did Dr. Smeyne first become a Syngenta consultant?

A. I'm sorry. I don't know exactly the year. Circa 2013, '14, I believe. Possibly the year after that.

Q. Dr. Smeyne advised Syngenta about Parkinson's disease?

A. Yeah. He -- because of the work that he had done previously, particularly in the mouse model, he was engaged really to try to help us to better understand the -- the way in which the mouse model might be following paraquat and Parkinson's disease.

Q. And he also advised Syngenta about doing paraquat experiments with the black mouse model, didn't he?

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A. Yeah. That's -- that's correct, yes.

Q. And you knew that he had a person in his laboratory that he relied upon to run his lab by the name of Dr. Yun Jiao, right?

A. Yes, we did. That's correct, yes.

Q. Did you meet her?

A. I think that I met her once, but Dr. Breckenridge is the person who had more interaction with her.

Q. And you understood that he did -- strike that.

You understood that Dr. Jiao also did a lot of Dr. Smeyne's stereology?

A. Yes. Yes, we knew that.

Q. Now, let's go to Plaintiffs' Deposition Exhibit Number 146.

(Exhibit 146 was identified for the record.)

BY MR. TILLERY:

Q. If you could familiarize yourself with this document and then identify it for the record, please.

A. So these are minutes of another of the paraquat health science team meetings dated the 2nd

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of October, 2013.
Q. Okay. And by this time, October 2nd, 2013, Dr. Smeyne had actually become a member of the Syngenta's paraquat health team on – on the outside member, correct?
A. Yeah. He was an external guest in the beginning, yes.
Q. And how did you identify people who were external – external guests from permanent members?
A. How did we identify them in terms of what, precisely?
Q. In other – in other words, how could you – was Professor Smith an external member, or was he a permanent member of the paraquat health science team?
A. Right. So that – it was a little bit of a loose boundary, I have to say. But people like Professor Smith and Sir Colin Berry in particular were really more permanent members of the – of the team. Others were temporarily associated with the team.
Q. How long did the association with Dr. Smeyne continue?
A. Really up until the – the time when

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his joint publication with us was -- was released. And, in fact, it is still gone on post the publication because we've needed to tie up some loose ends on internal reports and data to make sure it's all in good order.
Q. And so you still – as of this time?
(Reporter clarification.)
BY MR. TILLERY:
Q. So you still have your association with him as of this time?
A. We still have some contact with Richard Smeyne, yes.
Q. What was his role on the paraquat health sciences team?
A. Very much as -- as an adviser to the issue we've been discussing for the last hour or two on the -- the way in which the mouse -- the C57 black 6 mouse model should be conducted and in terms of the parameters that are important particularly as he and Dr. Jiao had done -- done work on this model themselves.
Q. Did you know that Dr. Smeyne is affiliated with Qualify – Quality Scientific Solutions?

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A. I don't know that I was aware of that. This is the organization that Dr. Breckenridge is now a part of?
Q. Yes. The Quality Scientific Solutions website shows Charles Breckenridge listed as principal.
A. Right. Yeah. I know there are a large number of scientists who have some connections with -- with Quality Science Solutions, yes.
Q. And he's also a Syngenta consultant, isn't he?
A. I'm not sure whether he is now, whether that is now finished. Again, as I said earlier, I'm not -- I don't get involved in those contracts.
Q. And on the same website of Qualified Settlement – or Scientific Solutions, Peter Hertl is listed as a principal?
A. Right. Yes.
Q. He's a former Syngenta employee, right?
A. Yes. Correct.
Q. And Jim Simkins is also listed as a principal in the same organization, Quality Scientific Solutions, and he is a long-time Syngenta consultant, right?

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A. That's right.
Q. And Lewis Smith is also listed as an associate with Quality Scientific Solutions. He is a long-term former employee and associate of Syngenta, correct?
A. Correct.
Q. Mark Butt is listed as an associate. He's been a Syngenta consultant for years, right?
A. Yes. He's been a collaborator and a consultant.
Q. Okay. Jeff Wolf is listed. What is his role in this?
A. Yeah. Jeff Wolf is also a -- a – an expert in – in neuropathology.
Q. Okay. And he has been a consultant for Syngenta for a number of years, right?
A. Yes, he was.
Q. And part of your paraquat health science team, right?
A. He was, indeed. As this -- the minutes indicate, he was an external member for a period of time.
Q. And Robert Sielken is listed as an association of that same organization. He too is a

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long-term Syngenta consultant, right?
A. Yes. As a statistician.
Q. Do you know how many hours a year Quality Scientific Solutions does work for Syngenta?
A. Are you referring to now?
Q. Yes.
A. No. I don't have that number at hand.
Q. Okay. Now, if you go to number 3, if you have the first page pulled up on the agenda items. "Outcome of investigative study with Richard Smeyne." Do you see that?
A. Yes.
Q. And it says "NTS." Who would that stand for?
A. That's Nick Sturgess.
Q. And then RS?
A. Richard Smeyne.
Q. And JW?
A. Jeff Wolf.
Q. Okay. Now, if we look about the fourth line, it says, "Similarly, the EPL." And what does that refer to?
A. EPL is the -- the organization that Jeff Wolf worked for -- works for.

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Q. And so did Dan Zadory, right?
A. And Dan Zadory too, correct.
Q. Right. And when the stereology work was done, it was done at EPL by Dan Zadory, right?
A. That's right.
Q. Okay. And this study -- strike that.
And this committee met about four days before the publication -- strike that.
And this study met on -- strike that.
And this health science team met on what date?
A. The 2nd of October, 2013.
Q. And you can look and see if you want, but I think that's about a week after the Minnema study was reported or submitted.
A. Yes. That's about right. It was published in early 2014, correct.
Q. Okay. Now, let's go back to that sentence. "Similarly, the EPL stereology data for this study are consistent with what we have seen previously (effect with the positive control MPTP, no effect for paraquat-treated mice) although the cell numbers as assessed by stereology at EPL are significantly higher than Smeyne's numbers and higher

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than those we have seen previously."
Do you see that?
A. Yes.
Q. Okay. Is this the meeting that you attended where there was an explanation given about the cell number count?
A. It may well have been. So I don't recall precisely; but, certainly, I think it's highly likely that it would have been discussed as a technical issue, yes.
Q. And you were listed as the very first person present at that meeting, weren't you?
A. Yes. Because I was chairing the committee.
Q. You were the chair of that group, weren't you?
A. Yes, I was.
Q. All right. So it continues on in -- under number 3 in that same paragraph and says, "Both group -- groups need to understand why the current study has failed to replicate Richard Smeyne's previously published data prior to a potential Smeyne-authored joint publication of the current investigation in an influential journal."

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Do you see that?
A. Yes.
Q. Okay. So this is referring to the results in the Minnema study, isn't it?
A. And the Breckenridge study.
Q. I'm sorry?
A. And the Breckenridge study.
Q. And both of them?
A. Yes.
Q. Breckenridge and Minnema, right?
Now, if you look at the next page -- actually, go to the next paragraph. "RS," Richard Smeyne, "outlined potential options for further investigation of the failure to reproduce the findings previously obtained in his investigations."
It says a PowerPoint presentation from Richard Smeyne, right?
A. Yes.
Q. "During the discussion, one difference which has emerged was that, in Smeyne's previously reported study, the paraquat-treated mice were placed on warming pads. In the Syngenta studies including the recent WIL study" -- which one is that?

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A. That's the study that we were -- the studies that we were talking about -- the Breckenridge and the Minnema studies.

Q. And Minnema, right?

A. Yeah.

Q. -- "which formed part of the Smeyne collaborative study, the paraquat-treated mice were not on heating pads. Richard Smeyne stated that in his original investigation which led to the publication, there was no assessment of slides for the presence of microglial activation." Okay?

A. Yes.

Q. "Richard Smeyne stated that based upon his earlier investigation using section evaluation interval, he believed the actual number of dopaminergic neurons in the substantia nigra to be about 8,800."

Do you see that?

A. Yes.

Q. Do you have any information that that's incorrect?

A. No, not at all. This is -- actually refers to the conversation we were having before the break.

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Q. Okay. And it's consistent with what his testimony was, isn't it?

A. It is.

Q. Now, if you continue to the next page and go into the second paragraph, "Richard Smeyne indicated that he believed that counting every third section, i.e., one in three, was unnecessarily labor intensive and that every fifth section, one in five, was sufficient."

Do you see that?

A. Yes.

Q. "The view of the meeting regarding the investigation of the potential for differences between Sigma-sourced versus Syngenta-sourced paraquat analytical standards due to possible presence of the significance and very highly potent impurity to account for differences in results was that this was probably better determined first by chemical analysis."

What does that have reference to?

A. Well, we were having a general discussion, a much broader discussion, I have to say, than is recorded in these short minutes about the reason why we were not getting the same effect

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on neuromal cells in the substantia nigra in the Minnema and the Breckenridge studies compared to the Jiao and Smeyne work in 2012, I think it was.

So, one, a number of hypotheses were put forward, one of which was a different standard of paraquat -- purity of paraquat was used, and potentially a more toxic impurity could have been in the material that was used by Richard Smeyne. And so that should be investigated to see if there's any evidence of that.

Q. You didn't find any evidence of that, did you?

A. No, we didn't.

Q. Okay. Now, what's the next number? Let's go to Exhibit 147.

(Exhibit 147 was identified for the record.)

BY MR. TILLERY:

Q. If you'd open that up, please. And this is a document entitled "Genetic Dissection of Strain Dependent Paraquat-induced Neurodegeneration in the Substantia Nigra Pars Compacta."

Do you see that in -- the investigator is Yun Jiao and then Lu Lu, Robert Williams, and

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Richard Smeyne. Do you see this?

A. I do.

Q. This is the 2012 Smeyne article, isn't it?

A. It is.

Q. In 2012 Dr. Smeyne coauthored a paper entitled "Genetic Dissection of Strain Dependent Paraquat-induced Neurodegeneration" at a time when he was not a consultant with Syngenta, correct?

A. Correct.

Q. He had never worked for Syngenta at that time, had he?

A. I don't believe he had, no.

Q. He used paraquat to induce parkinsonism symptoms in the C57 mouse, right?

A. He was using that to see particularly if there was any -- any impact on the substantia nigra.

Q. Right. And if you look at the page 1 of his study in the abstract about the fourth line down, he says in the abstract, "Paraquat acts as a direct redox cycling agent to induce formation of free radicals, and when administered to mice, induces the cardinal symptoms of parkinsonism, including loss of

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TH+ positive dopaminergic neurons in the ventral midbrain substantia nigra pars compacta," correct?
A. Correct.
Q. Okay. That's a direct quote from his paper, right?
A. Yes.
Q. And in 19 -- strike that.
In 2012 would you agree that Dr. Smeyne likely made that statement because it was well established at that time in the scientific literature that paraquat acts as a redox cycling agent to induce formation of free radicals, and when administered to mice, induces the cardinal symptoms of Parkinson's including the loss of TH+ positive dopaminergic neurons in the substantia nigra?
MR. NARESH: Objection. Calls for an expert opinion.
May I have a standing objection on this line?
MR. TILLERY: Yes.
THE WITNESS: Yes. I agree with your statement there that Dr. Smeyne was using the information that was in the public literature at that time.

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BY MR. TILLERY:
Q. And it was consistent -- the statement was consistent with it, wasn't it?
A. Yes.
Q. In that 2012 study by Dr. Smeyne, he showed that the C57 black mouse treated with paraquat lost about 50 percent of their neurons in the substantia nigra compared with untreated animals.
And if you need to see the reference, that's page 2, right column in the "Results" section if you want to verify that.
A. Yes, that's correct.
Q. Okay. To your knowledge, this was a valid study, wasn't it?
A. Yes, indeed. As, indeed, we always assume that most of the public literature was.
Q. Okay. Dr. Smeyne wrote that "Paraquat's mechanism of action involves the transfer of an electron usually from NADPH to form a P2+ radical," right? That's page 4, left column.
A. Yes. Indeed, I can see this.
Q. All right. "This free radical interacts with molecular oxygen to form a superoxide radical that damages lipids contained within cell membranes."

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That's what he said, right?
A. That's right.
Q. "Paraquat has been shown to induce extensive mitochondrial oxidative damage," correct? That's what he said?
A. Yes.
Q. "And in the brain, paraquat is actively transported through neutral amino acid transporters," he also said, correct?
A. Correct.
Q. "Paraquat generates free radicals through redox cycling." And that's page 1, left column, last sentence, if you want to verify that.
A. Okay. Yep.
Q. And if you go to page 4, the first column, line 10, "Experimentally," Dr. Smeyne wrote, "systemic administration of paraquat induces a relatively specific lesion in the substantia nigra that results in dopaminergic neuron loss," correct?
A. Correct.
Q. And he cited three references for that statement, right?
A. Yes.
Q. So that means at least three other

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published studies found those same results -- correct? -- at that time?
A. At that time, yes.
Q. In fact, by 2012 many laboratories worldwide had established the paraquat black mouse as a model to induce parkinsonian pathology and symptoms to study potential cures for Parkinson's disease, correct?
A. That's correct.
Q. Now, let's go to 148.
(Exhibit 148 was identified for the record.)
BY MR. TILLERY:
Q. After the publication of Dr. Smeyne's 2012 study, he became a Syngenta consultant in that same year; is that correct?
A. Yes.
Q. Dr. Smeyne was tasked with designing paraquat experiments to determine whether paraquat was neurotoxic in the C57 mouse. That's one of his jobs, right?
A. Yes.
Q. The same mouse strain that he used in his 2012 study that found paraquat was neurotoxic,

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right?
A. That's right.
Q. The work resulted in the publication of another study we can refer to as the Smeyne 2016 study of which you were a coauthor, correct?
A. That's correct.
Q. The results of that study were ultimately published in a paper entitled "Assessment of the Effects of MPTP and Paraquat on Dopaminergic Neurons and Microglia in the Substantia Nigra Pars Compacta of the C57BL/6 Mice," right?
A. That's right.
Q. And that is marked right now before you as Exhibit 148 for this deposition, correct?
A. That is correct, yes.
Q. All right. The paper was published. If we look at the publication date, it was received November 30th, 2015; accepted September 20th, 2016; and published October 27th, 2016.
Is that a fair statement?
A. It is.
Q. Okay. Dr. Smeyne performed experiments in his lab at St. Jude's Hospital in the United States, correct?

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A. Yes.
Q. And another Syngenta consultant Dan Zadory performed other experiments at EPL, the organization you previously described, correct?
A. Yes. So Dan Zadory was involved in one part of those experiments.
Q. Right. Just the stereology?
A. Just the stereology, yes.
Q. "EPL" stands for experimental pathology laboratory, correct?
A. That's correct.
Q. Okay. Did Syngenta pay for the study?
A. Yes, it did.
Q. Did Syngenta pay the study authors?
A. If they were consultants, there was a payment, yes.
Q. Did Syngenta pay for all the expenses associated with the lab experiments?
A. As far as I know, yes.
Q. Okay. One purpose of that paper was to use two different stereology methods to count neuronal cells in the substantia nigra, right?
A. Yes, that's right.
Q. Because loss of dopaminergic cells in

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the substantia nigra is a pathologic hallmark of human Parkinson's disease, correct?
A. Yes, that's right.
Q. Dr. Smeyne performed stereology on the mice that were part of the experiments taking place at his lab at St. Jude using what is known as 2D design method of stereology, right?
A. Right.
Q. And 2D is two-dimensional stereology, right?
A. Correct.
Q. And Dan Zadory used what is known as 3D, a three-dimensional stereology, right?
A. Yes.
Q. And Zadory was a paid Syngenta consultant at the time as well, right?
A. Yes, I believe he was.
Q. In that study you used the same strain of mice from two different suppliers; is that correct?
A. That's correct.
Q. That's page 6, Figure 1, if you want to verify that.
A. Just double-check. I'm pretty sure

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that's the case.
MR. NARESH: And by "that study," Steve, you're referring to the 2016?
MR. TILLERY: I am. I'm referring to the 2016 study which is marked as Plaintiffs' Deposition Exhibit 148.
MR. NARESH: Thank you.
THE WITNESS: Yes, you're correct. So we have – mice were sourced from Jackson and from Harlan.
BY MR. TILLERY:
Q. Right. And you used mice that were 9 or 16 weeks old at the start of the experiment, correct?
A. That's correct.
Q. And, again, just for the ladies and gentlemen of the jury and the court, what does that equate to in general terms with human population?
A. So, again, we're talking about mid to late teenage at the beginning of the study.
Q. Okay. You determined whether paraquat treatment caused the mice to have an immune response, inflammation, measured by microglial activation, correct?
A. Yes. In response to dying. If cells

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were dying in the substantia nigra, you would see that activation of microglia.

Q. And would you explain what microglial activation is?

A. Yeah. Microglia -- I mean, one way of explaining it, it's a bit like macrophage is responding to attack by bacteria. So they're one component of the response to external insult.

So if you get damage, then -- in the brain, then these cells called "microglia" would be activated as part of that response, which might include the death of neurons.

Q. You found that paraquat treatment did not result in the loss of dopaminergic neurons, right?

A. That's correct.

Q. That's what you reported in your paper, right?

A. In this paper, that's right.

Q. And you reported in the study that paraquat treatment did not result in microglial activation, right?

A. That's correct.

Q. And that's very important because

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microglial activation would tell you what?

A. I mean, micro – microglial activation is a way of confirming, according to our pathological consultants including Professor Smeyne, that there is -- there is genuine pathology, cell death in this case, actually happening.

Q. In other words, that the introduction of paraquat is actually causing cellular death in the substantia nigra?

A. That's right.

Q. Okay. And the paper was published in the journal PLOS One, right?

A. That's correct.

Q. Okay. Now, if I can just go through these microglial counts references quickly.

Microglial are immune cells found in the brain and spinal cord, right?

A. That's right.

Q. Okay. They're first responders to defend the central nervous system. Would you agree?

A. Yes. Yes. As I said, a little bit like macrophages.

Q. Right. Microglia are sort of scavenger cells constantly looking for toxins or damaged cells.

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Would you agree with that as well?

A. Yes. Yes. Yes, indeed.

Q. So activation means that there's a toxin to attack or damaged cell to dispose of, right?

A. Yes. And it's the latter that we were most concerned about here.

Q. Right. In other words, the death of a dopaminergic neuron would signal the activation of a microglial cell, right?

A. That's right.

Q. When microglial are resting, they have a small round center with tentacles, right?

A. Yes.

Q. And when activated, they change shape by withdrawing their tentacles, so more of a circular structure with a larger diameter than the resting cell. Correct?

A. That's right.

Q. Okay. And that's how you can tell they've been activated?

A. That's right.

Q. You measure whether microglial were activated by paraquat in the 2016 paper, right?

A. We did.

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Q. And you found that paraquat did not activate microglia, right?

A. That's correct.

Q. Because had you found that, that would have been an indication that paraquat was neurotoxic, correct?

A. It would have increased the likelihood that paraquat was causing the death of dopaminergic neurons, that's correct.

Q. Okay. In page – on page 8 of the 2016 paper under "Statistical Analyses," that's the last paragraph there. If you would pull that up and look at it.

A. Yeah. Okay. I'm on that.

Q. Where it says "Statistical Analyses," it says, "The mean number of activated resting and total microglia in the substantia nigra of vehicle controls was compared statistically to PQ- and MPTP-treated groups using a two-sided Welch t-test. A two-side test was used because it was considered equally likely that these agents could activate microglia as a result of dopaminergic neuron cell death or have a direct cytotoxic effect on glia. Both have a negative or positive response was possible."

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Do you see that?
A. Yes.
Q. What is a cytotoxic effect?
A. Well, that would mean that the external agent paraquat or MPTP was directly damaging the glia or activating the microglia rather than the microglia responding to dopaminergic cell death.
Q. Does paraquat have a direct cytotoxic -- cytotoxic effect on microglia?
A. I don't know that we've got evidence to that effect.
Q. Have you ever seen any science published anywhere in the world that paraquat is cytotoxic to microglia?
A. I can't recall that kind of information.
Q. And the next is -- we're going to go to Exhibit 149 now. If you could open that up.
(Exhibit 149 was identified for the record.)
BY MR. TILLERY:
Q. This is an email exchange. And lucky you, you're involved again. You're listed, aren't you?

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A. Yes, I am. I'm copied into it.
Q. This is an October 1st, 2014, email exchange, isn't it?
A. Yes.
Q. And it's -- the highlighted sentence is -- well, I don't think it's highlighted in yours.
A. No, it's not.
Q. Look at the very last of this. We have Andy Cook saying to Dan Minnema, "Any chance you can share information about the Smeyne data?"
And then you have a response from Charles Breckenridge saying, "I have an agreement with Smeyne that we do not decode the data until we resolve all discrepancies. Dan has not checked the Jackson mice data yet which we got on Monday."
And then it says, "Dan, go ahead and send the decoded Harlan data. We can discuss the results today."
A. Okay. Yeah. I can see that.
MR. NARESH: Is it frozen for anybody else?
THE WITNESS: Yeah. We lost -- we lost him, I think.
MR. NARESH: Let's go off the record.

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I'll send him a note.
THE VIDEOGRAPHER: Off the record. The time is 10:59. This ends Media Unit Number 8.
(Discussion off the record.)
THE VIDEOGRAPHER: We're going back on the record. The time is 11:01. This begins Media Unit Number 9.
BY MR. TILLERY:
Q. And if you would look at this email from Charles Breckenridge, October 1, 2014, 6:12 a.m., to Andy Cook, Dan Minnema, and to you re Smeyne data, it says, "Andy, I have an agreement with Smeyne. We do not decode the data until we resolve all discrepancies."
"Decode" means to unwind it, doesn't it?
A. It does, yes.
Q. Okay. And he says, "Dan, go ahead and send the decoded Harlan data."
And he says at the last line, he says, "In the Harlan mice, we have PQ effects on activated microglia but not TH neurons."
Do you see that?
A. I do.

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Q. Okay. And then there's a response. He -- the -- and he sends it, Dan Minnema, the top one, top email, which is sent a few hours later. And he sends it to Nick Sturgess, to Cook, to you. And it says, "See attached decoded Harlan data. We'll start checking the JAX data today."
That means they unblinded the data, didn't they?
A. Whether that means they were unblinding it all as they were doing some of the discrepancy checking, I wouldn't be able to comment on that.
Q. Okay. But that's certainly -- decoding, it means it makes it available from the controls to the test subjects. That's what it means, doesn't it?
A. Right. For the Harlan -- for the Harlan data, that's right, yes.
Q. Okay. All right. Did -- you did -- did you report the paraquat effects on activated microglia in Harlan mice in the 2016 paper?
A. I would have to look again at the paper. I mean, I don't know whether that was the final interpretation here. That may have been a preliminary analysis. I would have to check that detail.

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Q. Okay. Let's -- what's the next exhibit? It's 150.

(Exhibit 150 was identified for the record.)

BY MR. TILLERY:

Q. I think the next will clear this up for you. And here, if you wouldn't look -- if you wouldn't mind, you can go through and look at this four-page -- I think it's four pages of emails. And if you'd just skim through them, you'll see the discussions. And this is referencing microglial counts and what to do with the findings of Dr. Yun Jiao in Dr. Smeyne's laboratory. And you're included in some of these as well.

Do you see?

A. Yes.

Q. All right. Do you remember this exchange?

A. Well, some of it. As you say, I wasn't involved in some of the detailed interchange at the beginning.

Q. But it --

MR. NARESH: And, Dr. Botham, if you need, you know -- take whatever time you need to --

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to read the email and --

THE WITNESS: Yeah. I'm -- I'm still looking through this.

BY MR. TILLERY:

Q. Right. I'm not trying to rush you, but it looks like you were copied on all of this.

Tell me when you're ready to accept questions, please.

A. Okay. I'll do my best, but this is quite a -- quite a complicated set of information.

Q. Right. And Dr. Jiao, who worked in Dr. Smeyne's lab at St. Jude's, gives the first microglial counts for the 2016 paper from this if you read the first emails, correct?

A. Right.

Q. And she's the one who found the paraquat effects on microglia that Dr. Breckenridge wrote about in the prior exhibit, correct?

A. So which -- where -- just point to me exactly where --

Q. If you read the -- if you -- if you read the very first email, which would be on page 5 -- I'm sorry -- page 4. That's the end of it. It starts on page 3. And it's Smeyne to -- Monday, October 20th,

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to Breckenridge and Dan Minnema, microglia counts.

Do you see that?

A. Yes.

Q. And then if you go to the third paragraph, it says, "Although I am confident of the numbers provided, counts between Yun and I," and she says, "Inter investigator are within 10 percent and counts between Yun and herself and me and myself, intrainvestigator, have the same plus or minus 10 percent, I can understand given the many iterations Yun has sent you there are -- there may be questions on the microglia numbers."

Do you see that?

A. Yeah, I do.

Q. Okay. All right. So he's saying that he's confident in Yun's microglia counts, isn't he?

A. Yes.

Q. But then he offers to do a recount, doesn't he?

And if you want to see that, go to the next page, which is page 4, second paragraph, and it says for the record, "I know that Syngenta has invested a great amount of time and funds for this project and want to make sure that you feel both are

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good investments and, thus, want to make sure that you are comfortable with any decision you make. In terms of time and effort, I know that you would like data sooner than later. But as you said, it is more important to have complete confidence in the data."

Do you see that?

A. I do.

MR. NARESH: Steve, sorry to interrupt. But I think we just lost Shaun, the videographer.

MR. TILLERY: Oh.

MR. NARESH: I saw him drop in the middle of the question. I don't know if we can go off the record.

THE REPORTER: Yeah. We'll just go off the --

MR. NARESH: Why don't we go off the record.

MR. TILLERY: Yeah. Okay.

(Discussion off the record.)

THE VIDEOGRAPHER: We're going back on the record. The time is 11:12. This is the beginning of Media Unit Number 10.

BY MR. TILLERY:

Q. Dr. Botham, we lost video there for a

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little bit. I think the transcript was continuing, but I think we lost some video. But I'll continue on.

Dr. Smeyne offered -- I was in the process of going through that in the record, and I will go back and repeat it -- on the fourth page of the chain of emails. And he says, "I know that Syngenta has invested a great amount of time and funds for this project and want to make sure that you feel both are good investments and, thus, want to make sure that you are comfortable with any decision you make. In terms of time and effort, I know you would like data sooner rather than later. But as you said, it's more important to have complete confidence in the data."

Do you see that?

A. I do.

Q. All right. So Dr. Smeyne -- Smeyne justified doing the recount despite being confident that Yun's numbers were accurate because he wanted Syngenta to feel good about their investment, correct?

MR. NARESH: Objection to --

THE WITNESS: I think another way -- I

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think another --

MR. NARESH: Objection on foundation.

Go ahead.

THE WITNESS: Yeah. Sorry.

I think another way of putting that is that we wanted to make sure that the findings were scientifically sound.

BY MR. TILLERY:

Q. Okay. "Break the codes" means that you'd be unblinded as to whether tissue was treatment or control. Would that be a correct statement?

A. Yes, that's correct.

Q. Okay. And that's not what was reported in the study, right?

A. What was not reported in the study?

Q. Was there any indication that the codes were broken in the study?

A. I'm not quite sure how we've reported that. I'm pretty sure the study referred to reading the material in a blinded fashion.

Q. Yes. It reports that it was read in a blinded fashion?

A. Yes.

Q. Okay. But it wasn't read in a blinded

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fashion, was it?

A. To what are you referring?

Q. I'm talking about the fact that the data that was sent back for review was -- was where the code was broken and the review -- the second review after Dr. Jiao's by Dr. Smeyne was done unblinded.

A. Okay. So you're referring to specifically what Dr. Smeyne is suggesting --

Q. Right.

A. -- doing here?

Q. That's right. Would that be a fair statement?

A. I -- I don't know. I mean, I don't know whether we -- at this point he was unblinded to treatment.

Q. But Dr. Jiao, Yun Jiao, was blinded when she performed her microglial counts as far as you know, right?

A. As far as we know, yes.

Q. Yes. And Dr. Smeyne proposed to recount a subset of the brains that were analyzed by Dr. Jiao to compare numbers from Yun Jiao's initial counts, right? That's the way you understand this?

A. Yes.

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Q. Okay. On page 1 of this exhibit is an email exchange from Dr. Breckenridge to Dr. Smeyne dated October 21, if you go to that. Okay?

A. Yes.

Q. Do you see that?

A. Uh-huh.

Q. October 21, 2014. In the first paragraph, he says, "It is unfortunate that we cannot reconstruct the microglial counts from the raw data for the reads done by Yun. The good news is that the slide remains the authoritative raw data."

Paragraph two says, "We are considering the options you described and will discuss them in our PQ team meeting tomorrow morning. It is likely we will opt for a reread of microglia using 2D method."

Do you see that?

A. I do see that, yes.

Q. Okay. That's the part that he's referring to.

Now, let's pull up -- what is the next one? Exhibit 151.

(Exhibit 151 was identified for the record.)

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BY MR. TILLERY:
Q. All right. And if you look at this exhibit, it's Syngenta PQ -- SYNG-PQ-02143684. Okay? And it's entitled "Mouse Studies at St. Jude's Hospital."
Do you see that?
"Dr. Richard Smeyne, Status Update, November 19th, 2014," right?
A. Yes, I see that.
Q. All right. Now, this is a presentation that Dr. Smeyne wrote to give Syngenta as an update on those mouse studies, isn't it?
A. Yes, that's -- that's correct.
Q. Were you present at this or at least participating?
A. I'm pretty sure I was.
Q. Yes. And this -- if you'd go to the slide which appears on page 12. Tell me when you're there.
A. Okay. So number of microglia. Is that the slide?
Q. Right. And it says, "Assessment performed by YJ," Yun Jiao, right?
A. Yes.

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Q. And then you see it's got dark marked "Active Microglia," second is "Resting Microglia," "Total Microglia." And then it has an indication on them for significance. And statistical significance is noted with an asterisk.
Do you see that?
A. Yes.
Q. All right. Now, the very next slide is a validation study. "Redetermination of the number of microglia in the substantia nigra of the Harlan C57 mice."
Do you see that?
A. I do.
Q. And it says, "To confirm/validate the assessment of the number of microglia in the substantia nigra, Dr. Richard Smeyne reread the stain slides of Harlan C57 mice."
A. Yes. It does say that.
Q. All right. The next slide, number 14. If you'd look at that.
A. Okay. Go ahead.
Q. This shows the assessment of microglia on the Harlan mice that Dr. Smeyne did, right?
A. It does.

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Q. And it says, "Performed -- assessment perform by RS."
That's Richard Smeyne, right?
A. Yes.
Q. And Smeyne found that paraquat-treated mice activated microglia.
Do you see that?
A. Yes.
Q. The results were statistically significant as noted by the asterisk, correct?
A. Yes. Yes. Okay.
Q. But that's not what you reported in your 2016 paper. You didn't report this, did you?
A. Well, I would need to really understand what the status of this work was at the time compared to how we eventually or more accurately Professor Smeyne eventually interpreted these findings. So we're looking at a point in time on 14 --
Q. Well, I'll show you. If we look at the next slide and you look at this, this is the -- the next slide is 15 of 16. And it's entitled "Harlan C57 Mice, Number of Active Microglia Comparison of Richard Smeyne and Yun Jiao."

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Do you see that?
A. Yes.
Q. And -- and are you able to look at this and tell how he has reached a comparison?
Dr. Smeyne's initials are RS for Richard Smeyne, right?
A. Yes.
Q. And Yun Jiao's are YJ, right?
A. Right.
Q. And if you look up in the upper right-hand portion of this, you'll see the R-squared value?
A. Yes.
Q. Okay. And it represents the estimate of how similar Dr. Smeyne's counting was compared to Dr. Jiao's.
Do you see that?
A. Okay. Yes.
Q. Okay. So here the R-squared value is .895. Tells us that Smeyne's counts are 90 percent similar to Dr. Jiao's.
A. That was --
Q. That's exactly what he predicted.
A. That was --

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Q. That's within 10 percent.

The regression is for the pool data of all animals. That would be in controls, MPTP, and PQ treated together, right? Right?

A. Yes.

Q. Okay. Now, to do the statistics, you used, as in most of these studies, a 95 percent confidence interval, correct?

A. Right.

Q. And so anything less than a .05 is statistically significant, correct?

A. That's correct.

Q. Using both the one-tailed and a two-tailed t-test, Dr. Jiao's counts were statistically significant, weren't they?

A. That's what was indicated on the previous slide, yes.

Q. Okay. They were less than .05, right?

A. Uh-huh.

Q. Dr. Smeyne's microglial counts were statistically significant using a one-tail t-test, right?

A. Right. You're now getting down to a level of detail which I --

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Q. Well, just look at -- just look --

(Reporter clarification.)

MR. NARESH: You're interrupting.

BY MR. TILLERY:

Q. Okay. Look at the --

(Reporter clarification.)

BY MR. TILLERY:

Q. Go ahead, Dr. Botham. Finish.

A. I can't immediately confirm what you've said around about the one-sided statistics.

Q. Yeah. That's what I'm pointing you to. Okay? That's what I was trying to help point.

If you go to PQ under YJ column and RS, do you see that in the middle of the page at the bottom?

A. Yes.

Q. All right. And it says -- it shows one-tailed test, YJ, .0124 clearly within the -- the statistically significant range, right?

A. Okay. I've got it now, yes.

Q. And the two-tailed test, she's clearly, again, strongly within that range.

And then you go to RS, one-tailed test, .033. Again, statistically significant.

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And then the two-tailed test, he's just barely over at .06, where you said earlier an hour or so ago that that's what you look strongly at, correct?

A. Right. Yes. You can say -- you might say that that was a trend towards significance. That's what I said earlier.

Q. Right. Okay. So Dr. Smeyne's microglial counts were statistically significant using the one-tailed t-test, weren't they?

A. That's correct, yes.

Q. Using the two-tailed t-test, his were just above the .05 statistical significance level at .06, correct?

A. Yes.

Q. But in the 2016 study report, you chose to report only Dr. Smeyne's microglial counts, didn't you?

A. I would need to check that; so -- but I will take your word for now.

Q. Okay. You never disclosed Dr. Jiao's microglial counts despite having confidence in her counts, correct?

A. Well, this would have been a judgment

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of Dr. -- Professor Smeyne. So he was entirely accountable and, indeed, accepted the responsibility for the -- what were the definitive data.

Q. Okay. So -- because if you'd have reported that paraquat caused activated microglia, that would have been a negative effect, wouldn't it, sir?

A. Yes. If -- and particularly from the two -- two-tailed test, yes.

Q. It would have also been inconsistent with your findings that paraquat did not cause a loss of TH neurons in the substantia nigra pars compacta.

Would you agree with that?

A. Well, it would have suggested that the microglia had been activated in response to something, yes.

Q. The one-tailed test, you think, is the appropriate test or the two-tailed test?

A. I believe it's actually more of the two-tailed test. But, I mean, this is now memory from when we were discussing this. So, again, I would need to check that.

Q. And the -- the two-tailed test is fully dependent upon paraquat being cytotoxic with respect

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to glial cells.
Do you believe that?
A. I mean, now we're getting down to – to a level of detail where I really would need to – to check the – the information and the interpretation of this study.
Q. Well, beyond this, can you tell me this: Have you ever seen anything in the scientific literature that paraquat kills microglia directly?
A. I'm – I -- I'm not aware of anything as we sit here.
Q. So –
A. But I wouldn't rule it out.
Q. But if it – if it doesn't kill microglia directly, then the test would be a one-tailed test, right? One-sided?
A. Yes. Because it would be due to the microglia responding to dopaminergic neuron – neuron cell loss, that's correct.
Q. And that test with both your counts – well, both of their counts and Yun's was statistically significant? Both Smeyne's and Yun's on the one-tailed test was statistically significant, correct?

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A. Correct.
Q. Now, have you seen as a -- before we wrap up for the day, one final point.
Have you seen Dr. Smeyne's explanation of this?
A. I don't recall whether I have.
Q. Okay. Let's again look at number 1 -- Exhibit 152.
Here's 153. And 153 is the transcript of this clip. I want to show you this clip, and then I want to ask you a question or two. And that will be it for the day. Okay?
(Exhibits 152-153 were identified for the record.)
THE WITNESS: Okay. So I'll start playing the clip.
BY MR. TILLERY:
Q. Why don't you start playing yours, please.
MR. NARESH: Steve, while he's watching that, would you mind reading the transcript cite into the record?
Steve? Mr. Tillery?
MR. TILLERY: I'm sorry?

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MR. NARESH: Do you mind reading the transcript cite into the record while Mr. Botham is reading it.
MR. TILLERY: Yeah. It's -- I'm sorry about that. It's -- it's page 276, line 4, through page 280, line 3.
MR. NARESH: Thank you.
THE WITNESS: Okay. I've listened to that.
MR. NARESH: Steve?
THE WITNESS: I've listened to that. So ready when you are, Steve.
BY MR. TILLERY:
Q. All right. Sorry. I was engrossed in the – watching the film.
MR. NARESH: And I'll just object to the record on rule of completeness, similar to last time. I believe that the clip should include 280, line 4, through 282, line 1.
BY MR. TILLERY:
Q. So I would ask you the same question I asked Dr. Smeyne, Dr. Botham. And that is if you'd considered Dr. Yun Jiao's microglial counts, the results of the study would have been different,

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wouldn't they?
MR. NARESH: Objection. Foundation.
THE WITNESS: Well, if -- if, indeed, Dr. Yun's counts were based on a complete assessment of their quality by Dr. Smeyne, yes. I mean, we -- or Professor Smeyne. We were reliant on him doing that.
BY MR. TILLERY:
Q. All right. But I – I don't mean to – I'm just trying to get to the – to the bottom line.
The – had she been reported – the person who was blinded, the person who did the analysis blinded went through and did the microglial analysis, had you looked at her results in the one-tail or two-tail and reported those results, and she did not just a sampling, she did the entire analysis, if you'd considered her counts and published those and relied upon them, the results of the study would have been different, wouldn't they?
MR. NARESH: Objection. Foundation.
THE WITNESS: Well, they would if those were robust. I cannot imagine that Professor Smeyne would have been prepared to put into a publication data which she was not satisfied were robust.

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BY MR. TILLERY:
Q. Well, but --
A. Why would he do that?
Q. But he got statistical -- he got statistical significance on the one-tail himself, didn't he?
A. Well, that can be --
MR. NARESH: Objection.
THE WITNESS: Well, what you showed me in that correlation graph suggested that was the case, yes.
I can't explain that. I mean, I'm even one step further away from the detail than Professor Smeyne was.
BY MR. TILLERY:
Q. Let me ask you this: Do you have any way of disputing what Dr. Smeyne said in his sworn testimony that you just watched on video?
A. Well, clearly not, no.
Q. Do you -- from your knowledge and participation in that study and your recollection of the events of that occurrence, do you have any recollection today that's any different than what you just saw in the sworn testimony?

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A. Well, I don't know that I ever was a party to the kind of conversation about those data that we -- you were just having on that video with Professor Smeyne.
Q. All right. So let's go back now for the record and -- and take a look at this. This is exhibit -- so the video was an exhibit which will be attached or sent to the court reporter as 152, Plaintiffs' 152.
And if you would now look at 153 for me and verify that those portions -- and I think it's just for your reference, Dr. Botham. It would start on page 276, line 4, and continue through page 280, line 3. If you would look at that and confirm that that corresponds with what you watched.
A. Okay. That looks to be a transcription of that, yes.
Q. All right. You don't see any differences? I want to just confirm it as a foundation for the record. Okay?
MR. TILLERY: So at this point, Ragan, if you would stay on after we go off the record, but stay on where I can talk to you. But we'll suspend until 5:00 o'clock tomorrow morning in central time.

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Okay?
MR. NARESH: Okay. And just for the record, my rule of completeness objection is for both of the final two exhibits, not just the video but the transcript as well. But that's fine. 5:00 o'clock central tomorrow, 11:00 a.m. UK time tomorrow sounds fine. And I'll stay on.
MR. TILLERY: Okay.
THE REPORTER: Same original or same standing orders?
MR. TILLERY: Yes. Same for us.
MR. ORLET: Same thing.
MR. NARESH: Same.
(Discussion off the record.)
THE VIDEOGRAPHER: This concludes the video-recorded deposition of Philip Botham, Volume 6. We're going off the record at 11:39.
(Whereupon, signature was not waived and the witness was excused at 11:39 a.m.)
--oOo--

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CERTIFICATE OF REPORTER
I, RENEE COMBS QUINBY, a Registered Diplomate Reporter, Certified Realtime Reporter, Certified Court Reporter (MO), Certified Court Reporter (IL), and Notary Public within and for the State of Missouri, do hereby certify that the witness whose testimony appears in the foregoing deposition was duly sworn by me to testify to the truth and nothing but the truth; that the testimony of said witness was taken by stenographic means by me to the best of my ability and thereafter reduced to print under my direction.
I further certify that I am neither attorney nor counsel nor related nor employed by any of the parties to the action in which this deposition was taken; further, that I am not a relative or employee of any attorney or counsel employed by the parties hereto or financially interested in this action.
My Commission expires April 9, 2021.

Renee Combs Quinby, RDR, CRR, CCR (MO) #1291, CSR (IL) #084-004867

Alaris Litigation Services
711 North Eleventh Street
St. Louis, Missouri 63101
Phone (800)280-3376
Fax (314)644-1334

January 14, 2021
Ragan Naresh, Esq. (via videoconference)
Kirkland & Ellis, LLP
1301 Pennsylvania Avenue, N.W.
Washington, D.C. 20004

Re: DIANA HOFFMANN, individually and as Independent Administrator of the Estate of THOMAS R. HOFFMANN, Deceased, et al. vs. SYNGENTA CROP PROTECTION, LLC, et al.
Dear Mr. Naresh:
Please find enclosed your copy of the deposition of PHILIP BOTHAM, Volume 6, taken on January 5, 2021 in the above-referenced case. Also enclosed is the original signature page and errata sheets.

Please have the witness read your copy of the transcript, indicate any changes and/or corrections desired on the errata sheets, and sign the signature page before a notary public.
Please return the errata sheets and notarized signature page to Alaris Litigation Services, 711 North 11th Street, St. Louis, MO 63101 for filing prior to trial date.

Thank you for your attention to this matter.

Sincerely,

Renee Combs Quinby, RDR, CRR, CCR (MO), (IL) #084-004867
Enclosures
CC: All counsel

I, PHILIP BOTHAM, do hereby certify:

That I have read the foregoing deposition; That I have made such changes in form and/or substance to the within deposition as might be necessary to render the same true and correct;

That having made such changes thereon, I hereby subscribe my name to the deposition.

I declare under penalty of perjury that the foregoing is true and correct.

Executed the _____ day of _____, 20___, at _____.

_____.
Notary Public

My Commission Expires: _____
Signature: _____
PHILIP BOTHAM

Errata Sheet
Witness: PHILIP BOTHAM
In Re: DIANA HOFFMANN, individually and as Independent Administrator of the Estate of THOMAS R. HOFFMANN, Deceased, et al. vs. SYNGENTA CROP PROTECTION, LLC, et al.

Upon reading the deposition and before subscribing thereto, the deponent indicated the following changes should be made:

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Reporter: Renee Combs Quinby

EXHIBIT 16

FILED UNDER SEAL

IN THE CIRCUIT COURT
TWENTIETH JUDICIAL CIRCUIT
ST. CLAIR COUNTY, ILLINOIS
--o0o--

DIANA HOFFMANN, individually and as Independent Administrator) of the Estate of THOMAS R. HOFFMANN, Deceased, et al.,

Plaintiffs,

vs.) No. 17-L-517

SYNGENTA CROP PROTECTION, LLC, et al.,

Defendants.

VIDEO-RECORDED VIDEOCONFERENCE
DEPOSITION OF
PHILIP BOTHAM, Ph.D.
Volume 7 (pages 1684-1827)

January 6, 2021

(Beginning at 5:08 a.m.)

INDEX

(The original exhibits were provided to the court reporter electronically to be attached to the original and copies of the transcript.)

IN THE CIRCUIT COURT
TWENTIETH JUDICIAL CIRCUIT
ST. CLAIR COUNTY, ILLINOIS
--o0o--

DIANA HOFFMANN, individually and as Independent Administrator) of the Estate of THOMAS R. HOFFMANN, Deceased, et al.,

Plaintiffs,

vs.) No. 17-L-517

SYNGENTA CROP PROTECTION, LLC, et al.,

Defendants.

--oOo--

VIDEO-RECORDED VIDEOCONFERENCE DEPOSITION OF PHILIP BOTHAM, Ph.D., VOLUME 7, produced, sworn, and examined on Wednesday, January 6, 2021, taken on behalf of the Plaintiffs, with the witness appearing from Jealott's Hill, England, before RENEE COMBS QUINBY, a Certified Court Reporter (MO) #1291, Certified Shorthand Reporter (IL) #084-004867, Certified Shorthand Reporter (CA) #11867, Registered Diplomate Reporter, and a Certified Realtime Reporter.

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--oOo--

IT IS HEREBY STIPULATED AND AGREED by and between counsel for the Plaintiffs and counsel for the Defendants that this deposition may be taken in machine shorthand by RENEE COMBS QUINBY, a Certified Court Reporter and Notary Public, and afterwards transcribed into typewriting and the signature not waived by agreement of counsel and consent of the witness.

--oOo--

PROCEEDINGS 5:08 a.m.

THE VIDEOGRAPHER: We're on the record. The date is January 6th, 2021, and the time is 5:08 a.m. This is Volume 7 – I'm sorry. This is Volume 7 of Philip Botham. And we're on the record.

PHILIP BOTHAM, Ph.D.,
of lawful age, having been first duly sworn to testify to the truth, the whole truth, and nothing but the truth in the case aforesaid, deposes and says in reply to oral interrogatories propounded as follows, to-wit:

--o0o--

EXAMINATION

BY MR. TILLERY:

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Q. Okay. Dr. Botham, you understand this is a continuation of the deposition we started back in February, right?

A. Yes. I do understand that.

Q. And rules that we talked about are all the same. Everything is the same. Okay?

A. Okay.

Q. Are you familiar with the study that's referred to as the Howard study?

A. I think you may need to remind me about that.

Q. Okay. Sure. Actually, why don't I put up Plaintiffs' Deposition Exhibit 154 and give you a chance to see if you can take a look at it and familiarize yourself with it and see if you can answer questions about this.

THE VIDEOGRAPHER: And, excuse me, Counsel. Before we do, I missed a step. We're going off the record. The time is 5:09.

(Discussion off the record.)

THE VIDEOGRAPHER: We're going back on the record. The time is 5:09. This begins Volume Number 2 -- I mean, Media Unit Number 2.

BY MR. TILLERY:

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Q. Dr. Botham, I have placed in eDepoze a document which has been numbered 154 -- it's a plaintiffs' exhibit -- and wondering if you have any familiarity with that document?

(Exhibit 154 was identified for the record.)

THE WITNESS: Yes. Thank you. I've now been into eDepoze, and I'm just looking at the front page of that document.

So I -- I do remember seeing this in the past, but I -- it's not a paper that I studied in great detail.

BY MR. TILLERY:

Q. All right. This was done by -- let's see. Do you recognize any of these people? Howard? Sabapathy? Anne Whitehead?

A. Yeah. The only person that I knew was Dr. Sabapathy.

Q. Sabapathy. Okay. And these are people at ICI, right?

A. Yes, that's correct.

Q. Okay. So just for the court and jury's purposes, ICI is a predecessor corporation to Syngenta, correct?

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A. It is.

Q. So if you would look at this, I just have a few questions about it. And please take your time as you go through it if you need to spend time looking at it, but I wanted to ask you just a few questions.

This was a study performed in 1981 by ICI, correct?

A. Yes.

Q. All right. Do you happen to have any notion of the significance of that study one way or another with respect to the issues as you understand them to be in this case?

MR. NARESH: Objection. Vague.

THE WITNESS: Well, I -- as I say, I've not ever read this paper in great detail; so I'm not able to answer that question right now.

BY MR. TILLERY:

Q. Okay. Chevron was still the sole distributor of paraquat in the United States in 1981, weren't they?

A. Those dates, I don't carry in my head. I'll take your word for that.

Q. Okay. All I'm asking is, is Syngenta, to your knowledge, relying on this study as evidence that occupational exposure to paraquat does not cause long-term chronic health effects?

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A. I think it would be very doubtful to say that it was reliant on this study. This is perhaps part of the weight of evidence, but I wouldn't go any further than that.

Q. Okay. And I just wanted to go over it. To the extent that it is part of the weight of the evidence, I think we have to ask a few questions about the study.

Do you know if this study was ever submitted to any regulatory -- regulatory authority in the world in support of the continued registration of paraquat?

A. I'm afraid I can't answer that question. I don't know.

Q. All right. Let's go to page 1 if we can. It's an eight-page study. And if you look in the lower right-hand column beginning with the word "concern." Do you see that sentence?

A. Just bear with me. So, yes, the last paragraph on page 1 beginning "concern," yes, I can see that.

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Q. Would you just read those seven sentences, and then I'll ask you a question about it. You don't need to read it into the record. Just read it to yourself.

A. Okay. Yep. I've read that.

Q. Okay. So ICI did this study because they were concerned that paraquat may represent an important health hazard to paraquat spray mist, right?

A. That's what this indicates, certainly, yes.

Q. So would it be true that by 1981, the date that this study was undertaken -- we're dealing with about 15 years after the registration of paraquat in the United States -- ICI and Chevron had still not determined the potential long-term occupational health hazard of spraying paraquat?

MR. NARESH: Objection to scope. Foundation.

THE WITNESS: Well, I think I wouldn't put it quite that way. I would imagine that this was done to -- as we said earlier, to try to add to the existing weight of evidence because, obviously, as we discussed yesterday, there have been some

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long-term toxicity studies.
BY MR. TILLERY:
Q. Right. Are you familiar with any study of this type, "this" being the document marked for our purposes as 154 today. Are you familiar with any such study having ever been undertaken before 1981?
A. I can't bring to mind any particular study at this point. That's not to say there wasn't one that I may not know about, but I can't immediately indicate another one.
Q. All right. So if we can, let's go to the abstract. You have it in front of you there.
If you glance over it, I just want to ask a question, make sure you can confirm what I'm saying.
A. Okay. I've read the abstract.
Q. So the study compared 27 spray men who sprayed paraquat – paraquat and other herbicides with two control groups, right?
A. That's right.
Q. Okay. And if you go to page 2 now, there's a section that describes the control groups. One control group was a group of general manual

Page 1697

workers, some of whom may occasionally work in areas sprayed with paraquat.
Can you look at that? Do you see that?
A. Yes.
Q. All right. And the general manual workers control group included rubber tappers and harvesters. That's what they say?
A. Yes.
Q. Some members of the general workers control group had seen minimal exposure to paraquat as a result of working in areas of the plantations in which spraying had been recently completed.
That's what -- I took that straight out of the report. If you can confirm that?
A. Yes.
Q. The general workers control group, if you would look at it down at the bottom of page 2, I think you can confirm had 24 members in it?
A. Yes, that's right. In Table 1.
Q. In Table 1, correct. The other control group was a group of latex processing factory workers who were not exposed to paraquat at work at all. Okay? Do you see that?
A. Right. Yes.

Page 1698

Q. And they had 23 total members in it. Do you see that?
A. Yes, yes.
Q. Participants of the study were all male? If you look on page 2, you can confirm that.
A. Yes, I can confirm that.
Q. All right. The spray men averaged three to five years of spraying, right?
A. Yes, that's correct.
Q. Okay. And that is what the study authors considered to be a long-term spraying under their definitions, correct?
A. Yes. That's what they were defining here.
Q. Paraquat exposure was determined through an interview with the spray men; is that right?
A. Yes. The spraying history was obtained at an interview, yes. I can see that.
Q. Okay. And the spray men were defined as those who had sprayed a minimum of 1,000 hours?
A. Right.
Q. Okay. But since the – and there's – on column 2, last paragraph, I think the last full

Page 1699

paragraph, it indicates but since the spray men sprayed paraquat and other herbicides, they didn't know exactly how much paraquat was sprayed in those 1,000 hours. If you could confirm that as well?
A. Okay. Yep.
Q. Now, if we go to page – excuse me. Strike that.
Do you know if spray records for each spray man were maintained at that state by looking at this study?
A. I can't answer that question without looking at it in more detail. It does -- it does indicate that there were spraying records. I can see that on page 2 but --
Q. From what I can tell, and if you can take the time if you need to, to confirm. I know that you haven't looked at this study, I'm sure, for some time.
But I just wanted to – to ask you these questions because what I was trying to determine is whether spray records were kept at the plantation for each man and how they were kept, who maintained them. These questions – I would want to know if you can discern from the study how you can

Page 1700

answer those?
A. Well, what I'm reading on page 2 is that there was a spraying record of each man. So that's – those records did exist for each individual.
Q. But it doesn't – it doesn't say what the – it doesn't say if it was broken down by herbicide, does it?
A. I can't see that level of detail, no.
Q. Right. So they have sprayers that sprayed a thousand hours, but you don't know how many hours of those represented spraying of paraquat from what I can tell in this study.
A. I agree. I can't see that level of detail here.
Q. Okay. Other than having been selected for spraying history of paraquat and other herbicides for three years, the study doesn't tell us anything about how these men were chosen to participate in the study, does it?
A. No. It -- it just says where they were – they were – they were from.
Q. Right. They indicate some were Chinese, some were Indian, some were from Malaysia,

Page 1701

right?
A. Yes.
Q. If you'd look at that Table 1, age and racial structure of the working groups – that's SYNG-PQ-22611736 for counsel on the call. If you'd look at that.
A. Yes. I'm looking at Table 1.
Q. Okay. All right. So seven of the participants were under the age of 25, right?
A. Seven of the spray men, yes.
Q. And nine were between 25 and 34?
A. Yes.
Q. So 16 out of 27 were 34 or younger?
A. In the spray man group, that's correct.
Q. In the – in the so-called test group, not the control group?
A. Yes.
Q. Okay. So more than half the men were 34 and younger, right?
A. Yes.
Q. And if you could confirm this for me as well, those who participated had to be healthy in order to work? In other words, they were actually working? These people were actually spraying?

Page 1702

A. Yes, that's correct.
Q. And if he could not work because of illness, he would not have participated in the study. Is that your assumption from reading this?
A. Well, that would be an assumption. I don't think it spells that out.
Q. In other words, if any of the sprayers were sick or disabled using paraquat and couldn't work, they would be excluded from participation in the study at least as far as I see it. I would like your confirmation of that.
A. Well, I think this paper is silent on whether they actually excluded anybody because of illness. So I don't know -- I think maybe what you're saying is speculative.
Q. Right. Can you look, though, and see if, in fact, they were using from the abstract of the study and from the front page, if you just read that, that they were actually using people who were actively working?
A. Yeah. Sure. That is true.
Q. So they were actually working. So your assumption would be somebody who is afflicted with Parkinson's disease or neurological disorders would

Page 1703

find it quite difficult to be a spray man in a Malaysian plantation of this chemical. Would you agree?
A. Yes. That would be what you would normally expect.
Q. Okay. So do you know what a selection bias is for epidemiology?
A. I do.
Q. What does that mean?
A. It means that you're not necessarily selecting a full cross section of a population, for example.
Q. Like, if you wanted to know, for example, the impact of a chemical on an array of mice by age and you got mice who normally live between two and three years and you got all of your mice at age 15 weeks and you were trying to assess the impact across an age spectrum of the implications of paraquat exposure, you wouldn't be able to extrapolate about how that could impact mice that are 20 weeks or 50 weeks old, could you?
A. Well, I think we need to be careful not to conflate two different issues here. There's selection bias in epidemiology studies, and there's

Page 1704

the selection of appropriate age ranges in animal studies, and the considerations are different for those two.

So the analogy of animal studies is not -- is not one that is 100 percent relevant to epidemiology.

Q. Well, let's come back to that, then. Okay? Let's come back to that study.

Let's go back to epidemiology. If you're looking at the impact across a population, you'd want representative numbers in your test group from different age categories, particularly when you know the typical way age-wise when a disease like Parkinson's disease presents, correct?

A. In a study like this, you would -- I -- in a practical sense, you would only be able to look at the population that was working in the field. And it is possible that that working population here were largely of a younger age. They may not have been older workers who were engaged in this activity.

Q. But to the extent that you know, as you said in the deposition yesterday, that the typical average age of onset of Parkinson's disease is in

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the mid-'60s, if you're looking at a population like this of a group of men where 16 out of 27 of the study participants were 34 years or younger, it's difficult to draw any parallels or conclusions based upon a -- a -- the presentation of symptoms for Parkinson's disease, isn't it?

A. Well, the intention of the study, the purpose of the study was not to focus on Parkinson's disease. This was to look at long-term health effects, not -- not a specific neurotoxicology epidemiology study.

Q. And how did we -- in this study, how did -- how did Syngenta, ICI, define "long-term health effects"?

A. Well, again, I'd have to read the paper in full to see if there was some commentary on that.

Q. Okay. Do you know what they were testing? What they were observing?

A. Well, the paper was looking at various functions of the -- of the people that were monitored. Respiratory function, liver function, for example.

Q. And skin?

A. Yes. And renal function too.

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Q. Renal function. The study measured -- if you go to page 3 of the study, you'll see that it -- there's a reference to the study having measured respiratory function, liver function, renal function, and red and white blood cells.

Do you see that?

A. Yes. That's correct, yes.

Q. So there was no effort to tell us anything about the central nervous system effects of long-term spraying of paraquat from this study, was there?

A. No. This study was focusing on the -- on the known potential toxicity that paraquat has, so particularly on the lung and the kidney.

Q. Right. It wasn't designed and did not inform us about anything concerning neurotoxicity effects of long-term spraying of paraquat. Would you agree with that statement?

A. This study can't -- doesn't inform on that, no, directly. That's -- that is true.

Q. So this study would not tell us anything about long-term exposure to paraquat potentially causing Parkinson's disease or not, would it?

Page 1707

A. No. That was not the intention of the study.

Q. Right. If you go back to that Table 1, the range -- age range of the men was less than 25 to over 45, right?

A. Yes.

Q. There was seven spray men under 25?

A. Yes.

Q. Six spray men over the age of 45?

A. Yes.

Q. Okay. Was there ever any follow-up of these workers some years later to your knowledge?

A. I'm not able to answer that question. I really don't know.

Q. Okay. The study that you said is out for publication yesterday involving pharmacokinetics in primates -- is that a study you referred to as the Stevens study?

A. Yes, that's correct.

Q. Is Stevens the principal investigator in that study?

A. He was the principal investigator for Syngenta, yes.

Q. Right. And who else was involved in

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that study?
A. Quite a number of people, which I could list if you gave me a moment.
Q. Go ahead. Take your time, please.
A. Okay. Just bringing it up now.
So the authors are from Syngenta, Dr. Stevens; Dr. Travis, who of course is no longer with Syngenta but he was when the work was done; Dr. Hinderliter, similarly, was from – with Syngenta but is now not with the company.
Q. What do these people – if you don't mind as you're telling us about these people, could you please inform us as to what they're doing now?
A. Yes, of course. Right. So I'll start again.
So Dr. Stevens is still with Syngenta here at Jealott's Hill.
Dr. Travis was at Jealott's Hill. He's now working for Regulatory Science Associates. That's a consultancy company in the United Kingdom.
Dr. Hinderliter was working at the Syngenta Greensboro office and is now working for Alexion Pharmaceuticals in Boston, Massachusetts.
Myself, obviously, still working for

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Syngenta here at Jealott's Hill.
Andy Cook also Syngenta at Jealott's Hill, still working here.
Dan Minnema, Syngenta in the Greensboro office, still working for Syngenta.
Jeff Wolf, Syngenta, Greensboro -- sorry -- Syngenta, North Carolina, Research Triangle Park and still working for the company.
And then in addition, there were two scientists from the Ramboll, environment and health consulting company in Raleigh, North Carolina -- Jerry Campbell and Harvey Clewell.
Q. What was their roles?
A. They were -- they are experts in what we call PBPK modeling, so the mathematics that go into estimating the kinetics and distribution of chemicals.
Q. When was it submitted for publication? The so-called Stevens study?
A. So that was submitted in September of 2020.
Q. Okay. So we referred to it as a 2020 study?
A. No. Because it's not yet been finally

Page 1710

accepted for publication. It's been accepted pending some modifications. That occurred in November.
We are still working on that response. It will – that will be completed by the end of January. So we anticipate publication in a few months after that in 2021.
Q. And the modifications that you're referring to are what?
A. The normal kind of comments that you get from – from reviewers. There are – there were three reviewers who commented on this, and there were some comments that were very detailed. Again, exactly what you would normally expect from reviewers.
One or two comments which required us to add some additional wording in about the behavior of paraquat in the body, but nothing substantive, which is why the editor is happy to accept these papers subject to those modifications.
Q. What is the title of this paper?
A. "Paraquat Pharmacokinetics in Primates and Extrapolation to Humans."
Q. And let's pull this up. Number – next

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number would be, yeah, 155.
(Exhibit 155 was identified for the record.)
BY MR. TILLERY:
Q. So our next exhibit is 155. If you could take a look at this and tell us if Exhibit 155 is the so-called Stevens paraquat pharmacokinetic study you just referenced.
A. Yes, that's the one.
Q. Okay. Absent the changes that you're currently writing?
A. Well, yes, I'm not sure what version this is.
Q. This would have been – I can't – your counsel is on the call. He can tell us more specifically which version. It would have been produced sometime last year; so I don't know when last year.
Has there been any other laboratory work done since June of 2020?
A. Not lab work. There is a sister paper to this which was based on lab work and modeling work done at a similar time, which is a PBPK kinetics paper in – in rodents. And that's also

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been submitted to the same journal with similar authorship. But to answer your question directly, no lab work has been done since June.

Q. How many primate test subjects were used?

A. I'd need to do a count for that. Do you want me to give you an accurate number now or --

Q. Yeah, or your best estimate.

A. Right. Well, in Phase 1 and 2, there were six monkeys. In Phase 3, 4 -- so around about ten. I think that's -- that's the total number.

Q. Okay. And where was the study performed?

A. So the animals were housed and the -- the -- the dosing was conducted at Battelle, which is a contract research organization in Columbus, Ohio.

Q. Did they do all of the analyses while there? Was the -- withdraw the question.

Was the paraquat administered there?

A. Yes, the paraquat was administered there.

Q. Okay. So what was the limit to the involvement of that laboratory? What did they do?

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A. Yeah. So they -- the administered the -- they housed the animals. They administered the radioactive paraquat. They took the samples, the blood samples.

And they did the analyses and -- and also conducted the -- the final stages of the -- of the study. So that included the -- the analysis of the amount of paraquat that was remaining in the -- in the subjects at the end of the study.

So they basically did all the -- nearly all the practical work.

Q. And who was the principal lab contact for the study?

A. I don't know that person's name to hand; so I can give you that at some other point.

Q. Is that person listed on the -- on the study as a participant?

A. They are not included as an author, and I can't remember exactly where we ended up in terms of naming people as contributors.

There were -- we asked a number of people who were involved in this whether they wished to be named, and some did and some didn't.

Q. Did the people who were at the lab wish to be named?

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A. That's -- I would need to double-check.

Q. Do you have your paper there with a list of authors?

A. I've got the paper here with a list of authors, yes.

Q. Tell me looking at those authors if any of them from the lab wished to join?

A. There were no people from the CRO listed as author of this paper.

Q. Okay. Now, radio-labeled paraquat was administered by intravenous infusion, right?

A. That's right.

Q. Radio-labeled paraquat was administered in two different doses. Is that also correct?

A. That's correct.

Q. So radio-labeled paraquat was given via intravenous infusion at .1 milligram per kilogram body weight and .01 milligram per kilogram body weight, right?

A. That's right.

Q. And then how long after that were the primates euthanized? Killed?

A. A number of different times after

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administration. This was quite a complex protocol; so -- but we were essentially measuring the behavior of paraquat in those animals over a 14-day period. But we -- some animals remained on study beyond that time period.

Q. After their primate -- strike that.

After the primates were euthanized -- strike that question as well.

There was no pathological analysis of any organ performed, correct?

A. That's correct because that was not the purpose of this study. This was a pharmacokinetic study.

Q. Right. I understand that. I'm just trying to get some background information before we get to that, Dr. Botham.

Was there any pathological analysis of any organ of these monkeys?

A. No.

Q. Okay. So after the monkeys were euthanized, their carcass was separated from their skin, correct?

A. Yeah. More accurately, their skin was separated from the carcass, yes.

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Q. Okay. The carcass was then put in a blender, right?
A. Yes.
Q. And the carcass included the brain?
A. Yes.
Q. Ten percent of the radio-labeled paraquat was found in the carcass, right?
A. Yes.
Q. Radio-labeled paraquat was detected in excreta as well, right?
A. Yes.
Q. And if you look at this to verify whether the statements that I'm making are correct, 82.9 percent of the paraquat was found in excreta according to your study, right?
A. Yes. Just double-checking that. I think that's right.
Yes. 82.9. That is correct.
Q. And who did that analysis to come up with that number?
A. Well, it was based on the analyses done by the contract laboratory, but all the calculations were checked and monitored by our – by the Syngenta scientists.

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Q. Okay. So this part of the study wasn't created by an independent laboratory. The information was sent to you, and then various people from Syngenta completed the information.
Would that be a fair assessment?
A. A slight misrepresentation. I mean, clearly, this -- this – the conduct – the whole – the conduct of the study and the analyses was in the hands of a -- an independent CRO. We were obviously doing the necessary data quality checks that would be expected.
Q. Okay. What I'm trying to figure out is the number 82.9 that we – a percent that was found in excreta was placed in the study and calculated by Syngenta scientists, right?
A. Yes. That -- that's -- that is true.
Q. Okay. So if we take the 82.9 percent that was found in the excreta and we have 10 percent that was determined to be in the blended carcass, that totals 92.9 percent, correct?
A. Yes.
Q. So there's 7.1 percent of the dose unaccounted for, right?
A. Yes.

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Q. Now, where did that -- strike that.
You don't know where that 7.1 percent is, do you?
A. This is one of the -- the issues with this – with any kind of pharmacokinetic study in the primates, let alone with -- with paraquat.
The -- if you look at the experience of particularly pharmaceutical companies who do these kind of studies more routinely, it's – it's very generally the situation that you don't ever get 100 percent accounted for, for technical reasons.
But in the case of paraquat, that's further complicated by the fact that paraquat binds to metal surfaces, plastic surfaces. So you do lose some of the paraquat in the -- in the analysis.
It's not necessarily true that that 7 percent is in the carcass. It may be on the equipment or on the cage sides and so on.
Q. But the truth is you don't really know where that 7.1 percent went, do you?
A. Well, we can't – we can't specifically account for where it is.
Q. I mean, you're taking this as an indictment of the process. I'm trying to just get

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straight answers.
7.1 percent of the paraquat is unaccounted for. Would you agree with that statement?
A. It's not possible to -- to specifically identify where it was.
Q. All right. That could have been in the carcass, couldn't it?
A. Not likely in the carcass because we actually measured what was in the carcass.
Q. Well, and you say "not likely." How did you measure it, Dr. Botham?
A. Well, we -- as you indicated, the total carcass and the skin separately were essentially blended in order to be able to take samples and to measure exactly how much paraquat was there. So actually one of the more robust figures is how much was in the carcass.
Q. The brain was not specifically analyzed for any paraquat dose, was it?
A. No.
Q. It was blended as part of the carcass in the blender, right?
A. Correct.

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Q. Excuse me. So this study cannot tell us what specific concentration existed in the brain of the monkeys, can it?

A. No. That was not the intention of the study.

Q. But would you agree with me that it cannot?

A. It cannot, no.

Q. And in this study, kidneys were not specifically analyzed for any paraquat dose, were they?

A. No. No specific tissue was -- was measured in that way.

Q. Right. So you couldn't tell us from this study the specific concentrations in the kidneys either, correct?

A. Not as directly measured. But the point about this study is that from the measurements that were made using the mathematical modeling, then it is possible to estimate the concentrations that were in these tissues, including the brain and the kidney.

Q. Yeah. I move to strike that as unresponsive.

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My question is from this study, you couldn't tell us directly the specific concentrations in either the brain or the kidneys, could you?

A. Well, I -- I'm afraid I have to repeat what I just said. The whole purpose of this study was not to directly measure, to use your words, by separately blending a kidney or -- or a brain or -- or a liver. And we calculated those using the model, the mathematical model. That was the whole purpose of this study.

Q. Well, let me rephrase it, then.

Did you ever take the kidneys or brain out of these test monkeys and specifically measure any radio-labeled paraquat in those organs?

A. No.

Q. Okay. So if I ask you to look at this study and tell me how much radio-labeled paraquat was found in the brains of the squirrel monkey from this study, you couldn't tell me, could you?

A. Yes, I could tell you. We could -- because we used our mathematical model. And if you look at the --

Q. That --

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A. -- the Table 8, that will give you --

MR. NARESH: Steve, Steve. Please, don't interrupt him.

BY MR. TILLERY:

Q. You keep answering a different question. I'm asking you from specific measurements, not through some model that you're using. I'm asking you. You have the animals right there in this laboratory when they were taken and euthanized after the dosing. There was nothing prohibiting Syngenta from actually removing the brains and measuring the level of radio-labeled paraquat in the brain of the monkeys, was there?

A. We are using here 21st century technology, which is increasingly going to be using things like mathematical models in order to do exactly what you're saying.

So we have estimated the amount of paraquat that was in those brains with our mathematical models, which we believe to be a very accurate representation of the -- of what we might have found had we done what you suggested.

Q. Yeah. I move to strike your answer as unresponsive. Let's go back to my question.

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After the animals had been dosed with radio-labeled paraquat and euthanized, there was nothing preventing Syngenta from removing the brains of the test animals and actually measuring the amount of radio-labeled paraquat in the brains of the animals.

Is that a fair statement?

A. Well, of course, we could have done that. We could have done that with any of the tissues.

Q. All right. And you could have done that with the kidneys had you wanted to, right?

A. Yes.

Q. And you could have done that with the lungs too, right?

A. Yes.

Q. And you could have then determined from an assessment of those specific organs how much radio-labeled paraquat was in those organs, right?

A. We could have done that, yes.

Q. Okay. There was nothing preventing you from doing that, right?

A. Other than that was not the purpose of the study. It was to try to use modern technology

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to do that.

Q. So instead of doing those direct measurements, you chose to model the concentrations -- correct? -- using a mathematical model?

A. That's right.

Q. Okay. So you used a model with your own built-in assumptions about where this paraquat was located, where it was found in the bodies of these monkeys, instead of choosing to actually take a total of 10 monkeys and doing an analysis on their organs, correct?

A. Because that was the purpose of the study to actually provide such a model. And that part of it was done by the Ramboll Institute, not by Syngenta.

Q. So without having specifically analyzed the lungs for any radio-labeled paraquat, you can't tell us what specific concentrations were in the lungs before the carcass of the monkey was put in the blender, can you? Other than by looking at your mathematical model that you calculated?

A. I think I also have to bring in this point that the -- the validation of the model also

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comes from the work that was done, for example, in the rodents, the second paper that I mentioned, where we actually have got more of that information to confirm, if you like, that the models that we're using are an accurate representation of what you would have found had you physically analyzed those -- those organs.

Q. I'm afraid I have to move to strike your answer as nonresponsive to my question, which is so without having specifically analyzed the lungs for any radio-labeled paraquat, you can't tell us what specific concentrations were in the lungs before the carcass of the monkey was put in the blender, correct?

A. I can tell you what the mathematical model told -- told us. And I can tell you that we believe that that is an accurate representation of the reality.

I agree, however, of course, that we did not directly measure that by separately analyzing each tissue.

Q. Okay. Did it occur to you to take, let's say, half of the monkeys and measure the organs -- the amount of radio-labeled material in

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the organs by doing a careful measurement of them and then blending the other monkeys in whatever way you wanted to do it and applying your model and see how your model -- mathematical model you created compares to actually measured amounts in these organs?

A. Well, there are two answers to that, I'm afraid. One is that we did what you've suggested through -- as I indicated in my previous answer, through reference to the model -- the very similar model that was used in rodents where we have such information. So that was the validation part.

The second thing is, and it's a very important part, we wanted to minimize the number of nonhuman primates that we used in this study.

To do what you're suggesting would have required us to do, for example, probably twice the number of animals in this study, and that we didn't feel was appropriate or ethical.

Q. So I move to strike your answer as nonresponsive. Let's go back to my question.

No one involved in this test protocol ever suggested to take half of the sacrificed euthanized monkeys and do actual measurements of the

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brain, do actual measurements of the lungs, actual measurements in the kidneys, and compare those to your mathematical formula or math -- creation of which was by Syngenta folks, and compare the results. Nobody suggested doing that, right?

A. Well, of course, that was always one option for us. But we determined that that was not necessary to do for the reasons I've indicated because we could use our rodent data and to -- to -- to come up with that figure. And -- and the animal ethical position was an extremely important one.

Q. But you had no data about paraquat concentrations in monkey organs from your own work or published literature, did you?

A. Not from our own work, no.

Q. Okay. What published literature were you relying on, then?

A. Well, we -- for example, because we've been talking about the brain and we also did look at published papers by the Bartlett Group, as is indicated in this paper, to essentially confirm what -- or to represent, I should say, on our paper what they found in terms of the distribution of paraquat to -- to organs like the brain.

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Q. In the preliminary copy of this as I remember reading it, Bartlett 2009 is the study you're referencing, right?

A. That's right. There are two Bartlett papers. That's one of them.

Q. Well, is that the Bartlett paper you relied on, or is there another one? Because you --

A. Yeah. When I did –

Q. -- the first –

A. The Bartlett – excuse me. Sorry. Do ask the question again.

Q. Yeah. The Bartlett 2009 is what you referenced in your – in your paper, right?

A. Yeah. There are – there's -- there's a Bartlett 2009, and there's a Bartlett 2011. We actually include both of them in the paper.

Q. So you reference both of those papers?

A. Yes, we do.

Q. Okay. So is that what your model is based on? Those two Bartlett studies?

A. No. The model isn't based on that. That -- that was used to particularly try to better understand whether the figures that we got from our model made sense in terms of, for example, the

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amount of paraquat that we were seeing or modeling to be in the brain.

Q. Well, you had no data about paraquat concentrations in monkey organs from your own work in Syngenta laboratories.

Would that be a fair statement for purposes of creating your model?

A. No. We did not – we've -- we've no Syngenta data in nonhuman primates, no.

Q. Okay. And then you reference two studies that you got, and you said you didn't get your model information from Bartlett 2009 or 2011, right?

A. It would not actually – the -- the papers that -- that helped us to validate, if you wish, the whole model, they were being used specifically to -- to make sure we -- that the amount of paraquat that we believe is in the brain made some sense.

Q. Right. Well, here's – look, I'm trying to take us through what you built your model on. It wasn't, according to you, from Syngenta's own research on paraquat concentrations in primate organs. We've covered that, correct?

Page 1730

A. Right.

Q. And it's not from the 2009 or 2011 Bartlett studies.

A. No.

Q. Correct?

A. Correct.

Q. Right? Is it – I'm sorry?

A. Correct.

Q. Okay. And so that leaves us the rodent models that you built your model on, right?

A. Correct.

Q. All right. Now, tell me which rodent study did you build this mathematical formula on that you relied upon to extrapolate conclusions about where this chemical was located in the bodies of the primates? Which study?

A. Well, there are a number of different studies. And we'd have to go into the – the second paper, the paraquat pharmacokinetics in the rat and the mouse, and actually also the dog. It wasn't just rodents. And -- and there are a number of -- of studies that are listed in there.

Q. Well –

A. It's not – it's not just a single

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study.

Q. All right. So let's go through all of them. Here's what I want just for the ladies and gentlemen of the jury, the judge, and you. Okay?

I want you to tell me what you built your mathematical model on. I want everybody here who is watching you or listening to you sometime down the road and looking at this study to be able to know what Syngenta scientists built that study on.

Now, let's go through them. Take as much time as you need, but you tell me every single study you relied upon and how you relied upon it to build that mathematical formula. Okay?

A. Yes. Certainly, I'm now looking at that second paper.

Q. And before you speak about the paper, for the record give us the citation to that paper, where it was published, who were the authors, and what the title of the document was.

A. Okay. So the – the title is "Paraquat Pharmacokinetics in Rats, Mouse, and Dog." The lead author for this one is – is Dr. Campbell, Jerry Campbell, from Ramboll.

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Also on the paper were his colleague Harvey Clewell from Ramboll, who I mentioned before, and also Mel Anderson, who formerly was with Ramboll and is now a retired consultant.

In addition, the -- some of the Syngenta authors that were mentioned previously were -- are on this paper: Myself, Andy Cook, Paul Hinderliter at Syngenta, Alex Stevens, and Kim Travis.

Q. And when was this study published?

A. This is in the same status as the nonhuman primate study. They -- essentially, they were submitted in parallel. So we're -- all the dates that I gave you for the nonhuman primate study apply to this one as well.

Q. To your knowledge, has this study been disclosed in discovery in this case?

A. I don't know whether it has or not.

Q. Okay. Now, tell me how that paper that you just referenced told you how to build the mathematical formula.

A. Right. Well, I'm not going to go into a lot of technical detail here because I don't even know what would be appropriate.

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But to answer the question which you asked about, you know, name all -- name the studies, in Table 1 of this paper that we're now looking at, there are -- there's a list of studies. And it's entitled, "Summary of preexisting paraquat kinetic studies used in this paper." And they're listed in alphabetical order of first author.

And -- and if you can look, there are 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13 -- 14 papers that were used. And some of them are Syngenta or predecessor papers. I can tell you precisely. One, 2, 3, 4, 5 -- 6 of those 14 are ICI's or Zeneca or Syngenta papers.

So they -- so to answer your question they are -- they are live animal studies. They are conducted in either the rat, the mouse, or the dog. They are kinetic studies because that's what's important where you actually measure how much paraquat is in the plasma, in the urine, in the -- and in different tissues including the brain.

And -- and it was -- that was the data set that was used to build the model to allow us to extrapolate to the levels we -- we -- that were in the nonhuman primate and -- and could be in human

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beings because that's -- that was the whole purpose of this to build mathematical models, to estimate the amount of paraquat that would get into different tissues in the human being.

Q. Did the Bartlett Group in the two studies you referenced measure paraquat concentration in monkey organs?

A. They -- I mean, Bartlett -- at least our focus on the Bartlett was them using PET imaging to -- to have a -- to give a visual representation of the distribution of paraquat in the brain.

Q. So they used, you said, a PET scan analysis?

A. Yeah. PET scanning, basically. Yes. So it showed the distribution of paraquat in the brains of rodents and in the brains of the animals that they looked at, and you can see photographs of those PET images.

Q. Right. What I'm trying to say is, to your knowledge, did the Bartlett Group remove the brains and actually analyze the content in the brain itself? Do you know --

A. No. They -- they were doing PET scanning. So it was a visual -- a visual

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representation where the -- the deeper the staining, the more paraquat was present.

Q. Okay. So then you used the -- the studies that you referenced here in your other paper as the basis for your creation of your mathematical model, right?

A. That's right.

Q. Okay. Now. Let's go through the studies you relied on. Pull that paper. Tell us -- you said there were ten of them or something?

A. Fourteen in total.

Q. Fourteen. And I want you to tell me how they contributed to the creation of your model. And let's go pull them out one by one and go through them.

A. Well, this could take the whole day if we did it in that way.

The -- so the 14 -- let me give you an example. I don't really know what level of detail you'd like to get into.

Q. Well, I'm trying to figure out how you created a model using those studies and how they contributed to a mathematical model which gave you so much confidence that you and the other Syngenta

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scientists chose not to do an actual measurement – physical measurement of the content in the brains of the test animals.

So let's start with the oldest one first. Pull that –

A. No. I mean with respect, I think that's not really going to be very helpful. I mean, they – to give you an indication, they -- we're talking about studies that started in 1973 and went right away through to -- to papers that were published including the Breckenridge paper which have the kinetics as part of it, if you remember, and the – and the Minnema paper similarly in 2013 and 2014.

Q. Right. So this – this is what I'm trying to figure out, and I move to strike that last comment as – as not responsive to any question. But what I'm trying to figure out is what you used to build this algorithm or formula?

Let's start with the first one. What –

A. No. With respect, Mr. Tillery, starting with the first one won't help.

They -- they were all used and -- to

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build the mathematical model by taking the -- the actual data. This is the important part to answer your question. The -- these 14 papers were not themselves mathematical models of -- of -- or calculations of or estimations of how much paraquat was present in excreta or in blood or in tissues. They were actual measurements. They were actual --

Q. Okay. I understand. And this is why I wanted to talk to you about it because I don't know exactly what you're going to tell us as to which one, but I think I understand which studies you're referencing.

So you have references to the 14 studies. Let's start with the first one that you have referenced. What is that one?

A. Well, they're in alpha -- as I said, they're in alphabetical -- in the Table 1, they're in alphabetical order. The first –

Q. So this is the first one –

A. The first one is the Breckenridge.

Q. So the first one is the one that we discussed yesterday – Breckenridge 2013, right?

A. Yes.

Q. And that's the one that had Dan Zadory

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doing the – the stereology, right?

A. Yes.

Q. Okay. And we talked about – this is the one you referenced yesterday after we went through Dr. Smeyne's analysis of how Dan Zadory was doing his study, right?

A. Yes.

Q. Correct?

All right. And is this one of them you relied on?

A. Yes. Because this -- this -- the component of this Breckenridge study is the -- is the kinetic component.

Q. Right.

A. Not the toxicity or pathology component; so --

Q. Okay. So you – you – I'm just trying to figure out, sir, one of your studies was your Breckenridge study you're relying on, right?

A. Yes, that's correct.

Q. All right. What's the next one?

A. My -- Chui, et al., 1988.

Q. Okay. And tell me how that informed any portion of your analysis?

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A. I mean, I said, respectfully, I'm not sure where this particular deep line of questioning is going to take us because I – if we do that for every paper, we would be here until the end of today.

Q. Well, I'm just telling you, it's important. If you think you've reached or calculated through some mathematical formula information so accurate that you don't need – you have to – you can forgo standard laboratory analysis of organ tissue relying on your formula, I want to know how you built it.

I think everybody wants to know the standards. How – what did you do? How did you do this – create this formula? Let's go through.

What did Chui do, 1988? How did that study inform any aspect of this mathematical calculation that you reached?

MR. NARESH: And I'll object to the extent it's unfair to the witness. If you want to show – Dr. Botham told you where this is. And if you want to walk through each one, then I think you need to show them to him. Asking him to do this as a memory test is unfair to the witness.

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MR. TILLERY: We don't have this other study that he has published -- he hasn't even published yet.

MR. NARESH: Is it -- are you representing that the document that Dr. Botham is looking at hasn't been produced to you in draft form?

MR. TILLERY: I don't know whether it has or not. I haven't seen it.

MR. NARESH: Okay. Well --

MR. TILLERY: If you -- if you -- if you haven't -- if you have it, it should be. But it doesn't matter whether I have it here in front of me or not. He does have it, and he can answer questions from this.

Q. Now, you mentioned the Breckenridge 2013 study. You also mentioned the Chui 1988 study. I'm really not interesting in talking about the Breckenridge study. We discussed that yesterday.

I want to know how Chui, 1988, contributed to the creation of your mathematical formula?

A. Right. It was -- so the -- the summary of the detail of that study, it was a rat study.

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And the dose route was intravenous and also inhalation. And the paraquat dose was .039 milligrams per kilogram intravenous, .002 milligrams per liter for inhalation. The samples that were taken were blood, urine, feces, and eight different tissues.

And so, you know, that's the summary of -- of the -- of what was done. There is a lot more detail.

We could -- we could go through that level of detail for all of these studies. I'm not sure that that's very helpful in terms of trying to answer your question, which I really -- I really would like to be able to do. Believe me, I'm not trying to be evasive. I'm just the opposite. I'm trying -- I'm trying to help you to -- to understand it.

Q. Okay. So is there anything other than those details that you just stated on the record about the Chui 1988 study that -- anything else about that study that helped you form your mathematical modeling for the pharmacokinetic analysis?

A. Well, I'm sure that the people who were doing the mathematical modeling would have looked at the -- all the detail that actually appears in each publication. So the answer to that question for all of these papers is that the data points, the actual numbers, the analyses of paraquat in different tissues and -- were all fed into the model in order to validate whether the mathematics that -- that went into the model corresponded with actually how much paraquat was found by all of those different authors in all of these different papers.

And, I mean, the conclusion -- the overall conclusion of this paper was that they were a very good fit. The mathematics -- if you retrospectively use the model and say we believe that in, say, the Chui paper, they should have found this amount of paraquat in the blood or in the brain that they -- that they were a very good match.

Q. Okay. Did they use rats in the Chui paper?

A. They did, yes.

Q. Okay. And what did we discuss yesterday, if you remember, about how the rats show sensitivity or lack of sensitivity to paraquat? Do you remember that --

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A. Yeah. But that's --

Q. -- from that study? The Sprague Dawley?

A. This is -- this is irrelevant to this discussion because we're not talking about the sensitivity to pathology here. We're talking about how paraquat gets distributed around the body --

Q. Okay. Did --

A. -- and not toxicity.

Q. Did the Chui study measure the brain concentrations?

A. I'm -- I'm not that detailed here. I've just gone -- I'm just looking at the summary which says eight tissues; so I can't answer that.

Q. So you don't know whether the Chui study even measured whether or not paraquat entered the brain of the rats, do you?

A. I can't answer that for any of these studies at the moment without going back to the individual papers.

Q. Well, can --

A. And some of them -- some of them would have done.

Q. Can you tell me what else the Chui

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study added to the analysis of your pharmacokinetic formula?

MR. NARESH: And I'll again object to this. Again, I'll repeat that to the extent you would like to show Dr. Botham a copy of the study, then I think that you should show it to him. Asking him to do it as a memory test is unfair to the witness.

BY MR. TILLERY:

Q. Can you answer my question, sir?

A. No. I mean, I really can't answer the level of detail about any of these papers. We, you know -- we've got ourselves stuck at number 2 of 14 here.

Q. All right. So what's number 3?

A. Davis, et al., which is in the dog.

Q. Okay. And when was it done?

A. 1977.

Q. 1977 study. Was there any analysis of the brain of the dog?

A. This one says that it was -- this was a plasma measurement only, and it was intravenous and oral gavage.

Q. Okay. So -- okay. What's the next

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one?

A. Dey, et al., D-e-y, et al., 1990 in the rat, subcutaneous. Blood, urine, and seven tissues measured.

Q. Okay. And for that particular study, do you know how it contributed to the creation of your formula? Your mathematical formula?

A. I'm afraid I can't answer that for any of these studies specifically with the exception of Breckenridge because that would require me to go into the detail of each paper. And even then, the mathematical use of these and -- is -- is beyond my expertise. This -- this was the expertise of the mathematical models.

Q. So who was the modeler who used these studies and actually created the formula? Who was the person who did that?

A. So these -- this was predominantly the Ramboll experts. So Dr. Campbell, Dr. Clewell, Dr. Anderson. And -- but they were supported in this by particularly Dr. Stevens and Dr. Travis. But the models were -- were built by the Ramboll -- the three Ramboll scientists.

Q. And they took these 14 studies and

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created this model, right?

A. They did. That's correct.

Q. Okay. And they submitted the model to whom at Syngenta?

A. It wasn't submitted. It was -- it was a -- cocreated, if you wish. I mean, they did most of the work, but there were regular discussions with Dr. Stevens and Dr. Travis as the model was being built.

Q. And when did they build the model?

A. Over the previous two or three years. It was quite a long-term endeavor -- endeavor.

Q. And did they do it before they treated or dosed the monkeys?

A. Yes. Most of this work was done after the -- the treatment of the monkeys but was done in parallel with the analysis of the -- and development of the mathematical models in the monkeys.

Q. Back to the Stevens study that you have in front of you, the cartilage like the lungs, brain, kidneys was not specifically analyzed for any particular radio-labeled paraquat dose, correct?

A. That's correct. We added the cartilage as another component of the mathematical model.

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Q. You cannot tell us what specific concentration was in the cartilage from direct measurement, can you?

A. No. In the same way that I answered that question for other tissues, it's the same for cartilage, yes.

Q. It was blended as part of the carcass, right?

A. It was.

Q. So without direct analysis of the cartilage, you cannot attribute any of the dose specifically to the cartilage, correct?

A. No, we can't. But, again, if I may, just going back to Bartlett, that confirmed that there was -- and, in fact, there are other publications too, not just Bartlett, which confirm that paraquat does have a tendency to -- to bind to cartilage. And there are good chemical reasons why -- physical chemical reasons why that would be the case.

Q. Move to strike your answer as unresponsive. Here was my question. Please answer it.

So without direct analysis of the

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cartilage in the Stevens study, you could not attribute any of the specific dose to the cartilage, correct?

A. Yes. As we said is the case for other tissues.

Q. Would it be fair to say that in the 14 studies that you reference that these individuals used as a basis for this mathematical formula of primates, none of them involve monkey data?

A. No, they don't. And that's why you build mathematical models because in -- in theory, you would actually want to avoid doing nonhuman primate studies if you can but -- in order to be able to build a model for -- for estimating what happens in man. But we did actually go as far as doing nonhuman primates studies in order to be more certain about our model.

Q. I move to strike your answer as nonresponsive. Listen to my question, please.

Would it be fair to say that in the 14 studies that you reference in the study that provided the mathematical formula for your -- your Stevens study, none of those 14 studies used any monkey data?

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A. That's true, yes. It was mouse, rat, and dog only.

Q. They were only based on rodents and dogs, correct?

A. That's correct.

Q. All right.

MR. TILLERY: Okay. Let's take a few-minute break. Okay?

THE VIDEOGRAPHER: We're going off the record. The time is 6:24. This ends Media Unit Number 2.

(Recess taken.)

THE VIDEOGRAPHER: We're going back on the record. The time is 7:17. This begins Media Unit Number 3.

BY MR. TILLERY:

Q. Dr. Botham, before we took a break, you told me that the model used in Stevens was created from rodent and dog data, correct?

A. That's correct.

Q. Do you recall that we discussed in an earlier part of this deposition on the day before, some day before, a residue study that Syngenta performed on the frontal cortex of monkeys called

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"Analysis of Brain Samples from Paraquat-exposed Squirrel Monkeys for Residues of Paraquat"?

Do you remember that?

A. Is this the study that is linked to Dr. -- Dr. DiMonte's studies?

Q. It is, in fact. And I think you actually answered questions about that particular study. And just for reference, we're going to come back to it, but we'll pull up Plaintiffs' Deposition Exhibit Number 156. Yes.

(Exhibit 156 was identified for the record.)

BY MR. TILLERY:

Q. Do you have the study in front of you now on eDepoze, Dr. Botham?

A. It's just coming through now. Yes, I can now see it.

Q. All right. Would you familiarize yourself with that study for a moment before I ask questions.

A. Okay. I've just taken a look again at the executive summary just to give a headline refamiliarization.

Q. Now, it is entitled -- this exhibit is

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entitled, "Analysis of Brain Samples from Paraquat-exposed Squirrel Monkeys for Residues of Paraquat, Final Report," right?

A. Correct.

Q. And it is dated -- at least the study completion date is January 21, 2011, right?

A. Yeah. The experimental termination date was October 29th, 2010.

Q. Okay. And the author is Dr. William Ray?

A. That's right.

Q. Do you know him?

A. Yes, I do.

Q. And what is his role at Syngenta?

A. He is or was a -- an analytical chemist in the Greensboro campus of Syngenta.

Q. So he took data and analyzed it to produce to regulators?

A. No. It was largely because we offered to -- to do the analysis of the levels of paraquat in the brains of these monkeys to Professor DiMonte when we met him in 2009.

Q. Okay. Syngenta had 15 tissue samples from the frontal cortex of monkeys that were

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administered paraquat, right?
A. Yes, that's right.
Q. And those were the ones that came from Dr. DiMonte, right?
A. That's right.
Q. And Syngenta found paraquat residue in 12 out of 15 samples, didn't it?
A. Yes, that's correct.
Q. And if you want to verify that, that's Table 1, page 12, if you want to look at it. Do you remember this? But you can go ahead. I'll give you time to verify that.
A. Yeah. I was just agreeing that's what the summary said. I'll have a look at 10 and 12 again as well.
Q. Go ahead.
A. Yeah.
Q. Page 12, Table 1.
A. Yes. Table 1. But -- yes, that's right. Three were below the level of detection.
Q. Three below the level of detection. Twelve out of 15, residue of paraquat found within the monkey's brains, correct?
A. That's right.

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Q. And you didn't use any of this data when you created the model in the Stevens study, did you?
A. I don't believe we did.
Q. Okay. So Syngenta measured paraquat in the brains of monkeys, knew 12 out of 15 had paraquat residue in the exact same type of nonhuman primate species that you used in your Stevens studies, but you chose to use rodent and dog analyses from older studies instead, right?
A. Well, I don't think that I would characterize it that way.
The -- these were -- whilst they were in the -- in a relevant species. They were not a nonhuman primate. Not exactly the same. One was a squirrel monkey. One was a cynomolgus monkey, but that doesn't matter.
Now, the point is these were samples at a particular point in time. They're not measurements of kinetics. Single samples at a fixed point in time, and not necessarily all are helpful.
Q. So is that the reason you excluded them, sir?
A. I think it's one reason. Certainly,

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that would have made their value more limited.
Q. Did you give this information to the Columbus, Ohio, scientists who calculated this formula for them?
A. I don't know whether we did or not. I can't answer that. I'm sorry.
Q. Who was -- who was interacting with them? Was that Dr. Travis or Dr. Cook? Do you know?
A. It was Dr. Travis and Dr. Stevens.
Q. Dr. Stevens and Dr. Travis?
A. Yes.
Q. And they were located where when they did this?
A. They were both in Jealott's Hill.
Q. So they were both in England when they did this. And you don't know if they sent the DiMonte's information to them, do you?
A. No, I don't know whether they did.
Q. And you don't know, when they calculated their formula, if they had nonhuman primate study data that was in the hands of Syngenta, right?
A. I -- I honestly don't know whether this

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was taken into consideration at all. I mean, that is something we could check.
Q. And you knew what the dosing was for the animals that you had received from Dr. DiMonte, didn't you?
A. Yeah. We knew how much they had received as an external dose. That's true.
Q. And do you know why that wasn't provided to the U.S. EPA?
MR. NARESH: Objection. Assumes facts not in evidence.
Go ahead.
THE WITNESS: Yeah. As we've previously indicated, the mere presence of a chemical in any tissue does not necessarily represent the kind of information that would be needed by the EPA under 6(a)2.
BY MR. TILLERY:
Q. Yeah. So I move to strike your answer as unresponsive.
Do you know why -- strike that.
Were you part of the decision-making process, the PRF committee, which decided not to give the EPA the dosing information when you -- when

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you filed the report from Ray?
A. I think that we've – If you'll remember, we've been through this before. And what I've indicated is that I was involved in what we call the "approach committee" within the product safety function, which discusses potential referability. The final decision is with the United States-based PRF committee, which I'm not a member of. They made the final decision.
Q. Blame the Yanks.
A. No. I'm not blaming anybody.
Q. No.
A. I'm describing what happened.
Q. All right. So –
MR. NARESH: I'll object to that as –
BY MR. TILLERY:
Q. So – so let's do it this way. Okay?
Did you recommend – I – I forget the niceties of the committee structures that you have at Syngenta.
Did you recommend that the dosing information be turned over to the EPA or not?
MR. NARESH: I'll object to the attorney commentary at the beginning of the

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sentence.
THE WITNESS: What the approach committee said is that it was our belief that these kind of – this kind of information, not just in the nonhuman primate but actually in rodents too, kinetic information, we thought probably wasn't referable. And so that was the – that was part of our deliberation, but the final decision on that was taken by the appropriate committee.
BY MR. TILLERY:
Q. So you made the recommendation not to turn it over, right?
A. We – we believe from our understanding of the criteria that that was something that should – that could be considered.
Q. Would you agree with me that there was a dispute about whether it should be turned over?
A. I wouldn't describe a dispute that I was made aware of.
Q. Would you agree with me that there was certainly a nebulous area at least in the minds of Syngenta as to whether this should be turned over?
MR. NARESH: I'll object as vague and asked and answered.

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THE WITNESS: I don't think it was nebulous. I think we were doing – making our best professional judgment between the two committees on what constituted potential referable findings.
BY MR. TILLERY:
Q. Did anybody at Syngenta ever indicate they thought this should be turned over? This information?
MR. NARESH: Objection. Asked and answered. Foundation.
THE WITNESS: I don't recall that anybody was making a strong suggestion to that effect.
BY MR. TILLERY:
Q. Do you remember ever talking to the people who developed this – the Americans who developed this mathematical formula you used in the Stevens study? Did you ever interact with them yourself?
A. No. I have done no personal communication with this team on the development of this – this model. I've talked to those guys about other issues to do with modeling but not specifically the work they did for us.

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Q. Do you know if they were even told about the DiMonte monkey data?
A. No. I don't know whether they were or not.
Q. Do you know whether that would have been valuable to them or not?
A. I think I said earlier that I feel that, from a technical perspective, it would have limited value. It was a single observation in time. And we weren't even, I believe, absolutely sure how long after dosing that single measurement was – was taken.
Now, whether my colleagues discussed with the Ramboll consultants, we would have to take offline to determine.
Q. So you don't know whether or not they were given the opportunity to decide the relevance of the DiMonte monkey data that you had in your possession, right?
A. No. I don't – I don't know the definitive answer to that question.
Q. Okay. What year was it that Dr. DiMonte gave you this information?
A. I think I said earlier, if my memory

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serves me correctly, it was 2009.
Q. Let's put up exhibit – what's the next exhibit number? 156. 157. Excuse me.
(Exhibit 157 was identified for the record.)
BY MR. TILLERY:
Q. I'm going to show you now what's been marked as Plaintiffs' Deposition Exhibit 157. Okay. I hope you can read this.
A. Yes. Just about. Excuse me. Yes. Just about.
Q. If you'd familiarize yourself with the document, and then I'll ask you a couple questions.
A. Okay. Yes. So these are minutes of a health science meeting in 2009.
Q. Okay. And the guest speakers were Joan Abbott, right?
A. Yes.
Q. And then another guest speaker was Jeff Wolff?
A. Yes. This is Jeff Wolff, the lawyer.
Q. So the lawyer was there. And this is the Jeff Wolff from Houston, Texas?
A. By which you mean Jeff Wolff from

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Fulbright & Jaworski.
Q. Yes.
A. Yes.
Q. And then we have expert advisers on epidemiology, right?
A. Yes.
Q. And that's Jack Mandel, and who are the other people?
A. These are all academic epidemiologists. So I think certainly two of them are based in the United States. I can't remember exactly their affiliation.
Q. And what was the purpose of this meeting?
A. They – the whole meeting was one -- one of our regular strategic meetings of the health science team where we were reviewing the state of the science and our own research program.
Q. And – okay. And what's – what was the reason for having a presenter being an outside lawyer in a health science team?
A. The presence of an outside lawyer was generally there in order for us to be given advice on recordkeeping, general housekeeping of the way in

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which we managed the -- the records of the -- of the meeting.
Q. And give you advice on how to keep information from being disclosed in litigation, right?
A. Yeah. He was able to give advice on what might be able to attract privilege if that was required, but that had no impact on the scope of the discussions.
Q. Okay. So one of the speakers was guest speaker Joan Abbott, right?
A. Yes.
Q. And Joan Abbott at that session talked to you about the blood-brain barrier, didn't she?
A. Yes, she did.
Q. And she made a presentation that you and I have discussed in earlier portions of this deposition, correct?
A. That's correct.
Q. All right. And you also had under the health science team Lewis Smith, right?
A. Yes.
Q. Charles Breckenridge?
A. Yes.

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Q. And who is M.F. Wilks?
A. Martin Wilks. He was medical -- medically qualified product -- products adviser for Syngenta.
Q. And then Philip Botham.
A. Me.
Q. That's you. And then Nick Sturgess, right?
A. Yes.
Q. And then Kim Travis, right?
A. Yes.
Q. And then Andy Cook?
A. Yes.
Q. Janice McFarland?
A. Yes.
Q. And she was physically present at this meeting, right?
A. Yes, she was.
Q. And she traveled from America to come to this meeting, right?
A. She did.
Q. And then D.J. Berry, Dave Berry, right?
A. Yes.
Q. And then who was K. Mewes?

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A. Kersten Mewes or Mewes, he was the regulatory manager for herbicides including paraquat.

Q. And then under the extended health science team, these are team members. You had listed health science team plus Colin Berry, right?

A. Yes.

Q. Nicotera. That's the doctor that we talked about yesterday?

A. Yes.

Q. He is a scientist in Germany, right?

A. That's right.

Q. And then there's Dr. Dino DiMonte, right?

A. That's right.

Q. And then who's C. Campbell?

A. C. Campbell is Dr. Clive Campbell. He's the chief medical officer for Syngenta.

Q. And then J. Tomenson, right?

A. Yes.

Q. And then there's a Syngenta legal team. You have Alan Nadel; Jeff Wolff, Fulbright & Jaworski. J. Sullivan is another in-house counsel for Syngenta, right?

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A. He is or was, yes.

Q. You had dial-in participants Kim, Minnema, Tisdel, Butts, and Campbell. Who were they?

A. Well, David Kim was a kinetic – kinetics expert at the time working for Syngenta in Greensboro.

Dan Minnema. We've talked about him earlier. He's a toxicologist, still is with Syngenta in Greensboro.

Merrill Tisdel, also a toxicologist in the Greensboro team. He was mainly involved in study monitoring of our contracted research.

Mark Butt, an incorrect spelling there, is the pathologist that we're talking about yesterday on the Breckenridge and the Minnema papers.

And Clive Campbell is listed twice there because he was -- I presume he was actually dialing in and not present.

Q. Okay. And then there's a section under the minutes and actions, and you see the extended health science legal teams. And it says "Content -- Comments from Professor DiMonte."

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Do you see that?

A. Yes, I do.

Q. What is – what is that reference?

A. That – it references the presentation that we heard from Dr. DiMonte in that meeting.

Q. And what does -- what do these notes say he said?

A. I think, as we've discussed before, he was telling us the results that he got at that point from the dosing of monkeys both with MPTP and with paraquat and looking at potential neurotoxicity but also looking at the – or discussing with us the – the necessity for not only looking at the pathology but also understanding the kinetics.

Q. And – and the comment, first bullet under his name, would you read that into the record?

A. "In mice"? That first bullet point? Yes?

Q. Yes, sir.

A. "In mice paraquat exposure -- exposures show 25 percent reduction in dopaminergic neurons and upregulation of alpha-synuclein. It is believed the upregulation is a response to the insult and is not necessarily associated with the dying neurons."

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Q. Okay. And then it shows the results from the monkey studies, and what's the first bullet point underneath there? Actually, the first four. Would you read those, please?

A. Okay. So the results from the squirrel monkey studies started off by saying the monkeys were 8 to 12 weeks old. There were four of them. MPTP was dosed at 1 – between 1 to 6 milligrams per kilogram, and it resulted in reduced tyrosine hydroxylase one week and one month after dosing.

Paraquat was dosed subcutaneously at 5 milligrams per kilogram, but the monkeys died because of lung toxicity after the second and third dose.

At a lower dose, 2.5 milligrams per kilogram, our animals tolerated the dose with six weekly injections at which time they were sacrificed.

There were no clinical signs of -- of toxicity, and no difference in numbers of dopaminergic neurons was observed.

Q. Okay. Now, let's look at if we can – if you'll pull up Exhibit 158, which is 86, please.

(Exhibit 158 was identified

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for the record.)
BY MR. TILLERY:
Q. Can you look at this exhibit, please? Deposition Exhibit 158.
A. Okay. Got it.
Q. And it's entitled "Nonhuman" -- "NHP" stands for nonhuman primate, right?
A. That's right.
Q. And "Brain analysis results - samples from DiMonte studies," right?
A. That's right.
Q. Are these the analyses done by Dr. Ray?
A. That's correct, yes.
Q. And what do they show?
A. So these were showing the levels of paraquat that we found in the brain from those samples.
Q. Okay. All right. Now, as far as you know, the documents we've discussed, the three documents that we've put on here -- 158, 157, and 156 -- were never given to the people who created your mathematical model used in the Stevens case; is that correct?
A. No. I think I said I don't know

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whether they were given to the -- the people who created the model.
Q. Okay. Is there any indication in their paper that they relied upon this information?
A. No. I don't think there's anything in the paper which says that.
Q. Is there any reference in the footnotes? Any part of their paper?
A. I'd need to go back and double-check that.
Q. Are you listed as an author?
A. I am.
Q. And on both papers?
A. I am.
Q. Do you have any recollection of ever referencing this information about Dr. DiMonte's monkey studies?
A. I don't have a recollection of that.
Q. Do you recollect ever having seen this information referenced in either of those two studies?
A. I don't recollect that.
Q. Okay.
MR. TILLERY: All right. We're now

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going to move to a different topic. And I'm going to -- we're going to have to call up a different person and have IT come in and pull up a document for me to ask my next round of questions. So we'll go off for just a few minutes here while he does that, and we'll come back on. Okay?
THE WITNESS: Okay.
MR. TILLERY: Thank you.
THE VIDEOGRAPHER: We're going off the record. The time is 7:43. This ends Media Unit Number 3.
(Recess taken.)
THE VIDEOGRAPHER: We're going back on the record. The time is 7:52. This begins Media Unit Number 4.
BY MR. TILLERY:
Q. Dr. Botham, I'd like to move to a different topic at this point and discuss the databases and information that Syngenta has acquired over the years from the ingestion of paraquat, information related to that topic. Okay?
A. Okay.
Q. You're aware of the fact that after paraquat was placed on the market in the

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United States in the mid-1960s, people died from ingestion of the chemical, correct?
A. That's correct.
Q. And that happened in the '60s in a way that generated autopsy cadaver-type findings that were sent to the principal registrant of the chemical at that time, and that was Chevron, correct?
A. Yes. We discussed that very early in my deposition.
Q. We did. We went over that at length, and we talked about it. And we actually even looked at some of the autopsy findings if you remember. Okay?
A. We did.
Q. All right. And that number from deaths -- and the deaths include accidental exposures and -- where people mistakenly drank some of this to, unfortunately, include those folks who had decided to end their lives and to drink the stuff intentionally, correct?
A. That's right.
Q. And then -- and the results oftentimes resulted -- ended in the death of the person who

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either accidentally or intentionally ingested the chemical; isn't that right?
A. That's right, yes.
Q. Yes. And that happened. We saw documents where that happened not only in the United States, but it happened in England and Scotland and in other locations, didn't it?
A. It did.
Q. As the -- as the use of the chemical spread throughout the globe at that time in the '60s, '70s, '80s, 2000s before it was severely restricted after the beginning of this century, the 21st century, there were poisoning deaths that occurred in dozens of countries, weren't there?
A. There were.
Q. And that information in the United States that was acquired and shared with regulators ended up in 1978 resulting in paraquat being changed in status.
Do you remember that?
A. I do.
Q. And it became what's called a "restricted-use pesticide," correct?
A. That's right.

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Q. And that was due to the fact not that it was neurotoxic or not neurotoxic or would do this or do that. It had to do with the fact that if you either intentionally or accidentally drank it, it would poison you. A small bit could kill you, correct?
A. Yes, that's right.
Q. All right. So the process by which injuries and deaths from this chemical have taken place have occurred now about 55 years, haven't they?
A. Yes.
Q. And Syngenta has collected information. And the purpose of this line of questions is to sort of explore how the information has been maintained, where it's been maintained, et cetera, and go through what we have been provided so that you can help us understand the information that's been supplied to us. Okay?
A. I'll do my best.
Q. All right. So for convenience, can we refer to incidents where exposure to paraquat caused or was claimed to have caused injuries or deaths as "paraquat exposure incidents"? Is that fair?

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A. If you wish, that's fine.
Q. Okay. Now, when did Syngenta or its predecessors -- and when I say "predecessors," I principally mean ICI and Zeneca in this context. Okay?
But any company related to Syngenta which sold paraquat-containing products, when did they start maintaining a database concerning paraquat exposure incidents?
MR. NARESH: I'll object on scope and foundation.
But go ahead and answer if you can.
MR. TILLERY: And I'll give you a continuing objection on that.
MR. NARESH: Okay.
THE WITNESS: Right. So I can't give you a definitive answer as to when any kind of systematic database or collection may have started.
Back in -- in the time of ICI/Zeneca, which is prior to 1993 -- that's when Zeneca was formed -- I do know that in more modern times, which I'm more familiar with, that a database was formalized around about 2003. But I'm pretty sure that, although I don't know the detail, there was a

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collection of that kind of information in the years that preceded 2003.
BY MR. TILLERY:
Q. And that's really what I want to focus on first is the period of time preceding 2003. We have, as I think you and I just very, very briefly referenced, we've been provided this database. We talked about this yesterday at the beginning of the deposition.
We've been supplied some information in this database that tells us about some information concerning exposure, but it's very limited in time to about 15 years, okay, of the 55 years involved. And what I would like to know is, is everything you can tell us concerning the collection of information, the process of information, and using that information prior to 2003.
What -- can you tell me, number one, was there a place in the archives of Syngenta which would include Zeneca and ICI where information concerning exposure incidents was retained?
A. I can't give you any clear indication of exactly what that collection looked like. It's an area of -- of the company's responsibility that

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I had only marginal dealings with.

It certainly wasn't something that my base, CTL, the Central Toxicology Laboratory, was involved in. It was the product stewardship and the medical department's responsibility.

Q. And who would have been the person in the pre-2003 era who would have had charge of or responsibility for maintaining that type of information?

A. Again, I wouldn't -- I wouldn't want to speculate on their names, but the roles that we're talking about would be people like the products medical advisers and the heads of stewardship.

Q. Did this database serve any purpose in the creation or alteration of the paraquat formula?

MR. NARESH: I'll object to the use of the word "database." I'm not sure that -- well, I don't think any -- I'll object to the use of the --

MR. TILLERY: Let me withdraw it.

Q. Did the information that Syngenta had either pre- or post-2003 -- was it ever used for any purpose in terms of modifying the ultimate formula that was sold to consumers?

A. Yes, it was. And, likewise, I wouldn't

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describe this as a database but certainly, shall we say, a collection of information on paraquat poisoning incidents.

It was, to answer your question, used, for example, to add to the formulated product of -- products of paraquat, things that would help to make those formulations safer. And so the addition of things like an emetic, which we discussed in previous parts of my deposition, a dye, and a stench, a smell.

Q. And those were the three things that you undertook to try to make the product safer, correct?

A. That's right.

Q. And the dye was used for what purpose?

A. Well, to give it a color that was -- if I remember rightly, it's a deep blue. It's a color that was not similar to any fluid that would normally be consumed, so nothing that would be assumed to be safe to drink because you don't ever see any colorings in drinks or similar things with that color.

Q. And the stench was to tell those people who can smell those things to -- that they were near

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something that was of a very pungent odor, right?

A. Yes, that's right. Another alerting agent. That's right.

Q. And the emetic was to force them to vomit, right?

A. Yes, that's right. If they ingested, it would create emesis, which is vomiting, yes.

Q. And we talked about the need to have this emesis, as you referred to it, occur very quickly, right?

A. We did.

Q. And the reason for that, of course, was to avoid any absorption in the gut. And the quicker it comes out, the less opportunity there is for that purpose, right?

A. That's right.

Q. And once it's absorbed and gets into the circulating bloodstream and winds up in the lungs, pulmonary fibrosis develops, and the patient dies, right?

A. That's -- that's unfortunately one scenario, yes.

Q. Okay. Now, are you able to tell us today where we would go to ask questions of any

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Syngenta employee or former employee for what data was maintained in any form prior to 2003?

A. Well, I would point you to -- in our current organization to the global regulatory and stewardship function, which is based in Basel.

Q. And who would that person be?

A. Well, the head of global regulatory is Dave -- David French. There's also a head of -- stewardship is not quite his title -- but Juan Valero. So those -- those are the two people I think I would turn to first.

Q. How do you spell Valero for the reporter?

A. V-a-l-e-r-o.

Q. So Juan Valero and David French are the people you think who would have access to this information, right?

A. I think they would be better able than me to -- to give you some indications of -- of what, if anything, the record would show on that.

Q. Okay. You -- or strike that.

Are you telling me you don't have personal knowledge and cannot answer any questions regarding what information was maintained by

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Syngenta or Syngenta's corporate predecessors concerning ingestion data prior to 2003?

A. No. I'm – right at 2003, I'm -- I'm – was never familiar with the precise methodology and structure that was used to acquire and – and retain that information.

Q. Okay. So you wouldn't be able to tell me how Zeneca collected information about paraquat exposure incidents, right?

A. No. I wouldn't be able to give you any detail on that.

Q. Would you be able to tell me whether or not Chevron collected that data?

A. Even less so would I be able to tell you that.

Q. Okay. And you wouldn't be able to tell me about ICI and their collection procedures, their recordkeeping procedures, about the people around the world who had died or who had been injured as a result of ingesting this chemical?

A. No. In the ICI days, the people involved in that were based in the south of England in Fernhurst, not in my department.

Q. Did you know any of the people at ICI

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or Zeneca who were in this department?

A. Yes. I -- I worked with them from time to time.

Q. And who were the people who would have been in charge of the data at Zeneca?

A. Well, again, rather like I said before, if I gave you names, they wouldn't necessarily be accurate in terms of a point in time; so – but the senior medical advisers.

I mean, we did mention one name earlier today, Dr. Sabapathy, for example. We also mentioned Dr. Wilks, but he came later. There were other individuals. And -- and so I can't give you a complete list.

Q. Do you know how many different sources of information or potential databases were actually maintained?

A. Maintained by us? No, I can't.

Q. Do you know who today, other than Mr. Valero and Mr. French, would be able to answer our questions concerning the databases?

A. Well, I would particularly point you to Dr. Valero, who would undoubtedly say there are some other people in Basel that might be able to assist

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with that.

Q. Okay. Well, let's pull up at this point on screen share a database for you to look at – for us all to look at.

Now, this is –

MR. TILLERY: We have a place mark for this, Counsel, and we're going to refer to it as Exhibit 159. And we'll have more detailed description of the content of the document from the witness.

(Exhibit 159 was identified for the record.)

BY MR. TILLERY:

Q. Dr. Botham, this is a spreadsheet named "Paraquat AHI-DB Prosar report, Confidential" that I'll represent to you was produced in this litigation by Syngenta's counsel.

The "AHI" – does that stand for adverse health incidents?

A. Yes, it does.

Q. And is one database. And Prosar is the name of another database, or are they different or the same database?

A. I know a little bit about the history.

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Prosar was a database that was specifically covering the Americas and North America incidents.

Q. Okay. So Prosar was part of Syngenta?

A. Prosar was a database that was owned by Syngenta, but the operation of it was outsourced.

Q. Did it do other functions than monitor paraquat poisonings?

A. Yes. I mean, my understanding is that it was monitoring adverse health incidents to any product that Syngenta may have a registration for ourselves.

Q. How would people know to contact Prosar if there was an intentional or accidental exposure?

A. Again, my understanding is that, on the containers of our products, there are telephone numbers to use in the event of an accident or incident.

Q. And when they called that telephone number, it would put them in touch with Prosar people, right?

A. That's how I believe it works in America, yes.

Q. And that would be a call center, presumably, that would alert them or put them

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directly in touch with people who would be trying to take their information. Is that your understanding?
A. Yes, that's right.
Q. All right. Now, the AHI, adverse health incident -- is that a separate database?
A. Well, it was at one time. Certainly, when I first became familiar with this in the early 2000s, the adverse health incident database was essentially for the rest of the world.
Q. And these two apparently were combined when they were sent to us. This is how we received the document, I'm representing to you. It hasn't been changed on our end. Okay?
A. Okay.
Q. So I'm just trying to understand have you ever seen them combined into one single database captured in a spreadsheet?
A. The spreadsheet that you're just showing me now is something that my counsel let me see earlier this week, actually. And I've not seen this particular representation of the database. I was aware of its existence, but I hadn't seen recently, the account information that was now being captured.

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Q. So the adverse health incident information from the rest of the world, okay, would have been maintained or created where?
A. That was an accountability for the people based in Basel in -- certainly in 2003. And prior to that in the 1990s, if there was -- when there was some format of adverse health incident reporting, that would have been based in -- in the United Kingdom for Zeneca.
Q. Okay. So did you say prior to 1993?
A. No. Prior to 2003. So prior to the -- the adoption of what we're now calling AHI.
As I said earlier, I believe there was some form of collection of the data, but I can't give you a level of detail on that database.
Q. And do you know how they collected data? Was it along the same lines where they had a number on -- on the container and they called and then were connected to somebody at Basel who reported the information?
A. It -- it wasn't quite the same. So I know, for example, and certainly it was true in post-2003, that information that appeared on this database came from a variety of sources, a variety

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of routes -- routes. So particularly important were the global network of poison centers associated with the hospitals or government laboratories where information was provided to Syngenta or to Zeneca previously from those poison centers.
Q. Was this information shared with regulators?
A. I'm sure it was because that's part of -- particularly during reregistration processes for any product, it's expected that details of post-marketing health effects are -- are described.
Q. And do you know what Syngenta or its corporate predecessors have reported in terms of the type or number of poisonings that have taken place in various different countries?
A. That's a level of detail which I can't comment on. That was the responsibility of our regulatory and stewardship function.
Q. Okay. Okay. So if we look at this database, okay, there are, I think, on this particular database that starts at 2003, if you go to the very beginning. And do you see on the left -- far left column there's a number 1 assigned. Okay?

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A. Uh-huh.
Q. And then if you go all the way to the bottom of this, it will show 10,500 -- 10,856 entries in this database. I'll just show you to confirm that.
A. You're still going the wrong way.
Q. Okay. I think we finally got there.
A. Uh-huh.
Q. Do you see that last entry?
A. I do.
Q. Okay. It's an Australia entry, June 13th, 2007. There's an entry, and that's 10,580 -- 5 -- 10,857, correct?
A. Correct.
Q. And I think we started in line 2. So it would actually be, in terms of records, 10,856 records on this database.
A. Right.
Q. And that's primarily since 2003, right?
A. I believe it is, yes.
Q. And when was the emetic added to the chemical?
A. Twenty years before that.
Q. Okay. And was the amount of emetic --

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emetic changed over the course of time?
A. No.
Q. Okay. Has it always been the same level?
A. Well, let me caveat what I said. There were differences in the amount of the emetic in different formulations. So there wasn't a fixed emetic level in every formulation.
Q. Okay. Could you just very – in a summary form tell me how that emetic changed over time?
A. Well, it -- it changed --
MR. NARESH: And just -- sorry to interrupt. For the – just for the sake of the record, I assume my scope objection is continuing to run, Steve?
MR. TILLERY: It is.
MR. NARESH: Okay.
MR. TILLERY: It is. I'll raise my hand if it changes.
MR. NARESH: Well, I can't see you. I can only see a big Excel screen. So you'll have to do more than that.
MR. TILLERY: All right. All right.

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Sorry. Having some fun with you.
Q. All right. So, Dr. Botham, do you remember my question?
A. Yes. So you said, "How did the level of emetic change?"
And so there were changes to the level of emetic that -- on – on occasions when formulation changes were made. Generally speaking, the direction of travel was to somewhat increase the level of emetic.
Q. Well, yes, and it may be. But could you tell me in what ways or a specific, for example, amounts?
The emetic stayed the same, right? The type of emetic – there's been no change in the emetic itself from its first introduction into paraquat until today, right?
A. Yes. It's the same chemical emetic.
Q. And just for reference for the record, what's that called?
A. It goes under the title "PP796."
Q. PP –
A. – 796.
Q. 796. And this is the same chemical

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that you and I discussed earlier that came out of the pharma section of the company, right?
A. That's correct, yes.
Q. Yes. And so 796 is used to this very day, right?
A. It is.
Q. And the only variation would be the amount of PP796 that goes into the formulated product, right?
A. That's correct.
Q. Now, when it was first put in, what year was that? Twenty years before in – sometime in the '80s? Early '80s?
A. Yeah. I can't remember the exact date. We -- I'm sure the records were -- we wanted to define it in my previous deposition, but I don't have --
Q. All right. So it was in the early '80s when it first went in. And do you remember the amount that was added at that time?
A. Yeah. I mean, it was something like .5 grams per liter.
And to -- and to – to answer your other question, the kind of direction of travel in

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terms of changing that level, essentially, we're talking about up to three or five times the level of that emetic in some formulations. So there was a kind of fivefold difference between formulations at different times.
Q. Okay. And let's – and let's talk about that. When was the first time from your recollection that there was an increase in the .5 grams per liter of PP796 in a formulated paraquat product?
A. I'm sorry. I can't give you exact time and detail of formulation. I'd need to have some notice of that.
Q. When was –
THE VIDEOGRAPHER: Excuse me. Mr. Tillery?
MR. TILLERY: Yes.
THE VIDEOGRAPHER: I'm sorry to interrupt, but for the video's sake, you may want to drop that exhibit until you're actually referring to it.
MR. TILLERY: Okay. All right.
Q. So let's go ahead and talk about this. We'll come back to the emetic questions, and let's

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just go to this document. And if we go to the column A, this spreadsheet has a number of columns in it, and column A is a reference to the active ingredient, correct.

A. That's right.

Q. And if we go to the drop-down -- this is a drop-down that was supplied with this. If you see that?

A. Yes.

Q. That drop-down -- if you hit that button, it demonstrates that all of the records contain paraquat.

A. Yes.

Q. Okay. Right. And then columns B, C, and D appear to be other active ingredients involved in an incident. And then there's a call type in column E, and then cardiovascular system in column F. Okay? Do you see that?

A. Yep.

Q. Why is the cardiovascular system information important to the analysis of paraquat poisonings as far as you know?

A. Well, I don't know. I -- speculation, this is a spreadsheet that's used for recording

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incidents to products other than paraquat. So that may be more relevant to other products, but that's -- that's my speculation.

Q. Okay. Now, after column G that contains the case number -- do you see column G containing the --

A. Yes.

Q. -- case number? Is case priority in column H.

A. (Nods head.)

Q. By dropping down the filter, we see that the codes are high, low, medium, uncertain, and blank. Do you see those?

A. Yes.

Q. Do you know who assigns these categories?

A. I don't. I assume it's the individuals in stewardship who are accountable for this.

Q. Okay. And do you know what criteria are used in the assignments?

A. I'm sorry. I don't.

Q. And we look at the high priority. Let's look at those just under "High Priority." I'm going to pop those up.

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Okay. There are 299. And when we scroll down in that and look at country code in column J, we see that all of those are either from Canada with eight or the United States with the rest.

Do you see that?

A. I do.

Q. Do you have any idea why other countries don't have any high priority cases?

A. Oh, unless this was something specific to the Prosar capturing of these data, which was North America-specific as I indicated.

Q. Does high priority have anything to do with potential legal exposure Syngenta might face from these incidents?

A. I've got no idea. Like I say, I don't know what the criteria are based on.

Q. Okay. Column I is "Causal Link" category, right?

A. Yes.

Q. And when we drop down the filter arrow, we see that the choices are confirmed, insufficient information. Do you see that?

A. Yes.

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Q. Likely, open assignment, uncertain, and unrelated. Do you see that?

A. I do.

Q. Do you know what criteria were used in making these assignments?

A. Well, not in any detail. But I think it's easier to imagine what they do mean. So "confirm" would mean that there was good evidence that the person or the case that's recorded had involved an ingestion or other exposure to paraquat.

Q. Okay. When we look at the confirmed -- let's look at the confirmed cases. We see that the total is about 7,006 cases and are about 70 percent of the total incidents. Okay?

A. Okay.

Q. And can you tell me from the database -- strike that.

We can tell from this database at least how many countries are represented in this report by just going through and totaling them. I think there's 40 different ones. If you want to go through them and check my math, you can, but I'm showing the list of those on this now.

A. Uh-huh.

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Q. That includes Argentina, Australia, Belgium, Brazil, Canada, Chile, China, Colombia, Costa Rica, Ecuador. It goes on.
A. Yes.
Q. And that includes – for this list.
A. Yes.
Q. Okay. You wouldn't have any reason to dispute that number, right?
A. No.
Q. Okay. Highest number is, I think, about 5,000 from Thailand, right?
A. I haven't gotten to that; so I'll take your word.
Q. The UK has 14 reports?
A. Okay.
Q. Okay. Now, Thailand has about the same number of people as the UK, about 70 million.
Do you know the reasons for the huge disparity between 5,000 in Thailand and 70 in – or rather 14 in the UK?
A. Well, again, I don't want to overspeculate, but you would imagine that in the United Kingdom there is -- there's -- there has been for some time very strict regulatory control over

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the use of pesticides including paraquat and – and a lot of training of -- of farmers and growers and applicators.
Q. So --
A. And that may not be the same – may not have applied in Thailand.
Q. So let me propose another answer. How long has it been illegal to use paraquat in the UK?
A. Yes. Since the registration was -- the reregistration was denied about 15 years ago or so now, 10 to 15 years ago.
Q. So about 15 years ago, it's been – and this database goes to 2003. So it was after – two years after the data – database was initiated, it became illegal to even use it in the UK, correct?
A. I haven't given you an exact date of when the deregistration happened in the United Kingdom, I think, to -- so I don't know if it was two years or -- or more than that.
Q. I know. And whatever the date is, the date is. We agree with that, and I accept that. It could have been, I think, 2007 potentially?
A. Yeah. Maybe it was.
Q. But irrespective, one other explanation

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could be the fact that, after 2005 or 2007 in the UK, you couldn't use it anymore, right?
A. Right. I agree that would be another – another explanation or an additional explanation.
Q. All right. Okay. Now let's go to the incident date in column N and arrange it from the oldest to the newest. And with the exception of two incidents which took place in Morocco in 1995, do you see that the incidents first started in January 2003, right?
A. Yes.
Q. Now, let's look at the preceding column M that's has the title "Created." Do you know what those numbers stand for in that column?
A. I have no idea. I'm sorry.
Q. So when you select that column and change the format type to date, you can see that all those numbers actually correspond to a specific date.
A. Okay.
Q. Okay?
A. Yep.
Q. Well, it took a little detective work

Page 1799

on our part, but I'm wondering why – if you know why this database was sent in this capacity in a way which combined the information such that you had to separate it in order to get the correct date fields? Do you know anything about that?
A. No. No. I can't help you with that. I'm sorry.
Q. Okay. Is it possible they came from two separate databases which were melded together and that confused the data?
A. It may be. Dr. Valero -- or Mr. Valero may be able to help you with that.
Q. All right. I'm not going to take you through all the – the columns, Dr. Botham, but I do want to ask you a few more questions on this.
If we go to severity column, and that's in DD, and when we use the filter arrow again, we see the options fatal, minor, moderate, none, severe, right?
A. Right.
Q. And how many fatalities are indicated in the database?
I wouldn't expect you to know, but I can represent to you that what we've reported or

Page 1800

looked at is there is in this limited database back just 17 years, there's 3,536 deaths from exposure. Okay?

Now, you recall there's a total of 10,856 incident reports from around the world. So if my calculations are correct, that means that over 30 percent of the worldwide incidents resulted in death.

Would that be a fair assessment?

A. Yeah. I was just doing the math. Yes, that's correct.

Q. Okay. If we compare the outcome column in column CH. Okay?

A. Uh-huh.

Q. With the severity column in DD. Okay?

A. Uh-huh.

Q. Are we there?

A. Uh-huh.

Q. We see that one of the categories for outcome is fully recovered, and I'll show you that.

Do you see that?

A. I do.

Q. Okay. So the database has an entry in one column that shows that a person who was exposed

Page 1801

to this fully recovered, and that was selected.

If we then go to severity in column DD, okay, and look at the fatal code. Okay?

A. Uh-huh.

Q. Do you see that?

A. I do, yes.

Q. Okay. You can see there are 25 incidents that show that a person died but also fully recovered.

A. I've got no explanation to that.

Q. Yeah. All I'm just trying to say is, I mean, this – was there an effort to maintain this in an accurate way because it's showing people fully recovered who are dead, and they can't be both obviously.

So this is the kind of thing, the sort of thing, we saw. And you're saying I should go to Basel to ask these questions, correct?

A. I think you should, yes.

Q. Okay. Let's pull that down.

Oh, actually, there's another – there's another one. Is there another thing? Let's pull that up. What exhibit is that?

We're going to go in eDepoze to

Page 1802

exhibit – Plaintiffs' Deposition Exhibit Number 160.

(Exhibit 160 was identified for the record.)

(Discussion off the record.)

MR. TILLERY: Let's go off the record for just one second, please, sir. Okay?

THE VIDEOGRAPHER: We're going off the record. The time is 8:36. This ends Media Unit Number 4.

(Discussion off the record.)

THE VIDEOGRAPHER: We're going back on the record. The time is 8:38. This begins Media Unit Number 5.

BY MR. TILLERY:

Q. I – there's no particular reason for showing you this other than to get an explanation about what's referenced here.

Do you see the SOS International referenced in this Exhibit Number 160?

A. Yes.

Q. And you're listed as one of the recipients; so we pulled this up to look at this. You're one of – you were sent this email by

Page 1803

Dave Berry. Who is he?

A. Well, Dave Berry was a toxicology colleague working as a specific expert on paraquat at that time, and I know he used to get copied into some of the adverse health incidents.

Q. And GBAP following his name references what, sir?

A. Great Britain Alderley Park, which is where CTL was.

Q. And the date of the email was June 27th, 2007, and he copied Lewis Smith. What was his role at that time?

A. So Lewis previously at CTL had moved to be the head of global product development for crop protection, Syngenta.

Q. Okay. And then you're listed on this as well, right?

A. I was, yes.

Q. All right. And then it's reference to "Accidental exposure to Gramoxone with severe outcome, an eight-year-old boy in China," right?

A. Right.

Q. And what is SOS International?

A. Okay. I think this was an organization

Page 1804

that we also used as another route to acquiring information about adverse health incidents to our product.

Q. And do you know how they supplied information to Syngenta?

A. No. Again, I was never involved in those details; so I can't really comment any further on that.

Q. Do you know if there was a separate database for data from International SOS?

A. I was never aware of a separate database.

Q. Let's go to Exhibit 161, and this is a share screen.

(Exhibit 161 was identified for the record.)

BY MR. TILLERY:

Q. Now, have you looked at this exhibit before, sir?

A. Is this different than the spreadsheet we were looking at previously?

Q. Yes, sir, it is. It's a completely different spreadsheet. And this is a – this one was produced to us in discovery that had the file

Page 1805

name in the production "Prosar Year 1998 through 02/25/98 - 12/31/98." Okay?

And I don't know if you'd seen this before.

A. No, I've never seen this one before.

Q. And so it lists a number of columns of information, and do you know how this one was created or retained contrary or different from the first spreadsheet we looked at?

A. Well, the only hint that I've got is what you just described. If this refers to Prosar, this is what we were talking about earlier as the mechanism through which adverse health incidents in North America were – were brought into the company and then recorded.

Q. Okay. And you wouldn't know anything about the assignment of column headings or the information contained? I presume you would direct me to people in Basel to answer my questions?

A. Yeah. Or potentially people in -- and there may be people in Greensboro still who can help if there are real details there. But I would -- I would agree to start with Basel.

Q. Okay.

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MR. TILLERY: And there's one more spreadsheet, right? Can you pull that? And we'll call that Exhibit Number 162. 162.

(Exhibit 162 was identified for the record.)

BY MR. TILLERY:

Q. The last one we're going to refer to for hold in reference to that exhibit is 161; so I have one more to show you to see if you have any information about it, and it's 162.

A. Is this a screen share again?

Q. Yes, it is, sir.

(Discussion off the record.)

BY MR. TILLERY:

Q. Can you see this exhibit, sir, that's 162?

A. Now I can, yes.

Q. Okay. This is yet another database that's been sent to us. Do you have any information about this database?

A. No, I don't, although some of the names that I'm seeing there are in the regulatory department; so –

Q. Monty Dixon would be –

Page 1807

A. Monty Dixon and Janice McFarland, yeah.

Q. Right. So other than that, you'd direct me to them, I presume, to answer your questions, right?

A. Yes. Yes. Monty would be the best person, I think.

Q. Okay.

MR. TILLERY: All right. Let's take a three- or four-minute break and then go to another topic altogether. Thank you.

THE WITNESS: Okay.

THE VIDEOGRAPHER: We're going off the record. The time is 8:46. This ends Media Unit Number 5.

(Recess taken.)

THE VIDEOGRAPHER: We're going back on the record. The time is 8:55. This begins Media Unit Number 6.

BY MR. TILLERY:

Q. Dr. Botham, in the deposition yesterday, we discussed a connection with Dan Zadory and Dr. Richard Smeyne. We discussed stereology.

Do you remember that?

A. I do.

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Q. Stereology is a two-dimensional and three-dimensional tissue cell counting system, isn't it?
A. It is.
Q. A cell is sometimes identified by finding the cell nucleus as part of the counting from what you read, right?
MR. NARESH: Steve, may I have – may I have a standing objection to the extent this calls for expert testimony?
MR. TILLERY: Yes.
MR. NARESH: Go ahead, Phil.
THE WITNESS: Yes. I agree with Mr. Tillery's point.
BY MR. TILLERY:
Q. All right. Have you ever performed stereology yourself on animal tissue?
A. No. That's not a – not – I've never done any pathology myself.
Q. Okay. All right. Do you have familiarity with the general process by which it works from the fact that you do have or have had stereologists on staff who are trained to do this?
A. Yeah. I have a certain level of

Page 1809

understanding.
Q. All right. So were you aware that methods to perform 2D stereology were available in 1946?
A. No. That's not the thing that I would have known.
Q. Yeah. Let me show you an exhibit, and we'll call this Plaintiffs' Deposition Exhibit Number 163. If you'd open that.
(Exhibit 163 was identified for the record.)
MR. NARESH: And if I may add to that standing objection on scope.
MR. TILLERY: Of course. I understand your – and you have that objection. For the record, I'm consenting to that continuing objection.
Q. If you'd look at this, it's a very brief article. And this exhibit is entitled "Estimation of Nuclear Population from Microtome Sections."
A. Yes.
Q. Okay. And if you look at this document, this document was written by M. Abercrombie, Department of Zoology, University,

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Birmingham, England.
Do you see that?
A. I do.
Q. Now, if you look at – the "Summary" section is on the last page of – of text on page 246, if you go there. I believe it's page 8 of the document, "Summary."
Do you see that?
A. Yeah. I'm just getting there. It's not on page 8.
Q. It's -- yeah. It is on mine. The summary –
A. Maybe. Just give me a minute. Sorry. Yes. I'm sorry. It was underneath where I was looking.
Yes. I can see a summary.
Q. Yeah. It's a summary, just general. It's a -- all – my point is, is that this information was in the public domain about doing cell counting in 1946. Okay?
A. Okay.
Q. All right. And then if we go to – and we don't have to show this, but I would – did you – strike that.

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Did you happen to look at the Smeyne deposition last night?
A. I did not.
Q. Okay. I would just suggest -- represent to you that Dr. Smeyne on page 114 of his deposition referenced this particular exhibit that I just put up on the screen, which is Exhibit 163. And he referenced it as the original paper by Elizabeth Abercrombie in the Anatomical Record, which I think in 1946 was really the gold standard for estimating neurons.
And my only question to you is -- and if you would -- would you care to see that because I can show you that, what he testified to on the screen.
A. Well, why not? Why don't you share it.
Q. Well, let's do that. Okay. Can you pull up 164?
(Exhibit 164 was identified for the record.)
BY MR. TILLERY:
Q. Okay. This is just a hard copy of the transcript. And the first page of this says it's the videotaped deposition of Richard Smeyne dated

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October 2, 2020. Do you see that?
A. I do.
Q. All right. If you go to the next page, and the question is starting on line 9, and it says, "And in the '50s and '60s, those methods changed and improved. Is that also correct?"
And there was an objection. And then I said, "You can answer."
And then he answers on line 16, "I can only – the original paper by Elizabeth Abercrombie in the Anatomical Record, which I think is 1946, was really the gold standard for estimating neurons."
Do you see that?
A. I do.
Q. Okay. All right. Do you have any reason to dispute what Dr. Sworn – Dr. Smeyne's sworn testimony indicated?
A. No, not at all. He's an expert in his field.
Q. All right.
Now, were you aware there's an International Society for Stereology and Image Analysis?
A. I may have known at one time, but I

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have no memory of -- of that specifically at the moment.
Q. Do you have people at Syngenta who are part of that organization?
A. Certainly not now, no.
Q. And would that be after 2007 when your laboratories closed in England?
A. Yes, certainly. And I don't even know if there were prior to that.
Q. Okay. If you can, I'm going to pull this next exhibit up. It's number 165.
(Exhibit 165 was identified for the record.)
BY MR. TILLERY:
Q. And if you look on the first page.
A. Okay.
Q. There's a section under the little diagram there, and it says "International Society for Stereology and Image Analysis. ISSIA is an international scientific society aiming to promote stereology and image analysis in a wide range of disciplines."
Do you see that?
A. I do.

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Q. "ISSIA continues from a well-established International Society for Stereology, ISS, with expanded scope to all aspects of image analysis. Our members are coming from many different fields of science such as mathematics, biomedicine, computer science, material science, statistics, geology, stochastic geometry, et cetera."
Do you see that?
A. I do.
Q. All right. Do you know when this organization was formed?
A. No. I have no idea.
Q. Okay. Well, let's go to the next exhibit, which is 166.
(Exhibit 166 was identified for the record.)
BY MR. TILLERY:
Q. And I show you this just to show that it was founded – the International Society was founded in 1963. And if you look at this exhibit, and I think it's on page 3 of the exhibit. Actually, yes, if you go to the number 3.1.
A. Okay. That's on page 2.

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Q. All right. It's on page 2. "Purpose of association and scope of activity."
Do you see that?
A. I do.
Q. "Association professes the tradition of nonprofit organization International Society for Stereology founded as Internationale Gesellschaft fur Stereologie" – my German is not so good, okay? – "in Stuttgart in 1963. It continues its traditions and sets its own aim of holding within the framework of its activities the role of an international nongovernmental organization in the fields specified hereinbelow."
Do you see that?
A. I do.
Q. Well, it was formed as an international society in 1963. And did you know that 3D stereology had by that time already been created as a means to augment the 2D stereology that was used in 1946?
A. No, I didn't. I had no knowledge of the history of that.
Q. Okay. Do you have any scientific basis to dispute the facts that I'm asking you?

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A. No, I don't.
Q. All right. Now, if we can, let's go to exhibit now 167. Let's go to Exhibit 167.
(Exhibit 167 was identified for the record.)
BY MR. TILLERY:
Q. Have you heard of the Journal of Microscopy?
A. Yes. I'm pretty – I'm pretty sure I've heard of that.
Q. And this is – is the – basically the only peer-reviewed publication of the Royal Microscopical Society, right?
A. Yeah. That looks like that that's the case.
Q. All right. And – and do you understand that this Journal of Microscopy is the oldest journal dedicated to the science of microscopy? You wouldn't dispute that, I presume?
A. No. I have no reason to dispute that.
Q. Okay. And it – were you aware that it obtained its current name in 1869? You wouldn't dispute that, would you?
A. I wouldn't dispute it, no.

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Q. It's probably not far from where you live, I presume?
A. I assume so.
Q. Okay. And were you aware that one of the focuses of this journal is stereology?
A. No, I didn't know that.
Q. And you wouldn't dispute that, would you?
A. Nope.
Q. All right. And let's go to 168.
(Exhibit 168 was identified for the record.)
BY MR. TILLERY:
Q. This is Plaintiffs' Deposition Exhibit 168. And this is an abstract, if you look it up. A 1967 Journal of the Royal Microscopical Society, Volume 87, Issue 1. Do you see that?
A. I do.
Q. And -- and it says "Stereology techniques in microscopy." Okay?
A. Yep.
Q. And would you mind reading into the record the part that starts "The principal measuring

Page 1818

methods"?
A. "The principal measuring methods employed in morphometry, generally known as stereology, allow information on volumes, surface areas, numbers of structures and many other dimensions to be derived from simple counting operations. Until relatively recently, these techniques have found only limited application in biology, although they have been used for many years in the inorganic sciences. With the development of reliable quantitative methods in physiology and biochemistry, however, stereologic techniques are becoming increasingly important, and a number of interesting methods have been developed which are both rapid and simple. In this paper, a number of practical techniques are presented which have proved useful in light and electron microscopy."
Q. And would you agree that this was published in June of 1967?
A. Yes, it was.
Q. And would you agree that's just one year after the initial registration of paraquat in the United States in June of 1966?
A. Okay. Yes.

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Q. Okay. And the -- would you agree also that from these documents that I've shared with you that the technology and understanding of how to perform stereology was employed in multiple scientific disciplines including biology?
A. Yes. That seems to be true from what we've got here.
Q. Okay. I believe you told me in -- earlier in this deposition that before 2007, at least, when CPL laboratories was closed, okay, that laboratories ICI and Syngenta had in England were state-of-the-art labs, correct?
A. Yeah. In many – in many aspects, they were.
Q. Had ICI and then later Syngenta wanted to use available 2D or 3D stereology techniques in their laboratories in the 1960s or '70s or '80s to count dopaminergic brain cells, there was nothing preventing them from buying the stereology equipment and hiring a trained stereologist to do the studies, was there?
A. Conceivably, that's true.
Q. Did they do that?
A. I'm not aware that they employed a

Page 1820

specific expert in stereology.
Q. Okay. Until Louise Marks came on the scene in the early 2000s, correct?
A. That's right.
Q. To your knowledge, had Chevron wanted to use available 2D or 3D stereology techniques in their laboratories in the 1960s and 1970s to count dopaminergic brain cells, was there anything from where you're sitting that would prevent them from buying the stereology equipment, hiring a trained stereologist to do the studies?
A. Again, conceivably, there's nothing that could have stopped them from doing that.
Q. Okay. Was IP injection available as a laboratory tool for the introduction of chemicals into test animals by 1960?
A. It was.
Q. From a purely technological standpoint based upon what I've shown you about stereology and stereology availability, there was nothing preventing either ICI or Chevron from performing in the 1960s or 1970s the exact same type of studies performed by Dr. Louise Marks in the early 2000s, was there?

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A. No. In theory, that's right.
MR. TILLERY: Thank you. I have no further questions, Dr. Botham.
MR. NARESH: All right. Joe or Tony, do you have any questions?
MR. ORLET: I do not have any questions.
MR. HOPP: I do not have any questions for Growmark.
MR. NARESH: Okay. Can we take a break? I want to speak briefly with my client, and then we'll come back on the record.
MR. TILLERY: Yes, sir.
THE VIDEOGRAPHER: We're going off the record. The time is 9:14. This ends Media Unit Number 6.
(Recess taken.)
THE VIDEOGRAPHER: We're going back on the record. The time is 8:29 [sic]. This begins Media Unit Number 7.
MR. NARESH: Syngenta will reserve its questioning for Dr. Botham at trial. We don't have any further questions for Dr. Botham right now.
We will read and sign and designate

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this as confidential pursuant to the protective order.
MR. TILLERY: Doctor, let's go off the record.
THE VIDEOGRAPHER: Hold on a minute. Renee, orders?
THE REPORTER: Go off -- are we "done" done?
MR. NARESH: We're done.
THE REPORTER: Oh, okay. I guess the same copy orders, standing orders?
MR. NARESH: Yes, please, for Syngenta.
MR. TILLERY: It is for the same.
MR. ORLET: Same for Chevron.
MR. HOPP: Same for Growmark.
THE VIDEOGRAPHER: And same video orders for everybody?
MR. NARESH: Yes.
MR. TILLERY: Yes.
MR. ORLET: Same video orders.
THE VIDEOGRAPHER: This concludes --
MR. HOPP: Yes.
THE VIDEOGRAPHER: This concludes the video-recorded deposition of Philip Botham, Volume 7. We're going off the record at 9:30.
(Whereupon, signature was not waived and the witness was excused at 9:30 a.m.)
--oOo--

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CERTIFICATE OF REPORTER

I, RENEE COMBS QUINBY, a Registered Diplomate Reporter, Certified Realtime Reporter, Certified Court Reporter (MO), Certified Court Reporter (IL), and Notary Public within and for the State of Missouri, do hereby certify that the witness whose testimony appears in the foregoing deposition was duly sworn by me to testify to the truth and nothing but the truth; that the testimony of said witness was taken by stenographic means by me to the best of my ability and thereafter reduced to print under my direction.

I further certify that I am neither attorney nor counsel nor related nor employed by any of the parties to the action in which this deposition was taken; further, that I am not a relative or employee of any attorney or counsel employed by the parties hereto or financially interested in this action.

My Commission expires April 9, 2021

Renee Combs Quinby, RDR, CRR, CCR (MO) #1291, CSR (IL) #084-004867

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ALARIS LITIGATION SERVICES

January 15, 2021

Ragan Naresh, Esq.
Kirkland & Ellis, LLP
1301 Pennsylvania Avenue NW
Washington, D.C. 20004

IN RE: DIANA HOFFMANN, Individually and as Independent Administrator of the Estate of THOMAS R. HOFFMANN, Deceased, et al. v. SYNGENTA CROP PROTECTION, LLC, et al.

Dear Mr. Naresh:

Please find enclosed your copies of the deposition of PHILIP BOTHAM, Ph.D. taken on January 6, 2021 in the above-referenced case. Also enclosed is the original signature page and errata sheets.

Please have the witness read your copy of the transcript, indicate any changes and/or corrections desired on the errata sheets, and sign the signature page before a notary public.

Please return the errata sheets and notarized signature page to our office at 711 N 11th Street, St. Louis, MO 63101 for filing prior to trial date.

Sincerely,

RENEE COMBS QUINBY

Enclosures

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ERRATA SHEET

Witness Name: PHILIP BOTHAM, Ph.D.
Case Name: DIANA HOFFMANN, Individually and as Independent Administrator of the Estate of THOMAS R. HOFFMANN, Deceased, et al. v. SYNGENTA CROP PROTECTION, LLC, et al.
Date Taken: JANUARY 6, 2021

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Witness Signature: _____

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STATE OF _____)

COUNTY OF _____)

I, PHILIP BOTHAM, Ph.D., do hereby certify:

That I have read the foregoing deposition;

That I have made such changes in form and/or substance to the within deposition as might be necessary to render the same true and correct;

That having made such changes thereon, I hereby subscribe my name to the deposition.

I declare under penalty of perjury that the foregoing is true and correct.

Executed this _____ day of _____, 20___, at _____.

_____
PHILIP BOTHAM, Ph.D.

_____
NOTARY PUBLIC

My Commission Expires: