IN THE CIRCUIT COURT
TWENTIETH JUDICIAL CIRCUIT
ST. CLAIR COUNTY, ILLINOIS

- -

DIANA HOFFMANN, individually and as Independent Administrator of the Estate of THOMAS R. HOFFMANN, Deceased, et al.,
Plaintiffs,
Case No.: 17-L-517
v.

SYNGENTA CROP PROTECTION, LLC, et al.,
Defendants.
- -

February 26, 2020
9:13 a.m.

CONTINUED VIDEO DEPOSITION of DR. PHILIP BOTHAM, held at the offices of Kirkland & Ellis LLP, located at 30 St. Mary Axe, London EC3A 8AF, United Kingdom, before Laura Evans, Accredited Court Reporter of the United Kingdom and Europe.

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W I T N E S S I N D E X

Witness Page

PHILIP BOTHAM (continued) 251

Examination by MR. TILLERY (continued) 251

E X H I B I T I N D E X

No.	Description	Page
Exhibit 21	Patent with "Inventors/Applicants" John Doe, Nicholas Sturgess, Kim Travis, dated 31 August 2006.	256
Exhibit 22	Assignment of patent rights by John Doe, Nicholas Sturgess and Kim Zachary to Syngenta.	256
Exhibit 23	Syngenta presentation "Paraquat & Parkinson's Disease", Bates SYNG-PA-00493318 through 00493392.	296
Exhibit 24	Printed PowerPoint presentation "Paraquat and Parkinson's Disease Research Literature Update (External Publications)".	318
Exhibit 25	Printed PowerPoint presentation "Paraquat & Parkinson's Disease".	328
Exhibit 26	internal research report from Syngenta CTL by L. Marks.	330
Exhibit 27	Abstract for presentation "Lack of Effect of Paraquat on the Nigrostriatal Dopaminergic System of the Mouse" at the Society for Neuroscience Annual Meeting, October 23-27, 2004, San Diego, California.	342
Exhibit 28	Research report of study XM7258 by Dr. Marks. Study initiation date 17 September 2003.	347
Exhibit 29	Research report of study XM7371 by Dr. Marks, initiated April 6, 2004.	359
Exhibit 30	Document titled "Notes of	370

discussion with Lewis Smith to brief him on the latest Parkinson's disease findings on 3rd December 2004".

Exhibit 31 Document headed "Thoughts On Options For Challenging The PQ and C57Bl6 Mouse Model." 378

Exhibit 32 Research report for study XM7480 by Dr. Marks, initiation date 18 February 2005. 392

Exhibit 33 Letter to the US EPA from Syngenta dated February 24, 2006. 400

Exhibit 34 Research report of study XM7570 by Dr. Marks. Study initiation date 3 April 2006. 406

Exhibit 35 Presentation "Investigating the Nigrostriatal Toxicity of Paraquat Dichloride" by Dr. Marks. 408

Exhibit 36 Summary of a presentation "Paraquat & Parkinson's disease" at the Atlanta meeting on February 13th-14th 2008. 410

Exhibit 37 Document Bates numbered SYNG-PQ-01586117 through SYNG-PQ-01586606. 414

Exhibit 38 Product Safety Technical Evaluation Claimed Links Between Exposure to Paraquat and Development of Parkinson's Disease. Draft: September 2009. 422

Exhibit 39 Product Safety Technical Evaluation Claimed Links Between Exposure to Paraquat and Development of Parkinson's Disease. Draft: July 2011. 430

Exhibit 40 Printed PowerPoint presentation "Does the animal or human element support a causal relationship between Paraquat use and Parkinsonism", presented 2 March 443

2016, Brazil

Exhibit 41 Email exchange dated 22 June 2007 ...459
subject "Study titles".

PHILIP BOTHAM

having been duly sworn testified as follows:

THE VIDEOGRAPHER: Good morning. The date today is February 26, 2020. The time of commencement is 9:13 am. This is Day 2 in the deposition of Mr. Philip Botham.

I would just add for the record that the court reporter today is Ms. Laura Evans, and the videographer is Philip Viner, both of Veritext.

With that you may continue your questions.

MR. NARESH: Before you start, Steve, I think I didn't do this on the record yesterday: we will read and sign and the transcript should be marked "confidential" in accordance with the protective order in the case.

MR. TILLERY: Are you ready to resume the deposition, Mr. Botham?

THE WITNESS: I am.

EXAMINATION BY MR. TILLERY (continued):

Q. Can you give me your understanding and definition of Parkinson's disease.

A. Parkinson's disease is a neurodegenerative disease which is focused on the region of the brain called the substantia nigra. The specifics neurodegeneration is what are called dopaminergic cells in that region.

When a significant proportion of those cells have died, then that results in the clinical symptoms of

Parkinson's disease, which are related to changes in motor function but there are other clinical symptoms as well as, but in short, that's -- that is Parkinson's disease.

Q. What is alpha synuclein?

A. Alpha synuclein is a protein which can be found in -- including in cells in the brain.

Q. And what role does the misfolding of alpha synuclein have in Parkinson's disease?

A. It's, again, perhaps -- as I said yesterday, I'm not a clinical neurologist, but my understanding of alpha synuclein is that it's believed to play some role in Parkinson's disease.

Some people believe it has a pathological role, in other words it's in some way causing some of the symptoms that we have been describing; but I have heard others say that it has a protective effect. So I think there is still some uncertainty about precisely how alpha synuclein would work.

Q. What are the risk factors for Parkinson's disease?

A. The biggest factor that I am aware of is genetic. So there are a number of people who would have genetic susceptibility. I believe that that is particularly so for people who get early onset Parkinson's disease.

Q. And could you define what early onset Parkinson's disease is?

A. Again saying I'm not a clinical neurologist so my accuracy here may not be complete, but that would generally mean people who are under the age of 60. There are other risk factors which are known. Head jury is a similar one --

Q. I'm going to work through those.

A. Yes.

Q. Yes. When you used the word biggest factor, what do you mean by that?

A. In terms -- quantitatively, yes.

Q. Okay. What is Syngenta's position or conclusion as to whether exposure to paraquat causes or contributes to cause Parkinson's disease?

A. Our position is that whilst there is biological plausibility that the chemical properties of paraquat could cause damage to cells in the substantia nigra, so we certainly don't deny that that is a plausible hypothesis, but the overall evidence based on studies in animals -- the mouse model particularly -- and the epidemiology studies do not allow you to conclude that paraquat is a causative factor in Parkinson's disease.

Q. And were Syngenta to see the mass of scientific evidence shift to the point where all the key studies are replicable in independent laboratories, what would Syngenta's position be about the ongoing manufacture and sale of paraquat?

MR. NARESH: I object to the form and scope. You can answer.

A. Clearly if the evidence became more convincing that there was an association and indeed a causation, then we would need to consider what appropriate steps might be taken.

BY MR. TILLERY:

Q. And what quantum of evidence would Syngenta require to reach that stage?

MR. NARESH: Same objections.

A. That would include more evidence from the two strands that I mentioned previously. So if the experimental research studies were lending further evidence to paraquat being a causative agent, or epidemiology goes beyond what it currently does which is very equivocal on this subject, then we may be in a position where we need to take a different view.

BY MR. TILLERY:

Q. And would the different view include terminating the sale of the product -- product paraquat?

MR. NARESH: Same objections.

A. I wouldn't rule that out if the evidence became so strong. But at this stage I think we are some way from being in that position.

BY MR. TILLERY:

Q. You indicated a minute ago there was a plausible mechanism for paraquat causing damage -- neurological damage -- in the substantia nigra portion of the human brain; do you remember?

A. I do.

Q. How long has Syngenta been aware of that mechanism?

A. We have been aware that paraquat can cause what is called oxydative damage because of its redox cycling capability for many years. What we still don't know is whether that potential -- and I think it is important to talk about this as potential -- to have to express that effect, that mechanism, in a particular region of the brain, that that is still -- why it's plausible but not a proven hypothesis.

Q. Did ICI know that as well?

A. ICI have known that paraquat has that mode of action that I have just described, yes.

Q. At least for the time you were there, right?

A. Yes.

Q. Okay. Has Syngenta ever tried to market a treatment for Parkinson's disease?

MR. NARESH: Objection, scope.

A. I am not aware of a treatment. But we certainly are very actively -- we always actively support the use of general treatment procedures.

So we have not developed a treatment ourselves, but we would -- we encourage the use of appropriate treatments to -- that are used in acute poisoning, such as the use of Fuller's Earth and deactivating -- other deactivating materials.

Q. So you have not generated your own treatment for Parkinson's disease?

A. Not generated it per se, no. No, we have used existing mechanisms --

Q. Used it from other people?

A. Correct.

Q. Okay.

Now what is our next exhibit number you have?

(Exhibit 21 marked for identification)

BY MR. TILLERY:

Q. And would you mark this as 22, please.

(Exhibit 22 marked for identification).

BY MR. TILLERY:

Q. Have you ever seen exhibit 21 before?

A. No, I have not seen this exhibit.

Q. Were you aware of this process?

A. I was aware of the -- the research that had gone on with this, yes.

Q. And let's, first of all, describe for the record what number 21 is.

A. Would you like me to do that or --
Q. Yes, please.
A. Well, I just will take a little while to read this, if I may.
Q. My questions will be general in nature.
A. Okay.
Q. This is a patent, right?
A. It is. It is, yes.
Q. And it shows the "Inventors/Applicants" as John Doe -- and that is actually a man's name, right?
A. Yes, correct.
Q. And he works for Syngenta?
A. He did work for Syngenta.
Q. Okay. And then there is a person named Nicholas Sturgess; correct?
A. Yes.
Q. And Kim Travis, right?
A. Yes.
Q. They all work, or both worked, at one point --
A. That is correct.
Q. -- for Syngenta?
A. That is correct.
Q. And this was issued in what date? 2006?
A. That's correct.
Q. Okay. And in general terms what do you understand

this patent to involve?

A. Well, in very broad terms, this was a -- the patent was based on -- again I use the word "hypothesis", that this particular agent that is the subject of this patent could have utility in the treatment of Parkinson's disease. But I believe -- I believe -- that its actual use has actually never come to pass. But I maybe wrong about that, because this work originated with Syngenta but I believe was then passed on to another company.

Q. So would it be fair to say that the patent deals with the treatment by expanding the effectiveness of levadopa and other treatments in the substantia nigra of the human brain?

A. That was the hope in bringing this forward.

Q. And this was 2006, done by Syngenta employees while they were on duty?

A. Yes.

Q. And as a consequence of that, if you look at exhibit 22, they did, as is typical, assign their patent rights to Syngenta, didn't they?

A. Yes.

Q. Okay.

Do you know what the Brock theory is, sir?

A. I have an outline understanding of it, yes.

Q. Do you understand whether it includes the olfactory

bulb as a route of access to the mid-brain?

A. It certainly includes that, yes.

Q. Has the olfactory bulb been implicated as an initial site of Parkinson's disease pathology?

A. It has. As what is called one of the prodromal symptoms, where -- the loss of smell.

Q. Do you know if Chevron quit producing and selling paraquat because of the likelihood of it causing Parkinson's disease?

MR. NARESH: Objection to scope.

A. I cannot comment on behalf of Chevron.

BY MR. TILLERY:

Q. ICI and Chevron were working a joint venture at that time, weren't they?

MR. NARESH: Same objection.

A. They were.

BY MR. TILLERY:

Q. You don't know why Chevron told ICI that they no longer wanted to sell -- manufacture and sell the product?

A. I don't know why they -- they said that, no.

Q. Okay. Did you ever attempt to develop any formulation of paraquat products with the intent of reducing the exposure of users to paraquat? Again, when I say "you", I mean Syngenta.

A. Yes, we did.

Q. And that also includes ICI?
A. It would have started in the -- when ICI was the company, yes. That is correct.
Q. So you tried an alternative product --
A. We --
Q. Or a means of improving the safety of the product?
A. We did.
Q. What did you do?
A. We tried to develop formulations of paraquat which, if accidentally or deliberately, were ingested, would not be absorbed by the stomach as readily in order to be able to allow for more effective and quicker treatment.
Q. And this was a form of emetic, wasn't it?
A. Emetic was one of the agents that we used.
Q. And this contemplated a larger ingestion, for example, a teaspoon or more of paraquat?
A. It certainly contemplated that scenario, yes.
Q. Someone accidentally or perhaps even intentionally taking the product, you were designing a product that caused them, in addition to paraquat, to vomit to eliminate this product from their body and perhaps save their lives?
A. Because at that time that was considered by medical experts to be something that would have potential utility in the way in which you have described.
Q. With respect to the active ingredient of paraquat,

would it be safe to say that since 1962, when it was first used in the UK, and then three years later in the United States in 1965, has the molecule been the same?

A. As far as I'm aware, the molecule is the same.

Q. And so far as you know, there's been no effort to change the molecular structure of that chemical --

A. I'm not --

Q. -- in order to affect or change the potential health effects on users or consumers of the product?

A. I -- I'm not aware of any attempt to change the fundamental structure of the molecule.

Q. If you wanted to test a hypothesis that repeated low dose exposures to paraquat over several years could cause or potentially cause Parkinson's disease, how would you do that, sir?

MR. NARESH: Objection to form.

A. Well, the normal toxicological practice would be to see if you can see effects in an appropriate laboratory animal model, and to consider what the appropriate routes of exposure and duration of exposure should be.

BY MR. TILLERY:

Q. More granularly, how would you do it?

MR. NARESH: Same objection.

BY MR. TILLERY:

Q. In other words how would you design this, if you

were the lab lead scientist assigned to this product? How would you do that?

MR. NARESH: Same objection?

A. Well, you would first of all have to ascertain what end point, what effects you would want to detect in that animal model, regardless of the factors I have just been mentioning, and therefore you would want to see whether the hallmarks of Parkinson's disease that you see in a human could be seen and detected in such an animal model. So that would include the pathology in the relevant part of the brain, levels of dopamine and other such factors.

BY MR. TILLERY:

Q. Would your proposal include looking at the role of alpha synuclein in the development of Parkinson's disease?

MR. NARESH: Same objections.

A. It could. But as I said earlier, we are still unsure of exactly what role alpha synuclein has. So one would, I think, include that with some caution because it might be difficult to interpret the findings.

BY MR. TILLERY:

Q. How many studies has Syngenta done of alpha synuclein impact by paraquat?

A. We have not done very much in the way of addressing specifically alpha synuclein ourselves.

Q. Have you done one study?

A. I don't recall if we have done one study. We may have done. I don't recall.

Q. You don't remember ever seeing one?

A. Not -- I don't remember now seeing a Syngenta study where we have looked at --

Q. Have you -- sorry.

A. No, it's fine.

Q. Have you ever asked a third party to do a study that evaluated the role of alpha synuclein in the development of Parkinson's disease with respect to paraquat?

A. We have had conversations with other scientists about alpha synuclein, but again I can't recall that we've ever asked a third party to include this in any of their experiments.

Q. Is alpha synuclein included in the tests you did in the paraquat mouse model, such as the Breckenridge line of studies?

A. No, I don't believe it is included.

Q. Has paraquat been shown to cause an upregulation of alpha synuclein in laboratory animals?

A. I believe that in some other -- in some studies that other researchers have done, that that is the case.

Q. And for the record, would you describe briefly what upregulation of alpha synuclein means?

A. It means that there is a change -- usually meaning

an increase, when you talking about upregulation -- to the expression or the amount of alpha synuclein in a particular part of the body.

Q. Is Lewy body pathology a pathological hallmark of Parkinson's disease?

A. I think that is generally true.

Q. Does alpha synuclein misfolding comprise the majority of proteins in the Lewy bodies?

A. Again I think that is largely seen to be true, yes.

Q. And Parkinson's disease -- strike that question.

Can paraquat cause a misfolding of the alpha synuclein?

A. I'm not aware that there's any clear cut evidence of that.

Q. And there has been no test done by Syngenta to verify it one way or another?

A. We have certainly not looked at that specific parameter.

Q. Did Lewis Smith and Charles Breckenridge seek approval to perform exactly those studies?

A. We -- I certainly recall that we had discussions within our health scientists team about this on more than one occasion. But as I said earlier, the view was that although it was one possible avenue of research, the overall decision was that it was too uncertain that we would be able

to interpret the findings.

Q. And just so we are clear, when I mentioned those two scientists, Charles Breckenridge was until recently in what role at Syngenta?

A. He was a senior toxicologist in our North American toxicology department.

Q. And you described Lewis Smith, but he was in a similar position in the UK; correct?

A. He had a number of senior roles in product safety and in the company more widely.

Q. So two very high ranking scientists in the Syngenta organization sought that.

Who did they need approval from in order to secure the approval to do the test and to get the funding?

A. Discussions of that sort, where we were proposing possible lines of research, were discussed within the paraquat health scientists team, which Lewis Smith was initially the -- the head of that team, and subsequently I became the head.

And we would, ourselves, make recommendations -- in some cases a strong recommendation -- about which line of research we should take and they were then further discussed with a group of more senior leaders in the company called the Paraquat Issues Leadership Team.

Q. And who sat on that committee you are referring to?

A. The Paraquat Issues Leadership Team included -- and this is not an extensive list -- the head of research and development, a senior attorney -- a senior lawyer -- a senior person in the marketing department, other people in R&D, and the head of regulatory affairs.

Q. And let's assume they agreed that these studies should be undertaken. Was that the final authority or did they need to seek approval from yet a higher level in the company?

A. In normal terms, experiments would not require any further approval.

Q. Is the Syngenta executive committee involved in any of this process?

A. Only occasionally when there are some specific circumstances where we feel that we would like their opinion.

Q. Not just their opinion, their approval; correct?

A. And sometimes -- sometimes their approval.

Q. And for the record, describe what the Syngenta executive committee is?

A. The Syngenta executive committee, now called the Syngenta executive team, is the most senior group of leaders in the organization. So it is chaired by the Chief Executive Officer.

Q. These are the people who make the final decisions in

the company; correct?

MR. NARESH: Objection to scope and form.

A. They make the strategic decisions for the company. Of course, a lot of decision-making is delegated to appropriate organizations within the company.

BY MR. TILLERY:

Q. Is there any higher form of authority at the company than the Syngenta executive committee?

A. Well, the chairman of the executive committee reports to the Syngenta -- or did report to the Syngenta board, so in that sense there is a higher authority.

Q. Could you tell me the names of the people on the paraquat leadership team?

A. So the Paraquat Issues Leadership Team.

Q. Yes. You referred to it as PILT?

A. Yes, the PILT, that's right.

Q. Okay?

A. Well, that's quite a difficult thing to do. It has existed for a long period of time and the names have changed so ....

Q. So it's different. I'm not trying to put you through a memory test, so okay.

A. Yes.

Q. Is there a group now?

A. There is a group which acts in that same capacity,

although it's generally actually not used in the same way as it was before. It's a smaller group of people now who can help with this.

Q. Was the Syngenta executive committee involved in approving the studies that resulted in the Breckenridge and Minnema published studies?

A. The executive committee were informed about that at a point in time, but they were not -- we did not need to seek their approval to do those tests.

Q. Okay, but they were told about it?

A. I personally reported to them at one time, certainly, yes.

Q. Irrespective of whether or not they get involved at a level of approving or disapproving, are they informed of these types of studies at paraquat?

A. They are informed about the broad direction of the program, and from time to time they are given some detail where that is considered to be appropriate.

Q. Doesn't the Syngenta executive committee approve the entire Syngenta research project budget?

A. They -- the Syngenta executive committee would certainly approve the R&D budget, that is correct.

Q. Okay. What studies has Syngenta performed -- or had performed -- which investigated whether paraquat causes upregulation? Did we cover that?

A. We covered that.

Q. All right, forget that.

Now, you mentioned head injury before and I told you we would come back to that. Do you think head injury is a risk factor?

A. Well, I think there is certainly some evidence that suggests that, which is why I mentioned it. And head injury appears to be a potential risk factor for other neurodegenerative diseases, not just Parkinson's.

Q. Can you tell me the mechanism that you believe causes head injury to become a risk factor for Parkinson's disease?

MR. NARESH: Object to the scope, the form.

Go ahead.

A. No, I can't tell you that. Because that's, again, a level of knowledge which I've never really explored.

BY MR. TILLERY:

Q. And you mentioned earlier that more sporadic cases of Parkinson's disease, other than those that you said were early onset, they start around -- they average around 60?

A. Again, I think that I wouldn't -- I would say that early onset Parkinson's is generally something that would be in people who are under the age of 60. Parkinson's disease as a whole is a disease of older age.

Q. And is age itself -- aging itself -- a risk factor

for Parkinson's disease?

A. Indeed, that is probably in itself the biggest risk factor.

Q. And why is that? What is it doing in terms of the causative effects of Parkinson's disease, from your standpoint?

A. Again, really as a layperson in the clinical aspects of this, I would simply say that as you grow older things like repair processes and normal functioning of the body will tend to be less effective, thus leading us to be prone to a number of diseases.

Q. Let me ask you in terms of the research: you have a specific committee at Syngenta that deals with Parkinson's and paraquat, right?

A. We have a -- a health science team, yes.

Q. And that health science team has a name that applies to paraquat and Parkinson's studies, right?

A. Correct.

Q. What is that group called?

A. The paraquat health scientists team.

Q. And that explores and investigates the relationship between paraquat and Parkinson's, at least in part; correct?

A. It does.

Q. All right. Now, that committee and you -- you are heading it, that committee, or you did; right?

A. I still do.

Q. You understood that typical onset in the absence of a genetic -- strong genetic -- predisposition to have onset irrespective of any kind of external toxicant, okay, like an environmental factor, paraquat for example, would occur normally much earlier than 60 years, you knew that?

A. Early onset Parkinson's disease occurs before 60, yes.

Q. Okay. And you understood that in the literature that often ranged from late 20s to 30s and 40s?

A. It --

Q. You knew that, right?

A. We knew that, yes.

Q. All right.

But the traditional kind where scientists are investigating the effects that are not generated by some genetic predisposition, but instead by environmental factors, are in the sporadic group that typically -- not always but typically -- start around age 60; you knew that?

A. I would say it was generally above 60. I think that Parkinson's --

Q. Over 60, perhaps --

A. Certainly well over 60.

Q. And for those of us who are over 60, okay, the stage of life would be like, what, the last fourth of our life,

typically?

A. That's about right, yes.

Q. Right, okay. Now if we are using the model -- human model -- and we are talking about people exposed to paraquat or exposed to any other external toxicant and looking at those, and they typically wouldn't develop the condition until their 60s or later, can you tell me if you are using animal models whether it is appropriate to use a very, very young animal?

MR. NARESH: Objection to form, scope.

Go ahead.

BY MR. TILLERY:

Q. What I mean by that is let's say a mouse that lives for two years. We talked yesterday about mice and they were dying and you said that typically could be the end of their lives, two years, right? And these were six to eight week old mice that you were using in the studies, right?

A. When we first started to administer paraquat, that is correct.

Q. Okay. And can you extrapolate the effects of paraquat as a toxicant in these mice that are six to eight weeks old to the outcomes from the same exposure in the natural environment for people who have an onset at age 60 or later?

A. Toxicology is always based on an understanding that

the animal model cannot be necessarily an accurate mimic of the human being. And you sometimes have to compensate -- for example, for the factor that you have just mentioned -- by exaggerating the way in which you expose the animals to a substance, to give very high doses, for example.

And yes, you can use different ages of animals, and we ourselves did use older animals than six to eight weeks in some of our experiments. But you are never in a position to accurately replicate what might happen in the human being, and, if I may just add, it's not clear when the disease of Parkinson's disease -- of Parkinson's actually starts in the human being.

Q. Let's talk about that for a second. Let me ask you, what age does a six to eight week old mouse translate to in terms of the human being?

A. A mouse would normally have a life span of around 18 months.

Q. Okay. So a six to eight week old mouse is, what, just passed a -- not even a teenager yet, in human terms, right?

A. If you want to extrapolate that, yes.

Q. If you take the study out for four weeks or six weeks, you have moved them up to maybe the beginning of their teenage years in human terms, right?

A. Yes.

Q. Have you ever in your life read any accounts of people who were in their teens contracting Parkinson's disease that was not caused by some genetic predisposition?

A. No.

Q. All right, thank you.

Does well water cause Parkinson's disease?

A. I don't know. But there is, again, a hypothesis that it could, due to the presence of microorganisms in the well water.

Q. Or due to the presence of pesticides?

A. What I have seen is that microorganisms in well water have been hypothesised.

Q. But you have not done research to determine that; is that correct?

A. No, we have not.

Q. Do you know what percentage of people with Parkinson's disease have genes that give rise to the disease without any environmental factor?

A. I wouldn't be able to answer that.

Q. Are you aware of any geographical areas or occupational groups that have a greater than expected incidence of Parkinson's disease?

A. Again, I'm not a expert in this field. So again in broad terms, I sometimes read that there are such effects but they are not remarkable. There is nothing that strikes

you as being very clear in that area.

Q. So would a -- let's say a odds ratio of two or three or four to one, that odds ratio for developing Parkinson's disease, would that be something that would get your attention?

A. It's, again, an area where you would have to consult with epidemiologists as to what a significant odds ratio would be. But certainly, yes, again in general terms, odds ratios of that sort you would want to look at to see whether you could understand where that might have come from.

Q. And for the court and ladies and gentlemen of the jury, what that means, by odds ratios of those types, means odds ratio 2 means that you are twice as likely to get Parkinson's disease, right?

A. That's correct.

Q. Three, three times more likely?

A. Yes.

Q. Four, four times more likely?

A. Yes.

Q. Is that what your understanding is --

A. That's my -- that is what odds ratio means.

Q. What is a potentially referable finding?

A. This is associated with the United States Environmental Protection Agency legislation, which in shorthand is called 6(a)(2), where findings in, for example,

in toxicology studies but not exclusively in toxicology studies, may need to be reported to the US EPA.

Q. And does Syngenta have a committee known as the Potentially Referable Finding Committee?

A. It does, and that is a committee which is based in our United States organization.

Q. You mentioned using high doses of testing chemicals or tested chemicals in animals to exaggerate the exposure to make up for your inability to perfectly replicate real world exposure; do you remember that?

A. I do.

Q. Right. How would that make up for using animals that were the equivalent of teenagers at the end of the study?

A. I am not claiming that it necessarily would. I was making a broad point there that toxicology studies, because they can never accurately replicate what happens in a human being's lifetime, will take actions such as exaggerating the amount that is given to the animal, but not exclusively that.

Q. You agree with me that it would not make up for that difference of using young animals, would it?

A. You can't say that it would; equally, you can't say that it would not.

Q. Hasn't it been Syngenta's position that the high

doses in your paraquat mouse study are not relevant to real world exposure?

A. That is a different question. Because what our argument there is, is that it's the route of administration which is particularly of concern. Which I have to say is a view also shared by the US Environmental Protection Agency.

Q. And you actually suggested that to them, didn't you?

A. We certainly came to that view ourselves, because here, for the record, we are talking about injecting paraquat into the intra-peritoneal cavity, which was clearly a very big exaggeration, if you like, of the way --

Q. You have done that consistently for years in studies, haven't you?

A. We did that for two reasons. One for the reason we just indicated so that we are not trying to -- not -- look to see whether the mouse might have the capability of showing Parkinson's pathology, but also because our -- and more importantly -- because our research efforts were directed to see whether the finding that other people have shown using this route of exposure is repeatable.

Q. Did you suggest that to the US EPA or did they suggest it to you?

A. I -- neither applies.

Q. So you didn't go to the US EPA and suggest that

intra-peritoneal injections of mice for studies of paraquat are not appropriate, you never suggested that, is that what you are telling me?

MR. NARESH: I will object to the scope.

A. I may have misunderstood your question at first when you used the term "suggest". We certainly gave an opinion to the EPA that as a route of administration it was certainly not physiological.

BY MR. TILLERY:

Q. And you gave that opinion before they ever published a similar statement publicly, right?

MR. NARESH: Same objection.

A. I believe that would be correct in terms -- at the time, yes.

BY MR. TILLERY:

Q. Does your position with respect to the route of exposure being the issue mean that high doses themselves are not a concern?

A. No, high doses are -- in of themselves are still appropriate to consider. So we also did -- the Minnema paper that you referenced was where we gave paraquat through a more normal route of exposure, in their diet, but that was still at high doses.

Q. I'm going to come back later on the issue of potentially referable findings, okay. But I wanted to at

least inquire before the rest of this deposition today and just see if we can summarize, without getting into all of the details which we will touch later.

A potential referable finding refers to some adverse effect, doesn't it?

A. It does.

Q. And your committee evaluates whether certain adverse effects require reporting them, correct?

A. That is their responsibility, yes.

Q. And there's regulatory authorities all over the world which you have an obligation to report to, right, not just the US regulatory authority?

A. That is true.

Q. And those include where you sell, manufacture, market paraquat?

A. Yes.

Q. How many of those countries are there?

MR. NARESH: Object to scope.

A. Where we -- where we market paraquat?

BY MR. TILLERY:

Q. Yes.

A. I am not able to give you answer.

BY MR. TILLERY:

Q. How many countries -- strike that.

In how many countries has paraquat been banned?

MR. NARESH: Objection to scope.

A. Again, I can't give you an accurate number.

BY MR. TILLERY:

Q. If I told you it was over 32, would you dispute that?

MR. NARESH: Same objection.

A. I would not dispute that.

BY MR. TILLERY:

Q. Okay.

So the potential neurotoxic health effects of paraquat are required to be reported to regulatory authorities, correct?

A. It's not quite as straightforward as that. The reporting requirements are -- also say that the finding has to be new. A new finding. So if it is deemed already to be known by the agency, then that requirement is not -- is not in place.

Q. Well, more specifically, would you agree that withholding scientific findings from the regulatory agencies about the neurotoxic effects of paraquat would be inconsistent with compliance with the regulatory authorities?

MR. NARESH: I will just object to this. It calls for a legal conclusion.

You can answer to the extent you know.

A. If the -- if all the criteria had been addressed and we believed that the -- we needed to report, then we would certainly always have done so.

BY MR. TILLERY:

Q. You understood -- and I again mean Syngenta -- that when the US Congress amended FIFRA -- you know what FIFRA is?

A. I do.

Q. In 1972, it adopted a very broad reporting requirement, typically referred to as a section 6(a)(2) requirement, right?

MR. NARESH: I will object. It calls for a legal conclusion --

A. Indeed, 6(a)(2) is what I referred to in my earlier answer.

MR. NARESH: Steve, can I have -- to the extent that I suspect we are going to have a number of objections to the extent calling for a legal conclusion, can I just have a standing objection as to that?

MR. TILLERY: Absolutely.

BY MR. TILLERY:

Q. Do you understand that section 6(a)(2) requires pesticide registrants like Syngenta to report to the Environmental Protection Agency information concerning -- and I'm quoting:

"Any unreasonable risk to man or the environment."

Of their products? Did you know that?

A. I did know that.

Q. Okay. And do you know that FIFRA section 14(b) authorizes criminal prosecution of a registrant who knowingly violates FIFRA?

A. I did know that.

Q. All right. Sections 12(a)(2)(n) and (q) make it unlawful for a registrant:

"... to fail to file reports required by the subchapter."

Or to:

"Falsify all or part of any information relating to the testing of any pesticide including the nature of any observation made or conclusion or opinion formed submitted to the administrator or that person knows will be furnished to the administrator."

Did you know that?

A. I did know that.

Q. You are also aware that false statements to the EPA are also unlawful under the Criminal False Statement Statute which provides:

"Whoever falsifies, conceals or covers by any trick, scheme or device a material fact or makes an immaterially false fictitious or fraudulent statement or representation,

or makes or uses --..."

(Fire alarm test)

BY MR. TILLERY:

Q. "... or makes or uses any false writing or document knowing the same to contain any materially false, fictitious or fraudulent statement ... or shall be fined under this title or imprisoned for not more than five years."

Did you know that?

A. Yes, I did.

Q. That is 18 USC section 1001. You know that, right?

A. I don't know all the detailed numbers.

Q. But you knew in general --

A. I know in general what this says --

Q. You can't lie about this stuff and you can't withhold information, you knew that?

A. I knew that.

Q. If you've got information, you got to turn it over, right?

A. I know that.

Q. It is an absolute obligation to do it, if you are selling a product that they are in control of in terms of regulation and that can cause harm to the consumer, right?

MR. NARESH: Object to scope.

BY MR. TILLERY:

Q. Is that correct?

A. It is correct. But I would repeat that there are -- there is detailed guidance there on exactly what that means in terms of the findings.

Q. I am actually going to get into this, okay.

You are aware that the EPA regulations require registrants to report information that is relevant to the assessment of the risks or benefits of one or more specific pesticide registrations currently or formerly held by the registrant.

Correct?

A. Yes.

Q. And of course paraquat is one of those because Syngenta is a primary registrant of the chemical paraquat, right?

A. It is.

Q. In the United States and elsewhere, correct?

A. It is.

Q. And you knew that information is relevant to the assessment of the risks or benefits if it includes the conclusions or opinions of a person (i) who is employed or retained by the registrant and was likely to receive such information, (ii) from whom the registrant requested an opinion or conclusion, or (iii) who is a qualified expert as described in the codafel(?) regulations.

You knew that as well?

A. We did.

Q. Okay. You knew that conclusions and opinions of Syngenta employees and retained experts relevant to the assessment of the risks or benefits of a regulated chemical must be reported to the US EPA?

A. Yes, yes.

Q. Did you know that?

A. Yes.

Q. Okay. How long have you known this?

A. Personally, I've known this since the 1990s when I was --

Q. Okay. Syngenta knew that EPA regulations require that codafel(?) regulations section 159.165 makes mandatorily reportable adverse findings in toxicological studies not withstanding similar findings in prior studies:

"If relative to all previously submitted studies they show an adverse effect."

And then it lists a number of things: in a different organ or tissue of the test organism; at a lower dosage; after a shorter exposure period; after a shorter latency period; at a higher incidence or frequency; by a different route of exposure; in a different strain, sex or generation of test organism.

You knew that too?

A. That's right. Those are the qualifications I was --

Q. Those are the ones you were talking about?
A. Yes, yes.
Q. Would you agree that an adverse effect finding is a completely -- in a completely different species is a highly relevant mandatory reportable adverse effect finding under 40 CFR 159.165?
MR. NARESH: Objection to form.
A. In a different -- excuse me, in a different species, yes.
BY MR. TILLERY:
Q. Okay. You also knew that the EPA has a catchall regulation that makes "Other information" mandatorily reportable. A registrant must submit "information other than as described", in the section I just quoted 159.165: if the registrant knows or reasonably should know that if the information should prove to be correct, EPA might regard the information alone or in conjunction with other information about the pesticide as raising concerns about the continued registration of a product, or about the appropriate terms and conditions of registration of a product. Right?
MR. NARESH: Objection to form.
A. Yes. But if I could say at this point --
BY MR. TILLERY:
Q. Just tell me this: were you aware of that rule, 40 CFR 159.165?

A. Well, the script -- the last few words that you read out, I am less familiar with because my responsibility was largely to deal with toxicological information or opinion given to us by experts.

Q. What I'm asking is did you recognize this to be your duty at Syngenta?

MR. NARESH: Objection, asked and answered.

A. In broad terms, of course, yes.

BY MR. TILLERY:

Q. Okay. Syngenta never got a pass for compliance with these rules, did it?

MR. NARESH: Objection to form.

A. Would you repeat the question?

BY MR. TILLERY:

Q. Syngenta never got any kind of exoneration or pass from compliance with the rules?

A. You mean an exemption? No.

BY MR. TILLERY:

Q. Yes, exemption?

A. No, they didn't.

Q. Okay. At all relevant times Syngenta was required to fully comply with all of the rules that I just read to you about paraquat, wasn't it?

A. That is correct.

Q. Would you agree with me that in case of any doubt

about whether to make a report to the US EPA under any of these laws, the most responsible way to proceed would be to file a report?

A. That is correct. And I will have to say that that is absolutely the philosophy that I was encouraging.

Q. Okay.

A. If in doubt, we put it into the system to decide whether we should be submitting.

Q. I move to strike the answer as unresponsive.

Would you agree with me that in the case of any doubt about whether to make a report to the US EPA under any of these laws, the most responsible way to proceed is to file the report?

MR. NARESH: I will object as asked and answered.

BY MR. TILLERY:

Q. Would you agree with that?

A. It is. But I still believe that that is and should be done in accordance with understanding the specific requirements that you have been reading out.

Q. Were there others at Syngenta that argued the other side of this position?

A. Let me, at this point, say that the final decision for this was taken by the US PRF committee that I mentioned before. I personally was not a member of that committee. My responsibility was actually to give information to that

committee from studies or opinion that my department or my team were aware of or had found.

Q. So you may have never made a final report decision yourself?

A. I was never in the position of being part of that US committee that made those decisions.

Q. Right. And who was?

A. They were employees of ICI-Zeneca Syngenta in North America.

Q. And who was on the US PRF committee?

A. Rather like the answer to the previous question, the personnel have changed over the years so I could give a number of --

Q. It depends on the year is what you are saying?

A. It depends on the year, yes, yes.

Q. What are you saying is you could make recommendations but whether they followed them and reported it wasn't within your wheelhouse so to speak?

A. It was not my accountability to do that.

Q. Accountability, right. And would you agree with me that in case of doubt there should be a report made?

A. That was very much the philosophy of what -- what I was responsible for was what we called an approach process. So we had a PRF approach committee in my function and it -- absolutely, people were encouraged that if in

doubt they brought that for my committee to look at, and then we again would pass most of that information on to the US committee.

Q. How many times has a 6(a)(2) report about paraquat been considered but rejected in terms of advancement to the US EPA by either the PRF committee or someone above them?

A. I wouldn't want to speculate on that number. So I don't want to answer that question, because I don't -- I don't know.

Q. Okay. You know it's happened, don't you?

A. The word "rejected" is perhaps not quite the word I would use. Certainly a decision has been taken that certain findings did not meet those criteria that you read out.

Q. Right. That would be certainly something that you would put in a document perhaps. Would that be done by you or by the PRF committee or by the SEC?

A. By the US PRF committee who made that final decision.

Q. And would they make that decision or would that have to be approved by the managing board of the company?

A. My understanding is that that would be the accountability of the US PRF committee.

Q. Okay.

Would you agree that science is built on the sharing

of information; that scientists generate knowledge building on the information produced and shared by other scientists?

MR. NARESH: Objection to form, scope.

A. I think that's a very sound description.

BY MR. TILLERY:

Q. Okay. You would agree with it?

A. Yes.

Q. Would you agree that science flourishes best in conditions of the open and public exchange of ideas, methods, findings and interpretation; openness facilitates vetting new findings and new theories through continued study and analysis?

MR. NARESH: Same objection.

A. I would have to agree with that.

BY MR. TILLERY:

Q. Would you agree that the absence of disclosure of scientific information inevitably causes society to be the loser?

MR. NARESH: Same objections --

A. It could -- it could be one consequence.

BY MR. TILLERY:

Q. You would agree also that secrecy regarding scientific findings diminishes our ability to both identify public health and safety hazards and to prevent harm from them?

MR. NARESH: Same objections.

A. As a general statement, I think that is true.

BY MR. TILLERY:

Q. On the other hand, awareness of scientific studies and findings helps redirect precious efforts and dollars and avoids unnecessary delay and expense?

MR. NARESH: Same objections.

A. Yes.

BY MR. TILLERY:

Q. Okay. Scientific results establishing possible links between heavily used products and very serious health effects are all the more important to disclose because of the potential enormous cost and suffering to human victims specifically and to our society generally.

Would you agree with that statement?

MR. NARESH: Same objection.

A. Yes, I would agree with that.

BY MR. TILLERY:

Q. Okay. Would you agree that scientific research is often a cumulative process built on the knowledge learned from laboratory and epidemiological studies. Disclosing all scientific research is vital to this process and failing to do so interferes with the advancement of objective research and knowledge?

MR. NARESH: Same objection.

A. I would -- I would add one qualifier if I may at this point. What is just as important is that the sharing of information must be done so in a way in which the quality of that information is also properly understood because --

BY MR. TILLERY:

Q. The quality of the studies?

A. Whether it is preliminary findings or whether it is confirmed findings.

Q. Would you say that would also be sharing information about whether the sponsor of a study or the people paid for a study or to do a study had a financial interest in the outcome?

A. Some people would believe that that was an important factor. And I have no problems in transparency of that issue.

Q. Right. Would you agree that the importance of public disclosure of adverse effects of chemicals is especially true when studies link that chemical to a pervasive and progressive disease like Parkinson's disease?

MR. NARESH: Same objections.

A. I think that that would be not unreasonable.

BY MR. TILLERY:

Q. Okay.

What is neurotoxicity? What does that mean?

A. Neurotoxicity is the effects of agents on the nervous system.

Q. How would you define neurotoxicity?

A. It is toxicity to the parts of the nervous system, the nerves, the brain and so on, and to neurological function.

Q. Let me propose a sort of a textbook definition of neurotoxicity and see if you agree with it so that we can agree to use it for the next round of questions I'm about to ask you.

A. Okay.

Q. Neurotoxicity is a form of toxicity in which a biological, chemical or physical agent produces an adverse effect on the structure or function of the central and/or peripheral nervous system. It occurs when exposure to a neurotoxin alters the normal activity of the nervous system in such a way as to cause damage to nervous tissue. This can eventually disrupt or kill neurons and other parts of the nervous system.

Do you understand that?

A. I do.

Q. Does that make sense to you?

A. It makes sense.

Q. Okay. Can we use that definition for the purpose of this line of questions?

A. I am fine with that.
Q. Is paraquat neurotoxic?
A. I believe that that is not yet shown to be the case.
Q. So your answer is it is not?
A. At this point in time, it is not.
Q. Okay. In the Charles River black mouse, does paraquat kill dopaminergic neurons in the substantia nigra?
A. In some laboratory experiments, some investigators, but not all, have found -- have found that.
Q. So if it did kill dopaminergic neurons, under the definition it would be neurotoxic at least as to the Charles River black mouse, right?
A. If that were a consistent and reproducible finding, yes.
Q. When did you first learn that paraquat was neurotoxic in the Charles River black mouse?
MR. NARESH: Objection to form.
A. When some of the publications from other researchers began to appear in peer-reviewed journals.
BY MR. TILLERY:
Q. Why did you conduct paraquat studies using the Charles River black mouse?
A. Because we were trying to do as I have just indicated, to see whether that apparent toxicity, neurotoxicity, could be repeated and therefore could

potentially be a real effect.

MR. TILLERY: Let's go off the record for a minute.

THE VIDEOGRAPHER: We are going off the record at 10:15.

(Break taken.)

THE VIDEOGRAPHER: We are back on the record as of 10:27. This is now media number 2. You may continue.

BY MR. TILLERY:

Q. Before we move on to this line of questions, just for clarification's sake for this record: the PRF committee, you said, could make a recommendation to the US Syngenta folks -- that would be Syngenta Crop Protection LLC, correct?

A. That is right.

Q. And they had the final authority about whether or not to report it to the US EPA?

A. That is correct.

Q. Okay. Now I would like to direct your attention to exhibit number 23.

(Exhibit 23 marked for identification)

BY MR. TILLERY:

Q. This starts at a Bates range of Syngenta 493318. Is that correct, sir?

A. That is correct.

Q. I will be using those numbers as references to guide you to different pages of this document.

A. Okay.

Q. Okay. This is a document I will represent to you that was produced in discovery by your counsel to us --

A. Um-hm.

Q. -- as one of Syngenta's documents. This is a Syngenta presentation entitled:

"Paraquat & Parkinson's Disease."

Correct?

A. Yes.

Q. And when was this presentation given?

A. I'm not able to answer that question at the moment. I can't see a date.

Q. All right. And if you would go to -- I will just refer to the last three numbers on the Bates number -- to 319.

A. Okay.

Q. The presenters of this -- it looks like a presentation and a PowerPoint presentation, doesn't it?

A. It does.

Q. All right. The presenters were Mr. Sturgess -- Nick Sturgess -- Louise Marks and Alison Foster; correct?

A. Yes.

Q. And Nick Sturgess is the person that you described

yesterday in the deposition. He was the former technical -- senior technical expert product safety at Syngenta; correct?

A. That is correct.

Q. Okay. He served as senior technical expert in product safety from 1989 to 2018. Is that also correct?

A. Those dates sound familiar. I can't be sure those are absolutely accurate, but I think that that's correct.

Q. Okay. And for this presentation, and from this exhibit, Mr. Sturgess presented an introduction to paraquat and Parkinson's disease, and the summary comments as well. Okay?

A. Yes.

Q. Is that what --

A. That's what that says, yes.

Q. And Dr. Marks was a research scientist at Syngenta CPL in the neurotoxicity group in the investigating toxicology section; correct?

A. That is correct.

Q. And she worked for Syngenta?

A. She did.

Q. And Dr. Marks presented the part of this presentation referenced as "In vivo studies with paraquat", right?

A. That is correct.

Q. Now if we go to 328, Dr. Sturgess in his

presentation said that:

"Paraquat is unlikely to be neurotoxic owing to the fact that it has a chemical structure and physical properties (charged, polar molecule) which mean it will not readily cross the blood brain barrier ..."

Correct?

A. That's what that says.

Q. That's what it says.

Syngenta, however, knew that paraquat crossed the blood-brain barrier when this presentation was given, didn't it?

A. As we discussed yesterday, it depends on how you define "readily", yes.

Q. But it did cross it?

A. Of course.

Q. All right.

If you go to the next page, Dr. Sturgess actually refers to the radio-labeled paraquat studies that we talked about yesterday, didn't he?

A. Yes.

Q. And he said "some of this material gets into the brain"; he acknowledges that, right?

A. Yes.

Q. Yes. Now if we go to 330, the following page, it's entitled:

"Literature Developments of Concern."

It lists a number of them. One, the first one it starts with, is Fredriksson et al 1993, right, do you see that?

A. I do.

Q. It is listed as a literature development of concern, isn't it?

A. It is.

Q. And the study found behavioural effects in mice given oral doses of paraquat, right?

A. Correct.

Q. And it found reductions in striatal dopamine in mice given oral doses of paraquat too, didn't it?

A. That's what this says.

Q. So this was a presentation that the Syngenta scientists were presumably making to other people at Syngenta?

A. I'm not sure exactly where this presentation was made.

Q. But we weren't given any information as well. Had we been given that in discovery, I would have given it to you.

A. Right.

Q. So you would have it.

A. Okay.

Q. This is as best I have. You have to go to your lawyer to get more information.

MR. NARESH: I will object to all this.

BY MR. TILLERY:

Q. So based upon where we are right now with the document, is that what you would think the situation would be?

MR. NARESH: Just for the record, I object to the whole attorney commentary.

Could you please just ask your question again?

BY MR. TILLERY:

Q. Yes. Does it appear to be a presentation by Syngenta scientists to other Syngenta employees?

A. It appears to be a presentation by Syngenta scientists, but I don't know to whom this particular presentation was made.

Q. Okay. All right.

Okay. Continuing on, and this would be 331 --

A. Yes.

Q. -- and this was again under the topic heading: "Recent Literature Developments of Concern."

Right?

A. Yes.

Q. And here it says, by Dr. Sturgess, there is a note that:

"Two US based research groups have produced a series of publications since 1999 implicating paraquat in a Parkinson's disease ..."

Model in the mouse, right?

A. It does.

Q. And that references a Cory-Slechta Group and that is Rutgers, New Jersey?

A. Correct.

Q. And the Di Monte Group at the Parkinson's Disease Institute in Sunnyvale, California?

A. Correct.

Q. And he's the person that you mentioned yesterday as the person who educated, I think Dr. Louise Marks about stereology, right?

A. Yes, she visited Dr. Di Monte in his institute.

Q. At his facility?

A. Yes.

Q. And he acquainted her with techniques about how to do that?

A. He did.

Q. Okay. Continuing, the studies observed neurotoxicity in paraquat in three biological endpoints that are referenced: loss of neurones from the substantia nigra; loss of dopamine from the striatum; and reduction in locomotor activity. Correct?

That's what Dr. Sturgess is telling the people in the audience?

A. Yes, he was saying that those were the endpoints that were looked at in those studies.

Q. In those studies that he's reporting. Okay.

If you look at the next three slides in the presentation, all three of these fall under the heading:

"Recent external pressures on paraquat quoting links with Parkinson's disease."

Do you see that?

A. I do.

Q. Now, one of them, the first one, is a reference to PAN Europe. Do you remember that?

A. Yes.

Q. Where that was a group of people who had as their position or their mission statement to fight against chemicals that they thought were destructive to human health. Did you understand that?

A. This is the Pesticides Action Network, as it says.

Q. What do they do?

A. They are an NGO, a nongovernmental organization, whose aim is to promote that pesticides should, essentially, be used as little as possible.

Q. Well, at least the ones that kill people, right?

A. They have concerns -- obviously more concerns about

more toxic pesticides, but they campaign against pesticides generally.

Q. That's how you see them, right?

A. Yes.

Q. And they really, really burn up over those that cause horrible, long-lasting miserable deaths too, right?

MR. NARESH: Objection to form.

A. They will certainly --

BY MR. TILLERY:

Q. They don't like those at all?

A. They will certainly focus on those that they perceive in that manner.

Q. Right. Okay. So were they at that time writing an open letter for a ban of this chemical across all of the European Union?

A. I can only read what I've got in front of me. At the time that this was written, I was not familiar with this.

Q. Okay. But you are the corporate designee and you are sitting there as the two Syngenta entities, so I have nobody else to ask.

A. Well, I -- they clearly -- this suggests they did write such an open letter.

Q. They wrote a letter dated August 4, 2003, saying they wanted it banned in Europe; right?

A. That's what this suggests, yes.
Q. And you know that it was banned in Europe?
A. It was subsequently, um, deregistered in Europe.
Q. That's right. Isn't that about the same?
Let me ask you this: can you sell it in Europe?
A. We are not able to sell it in Europe.
Q. Okay.
A. And --
Q. I view that as a ban.
A. Well, we voluntarily withdrew our registration.
Q. Okay. So you just, out of the goodness of your heart not because everybody was trying to ban your chemical, like the open letter from PAN Europe, you just decided not to engage, right?
MR. NARESH: I will object to the form.
A. The situation in Europe is much more complicated than you portray it.
BY MR. TILLERY:
Q. Okay. Well, let's continue on. Let's look at the next one.
What is the next page?
A. "The Swedish government is suing the EU Commission", yes.
Q. So let me ask you this. You withdrew it when you were asked to prove that it was safe, didn't you?

A. No, we withdrew it because of what it says here, that the process that the EU had gone through in the new legislation for registering pesticides was considered by Sweden to have been a process that had not been followed through appropriately.

Q. They actually filed a lawsuit, didn't they?

A. That, I believe, is the case.

Q. And that's, if you look at 333, that page --

A. Yes.

Q. -- "Swedish government is suing the [European Union] Commission", right?

A. That's right.

Q. And they filed a law suit?

A. Yes.

Q. They decided that day, 6 February 2004, to sue the EU Commission for their decision about paraquat in pesticides in the European Union, didn't they?

MR. NARESH: Objection to form.

A. They did. And I would like to reiterate that it was suing the EU because they had not followed the process correctly.

BY MR. TILLERY:

Q. Well, look at what Mr. Sturgess says. He says:

"The suit means that the EU Court of Justice is trying the government's partition to nullify the

commission's decision."

Right? That's what Mr. Sturgess says, if you could just answer that question.

A. That's -- that is what that says, yes.

Q. Okay. That's what he's submitting.

Were you there at this meeting?

A. I don't know if I was.

Q. Okay.

Now go to the next page. It says at the top:

"Recent external pressures on paraquat quoting links with Parkinson's disease."

Right?

A. Yes.

Q. And that was:

"Stockholm to seek ban on paraquat herbicides By Nicholas George."

Who is Nicholas George?

A. I don't know. But that -- this page suggests he may have been a journalist.

Q. A journalist from the Financial Times seeking -- strike that.

A journalist from the Financial Times quoting Stockholm seeking a ban on paraquat herbicides, right?

A. Okay.

Q. Okay.

Now -- now let's go to 335 if we can. This is a slide entitled:

"Research Activity at Syngenta CTL Strategy Being Followed."

Okay. You agree?

A. Yes.

Q. All right. And it starts off with a first bullet point:

"Establish whether there is a sound scientific basis ..."

For claims, right?

A. Yes.

Q. And second one:

"If findings are not reproducible, aim to publicly refute the claims in the literature by offering our own alternative experimental findings."

Right?

A. That's what that says.

Q. Did Syngenta at that time and earlier have a group whose job it was to monitor publications about its products?

A. Not knowing the exact date of this, but this preceded what I have been referring to as the paraquat health science team --

Q. Irrespective of whether it is paraquat, I am talking about products in general: did it have a group of people

whose job it was to monitor publications that were -- that were published about their products?

A. It -- it did not, as far as I am aware, have a specific group whose objective was to do that. We expected the scientists who were engaged in either having responsibility for products or particular areas of science to monitor the literature.

Q. So you had groups of scientists -- of these 2000 chemists and other scientists that you had, you had these groups who had portions of them assigned particular products to monitor?

A. I am just talking specifically about what we now call the product safety organization, where we were looking -- where we were expecting our researchers to be aware of the appropriate literature.

Q. If you look at the next bullet:

"If findings are repeatable, Syngenta CTL generated data will be used to build a defensive position for [paraquat] based on establishing a no effect dose (under various dosing regimens) in the C57Bl6 mouse model, based on a biological endpoint -- neuronal cell loss in the substantia nigra."

Right?

A. That's what that says.

Q. So Dr. Sturgess was coming up with a game-plan to

refute findings that you made in your own laboratories that duplicated what was done in the public literature, right?

A. I would not put it that way. What the intent here was to say if the finding that we are talking about here was indeed repeatable, as would always be the case with any toxicological finding, you don't simply say you have that finding, at very high doses quite often, and you leave it at that. You actually say at what dose levels do you stop seeing that finding? You go down the dose levels --

Q. Okay.

A. -- to find a "no effect" level.

Q. Have you seen this before?

A. I have may have done. I don't today recall whether I have or not.

Q. Okay. So -- and you don't remember being here, right, at this meeting?

A. Because I don't exactly know which meeting this was.

Q. Okay. Let's go to the last point that Dr. Sturgess made, which says:

"Avoided measuring PQ levels in the brain ..."

So Syngenta was avoiding measuring PQ levels in the brain, right? That's what he says?

A. At that point clearly that was what some people felt was the right thing to do.

Q. Right. And to, in other words, when you do

laboratory analysis avoid measuring that level in the brain?

A. That would not be our position today, and it wasn't our position --

Q. Well, what it -- excuse me, sir.

A. -- at a later time.

Q. Excuse me. I move to strike your answer as unresponsive.

Did he at that time say --

MR. NARESH: Hang on, Steve, your question was: when do you do laboratory --

MR. TILLERY: No.

MR. NARESH: -- analysis avoid measuring that level in the brain, and he was trying to answer your question.

MR. TILLERY: I said did he -- "avoiding measuring PQ levels in the brain", is that what he said?

MR. NARESH: That wasn't your question --

MR. TILLERY: Well, I will withdraw the question and I will ask him.

BY MR. TILLERY:

Q. He said, Dr. Sturgess said:

"Avoided measuring PQ levels in the brain, ..."

That means Syngenta was avoiding measuring paraquat levels in the brain, doesn't it?

A. At that point in time, that was the opinion of the

people who were engaged in this conversation.

Q. Right. And continuing on with that same bullet, he says:

"... since the detection of any [paraquat] in the brain (no matter how small) will not be perceived externally in a positive light."

Correct?

A. That's --

Q. Is that what he says?

A. That's what it says.

Q. All right.

A. But I would like to add --

Q. Excuse me, sir: is that what it says or not?

A. That's what it says.

Q. All right. So at this time, based upon what he said, Syngenta knew that any amount of paraquat in the brain, "no matter how small", would be perceived negatively outside the company; correct? That's what he was saying?

A. That is what he was saying.

Q. All right.

So the research program at Syngenta CTL described here, Syngenta simply didn't do studies to determine how much paraquat was getting into the brains of animals and they did that intentionally?

A. That's what I was about to follow on by saying. The

record shows that in our research program which followed --

Q. Not followed -- excuse me.

MR. NARESH: Steve, you have to stop interrupting him --

MR. TILLERY: Now that is -- we are not going to do this. You are not going to do it. You may try to override and state another answer. Not with me. Okay. You are not going to do it. I'm not going to let you.

So here's what you are going to do, you are going to answer my questions, or we are going to do this -- and this is for you, counsel -- we are going to terminate it, if you want it that way, and you will go to St. Clair County Illinois and finish this in front of our judge.

Now I know you have prepared him very well. Okay. But you are going to answer my questions, not what your counsel told you to say.

A. Can I just say my counsel has not told me to say that --

BY MR. TILLERY:

Q. Well, here's what we're going to do. I want you to answer my specific --

MR. NARESH: Steve, you've got to stop interrupting him.

MR. TILLERY: -- question.

MR. NARESH: You have interrupted him over and

over again.

MR. TILLERY: No, I wasn't talking to him about anything else.

MR. NARESH: You just interrupted him again.

MR. TILLERY: I want you to answer my question and my question only. Not something else.

MR. NARESH: Why don't you ask your question again? Ask your question again. I don't think -- the question you are asking in your mind is not the question that's showing up on the transcript.

MR. TILLERY: Well, maybe --

MR. NARESH: He's answering the question that you're asking. Why don't you ask your question --

MR. TILLERY: I'm reading it, and I have it right here, okay.

MR. NARESH: The one that you just asked was the one he was answering and you interrupted him.

MR. TILLERY: So --

MR. NARESH: So why don't you try it again --

MR. TILLERY: What we are going to try is this -- and we are going to continue it for a bit -- and then we are going to see what the judge says.

MR. NARESH: Ask your question.

MR. TILLERY: It is 10 to 5 there right now, and we will go to the court and see what the judge says whether

or not -- and we can email the rough to the judge and see if the judge feels that this deposition should go forward.

MR. NARESH: That's fine. Ask your question.

BY MR. TILLERY:

Q. So I'm asking you, sir, to answer my specific questions and not volunteer information. If you want to do that at the trial, called by Syngenta as a witness, that is up to you.

Do we have an understanding, clearly what I want at least?

A. I understand what you are saying.

Q. All right. Thank you.

Syngenta knew at that time -- at the time this was done, this presentation -- Syngenta knew that any amount of the brain -- strike that.

Syngenta knew at that time that any amount of paraquat in the brain, no matter how small, would be perceived negatively outside the company; correct?

A. It is correct that that was the view at that time.

Q. Right. And Syngenta at that time, as reported by Dr. Sturgess, didn't do studies to determine how much paraquat was getting into the brains of animals, correct?

A. It is correct to say that at that time that is the case.

Q. And those studies couldn't -- strike that.

Those studies could have been done at that time, couldn't they?

A. They -- further studies could always have been done at any time.

Q. Right. But Syngenta had not been doing them, had they?

A. That's not quite true, if I may say so. There had been studies done by Syngenta earlier than this time.

Q. That we have talked about?

A. Which included measuring paraquat in the brain.

Q. Okay. Now if you would go to 36 -- I'm sorry, yes, to 36 -- and that is:

"Research Activity at Syngenta CTL in vivo Studies."

And that references Louise Marks, do you see that?

A. I do.

Q. Okay. And the first bullet says:

"Repeat of published in vivo experiments with [paraquat] alone being dosed to C57Bl6 mice."

Right?

A. It does.

Q. What does that mean?

A. It means to repeat the studies done by, for example, the researchers that were referred to in earlier slides, Di Monte and Cory-Slechta, whether paraquat if given to the -- this particular strain of mice may cause the same

effects.

Q. Okay. "In vivo" just means live animals, right?

A. It means -- to live mice in this case.

Q. So Dr. Marks' research was intended to repeat the independent research in the published literature and determine whether she could reproduce the neurotoxic effects in the mouse; correct?

A. That was correct, yes.

Q. Okay. The last bullet, if you would see on the very last one on that page, notes Syngenta intended:

"... to seek peer review of our findings."

Correct?

A. Correct.

Q. Did Syngenta ever seek peer review of any of Dr. Marks' findings?

A. No, it didn't at the time that they were conducted because the, er --

Q. Did I ask you about "because"?

A. Yes, right.

Q. Okay. Read back my question to this gentlemen, please.

COURT REPORTER: "Did Syngenta ever seek peer review of any of Dr. Marks' findings?"

A. I don't believe that we did.

Q. Thank you.

Did Syngenta publish any of Dr. Marks' studies anywhere?

MR. NARESH: Objection to form.

A. I don't believe that Dr. Marks' studies specifically were ever published.

BY MR. TILLERY:

Q. Okay. Now, let us go to next exhibit number 98, please, our internal number 98.

Next exhibit is 24, counsel.

(Exhibit 24 marked for identification).

A. Thank you.

MR. NARESH: Is this the first page of the document?

BY MR. TILLERY:

Q. It is.

Is this another presentation so far as you can tell, sir?

A. This looks like it is another paraquat presentation -- PowerPoint presentation, yes.

Q. PowerPoint?

A. A PowerPoint presentation.

Q. And this has a date of -- can you see a date on it? We may see one.

A. I don't immediately see one.

Q. It discusses work to be done at CTL with paraquat in

the mouse, right?

A. Starting at 628, it's moving into the in vivo studies that we were just discussing.

Q. Right. The studies that Dr. Marks undertook, is that correct?

A. This looks like it is the case.

Q. And who authored the presentation?

A. I can't see an author on the copy that you've given me.

Q. Okay. If you wouldn't mind turning to 633 of that document.

Do you see that page, sir?

A. I do.

Q. Okay. The first bullet in this PowerPoint presentation is entitled -- it's under "Investigative Toxicology Input," correct?

A. Correct.

Q. And it says:

"Investigative toxicology is involved in establishing whether there is a sound scientific basis for the claims by some research groups that exposure to paraquat causes Parkinsonian like [symptoms] in animal models."

Correct?

A. Correct.

Q. And Investigative Toxicology is a group at CTL that

conducted paraquat mouse research, correct?

A. That is correct.

Q. Did that group include Drs. Sturgess and Marks?

A. That is correct.

Q. Okay. And on this slide, Syngenta is concerned whether the findings that paraquat is neurotoxic that have been made in the independent published literature are accurate.

Would that be a fair statement?

A. I would use the word "repeatable".

Q. And that means, if they are not repeatable, there would be some question about whether they are legitimate?

A. That is right. That is normal scientific practice.

Q. And replication in science is kind of the gold standard, isn't it?

A. It is the hallmark of quality science, of course.

Q. And if they are not replicable in laboratories that are well-run and well-organized and using the same technology and people who don't distort and alter the results intentionally or not intentionally --

A. Yes.

Q. -- then if they get those results and keep repeating them at different labs, it becomes more or less an established fact among the scientific community; right?

A. That is -- you have described the scientific process

well, yes.

Q. Okay. Let's turn to, if we can -- actually on that same list, if you don't mind, going down it says:

"Are their findings repeatable?"

It asks that question.

A. Yes.

Q. And then it says:

"If so can we offer a mechanistic explanation for their results?"

Right?

A. Yes.

Q. What is a "mechanistic explanation" as you understand it referenced in that slide?

A. Again, not knowing exactly what point in time this was, I believe the most likely explanation for what they meant here was to say if you see -- let me call them discrepant results, one laboratory has seen this, another laboratory has seen something different so they are not repeatable -- in an ideal world you would like to understand why. So is there an explanation, a mechanistic explanation, as to why one lab has seen something and another has not? That's what I suspect may have been --

Q. Actually look at it again, sir. It says the exact opposite. It says:

"Are their findings repeatable?"

And it says:

"If so can we offer a mechanistic explanation ..."

So in other words, they are saying here that if we repeat their same findings, can we offer an explanation? Correct?

A. Oh sorry, yes, I do -- sorry, there's -- I should have looked at this more carefully. You are quite right. As written there, I think what I said --

Q. As written here it means --

A. Yes.

Q. -- that they are saying, the presentation: if we reproduce the results, we better come up with a mechanistic explanation for why we are reaching the same results.

A. Right. So I think that's true. I mean, what I also said is equally true, but yes, you are right, as written you would need to understand what the mechanism they are --

Q. I mean, what is the final bullet? Read that one into the record.

A. "If findings are not reproducible, can we refute the claims in the literature and offer alternative experimental findings?"

Q. Was that the course of Syngenta at that time: when the findings were not reproducible in their labs, they could refute the claims in the literature and offer alternative experimental findings in the literature; was that the

standard?

A. The standard is if the -- if findings are not reproducible, then you don't necessarily just leave it at that. That's why I made my previous answer, if I may say so, which is to say that you do need to understand why that might be the case, and not just assume that we are right and somebody else is wrong.

Q. But it says here very clearly:

"... can we refute the claims in the literature and offer alternative experimental findings?"

A. Yes.

Q. That's what they intended to do --

A. That's a question --

Q. -- if they didn't reproduce the results?

A. That is a question at the time.

Q. Right. Now please turn to 638 on that document.

It's entitled "Paraquat and Parkinson's Disease Investigative Toxicology Research", isn't it?

A. It is.

Q. The first bullet says:

"The issue around the claims that paraquat exposure and Parkinson's disease are linked needs to be addressed if the future Syngenta aspirations for the product are to be realized."

The future aspirations for the product mean selling

it on the market and making profits from the sale, don't they?

MR. NARESH: Objection to scope.

A. That's an assumption which you can certainly take from the way that's written.

BY MR. TILLERY:

Q. Yes. You would not disagree with that interpretation, would you?

A. I think that is one plausible interpretation.

Q. That is probably the most plausible, would you agree?

A. It may well have been.

Q. Okay. So Syngenta's aspiration for products, paraquat products, would not be realized if the link between paraquat exposure and Parkinson's disease was established; is that right?

A. That's what you would infer from that.

Q. So going to the next bullet:

"Data generated will be used to build a scientifically robust, defensive position for paraquat in response to the issues already in the scientific literature, and to questions raised by the media, customers and regulatory authorities."

Is that what that says?

A. That's what that says.

Q. Okay. Now let's go to 641 of that document. The third bullet says:

"External publication of findings at scientific meetings to assist our influencing strategy."

Do you see that?

A. Yes.

Q. And "influencing strategy" was a strategy intending -- intended to influence publications, scientists around the world, wasn't it?

A. As written that would be what it suggests it -- yes, yes.

Q. Okay. And Syngenta's paraquat mouse research was intended to influence independent researchers regarding the safety of paraquat, wasn't it?

A. It was intended to ensure that we understood the validity of those findings that other researchers had published, including the aspects, as it said earlier, about repeatability.

Q. And it says very clearly in bullet three there -- were you at this presentation, sir?

A. I don't know that I was.

Q. All right. It says very clearly in this bullet, the:

"External publication of findings at scientific meetings to assist our influencing strategy."

Right?

A. Yes, but I can say that --

Q. Can you answer that question?

A. Yes, that's what it says.

Q. And scientific meetings are meetings where Syngenta's people would go with boards or presentations and speak and present to scientists around the world the findings from their studies; right?

A. Yes, yes.

Q. And you have done that yourself, haven't you?

A. I have.

Q. Okay. And what's the purpose? It is to get that information -- your position or your findings -- out, right?

MR. NARESH: Objection to form.

A. That's -- that's correct.

BY MR. TILLERY:

Q. Okay. And that, if there was a strategy, it's referenced here as "spring 2003", there was a strategy that had been adopted by paraquat -- sorry, strike that.

There had been a strategy announced in spring 2003 by Syngenta scientifics meetings within them to influence other scientists around the world?

A. To give transparency, as we have said before, to the fact that the science behind this issue is still a work in progress.

Q. Okay. Would you see where it says -- read where it says that in bullet 3, what you just said?

It doesn't say that at all. You made that up.

MR. NARESH: Objection --

A. I didn't, I was --

MR. NARESH: Objection to form, argumentative.

Ask your question.

BY MR. TILLERY:

Q. Did you make that up?

A. No, I didn't make it up. I agree that this is what it says.

Q. All right. It says that in spring 2003 there was an influencing strategy adopted, okay?

A. Yes, I was trying to describe what I believe "influencing strategy" meant.

Q. Okay. But the document doesn't say what you say, does it?

A. The document does not say that.

Q. All right, okay.

The bottom line is the paraquat mouse research by Syngenta was intended to convince others outside of Syngenta that paraquat was safe, correct?

A. It was at that time trying to see whether the findings were replicable in order for a judgment to be made about that point.

(Exhibit 25 marked for identification)

BY MR. TILLERY:

Q. Can you identify exhibit number 25, please?

A. Again, this is a PowerPoint presentation on paraquat and Parkinson's disease.

Q. It's another presentation or excerpt entitled:

"Paraquat & Parkinson's disease."

Right?

A. That's right.

Q. And the front page says:

"Paraquat and Parkinson's Disease Experimental Strategy."

A. Correct.

Q. And it says:

"Carry out in-house research to further our understanding of paraquat and it's role in Parkinson's disease models ... to ensure safety in use."

And it says:

"Use these data to gain a presence in the International Scientific Community and promote a balanced view for the use of paraquat as a non selective herbicide."

A. That's what that says.

Q. That's what it says.

And all of "these data", as mentioned, refers to paraquat mouse research at CTL; correct?

A. I believe that that is correct, yes.
Q. Okay. If you go to 238, please, you see in the second bullet -- the top of this one says, the first line says:
"Paraquat & Parkinson's Disease."
And then the second bullet says:
"Threats to paraquat from ... recent scientific literature."
A. That's right.
Q. Those were threats to Syngenta's continued ability to manufacture and sell paraquat, weren't they? Is that a fair reading?
A. That would be an ultimate consequence that was intended.
Q. Okay. And the ultimate threat was that the scientific literature would cause paraquat to be banned, correct?
A. If the -- if the evidence eventually came together to make -- to lead to that possible conclusion.
Q. Okay.
If you go to the next page. This presentation, if you look at the next page and that is 484239, you see that?
A. Yes.
Q. Also refers to the Di Monte group at the Parkinson's Institute in California?

A. Yes.
Q. And both groups had shown paraquat was neurotoxic in the C57B16 mouse; correct?
A. They had seen findings which suggest that that was a possibility.
Q. Syngenta considered the work by Dr. Cory-Slechta and Dr. Di Monte to threaten its aspiration for paraquat product sales, didn't they?
A. The findings, if they had -- if indeed they were replicable -- could lead to a view being taken on the safety of paraquat. That is correct.
Q. And that would ultimately lead into the decision that it would not be allowed to be used?
A. That was always one possible outcome, yes, as we said before.
Q. That's a fair interpretation of this slide?
A. Yes.
Q. If you go to 889 --
MR. NARESH: 889?
(Exhibit 26 marked for identification)
A. Thank you.
BY MR. TILLERY:
Q. We've handed you what's been marked as plaintiff's exhibit number 26.
Do you see that, sir?

A. I do.
Q. Can you identify what this document is?
A. It's an internal research report from Syngenta. And specifically from Syngenta CTL.
Q. Okay. Could you repeat -- read the report title and date?
A. It's:
"Paraquat Dichloride Hydrate.
"Investigating reported paraquat-induced neurotoxicity in the Alderley Park C57 black mouse: The neurochemical and pathological effects on the dopaminergic system of 3 weekly injections of 10mg/kg 1,1'dimethyl-4,4'bipyridinium (Paraquat)."
Q. And this is a report of a study that Dr. Marks did, right?
A. That's correct, yes.
Q. It says "Author(s): L. Marks"?
A. Correct, yes.
Q. That was conducted by Syngenta at its CTL laboratory in Alderly Park; right?
A. That is correct.
Q. The study was part of the paraquat mouse research program at Syngenta that was discussed in the presentations we just looked at, correct?
A. That is right, yes.

Q. And the author was -- was Louise Marks?
A. Yes.
Q. And she also served as the study director and principal investigator?
A. That is correct, yes.
Q. And Mr. Sturgess served as a contributor to the report and study reviewer, correct?
A. That is correct.
Q. Okay. And that's the same Dr. Nick Sturgess we have been talking about, right?
A. It is.
Q. Okay. Dr. Marks reports the study was initiated on April 17, 2003?
A. Yes.
Q. And the experimental phase terminated August 21, 2003; correct?
A. Yes.
Q. And that just means the experiments on these mice were terminated at that time?
A. That's right.
Q. But the study report was not issued until four years later --
A. That's --
Q. -- July 21, 2007; right?
A. That is correct.

Q. Okay. And do you have knowledge of why it was delayed for four years?

A. I have some knowledge of that.

Q. Okay. Who has all of the knowledge? Dr. Marks?

A. Dr. Marks would be able to give you more knowledge than me.

Q. You talked to her recently. Did she talk to you about this?

A. Not specifically about this point.

Q. Okay. Dr. Marks issued this report during her last week of employment with Syngenta, didn't she?

A. I can't comment on that accurately. But certainly 2007 was, I believe, the last year of her employment.

Q. Okay. The study was designed to investigate the reproducibility of claims in the literature of what?

A. Um, of the ability of paraquat to cause damage to the substantia nigra in the mouse brain.

Q. Okay. And that's exactly what she was designing this study to do, right?

A. Yes. And this was one of -- there were more than one study performed, just to add.

Q. Okay. And other independent laboratories had observed loss of striatal dopamine and the loss of dopamine neurons in the substantia nigra of mice given paraquat --

A. Correct.

Q. -- and she was trying to replicate those studies?
A. That is correct.
Q. Okay. And it involved dosing male C57Bl6J mice with paraquat once a week for three consecutive weeks, correct?
A. That is correct.
Q. And the dose was 10 milligrams per kilogram body weight of the test animals; is that also correct?
A. That is also correct.
Q. The administration of paraquat resulted in a small reduction in dopaminergic cell number, correct, in the substantia nigra portion of the brain?
A. Yes. What it says precisely is a small but non-statistically significant reduction in dopaminergic cell number.
Q. And she found that it was not statistically significant?
A. Yes.
Q. Okay. And the dopaminergic cell number in the study was counted -- counting -- strike the question.
The dopaminergic cell number in this study was counted using a technique called stereology, wasn't it?
A. Yes.
Q. Specifically, she used an optical fractionator method for stereology, didn't she?
A. That is correct.

Q. What is that?

A. It's essentially a device -- a microscopic device -- that allows you to accurately identify the region of the brain that you are looking to investigate and to count the number of cells. So it is quantitative microscopy, in other words.

Q. And she was actually nominated for what is called the Ashby Prize because she was the first scientist at Syngenta to use that technique, right?

A. Now you mention it, I think that is correct.

Q. And she was nominated by Dr. Sturgess --

A. I think that is correct, yes.

Q. -- for the Ashby Prize. And she was one of the finalists for the prize. Correct?

A. I think -- yes, I think that's right.

Q. Okay. And the reason being that she came up with this. And she had not yet been to Sunnyvale but she used this optical fractionator; right?

A. Back in 2003, that is correct.

Q. Okay. What is the Ashby Prize?

A. It was a prize which was initiated in CTL to recognize scientific achievement.

Q. Okay. In other words, to reward people who you thought had done a very good job?

A. A good technical job, yes.

Q. Yes. And who maybe were innovative, creative and doing sound scientific work?

A. Absolutely.

Q. Okay. And that's why Dr. Sturgess, who was one of the advisers to this study, recognized that work and nominated her for that award; right?

A. Yes.

Q. Okay. The studies in the independent literature to that point had reported that paraquat was neurotoxic using an optical fractionator stereology to count dopaminergic cell loss; right?

A. Yes.

Q. They had used the same technology or similar technology?

A. Yes, similar technology is the best way to describe it.

Q. All right. Now let's go back, if we can, to 2905 here. 2905.

You see the heading "Stereology", 3.9?

A. Yes.

Q. Okay. You have seen this study before, haven't you?

A. I have.

Q. You read this in preparation --

A. I have seen this study before.

Q. And you read it in preparation. It is all in your

reliance materials.

A. I certainly have read this study relatively recently.

Q. Right. In preparation for this deposition?

A. Not specifically for this, actually, no.

Q. Okay. So under the heading "Stereology" --

A. Yes.

Q. -- you see where it says "All cell counts"? I'm going to read that into the record, and you tell me if I have read it correctly when I'm finished, okay:

"All cell counts were carried out with the help of an interactive computer system and stereology software (Digital Stereology, Kinetic Imaging, UK) connected to a Zeiss Axioplan microscope. The stage itself was not automated and had to be moved from sampling point to sampling point."

Is that correct?

A. That's what it says.

Q. Okay. And if you go to 2910, at the bottom there, Dr. Marks reports that the optical fractionator method was used by the majority of studies in the independent literature. Okay?

A. Yes.

Q. And it says at the very last part of that page, if you read it:

"Our method..."

Do you see that sentence where she's talking about this? This is within her study still, isn't it?

A. Yes, yes.

Q. Okay:

"Our method, in which the counting frame is moved manually from sampling point to sampling point, has been tested for sensitivity and has produced consistent values for the total number of cells in control and MPTP treated animals ... Our technique has been proven sensitive enough to detect a 13.8% reduction in TH+ cell number following MPTP administration and therefore should be sensitive enough to detect the reported 25-30% loss ... observed following PQ exposure: ..."

Do you see that?

A. I do.

Q. Now the last sentence of that, if you read that into the record, that last sentence that starts "Nevertheless ..." and continues to the next page?

A. "Nevertheless, even small differences in methodology could lead to our system potentially being deemed less accurate than the automated systems available and this may explain in part the differences in total cell counts obtained."

Q. So she was reporting in her report that she was

using a manual system that could be the reason her cell counts were different from the independent literature that had already found that this chemical could produce loss of dopaminergic neurones in the same mouse, right?

A. At that time, that was a reasonable possibility for any discrepancy.

Q. And she was -- she was reporting that, right?

A. Yes.

Q. Putting that in the study. The independent researchers had been using an automated system. She was using a manual system. That's what she was saying?

A. That's what she said.

Q. Okay. And she said the automated set up may confer a greater degree of accuracy to the counting process; do you see that?

A. Yes, I do.

Q. All right. In contrast in this study, Dr. Marks used a manual method to move the counting frame from sampling point to sampling point, didn't she?

A. Yes.

Q. She goes on to say:

"It is therefore important to further investigate PQ [paraquat] toxicity and attempt to replicate our findings."

Correct?

MR. NARESH: Where are you?

A. Where are you now, please? Yes, at the bottom of the page.
BY MR. TILLERY:
Q. It's the bottom of the page.
A. Yes, I see, yes.
Q. Read it into the record, please?
A. Yes: "It is therefore important to further investigate PQ toxicity and attempt to replicate our findings."
Q. "Further input is required", I am reading now, follow along with me, please?
A. Yes.
Q. "Further input is required to determine whether the stereology set-up and parameters used in the present study are accurate enough to detect the reported cell loss."
Is that right?
A. That's what it says.
Q. Okay. Was that the first optical fractionator stereology study done at Syngenta?
A. This was the first one, other than the -- some of the method development which I think this report refers to, where we were trying to get the methods that we are now describing to work appropriately.
Q. And she was the first researcher at CTL to use that stereology unit technique?

A. That is correct.
Q. And she was credited with establishing the technique at CTL?
A. That's correct.
Q. And that's one of the reasons she was nominated for the Ashby Prize?
A. I think that was certainly one of the factors, I agree.
Q. Okay. I have her nomination if you want to see it. That's up to you. If you wish to, I will give it to you --
A. I don't think I need to see that.
Q. All right, okay.
She was, you would agree, concerned that the technique she used was not comparable to the technique used by independent researchers in the published literature. Would you agree?
A. She clearly wanted to make sure that we understood where methodological differences could lie.
Q. Right. She was also concerned the technique she used might be less accurate than the technique used by independent researchers in the published literature?
A. Yes, and it is important that you --
Q. Can you just answer my question?
A. Yes.
Q. Okay. And she was also concerned that the manual

technique was not as accurate as the automated, newer technique?

A. Accurate, but not necessarily sensitive. I think those are -- those are two different issues here.

Q. Okay.

Now, despite Dr. Marks' concerns about the accuracy of this study, Syngenta published the results of the study. We are going to refer to that first study by her number -- you assign numbers to studies at Syngenta, don't you?

A. Yes, we do.

Q. That number for that study was XM7229. Correct?

A. Correct.

Q. Okay. And Syngenta published the results of that study, didn't they?

A. Can you remind me where we published that?

Q. I will, okay.

(Exhibit 27 marked for identification)

BY MR. TILLERY:

Q. What number is this document you are referring to, sir, so we are clear?

A. The Bates number, do you want?

Q. No, the --

A. Oh, the reference --

Q. The exhibit number is 27?

A. Exhibit number 27.

Q. Thank you. Exhibit number 27 is an abstract for a presentation at the Society for Neuroscience Annual Meeting, October 23 through 27, 2004, in San Diego in California?

A. That is correct.

Q. Okay. The title of that is:

"Lack of Effect of Paraquat on the Nigrostriatal Dopaminergic System of the Mouse."

Correct?

A. Correct.

Q. It shows Louise Marks as the principal investigator with that asterisk underlying her name?

A. That asterisk would represent that she was the presenter of this.

Q. Oh, she was the presenter as well?

A. Yes, that's what --

Q. Okay.

A. -- the convention would normally suggest that she was.

Q. And it says "a control group of mice received injections of ... paraquat did not alter the concentrations ..."

Do you see that?

A. Yes.

Q. It comes through and says it was basically a finding

of no impact, no loss of dopaminergic neurones in a statistically significant way, right?

MR. NARESH: Objection to form.

A. Yes, that's what that says.

BY MR. TILLERY:

Q. And the abstract would have been published in the symposium materials, wouldn't it, is that right?

A. I don't know exactly what this particular annual meeting's procedures are. Certainly this is not a peer-reviewed publication.

Q. Absolutely. Is it customary that the abstract be published in the symposium materials?

A. In some meetings, yes. In other meetings, no.

Q. And it is made available -- it's published to the people who are there and there's a presentation made?

A. That is correct.

Q. Okay. The presentation would be -- would announce -- that a Syngenta study showed that there was no impact on the substantia nigra in that mouse, correct?

A. In this study that is correct, yes.

Q. Okay. All right.

Did Syngenta at any time report Dr. Marks' reservation about the study technique using a manual system?

A. Well, I was not in this particular meeting so I don't know whether Dr. Marks took the opportunity to make

that point.

Q. Did Syngenta otherwise -- did anybody at Syngenta -- not just Dr. Marks, she made it clear in her entire study which was, not to your knowledge, distributed to the attendees at that Society for Neuroscience Annual Meeting, was it?

A. This, if you are referring to the detail in this report, no.

Q. It was kept highly confidential at Syngenta?

A. At this time, that report had not even been finalized.

Q. That's right. It wasn't printed, right?

A. Right.

Q. Okay. So none of her reservations were announced, to your knowledge?

A. But normal scientific practice in a meeting of this sort is that this will lead to conversations with other research people, and I can't rule out that Dr. Marks may have had such conversations about some of those technical reservations.

Q. I move to strike your answer as unresponsive.

Would you read back my question to the witness?

COURT REPORTER: "So none of her reservations were announced, to your knowledge?"

A. Well, to my knowledge, that's true.

Q. Okay.

Do you know of anyone at Syngenta who ever publicly stated or admitted that the manual cell counting method Dr. Marks used could account for the differences in the studies?

A. I'm not aware of any such occurrences.

Q. Was that ever reported to the US EPA?

A. Um, this --

Q. Her reservations?

A. Her reservations were not reported to the EPA, no.

Q. So the principal investigator acknowledged that her manual counting technique was not as accurate as automated techniques, and could explain the difference in results, but it was never announced by anybody else at Syngenta to your knowledge?

A. To my knowledge.

Q. Okay. Did you ever report her reservations about her study technique to your knowledge?

A. Report in -- in what sense?

Q. In any sense. Publicly?

A. Well, I -- the only thing that I could offer there is that Dr. Marks certainly did discuss that as part of her discussions with Dr. Di Monte.

Q. Okay. So that's the public disclosure is to another scientist who was teaching her how to improve her technique?

A. If you call that public. I mean, that is part of normal scientific discourse as we have said many times.

Q. Okay, all right.

(Exhibit 28 marked for identification)

BY MR. TILLERY:

Q. We are giving you the full study as well as the quotes that you may want to look at.

We have handed you plaintiff's exhibit number 28.

A. Correct.

Q. Okay. What is this document?

A. It's another research report from CTL of a study, authored again by Dr. Louise Marks, again looking at the effect of neurotoxicity in the same strain of mouse using the same techniques that we were describing previously.

Q. So this is the second paraquat study that was conducted at Syngenta by Dr. Marks, right?

A. You may be right. I don't have accurate knowledge of the -- of the order of which these studies were done. But this was -- there were four or five studies in total.

Q. And this is the study Dr. Marks recommended to try to replicate the first study's findings that paraquat was not neurotoxic; correct?

A. If this is the second study, that would be the case.

Q. Okay. It was part of the paraquat mouse research program at Syngenta CTL?

A. At that time, yes.
Q. Dr. Louise Marks was the report author?
A. Correct.
Q. Did she use different techniques?
A. I'd need to read the detail of, um, what she said in here --
Q. Actually, let me withdraw that for a second. We will get to it, okay. Rather than going through in sequence, I would rather go through the whole thing in sequence and then get to the different technique.
A. Okay.
Q. Dr. Sturgess contributed to the reported -- report as a study reviewer as well, didn't he?
A. Yes, that is correct.
Q. Okay. And Dr. Marks reports that this study was initiated on September 17, 2003?
A. Correct.
Q. And it terminated on December 22, 2003.
A. Correct.
Q. Okay. That just means the mice were terminated on that day?
A. I'm not sure if that means that the experiment as a whole was terminated on the 22 December --
Q. Okay. The study report was issued three and a half years later, June of 2007?

A. That's because the reports of all of that series of studies were written up together.

Q. And they were generated in the last week of her employment?

A. As you said earlier, that is what you -- your information suggests.

Q. The study completion date is June 21, 2007?

A. The -- yes, in terms of writing the report --

Q. Instead --

A. -- yes.

Q. I should have said "the report completion date"?

A. Yes, yes.

Q. That would have been a more accurate question?

A. Yes, it would.

Q. Thank you. Okay. You have answered.

Dr. Marks announced the study purpose on page 6791, didn't she?

A. Yes.

Q. And the purpose she announced is:

"The aim of this study was to assess whether at a dose of 10 mg/kg, paraquat dichloride caused changes in the concentrations of striatal dopamine and its metabolites, and a loss of dopamine containing neurons in the substantia nigra pars compacta when dosed i.p. ..."

That is intra-peritoneally.

"... to Charles River male C57Bl6J mice."

Is that correct?

A. That is correct, and that part of the purpose is the same as the purpose of the same previous experiment.

Q. It is exactly the same, isn't it?

A. Yes.

Q. Okay. And continuing on, she says:

"This study was conducted in order to determine the reproducibility of findings from an earlier CTL study ... where no apparent effect of [paraquat] was observed at these toxicity endpoints. The stereology methodology used in the present study has been modified from that detailed in ..."

The study that she reports as XM7229. Is that the first study?

A. That's what we were talking about previously.

Q. And continuing on, she says:

"This was as a result of information obtained following a lab visit to the Parkinson's Institute, California, and discussions with Dino Di Monte's research group."

Correct?

A. Indeed, as I have indicated.

Q. And she was educated in the use of an automated stereology technique, correct?

A. That's right, as used in his laboratory.

Q. Right.

Now what were the results of this study? I think that is probably 6808?

A. Actually, I was looking at the executive summary of that --

Q. Okay.

A. -- on 6790, where it states that on this occasion, again, paraquat did not result in any significant reduction in the concentration of dopamine or its metabolites, whereas the positive control substance did. But on this occasion -- in this study, administration of paraquat did result in a statistically significant reduction, 23.7 percent.

Q. 23.7 percent reduction?

A. Yes.

Q. Okay.

A. In dopaminergic neuronal cells.

Q. And she reported that as statistically significant?

A. Yes.

Q. And that finding is comparable with the findings reported by independent laboratories who investigated the effects of paraquat on the black mouse; correct?

A. Absolutely. This is more, if you like, similar to the findings that you've described, yes.

Q. So she, effectively, in your laboratories replicated what the other scientists in the independent labs had done?

A. Yes.

Q. Correct?

A. Yes.

Q. Okay. Now she reported a 23.7 percent reduction in dopaminergic neurons found in the study, and that was comparable to the other publications finding between 25 and 30 percent reduction in dopaminergic neurons in the substantia nigra; all right?

A. Yes.

Q. And she refers in this to the McCormack studies, didn't she? Do you see that? If you want to go to the top of 6808 that will give you a reference. On the preceding page, as well. Bottom of the preceding page 6807 and to the top of the page. Do you see that?

A. Yes, yes.

Q. And she shows you the results from the preceding page, reduced by 24 percent. It is comparable to the findings in publications observing a 25 to 35 percent reduction in cell numbers in the substantia nigra?

A. Yes.

Q. And she references studies and those -- one is McCormack et al, and that is 2002.

A. Yes.

Q. Can you tell me how to pronounce the second scientist's name?

A. We pronounced it Thiruchelvam.
Q. Thiruchelvam?
A. I don't know whether that's the right pronunciation, but that's the one we used.
Q. And that is 2002; and Thiruchelvam et al 2003; and McCormack & Di Monte 2003. Right?
A. Yes.
Q. These were the studies by independent researchers in the published literature who had found paraquat to be neurotoxic in that mouse, hadn't they?
A. Yes.
Q. And these were published literature findings that CTL was trying to replicate?
A. Yes.
Q. Okay. And this study, in fact, replicated those independent scientific findings?
A. On this occasion, that is true.
Q. Those were in peer-reviewed journals as well, weren't they?
A. The publications that are cited here, yes.
Q. That she refers to?
A. Yes.
Q. And then the last -- okay, she reports the results and compares them to the XM7229 study; do you see that?
A. Yes.

Q. Look on page 6808:

"With respect to the apparent cell loss ..."

A. Yes.

Q. Okay. And Dr. Marks -- would you take a minute to read that, please?

A. Yes, I would like to do that, please.

Q. Yes. And, sir, that whole page or at least the last two paragraphs. Take your time.

A. Okay.

Q. Have you read it?

A. Yes.

Q. Dr. Marks attributes the failure to detect neuronal cell loss in study XM7229 to differences in the stereology methodology, software and hardware used in that study; correct?

A. She does.

Q. And she also reports that in the study that you have in front of you, the newer one or the more recent one, XM7258, she:

"... used one of the most widely used and accurate stereology systems currently available and the methodology was refined to further improve the accuracy of the cell count data."

Correct?

A. Indeed.

Q. "These changes to the stereology hardware and software were implemented following ... "

The visit and training by Dr. Dino Di Monte. Is that right?

A. That is correct.

Q. And that was in the Parkinson's Institute in Sunnyvale, California?

A. That's right.

Q. The previous study used "a non automated stage and used much older stereology software."

Correct?

A. Yes.

Q. Dr. Marks also notes that brain tissue in the previous study had deteriorated and thus could not be examined using the new, improved stereology equipment?

A. Correct.

Q. So what she did is she actually used the old methodology on the second group of mouse brains to count, didn't she? And when she did, she found negative results. She would have reached the same conclusion, that's what she found.

MR. NARESH: Objection to form.

A. Could you just repeat that?

BY MR. TILLERY:

Q. Of course. Did you understand or did you know that

Dr. Marks had actually repeated the same manual technique on the second round analysis, and came up with the same results as the first study.

When she used the automated technique --

A. Right.

Q. -- she got an accurate result because of the difference in techniques?

A. I don't understand that I actually knew that --

Q. But you do now?

A. But I do now.

Q. All right. She re-examined the tissue with new, improved stereology equipment and found the loss of neurons in the substantia nigra that she reports here?

A. Okay, that's fine.

Q. Now, did -- strike that.

Did Syngenta send Dr. Marks to Sunnyvale?

A. Yes.

Q. Okay. Did Syngenta ever publish the results of the second study?

A. Again, not that I remember, unless, like on the previous occasion, it was at a scientific meeting. But I've no evidence for that.

Q. Did Syngenta ever notify the Society of Neural Science where the first study was reported to tell them that the first study was wrong?

A. I have no evidence we did that.
Q. Okay. Based upon what you have seen from these two studies, would you agree with me that the results of the first study was wrong?
A. The -- it points to the possibility that the first study was wrong.
Q. Do you have any reason to dispute her statements that the difference in automated versus manual technology accounted for the difference in the results?
A. No reason to dispute that at all.
Q. Okay. Did Syngenta ever inform the Environmental Protection Agency about the loss of dopaminergic neurones found in the study?
A. In this study, no, because they were not new findings.
Q. I am just asking whether they did.
A. Right.
Q. Did they?
A. So far as I'm aware, they did not.
Q. Okay. So you weren't aware that on December 13, three months ago, your counsel notified them of this study --
A. I thought you meant at the time, sir, so I --
Q. Oh, that would be the logical thing to do --
A. Right.

Q. -- would be to tell them.

Would you think it would be appropriate to wait 16 years and a half -- 16.5 years -- to tell them?

MR. NARESH: And I will object to the attorney commentary.

BY MR. TILLERY:

Q. We're just asking you. Is 16.5 years an appropriate time period to make a report?

A. I believe it was still the correct decision at the time that these findings were not reportable.

Q. Okay. So when it changed and suddenly you decided to notify the US EPA on December 13, 2019, sixteen and a half years after the report was finalized --

A. Well, that was not a decision that I was involved in taking.

Q. Okay. Would you have done that?

A. I wouldn't want to comment on that. I'm not an expert in whether these things should be done.

Q. You don't want to go down that path, do you?

A. I --

MR. NARESH: I object to the form, argumentative.

BY MR. TILLERY:

Q. Okay. So can you explain to me why there was a 16.5-year delay?

A. I don't want to venture in any speculative way,

because I'm not involved in that process.

Q. Were you aware that I wrote your counsel a letter demanding that they notify the US EPA?

A. I saw that letter.

Q. Okay. That might account for why they did it a week later, do you think?

MR. NARESH: Objection to form, argumentative.

BY MR. TILLERY:

Q. Do you think there's a connection?

A. I wouldn't want to comment on that.

MR. TILLERY: Okay. Let's take a lunch break. Is this a good time? Or we can keep going --

MR. NARESH: Let's go off the record for a second.

THE VIDEOGRAPHER: Off the record at 11:49.

(Break taken.)

THE VIDEOGRAPHER: We are back on the record at 12:08. This is now media number 3 in the deposition of Philip Botham.

You may continue.

(Exhibit 29 marked for identification)

BY MR. TILLERY:

Q. I'm directing your attention, sir, to plaintiff's exhibit 29. Can you tell us what that is?

A. Again, another study on paraquat dichloride

investigating the reported paraquat-induced dopaminergic neurotoxicity in the black mouse.

Q. And this was at Central Toxicology Laboratory Alderley Park, right?

A. It was.

Q. And the principal investigator was Louise Marks?

A. That is correct.

Q. And the study number is XM7371?

A. Yes.

Q. This was a study that was part of the paraquat mouse research program at Syngenta CTL, right?

A. At that time, yes.

Q. Dr. Sturgess again was the study reviewer?

A. Correct.

Q. The study was initiated on April 26th, 2004?

A. Yes.

Q. And was terminated on November 17, 2004?

A. Yes.

Q. And reported in June 2007?

A. Correct, along with the other reports we have been discussing.

Q. Right.

If you would go to 911 in the "Study Design" section, Dr. Marks reports that the purpose of the study was to investigate whether the loss of dopaminergic neurons in

the substantia nigra observed in XM7258 could be further enhanced by increasing the frequency of dosing; correct?

A. Correct.

Q. And then if you go to the "Results" section, Dr. Marks reports dosing of paraquat resulted in a statistically significant loss of dopaminergic neurons in the substantia nigra pars compacta of mice; correct?

A. Correct.

Q. But the increased doping frequency did not result in a greater magnitude of cell loss, correct?

A. Correct.

Q. At the bottom of that page, that is on 911, Dr. Marks reports:

"These results support the findings of study XM7258 and demonstrate that paraquat, when administered to [C57Bl6] mice ... induces nigral, but not striatal, toxicity."

Correct?

A. Correct.

Q. And nigral toxicity is a form of neurotoxicity, isn't it, sir?

A. It is an effect on that part of the -- of the brain, yes.

Q. The results support the findings that paraquat is neurotoxic, correct?

A. They support the possibility that paraquat could be

neurotoxic, yes.

Q. Support the findings of it as well, at least in mouse, right?

A. The findings are now becoming more replicable, yes.

Q. As a matter of fact, this result replicates the studies in the independent literature she found as well, correct?

A. It does. As did the previous one. Although, interestingly, there was no exacerbation of the effect compared to the previous study.

Q. All right. And if you go to 25, Dr. Marks reports:

"The present study has confirmed that administration of 3 weekly injections of 10 mg/kg paraquat dichloride to ... C57Bl6J mice, results in a statistically significant reduction in the number of ... dopaminergic neurons in the [substantia nigra] ..."

Correct?

A. That's what that says, yes.

Q. Yes. She further reports this reduction is comparable with the loss reported in the public literature?

A. Yes.

Q. And she references several studies by independent researchers, right?

A. Yes.

Q. And who does she list as the source: McCormack et al

2002; McCormack & Di Monte 2003; correct?

A. Correct.

Q. Did Syngenta ever publish the results of this study in a peer-reviewed journal?

A. I'm not aware that it did.

Q. Okay. Did the results of this study ever appear anywhere in any public literature?

A. I am not aware of -- of whether that actually did happen.

Q. Did Syngenta ever inform the United States Environmental Protection Agency about the loss of dopaminergic neurons observed in this study?

A. At the time of this study, there was -- this was not reported to the EPA, that I do know.

Q. This was reported sixteen and a half years later in December 2019; correct?

A. As you were indicating on the previous occasion, yes.

Q. You saw that report, and you saw my letter demanding that it be reported?

A. I saw your letter, yes.

Q. You saw my -- I'm sorry, strike that.

You saw my letter and you saw the report that was filed?

A. I'm not sure that I've seen the report.

Q. Okay. Do you know who made the decision to file the report?

A. I don't.

Q. Did Syngenta ever disclose the study to any other regulatory agency around the world?

A. I -- I'm not able to answer that accurately. I am not sure.

Q. Okay. You've dealt with other regulatory bodies yourself, haven't you, outside the United States?

A. I have.

Q. You haven't dealt with the US EPA?

A. I have not engaged with the US EPA on this issue, no.

Q. Okay. And you have engaged with other regulatory authorities?

A. Yes.

Q. Okay. Which countries have you dealt with?

MR. NARESH: You are asking him personally?

MR. TILLERY: Yes.

A. Right. So for me personally, I have had some engagement with Brazil. But I have had -- there has been indirect contact with other -- Australia by members of my team, but not me personally.

BY MR. TILLERY:

Q. Are those the only two countries that you know of

that -- that you interact with in terms of this?

A. Well, certainly in terms of personal interaction, there were no other countries.

Q. Do you know of any other regulatory bodies in other countries besides Brazil and Australia?

A. There are other regulatory authorities who will have had -- where there will have been discussions about this topic.

Q. You don't know whether this study was reported to them?

A. I can't give you any indication of that, I am afraid.

Q. Was it given to Brazil?

A. I don't think it was specifically given to Brazil.

Q. Was it given to Australia?

A. I don't believe so.

Q. Are you aware of any disclosures of Dr. Mark's study results to any regulatory agency in the world?

A. I am not aware of that.

Q. When Dr. Marks -- strike that.

When Dr. Marks reported the results of the studies to her superiors, her superiors did not want her to accept the findings that paraquat causes neuronal cell loss in the black mouse; is that a fair statement?

A. I would not say that was a fair statement because

I don't know what your evidence is to -- to back that up.

Q. Okay, okay.

Were you aware that her superiors wanted her to find a flaw in her methodology?

A. Again, I would not -- I would like to understand what the basis of that is.

Q. Okay. Before we get into the documents, because I promise you I will -- after lunch I will share that with you, I will -- were you aware that they were doing that?

A. No, I was not aware that there was such -- such conversations were going on at the time.

Q. Have you ever heard of a scientist being asked to find -- search for flaws in her own methodology in order to disprove her own scientific results?

A. Well, put that way, I think that is something that you wouldn't expect. But you would expect that people would be -- would say: are you really sure that the methodology that you are using is actually being used as well as possible?

Q. But you've studied -- you've looked at these studies and this is a scientist who has gone through -- who has criticized her first result because it was manual technique, who has gone to the trouble of educating herself at Sunnyvale, California, in a -- in a more automated technique in order to enhance the accuracy of her scientific findings.

For that, she's been recognized with the highest prize for professionalism that your company even recognizes; correct?

A. Correct.

Q. Okay. Now in that context, right, can you imagine a scientist being told, of that type, to discredit her own findings?

MR. NARESH: Objection to form.

A. I would personally never put such a -- a proposal to a scientist.

BY MR. TILLERY:

Q. You wouldn't do that, would you?

A. I would not do that personally.

Q. Okay. And that would be unethical, would you agree?

MR. NARESH: Objection to form, scope.

A. As you -- as you actually stated it, that would, to my mind, be an inappropriate way of dealing with a scientist.

BY MR. TILLERY:

Q. All right.

Do you, as Syngenta's representative who prepared to testify on the subjects that included what we are talking about here today, need to know what evidence I have before you are able to testify about what Dr. Marks' superiors wanted?

A. As I said a minute ago, yes, I would like to see

that evidence.

MR. NARESH: Steve, just so we have a clear record, you mentioned the Marks studies. You are referring to the three studies you have introduced as evidence?

MR. TILLERY: No, all of the studies. Every one she did for Syngenta.

MR. NARESH: Including the studies you have not yet introduced?

MR. TILLERY: Yes.

MR. NARESH: All right, then --

MR. TILLERY: I'm going to go through them all.

MR. NARESH: Okay. Well, I'm concerned that there might be confusion from the witness because you asked some questions about disclosure to the EPA --

MR. TILLERY: Yes.

MR. NARESH: -- and referred to the Marks studies. And if you are referring to all, as opposed to the ones you have introduced, I think there maybe some confusion on the record. So I don't know if you want to --

MR. TILLERY: I don't want an incorrect record. So if I -- if my question did -- was too broad and encompassed it, I am willing to allow you to have him correct that so he's not impeached by it later.

MR. NARESH: You want to do it now or later --

MR. TILLERY: We can do it later. Then you can

use the hour time to fix that with him. I'm happy to let you do that.

MR. NARESH: Let me put it this way, I do anticipate having more fulsome redirect than just on that question. Would you want me to do that, do all of it at the conclusion of your examination, or do you want me to do that at some other point?

MR. TILLERY: Probably at the conclusion of the examination.

MR. NARESH: I will reserve the right to do redirect on that point and all of the points at the conclusion of your deposition.

MR. TILLERY: I'm not saying that I agree that you are entitled to do that, so that you understand, okay?

MR. NARESH: Okay.

MR. TILLERY: Thank you.

BY MR. TILLERY:

Q. Were you aware that her superiors wanted Dr. Marks to come up with other explanations for why paraquat could have caused the same findings that were not consistent with it being a potential cause for neuronal cell loss?

A. I can't speak about the specific conversations at the time. But such conversations were certainly had at a later time which I was involved with, when we continued to find an apparent loss of dopaminergic neurons, and which

indeed we have subsequently published.

Q. Well, let us go to the next exhibit.

(Exhibit 30 marked for identification)

BY MR. TILLERY:

Q. Now, on that last point that you made, could you tell me where Syngenta published a Syngenta study finding loss of dopaminergic neurons after the use of paraquat?

A. Yes.

Q. Where?

A. In the neurotoxicology publication of Breckenridge et al. One of the studies that was reported in that showed an apparent loss of dopaminergic neurons.

Q. And which study specifically, could you tell us on the record, please?

A. I would have to go back and look at the publication to see exactly what study number it was referred to in that, but it was -- I know the dose level was 15 milligrams per kilogram of paraquat.

Q. Okay. Now look at exhibit number 50, please -- I'm sorry, number 30.

A. 30.

Q. Can you read into the record the title of this document?

A. "Notes of discussions with Lewis Smith to brief him on the latest Parkinson's disease findings on

3rd December 2004".

Q. And present were, can you tell us?

A. Lewis Smith, Nick Sturgess, Louise Marks and Mike Clapp.

Q. And Nick Sturgess and Louise Marks presented the latest findings, correct?

A. That's what the next line says.

Q. Okay. And the first bullet point of number 1 paragraph says:

"Is the loss of neurones indicating generalised neuronal toxicity in the brain rather than a specific effect in the Substantia Nigra? This is not ... clear, however data from other brain areas (e.g. hippocampus) suggest that it is specific, but it may be difficult to detect changes in dopaminergic neurone number in other brain regions where the density of dopamine containing neurones is lower than in the [substantia nigra], thus making a loss of neurones more difficult to detect."

Right?

A. Yes.

Q. Okay. Lewis Smith, who is listed here, is the same Lewis Smith that we have been talking about, right?

A. He is.

Q. And what was his role at that time?

A. I think in 2004 it would be when he was the head of

the Central Toxicology Laboratory.

Q. Who is Mike Clapp?

A. Mike Clapp was the product toxicologist for -- based at CTL who had paraquat as one of his product responsibilities.

Q. Is he still employed with the company?

A. He is not.

Q. Where is he now?

A. He's retired.

Q. Okay. The purpose of the meeting was to brief Lewis Smith regarding the latest Parkinson's disease findings from Dr. Marks; correct?

A. That's what the title suggests.

Q. Now if you would look at page 2 of that two-page document, that's dated what, if you look at the bottom of the second page?

A. 7 December 2004.

Q. 7 December 2004?

A. Yes, if this is an English document, the --

Q. Okay. All right.

Were Dr. Smith and Dr. Clapp, Louise Marks' and Sturgess's superiors?

A. Dr. Smith, yes; Dr. Clapp, no.

Q. But Dr. Smith was their boss?

A. He was the head of the laboratory at that time.

Q. He was the head of the entire operation?
A. I believe at that time that is correct.
Q. Okay. So if you would read this, does it report that Dr. Smith wanted to have the research team investigate other reasons for dopaminergic neuronal death in paraquat-dosed mice?
A. I would just like to read it a little bit more if I could.
Q. Sure, take your time.
A. Okay. Would you like to repeat the question?
Q. Of course, thank you.
The question -- the first question I would ask is whether Dr. Smith wanted the research team to investigate other reasons for dopaminergic neuronal cell death in paraquat-dosed mice? He was looking for other explanations?
A. He was suggesting that some methodological things needed checking and that there were other hypotheses that might explain the findings.
Q. Trying to think of other ways this could account for the results?
A. Yes, to see -- yes.
Q. Okay. Right. That's what he was doing.
Because Syngenta had replicated the paraquat neurotoxicity findings in the independent published literature, correct?

A. Yes.

Q. And unless those findings could be attributed to a cause other than paraquat, Syngenta had established a sound scientific basis for the claims made in the public literature that paraquat is neurotoxic; correct?

A. That would be the implication of the replication and confirmation.

Q. And those claims were a threat to Syngenta's aspirations for paraquat too, weren't they?

A. That would undoubtedly have led to discussions about the -- paraquat and how it should be continued, I agree.

Q. In fact, a threat to the bottom line of the company?

A. Well, that's a -- possibly what some people had in mind. Certainly it wasn't, within the scientific community, something that was prominent.

Q. Well, I mean, look at the last paragraph of the conclusion. He says, second sentence, "HA."

Who is that? At that time, what is HA?

A. That would be "Health Assessment".

Q. "[Health Assessment] have a responsibility to create the scientific understanding and there will be no intention to slow down this understanding, although business risk will need to be considered in the decision making process."

"Business risk" means selling paraquat, doesn't it?

A. It does.

Q. Right.
A. But it did reinforce the point I was making about creating scientific understanding, so I think it --
Q. Right.
A. -- said the same as I did.
Q. So HA at Syngenta had the responsibility to create the scientific understanding regarding paraquat's neurotoxicity?
A. That's right. That was our accountability.
Q. The business threats which needed to be considered in the decision-making process for creating the scientific understanding of paraquat was that they could further prove paraquat was neurotoxic. That was the business risk?
A. Of course.
Q. Yes. There was a business risk that paraquat would be banned in more countries if it were established by additional tests; correct?
A. I would put it differently. It was always our role, in health assessment as it was called then, to -- to say if there was a scientific basis for there being a risk associated with the product, we would want that to be understood by the business.
Q. How many of these studies need to be repeated before you're happy with the fact that this stuff causes brain injury?

A. That's a -- you can never put an exact number on that. And don't forget, this was still very much at the forefront of research which is why, um, Louise Marks received that award, because, you know, this was new technology. We were still understanding how it worked.

Q. It was new technology with you. It wasn't new technology around the world, was it?

A. Even around the world, if we had -- conversations were made as an example when we spoke to Professor Nyengaard, I think I mentioned his name yesterday, where -- which said this is technology where we are all still learning how to use it properly.

Q. Let me ask you: you knew that this automated technology was already being used by the independent researchers before this, right?

A. Yes.

Q. They had access to this; they were using it.

Do you know how long they had it in use before you got it?

A. I can't answer that question.

Q. You don't know?

A. I don't know.

Q. Let me ask you this. Do you think had you wanted to get it at the time that these independent researchers got it, you could have done exactly the same thing at CTL

laboratory?

A. Of course we could have done that, yes.

Q. Sure. And hired the best researchers in the world to do it?

A. We could. But there was no reason for us to do it, because at that time there were no findings in the literature. So things go in a -- in an order.

Q. Okay.

And this technology, stereology, wasn't the first technology the scientists could use to detect the death of dopaminergic neurons in the substantia nigra, was it?

A. Well, there are some other pathological techniques you could use, of course.

Q. Of course. And they long pre-dated stereology techniques, didn't they?

A. They are, but those pathological techniques are not necessarily specific to the cells that you are -- that are involved here.

Q. Okay.

THE VIDEOGRAPHER: In that case, we will go off the record at 12:33.

(Break taken.)

THE VIDEOGRAPHER: In which case we are back on the record as of 1:26.

You may continue.

(Exhibit 31 marked for identification)

BY MR. TILLERY:

Q. Sir, we have handed you what's been marked as plaintiff's exhibit number 31.

This is Bates range Syngenta 1981435. Do you see that?

A. I do.

Q. Okay. And the top of this page says what?

A. "Thoughts On Options For Challenging The PQ and C57Bl6 Mouse Model."

Q. And if you look on the second page, it's got a reference to Nick Sturgess and Louise Marks, 6 December 2004. Do you see that?

A. I do.

Q. Okay. Are these notes Drs. Sturgess and Marks made on December 6 regarding challenging the paraquat results they had seen in the C57B6 mouse?

A. It suggests that this is a record of their conversation.

Q. Okay. And these notes were made one day before the meeting with Dr. Smith on the paraquat results in the C57 black mouse, weren't they?

A. They were made -- well, that meeting itself was on 3 December.

Q. On the 3rd?

A. Yes. So the meeting minutes were dated 7 December, but the title says that the meeting itself was on 3 December, if I have read this correctly.

Q. This meeting minutes says 6 December 2004. And you read the other one as being --

A. I do, sir, yes.

Q. -- later?

A. Yes. Well, earlier --

Q. Earlier, right?

A. So the meeting here is earlier, yes.

Q. So Lewis Smith, from your prior review of the meeting with Lewis Smith, was of the opinion that CTL should aggressively challenge the results in the Marks studies; do you agree?

A. And by "aggressively", it is to get on with it.

Q. Yes. He wanted them to aggressively challenge the methodological issues with the --

A. That was one of the factors, yes.

Q. Okay. And did Lewis Smith ask Drs. Sturgess and Marks, or both, to come up with ways to challenge the paraquat mouse model in preparation for the briefing?

A. Which briefing are you talking about?

Q. Assuming you are right about the times, then it wouldn't be a briefing: this would be a meeting that occurred after they met with Dr. Smith, is that what you are

thinking?

A. Well, I'm taking it to be that way. That they have met with Dr. Smith, and maybe this was Dr. Sturgess and Dr. Marks saying, "Well, where do we go from here?"

Q. So your meeting -- the first meeting with Dr. Smith, and then this is notes of meetings that these two scientists had after they met with Dr. Smith, is that what you are saying?

A. If the dates on these pieces of paper are accurate, then you would conclude that.

Q. Okay. So if you look at the fifth bullet, it says Drs. Sturgess and Marks note, on the fifth one down:

"It has not been reported that C57Bl6J mice are more sensitive to PQ induced toxicity than other strains of mice. In fact, given that the animals have been obtained from different suppliers including our own data, would suggest that subtle differences between strains in their susceptibility to PQ are unlikely."

A. Correct, yes.

Q. So one of the things they were looking at was to try to change the mice to come up with different results, potentially?

A. One of the things they were looking at was asking the question about is there strain sensitivity, which may be important.

Q. Okay. The next says:

"The only studies we are aware of involving non-C57Bl6 mice with [paraquat] relate to studies investigating PQ induced cell loss in alpha synuclein over-expressing animals."

Correct?

A. Yes.

Q. So Syngenta was aware of studies involving other strains of mice where paraquat induced cell loss occurred, right?

A. Yes.

Q. And this was neuronal cell loss, correct?

A. Yes, that would be correct.

Q. And this paraquat induced neuronal cell loss occurred in mice who were over-expressing alpha synuclein?

A. That's what the Swiss Webster was describing, yes.

Q. And over-expressing alpha synuclein means the same thing as upregulation of alpha synuclein, would you agree?

A. It is expressing more of the protein, yes.

Q. You are aware that upregulation of alpha synuclein is part of the Lewy body pathology in human Parkinson's disease patients, correct?

A. Yes.

Q. Syngenta was fully aware of that fact in 2004 --

A. Yes.

Q. -- would you agree?

When was that first known to be true?

A. I can't give you a date as to when that was first known.

Q. Okay. The next bullet point says:

"If we were concerned that the pigmented mouse was more sensitive to [paraquat] than other strains, one option would be to dose 10mg/kg [of paraquat] to variety of different mouse strains including BALB/c, Swiss Webster and CFI, and observe the extent of the neuronal cell loss."

Right?

A. Yes.

Q. What are those?

A. They are different strains of mice.

Q. Okay. Then it says, "however" -- it goes on to say:

"However, this would generate a PRF since no one else has dosed [paraquat] to these strains."

A. That is absolutely correct.

Q. And a PRF there means what?

A. As we were discussing this morning, the potentially referable findings under 6(a)(2).

Q. So they didn't do that, because had they made the finding they would have had to report it?

A. That doesn't say that. It says:

"However, this would generate a PRF ..."

Q. And do you know if they ended up doing that study?
A. I don't believe that they did.
Q. Okay. Do you think that the reason they didn't do it is because it might generate a PRF?
A. I don't know what the full reasoning was. It may have been taken into consideration but I wasn't involved in these discussions.
Q. Okay. Do you agree with their conclusion that there was not strain sensitivity?
A. I -- it depends whether you are looking at that question as it was seen at that time or with the benefit of hindsight, because with the benefit of hindsight more research has shown that there is perhaps some strain -- difference in the sensitivity.
Q. Statistically significant strain sensitivity?
A. That is on the borderline, I have to say.
Q. Okay. Are PRFs something that Syngenta generally wants to avoid?
A. We don't avoid them if it actually is doing the right scientific study.
Q. Okay. The next page -- flip this over -- fifth bullet down says:
"The reported PQ induced nigrostriatal toxicity is not just mouse specific."
Do you see that?

A. Yes.
Q. And then it cites another name you are going to have to pronounce for me.
A. Chanyachukul.
Q. We probably should spell that for the reporter, please?
A. C-H-A-N-Y-A-C-H-U-K-U-L.
Q. "... (work in part carried out at University of Nottingham) investigated the effect of acute [paraquat] exposure to Wistar rats, demonstrating neurochemical and behavioural deficits, which were attenuated by the administration of L-valine."
Q. What is L-valine?
A. It is an amino acid.
Q. "Also neurochemical, pathological and behavioural changes have been reported following intracerebral injection of [paraquat] into rats."
Correct?
A. Yes.
Q. Do you agree with that statement?
A. Yes, those are published papers.
Q. Okay. So Syngenta knew the same types of results would occur in rats as well, wouldn't it?
A. There was clearly a potential for that to be the case, yes.

Q. Drs. Sturgess and Marks note:

"The options for challenging the [paraquat] mouse model would appear to be somewhat limited."

Okay?

A. That's what it says.

Q. Dr. Sturgess and Dr. Marks considered the options to be challenging -- strike that.

Dr. Sturgess and Dr. Marks considered that the options to challenging the methodology of the paraquat mouse model appeared very limited, didn't they?

A. Yes. And I think what was meant there is challenging its relevance to human Parkinson's disease potential from paraquat.

Q. What options for challenging the paraquat mouse model did they provide?

A. Well, what was being discussed at the time, and certainly was discussed subsequently, was whether there were more relevant models. The rat was discussed frequently as -- as another option. Indeed we did go on to do a rat study ourselves.

Q. Well, didn't they say in the same bullet point there, they wrote:

"The best way of challenging the model would be based on the dose, duration and route of exposure ..."

A. Indeed, and that was going to be my second point.

So human relevance is much more going to be directed to how you administer the compound, indeed.

Q. They are not challenges to the methodology of the model, so much as changing certain aspects of the model?

A. Yes, it is back to what we discussed this morning: the relevance of your model is always an important consideration.

Q. What is NOEL?

A. A no effect level.

Q. What does that mean?

A. It is the dose that when you do a toxicology study and you use more than one dose level -- so in other words you feed or inject different concentrations of a chemical to your animals -- it is the dose at which you saw no effects.

Q. And the very next bullet point says:

"I still believe our best defence is to conduct an exposure based risk assessment based upon a dietary/dermal NOEL using the mouse model of neuronal cell loss."

Correct?

A. Correct.

Q. Best defense?

A. And that -- if I may, again I would say that that was being positioned at the time on the assumption that the effect is real. It is reproducible. You know, it would be perhaps not easy to deny it with the information that was

available at that time.

But is that model that's being used relevant to humans because it is an injection model? And actually, even if you do see an effect at a high dose, if you can find a dose which is still orders of magnitude above anything a human would be exposed to, then that would say that that -- your concern would be reduced.

Q. I move to strike the answer as unresponsive.

So it says, my question was:

""I ... believe our best defence is to conduct an exposure based risk assessment based upon a dietary/dermal NOEL using the mouse model of neuronal cell loss."

Doesn't it?

A. Yes.

Q. And it says the word "defence", that was the question I had. "Defence", do you see that?

A. Yes.

Q. And defense is defense against the fact that the study showed damage to the substantia nigra and to the production of dopamine by the dopaminergic neurons?

A. No, I disagree, sir. The defense at that time, I am sure, was not to say we are trying to discredit the possibility that you see the neuronal cell loss in the conditions that we have been talking about; but actually to say -- to, if you wish, discredit its relevance to human

risk assessment. And that's why they used "exposure based risk assessment" as a shorthand way of describing what I just said to you.

Q. Well, aren't they really saying that Syngenta should accept the results of the Marks studies and the findings of independent researchers that paraquat causes neuronal cell loss? Isn't that what they were suggesting?

A. I don't dispute that and actually agree with it.

Q. And you agree with it too?

A. Indeed. And as I said to you this morning, when we continued our work and published the Breckenridge paper, that was a position we were first in. We again replicated that finding.

Q. And when you found that -- in the Breckenridge paper, you found that it caused neuronal cell loss in the substantia nigra, didn't you?

A. In one study at one dose level.

Q. In one study and one dose level in one type of rat, I apologize --

A. Mouse.

Q. A rat, right?

A. Mouse.

Q. Mouse, sorry, excuse me. In one type of mouse you found it and it was attributable to paraquat exposure?

A. It appeared to be at the time. But then, as that

Breckenridge paper says, we did many more experiments as part of that publication and in none of the others were we able to replicate it nor were we able to see any evidence that you would -- that other pathologists who we were now consulting with said you should see if that was a genuine death of cells. Because pathologists were telling us that if cells were dying other things would happen around them.

Q. I just wanted to clarify one thing. My question was really this -- I move to strike your answer as unresponsive.

My question was simply this: did you find damage in that single mouse study that was reported there as a result of paraquat exposure in the mouse?

A. Yes. In that single study, yes.

Q. Okay. And that was reported, correct?

A. As part of our publication.

Q. Okay, all right.

Would you agree that instead of challenging the results, Syngenta should use them as the basis for a human health risk assessment of paraquat?

A. Now that we have done many more experiments, including those we have just been referring to in neurotoxicology, I believe quite strongly that our position is that the replicability has not been established, so I don't think it would be appropriate to do that.

Q. Okay.

You see the next section says, bottom of the second page:

"Potential experimental follow-ups suggested by Lewis Smith include:

"Can the changes observed be accounted for by tissue shrinkage owing to the diuretic effect of PQ? Suggests dosing with a diuretic to look for changes in ... cell counts."

Do you see that?

A. Yes, yes.

Q. Okay. And it says:

"Are the effects observed with the mouse model irreversible? Conduct a ip study ..."

What does "ip" mean?

A. Intra-peritoneal.

Q. Intra-peritoneal study:

"... at 3 x 10 mg/kg, and assess the extent of neuronal cell loss 7, 14, 28, and 90 days post final dose."

A. Yes.

Q. "This will confirm the loss detected so far is irreversible."

Do you see that?

A. I do.

Q. Okay. And those were suggested by Lewis Smith, apparently, from this report --

A. From what this says, yes.

Q. Okay.

He suggested -- he being Lewis Smith -- suggested dosing mice with a diuretic to determine if the loss of neuronal cell loss could be attributed to the diuretic effect of paraquat on tissue samples; right?

A. Yes.

Q. That was one of the theories that they had for why these results could have come back the way they did?

A. Indeed, and it was --

Q. It's a diuretic?

A. It was included in the notes of that other meeting we were talking about.

Q. Right. And Lewis Smith has also suggested conducting a paraquat mouse study with animal sacrifice at 7, 14, 28 and 90 days to confirm whether paraquat induced neuronal cell loss was irreversible, whether it was permanent?

A. Yes. And an experiment of that sort was actually subsequently done.

Q. It was done, wasn't it?

A. Yes.

Q. Okay.

MR. NARESH: Steve, just as housekeeping thing, can I move some of these --

MR. TILLERY: Yes, you do whatever you need.

(Exhibit 32 marked for identification)

BY MR. TILLERY:

Q. The next exhibit is number 32, correct, sir?

A. That is correct.

Q. What is this?

A. This is another study in the series of studies conducted with the title "Paraquat Dichloride Hydrate", looking at, in this case, the time course and reversibility of dopaminergic cell loss in that same mouse model following the administration of paraquat.

Q. And this is XM7480, right?

A. That is correct.

Q. And it started June 21, 2007, right?

A. That was when it was reported.

Q. I'm sorry, that was the report date. The study dates were February 18, 2005, and the termination date was September 1, 2005; right?

A. Which I think it must be misprint -- no, it may not be. I beg your pardon, forgive me. Yes, that is probably correct, yes. Yes.

Q. Okay. This study was designed to investigate the time course and potential reversibility --

A. Yes.

Q. -- of the loss of dopaminergic neurons in the

substantia nigra after three months of dosing; right?

A. Yes.

Q. And using paraquat?

A. Well, if I may, I believe -- I would just like a little time to double-check this.

Q. Go ahead and take your time.

A. Okay.

Q. If you look at 2793 under "Purpose"?

A. Yes. So I think I would just need to, if I've heard you correctly, slightly qualify. So paraquat was given as three weekly injections but then it was not continued to be administered. I believe the animals were then rested, if you like, and sacrificed at different time points.

Q. Yes. For clarity in the record, the purpose set out at page 2793 by Dr. Marks was:

"The aim of this study was to investigate the time course and potential reversibility of nigrostriatal effects following 3 weekly injections of 10 mg/kg paraquat dichloride by assessing dopaminergic cell loss in the [substantia nigra] and concentrations of striatal dopamine and its metabolites at 7, 28 and 90 days after the final dose of paraquat."

A. That is correct, yes.

Q. That's what you --

A. That's what I was qualifying, yes.

Q. In the previous studies, Dr. Marks had observed loss of dopaminergic neurons in mice dosed with paraquat and sacrificed seven days later, correct?

A. Yes.

Q. In this study she observed loss of dopaminergic neurons dosed with paraquat, didn't she?

A. Yes.

Q. And the loss was statistically significant too, wasn't it?

A. Yes.

Q. The study also measured the loss of dopaminergic neurons 28 and 90 days after the last dose was given?

A. Yes.

Q. And the degree of dopaminergic neuron loss at 28 and 90 days was similar to the loss at 7 days, wasn't it?

A. That is correct.

Q. In other words, the animals did not recover dopaminergic neuron function after a passage of 28 or 90 days?

A. That's right. Using that measurement they stayed the same, correct.

Q. The loss of dopaminergic neuron function was permanent throughout the 90 days of the study?

A. That's right.

Q. It was not reversible, is what you found?

A. Within that timescale, it did not reverse.

Q. The last paragraph, okay -- and that is 2792 -- Dr. Marks says:

"These results support the findings of two previous CTL studies XM7258 and XM7371 ... and demonstrate that paraquat, when administered to C57Bl6J mice ... would appear to be capable of inducing nigral but not striatal toxicity."

Right?

A. Yes.

Q. And nigral toxicity is a form of neurotoxicity again?

A. Nigral is meant to be the substantia nigra.

Q. The substantia nigra, yes, okay. The studies suggest -- support -- the findings that paraquat is neurotoxic, don't they?

A. They support that, that finding yes.

Q. Yes. This is the third Syngenta CTL study that found that paraquat causes loss of dopaminergic neurons; correct?

A. Correct.

Q. And the third Syngenta CTL study where Dr. Marks found the loss of dopaminergic neurons were comparable to the loss reported by independent researchers in published scientific literature; correct?

A. Correct.

Q. The third Syngenta study to repeat the results of independent researchers' finding that paraquat is neurotoxic?

A. As specifically defined by the loss of dopaminergic cells. There were other findings that were not seen. Like the loss of dopamine has not been seen consistently in the studies --

Q. But in the limited context in which I asked the question, to repeat the findings means replicate the findings?

A. In that area, that is correct --

Q. So this is the third one in a row to replicate the work by independent researchers?

A. Can you just say that again?

Q. By independent researchers?

A. Yes.

Q. And it also means, for these purposes, that these studies reproduce the findings of the independent researchers?

A. They do.

Q. If you look at 2807, the first full paragraph, sir, tell me when you are there.

Dr. Marks says:

"Our data would appear to be supportive of the hypothesis that a sensitive subpopulation of dopaminergic

neurons may exist which are vulnerable to paraquat induced toxicity."

Do you see that?

A. I do.

Q. Do you agree with that?

A. That's what it says.

Q. Okay. Did Syngenta publish the results of this study in any journal?

A. I'm not aware that we did.

Q. Did Syngenta publish this anywhere, or post it, or present it, or talk about it in any scientific symposium?

A. I'm not sure that we did that.

Q. Okay. Are you aware of anybody ever saying they did?

A. I'm not aware.

Q. Did Syngenta ever disclose this study to any regulatory authority in the world, including the United States Environmental Protection Agency?

A. This study was the subject of a disclosure to the EPA --

Q. You did report it, didn't you?

A. We did.

Q. Okay. When did you file that report?

A. I don't have the date to hand, so I would need to check the record of that date.

Q. Okay. Why did you report this one?
A. Because the conditions -- some of the conditions of the study were different to what had been used by other researchers. So it fulfilled some of those detailed criteria that we were talking about this morning under 6(a)(2).
Q. Do you not know when you filed it with US EPA?
A. I can't give you the date off the top of my head.
Q. It certainly wasn't when the study was done, was it?
A. It was obviously after the study had been interpreted.
Q. It was years before it was reported --
A. It was before it was reported, yes. Yes.
Q. All right. You reported it as an adverse finding?
A. Yes, as defined by 6(a)(2), yes. Yes, where adverse --
Q. Adverse effect?
A. Adverse effect seen in -- because it was seen with different experimental conditions.
Q. Why was it considered to be an adverse effect?
A. Because we had, as we have been discussing, concluded that we now appeared to have a replicable finding showing loss of dopaminergic neurons which could be interpreted as neurotoxicity. And the reason that it was reported -- not reported before, as we said, is because up

until that point that was not a new finding. Now the conditions of the experiment had changed which meant that it was appropriate to report it.

Q. So when you made this report, why didn't you include the other two prior reports at that time?

A. When -- I was certainly involved in -- you remember I talked about the approach, the PRF approach committee this morning? So we discussed that. And in the record of that meeting, it very clearly shows that we discussed the totality of those experiments not just this one in isolation.

And we proposed -- if my memory serves me right but it would be useful to check the record -- to the US PRF committee that that bigger picture should be -- should be included.

Q. All of them?

A. That was what I believe the record of our communications --

Q. So the PRF committee recommended to the US people that they report all of them?

A. That they could consider that, yes.

Q. They didn't do that, did they?

A. I would have to check the record of that.

Q. Well, you know that the earlier two studies were never reported until December 13, 2019; correct?

A. They were -- you were telling me that they had been reported in some way in that time, yes. I have not seen that.

Q. Okay, all right.

(Exhibit 33 marked for identification)

BY MR. TILLERY:

Q. Do you have exhibit 33 before you, sir?

A. I do.

Q. Okay. Is this a report to the United States EPA?

A. Yes, this is a letter to the US EPA, yes.

Q. Okay. Let me ask you, wouldn't the evidence for the neurotoxic effect of paraquat be stronger if all three of the studies done by Dr. Marks were reported?

A. I think there's -- there's certainly a reasonable thing to -- to propose. And as I said, the approach committee suggested that was one possibility.

Q. And that was one of the reasons you told them, wasn't it?

A. It was, yes.

Q. Yes. Now, if you take a look at this document, number 33, what's the document date?

A. February 24, 2006.

Q. Syngenta made this disclosure under FIFRA 6(a)(2), correct?

A. Correct.

Q. The only study results reported in this letter were XM7480; is that correct?

A. That is correct, yes.

Q. The study itself, which referenced the two earlier positive studies with similar results, was not sent to them, was it?

A. Not in this -- in this letter, certainly.

Q. Do you know if the study itself has ever been sent to them?

A. I would need to check that. I don't know for sure.

Q. Okay. Would it be your recommendation to include the entire study?

A. As part of the normal process, it wouldn't necessarily be the case. And sometimes studies of this sort are sent to them for other purposes, but I can't comment about this specific.

Q. In Dr. Marks' conclusions, at the "Results" section of study XM7480, she says the study results:

"... support the findings of two previous CTL studies XM7258 and XM7371 ... and demonstrate that paraquat, when administered to C57BL6J mice ... would appear to be capable of inducing nigral but not striatal toxicity."

That's what she says.

A. Where are you reading from?

Q. That would be from the document you are looking at,

the study --

A. Which page?

Q. 492792?

A. Okay.

Q. I will read that question over if you want it, because you were looking.

MR. NARESH: Could you, please?

A. Yes, I'm there, thank you.

BY MR. TILLERY:

Q. All right. Dr. Marks concluded in the results section of that study that you are looking at -- that is 7480 you are looking at, right?

A. I'm now looking at --

Q. I am sorry, the study number?

A. Yes, the study number is --

Q. 7480?

A. 7480, yes.

Q. She stated in the study number -- and 792 is the page?

A. Okay.

Q. That the results:

"... support the findings of two previous CTL studies XM7258 and XM7371 ... and demonstrate that paraquat, when administered to C57BL6J mice ... would appear to be capable of inducing nigral but not striatal toxicity."

Right?

A. That's right.

Q. Okay. That conclusion was not reported, was it?

A. It was not reported --

Q. To the US --

A. -- to the US EPA.

Q. Is that right?

A. No, it was not in its entirety. No, that's right.

Q. Dr. Marks concluded about 7480, that:

"Our data would appear to be supportive of the hypothesis that a sensitive subpopulation of dopaminergic neurons may exist which are vulnerable to paraquat induced toxicity."

She said that as well?

A. Yes.

Q. Okay. But that report and that conclusion was not contained within the February 24, 2006 report to the US EPA, was it?

A. It was not.

Q. You did not report in this letter that paraquat was neurotoxic in three separate studies, did you?

A. We did not in this letter, no.

Q. You did not report in this letter that you had conducted three studies with paraquat where the loss of dopaminergic neurons in the substantia nigra of the black

mouse was comparable to the findings reported in the published literature, did you?

A. Indeed. Because the 6(a)(2) regulations did not require us to do so, because they were the same conditions and therefore the finding was not new.

Q. Let me ask you -- let me ask you, would that be the prudent thing to do and was that the reason you recommended that they do it?

A. The reason that I recommended that they should consider including that in the letter was that it would allow them to understand the totality of the program that we had done, which I didn't think was something which was unreasonable.

Q. Would you think it would be unreasonable to wait 16 and a half years to do that?

A. I can't comment on that. Certainly that was --

Q. You don't want to comment on that?

A. Well, I'm not able to comment on that, because I was not involved in that decision process.

Q. Okay. Okay. Who was involved in that decision process?

A. I don't know.

Q. Okay. You did not report to the US EPA in this February 24, 2006 letter that three different studies at CTL had replicated neuronal cell loss findings with

paraquat in the C57 black mouse, did you?

A. We did not.

Q. Who was on the US PRF committee at that time, or was there one? Was the PRF committee here?

A. The US PRF committee, which is who would be responsible for writing this letter, would have included a number of people whose names I wouldn't be able to say at this point in time who they exactly were.

Q. Would you think that would be Montague Dixon?

A. It may not have been Monty Dixon in 2006 but I would need to check.

Q. Would it also have been Janice McFarland?

A. It could have been Janice McFarland. She was the head of regulatory in North America at that time, but I don't know.

Q. What did you send along, after the committee met here and made their recommendations about these -- all of these studies being reported -- did you send along any specific writings or papers to the committee?

A. Yes. As always we completed a proforma document.

Q. And sent it to them?

A. And sent it to them.

Q. And made that recommendation that they report the studies?

A. Indeed. You may well have seen that document.

(Exhibit 34 marked for identification)

BY MR. TILLERY:

Q. We've handed you what's been marked as plaintiff's exhibit 34. I will give you some time to look it over, sir.

A. Okay.

Q. Tell me when you are ready to talk about the document.

A. Okay.

Q. Okay. What is this, please?

A. This is the fifth in the series of reports -- of studies conducted by Dr. Louise Marks. This one was looking at the effects on -- in the nigrostriatal region, including the substantia nigra, of a range of other compounds to the same strain of mice. And these were compounds which were toxic and -- were toxic compounds and they were given at high doses as one line of research that was suggested in that meeting that we were looking at earlier in this discussion.

Q. Let me see if I can state this as a layperson would in the best understanding I have of the study.

After the first couple of reports came back positive, Dr. Smith suggested that perhaps it was the study itself, the injection of the paraquat, that caused toxicity throughout the body; that the toxicity itself could have caused the results of seeing damaged or dead dopaminergic

neurons, and that could account for this. That could be the explanation why not only Dr. Marks but the other folks who were publishing this in the sort of independent peer-reviewed literature, correct?

A. That was the hypothesis.

Q. And let's figure this out about by getting away from paraquat, and let's use other things in a toxic injection format?

A. That's right.

Q. And then if they create toxicity sufficient to actually kill the animal, or up to that point or close to it, then we can see if the injection of them could result in the same thing; correct?

A. That is correct.

Q. Have I said that accurately and fairly?

A. You have indeed, yes.

Q. All right. What were the results?

A. The results were that none of these compounds induced the same effect on TH positive cells, the dopaminergic neurons in the substantia nigra.

Q. So I'm looking at her discussion section. In the discussion section on 939, she says:

"The aim of the present study was to determine whether the degree of [dopaminergic] cell loss observed following administration of [paraquat] to C57 black mice

could be attributed to a 'general toxicity' associated with dosing any compound at a high enough dose."

Correct?

A. That is correct.

Q. All right. And her results were that it didn't.

Now what did that mean for you as a scientist?

A. It meant that we had --

Q. Excuse me, I don't mean to interrupt you, I apologize to you. But when I asked that, I didn't say it right.

I meant: what did it mean to you in terms of the reliability of the prior studies in terms of the toxicity being the cause, if you could explain?

A. Well, it made it more likely that what we had seen with paraquat could be genuinely due to the -- to paraquat.

Q. Right. Instead of just the overall toxicity to the body of this mouse?

A. Yes, the stress -- in other words, putting it in a different way, the stress that you can cause in an animal if you are dosing anything at substantially high doses.

Q. Yes. All right. And what you "had seen with paraquat", meaning the loss of dopaminergic neurons?

A. Yes.

Q. Okay.

(Exhibit 35 marked for identification)

BY MR. TILLERY:

Q. Please take a look at exhibit number 35.

After you are familiar, I am going to ask you couple of questions about it. If you go specifically to page 3432?

This is a presentation that Dr. Marks gave, isn't it?

A. Yes, I believe that is the case.

Q. All right. If you look at 3432, she's discussing the study that you just commented on, isn't she?

A. She is.

Q. And she concludes, in reference to that study, that:

"The data would suggest that [paraquat] induced cell loss in the [substantia nigra] is not likely to be attributable to a 'general toxicity' associated with dosing a compound at high doses rather it suggests a selective effect on vulnerable dopaminergic cells within the [substantia nigra]."

Is that right?

A. That's right.

Q. You agree with that?

A. That was not an unreasonable conclusion at the time.

Q. What is the significance scientifically of the effect of paraquat being selective?

A. Well, if it is selective to dopaminergic cells within that region, then clearly that could lead to

emphasizing a possible concern for Parkinson's disease.

Q. Right.

(Exhibit 36 marked for identification)

A. Okay.

BY MR. TILLERY:

Q. This is a presentation or a summary of a presentation at a meeting in Atlanta on February 13 and 14, 2008; correct?

A. It was.

Q. This would have been a Syngenta meeting?

A. Yes.

Q. And it is "Paraquat & Parkinson's disease" as the subject matter of the meeting?

A. Yes.

Q. Okay. And this would be an internal presentation about Syngenta's research into paraquat and Parkinson's disease, right?

A. It was. But we were -- I was aware -- I was actually at this meeting, I believe.

Q. Okay.

A. And I believe also we did have people from outside Syngenta in that meeting.

Q. Okay. This meeting was held over two years after Dr. Marks had completed the paraquat mouse studies --

A. Yes.

Q. -- as you know.

Did Dr. Sturgess give this presentation?

A. I don't recall who gave this presentation, whether it was one person or more than one person.

Q. Do you know who was in attendance?

A. I -- there would be a number of people, including myself, Dr. Sturgess and Dr. Smith, and a number of other people.

Q. And other of the people from Syngenta Crop Protection?

A. I couldn't give you an exact list. I would need check that.

Q. If you turn to 742, please, at the top of this particular slide it says:

"Syngenta CTL Investigative Studies."

Right?

A. It does.

Q. The first paragraph says:

"In vivo studies -- replicating studies conducted in the C57Bl6 mouse model with paraquat to validate the literature claims."

Correct?

A. Correct.

Q. And that refers to the studies Dr. Marks conducted with paraquat in the mouse at CTL, correct?

A. It does.
Q. Please turn to the last slide. That would be -- I think that is at 754.
A. Yes.
Q. Is that right?
A. That is correct.
Q. And that's a summary slide: paraquat and Parkinson's disease literature findings; right?
A. That is correct.
Q. The first bullet says:
"Reports in the literature suggest that in a certain strain of pigmented mouse (C57Bl6), multiple i.p. [again that is intraperitoneal] injections of paraquat at relatively high doses can result in a 30% loss of dopaminergic neurones in the substantia nigra."
Okay?
A. Yes.
Q. And then it says:
"These findings have been replicated in Syngenta studies."
Is that what it says?
A. Yes, it does.
Q. Then it says:
"There are also claims that the effect can be observed in another rodent species ... however Syngenta

studies have failed to repeat this finding."

Okay?

A. Yes. And we have not talked about those studies but that is true: in the Louise Marks period, we also looked in the rat as well as the mouse, and we did not see such a finding.

Q. And then the final bullet says:

"We should be aware that there may be NHP data with paraquat emerging in the near future that may replicate the findings already reported in rodent species -- potential relevance to humans."

All right?

A. Yes.

Q. All right.

A. I don't know if you will allow me to just restate that I believe this meeting had some external people to Syngenta -- we should check the record -- but I think if that is the case, it shows we were being very transparent about those findings with those people.

Q. To follow up on that point, meaning being very transparent to the public?

A. To other researchers engaged --

Q. Which would be the public?

A. That's right, yes.

Q. And transparency, to follow up on your point which

I allowed you to make to clarify, would mean that you wanted to set the record straight and be honest and straightforward with everybody?

A. We wanted to make sure that the scientific community and, as you put it --

Q. And the public?

A. -- and the public knew that at that point in time we had come to a conclusion that the findings appeared to be replicable.

Q. Right. They were replicable?

A. At that time.

Q. At that point. And that was 2008, right?

A. Yes.

Q. Was Dr. Cory-Slechta there?

A. That's what I was wanting to check, exactly who the attendees were. We had a number of meetings and I can't remember who was present at which.

(Exhibit 37 marked for identification)

BY MR. TILLERY:

Q. The next document is included in such a voluminous format because only it includes one or two pages that are relevant --

A. Okay.

Q. -- but I didn't want to include a bunch of -- I didn't want to include just a page or two of the document.

So very little relevance to virtually all of it, but I want to direct your attention to a particular section and follow up to a statement that you just made on the record, okay.

If you would go to -- and feel free to refresh yourself about any of this as you wish, it just wasn't contained within this document -- but what I'm going to direct your attention to is 86601.

Please take a look at that document. Again it is 86601.

A. Okay, got it. And, sorry, that was the one that you printed out separately but --

Q. Go ahead --

A. -- thank you for --

Q. Go ahead and read that. Does it say "Paraquat Information Center" at the top?

A. Yes, it does.

Q. All right. And when you are finished, you let me know, please. Okay?

A. Okay.

Q. You had just clarified the record a minute ago and said that a document that I had put in the record mark and dated February 8, 2008, right?

A. Yes.

Q. Was the summary of a presentation -- February 13 and

14th --

A. Yes.

Q. -- of 2008 was a summary of a meeting where you had invited people and you had been transparent. That's what you told me.

A. To those people, yes.

Q. All right. Now I want to direct your attention to this exhibit, which is marked as exhibit 37, okay? And I want you to tell me if this is a clip from the Paraquat Information Center, and what appears to be a --

A. Yes.

Q. -- page from the internet, right?

A. It is. It is from, as it says at the bottom, from paraquat.com, yes.

Q. What is paraquat.com?

A. It's information resource which is provided for customers and for the public generally to understand more about the benefits, the use -- the appropriate use -- and some aspects of the safety of paraquat.

Q. And, actually, it tells them about farming uses, explains things, gives them references to application, to its effectiveness, all kinds of information?

A. It does.

Q. And it's designed for use by the consuming public?

A. Indeed. And especially the farmer and grower who

may be using it.

Q. The farmer and grower. The person like Freeman Schmidt in this case, or Mr. Hoffmann or Mr. Mills or any of these people who could -- who could, either by themselves or with help, get on the internet and ask questions or do research, correct?

A. Of course.

Q. Now look at this. And this is maintained by Syngenta, correct?

A. It is certainly -- the content is certainly maintained by Syngenta.

Q. Right. Whether it is housed by a third party, the content is supplied by Syngenta?

A. Yes.

Q. And then it contains paraquat frequently asked questions, doesn't it?

A. It does.

Q. And a frequently asked question is a question that you would expect the people out there who buy your product to perhaps want answered about that product?

A. Yes.

Q. One of those might be whether it causes me to get sick?

A. Yes.

Q. Whether it causes me to get Parkinson's disease?

A. Yes.
Q. Because there had been some rumblings, right?
A. There had.
Q. All right. Let's take a look at what Syngenta had on its website three weeks before that meeting that you just told me they were so transparent at, okay?
Let's look at this. First question:
"Is paraquat safe to farmers and their families?"
Next question:
"What is the safety of paraquat to farmers when used long-term?
"Has paraquat been found to cause cancer ...?
"Does paraquat cause Parkinson's Disease?"
Do you see those?
A. I do.
Q. The answer given is:
"There is no scientific or reliable epidemiological evidence so far to link paraquat with Parkinson's Disease. Previous studies have demonstrated that paraquat does not cross the blood-brain barrier easily, meaning that it does not reach the specific location in the brain necessary to produce Parkinson's symptoms.
Am I reading that correctly?
A. You are reading it correctly.
Q. I will continue:

"Epidemiology studies in areas of high and long-term paraquat usage have shown no increase in neurotoxic incidents."

Right?

A. That's what it says.

Q. Now, were all those statements true?

A. Well, you have to remember --

Q. I am just asking you if they are true, in 2008?

A. In 2008, I think that it is still broadly true because we were not yet seeing the totality of evidence that was sufficiently convincing to say that paraquat was a clear causative agent for paraquat -- for Parkinson's disease.

Q. In the preceding five years, you just had test after test after test showing you that this chemical gets into the brain -- the substantia nigra -- of the exact location where paraquat can cause damage and cause Parkinson's disease, didn't you?

A. Let me qualify --

Q. If you could answer that?

A. I need to answer it with a qualification, if I may.

Q. All right.

A. We had shown that paraquat had got potential to get into the brain. That a small amount of blood would get into the -- cross the blood-brain barrier into the brain. We hadn't definitely looked in the substantia nigra. We had

not teased out that area of brain and measured paraquat in that region.

Q. Do you think it mattered to the average farmer whether you had teased that out --

A. No, of course not.

Q. Okay. Don't you think they are really worried about whether or not this stuff can make me sick generally?

A. Of course.

Q. And you think they might be concerned about whether or not it is going to cause them to get Parkinson's disease?

A. Of course.

Q. Do you know what the Illinois plaintiffs said when asked in their depositions whether they would have used this chemical if they had known there was any chance of getting Parkinson's disease? Do you know what they said?

A. I do not.

Q. Do you think that statement was transparent?

A. It was transparent in terms of it being a conclusion that was appropriate at the time in that we did not believe -- and indeed still do not believe -- that the totality of evidence, not just the mouse models that we were talking about earlier but also the epidemiology, has yet come to a clear conclusion that paraquat is a causative agent in Parkinson's disease.

Q. Didn't Dr. Marks conclude after repeated studies

that paraquat selectively targeted the substantia nigra?

A. She did. But that's not the same as saying that in the conditions at which people would be exposed to paraquat that that would pose a risk to those farmers and growers.

Q. But telling them that it would cause this kind of dreadful disease would impact the bottom line, wouldn't it?

MR. NARESH: Objection to form.

BY MR. TILLERY:

Q. If you told all the farmers in America that you -- had brought your product that it could cause them to have Parkinson's disease, what do you think that would do to your sales?

MR. NARESH: Objection to form, scope.

A. Well, it absolutely --

BY MR. TILLERY:

Q. Absolutely what?

A. If I may say, it is a bit like me saying to you if you knew if you knew that you took twice the dose of acetaminophen or paracetamol that your liver may pack up, then you might be scared of taking paracetamol.

Q. You bet I would.

A. Yes, and that is the truth of the matter. But we don't suggest that you should stop using paracetamol.

Q. Isn't damage to the substantia nigra the part of the brain associated with Parkinson's disease?

A. Yes.

Q. How long did this statement appear on your Parkinson's -- on your paraquat website?

A. I am afraid I don't know the answer to that.

(Exhibit 38 marked for identification)

MR. NARESH: Steve, could we go off the record and discuss this for a moment?

MR. TILLERY: Sure.

THE VIDEOGRAPHER: We are off the record at 2:34.

(Break taken.)

MR. NARESH: For the record we have discussed and we are willing to let you go forward on questioning on documents marked exhibit 38 -- which I assume will be exhibit 39 -- which were marked 502D documents by Syngenta, with all parties reserving the rights and to the extent that we believe that any of the questioning calls for the divulging of privileged or otherwise protected content, we will object on the record.

MR. TILLERY: Okay. Back on the video record, please.

THE VIDEOGRAPHER: We are back on the record as of 2:57. This is now media number 4 in the deposition of Philip Botham. You may continue.

BY MR. TILLERY:

Q. What is the number of the exhibit in front of you

now, sir?

A. Exhibit 38.

Q. Okay. Do you know what 38 is?

A. I know what the document is, yes.

Q. Yes. What is it?

A. It's an internal -- i.e. product safety, the department that I was responsible for evaluation of -- essentially doing a risk assessment of the possibility that the findings that we have been discussing are real, and therefore we were looking to see what margins of exposure and safety margins would be -- occur if we assume that those findings were real.

Q. And when you say "findings are real", what is it, more specifically, that you are referring to?

A. We are referring to the findings we have just been discussing around the loss of dopaminergic cells in the brain.

Q. That paraquat causes Parkinson's disease?

A. That paraquat causes in the mouse model a loss of dopaminergic cells.

Q. So you are limiting your evaluation in this product safety technical evaluation to the mouse model?

A. That's -- the calculations are based on the data from the mouse model.

Q. Okay. What I'm trying to figure out is the scope of

this. You were evaluating product safety in terms of a mouse model?

A. Yes. And it is a standard toxicological practice to take things like the no effect level we were discussing earlier and to do risk assessments from that.

Q. Okay. Do you see the names listed on this document? I think, if you look at 14 --

A. Yes.

Q. -- who was the document's author?

A. It is the four people that you see on page 14.

Q. And that's Nick Sturgess, Kim Travis, Andy Cook and Phil Botham?

A. Correct.

Q. You are one of those authors?

A. I am.

Q. Okay.

Was this kind of document prepared regularly at Syngenta?

A. This kind of document is somewhat atypical in that we were taking a very precautionary approach, as I said a few minutes ago, assuming that this is an effect of real concern. But the principles of calculating no effect levels, doing risk assessment, is standard practice.

Q. Why was the document prepared?

A. In order for product safety, the function that I was

responsible for, to be fulfilling its duty of care to do risk assessment.

Q. Was it prepared for any litigation?

A. It was not in any sense done for litigation -- purposes of future litigation.

Q. Okay. On the first page, it says:

"There is consistent evidence..."

Do you see that?

A. Yes.

Q. Why don't you read that paragraph into the record?

A. "There is consistent evidence in animal studies for the loss of dopaminergic neurones in the substantia nigra of male [C57Black6J] mice when dosed with paraquat (at up to one third of the median lethal dose) via the i.p. route."

Q. And the next, if you wouldn't mind, where it starts:

"There is no evidence..."?

A. "There is no evidence to indicate that the observed effect on neuronal cell loss is an artefact of the test system, though this remains a possibility. Therefore it is prudent to assume at this stage that the finding is real, and that it is related to paraquat treatment in this strain of mice."

Q. Okay. The next bullet reads, "In the absence..." Would you read that?

A. "In the absence of evidence to the contrary, it is

assumed that this finding is potentially qualitatively relevant to man for the purposes of a re-evaluation of the reference dose."

Q. What is a reference dose?

A. It is a dose that is used in order to determine the -- again, the margin of safety as part of risk assessment.

Q. And the sixth bullet reads, please check me for accuracy:

"The estimated reference dose for neuronal cell loss is ... less than the current sub-chronic and chronic reference doses."

MR. NARESH: Steve, I think you misspoke.

MR. TILLERY: Really?

MR. NARESH: I think you missed a word.

MR. TILLERY: Okay, let me start over. Thank you, counsel.

BY MR. TILLERY:

Q. Why don't you read it, the sixth bullet, where it says "The estimated reference dose"?

A. "The estimated reference dose for neuronal cell loss is a little less than the current sub-chronic and chronic reference doses, but given the uncertainties of the calculation Product Safety considers the difference not to be significant."

Q. Okay. And the sub-chronic and chronic reference doses were based upon damage to the lungs as an endpoint, right?

A. That is correct.

Q. Product safety calculated the reference dose based on neuronal cell loss in the substantia nigra pars compacta as the endpoint, and that reference dose was lower; correct?

A. The reference -- we took the no effect level from studies -- not our studies, actually, the studies of other researchers we have spoken about -- as the no effect level and then the reference dose is calculated by dividing that by some usual factors.

Q. It was a lower number, wasn't it?

A. Yes, yes.

Q. The technical evaluation gives the position of Syngenta's Product Safety department in September 2009?

A. That's correct.

Q. With respect to paraquat's neurotoxic potential in the substantia nigra portion of the brain?

A. Correct.

Q. When did the product safety department or product safety group -- what do you refer to it as?

A. It doesn't really matter, product safety team is fine.

Q. Team?

A. Um-hm.
Q. When did the product safety team first adopt this position?
A. I believe that this was the first time that we put together the information in such a way.
Q. Was it the position of Syngenta's product safety team in 2008?
A. Well, I don't think we had actually -- we certainly hadn't done these kind of calculations in 2008.
Q. Would it be different -- had you asked the same group of professionals in 2008 for their answer, would they have given you the same results?
A. It would have been the same.
Q. Would have been the same?
A. Yes.
Q. So the statement on the paraquat.com website "paraquat does not reach" the substantia nigra pars compacta is not all consistent with the position adopted in this technical evaluation, is it?
A. It is not consistent, I would agree.
Q. Okay. The second paragraph on the second page, starting with "A number", would you read that first full sentence?
A. "A number of laboratories, including Syngenta CTL, have observed a reduction in neuronal cell counts in

dopaminergic neurones in the substantia nigra pars compacta brain region following paraquat administration [using] a dosing regimen of 10 mg/kg paraquat once or twice a week for three weeks (McCormack et al, 2002; Barlow et al, 2004; Cory-Slechta et al, 2005; CTL report number XM7258 ...)"

Q. So the CL studies referred to here are Dr. Marks' studies, right?

A. That is correct.

Q. And the third party or independent scientific references are the same ones that Dr. Marks used in her studies and referenced?

A. That -- that is correct.

Q. Did Syngenta share this document with the United States Environmental Protection Agency?

A. I don't believe we did.

Q. Did Syngenta share this with any pesticide regulatory agency in the world?

A. I cannot answer that. I don't know.

Q. Did Syngenta ever publish these conclusions and share them with the public health committee?

A. I don't believe it did.

Q. Was this document restricted to internal use at Syngenta?

A. It was largely intended to be our own internal evaluation, as I said, as part of our duty of care.

Q. Okay. Now let's go to the next document which will be 39.

(Exhibit 39 marked for identification)

BY MR. TILLERY:

Q. Would you please take a minute and familiarize yourself with this document?

A. Okay.

Q. Could you on the record please describe or identify the document?

A. This is an update of the document we have just been talking about. So it has the same title as the previous one "A consideration of the Potential Implications for Reference Doses" now dated draft July 2011. So just under two years after the previous version.

Q. Does a final document have draft on it? They have "draft" for years. They just keep putting the word "draft" on it. Do you know why?

A. Because we were using draft to recognize that we were still in the middle of a research program, so new data were going to continue to emerge.

Q. Right. But you, as of the date of the issuance of the document, it was at that point in time final?

A. With the information that was available at that time. This was our best estimation of this situation, yes.

Q. All right. Okay.

And this document wasn't produced for litigation purposes, was it?

A. It was not, in my understanding, no.

Q. Okay. Were you the head of this group?

A. Yes. By that time I was the head of the paraquat health science team and also I had a leadership position in the product safety organization.

Q. And the authors of this were Nick Sturgess, Kim Travis, Andy Cook and you, is that right?

A. That is correct.

Q. And were others in attendance, do you remember?

A. By "attendance", this wasn't a meeting, this was a document that was generated by that team working together.

Q. Okay. So there was no meeting to discuss the content. It was just sent back and forth to reflect the 2011 --

A. It was a combination of the four of us having discussions and also looking at various drafts of this document.

Q. As a matter of fact, you anticipated that 18 months later you would have a next review, right?

A. That's right. Because as it said there, and as I indicated a few moments ago, we were in the middle of a research program and we were doing what we thought was going to be a very relevant study, which is the 90 day data

study.

Q. Does this document give the position of the Syngenta product safety with respect to paraquat's neurotoxic potential as of July 2011?

A. I will qualify that if I may. It establishes as I indicated a conservative position that paraquat could cause the neuronal cell loss and therefore we were establishing if that were the case whether we believed that there were adequate margins of safety.

Q. Okay. The first bullet, if you read that, "Executive summary."

A. "There is some evidence in animal studies for the loss of dopaminergic neurones in substantia nigra of male [C57 black 6J] mice when dosed with paraquat (at up to one third of the median lethal dose) by the i.p. route."

Q. And the next, starting with "Recent"?

A. "Recent Syngenta studies have failed to consistently replicate the findings reported in the literature of the loss of dopaminergic neurons at doses of paraquat up to 10 mg/kg or at higher doses up to the maximum tolerated dose (25 mg/kg). In addition, comprehensive neuropathology studies have consistently indicated no evidence for neuronal cell damage, cell loss or an inflammatory response following paraquat exposure. It therefore remains a possibility that the reported findings described in the literature on

neuronal cell loss are an artefact of the test system. It is however prudent to assume at this stage that the reported finding of neuronal cell loss is real, and that it is related to paraquat treatment in this strain of mouse."

Q. And the recent Syngenta studies referred to in that paragraph that you just read were experiments that would later be published as the Breckenridge et al, 2013 study; correct?

A. That is correct.

Q. What does "artefact of the test system" mean in this context?

A. Rather like some of the discussions we were having earlier today, that there may have been other explanations that could have explained why there was an apparent loss of dopaminergic neurons. Technical -- technical reasons, in other words.

Q. The last sentence concludes:

"It is however prudent to assume at this stage that the reported finding of neuronal cell loss is real, and that it is related to paraquat treatment in this strain of mouse."

Correct?

A. Yes.

Q. The next bullet reads:

"In the absence of evidence to the contrary, it is

assumed that this finding is potentially qualitatively relevant to man for the purposes of a re-evaluation of the reference dose."

Correct?

Yes.

Q. On page 4, if you look at that, in the product safety evaluation, is 44.0004?

A. I have that.

Q. Okay. It begins:

"The most consistent finding from the body of animal studies reported in the literature is the loss of dopaminergic neurons in the substantia nigra pars compacta of male C57Bl6J mice, when compared to control animals."

Correct?

A. Correct.

Q. Did Syngenta share this document with the United States Environmental Protection Agency?

A. I don't know, but I don't believe so.

Q. Did it share this document with any pesticide regulatory agency?

A. I am not aware that it did.

Q. With the public health community?

A. I am not aware that it did.

Q. Was it restricted to internal use?

A. That is my understanding of this document.

Q. I'm going to go backwards. How does one arrive at the conclusion that an effect noted by a study result is an artefact of the test system?

A. How would one conclude that it was an artefact --

Q. How would you, as a scientist, conclude that?

A. By finding a technical explanation that it was due to some way in which the effect was measured, for example.

Q. Have you ever done that?

A. We have done a lot of work to do -- to check that out, yes.

Q. What was the artefact of the test system that you found?

A. We -- I'm not saying that we found an artefact as such. What we found was that what the -- the results that you got when you measured the number of neurons in that part of the brain was very critically dependent on a number of factors. Not just the stereology machinery we were talking about this morning, but also the way in which you prepared the material, the brain, how you cut it, how you stained it, how -- whether you had -- were reading it blind to treatment. So a number of factors seemed to be at play here.

Q. Well, did you find that any of the preparation had been done incorrectly in any of the studies of the public health community?

A. It's -- again, I wouldn't quite put it "incorrectly". As we said this morning, this was -- and is still -- a relatively new technique. Not that many people used it. And I think the community as a whole, not just us, was still learning that you could get different results simply as an example that I was showing there how thick the sections were that you put under the microscope.

Q. Right. But you did take note as the group, didn't you, that Dr. Marks' results were consistently virtually identical to laboratories doing the same test in different parts of the world; right?

A. Of course, yes. Yes.

Q. Okay. And presumably doing it slightly differently, following the same test protocol but different people, different -- perhaps different protocols for the test, but arriving at the same results. Did you take that into account?

A. We took that into account. But I think as this also said, we were, by this time as reported in Breckenridge et al, given advice by again independent pathologists that you needed to look in addition to just measuring the TH positive cells, at other histopathological or pathological measurements that you should see if those cells were genuinely dying.

Q. What is a TH positive cell?

A. That is a dopaminergic cell for the purposes of the discussion here, because dopaminergic cells express on their cell surface an enzyme tyrosine hydroxylase, and that's actually what you see when you stain -- it is a marker for tyrosine hydroxylase.

Q. What is the purpose of that enzyme?

A. That is involved in the utilization of dopamine.

Q. That is involved in using it, creating it, isn't it?

A. Yes, yes.

Q. That's what you need for that cell to be able to help you?

A. Yes.

Q. Without it, it may be there -- may or may not be showing up as dead or alive or one way or another, but without it, it is obviously not able to help you --

A. If it is nonfunctioning.

Q. If it is nonfunctioning?

A. And there is a difference between not being able to see it with the markers we were using and it necessarily being nonfunctioning.

Q. You mentioned cut as well. Did you see any evidence of a problem with the cut in Dr. Marks' studies?

A. We didn't obviously go back and look at Dr. Marks' studies because the tissue was then too old to do that.

Q. You never evaluated hers and thought that they were

done incorrectly?

A. We were not able to do that.

Q. Okay. And you didn't find her prep was wrong?

A. We were not able to do that.

Q. You did not find that her staining method was wrong?

A. We are not saying that anything was wrong.

Q. Or that anything else she did was wrong?

A. We are not saying that anything she did was wrong.

Q. What about McCormack or Di Monte, or any of these other people?

A. I would say we would never have said that what they did was wrong.

Q. Maybe that's word is too harsh. Okay, that they used an incorrect technique: did you ever find that anything done scientifically by way of technique achieved an unreliable result?

A. I think the issue is that we know that the particular -- particularly the stereology technique is subject to the variability that we were able to see when we started to look at various things like the thickness of the tissues, how you looked down the microscope, at what depth. There were lots of technical detail there which started to uncover variability which maybe other researchers apart from ourselves were not aware of.

Q. That's what I'm trying to find out. What are those

that you found to be an explanation for why these consistent independent researchers and independent laboratories published in peer-reviewed journals and Dr. Marks reached virtually identical results showing that the substantia nigra was being impacted by paraquat? What did you find that could explain the consistent results that they got?

A. I would say the right thing to say is that we didn't find a specific issue which said "yes, it's that which must be responsible for the difference in the results".

What I'm saying to you is that the large body of evidence that we accumulated with other external pathologists gave us some possible explanations which I have just been explaining to you, which could cause variability in results.

Q. Is that the extent of your answer as far as deep as it can go and detail?

A. I think that's probably adequate for now.

Q. That makes me nervous. Okay, I am trying to find out if you have any specifics to answer my question.

A. Well, I can repeat what I said earlier.

Q. No, that's not necessary. You don't need to do that.

A. Okay, fine.

Q. I'm trying to find did you -- was there one of these

"aha" moments when you looked at it and said you have got the answer. Did you do that?

MR. NARESH: I object to the form of the question. I think if you would like him to answer the question, he was offering to give you more detail.

MR. TILLERY: He was offering to repeat what he said before.

A. Let me say that one of the number of factors that I said before, one thing which came closest to being a critical factor -- not necessarily the critical factor but closest to it -- was actually for the pathologist to be blinded to treatment; to not know that he or she was looking at control animals not dosed with paraquat versus those that had been treated.

BY MR. TILLERY:

Q. And that would be the one thing you would point to?

A. No, that's why I said that very carefully. I said that that was the closest thing that we came to which could be the biggest factor. But we did not finally conclude that any of these factors was the sole definite reason for that.

Q. Of all of them that you can think of, would you think not being blinded would be the most telling explanation?

A. Well, when we looked at what it said in the publications of other people -- and actually what Dr. Marks

herself said -- then it seemed to be that some of those studies were certainly not read blinded to treatment. Either it said they weren't, or the matter was silent.

Q. Okay.

A. So that's why we wondered if that, indeed, may be an important factor.

Q. And you are referring to the Minnema study, is that what you are --

A. Yes, subsequently we have made that point in other papers.

Q. And that's a study that you rely on, too, isn't it?

A. It is, yes.

Q. Okay. And that was one where a number -- the report was that a large number of the results were -- were not blinded?

A. Yes, yes.

Q. And that was a significant finding for you?

A. I think it was certainly an important finding, I agree, yes.

Q. Okay. But you never identify the flaw in the paraquat mouse model itself which could lead you to conclude that the neurotoxic effects are an artefact of the test system, right? That's right. Although if I may just speak from a toxicological principles perspective, again if the effect was real one would anticipate that had you dosed at

higher dose levels -- which we did do, we went up to 25 milligrams per kilogram, as high as we could possibly go without killing a lot of the animals -- that you would see that effect. It is another factor which says "if this is really real, you would perhaps see it in a more pronounced form" and we didn't.

Q. You mentioned you got advice from independent pathologists. Are you saying that the pathologists you took advice from were not in any way compensated by Syngenta?

A. No, I am not saying that.

Q. When you use the word "independent" do you include people that you pay?

A. I do. Because although we paid them, at no time were we sitting in their laboratory or sitting alongside them when they were doing their microscope readings or changing their reports.

Q. You are saying independent means that they are not in your employ?

A. Indeed, and working independently from our scientists.

Q. Okay. Are you aware that other people refer to independents as people who do not have a pecuniary relationship with Syngenta, are you aware of that?

A. Of course.

Q. Okay. And other independent people might be people

who don't have a financial interest to where the results could be impacted one way or another.

You understand that?

A. Of course, yes.

Q. That's why in peer-reviewed journal articles if any part of your paying -- compensation, honorariums, anything that is paid for by the company that is making the product -- you have to report it?

A. Indeed.

Q. Why is that, do you think?

A. So that we are being transparent.

Q. Don't you think it might be that those editors of those peer-reviewed journals want to make sure that the people don't have another motive for what they found in their science?

A. Of course.

Q. Okay. That's what I am thinking.

A. Yes.

Q. So when we use the word "independent", your definition is that they are not sitting in your laboratory; my definition is that they are not paid by you?

A. Okay. That's fine.

Q. All right. Let's go to the next one.

(Exhibit 40 marked for identification)

BY MR. TILLERY:

Q. Can you identify and describe plaintiff's exhibit 40?
A. Just give me a minute or two to check, please.
Q. Of course, of course.
A. Okay.
Q. What is the document?
A. It is a PowerPoint presentation.
Q. And it is dated March 2, 2016?
A. That's correct.
Q. And it was done in Brazil?
A. That is correct.
Q. Okay. And did Syngenta sell paraquat in Brazil?
A. Yes.
Q. Okay. This is a presentation Charles Breckenridge made to a expert panel at the Brazil pesticide regulator ANVISA when the agency was considering banning paraquat, is that right?
A. That is correct.
Q. And the topic here or the title is: "Does the animal or human element support a causal relationship between Paraquat use and Parkinsonism."
Correct?
A. Yes.
Q. You were asked to address that topic there, weren't you?

A. Yes, because the agency had asked a number of questions.

Q. And the agency was concerned about that connection?

A. They were.

Q. And they wanted you to come there and answer questions about it, right?

A. That is correct.

Q. So if turn to page 18, the top of it is "ANVISA's Question on PQ as a Model for Parkinson's Disease". If you can find that page, my number is cut off.

A. Can you just --

Q. What is your page reference at the bottom?

A. Did you say page 18?

Q. I think so.

A. That is 116230.

Q. Thank you. It is actually page 14 of the PowerPoint, isn't it? It looks like. But if you look at the Bates number, I think it is 6223.

A. Yes, I am on that page.

Q. All right. And it's at the top of that says:

"ANVISA's Question on PQ as a Model for Parkinson's Disease."

Do you see that?

A. I do.

Q. Two questions are presented and they both ask about

animal studies investigating the relationship between paraquat and Parkinson's disease, right?

A. Yes.

Q. And Syngenta's response is that animal studies should produce a constellation of neurochemical, neuropathological and motor symptoms observed in human cases of PD or Parkinsonism; right?

A. Yes.

Q. And one of the neuropathological symptoms listed is loss and neurodegeneration of dopaminergic neurons?

A. Yes.

Q. Now the last bullet says:

"Paraquat had no effect on these parameters in our experiments after either [intra-peritoneal] ..."

And that references Breckenridge et al:

"... or oral administration at maximum tolerated doses, (Minnema et al 2014)."

A. Yes.

Q. Did you inform ANVISA -- the expert panel of ANVISA -- that Syngenta had observed the loss of dopaminergic neurons in paraquat-treated mice in previous studies?

A. I'm not sure whether that came up in the discussion because I was not actually present in the meeting.

Q. Who did that presentation?

A. Dr. Breckenridge.
Q. It looks like, if he didn't, he never told them anything about Dr. Marks' studies, did he?
A. It is a possibility.
Q. Look at this document and show me where he --
A. No, there is nothing on the slide, I agree.
Q. There is nothing there that he said one single word about it.
Would you agree with me that making that statement without producing those studies and telling those people about it was absolutely a misrepresentation?
MR. NARESH: Objection form, foundation.
A. I think that there's a reasonable argument that we could have actually included the word "consistent" in that. Then that would have included the reality of what we found, no consistent effect.
BY MR. TILLERY:
Q. Were you involved in drafting this presentation?
A. Actually, yes, I was. And it's a point I think with -- sometimes these things happen with the benefit of hindsight, it is probably something that we should have done.
Q. Would you, as a scientist, tell me right now that you should have put it in there, shouldn't you?
A. I think that's not unreasonable. But it doesn't

take away the overall conclusion that we were presenting.

Q. Right. You were trying to keep it from getting banned, weren't you?

A. No. I would object to that. At no point did we have a conversation where we said we would deliberately take that information out.

Q. Was it banned in Brazil?

A. No.

Q. Okay. Do they know today about those studies? Have you told them?

A. I don't know whether any further communication on those studies has been made.

Q. Are you still selling the product in Brazil?

A. We are.

Q. Okay. What do you think the reaction will be when this case comes out, all of the information comes out, that you didn't tell them?

MR. NARESH: Objection to form, scope.

A. I would still maintain that what we were presenting here -- as one often does in science -- was an overall weight of the evidence.

BY MR. TILLERY:

Q. Okay. So the weight of evidence you presented happened to be in favor of continuing to sell it; the weight of the evidence you omitted would be against continuing to

sell it, right?

A. Well, weight is weight, sir. The fact that we were finding effects in some of the studies, as were other people, was, in the context of this larger amount of information, a smaller proportion of that weight of evidence.

Q. You knew when you drafted this -- or helped draft it -- that you were omitting Louise Marks' words, right?

A. I think if you were inferring that we made a deliberate decision to do that then --

Q. No, excuse me. I move to strike that answer as unresponsive.

A. That is fine.

Q. Did you know, when you drafted this, did you happen to remember about Louise Marks' words?

MR. NARESH: Objection to form.

A. I think at the time these were drafted we were not considering the Marks studies in our weight of evidence thinking.

BY MR. TILLERY:

Q. Because they didn't reach the same conclusion, did they?

A. At the time they were suggesting otherwise, yes.

Q. So you left them out?

A. I say again, I'm not aware that I or anybody else

deliberately left them out.

Q. Did you just forget about them? Did you happen to forget about multiple studies of consistent results parallelling virtually identically the results of independent researchers in published literature, did you just forget about them?

A. We were aware that ANVISA, because they had told us that, were well aware that there was published literature showing that there was an effect in this mouse model. So they were not blind to the fact that there was another part of the weight of evidence that would suggest that that should be taken into consideration.

Q. So you are thinking they knew about McCormack, they knew about Di Monte's results?

A. I believe they had already told us about that in some of the responses they gave us.

Q. But they didn't know about the Marks studies, did they?

A. I imagine that they didn't.

Q. And you have never told them to this day, have you?

A. I don't know. I would have to check that. I don't believe so.

Q. All right.

Has paraquat been phased out in Brazil?

MR. NARESH: Objection, scope.

A. Not so far as I'm aware.
BY MR. TILLERY:
Q. If you look at the same page where you were under the questions that were asked by the regulatory authorities in Brazil?
A. Mm-hm.
Q. If you would like under "Response", the first bullet. Read that into the record, and that response is to which question?
A. Well, there are two questions above:
"Why could the results obtained in a study using PQ as a model for the induction of [Parkinson's disease] not be enough to consider such a substance as a potential causer of [Parkinson's disease] or Parkinsonism in humans?"
Q. So your response, the first bullet, responds to all of that?
A. Well, there is a second question which is:
"What would be necessary to conclude that the animal model studies show evidence of [Parkinson's disease] or Parkinsonism resulting from human exposure to [paraquat]?
Q. And your first bullet, would you read that?
A. "Only human epidemiological evidence can be used to conclude that a causal relationship exists between Parkinsonism in humans and paraquat exposure."
Q. Is that Syngenta's position today?

A. Causal means that you've got direct evidence in humans that there is a direct relationship between exposure to paraquat and the development of Parkinson's.

Q. What I'm asking you is, is the Syngenta position consistent with that today, that statement?

A. I would say that today we would still say that human epidemiological information would carry more weight in that weight of evidence that I was describing --

Q. That is not --

A. -- but animal model data are still part of that.

Q. Well, then your answer to them was wrong, wasn't it?

A. No, because the important word there is "causal" --

Q. No, the important word is the first one. Do you see that?

MR. NARESH: Steve, stop interrupting him.

BY MR. TILLERY:

Q. What does the sentence say? "Only", that's what I'm asking.

MR. NARESH: Just please let him finish his answers to your questions --

MR. TILLERY: He's not answering it.

BY MR. TILLERY:

Q. Just answer my question --

A. Yes.

Q. Is that statement --

MR. NARESH: Why don't you withdraw your prior --
BY MR. TILLERY:
Q. I will withdraw it. Let me ask you, here's what it says:
"Only human epidemiological evidence can be used to conclude that a causal relationship exists between Parkinsonism in humans and paraquat exposure."
Is that what it says?
A. That's what it says.
Q. Is that Syngenta's position today?
A. It is Syngenta's position that human epidemiological evidence is the only evidence, if you like, that can definitively lead to a conclusion about causality.
Q. Okay.
Would you go to the next page, sir, which is 116224? There's "Questions #3 and 4", do you see that, at the top?
A. Yes.
Q. And then down at the middle of the page, it says number 2:
"Establish that the results are reproducible."
A. Yes.
Q. Okay. And you said:
"The results from such studies must be robust and reproducible when investigators are blinded to treatment using confirmatory independent assessments both within and

between labs/research groups ..."

Okay?

A. Right.

Q. And then you say:

"In our experiments we have not been able to reproduce the results reported by others."

A. Yes.

Q. That's an absolute misrepresentation, isn't it?

A. Well, in the context of the conversation we have been having then clearly that, as we said before, did not fully include the, um, the earlier findings of our lab, yes.

Q. You agree with me?

A. Yes. As I said before, yes. With the benefit of hindsight, we might have put an additional clause in that to qualify.

Q. Namely all of the tests --

A. "Consistently" or --

Q. All of the studies that Dr. Marks did which verified the results of the independent researchers, correct?

A. That's something which we could have taken more consideration of, yes.

Q. And put it in there and told the truth, right, okay?

MR. NARESH: Objection to form.

A. I still believe that the truth is based on that overall weight of evidence, but that's, I think, a point we

have covered before.
BY MR. TILLERY:
Q. Did you ever tell ANVISA that Dr. Marks' studies provided evidence that dopamine were lost -- or had lost dopamine function?
A. As I said earlier, I'm not aware that we did that.
Q. Did you ever disclose to the ANVISA panel in Brazil that Syngenta CTL had replicated the loss of dopaminergic neurons in the paraquat treated mouse that Di Monte's group had observed?
A. I am not aware that we did that.
Q. Did Syngenta disclose to ANVISA that it had observed loss of dopaminergic neurons at lower doses in the Marks studies?
A. Lower doses than?
Q. Than the NOEL of 10.2 milligrams per kilogram per day that you had identified?
A. On which study -- which study are you referring to?
Q. What is a NOEL again, sir?
A. A no effect level.
Q. Okay. Do you reference that here?
A. The "no effect level" is in the notes, 10.2 milligrams per kilogram.
Q. Per day?
A. Per day.

Q. And did you tell them that it had observed a loss of dopaminergic neurons at lower doses in the Marks studies?

A. That isn't lower doses than the Marks studies.

Q. One of them had 10.0, do you know that?

A. Well, that's very marginal, I think, yes. Yes, yes. I think with the -- the analytical and other factors involved, 10 and 10.2 are essentially the same.

Q. So they are the same?

A. Yes.

Q. Okay.

Syngenta did not disclose to the Brazilian regulatory authorities that it had estimated a reference dose for paraquat based upon the loss of dopaminergic neurons in the substantia nigra, did it?

A. It did not talk about the work we were talking about here earlier.

Q. Okay.

Syngenta also made a number of presentations to update the United States EPA regarding its paraquat mice research, didn't it?

A. I believe it did, yes.

MR. NARESH: I will object to the scope of this line of questioning.

I think there is no (inaudible) about the interaction with the EPA. You can ask him in his personal

capacity --

BY MR. TILLERY:

Q. Okay. In your personal capacity is fine.

Did Syngenta ever disclose the full paraquat mouse research program conducted by Louise Marks in those updates to the US EPA?

A. I can't answer that question. I was not involved in those presentations.

Q. Okay. Did Syngenta ever disclose in those updates to the US EPA that CTL, the laboratory, had replicated the loss of dopaminergic neurons the substantia nigra seen in published literature?

A. Again, I was not involved in those presentations so I don't know the answer to that question.

Q. Did Syngenta ever represent to the US EPA that they could not replicate the loss of dopaminergic neurons seen in the published literature?

A. So we were not able to replicate?

Q. Yes.

A. Yes, that --

Q. Did you tell them that?

A. That was the nature of the research that we've just been talking about.

Q. Would that statement have been false?

A. Well, it depends on the context in which it was

said.

Q. Well, in the context of having known that Louise Marks did these studies that replicated the prior results?

A. Yes. But then, as we have said at some length, when these presentations were made we had done a lot more detailed research which had failed to replicate the findings.

Q. So at no time did you ever tell them about Louise Marks --

A. That I would need to check. Because, as I say, I have not been involved in all those communications.

Q. Wouldn't transparency have required you to disclose the Marks studies and allow the agency to decide their significance or relevance?

A. One thing of course we can say, because we mentioned it earlier, is that one of those Marks studies was submitted to the EPA.

Q. Yes. But wouldn't transparency -- and when in case of doubt doing the right thing, in terms of being fully transparent, as you said it's your desire to do -- have pushed you to the direction of full disclosure?

A. I -- as we said with Brazil, it is possible that with the benefit of hindsight, you could make that judgment. It would still -- and I would repeat -- not change our

conclusion that the overall weight of the evidence suggests that their -- that paraquat does not have a reproducible effect on the substantia nigra.

Q. That was not my question. I will move to strike it as unresponsive.

My question is: would you agree that in the interests of full compliance in case of doubt, that it would be best to err in terms of being fully transparent with the agency, the regulatory agencies, responsible for guarding the public's interest; would you agree with that?

A. Yes, but they were aware of the Marks study that we talked about earlier through the 6(a)(2) process.

Q. I'm talking about all of the studies. Would you agree it would be best to err towards inclusion and to make them aware of all the findings?

A. That is -- I have said several times that a different judgment could be made which would incorporate those findings as well.

Q. And you actually made that judgment and recommended that course, didn't you?

A. With regard to reporting under 6(a)(2), I said it might be something that was considered, yes.

(Exhibit 41 marked for identification)

BY MR. TILLERY:

Q. Please read this email exchange including

Dr. Louise Marks in her last week of employment.

A. So you want me to read everything right from the first email?

Q. No, I just want you to read it yourself.

A. Okay, that's fine.

Okay.

Q. She issued her study reports on June 21, 2007, didn't she?

A. That's the date we saw earlier.

Q. This email exchange is 2007, June 22nd, the following day. Right?

A. Mm-hm.

Q. And in her first email, she says:

"From 30th June my contact email will be ..."

And she points out that that's her last week, okay?

A. Yes.

Q. And then she sends this to Barry Elliott. Who is that?

A. Yes. Barry Elliott by that time had taken over the role that Mike Clapp had, if you remember Dr. Clapp earlier? So he was the product toxicologist for paraquat.

Q. What did she send in that email?

A. She sent details of the studies that we were discussing earlier and that they -- the studies had been issued, as we saw earlier, and that in accordance with

proper practice the raw material, the data and the slides had been archived.

Q. And she sent along XM7229, XM7258, XM7371, XM7480, XM7552, XM7570, XR7641; correct?

A. That's correct.

Q. All of the study materials she sends along?

A. Yes.

Q. And then this information is sent on by Barry Elliott to a person named Sheldon Ros, right?

A. Mm-hm.

Q. And he says:

"Can you check this SAMSON part please."

What is a SAMSON part?

A. SAMSON is essentially -- or was at that time -- our document management system.

Q. And he says to Mr. Sheldon Ros --

A. It is Ros Sheldon. It is a lady.

Q. Okay. So says to Ros Sheldon:

"We must control the accessibility of them to that usual for any such investigate reports."

Right?

A. Yes.

Q. And Ros Sheldon says:

"They are all entered as Research reports not for submission."

A. Yes.
Q. What does "submission" mean?
A. Submission to a regulatory authority.
Q. That means they are not to be submitted to the regulatory authority. That's where they are filed?
A. And this, let me say, is absolutely normal practice and was nothing specific to these reports.
Q. Okay. All right, got it.
But just coincidentally, they didn't get submitted to regulatory authorities, did they?
A. They did not, I believe.
MR. TILLERY: Thank you. We will take a break right now.
THE VIDEOGRAPHER: We are going off the record at 3:53.
(Break taken.)
THE VIDEOGRAPHER: We are back on the record as of 4:08. You may continue.
BY MR. TILLERY:
Q. Earlier in the day I told you that I would come back to the topic of potentially referable findings, remember that?
A. Yes.
Q. Let's go back to the history of that group. When was the first time that Syngenta -- and by that I mean the

definition we agreed to yesterday at the beginning of the deposition, to include all of the entities -- when was a potentially referable finding committee first created in the Syngenta organization or by its corporate predecessors?

A. Well, again, remembering that we have to make the distinction between the US PRF committee which is the one that is accountable for fulfilling the obligations of the law, I can't speak directly as to when that committee was formed because I was never part of it. But we certainly set up the -- the approach committee within our function at the time that was required in order for us to start complying. I can't give you a date for that either off the top of my head.

Q. I didn't understand what you said, approach committee?

A. You remember I said this morning that the product safety organization as we now call it met to consider if findings were truly adverse as defined by the legislation, and then sent our recommendations to the US committee.

Q. So the product safety committee?

A. That's the product safety -- what we call the PRF approach committee.

Q. Okay, the PRF approach committee?

A. Yes.

Q. And that's the group that you discussed about your

2009 and 2011 documents discussing the impact paraquat would have?

A. No, that's different. No, we are talking about when studies are conducted, and we get the results and we have interpreted them, whether the -- they would meet the criteria of, or could potentially meet the criteria, of 6(a)(2).

Q. Okay. I want to start over if we can. I want to try to understand every single one of these different groups, subgroups, that impact paraquat.

A. Right.

Q. And I want to talk about them and then their interrelationship with America, okay?

A. Okay.

Q. So let's start over, if we can?

A. Sure.

Q. And let's go through each one of them. You have a Paraquat Parkinson's group, what is that called?

A. So we have since 2008 --

Q. Okay, in 2008 --

A. Yes, we created the paraquat health science team.

Q. And you certainly by that don't mean the health of paraquat, do you?

A. No. No, we don't.

Q. Okay. So the paraquat health science team?

A. Yes.
Q. Let's get them all down first --
A. Okay.
Q. -- and then let's come back and see how they inter-relate.
A. Right.
Q. And then what's next?
A. Well, maybe the closest related to that, which we talked about yesterday, is the paraquat issues leadership team.
Q. The paraquat issues leadership team.
A. Correct. And that was responsible for overall governance. Remember we discussed who authorizes studies, et cetera.
Q. Okay. When was that started?
A. I am not -- I can't give a date, precise date to that. As I say, 2008 for the health sciences team. I can't remember when the PILT -- this is the PILT -- when that was created.
Q. Before or after the paraquat health science team?
A. I think it would be around about the same time, actually, yes.
Q. Okay.
A. Right. So they -- they were tasked with our research program on paraquat, particularly the health

sciences team, with some governance from the PILT.

Q. Okay.

A. Right. Now if you then look at the product safety function, which is the organization that I for a time was leading, a separate committee to what we have just been talking about because it dealt with any potentially -- any findings from studies on any compounds that we were testing or any information that we were getting from the outside world, the PRF approach committee --

Q. PRS approach --

A. PRF, potentially referable findings, approach committee was set up within what we now call product safety in order to discuss whether the findings might meet the criteria for a 6(a)(2) as defined in that regulation we were reading out this morning.

And they would send on their recommendations or their -- the outcome of their discussion to the US PRF committee. So a separate committee -- this is coming to your point -- was the United States PRF committee, and it was that committee which had the accountability to make the final determination of what was submitted to the US EPA.

Q. And so it is potentially referable --

A. Findings, yes.

Q. -- referable findings committee?

A. Yes.

Q. Now, so we have identified four different committees?

A. Yes.

Q. Are they the only ones that could have anything to do with paraquat?

A. Well, if we go back further in history, there were other bodies --

Q. I will get to those. But right now, those are in existence?

A. Right now, those are indeed all in existence still.

Q. How many PRF committees are there in the entire umbrella of Syngenta?

A. Well, there are other PRF committees in other regions. I believe, for example, although I don't have any direct contact, that there may still be a European PRF committee that has a similar task to the US to comply with the appropriate legislation in the EU.

Q. Well, is there one or not?

A. I don't know, because I no longer have any interactions in that area. There certainly was for a -- a period -- significant period, when I was directly involved with the PRF process. I no longer am directly involved with the PRF process.

Q. And they would then make potentially referable finding conclusions about notifying regulatory authorities

in different countries?
A. Correct.
Q. And that might include, of course, the fact that as Syngenta sells paraquat in multiple different countries --
A. Yes.
Q. -- it may include reporting or making reports in those countries --
A. Yes.
Q. -- about paraquat?
A. Yes, yes.
Q. Okay. In how many countries is paraquat sold by Syngenta?
A. I don't have that figure in my head.
MR. NARESH: Object to the scope on that.
MR. TILLERY: Actually, it is one of his topics.
MR. NARESH: Which topic?
MR. TILLERY: I don't have the topic list. It is right there in front, in your stack of papers.
BY MR. TILLERY:
Q. Does the Syngenta executive committee have anything to do with this?
A. With what, sir?
Q. With any oversight of paraquat?
A. Well, in the sense that it has oversight of the way in which paraquat is used and sold and marketed, of course,

as one of the key products in the company.

Q. And as a result of that, the SEC that you identified this morning and described in terms of their authority, would be put on notice and -- about items that might have some bearing on the sales of the product?

A. They would, yes.

Q. Okay. And research concerning the product?

A. Any significant research they would potentially be informed about, yes.

Q. And how many members are on the SEC?

A. At the moment less than ten. This has changed very recently because we are now Syngenta Group so the numbers change actually from one -- almost from one year to another.

Q. Syngenta's headquarters are in Basel, Switzerland?

A. They are.

Q. And in what parts of the world are you located?

A. In virtually all parts of the world.

Q. Okay. So you have operations in South America, and the Pacific Rim, all over North America, Canada, Australia?

A. Yes.

Q. China?

A. Yes.

Q. Africa?

A. Yes.

Q. Is there an area of the world where you don't have

a dominant position in terms of agricultural chemicals?

MR. NARESH: Objection to form and scope.

I am not seeing it in the -- if you can point me to something, I am just not seeing anything -- I am fine with you asking questions in his personal capacity on Syngenta sales, but I am not seeing it in the topics.

MR. TILLERY: No, no, I was talking to it -- well okay.

BY MR. TILLERY:

Q. Go ahead.

A. Well, we are a leading crop protection company in what we call all the four main regions of the world: Asia Pacific; European -- Europe, Middle East and Africa; North America and South America.

Q. Has there been any significant change in the way Syngenta is managed since the acquisition by ChemChina?

MR. NARESH: Objection to scope.

A. We still have the Syngenta executive committee who is responsible for the strategy and operation of Syngenta and its associated businesses.

BY MR. TILLERY:

Q. But in terms of its leadership teams, its hierarchy of responsibility, is it generally the same?

MR. NARESH: Same objection.

A. It is generally the same, although recently we have

formed this Syngenta Group which -- where other companies are now part of that group, and the leadership team has changed as a consequence of that.

BY MR. TILLERY:

Q. Now the descriptions that you have given to me -- you talked about the paraquat health science team -- is that comprised of members of Syngenta employees only?

A. The team is -- the core team is certainly Syngenta employees. But we have consistently, since 2008, included in our teams and our team meetings external experts. Some have had a longstanding relationship with us, others have had -- come in from time to time.

Q. And what is the overall responsibility of that team?

A. To address the issue of whether paraquat could be a causative agent in Parkinson's disease.

Q. And you have involved outside lawyers in that team as well?

A. Occasionally outside lawyers have come in to talk to us.

Q. But actually, more than talk to you; right?

A. Perhaps you could clarify what you mean?

Q. Well, have you had lawyers from Fulbright Deloitte sit in on your meetings, presentations at science committees?

A. That has occurred, yes.

Q. And they have actually made presentations?
A. Yes, that's true.
Q. All right. You have been there when they have made presentations?
A. Yes.
Q. And they are there during scientific reports and giving advice about the inclusion of information in those reports; correct?
A. By reports, you mean what?
Q. Well, let's say this: PowerPoints with the rest of the group, editing PowerPoints, are you aware they did that?
MR. NARESH: Objection to form.
A. I was not aware that external counsel were involved in editing our PowerPoints.
BY MR. TILLERY:
Q. Would you think that that would be inappropriate?
A. I think under some circumstances it certainly would.
Q. Why? Why would you that having some outside lawyer from some private law firm in America editing your reports and telling scientists what they can and cannot say about paraquat would be inappropriate?
MR. NARESH: Objection to form.
A. I don't believe in my experience that has happened.
BY MR. TILLERY:
Q. Okay. So you certainly would not put up with it,

would you?

A. No.

Q. Okay, what would you tell them?

MR. NARESH: Objection to form.

A. I would tell them that they are perfectly entitled to give advice about how we are made aware of the situation that exists in terms of things like potential litigation. But we -- we would not expect them to be saying "you do this experiment and not that experiment".

BY MR. TILLERY:

Q. Or that you say this about this chemical, or you say that about this chemical?

A. Absolutely, absolutely.

Q. You would think that that should rest within the discretion of the Syngenta scientists and leadership team within Syngenta; correct?

A. That is part of the ethos of the team exactly, yes.

Q. Right, right.

Now, can you tell me in terms of the paraquat health science team, is it made up of people from around the world, or are you located in one particular geographic area?

A. No, it's from more than one part of the world. So we have people -- or have had people, again there is history of people, some people being in it at one time and not at others -- but we generally have people from both Europe and

North America, particularly.

Q. Any other parts of the world besides Europe and North America?

A. Generally speaking, no. It has largely been from those two regions.

Q. Has there been any specific accomplishment by the paraquat health science team in terms of the progression of your thinking about paraquat and Parkinson's disease?

MR. NARESH: Objection to form.

A. Well, I think you have seen that the work program that we have conducted in the form -- and how it has been published, the kind of experiments that we have done -- and we spoke yesterday about experiments which are still in progress to completion and publication.

So our achievements have been to conduct a large body of research and to put that into the public domain as much as we can.

BY MR. TILLERY:

Q. Have you received advice from any outside lawyers about what studies you should do?

A. Not in terms of what studies we should do, no.

Q. Okay. Again, would that fall into the realm of things that you would think would be inappropriate?

A. Unless there was a particularly good reason to -- to give out that kind of advice then, generally speaking,

I wouldn't want the science -- good science to be not allowed to progress.

Q. Would you agree with me that an outside lawyer who is retained primarily to represent the company in terms of potential exposure from the sale of its product would have different kinds of motives than that of a scientist whose motives are to obtain an accurate objective reproducible scientific result?

MR. NARESH: Objection to scope, form.

A. Call it motives, different agendas, what you will, of course, yes, that's true.

BY MR. TILLERY:

Q. That seems pretty fundamentally correct, yes?

A. Of course.

Q. And that's the reason why you wouldn't want them telling you what science to do, would you?

MR. NARESH: Same objection.

A. And why in my experience, I don't recall ever having been told by lawyers not to do --

BY MR. TILLERY:

Q. Ever saying that?

A. No.

Q. And if that happened, they didn't tell you about it?

A. Indeed.

Q. Okay.

Let's talk about -- I don't remember the name of the group that you headed up.

A. Yes, yes.

Q. What was the name of that group?

A. It didn't have a particular name. I think you're referring to the documents where we were talking about reference doses and so on.

Q. It was you, Dr. Sturgess and --

A. Dr. Travis.

Q. Dr. Travis.

A. And Mr. Cook.

Q. And you had two documents, 2009 and 2011. What was the name of that group?

A. Well, we didn't call ourselves -- there wasn't an official title. We were part of what we called a -- the paraquat technical team, which was a subset of the paraquat health science team.

Q. And how do you keep all these teams, committees, groups, straight?

A. That's part of my leadership responsibilities.

Q. So that's the paraquat --

A. Let's describe it as the paraquat technical team.

Q. Technical team?

A. Yes.

Q. Okay.

And are you no longer on that team?
A. No, I'm still part of that team.
Q. All right. Are you the head of that team?
A. I still act to head that team, yes.
Q. All right. And how long has that team been in existence?
A. It's been part of the modus operandi of the health science team, i.e. being a group which feeds into the health science team, for as long as the health science team has been in existence.
Q. Okay. So in 2008 or thereabouts when the paraquat health science team started, you started a technical team to support it --
A. We had something similar to what we've got now. Different people -- some different people, but broadly having the same --
Q. Do you have marketing people on the paraquat health science team?
A. No.
Q. Okay. Do you have marketing people on the paraquat issues leadership team?
A. Yes.
Q. And who are those people?
A. I -- I can't give you names off the top of my head. And today the paraquat issues leadership team is a looser

association, it is a looser organization than it used to be until a few years ago.

Q. Can you explain why you have marketing people on the paraquat issues leadership team?

A. I believe that it was thought wise to have -- to give again transparency to the marketing organization about, um, safety and regulatory issues regarding paraquat, so it is giving them foresight of things that could affect their ability to sell paraquat.

Q. Anybody from the business side on the paraquat health science team?

A. No.

Q. Okay. You talked about different PRF committees, and you mentioned the difference between the US and Europe. Are you aware of any other PRF committees with respect to regulatory oversight by other countries?

A. No, I am not aware. I am not saying that there aren't, but I don't remember having visibility of any other PRF committees other than the one in Europe.

I don't even know whether that still works. I assume it does, but I don't see evidence of that, or the North American one.

Q. When an adverse effect is reported to the regulatory authority in the United States, the US EPA, is it automatically reported in other countries where the product

is sold?

A. I'm not sure if that process is in place. I don't know.

Q. Was it when you were on the committee?

A. I -- at the time I was on the committee I don't know, because I think as I said earlier the US PRF committee I was not a member of that, so I don't exactly know what their onwards process of communication was, other than into the EPA.

Q. When a person makes -- or scientist makes -- a finding and sends it to, you said, a PRF approach committee, do they get it before the PRF committee?

A. Yes. Because the PRF approach committee is within the function that is generating the data doing the studies, either within the function itself or at contract research organizations. So they are the scientists who first become aware of the findings.

Q. And they then do an evaluation?

A. They evaluate whether the findings -- whether they are real, whether they are related to treatment, if they are adverse and if they fulfill the criteria for 6(a)(2).

Q. And they say it doesn't, does that stop it? Right there it ends?

A. If the committee -- if that approach committee makes -- if it is clear to that approach committee, and this

is my experience from sometimes chairing that committee as well as being part of it, if it is clear that the criteria are not fulfilled then the record is there that we had that discussion, but it does not get submitted to the US committee.

If it is clear that they do meet the criteria, or if there is any doubt, then they are submitted to the US committee.

Q. Okay. It goes to the PRF committee?

A. To the US PRF committee, yes.

Q. Okay.

So along the process, the PRF approach committee has the authority to stop the advancement of an adverse effect potentially being sent on to a regulatory authority, and the PRF committee itself does, right?

A. Yes.

Q. And then after the PRF committee makes the recommendation, where does it go from there?

A. Are you there referring to the approach committee or the US committee?

Q. No, the US committee. The PRF committee in the United States?

A. If the US committee believes that it meets the criteria of 6(a)(2), it will submit to the US EPA.

Q. Without further ado?

A. I don't believe there is another check in that process.

Q. Okay. So you don't believe the Syngenta executive committee has to approve any decision or recommendation by a potentially referable finding committee about whether to report adverse effects to regulatory authorities?

A. I don't believe that the Syngenta executive committee gets involved in that kind of decision.

Q. Now have we identified all people outside of Syngenta in all the committees? Are there other people who are not fully employed by Syngenta who occupy roles in any of these committees other than one you've described for me?

A. Right. So certainly there are no outside non-employed -- Syngenta employed -- people on either of the PRF committees. So we can exclude those.

Q. Okay. All right.

A. There is nobody outside of Syngenta on the PILT.

Q. Okay.

A. Paraquat issues leadership team.

Q. All right.

A. As I said earlier, when it comes to the paraquat health scientists team, we have had people, consultants, outside experts, be part of that team for in some cases quite a long period and other cases for a short period.

Q. Okay. Is a notifiable effect the same as

a potentially referable finding?

MR. NARESH: Objection, calls for a legal conclusion.

A. Possibly, yes. It sounds a reasonable conclusion.

BY MR. TILLERY:

Q. Have you ever heard of the term "notifiable effect" being used at Syngenta?

A. Yes, it is a term which is sometimes used, yes.

Q. Interchangeably with --

A. Yes, my understanding of how that would be used would be interchangeable with potentially referable, yes. That's not to say that other people might have a different view, but that would be my understanding.

Q. If a product is determined to be potentially neurotoxic does that indicate to you that much more care in analysis is required because of possible serious harm or death to consumers?

A. We take all potential findings in studies that may have consequences for human health very seriously, so not just neurotoxicity.

Q. So, in other words, you don't treat products that are determined to be potentially neurotoxic any more seriously than any other product?

A. That is in no way to diminish what you -- what you are inferring, that any potential health effect is something

which we need to take seriously.

Q. Okay. Would you agree with me that if a product is determined to be potentially neurotoxic, it sends an indication, a red flag to you that care, deliberation, caution is required because of the potential side effects to, impact caused -- whatever you want to call it -- to the consuming public, the people who by your product?

MR. NARESH: Objection to form.

A. Of course. And that has always been the ethos of the approach committee which I was apart of, indeed.

BY MR. TILLERY:

Q. Let's talk about countries that have banned the chemical paraquat, okay?

Does Switzerland allow paraquat to be used?

A. I believe it does not.

Q. Okay. Does England?

A. No.

Q. Does France?

A. No.

Q. Germany?

A. No EU country does.

Q. So I could go through the whole list --

A. You could.

Q. -- and none of them, okay?

When you say "EU", every country ever of the

European Union has banned it?

A. It was part -- well, because the decision-making is done at the EU level and we were talking about that list just now.

Q. All right. So it can't be sold in the EU?

A. That's the current position, yes.

Q. All right. What other countries have banned it?

A. Well, a number of other countries in the Far East, China for example. Again, I would have to check back on the list that -- yes, the number of countries have banned it.

Q. Who keeps that list?

A. The marketing organization.

Q. Okay. And you say China. When did China ban it?

A. Again, I can't remember the exact date.

Q. And did Vietnam ban it?

A. I can't remember whether that was one of the countries.

Q. What other Pacific Rim countries have banned paraquat from being sold in their countries?

A. Well, I think I would need notice of that question to check. It is not a list that I tend to keep in my head.

Q. Do you know the rough number of countries --

A. I think you indicated a number this morning --

Q. I told you 32, but I think my information might be out of date.

A. Yes, I can neither confirm nor deny that.
Q. Who is -- strike that.
Who owns Syngenta?
MR. NARESH: Objection, scope.
A. ChemChina.
BY MR. TILLERY:
Q. Where is Syngenta headquartered?
A. Basel.
Q. Okay.
Was paraquat banned by any country because of its neurotoxicity, or its potential to be neurotoxic?
A. I don't believe so. But I would -- again a detail that I would need to check. My understanding is most of the bans have been associated with its acute toxicity.
Q. Has paraquat been banned by any country because Syngenta could not establish that it was not neurotoxic?
A. I'm not aware of that, but again I would need to check the detail.
Q. Has any country banned paraquat because of a risk of brain injury?
A. I am not aware of that.
Q. But you can't deny --
A. I would need to check that.
Q. Has Syngenta been asked by any country considering the registration and permission to continue to sell it to

provide evidence that it is not neurotoxic?
A. Well, we did discuss earlier on this afternoon Brazil, for example.
Q. We went through that.
A. They were asking questions about that matter --
Q. So excluding Brazil and their request for information about neurotoxicity?
A. Yes.
Q. Any other country ask for that same information?
A. I can think of another example in the form of Australia.
Q. Have they asked for that?
A. They asked for our evidence which we discussed with their regulatory authority, yes.
Q. And when did they ask for that?
A. I can't give you the date. It was -- I think we are talking about over the last ten years or so as they have been rereviewing.
Q. And Charles Breckenridge made a presentation to them there, didn't he?
A. He did, yes.
Q. Just like he did to the folks in Brazil?
A. Yes.
Q. And in that presentation he didn't mention anything about Louise Marks, did he?

MR. NARESH: Objection to form.

A. And I think the same applies to what -- to the discussion we had earlier that two things are important.

First of all, Australia were well aware of the published literature suggesting that paraquat has an effect on the mouse brain, so they were starting from an assumption that that might be something of significance. But they saw from the extensive research that we have done that that was giving a different weight of the evidence.

BY MR. TILLERY:

Q. Okay. I move to strike the answer as unresponsive.

Could you repeat my question, please?

COURT REPORTER: "And in that presentation he didn't mention anything about Louise Marks, did he?"

A. I believe he did not.

Q. To your knowledge, the Australians selling or allowing paraquat to be sold today know nothing about the studies that you did internally in CTL by Louise Marks, right?

A. That is a possibility. But again I would need to confirm that with other colleagues.

Q. Okay.

Has Syngenta ever reported to any regulatory agency anywhere on this globe that paraquat is neurotoxic?

MR. NARESH: Objection to scope.

A. I do not believe so.
BY MR. TILLERY:
Q. Okay. Has Syngenta ever reported to any regulatory agency that paraquat has the potential to be neurotoxic?
MR. NARESH: Objection to scope.
A. Yes, because as exemplified by the discussions we had with Brazil, we said the potential was there, which was why we were conducting our research program.
BY MR. TILLERY:
Q. You were telling them about the potential. Why didn't you tell them about Louise Marks?
A. Well, as I say, hindsight is a wonderful thing, and we could have added the Marks studies to what these regulatory authorities already knew, which is that that mouse model has, in the hands of some researchers, shown an effect, an apparent effect, of the paraquat.
Q. You don't think it makes a little bit of difference if the people involved in the manufacturing and sell -- sale -- and who have an obligation to go forward with the registration of the chemical, if the same people behind that chemical had done testing within their own laboratories and made findings that are consistent with outside scientists, you don't think that's important to regulators?
MR. NARESH: Objection to form.
A. I don't think I have ever said that it is not

important to regulators. And I have said, I think, several times now that in my view it would have been not an unreasonable course of action to include that, but obviously the overall weight of evidence was telling us something differently.

BY MR. TILLERY:

Q. Have you ever told anyone not to report an adverse effect of paraquat to any regulatory agency?

A. I am not aware that I have ever done that.

Q. Are you aware of anyone at Syngenta who has ever told anyone not to report the results of an adverse effect of paraquat to any regulatory agency?

A. Again, I'm not aware of that being said in any -- in any direct way, no.

Q. Have you ever participated in a group that discussed whether to report an adverse effect of paraquat?

A. The PRF approach committee is the closest that I've got to. But again that's making recommendations, not decisions.

Q. And you told us about that earlier.

A. I did.

Q. When you made the recommendation for the US EPA?

A. That is correct.

Q. Did the Syngenta executive committee ever decide not to report a potential adverse effect of paraquat to

a regulatory agency?

A. Again, as I have said before, in my experience I don't think the SEC have ever been involved in making those decisions.

Q. Would you agree with me, sir, that companies engaged in the development and sale of a product subject to ongoing regulation like paraquat have an obligation to be truthful to those regulatory bodies and to the public when they report their scientific findings?

A. I do agree with that.

Q. Okay. Would you agree with me that companies engaged in the development and sale of a product subject to ongoing regulation like paraquat have an obligation to the public to share their scientific findings?

A. Yes, I agree with that.

Q. Would you agree with me that Syngenta scientists are ethically required to share their scientific findings about paraquat?

MR. NARESH: Objection to scope.

A. I do agree.

BY MR. TILLERY:

Q. Would you agree with me that the amount of money Syngenta makes should never, ever, be a reason or justification for concealing health risks of paraquat?

A. Very much so, yes. I agree.

Q. Okay. Can you think of any justification for concealing or withholding information about an adverse effect concerning paraquat?

A. Only if the -- the definition of a PRF, for example, has not been felt to have applied, which is the case we were discussing earlier.

Q. Would you agree with me that withholding scientific findings from the public about the neurotoxic effects of paraquat would be unethical?

A. If we truly believed that paraquat had genuine neurotoxicity, then of course we would not wish to withhold that.

Q. And do you agree with me that would be improper and unethical?

A. If we genuinely believed that that was the property of paraquat.

Q. But it is only when you subjectively believe it, right?

MR. NARESH: Object to form, argumentative.

A. Could you repeat the question?

BY MR. TILLERY:

Q. It is only when you believe it, that is the standard?

MR. NARESH: Objection.

A. No, let me qualify that by saying that this is

dependent on the best possible scientific evidence which, when I have been talking about weight of evidence, is what we have been engaged for many years in trying to create.

BY MR. TILLERY:

Q. Would you agree with me that withholding scientific findings from the public about the neurotoxic effects of paraquat would be fraudulent?

MR. NARESH: Objection to form.

A. If there were -- if the weight of evidence had suggested there was clear neurotoxicity, then I don't know whether you call that fraudulent, but I think it is certainly not something that we would -- we would do.

BY MR. TILLERY:

Q. Well, whether or not you would do it or not, would you agree with me that if you did it, it would be fraudulent?

MR. NARESH: Same objections.

A. I don't know that I would be happy to -- to use the word "fraudulent".

BY MR. TILLERY:

Q. Okay, let's substitute a word. Let's substitute the word "dishonest"?

A. I think that is probably a better --

Q. Are you okay with that word?

A. Yes.

Q. Let me start over again. Would you agree with me that withholding scientific findings from the public about the neurotoxic effects of paraquat would be dishonest?

MR. NARESH: Same objection.

A. Yes, and again if we had come to a conclusion on that subject based on the best science.

MR. TILLERY: I am at your magic number. I will see on you the 31st.

A. I understand, sir.

MR. NARESH: Let me just make on the record, I do anticipate having redirect for this witness. I understand that my opportunity for redirect will come at the conclusion of your questioning and I do object to the use of this deposition until I have my opportunity for redirect.

THE VIDEOGRAPHER: At that point, are we concluding for today?

MR. TILLERY: We are.

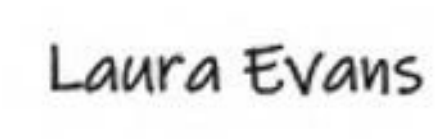
THE VIDEOGRAPHER: In which case we shall go off of the record at 4:49 pm concluding today's part of the deposition.

(Whereupon, the deposition concluded at 4:49 p.m.)

CERTIFICATE OF COURT REPORTER

I, Laura Evans, an Accredited Real-time Reporter, hereby certify that the testimony of the witness Philip Botham in the foregoing transcript, numbered pages first page 244 through last page 495, taken on this 26th day of February, 2020 was recorded by me in machine shorthand and was thereafter transcribed by me; and that the foregoing transcript is a true and accurate verbatim record of the said testimony.

I further certify that I am not a relative, employee, counsel or financially involved with any of the parties to the within cause, nor am I an employee or relative of any counsel for the parties, nor am I in any way interested in the outcome of the within cause.



Signed: .....

Name: Laura Evans

Date: February 27, 2020

Ragan Naresh, Esq.
ragan.naresh@kirkland.com
March 3, 2020
RE: Hoffmann, Diana v. Syngenta Crop Protection LLC
2/26/2020, Dr. Philip Botham, V2 (#3984465)

The above-referenced transcript is available for review.

Within the applicable timeframe, the witness should read the testimony to verify its accuracy. If there are any changes, the witness should note those with the reason, on the attached Errata Sheet.

The witness should sign the Acknowledgment of Deponent and Errata and return to the deposing attorney. Copies should be sent to all counsel, and to Veritext at cs-ny@veritext.com.

Return completed errata within 30 days from receipt of testimony.

If the witness fails to do so within the time allotted, the transcript may be used as if signed.

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Dr. Philip Botham, V2 (#3984465)

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Dr. Philip Botham, V2 Date

Hoffmann, Diana v. Syngenta Crop Protection LLC

Dr. Philip Botham, V2 (#3984465)

ACKNOWLEDGEMENT OF DEPONENT

I, Dr. Philip Botham, do hereby declare that I have read the foregoing transcript, I have made any corrections, additions, or changes I deemed necessary as noted above to be appended hereto, and that the same is a true, correct and complete transcript of the testimony given by me.

_____ _____

Dr. Philip Botham, V2 Date

*If notary is required

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& 245:16 246:9,14 248:9,14 249:13 297:9 328:7 329:5 353:6 363:1 410:12

0

00493318 248:10
00493392 248:10
01586117 249:15
01586606 249:16

1

1 371:8 392:18
1,1'dimethyl 331:13
10 314:24 334:6 349:21 362:13 390:17 393:18 429:3 432:20 456:7
10.0 456:4
10.2 455:16,22 456:7
1001 283:10
10:15 296:5
10:27 296:8
10mg 331:12 382:8
116224 453:15
116230 445:15
11:49 359:15
12 282:8
12:08 359:18
12:33 377:21
13 357:20 358:12 399:25 410:7 415:25
13.8 338:11
1301 246:14
13636 494:19
13th 249:14
14 282:4 390:18 391:16 410:8 424:7,10 445:16
14th 249:14 416:1
15 370:17
159.165 285:13 286:6,14,25
16 358:3 404:14
16.5 358:3,7,24
17 245:7 248:22 332:13 348:16 360:17
18 249:5 273:17 283:10 392:17 431:20 445:8,13
190 246:19
1962 261:1
1965 261:3
1972 281:9
1981435 378:5
1989 298:5
1990s 285:10
1993 300:3
1999 302:2
1:26 377:24

2

2 249:25 251:5 275:13,25 281:10 281:14,22 282:8 290:4 296:8 372:14 382:21 398:6,15 400:23 404:3 444:8 453:19 459:12,21 464:7 466:14 479:21 480:24
2/26/2020 495:5
20 497:15
2000 309:8
20004 246:15
2002 352:22 353:5 363:1 429:4
2003 248:22 304:24 326:18,20 327:12 332:13,16 335:19 348:16,18 353:5,6 363:1
2004 248:19,24 249:2 306:15 343:3 360:15,17 371:1,25 372:17 372:18 378:13 379:4 381:24 429:4
2005 249:6 392:17 392:18 429:5
2006 248:6 249:7,9 257:23 258:15 400:22 403:17 404:24 405:10
2007 250:2 332:24 333:13 348:25 349:7 360:19 392:14 460:7,10
2008 249:14 410:8 414:12 415:23 416:3 419:8,9 428:7,9,11 464:19 464:20 465:17 471:9 477:11
2009 249:19 427:16 464:1 476:12
2011 249:22 430:13 431:16 432:4 464:1 476:12
2013 433:7
2014 446:17
2016 250:1 444:8
2018 298:5
2019 358:12 363:16 399:25
202 246:15
2020 245:12 251:4 494:7,22 495:3
20s 271:10
21 248:5 256:14,19 256:25 332:15,24 349:7 392:14 460:7
22 248:7 250:2 256:16,17 258:19 348:18,23
22nd 460:10
23 248:9 296:20,21 343:3
23-27 248:19
23.7 351:12,13 352:4
238 329:2
24 248:11 249:7 318:9,10 352:17 400:22 403:17 404:24
241-4844 246:5
244 494:5
25 248:14 328:1,3 352:6,18 362:11 432:21 442:1
25-30 338:13
251 247:4,5
256 248:5,7
26 245:12 248:15 251:4 330:20,24
26th 246:10 360:15 494:6
27 248:17 342:17 342:24,25 343:1,3

494:22
2792 395:2
2793 393:8,15
28 248:21 347:4,8 390:18 391:16 393:21 394:12,14 394:18
2807 396:21
29 248:23 359:21 359:24
2905 336:17,18
2910 337:19
296 248:9
2:34 422:9
2:57 422:22

3

3 249:9 327:2 331:12 359:18 362:13 378:24 379:3 390:17 393:18 453:16 495:3
3.9 336:19
30 245:17 248:25 352:7 370:3,20,21 412:14 495:17
30s 271:10
30th 460:14
31 248:6 249:3 378:1,4
314 246:5,20
318 248:11
319 297:17
31st 493:8
32 249:5 280:4 392:2,4 484:24
328 248:14 298:25
33 249:7 400:5,7 400:21
330 248:15 299:24
331 301:18
333 306:8
335 308:1
34 249:8 406:1,4
342 248:17
3432 409:4,8
347 248:21
35 249:10 352:18 408:25 409:2
359 248:23
36 249:12 316:11 316:12 410:3
3600 246:4
37 249:15 414:18 416:8
370 248:25
378 249:3
38 249:17 422:5,13 423:2,3
389-5267 246:15
39 249:20 422:14 430:2,3
392 249:5
3984465 495:5 496:2 497:2
3:53 462:15
3rd 249:2 371:1 378:25

4

4 304:24 422:22 434:6 453:16
4,4'bipyridinium 331:13
40 249:23 286:6,24 443:24 444:2
400 249:7
406 249:8
408 249:10
40s 271:10
41 250:2 459:23
410 249:12
414 249:15
415 246:11
422 249:17
430 249:20
44.0004 434:7
443 249:23
459 250:2
480-1927 246:20
484239 329:22
492792 402:3
493318 296:23
495 494:6
4:08 462:18
4:49 493:19,21

5

5 314:24
50 370:19
502d 422:14
505 246:4
517 245:7

6

6 248:23 275:25 281:10,14,22 290:4 306:15 378:13,16 379:4 382:21 398:6,15 400:23 404:3 459:12,21 464:7 466:14 479:21 480:24
60 253:3 269:20,23 271:6,7,19,20,22 271:23,24 272:23
600 246:19
60s 272:7
6223 445:18
628 319:2
63101 246:5
63105 246:19
633 319:10
638 323:16
641 325:1
650 246:10
6790 351:7
6791 349:16
6807 352:13
6808 351:3 352:12 354:1
6j 432:14

7

7 372:17,18 379:1 390:18 391:16 393:21 394:15
742 411:13
7480 402:12,16,17 403:9
754 412:3
792 402:18
7th 246:4

8

8 415:23
86601 415:8,10
889 330:18,19
8af 245:17

9

90 390:18 391:16 393:21 394:12,15 394:18,23 431:25
911 360:23 361:12
939 407:22
94108 246:10
98 318:7,8
981-7210 246:11
9:13 245:13 251:4

a

a.m. 245:13

ability 291:23 329:10 333:16 478:9
able 260:11 264:25 274:19 279:22 297:13 305:6 333:5 364:6 367:23 389:3,3 404:18 405:7 437:10,15,18 438:2,4,19 454:5 457:18
absence 271:2 291:16 425:23,25 433:25
absolute 283:20 454:8
absolutely 281:20 288:5 289:25 298:7 336:3 344:11 351:22 382:18 421:14,16 447:11 462:6 473:13,13
absorbed 260:11
abstract 248:17 343:1 344:6,11
accept 365:22 388:5
access 259:1 376:17
accessibility 461:19
accidentally 260:10,18
accomplishment 474:6
account 346:4 359:5 373:19 407:1 436:17,18
accountability 289:19,20 290:23 375:9 466:20
accountable 463:7
accounted 357:9 390:5
accounts 274:1
accredited 245:18 494:3
accumulated 439:12
accuracy 253:2 339:14 342:6 354:22 366:25 426:9 495:9
accurate 273:1 280:2 298:7 320:8 338:22 340:15 341:20 342:1,3 346:12 347:17 349:13 354:20 356:6 380:9 475:7 494:9
accurately 273:9 276:17 333:12 335:3 364:6 407:15
acetaminophen 421:19
achieved 438:15
achievement 335:22
achievements 474:15
acid 384:14
acknowledged 346:11
acknowledgement 497:3
acknowledges 299:22
acknowledgment 495:12
acquainted 302:18
acquisition 470:16
act 477:4
action 255:16 303:19 489:3
actions 276:18
active 260:25
actively 255:24,24
activity 294:16 302:25 308:3 316:13
acts 267:25
actual 258:6
acute 256:3 384:9 485:14
add 251:6 273:10 293:1 312:12 333:21
added 488:13
addition 260:20 432:21 436:21
additional 375:17 454:14
additions 497:6
address 444:24 471:14
addressed 281:1 323:22
addressing 262:23
adequate 432:9 439:18
administer 272:18 386:2
administered 361:15 393:12 395:6 401:21 402:24
administration 277:4 278:7 334:9 338:12 351:11 362:12 384:12 392:11 407:25 429:2 446:16
administrator 245:5 282:16,17
admitted 346:3
ado 480:25
adopt 428:2
adopted 281:9 326:19 327:13 428:18
advancement 290:5 292:23 480:13
adverse 279:4,7 285:14,17 286:3,5 293:17 294:13 398:14,16,17,18 398:20 463:18 478:23 479:21 480:13 481:6 489:7,11,16,25 491:2
advice 436:20 442:7,9 472:7 473:6 474:19,25
advisers 336:5
affairs 266:5
affect 261:8 478:8
afraid 365:12 422:4
africa 469:23 470:13
afternoon 486:2
age 253:3 269:23 269:24,25 271:19 272:23 273:14
agencies 280:19 459:9

agency 275:24 277:7 280:16 281:24 357:12 363:11 364:5 365:18 397:18 429:14,17 434:17 434:20 444:16 445:1,3 458:14 459:9 487:23 488:4 489:8,12 490:1
agendas 475:10
agent 254:14 258:4 294:13 419:12 420:24 471:15
agents 260:14 294:1
ages 273:6
aggressively 379:13,15,16
aging 269:25
ago 255:1 357:21 367:25 415:21 424:21 431:23 478:2
agree 276:21 280:18 286:3 287:25 288:10,16 289:20 290:25 291:6,8,14,16,22 292:15,17,19 293:16 294:8,9 308:5 324:11 327:10 341:8,13 341:16 357:3 367:13 369:13 374:11 379:14 381:18 382:1 383:8 384:20 388:8,9 389:17 397:5 409:20 428:20 441:19 447:6,9 454:12 459:6,10,14 475:3 483:2 490:5,10,11 490:15,16,20,22 490:25 491:7,13 492:5,15 493:1
agreed 266:6 463:1
agricultural 470:1
aha 440:1
ahead 269:14 272:11 393:6 415:13,15 470:10
aim 303:22 308:14 349:20 393:16 407:23
al 245:6,8 300:3 352:22 353:5 362:25 370:11 429:4,4,5 433:7 436:20 446:15,17
alarm 283:2
alderley 331:10 360:4
alderly 331:20
alison 297:23
alive 437:14
allotted 495:20
allow 253:19 260:12 368:22 404:11 413:15 458:14 483:14
allowed 330:13 414:1 475:2
allowing 487:17
allows 335:3
alongside 442:14
alpha 252:4,5,7,10 252:17 262:14,17 262:21,24 263:9 263:12,15,20,24 264:2,7,11 381:4 381:15,17,18,20
alter 320:19 343:21
alternative 260:4 308:16 322:20,24 323:10
alters 294:16
amended 281:6
america 289:9 405:14 421:9 464:13 469:18,19 470:14,14 472:19 474:1,3
american 265:5 478:22
amino 384:14
amount 264:2 276:19 312:16 315:14,16 419:23 449:4 490:22
analysis 291:12 311:1,12 356:2 482:16
analytical 456:6
andy 424:11 431:9
animal 249:23 261:19 262:6,9 272:8,9 273:1 276:19 319:22 391:15 407:11 408:19 425:11 432:12 434:10 444:19 446:1,4 451:18 452:10
animals 253:17 263:20 273:4,6,7 276:8,12,22 312:23 315:22 317:2 334:7 338:10 380:15 381:5 386:14 393:12 394:17 434:13 440:13 442:3
announce 344:18
announced 326:20 345:14,24 346:14 349:16,19
annual 248:19 343:2 344:8 345:5
answer 254:2 274:19 279:22 280:25 281:15 288:9 289:11 290:8 295:4 297:13 307:3 311:6,13 313:7,10 313:15,21 314:5 315:5 323:4 326:3 341:23 345:21 364:6 376:20 387:8 389:9 418:16 419:19,20 422:4 428:11 429:18 439:16,20 440:2,4 445:5 449:11 452:11,23 457:7,14 487:11
answered 287:7 288:14 349:15 417:20
answering 314:12 314:17 452:21
answers 452:20
anticipate 369:4 441:25 493:11
anticipated 431:20
anvisa 444:16 446:19,20 450:7

455:3,7,12
anvisa's 445:8,21
anybody 345:2 346:14 397:13 449:25 478:10
apart 438:23 483:10
apologize 388:19 408:9
apparent 295:24 350:10 354:2 369:25 370:12 433:14 488:16
apparently 390:25
appear 295:19 301:12 363:6 385:3 395:6 396:24 401:21 402:24 403:10 422:2
appeared 385:10 388:25 398:22 414:8
appears 269:8 301:14 416:10
appended 497:7
applicable 495:8
applicants 248:5 257:9
application 416:21
applied 491:5
applies 270:16 277:24 487:2
approach 289:23 289:24 399:7,7 400:15 424:20 463:10,14,22,23 466:9,10,11 479:11,13,24,25 480:12,19 483:10 489:17
appropriate 254:5 256:2 261:18,19 267:5 268:18 272:8 278:2,20 286:19 309:15 358:2,7 389:24 399:3 416:18 420:19 467:17
appropriately 306:5 340:23
approval 264:20 265:13,14 266:8 266:11,17,18 268:9
approve 268:19,22 481:4
approved 290:21
approving 268:5 268:14
april 248:23 249:9 332:13 360:15
archived 461:2
area 275:1,6 396:11 420:1 467:20 469:25 473:21
areas 274:20 309:6 371:13 419:1
argued 288:20
argument 277:4 447:13
argumentative 327:6 358:21 359:7 491:19
arrive 435:1
arriving 436:16
artefact 425:18 433:1,10 435:3,4 435:11,13 441:22
articles 443:5
ascertain 262:4
ashby 335:8,13,20 341:6
asia 470:12
asked 263:8,13 287:7 288:14 305:25 314:16 366:12 368:13 396:8 408:9 417:15,18 420:13 428:10 444:24 445:1 451:4 485:24 486:12,13
asking 287:5 314:9,13 315:5 357:16 358:7 364:18 380:23 419:8 452:4,18 470:5 486:5
asks 321:5
aspects 270:7 325:17 386:4 416:19
aspiration 324:13 330:7
aspirations 323:23 323:25 374:9
assess 349:20 390:17
assessing 393:19
assessment 284:7 284:19 285:4 374:19,20 375:19 386:17 387:11 388:1,2 389:19 423:8 424:23 425:2 426:7
assessments 424:5 453:25
assign 258:19 342:9
assigned 262:1 309:10
assignment 248:7
assist 325:4,25
associated 275:23 375:21 408:1 409:14 421:25 470:20 485:14
association 254:4 478:1
assume 266:6 323:6 422:13 423:11 425:20 433:2,18 478:21
assumed 426:1 434:1
assuming 379:23 424:21
assumption 324:4 386:23 487:6
asterisk 343:12,13
atlanta 249:13 410:7
attached 495:11
attempt 259:21 261:10 339:23 340:8
attendance 411:5 431:11,12
attendees 345:5 414:16
attention 275:5 296:19 359:23 415:2,8 416:7
attenuated 384:11
attorney 266:3 301:9 358:4 495:13

attorneys 246:3,13 246:18
attributable 388:24 409:14
attributed 374:2 391:5 408:1
attributes 354:12
atypical 424:19
audience 303:2
august 248:6 304:24 332:15
australia 364:22 365:5,15 469:19 486:11 487:4
australians 487:16
author 319:8 331:17 332:1 348:2 424:9
authored 319:7 347:12
authorities 279:10 280:12,22 324:23 364:15 365:6 451:4 456:12 462:10 467:25 481:6 488:14
authority 266:7 267:7,11 279:12 296:16 397:17 462:3,5 469:3 478:24 480:13,14 486:14
authorizes 282:5 465:13
authors 424:14 431:8
automated 337:15 338:22 339:10,13 342:1 346:12 350:23 355:9 356:4 357:8 366:24 376:13
automatically 478:25
available 338:22 344:14 354:21 387:1 430:23 495:6
avenue 246:14 264:24
average 269:20 420:3
avoid 311:1,12 383:18,19
avoided 310:20 311:22
avoiding 310:21 311:15,23
avoids 292:6
award 336:6 376:4
aware 252:20 255:6,7,23 256:21 256:22 261:4,10 264:13 274:20 282:20 284:5 286:24 289:2 309:3,15 346:6 357:19,20 359:2 363:5,8 365:17,19 366:3,9,10 369:18 381:2,8,20,24 397:9,13,15 410:18 413:8 434:21,23 438:24 442:21,23 449:25 450:7,8 451:1 455:6,11 459:11 459:15 472:11,13 473:6 478:15,17 479:17 485:17,21 487:4 489:9,10,13
awareness 292:4
axe 245:17
axioplan 337:14

b

b 248:1 282:4
back 269:4 278:24 296:7 317:20 335:19 336:17 345:22 359:17 366:1 370:15 377:23 386:5 391:9 406:21 422:19,21 431:15 437:23 462:17,20 462:24 465:4 467:6 484:9
backwards 435:1
balanced 328:20
balb 382:9
ban 304:14 305:9 305:12 307:15,23 484:13,15
bank 246:4
banned 279:25 304:25 305:2 329:16 375:16 448:3,7 483:12 484:1,7,10,18 485:10,15,19
banning 444:16
bans 485:14
barlow 429:4
barrier 299:5,10 418:20 419:24
barry 460:17,19 461:8
based 253:17 258:3 272:25 276:5 301:5 302:1 309:19,20 312:15 357:2 372:3 385:24 386:17,17 387:11,11 388:1 423:23 427:2,5 454:24 456:13 493:6
basel 469:14 485:8
basically 343:25
basis 308:9 319:20 366:6 374:4 375:20 389:18
bates 248:10 249:15 296:23 297:16 342:21 378:5 445:18
bearing 469:5
becoming 362:4
beg 392:20
began 295:19
beginning 273:23 463:1
begins 434:9
behalf 259:11
behavioural 300:9 384:11,15
being's 276:18
believe 252:13,22 258:6,6,8 263:18 263:21 269:10 278:13 288:17 293:13 295:3 306:7 317:24 318:4 321:15 327:14 329:1 333:13 358:9 365:16 373:2 383:2 386:16 387:10 389:22 393:4,12 399:17 409:7 410:19,21 413:16 420:20,20 422:16 428:4

429:15,21 434:18 450:15,22 454:24 456:21 462:11 467:14 472:23 478:5 481:1,3,7 483:15 485:12 487:15 488:1 491:17,22
believed 252:11 281:2 432:8 491:10,15
believes 480:23
benefit 383:11,12 447:20 454:13 458:24
benefits 284:7,19 285:4 416:18
best 291:8 301:1 336:15 377:3 385:23 386:16,21 387:10 406:20 430:24 459:8,14 492:1 493:6
bet 421:21
better 322:12 492:23
beyond 254:14
big 277:12
bigger 399:14
biggest 252:20 253:7 270:2 440:19
biological 253:13 294:13 302:22 309:21
bit 314:21 373:7 421:17 488:17
black 295:6,12,16 295:22 331:10 351:21 360:2 365:24 378:22 403:25 405:1 407:25 432:14
blackwell 246:18
blind 435:20 450:10
blinded 440:12,22 441:2,15 453:24
blood 299:5,10 418:20 419:23,24
board 267:11 290:21
boards 326:6
bodies 264:8 364:8 365:4 467:7 490:8
body 260:21 264:3 264:4 270:9 334:6 381:21 406:24 408:17 434:10 439:11 474:16
borderline 383:16
boss 372:24
botham 245:15 247:4 251:1,5,15 359:19 422:23 424:12 494:4 495:5 496:2,24 497:2,4,12
bottom 327:20 337:19 340:1,4 352:13 361:12 372:15 374:12 390:1 416:13 421:6 445:12
brain 251:21 252:6 255:4,12 258:13 259:1 262:11 294:5 299:5,10,22 310:20,22 311:1 311:13,16,22,24 312:5,17 315:15 315:17 316:10 333:17 334:11 335:4 355:13 361:21 371:11,13 371:15 375:24 418:20,21 419:15 419:23,24,24 420:1 421:25 423:17 427:19 429:2 435:16,19 485:20 487:6
brains 312:23 315:22 355:18
brazil 250:1 364:21 365:5,13 365:14 444:10,12 444:15 448:7,13 450:24 451:5 455:7 458:23 486:3,6,22 488:7
brazilian 456:11
break 296:6 359:11,16 377:22 422:10 462:12,16
breckenridge 263:16 264:19 265:3 268:5 370:10 388:11,14 389:1 433:7 436:19 444:14 446:15 447:1 486:19
brief 249:1 370:24 372:10
briefing 379:21,22 379:24
briefly 263:23
bringing 258:14
broad 258:2 268:16 274:24 276:16 281:9 287:8 368:21
broadly 419:9 477:15
brock 258:23
brought 290:1 421:10
budget 268:20,22
build 309:18 324:19
building 291:1
built 290:25 292:20
bulb 259:1,3
bullet 308:7 309:16 312:2 316:16 317:9 319:14 322:17 323:20 324:18 325:2,19,22 327:2 329:3,6 371:8 380:11 382:5 383:22 385:21 386:15 412:10 413:7 425:23 426:8,19 432:10 433:24 446:12 451:8,15,21
bunch 414:24
burn 304:5
business 374:22 374:24 375:10,13 375:15,22 478:10
businesses 470:20
buy 417:19

c

c 245:22 246:1,20 382:9 384:7,7
c57 331:10 378:21 405:1 407:25 432:14

c57b16 330:3
c57b6 378:17
c57bl6 249:4 309:20 316:18 361:15 378:10 381:3 411:20 412:12
c57bl6j 334:3 350:1 362:14 380:13 395:6 401:21 402:24 434:13
c57black6j 425:13
ca 246:10
calculated 427:5 427:11
calculating 424:22
calculation 426:24
calculations 423:23 428:9
california 246:10 248:20 302:10 329:25 343:4 350:19 355:7 366:24
call 309:13 321:16 347:1 463:17,21 466:12 470:12 475:10 476:14 483:6 492:11
called 251:21,23 255:8 259:5 265:23 266:21 270:19 275:25 289:23 315:7 334:21 335:7 375:19 464:18 476:15
calling 281:18
calls 280:24 281:12 422:16 482:2
campaign 304:1
canada 469:19
cancer 418:12
capability 255:9 277:17
capable 395:7 401:22 402:25
capacity 267:25 457:1,3 470:5
care 425:1 429:25 482:15 483:4
carefully 322:7 440:17
carondelet 246:19
carried 337:11 384:8
carry 328:15 452:7
case 245:7 251:13 263:22 287:25 288:10 289:21 295:3 306:7 310:5 315:24 317:3 319:6 323:6 347:23 377:20,23 384:25 392:9 401:14 409:7 413:18 417:3 432:8 448:16 458:19 459:7 491:5 493:18
cases 265:21 269:18 446:6 481:23,24
catchall 286:11
causal 249:24 444:20 451:23 452:1,12 453:6
causality 453:13
causation 254:4
causative 253:19 254:14 270:5 419:12 420:23 471:15
cause 253:12,15 255:7 261:13,14 263:19 264:11 274:6 283:22 294:17 304:6 316:25 329:16 333:16 369:21 374:3 408:13,19 418:12,13 419:16 419:16 420:10 421:5,10 432:7 439:14 494:15,17
caused 260:19 274:3 349:21 369:20 388:15 406:23,25 483:6
causer 451:13
causes 253:11 268:24 269:11 291:17 319:22 365:23 375:24 388:6 395:18 417:22,25 423:18 423:19
causing 252:14 255:2 259:8
caution 262:18 483:5
cavity 277:11
cell 309:21 334:10 334:13,18,20 336:11 337:8,11 338:11,23 339:1 340:15 346:3 352:19 354:2,13 354:22 361:10 365:23 369:21 373:14 381:4,9,12 381:14 382:10 386:18 387:12,23 388:6,15 390:7,18 391:5,17 392:10 393:19 404:25 407:24 409:12 425:18 426:10,21 427:6 428:25 432:7,23,23 433:1 433:3,19 436:25 437:1,3,10
cells 251:23,24 252:6 253:15 335:5 338:9 351:16 377:17 389:6,7 396:5 407:19 409:16,24 423:16,20 436:22 436:23 437:2
center 415:16 416:10
central 294:14 360:3 372:1
certain 279:7 290:13 386:4 412:11
certainly 253:16 255:23 259:2 260:17 264:17,21 268:12,22 269:6 271:23 275:8 277:9 278:6,8 281:3 290:12,15 304:8,11 324:4 333:12 337:2 341:7 344:9 346:22 365:2 369:23 374:14 385:17 398:9

399:6 400:14 401:7 404:16 417:10,10 428:8 441:2,18 463:9 464:22 467:20 471:8 472:17,25 481:13 492:12
certificate 494:1
certify 494:4,13
cetera 465:14
cfi 382:10
cfr 286:6,25
chaired 266:23
chairing 480:1
chairman 267:9
challenge 379:13 379:16,20
challenges 386:3
challenging 249:3 378:9,16 385:2,7,9 385:12,14,23 389:17
chance 420:14
change 261:6,8,10 263:25 380:21 458:25 469:13 470:15 496:4,7,10 496:13,16,19
changed 267:19 289:12 358:11 399:2 469:11 471:3
changes 252:1 349:21 355:1 371:14 384:16 390:5,7 495:10 497:6
changing 386:4 442:16
chanyachukul 384:4
charged 299:4
charles 264:19 265:3 295:6,12,16 295:22 350:1 444:14 486:19
check 393:5 397:25 399:13,23 401:10 405:11 411:12 413:17 414:15 426:8 435:9 444:3 450:21 458:11 461:12 481:1 484:9,21 485:13 485:18,23
checking 373:17
chemchina 470:16 485:5
chemical 253:14 261:6 284:13 285:4 293:18 294:13 299:3 304:14 305:12 339:3 386:13 419:14 420:14 473:11,12 483:13 488:20,21
chemicals 276:7,8 293:17 303:17 470:1
chemists 309:9
chevron 246:18 259:7,11,13,18
chief 266:23
china 469:21 484:9,13,13
chronic 426:11,11 426:22,22 427:1,1
circuit 245:1,1
circumstances 266:15 472:17
cited 353:20
cites 384:2
cl 429:6
claimed 249:17,20
claiming 276:15
claims 308:11,15 319:21 322:20,24 323:9,21 333:15 374:4,8 411:21 412:24
clair 245:2 313:12
clapp 371:4 372:2 372:3,21,23 460:20,20
clarification's 296:11
clarified 415:21
clarify 389:8 414:1 471:21
clarity 393:14
clause 454:14
clear 264:13 265:2 273:10 275:1 342:20 345:3 368:2 371:12 419:11 420:23 479:25 480:2,6 492:10
clearly 254:3 277:11 304:22 310:23 315:9 323:8 325:19,22 341:17 384:24 399:9 409:25 454:10
clinical 251:25 252:2,10 253:1 270:7
clip 416:9
close 407:11
closest 440:9,11,18 465:8 489:17
codafel 284:24 285:13
coincidentally 462:9
colleagues 487:21
combination 431:17
come 258:7 269:4 275:10 278:24 322:12 369:19 379:20 380:21 391:9 414:8 420:23 445:5 462:20 465:4 471:12,18 493:5 493:12
comes 343:25 448:16,16 481:21
coming 309:25 466:18
commencement 251:4
comment 259:11 333:12 358:17 359:10 401:15 404:16,17,18
commentary 301:9 358:5
commented 409:9
comments 298:10
commission 305:22 306:11,16
commission's 307:1
committee 265:25 266:12,20,21 267:8,9 268:4,7,19 268:21 270:13,24 270:25 276:3,4,5

279:7 288:23,24 289:1,6,10,24 290:1,3,6,17,18,23 296:11 399:7,14 399:19 400:16 405:3,4,5,16,19 429:20 463:3,6,8 463:10,15,19,20 463:22,23 466:5,9 466:12,18,18,19 466:20,24 467:16 468:20 470:18 479:4,5,6,12,12,13 479:24,24,25 480:1,5,8,9,10,12 480:15,17,19,20 480:21,21,23 481:4,5,8 483:10 489:17,24

committees 467:2 467:11,13 471:24 476:18 478:13,15 478:19 481:10,12 481:15

communication 448:11 479:8

communications 399:18 458:12

community 320:24 328:20 374:14 414:4 434:22 435:25 436:4

compacta 349:24 361:7 427:6 428:17 429:1 434:12

companies 471:1 490:5,11

company 258:9 260:3 265:10,23 266:9 267:1,3,5,7 290:21 312:18 315:18 367:2 372:6 374:12 443:7 469:1 470:11 475:4

comparable 341:14 351:19 352:6,17 362:20 395:22 404:1

compared 362:10 434:13

compares 353:24

compensate 273:2

compensated 442:9

compensation 443:6

complete 253:2 497:8

completed 405:20 410:24 495:17

completely 286:4 286:4

completion 349:7 349:11 474:14

compliance 280:21 287:10,16 459:7

complicated 305:16

comply 287:22 467:16

complying 463:11

compound 386:2 408:2 409:15

compounds 406:13,14,15 407:18 466:7

comprehensive 432:21

comprise 264:7

comprised 471:7

computer 337:12

concealing 490:24 491:2

conceals 282:23

concentration 351:9

concentrations 343:21 349:22 386:13 393:20

concern 277:5 278:18 300:1,6 301:21 387:7 410:1 424:22

concerned 320:5 341:13,19,25 368:12 382:6 420:9 445:3

concerning 281:24 469:7 491:3

concerns 286:18 303:25,25 342:6

conclude 253:19 380:10 420:25 435:4,5 440:19 441:21 451:18,23 453:6

concluded 398:22 402:10 403:9 493:21

concludes 409:11 433:17

concluding 493:16 493:19

conclusion 253:10 280:24 281:13,18 282:15 284:23 329:19 355:20 369:6,8,12 374:17 383:8 403:3,16 409:21 414:8 420:18,23 435:2 448:1 449:21 453:13 459:1 482:3,4 493:5,12

conclusions 284:20 285:2 401:17 429:19 467:25

condition 272:6

conditions 286:20 291:9 387:24 398:2,2,19 399:2 404:4 421:3

conduct 295:21 386:16 387:10 390:13 474:15

conducted 317:16 320:1 331:19 347:16 350:8 392:8 403:24 406:11 411:19,24 457:5 464:4 474:11

conducting 391:15 488:8

confer 339:13

confidential 251:12 345:9

confirm 390:20 391:16 485:1 487:21

confirmation 374:7

confirmatory 453:25

confirmed 293:8 362:12

confusion 368:13 368:18

congress 281:6
conjunction 286:17
connected 337:13
connection 359:9 445:3
consecutive 334:4
consequence 258:18 291:20 329:13 471:3
consequences 482:19
conservative 432:6
consider 254:5 261:19 278:20 399:21 404:10 451:13 463:17
consideration 383:6 386:7 430:12 450:12 454:21
considered 260:22 268:18 290:5 306:3 330:6 374:23 375:10 385:6,8 398:20 459:22
considering 444:16 449:18 485:24
considers 426:24
consistent 295:13 338:8 369:20 425:7,11 428:18 428:20 434:10 439:1,6 447:14,16 450:3 452:5 488:22
consistently 277:13 396:6 432:17,22 436:9 454:17 471:9
constellation 446:5
consult 275:6
consultants 481:22
consulting 389:5
consumer 283:22
consumers 261:9 482:17
consuming 416:24 483:7
contact 364:22 460:14 467:15
contain 283:5
contained 403:17 415:7
containing 349:23 371:16
contains 417:15
contemplated 260:15,17
content 417:10,13 422:17 431:15
context 367:4 396:8 433:11 449:4 454:9 457:25 458:2
continue 251:9 296:8 305:19 314:21 359:20 377:25 418:25 422:23 430:20 462:18 485:25
continued 245:15 247:4,5 251:17 286:18 291:11 329:10 369:24 374:11 388:11 393:11
continues 338:19
continuing 301:18 302:21 312:2 350:7,16 448:24 448:25
contract 479:15
contracting 274:2
contrary 425:25 433:25
contrast 339:17
contributed 348:12
contributes 253:11
contributor 332:6
control 283:21 338:9 343:20 351:10 434:13 440:13 461:19
convention 343:18
conversation 312:1 378:19 448:5 454:9
conversations 263:11 345:17,19 366:11 369:22,23 376:8
convince 327:21
convincing 254:3 419:11
cook 424:11 431:9 476:11
copies 495:14
copy 319:8
core 471:8
corporate 304:19 463:4
correct 256:11 257:11,15,20,22 257:24 260:3 265:8 266:17 267:1 268:22 270:18,22 272:19 274:14 275:15 278:13 279:8 280:12 283:25 284:1,10,16 286:16 287:24 288:4 296:14,18 296:24,25 297:10 297:23 298:2,3,5,7 298:17,18,24 299:6 300:11 302:8,11,25 312:7 312:18 315:18,19 315:22,23 317:7,8 317:12,13 319:5 319:16,17,23,24 320:1,2,4 322:5 326:15 327:22 328:13,25 329:1 329:17 330:3,11 331:16,18,21,24 332:5,7,8,16,25 333:25 334:2,4,5,7 334:8,10,25 335:10,12,14,19 337:17 339:24 341:1,4 342:11,12 343:5,9,10 344:16 344:19,20 347:9 347:22 348:3,14 348:17,19 350:2,3 350:21,24 351:21 352:2 354:15,24 355:5,11,16 358:9 360:7,14,20 361:2 361:3,7,8,10,11,17 361:18,24 362:7 362:17 363:1,2,16 367:2,3 368:23 371:6 372:12

373:2,25 374:5 375:17 380:19 381:6,12,13,22 382:18 384:18 386:19,20 389:14 392:4,5,13,21 393:23 394:3,16 394:21 395:19,20 395:24,25 396:11 399:25 400:24,25 401:2,3 407:4,13 407:14 408:3,4 410:8 411:22,23 411:25 412:6,9 417:6,9 424:13 427:4,7,17,20 429:8,12 431:10 433:8,9,22 434:4 434:14,15 444:9 444:11,18,22 445:7 454:19 461:4,5 465:12 468:2 472:8 473:16 475:13 489:23 497:8
corrections 497:6
correctly 306:21 337:10 379:3 393:10 418:23,24
cory 302:6 316:24 330:6 414:14 429:5
cost 292:13
counsel 297:5 313:11,16,17 318:9 357:21 359:2 426:17 472:13 494:14,16 495:14
count 335:4 336:10 354:23 355:18
counted 334:19,21
counting 334:19 338:6 339:14,18 346:3,12
countries 279:17 279:24,25 364:17 364:25 365:3,5 375:16 468:1,4,7 468:11 478:16,25 483:12 484:7,8,10 484:17,18,19,22
country 483:21,25 485:10,15,19,24 486:9
counts 337:8,11 338:23 339:2 390:8 428:25
county 245:2 313:12
couple 406:21 409:3
course 267:4 284:12 287:8 299:15 320:16 322:22 355:25 373:11 375:14 377:2,13,14 392:9 392:23 393:17 417:7 420:5,8,11 436:12 442:24 443:4,16 444:4,4 458:16 459:20 468:3,25 475:11 475:14 483:9 489:3 491:11
court 245:1,18 251:6 275:11 306:24 314:25 317:22 345:23 487:13 494:1
cover 268:25
covered 269:1 455:1
covers 282:23
cpl 298:16
craig 246:7
create 374:20 375:6 407:10 492:3
created 463:3 464:21 465:19
creating 375:3,11 437:8
creative 336:1
credited 341:2
criminal 282:5,21
criteria 281:1 290:13 398:5 464:6,6 466:14 479:21 480:2,6,24
critical 440:10,10
critically 435:16
criticized 366:22
crop 245:8 296:13 411:9 470:11 495:4 496:1 497:1
cross 299:5,14 418:20 419:24
crossed 299:9
cs 495:15
ctl 248:16 308:3 309:17 312:21 316:13 318:25 319:25 328:25 331:4,19 335:21 340:24 341:3 347:11,25 350:9 353:13 360:11 372:4 376:25 379:12 395:5,17 395:21 401:19 402:22 404:25 411:15,25 428:24 429:5 455:8 457:10 487:18
cumulative 292:20
current 426:11,22 484:6
currently 254:15 284:8 354:21
customary 344:11
customers 324:22 416:17
cut 264:13 435:19 437:21,22 445:10
cycling 255:8

d

d 245:22 247:1 248:1
d.c. 246:15
damage 253:15 255:2,3,8 294:17 333:16 387:19 389:10 419:16 421:24 427:2 432:23
damaged 406:25
data 309:18 324:19 328:19,24 354:23 371:13 380:16 396:24 403:10 409:12 413:8 423:23 430:19 431:25 452:10 461:1 479:14
date 248:22 249:5 249:9 251:3 257:23 297:14 308:21 318:22,22 331:6 349:7,11 382:3 392:16,17

397:24,25 398:8 400:21 430:21 460:9 463:12 465:16,16 484:14 484:25 486:16 494:22 496:24 497:12
dated 248:6 249:7 250:2 304:24 372:15 377:14 379:1 415:23 430:13 444:8
dates 298:6 380:9 392:17
day 251:5 306:15 348:21 378:20 431:25 450:20 455:17,24,25 460:11 462:20 494:6 497:15
days 390:18 391:16 393:21 394:3,12,15,15,19 394:23 495:17
deactivating 256:4 256:4
dead 406:25 437:14
deal 287:3
dealing 367:16
deals 258:10 270:13
dealt 364:8,11,17 466:6
death 373:5,14 377:10 389:6 482:17
deaths 304:6
deceased 245:6
december 249:2 348:18,23 357:20 358:12 363:16 371:1 372:17,18 378:13,16,24 379:1,3,4 399:25
decide 288:7 458:14 489:24
decided 305:13 306:15 358:11
decision 264:25 267:4 288:22 289:3 290:12,19 290:20 306:16 307:1 330:12 358:9,14 364:1 374:23 375:11 404:19,20 449:10 481:4,8 484:2
decisions 266:25 267:3 289:6 489:19 490:4
declare 497:4
deemed 280:15 338:21 497:6
deep 439:16
defence 386:16 387:10,15,16
defendant 246:18
defendants 245:9 246:13
defense 386:21 387:18,18,21
defensive 309:18 324:20
deficits 384:11
define 252:24 294:3 299:13
defined 396:4 398:15 463:18 466:14
definite 440:20
definitely 419:25
definition 251:18 294:7,24 295:11 443:20,21 463:1 491:4
definitively 453:13
degree 339:14 394:14 407:24
delay 292:6 358:24
delayed 333:2
delegated 267:4
deliberate 449:10
deliberately 260:10 448:5 450:1
deliberation 483:4
deloitte 471:22
demanding 359:3 363:19
demonstrate 361:15 395:5 401:20 402:23
demonstrated 418:19
demonstrating 384:10
density 371:16
deny 253:16 386:25 485:1,22
department 265:6 266:4 289:1 423:7 427:16,21
dependent 435:16 492:1
depends 289:14,15 299:12 383:10 457:25
deponent 495:13 497:3
deposing 495:13
deposition 245:15 251:5,15 279:1 298:1 315:2 337:4 359:18 369:12 422:22 463:2 493:14,20,21
depositions 420:13
depth 438:21
deregistered 305:3
dermal 386:17 387:11
describe 256:24 263:23 266:19 327:14 336:15 430:8 444:1 476:22
described 255:17 260:24 265:7 284:24 286:14 297:25 312:21 320:25 351:23 432:25 469:3 481:12
describing 252:15 340:23 347:14 381:16 388:2 452:8
description 248:3 291:4
descriptions 471:5
design 261:25 360:23
designed 333:14 392:22 416:24
designee 304:19
designing 260:19 333:18
desire 458:21
despite 342:6

destructive 303:17
detail 268:17 345:7 348:5 438:22 439:17 440:5 485:12,18
detailed 283:11 284:2 350:12 398:4 458:7
details 279:3 460:23
detect 262:5 338:11,13 340:15 354:12 371:14,18 377:10
detected 262:9 390:20
detection 312:4
deteriorated 355:14
determination 466:21
determine 274:13 312:22 315:21 317:6 340:13 350:8 391:4 407:23 426:5
determined 482:14,22 483:3
develop 259:21 260:9 272:6
developed 256:1
developing 275:3
development 249:18,21 262:14 263:9 266:3 300:6 340:21 452:3 490:6,12
developments 300:1 301:21
device 282:24 335:2,2
di 302:9,15 316:24 329:24 330:7 346:23 350:19 353:6 355:3 363:1 438:9 450:14 455:9
diana 245:4 495:4 496:1 497:1
dichloride 249:11 331:8 349:21 359:25 362:13 392:8 393:19
died 251:25
diego 248:19 343:3
diet 278:22
dietary 386:17 387:11
difference 276:22 346:13 356:7 357:8,9 383:14 426:24 437:18 439:10 478:14 488:17
differences 338:20 338:23 341:18 346:4 354:13 380:17
different 254:16 254:19 267:21 273:6 277:3 285:18,21,22 286:4,8,8 297:2 320:23 321:18 339:2 342:4 348:4 348:10 380:16,21 382:9,14 386:13 393:13 398:3,19 404:24 408:19 428:10 436:5,10 436:14,15,15 459:17 464:3,9 467:1 468:1,4 475:6,10 477:15 477:15 478:13 482:12 487:9
differently 375:18 436:13 489:5
difficult 262:19 267:18 371:14,18
digital 337:13
diminish 482:24
diminishes 291:23
dino 350:19 355:3
direct 296:19 415:2,8 416:7 452:1,2 467:15 489:14
directed 277:20 386:1
directing 359:23
direction 268:16 458:22
directly 463:8 467:21,22
director 332:3
disagree 324:7 387:21
disapproving 268:14
disclose 292:12 364:4 397:16 455:7,12 456:11 457:4,9 458:13
disclosing 292:21
disclosure 291:16 293:17 346:24 368:14 397:19 400:23 458:22
disclosures 365:17
discourse 347:2
discovery 297:5 300:21
discredit 367:5 387:22,25
discrepancy 339:6
discrepant 321:17
discretion 473:15
discuss 346:22 422:7 431:14 466:13 486:2
discussed 265:16 265:22 299:12 331:23 385:16,17 385:18 386:5 399:8,9 422:11 463:25 465:13 486:13 489:15
discusses 318:25
discussing 319:3 360:21 382:20 398:21 409:8 423:9,16 424:4 460:24 464:1 491:6
discussion 249:1 406:18 407:21,22 437:2 446:23 466:17 480:4 487:3
discussions 264:21 265:15 346:23 350:19 365:7 370:24 374:10 383:7 431:18 433:12 488:6
disease 248:10,12 248:14 249:1,13 249:18,21 251:19 251:20,20 252:1,3 252:8,12,19,23,25 253:12,20 255:21

256:7 258:5 259:4 259:9 261:14 262:8,14 263:10 264:5,10 269:12 269:19,23,24 270:1,5 271:7 273:11,11 274:3,6 274:17,17,22 275:4,14 293:19 293:20 297:9 298:10 302:3,9 303:9 307:11 323:17,22 324:15 328:5,7,11,17 329:5 370:25 372:11 381:22 385:12 410:1,12 410:17 412:8 417:25 418:13,18 419:12,16 420:10 420:15,24 421:6 421:11,25 423:18 445:9,22 446:2 451:12,14,19 471:15 474:8

diseases 269:9 270:11

dishonest 492:22 493:3

disprove 366:14

dispute 280:4,7 357:7,10 388:8

disrupt 294:18

distinction 463:6

distort 320:19

distributed 345:4

diuretic 390:6,7 391:4,5,11

dividing 427:11

divulging 422:17

dixon 405:9,10

document 248:25 249:3,15 283:4 290:16 297:2,4 301:6 318:13 319:11 323:16 325:1 327:16,18 331:2 342:19 347:10 370:23 372:15,19 400:20 400:21 401:25 405:20,25 406:7 414:20,25 415:7,9 415:22 423:4 424:6,17,19,24 429:13,22 430:1,6 430:9,10,15,22 431:1,13,19 432:2 434:16,19,25 444:6 447:5 461:15

document's 424:9

documents 297:7 366:7 422:13,14 464:1 476:6,12

doe 248:5,8 257:10

doing 270:4 316:5 336:2 366:9 373:22 383:1,19 423:8 424:23 431:24 436:10,13 442:15 458:20 479:14

dollars 292:5

domain 474:16

dominant 470:1

dopamine 262:11 300:12 302:24 333:23,23 349:22 349:23 351:9 371:16 387:20 393:20 396:6 437:7 455:4,5

dopaminergic 248:18 251:23 295:7,10 331:11 334:10,13,18,20 336:10 339:4 343:8 344:1 351:16 352:5,7 357:12 360:1,25 361:6 362:15 363:12 369:25 370:7,12 371:15 373:5,14 377:11 387:20 392:10,25 393:19 394:2,5,11 394:14,18,22 395:18,22 396:4 396:25 398:23 403:11,25 406:25 407:20,24 408:22 409:16,24 412:15 423:16,20 425:12 429:1 432:13,19 433:15 434:12 437:1,2 446:10,21 455:8,13 456:2,13 457:11,16

doping 361:9

dosage 285:19

dose 261:13 309:19 310:8,9 334:6 349:21 370:17 382:8 385:24 386:11,12 386:14 387:4,5 388:17,18 390:18 393:22 394:12 408:2 421:18 425:14 426:3,4,5 426:10,20,21 427:5,7,11 432:15 432:20 434:3 442:1 456:13

dosed 316:18 349:24 373:6,15 382:17 394:2,6 425:13 432:14 440:13 441:25

doses 273:5 276:7 277:1 278:17,19 278:23 300:10,13 310:7 406:16 408:20 409:15 412:14 426:12,23 427:2 430:13 432:19,20 446:17 455:13,15 456:2,3 476:7

dosing 309:20 334:3 361:2,5 390:7 391:4 393:1 408:2,20 409:14 429:3

double 393:5

doubt 287:25 288:7,11 289:21 290:1 458:20 459:7 480:7

dr 245:15 248:21 248:23 249:5,9,11 298:15,21,25 299:17 301:24 302:13,15 303:1 309:25 310:18 311:21 315:21 317:4,15,23 318:1 318:4 319:4 330:6 330:7 331:14 332:9,12 333:4,5 333:10 335:11 336:4 337:20

339:17 342:6 344:22,25 345:3 345:18 346:4,22 346:23 347:12,16 347:20 348:2,12 348:15 349:16 354:4,12 355:3,13 356:1,16 360:13 360:24 361:5,13 362:11 365:17,20 365:21 367:23 369:18 372:12,21 372:21,23,23,24 373:4,13 378:21 379:25 380:3,3,4,5 380:7 385:6,6,8,8 393:15 394:1 395:3,21 396:23 400:13 401:17 402:10 403:9 406:11,22 407:2 409:5 410:24 411:2,7,7,24 414:14 420:25 429:6,10 436:9 437:22,23 439:3 440:25 447:1,3 454:18 455:3 460:1,20 476:8,9 476:10 495:5 496:2,24 497:2,4 497:12

draft 249:19,22 430:13,15,16,16 430:18 449:7

drafted 449:7,14 449:17

drafting 447:18

drafts 431:18

dreadful 421:6

drs 320:3 378:15 379:19 380:12 385:1

due 274:8,10 408:15 435:6

duly 251:2

duplicated 310:2

duration 261:20 385:24

duty 258:16 287:6 425:1 429:25

dying 272:15 389:7 436:24

e

e 245:22 246:1,1 247:1,1 248:1,1 496:3,3,3

e.g. 371:13

earlier 262:16 264:23 269:18 271:6 281:14 308:19 316:8,23 325:17 349:5 350:9 379:8,9,10 399:24 401:4 406:17 420:22 424:5 433:13 439:21 454:11 455:6 456:16 458:17 459:12 460:9,20,24,25 462:20 479:6 481:21 486:2 487:3 489:20 491:6

early 252:23,24 269:20,22 271:7

earth 256:4

easily 418:20

east 470:13 484:8

easy 386:25

ec3a 245:17

editing 472:11,14 472:19

editors 443:12

educated 302:13 350:23

educating 366:23

effect 248:17 252:16 255:12 279:5 285:17 286:3,5 294:14 296:1 309:19 310:11 343:7 347:13 350:10 361:21 362:9 371:11 384:9 386:9,24 387:4 390:6 391:6 398:17,18,20 400:12 407:19 409:16,23 412:24 424:4,21,22 425:18 427:8,10 435:2,7 441:25 442:4 446:13 447:16 450:9 455:20,22 459:3 478:23 480:13 481:25 482:6,25 487:5 488:16,16 489:8,11,16,25 491:3

effective 260:12 270:10

effectively 351:24

effectiveness 258:11 416:22

effects 261:9,18 262:5 270:5 271:16 272:20 274:24 279:8 280:10,20 292:12 293:17 294:1 300:9 317:1,6 331:11 351:21 386:14 390:12 393:17 406:12 441:22 449:3 481:6 483:5 491:8 492:6 493:3

effort 261:5

efforts 277:19 292:5

eight 272:16,21 273:7,14,18

either 290:6 309:5 417:4 441:3 446:14 463:12 479:15 481:15

element 249:23 444:20

eliminate 260:20

elliott 460:17,19 461:9

ellis 245:16 246:14

email 250:2 315:1 459:25 460:3,10 460:13,14,22

emerge 430:20

emerging 413:9

emetic 260:13,14

emphasizing 410:1

employ 442:18

employed 284:20 372:6 481:11,14 481:14

employee 494:13 494:15

employees 258:15 285:3 289:8

301:13 471:7,9
employment 333:11,13 349:4 460:1
encompassed 368:22
encourage 256:2
encouraged 289:25
encouraging 288:5
ended 383:1
endpoint 309:21 427:2,7
endpoints 302:22 303:3 350:11
ends 479:23
engage 305:14
engaged 309:5 312:1 364:12,14 413:22 490:5,12 492:3
engagement 364:21
england 483:16
english 372:19
enhance 366:25
enhanced 361:2
enormous 292:13
ensure 325:15 328:17
entered 461:24
entire 268:20 345:3 373:1 401:12 467:11
entirety 403:8
entities 304:20 463:2
entitled 297:8 299:25 308:2 319:15 323:17 328:6 369:14
473:5
environment 272:23 282:1
environmental 271:5,17 274:18 275:24 277:6 281:24 357:11 363:11 397:18 429:14 434:17
enzyme 437:3,6
epa 249:7 276:2 277:22,25 278:7 282:20 284:5 285:5,12 286:11 286:16 288:1,11 290:6 296:17 346:7,10 358:12 359:3 363:14 364:11,12 368:14 397:20 398:7 400:9,10 403:6,17 404:23 456:19,25 457:6,10,15 458:18 466:21 478:24 479:9 480:24 489:22
epidemiological 292:21 418:17 451:22 452:7 453:5,11
epidemiologists 275:7
epidemiology 253:18 254:14 419:1 420:22
equally 276:23 322:15
equipment 355:15 356:12
equivalent 276:13
equivocal 254:15
er 317:17
err 459:8,14
errata 495:11,13 495:17
especially 293:18 416:25
esq 495:1
essentially 303:22 335:2 423:8 456:7 461:14
establish 308:9 453:20 485:16
established 320:24 324:15 374:3 375:16 389:23
establishes 432:5
establishing 292:10 309:19 319:20 341:2 432:8
estate 245:5
estimated 426:10 426:20,21 456:12
estimation 430:24
et 245:6,8 300:3 352:22 353:5 362:25 370:11 429:4,4,5 433:7 436:19 446:15,17 465:14
ethically 490:17
ethos 473:17 483:9
eu 305:22 306:2,16 306:20,24 467:17 483:21,25 484:3,5
europe 245:19 303:13 304:25 305:2,3,5,6,13,16 470:13 473:25 474:2 478:14,19
european 304:15 306:10,17 467:15 470:13 484:1
evaluate 479:19
evaluated 263:9 437:25
evaluates 279:7
evaluating 424:1
evaluation 249:17 249:20 423:7,21 423:22 426:2 427:15 428:19 429:25 434:2,7 479:18
evans 245:18 251:7 494:3,21
eventually 294:18 329:18
everybody 305:12 414:3
evidence 253:17 253:22 254:3,8,11 254:13,22 264:13 269:6 329:18 356:22 357:1 366:1 367:22 368:1,4 389:3 400:11 418:18 419:10 420:21 425:7,11,16,17,25 432:12,22 433:25 437:21 439:12 448:21,23,25 449:6,18 450:11 451:19,22 452:1,8 453:5,12,12 454:25 455:4 459:1 478:21 486:1,13 487:9 489:4 492:1,2,9

exacerbation 362:9
exact 308:21 321:23 376:1 411:11 419:15 484:14
exactly 262:17 264:20 284:2 300:18 310:17 321:14 333:18 344:8 350:5 370:16 376:25 405:8 414:15 473:17 479:7
exaggerate 276:8
exaggerating 273:4 276:18
exaggeration 277:12
examination 247:5 251:17 369:6,9
examined 355:15 356:11
example 260:16 271:5 273:3,5 275:25 316:22 376:9 435:7 436:6 467:14 484:9 486:3,10 491:4
excerpt 328:6
exchange 250:2 291:9 459:25 460:10
exclude 481:15
excluding 486:6
exclusively 276:1 276:19
excuse 286:8 311:4,6 312:13 313:2 388:23 408:8 449:11
executive 266:12 266:20,21,22,24 267:8,9 268:4,7,19 268:21 351:4 432:11 468:20 470:18 481:3,7 489:24
exemplified 488:6
exemption 287:17 287:19
exhibit 248:5,7,9 248:11,14,15,17 248:21,23,25 249:3,5,7,8,10,12 249:15,17,20,23 250:2 256:13,14 256:17,19,20 258:19 296:20,21 298:9 318:7,9,10 328:1,3 330:20,24 342:17,24,25 343:1 347:4,8 359:21,24 370:2,3 370:19 378:1,4 392:2,4 400:5,7 406:1,4 408:25 409:2 410:3 414:18 416:8,8 422:5,13,14,25 423:2 430:3 443:24 444:2 459:23
exist 397:1 403:12
existed 267:19
existence 467:9,10 477:6,10
existing 256:9
exists 451:23 453:6 473:7
exoneration 287:15
expanding 258:11
expect 366:16,16 417:19 473:8
expected 274:21 309:5
expecting 309:14
expense 292:6
experience 472:23 475:18 480:1 490:2
experiment 348:22 350:4 391:19 399:2 473:9,9
experimental 254:12 308:16 322:20,25 323:10 328:11 332:15 390:3 398:19
experiments 263:14 266:10 273:8 295:8 316:17 332:18 389:1,20 399:10 433:6 446:14 454:5 474:12,13
expert 274:23 284:23 298:2,4 358:18 444:15 446:19
experts 260:23 285:3 287:4 471:10 481:23
explain 338:23 346:13 358:23 373:18 408:13 439:6 478:3
explained 433:14
explaining 439:14
explains 416:21
explanation 321:8 321:12,15,20,20 322:2,4,13 407:2 435:6 439:1 440:23
explanations 369:19 373:15 433:13 439:13
explored 269:16
explores 270:21
expose 273:4
exposed 272:4,5 387:6 421:3
exposure 249:18 249:21 253:11 259:23 261:20,20 272:22 276:8,10 277:2,21 278:17 278:22 285:20,22 294:15 319:21 323:21 324:15 338:14 384:10 385:24 386:17 387:11 388:1,24 389:12 423:10 432:24 451:20,24 452:2 453:7 475:5
exposures 261:13
express 255:11 437:2
expressing 381:5 381:15,17,19
expression 264:2
extensive 266:2 487:8
extent 280:25 281:16,18 382:10 390:17 422:15 439:16
external 248:13 271:4 272:5 303:8

307:10 325:3,24 413:16 439:12 471:10 472:13
externally 312:5
extrapolate 272:20 273:21

f

f 245:22
facilitates 291:10
facility 302:16
fact 282:24 299:3 320:24 326:24 353:15 362:5 374:12 375:24 380:15 381:24 387:18 431:20 449:2 450:10 468:3
factor 252:20 253:7,20 269:5,8 269:11,25 270:3 271:5 273:3 274:18 293:14 440:10,10,19 441:6 442:4
factors 252:19 253:4 262:6,11 271:18 341:7 379:18 427:12 435:17,21 440:8 440:20 456:6
fail 282:10
failed 413:1 432:17 458:7
failing 292:22
fails 495:19
failure 354:12
fair 258:10 320:9 329:12 330:16 365:24,25
fairly 407:15
fall 303:7 474:22
false 282:20,21,25 283:4,5 457:24
falsifies 282:23
falsify 282:13
familiar 287:2 298:6 304:17 409:3
familiarize 430:5
families 418:8
far 261:4,5 309:3 318:16 357:19 390:20 418:18 439:16 451:1 484:8
farmer 416:25 417:2 420:3
farmers 418:8,10 421:4,9
farming 416:20
favor 448:24
february 245:12 249:6,7,13 251:4 306:15 392:17 400:22 403:17 404:24 410:7 415:23,25 494:6 494:22
feed 386:13
feeds 477:8
feel 266:15 415:5
feels 315:2
felt 310:23 491:5
fictitious 282:25 283:5
field 274:23
fifra 281:6,6 282:4 282:6 400:23
fifth 380:11,12 383:21 406:10
fight 303:16
figure 407:6 423:25 468:13
file 282:10 288:3 288:13 364:1 397:23
filed 306:6,13 363:24 398:7 462:5
final 266:7,25 288:22 289:3 290:18 296:16 322:17 390:18 393:21 413:7 430:15,22 466:21
finalists 335:14
finalized 345:11 358:13
finally 440:19
financial 293:11 307:20,22 443:1
financially 494:14
find 310:11 366:3 366:13 369:25 387:4 389:10 435:23 438:3,5,14 438:25 439:6,9,19 439:25 445:10
finding 275:22 276:4 277:20 279:4 280:14,15 286:3,6 295:13 310:4,6,7,9 343:25 351:19 352:6 370:6 382:23 388:13 395:16 396:2 398:14,22 399:1 404:5 413:1 413:6 425:20 426:1 433:3,19 434:1,10 435:6 441:17,18 449:3 463:3 467:25 479:11 481:5 482:1
findings 249:2 262:19 265:1 275:25 278:25 280:19 284:3 285:14,15 290:13 291:10,11,23 292:5 293:7,8 308:14,16 309:17 310:1 317:11,15 317:23 320:6 321:4,25 322:4,19 322:21,23,25 323:2,10 325:3,16 325:24 326:8,13 327:24 330:4,9 339:23 340:9 347:21 350:9 351:19,23 352:18 353:12,16 357:15 358:10 361:14,23 362:2,4 365:23 366:25 367:6 369:20 370:25 371:6 372:12 373:18,24 374:2 377:6 382:21 388:5 395:4,14 396:5,9,10,18 401:19 402:22 404:1,25 412:8,19 413:10,19 414:8 423:9,12,13,15 432:18,25 454:11 458:8 459:15,18 462:21 463:18 466:7,11,13,23,24 479:17,19 482:18

488:22 490:9,14 490:17 491:8 492:6 493:2
fine 263:7 295:1 315:3 356:14 427:24 439:24 443:22 449:13 457:3 460:5 470:4
fined 283:6
finish 313:13 452:19
finished 337:10 415:18
fiorillo 246:8
fire 283:2
firm 472:19
first 256:24 261:1 262:4 272:18 278:5 295:15 300:2 303:12 308:7 316:16 318:12 319:14 323:20 329:3 335:8 340:18,20 340:24 342:8 347:21 350:14 356:3,24,25 357:4 357:5 366:22 371:8 373:12 377:9 380:5 382:2 382:3 388:12 396:21 406:21 411:18 412:10 418:7 425:6 428:2 428:4,22 432:10 451:7,15,21 452:13 460:3,13 462:25 463:3 465:2 479:16 487:4 494:5
five 283:7 347:19 419:13
fix 369:1
flag 483:4
flaw 366:4 441:20
flaws 366:13
flip 383:21
floor 246:10
flourishes 291:8
focus 304:11
focused 251:21
folks 296:13 407:2 486:22
follow 312:25 340:11 390:3 413:20,25 415:3
followed 289:17 306:4,20 308:4 313:1,2
following 299:24 338:11,13 350:18 355:2 384:16 392:10 393:18 407:25 429:2 432:23 436:14 460:11
follows 251:2
forefront 376:3
foregoing 494:5,8 497:5
foresight 478:8
forget 269:2 376:2 450:2,3,6
forgive 392:20
form 254:1 260:13 261:16 267:2,7 269:13 272:10 286:7,21 287:12 291:3 294:12 295:17 304:7 305:15 306:18 318:3 326:14 327:6 344:3 355:22 358:21 359:7 361:19 367:7,14 395:10 421:7,13 440:3 442:6 447:12 448:18 449:16 454:23 470:2 472:12,22 473:4 474:9,11 475:9 483:8 486:10 487:1 488:24 491:19 492:8
format 407:8 414:21
formed 282:15 463:9 471:1
former 298:1
formerly 284:8
formulation 259:22
formulations 260:9
forth 431:15
forward 258:14 315:2 422:12 488:19
foster 297:23
found 252:5 289:2 295:9,9 300:9,12 334:15 339:3 352:5 353:9 355:19,21 356:12 357:13 362:6 388:14,15,24 394:25 395:18,22 418:12 435:12,13 435:14 439:1 443:14 447:15
foundation 447:12
four 273:22 275:3 275:18,18 332:21 333:2 347:19 424:10 431:17 467:1 470:12
fourth 271:25
fractionator 334:23 335:18 336:10 337:20 340:18
frame 338:6 339:18
france 483:18
francisco 246:10
fraudulent 282:25 283:6 492:7,11,16 492:19
fredriksson 300:3
free 415:5
freeman 417:2
frequency 285:21 361:2,9
frequently 385:18 417:15,18
front 304:16 313:13 328:10 354:18 422:25 468:18
fulbright 471:22
fulfill 479:21
fulfilled 398:4 480:3
fulfilling 425:1 463:7
full 347:6 383:5 396:21 428:22 457:4 458:22 459:7
fuller's 256:4

fully 287:22 381:24 454:11 458:20 459:8 481:11
fulsome 369:4
function 252:2 289:24 294:6,14 394:18,22 424:25 455:5 463:10 466:4 479:14,15
functioning 270:9
fundamental 261:11
fundamentally 475:13
funding 265:14
furnished 282:16
further 254:13 265:22 266:11 316:3 328:15 339:22 340:7,10 340:13 354:22 361:1 362:19 375:12 448:11 467:6 480:25 494:13
future 323:23,25 413:9 425:5

g

gain 328:19
game 309:25
general 255:25 257:5,25 275:8 283:12,13 292:2 308:25 408:1 409:14
generalised 371:10
generally 253:2 264:6 268:1 269:22 271:20 292:14 304:2 383:17 416:17 420:7 470:23,25 473:25 474:4,25
generate 291:1 382:16,25 383:4
generated 256:6,8 271:16 309:17 324:19 349:3 431:13
generating 479:14
generation 285:22
genes 274:17
genetic 252:20,21 271:3,3,17 274:3
gentlemen 275:11 317:20
genuine 389:5 491:10
genuinely 408:15 436:24 491:15
geographic 473:21
geographical 274:20
george 307:16,17
germany 483:20
getting 279:2 312:23 315:22 407:6 420:14 448:2 466:8
give 251:18 273:5 274:17 279:22 280:2 288:25 289:12 326:23 333:5 341:10 352:12 365:11 382:3 398:8 406:4 411:2,11 432:2 440:5 444:3 463:12 465:16 473:6 474:25 477:24 478:6 486:16
given 268:17 276:19 287:4 297:12 299:10 300:10,13,20,21 300:21 316:24 319:8 333:24 365:13,14,15 380:15 393:10 394:12 406:15 418:16 426:23 428:12 436:20 471:5 497:9
gives 416:21 427:15
giving 347:6 472:7 478:8 487:9
globe 487:24
go 269:14 272:11 277:25 296:2 297:15 298:25 299:17,24 301:1 307:9 308:1 310:9 310:18 313:12 314:25 315:2 316:11 318:7 325:1 326:6 329:2 329:21 330:18 336:17 337:19 348:9 352:11 358:19 359:13 360:23 361:4 362:11 368:11 370:2,15 377:7,20 380:4 385:19 393:6 409:4 415:5 415:13,15 422:6 422:12 430:1 435:1 437:23 439:17 442:2 443:23 453:15 462:24 464:17 467:6 470:10 480:18 483:22 488:19 493:18
goes 254:14 339:21 382:15 480:9
going 253:5 278:24 281:17 284:4 296:4 313:5 313:6,8,8,9,9,10 313:11,15,20 314:20,21,22 321:3 324:18 337:9 342:8 348:8 359:12 366:11 368:11 384:2 385:25 386:1 409:3 415:7 420:10 430:20 431:25 435:1 462:14
gold 320:14
good 251:3 335:24 335:25 359:12 474:24 475:1
goodness 305:11
governance 465:13 466:1
government 305:22 306:10
government's 306:25
graham 246:23
granularly 261:22
greater 274:21 339:14 361:10
group 265:23 266:22 267:24,25 268:2 270:19

271:18 298:16 302:6,9 303:15 308:19,25 309:4 319:25 320:3 329:24 343:20 350:20 355:18 427:22 428:11 431:4 436:8 455:9 462:24 463:25 464:18 469:12 471:1,2 472:11 476:2,4,13 477:8 489:15
groups 274:21 302:1 309:8,10 319:21 330:2 454:1 464:10 476:19
grow 270:8
grower 416:25 417:2
growers 421:4
guarding 459:9
guidance 284:2
guide 297:1

h

h 248:1 384:7,7 496:3
ha 374:17,18 375:6
half 348:24 358:3 358:13 363:15 404:15
hallmark 264:4 320:16
hallmarks 262:8
hand 292:4 397:24
handed 330:23 347:8 378:3 406:3
hands 488:15
hang 311:9
happen 273:9 363:9 389:7 447:20 449:14 450:2
happened 290:10 448:24 472:23 475:23
happens 276:17
happy 369:1 375:24 492:18
hardware 354:14 355:1
harm 283:22 291:24 482:16
harsh 438:13
hazards 291:24
head 253:4 265:18 265:19 266:2,5 269:3,4,7,11 371:25 372:25 373:1 398:8 405:14 431:4,5 463:13 468:13 477:3,4,24 484:21
headed 249:3 476:2
heading 270:25 301:20 303:7 336:19 337:6
headquartered 485:7
headquarters 469:14
health 261:8 264:22 265:17 270:15,16,20 280:10 291:24 292:11 303:18 308:23 374:19,20 375:19 389:19 429:20 431:6 434:22 435:25 464:21,22,25 465:17,20,25 471:6 473:19 474:7 476:17 477:7,8,9,12,17 478:11 481:22 482:19,25 490:24
heard 252:15 366:12 393:9 482:6
heart 305:12
heavily 292:11
held 245:16 284:8 410:23
help 268:3 337:11 417:5 437:11,15
helped 449:7
helps 292:5
herbicide 328:21
herbicides 307:15 307:23
hereto 497:7
hierarchy 470:22
high 265:11 273:5 276:7,25 278:17 278:19,23 310:7 387:4 406:16 408:2,20 409:15 412:14 419:1 442:2
higher 266:8 267:7,11 285:21 432:20 442:1
highest 367:1
highly 286:5 345:9
hindsight 383:12 383:12 447:21 454:14 458:24 488:12
hippocampus 371:13
hired 377:3
histopathological 436:22
history 462:24 467:6 473:23
hm 297:6 428:1 451:6 460:12 461:10
hoffmann 245:4,5 417:3 495:4 496:1 497:1
honest 414:2
honorariums 443:6
hope 258:14
horrible 304:6
hour 369:1
house 246:24 328:15
housed 417:12
housekeeping 391:24
human 249:23 255:3 258:13 262:8 272:3 273:2 273:9,12,15,19,24 276:17 292:13 303:17 381:21 385:12 386:1 387:6,25 389:18 444:20 446:6 451:20,22 452:6 453:5,11 482:19
humans 387:3 413:11 451:14,24 452:2 453:7
husch 246:18
huschblackwell.... 246:21

hydrate 331:8 392:8
hydroxylase 437:3 437:5
hypotheses 373:17
hypothesis 253:16 255:14 258:3 261:12 274:7 396:25 403:11 407:5
hypothesised 274:12

i

i.e. 423:6 477:8
i.p. 349:24 412:12 425:14 432:15
ici 255:15,16 259:13,18 260:1,2 289:8
ideal 321:19
ideas 291:9
identical 436:10 439:4
identically 450:4
identification 256:14,17 296:21 318:10 328:1 330:20 342:17 347:4 359:21 370:3 378:1 392:2 400:5 406:1 408:25 410:3 414:18 422:5 430:3 443:24 459:23
identified 455:17 467:1 469:2 481:9
identify 291:23 328:3 331:2 335:3 430:8 441:20 444:1
ii 284:22
iii 284:23
illinois 245:2 313:13 420:12
imagine 367:4 450:19
imaging 337:13
immaterially 282:24
immediately 318:24
impact 262:22 344:1,19 421:6 464:1,10 483:6
impacted 439:5 443:2
impeached 368:23
implemented 355:2
implicated 259:3
implicating 302:2
implication 374:6
implications 430:12
importance 293:16
important 255:10 292:12 293:2,13 339:22 340:7 341:22 380:25 386:6 441:6,18 452:12,13 487:3 488:23 489:1
importantly 277:19
imprisoned 283:7
improper 491:13
improve 346:25 354:22
improved 355:15 356:12
improving 260:6
inability 276:9
inappropriate 367:16 472:16,21 474:23
inaudible 456:24
incidence 274:22 285:21
incidents 419:3
include 254:11,19 262:10,13,18 263:13 279:14 320:3 390:4 399:4 401:11 414:24,25 442:11 454:11 463:2 468:3,6 489:3
included 263:15 263:18 266:1 316:10 367:21 391:12 399:15 405:6 414:20 447:14,15 471:9
includes 258:25 259:2 260:1 284:19 414:21
including 252:6 282:14 325:17 368:7 380:16 382:9 389:21 397:17 404:10 406:12 411:6 428:24 459:25
inclusion 459:14 472:7
inconsistent 280:21
incorporate 459:17
incorrect 368:20 438:14
incorrectly 435:24 436:2 438:1
increase 264:1 419:2
increased 361:9
increasing 361:2
independent 245:5 253:23 317:5 320:7 325:13 333:22 336:8 337:21 339:2,9 341:15,21 351:20 351:25 353:8,16 362:6,22 373:24 376:14,24 388:6 395:23 396:2,13 396:15,18 407:3 429:9 436:20 439:2,2 442:7,11 442:17,25 443:19 450:5 453:25 454:19
independently 442:19
independents 442:22
indicate 425:17 482:15
indicated 255:1 277:16 295:24 350:22 431:23 432:6,22 484:23
indicating 363:17 371:10
indication 365:11 483:4
indirect 364:22
individually 245:4
induced 331:9 360:1 380:14 381:4,9,14 383:23

391:16 397:1 403:12 407:19 409:12
induces 361:16
inducing 395:7 401:22 402:25
induction 451:12
inevitably 291:17
infer 324:17
inferring 449:9 482:25
inflammatory 432:23
influence 325:8,13 326:21
influencing 325:4 325:7,25 327:13 327:15
inform 357:11 363:10 446:19
information 281:24 282:13 283:15,17 284:6 284:18,22 286:12 286:13,16,17,17 287:3 288:25 290:2 291:1,2,17 293:3,4,9 300:20 301:2 315:6 326:13 349:6 350:17 386:25 415:16 416:10,16 416:22 428:5 430:23 448:6,16 449:5 452:7 461:8 466:8 472:7 484:24 486:7,9 491:2
informed 268:7,14 268:16 469:9
ingested 260:10
ingestion 260:15
ingredient 260:25
initial 259:3
initially 265:18
initiated 248:23 332:12 335:21 348:16 360:15
initiation 248:21 249:5,9
inject 386:13
injecting 277:10
injection 384:16 387:3 406:23 407:7,12
injections 278:1 331:12 343:21 362:13 393:11,18 412:13
injury 269:3,4,7 269:11 375:25 485:20
innovative 336:1
input 319:16 340:10,13
inquire 279:1
institute 302:10,15 329:25 350:18 355:6
intended 317:4,10 323:12 325:8,13 325:15 327:21 329:14 429:24
intending 325:8
intent 259:22 310:3
intention 374:21
intentionally 260:18 312:24 320:20,20
inter 465:5
interact 365:1
interaction 365:2 456:25
interactions 467:20
interactive 337:12
interchangeable 482:11
interchangeably 482:9
interest 293:11 443:1 459:10
interested 494:16
interestingly 362:9
interests 459:7
interferes 292:23
internal 248:15 318:8 331:3 410:15 423:6 429:22,24 434:24
internally 487:18
international 328:20
internet 416:12 417:5
interpret 262:19 265:1
interpretation 291:10 324:8,9 330:16
interpreted 398:11,24 464:5
interrelationship 464:13
interrupt 408:8
interrupted 313:25 314:4,17
interrupting 313:3 313:23 452:15
intra 277:11 278:1 349:25 390:15,16 446:14
intracerebral 384:16
intraperitoneal 412:13
introduced 368:4 368:8,18
introduction 298:9
inventors 248:5 257:9
investigate 333:14 335:4 339:22 340:8 360:25 373:4,13 392:22 393:16 461:20
investigated 268:24 351:20 384:9
investigates 270:21
investigating 249:10 271:16 298:16 331:9 360:1 381:4 446:1
investigative 319:15,19,25 323:18 411:15
investigator 332:4 343:11 346:11 360:6
investigators 295:8 453:24
invited 416:4
involve 258:1
involved 266:12 268:4,13 319:19 334:3 358:14 359:1 369:24

377:18 383:6 399:6 404:19,20 437:7,8 447:18 456:7 457:7,13 458:12 467:21,22 471:16 472:13 481:8 488:18 490:3 494:14
involving 381:2,8
ip 390:13,14
irrespective 268:13 271:4 308:24
irreversible 390:13,21 391:17
isolation 399:11
issuance 430:21
issue 278:17,24 293:15 323:21 326:24 364:12 438:17 439:9 471:14
issued 257:23 332:21 333:10 348:24 460:7,25
issues 265:24 266:1 267:14 324:21 342:4 379:17 465:9,11 477:21,25 478:4,7 481:19
items 469:4

j

janice 405:12,13
jcraig 246:7
jersey 302:7
job 308:20 309:1 335:24,25
john 246:7 248:5,8 257:9
joint 259:13
joseph 246:20
joseph.orlet 246:21
journal 363:4 397:8 443:5
journalist 307:19 307:20,22
journals 295:19 353:18 439:3 443:13
judge 313:13 314:22,25 315:1,2
judgment 327:24 458:24 459:17,19
judicial 245:1
july 249:22 332:24 430:13 432:4
june 250:2 348:25 349:7 360:19 392:14 460:7,10 460:14
jury 253:4 275:12
justice 306:24
justification 490:24 491:1

k

k 384:7
keep 320:22 359:12 430:16 448:2 476:18 484:21
keeps 484:11
kelly 246:9,11
kept 345:9
key 253:22 469:1
kg 331:12 349:21 362:13 382:8 390:17 393:18 429:3 432:20,21
kill 294:18 295:7 295:10 303:24 407:11
killing 442:3
kilogram 334:6 370:18 442:2 455:16,23
kim 248:6,8 257:17 424:11 431:8
kind 271:4,15 287:15 320:14 421:5 424:17,19 428:9 474:12,25 481:8
kinds 416:22 475:6
kinetic 337:13
kingdom 245:17 245:19
kirkland 245:16 246:14
kirkland.com 246:16 495:2
knew 271:6,12,13 271:19 283:12,15 283:16 284:18,25 285:2,12,24 286:11 299:9 312:16 315:13,14 315:16 356:8 376:13 384:22 414:7 421:18,18 449:7 450:13,14 488:14
know 255:9,15 258:23 259:7,18 259:20 261:5 274:7,16 280:25 281:6 282:2,3,4,7 282:18,19 283:8 283:10,11,13,19 285:7 286:15 290:9,10 301:15 305:2 307:7,18 310:17 313:14 325:21 344:8,25 346:2 353:3 355:25 363:14 364:1,25 365:4,9 366:1 367:22 368:19 370:17 376:4,18,21,22 383:1,5 386:24 398:7 399:24 401:8,10 404:22 405:15 411:1,5 413:15 415:19 420:12,15 422:4 423:3,4 429:18 430:17 434:18 438:17 440:12 448:9,11 449:14 450:17,21 456:4 457:14 467:19 478:20 479:3,6,7 484:22 487:17 492:10,18
knowing 283:5 308:21 321:14
knowingly 282:6
knowledge 269:16 291:1 292:20,24 333:1,3,4,5 345:4 345:15,24,25 346:15,16,18 347:17 487:16
known 253:4 255:16 276:3 280:16 285:9,10 382:2,4 420:14 458:2

knows 282:16 286:15
korein 246:3,23
koreintillery.com 246:6,7,8

l

l 245:7,22 248:16 331:17 384:7,12 384:13
lab 262:1 321:21 350:18 454:11
labeled 299:18
laboratories 253:23 310:1 320:17 333:22 351:20,24 428:24 436:10 439:2 488:21
laboratory 261:18 263:20 292:21 295:8 311:1,10 321:17,18 331:19 350:25 360:3 372:1,25 377:1 442:14 443:20 457:10
labs 320:23 322:23 351:25 454:1
lack 248:17 343:7
ladies 275:11
lady 461:17
large 439:11 441:14 474:15
largely 264:9 287:3 429:24 474:4
larger 260:15 449:4
lasting 304:6
late 271:10
latency 285:20
latest 249:1 370:25 371:6 372:11
laura 245:18 251:7 494:3,21
law 306:13 463:8 472:19
laws 288:2,12
lawsuit 306:6
lawyer 266:3 301:2 472:18 475:3
lawyers 471:16,18 471:22 474:19 475:19
layperson 270:7 406:19
lead 262:1 329:19 330:10,12 338:21 345:17 409:25 441:21 453:13
leaders 265:23 266:22
leadership 265:24 266:1 267:13,14 431:6 465:9,11 470:22 471:2 473:15 476:20 477:21,25 478:4 481:19
leading 270:10 466:5 470:11
learn 295:15
learned 292:20
learning 376:12 436:5
leave 310:7 323:3
led 374:10
left 449:24 450:1
legal 280:24 281:12,18 482:2 495:23
legislation 275:24 306:3 463:18 467:17
legitimate 320:12
lending 254:13
length 458:5
lethal 425:14 432:15
letter 249:7 304:14,23,24 305:13 359:2,4 363:19,21,23 400:10 401:1,7 403:20,22,23 404:10,24 405:6
levadopa 258:12
level 266:8 268:14 269:16 310:11 311:1,13 370:17 386:9,12 388:17 388:18 424:4 427:8,10 455:20 455:22 484:3
levels 262:11 310:8,9,20,21 311:16,22,24 424:23 442:1
lewis 249:1 264:19 265:7,17 370:24 371:3,21,22 372:11 379:11,12 379:19 390:4,24 391:3,14
lewy 264:4,8 381:21
lie 283:14 341:18
life 271:25,25 273:16 274:1
lifetime 276:18
light 312:6
likelihood 259:8
limited 385:3,10 396:8
limiting 423:21
line 263:16 265:21 294:25 296:10 327:20 329:3 371:7 374:12 406:16 421:6 456:23 496:4,7,10 496:13,16,19
lines 265:16
link 293:18 324:14 418:18
linked 323:22
links 249:17,20 292:11 303:8 307:10
list 266:2 321:3 362:25 411:11 468:17 483:22 484:3,10,11,21
listed 300:6 371:21 424:6 446:9
lists 285:18 300:2
literature 248:12 271:9 300:1,6 301:21 308:15 309:7,15 310:2 317:5 320:7 322:20,24,25 323:9 324:21 329:8,16 333:15 336:8 337:22 339:2 341:15,21 353:9,12 362:6,20 363:7 373:25 374:5 377:7

395:24 404:2 407:4 411:21 412:8,11 432:18 432:25 434:11 450:5,8 457:12,17 487:5
litigation 425:3,4 425:5 431:1 473:7
little 257:3 303:23 373:7 393:5 415:1 426:22 488:17
live 317:2,3
liver 421:19
lives 260:21 272:13,16
llc 245:8 246:3 296:13 495:4 496:1 497:1
llp 245:16 246:14 246:18
located 245:16 469:16 473:21
location 418:21 419:15
locomotor 302:25
logical 357:24
london 245:17
long 255:6 267:19 285:9 304:6 376:18 377:14 418:11 419:1 422:2 477:5,9 481:24
longer 259:19 467:19,22 477:1
longstanding 471:11
look 258:18 275:9 277:16 290:1 303:6 305:19 306:8,23 309:16 321:23 329:22 347:7 354:1 370:15,19 372:14 372:15 374:16 378:11 380:11 390:7 393:8 396:21 400:20 406:4 409:2,8 415:9 417:8 418:4 418:7 424:7 434:6 436:21 437:23 438:20 445:17 447:5 451:3 466:3
looked 263:5 264:17 303:4 322:7 331:24 366:20 413:4 419:25 438:21 440:1,24
looking 262:13 272:5 309:14 335:4 347:12 351:4 373:15 380:20,23 383:10 392:9 401:25 402:6,11,12,13 406:11,17 407:21 423:10 431:18 440:12
looks 297:19 318:18 319:6 445:17 447:2
looser 477:25 478:1
loser 291:18
loss 259:6 302:23 302:24 309:21 333:23,23 336:11 338:13 339:3 340:15 344:1 349:23 354:2,13 356:12 357:12 360:25 361:6,10 362:20 363:11 365:23 369:21,25 370:7,12 371:10 371:17 381:4,9,12 381:14 382:10 386:18 387:12,23 388:7,15 390:18 390:20 391:4,5,17 392:10,25 393:19 394:1,5,8,11,14,15 394:22 395:18,22 395:23 396:4,6 398:23 403:24 404:25 407:24 408:22 409:13 412:14 423:16,19 425:12,18 426:10 426:21 427:6 432:7,13,19,23 433:1,3,14,19 434:11 446:10,20 455:8,13 456:1,13 457:11,16
lost 455:4,4
lot 267:4 435:9 442:3 458:6
lots 438:22
louis 246:5,19
louise 297:23 302:13 316:14 332:1 343:11 347:12 348:2 360:6 371:3,5 372:21 376:3 378:12 406:11 413:4 449:8,15 457:5 458:3,10 460:1 486:25 487:14,18 488:11
low 261:12
lower 285:19 371:16 427:7,13 455:13,15 456:2,3
lunch 359:11 366:8
lungs 427:2

m

m 246:6
machine 494:7
machinery 435:17
magic 493:7
magnitude 361:10 387:5
main 470:12
maintain 448:19
maintained 417:8 417:11
majority 264:8 337:21
making 267:4 276:16 300:16 324:1 371:17 374:23 375:2,11 443:7 447:9 468:6 484:2 489:18 490:3
male 334:3 350:1 425:13 432:13 434:13
man 282:1 426:2 434:2
man's 257:10
managed 470:16
management 461:15
managing 290:21
mandatorily 285:14 286:12
mandatory 286:5

manner 304:12
manual 339:1,11 339:18 341:25 344:23 346:3,12 356:1 357:8 366:22
manually 338:7
manufacture 253:24 259:19 279:14 329:11
manufacturing 488:18
march 249:25 444:8 495:3
margin 426:6
marginal 456:5
margins 423:10,11 432:9
mark 246:24 256:16 415:22
mark's 365:17
marked 251:12 256:14,17 296:21 318:10 328:1 330:20,23 342:17 347:4 359:21 370:3 378:1,3 392:2 400:5 406:1 406:3 408:25 410:3 414:18 416:8 422:5,13,14 430:3 443:24 459:23
marker 437:4
markers 437:19
market 255:20 279:15,19 324:1
marketed 468:25
marketing 266:4 477:17,20 478:3,6 484:12
marks 248:16,21 248:23 249:5,9,11 297:23 298:15,21 302:13 316:14 317:4,15,23 318:1 318:4 319:4 320:3 331:14,17 332:1 332:12 333:4,5,10 337:20 339:17 342:6 343:11 344:22,25 345:3 345:18 346:4,22 347:12,16,20 348:2,15 349:16 354:4,12 355:13 356:1,16 360:6,24 361:5,13 362:11 365:20,21 367:23 368:3,16 369:18 371:3,5 372:12,21 376:3 378:12,15 379:13,20 380:4 380:12 385:1,6,8 388:5 393:15 394:1 395:3,21 396:23 400:13 401:17 402:10 403:9 406:11 407:2 409:5 410:24 411:24 413:4 420:25 429:6,10 436:9 437:22,23 439:3 440:25 447:3 449:8,15,18 450:17 454:18 455:3,13 456:2,3 457:5 458:3,10,14 458:17 459:11 460:1 486:25 487:14,18 488:11 488:13
mary 245:17
mass 253:21
material 282:24 299:21 435:19 461:1
materially 283:5
materials 256:5 337:1 344:7,12 461:6
matter 312:5,17 315:17 362:5 410:13 421:22 427:23 431:20 441:3 486:5
mattered 420:3
maximum 432:20 446:16
mccormack 352:10,22 353:6 362:25 363:1 429:4 438:9 450:13
mcfarland 405:12 405:13
mean 253:3,8 259:24 272:13 278:17 281:5 287:17 293:25 299:4 316:21 322:14,17 323:25 347:1 374:16 386:10 390:14 408:6,8,11 414:1 433:10 462:2,25 464:22 471:21 472:9
meaning 263:25 408:22 413:20 418:20
means 260:6 263:24,25 275:12 275:12,13,21 284:2 306:24 311:23 316:22 317:2,3 320:11 322:9 332:18 348:20,22 374:24 381:17 382:19 396:9,17 442:17 452:1 462:4
meant 321:16 327:15 357:23 385:11 395:12 399:2 408:7,11
measured 394:11 420:1 435:7,15
measurement 394:20
measurements 436:23
measuring 310:20 310:21 311:1,12 311:16,22,23 316:10 436:21
mechanism 255:2 255:6,12 269:10 322:16
mechanisms 256:9
mechanistic 321:8 321:12,20 322:2 322:12
media 296:8 324:22 359:18 422:22
median 425:14 432:15
medical 260:22
meet 290:13 464:5 464:6 466:13 480:6

meeting 248:19 249:13 307:6 310:16,17 343:3 344:24 345:5,16 356:21 372:10 378:21,23 379:1,2 379:4,10,12,24 380:5,5 391:12 399:9 406:17 410:7,10,13,19,22 410:23 413:16 416:3 418:5 431:12,14 446:24
meeting's 344:9
meetings 325:4,25 326:5,5,21 344:13 344:13 380:6 414:16 471:10,23
meets 480:23
melodia 246:9
member 288:24 479:7
members 364:22 469:10 471:7
memory 267:22 399:12
mention 335:10 486:24 487:14
mentioned 254:12 265:2 269:3,7,18 273:3 276:7 288:23 302:12 328:24 368:3 376:10 437:21 442:7 458:16 478:14
mentioning 262:7
met 379:25 380:3 380:7 405:16 463:17
metabolites 349:22 351:9 393:21
method 334:24 337:20 338:1,6 339:18 340:21 346:3 438:5
methodological 341:18 373:16 379:17
methodology 338:20 350:11 354:14,21 355:18 366:4,13,17 385:9 386:3
methods 291:10 340:22
mg 349:21 362:13 390:17 393:18 429:3 432:20,21
mice 272:14,17,21 278:1 300:9,12 316:18,25 317:3 332:18 333:24 334:3 343:20 348:20 350:1 361:7,16 362:14 373:6,15 380:13 380:14,21 381:3,9 381:15 382:14 391:4 394:2 395:6 401:21 402:24 406:14 407:25 425:13,22 432:14 434:13 446:21 456:19
michael 246:11
microorganisms 274:8,11
microscope 337:14 436:7 438:21 442:15
microscopic 335:2
microscopy 335:5
mid 259:1
middle 430:19 431:23 453:18 470:13
mike 371:3 372:2 372:3 460:20
milligrams 334:6 370:17 442:2 455:16,23
mills 417:3
mimic 273:1
mind 314:9 319:10 321:3 367:16 374:14 425:15
minnema 268:6 278:20 441:7 446:17
minute 255:1 296:3 354:4 367:25 415:21 430:5 444:3
minutes 379:1,4 424:21
miserable 304:6
misfolding 252:7 264:7,11
misprint 392:19
misrepresentation 447:11 454:8
missed 426:15
mission 303:16
misspoke 426:13
misunderstood 278:5
mkelly 246:12
mm 451:6 460:12 461:10
mo 246:5,19
mode 255:16
model 249:4 253:18 261:19 262:6,9 263:16 272:3,4 273:1 302:4 309:20 378:10 379:21 385:3,10,15,23 386:4,4,6,18 387:2 387:3,12 390:12 392:10 411:20 423:19,22,24 424:2 441:21 445:9,21 450:9 451:12,19 452:10 488:15
models 272:8 319:22 328:17 385:18 420:21
modified 350:12
modus 477:7
molecular 261:6
molecule 261:3,4 261:11 299:4
moment 297:13 422:7 469:11
moments 431:23 440:1
money 490:22
monitor 308:20 309:1,7,11
montague 405:9
monte 302:9,15 316:24 329:24 330:7 346:23 353:6 355:3 363:1 438:9
monte's 350:19 450:14 455:9

months 273:17 357:21 393:1 431:20
monty 405:10
morning 251:3 382:20 386:5 388:10 398:5 399:8 435:18 436:2 463:16 466:15 469:3 484:23
motive 443:14
motives 475:6,7,10
motor 252:1 446:6
mouse 248:18 249:4 253:18 263:16 272:13 273:14,16,18 277:1,17 295:6,12 295:16,22 302:4 309:20 317:7 319:1 320:1 325:12 327:20 328:25 330:3 331:10,22 333:17 339:4 343:8 344:19 347:13,24 351:21 353:10 355:18 360:2,10 362:3 365:24 378:10,17,22 379:21 382:6,9 383:24 385:2,9,14 386:18 387:12 388:20,22,23,23 389:11,12 390:12 391:15 392:10 404:1 405:1 408:17 410:24 411:20,25 412:12 413:5 420:21 423:19,22,24 424:2 433:4,21 441:21 450:9 455:9 457:4 487:6 488:15
move 288:9 296:10 311:6 339:18 345:21 387:8 389:9 391:25 449:11 459:4 487:11
moved 273:23 337:15 338:6
moving 319:2
mptp 338:9,12
multiple 412:12 450:3 468:4

n

n 245:22,22 246:1 246:4 247:1,1 248:1 282:8 384:7
n.w. 246:14
name 257:10 270:16 343:12 352:25 376:10 384:2 476:1,4,5,13 494:21
named 257:14 461:9
names 267:12,19 405:7 424:6 477:24
naresh 246:16 251:10 254:1,10 254:21 255:22 259:10,15 261:16 261:23 262:3,15 267:2 269:13 272:10 278:4,12 279:18 280:1,6,23 281:12,16 283:23 286:7,21 287:7,12 288:14 291:3,13 291:19 292:1,7,16 292:25 293:21 295:17 301:3,8 304:7 305:15 306:18 311:9,12 311:17 313:3,22 313:25 314:4,7,12 314:16,19,23 315:3 318:3,12 324:3 326:14 327:4,6 330:19 339:25 344:3 355:22 358:4,21 359:7,13 364:18 367:7,14 368:2,7 368:10,12,16,24 369:3,10,15 391:24 402:7 421:7,13 422:6,11 426:13,15 440:3 447:12 448:18 449:16 450:25 452:15,19 453:1 454:23 456:22 468:14,16 470:2 470:17,24 472:12 472:22 473:4 474:9 475:9,17 482:2 483:8 485:4 487:1,25 488:5,24 490:19 491:19,24 492:8,17 493:4,10 495:1
natural 272:23
nature 257:5 282:14 457:22
near 413:9
necessarily 273:1 276:15 323:3 342:3 377:17 401:14 437:19 440:10
necessary 418:21 439:22 451:18 497:6
need 254:5,16 265:13 266:8 268:8 276:2 322:16 323:5 341:11 348:5 367:22 374:23 375:23 392:1 393:9 397:24 401:10 405:11 411:11 419:20 437:10 439:22 458:11 483:1 484:20 485:13,17 485:23 487:20
needed 281:2 373:17 375:10 436:21
needs 323:22
negative 355:19
negatively 312:17 315:18
neither 277:24 485:1
nerves 294:5
nervous 294:2,4 294:15,16,17,19 439:19
network 303:19
neural 356:23
neurochemical 331:11 384:10,15 446:5
neurodegeneration 251:22 446:10

neurodegenerative 251:20 269:9
neurological 255:2 294:5
neurologist 252:10 253:1
neuron 394:14,18 394:22
neuronal 309:21 351:16 354:12 365:23 369:21 371:11 373:5,14 381:12,14 382:10 386:18 387:12,23 388:6,15 390:18 391:5,17 404:25 425:18 426:10,21 427:6 428:25 432:7,22 433:1,3 433:19
neurone 371:15
neurones 302:23 339:4 344:1 357:12 371:10,16 371:17 412:15 425:12 429:1 432:13
neurons 294:18 295:7,10 333:24 349:23 352:5,7 356:12 360:25 361:6 362:15 363:12 369:25 370:7,12 377:11 387:20 392:25 394:2,6,12 395:18 395:22 397:1 398:23 403:12,25 407:1,20 408:22 432:19 433:15 434:12 435:15 446:10,21 455:9 455:13 456:2,14 457:11,16
neuropathological 446:6,9
neuropathology 432:21
neuroscience 248:19 343:2 345:5
neurotoxic 280:10 280:20 295:2,11 295:16 299:2 317:6 320:6 330:2 336:9 347:22 353:10 361:24 362:1 374:5 375:13 395:15 396:3 400:12 403:21 419:2 427:18 432:3 441:22 482:15,22 483:3 485:11,16 486:1 487:24 488:4 491:8 492:6 493:3
neurotoxicity 293:25 294:1,3,8 294:12 295:25 298:16 302:22 331:10 347:13 360:2 361:19 373:24 375:8 395:10 398:24 482:20 485:11 486:7 491:11 492:10
neurotoxicology 370:10 389:22
neurotoxin 294:16
never 258:7 269:16 273:8 276:17 278:2 287:10,15 289:3,5 346:14 367:8 376:1 399:25 437:25 438:11 441:20 447:2 450:20 463:9 490:23
nevertheless 338:18,20
new 280:15,15 291:11,11 302:7 306:2 355:15 356:11 357:14 376:4,6,6 399:1 404:5 430:19 436:3
newer 342:1 354:18
ngo 303:21
nhp 413:8
nicholas 248:6,8 257:14 307:16,17
nick 297:22,25 332:9 371:3,5 378:12 424:11 431:8
nicole 246:23
nigra 251:22 253:15 255:3 258:12 295:7 302:23 309:22 333:17,24 334:11 344:19 349:24 352:8,19 356:13 361:1,7 362:16 371:12,17 377:11 387:19 388:16 393:1,20 395:12 395:13 403:25 406:13 407:20 409:13,17 412:15 419:15,25 421:1 421:24 425:12 427:6,19 428:17 429:1 432:13 434:12 439:5 456:14 457:11 459:3
nigral 361:16,19 395:7,10,12 401:22 402:25
nigrostriatal 248:18 249:11 343:7 383:23 393:17 406:12
noel 386:8,18 387:12 455:16,19
nominated 335:7 335:11 336:6 341:5
nomination 341:9
non 328:21 334:13 355:9 381:3 481:14
nonfunctioning 437:16,17,20
nongovernmental 303:21
normal 261:17 266:10 270:9 278:22 294:16 320:13 345:16 347:2 401:13 462:6
normally 271:6 273:16 343:18
north 265:5 289:9 405:14 469:19 470:14 474:1,3

478:22
notary 497:13,19
note 301:24 380:12 385:1 436:8 495:10
noted 435:2 497:7
notes 248:25 317:10 355:13 370:24 378:15,20 380:6 391:12 455:22
notice 469:4 484:20
notifiable 481:25 482:6
notified 357:21
notify 356:23 358:12 359:3
notifying 467:25
nottingham 384:9
november 360:17
nullify 306:25
number 252:21 256:13,25 265:9 270:11 280:2 281:17 285:18 289:13 290:7 296:8,20 297:16 300:2 318:7,8 328:3 330:24 334:10,14,18,20 335:5 338:9,11 342:8,11,19,21,24 342:25 343:1 347:8 359:18 360:8 362:15 370:16,19,20 371:8,15 376:1 378:4 392:4 400:21 402:14,15 402:18 405:7 409:2 411:6,7 414:16 422:22,25 427:13 428:22,24 429:5 435:15,16 435:21 440:8 441:13,14 445:1 445:10,18 453:19 456:18 484:8,10 484:22,23 493:7
numbered 249:15 494:5
numbers 283:11 297:1,16 342:9 352:19 469:12
ny 495:15
nyengaard 376:10

o

o 245:22
object 254:1 269:13 278:4 279:18 280:23 281:12 283:23 288:14 301:3,8 305:15 358:4,21 422:18 440:3 448:4 456:22 468:14 491:19 493:13
objection 255:22 259:10,15 261:16 261:23 262:3 267:2 272:10 278:12 280:1,6 281:19 286:7,21 287:7,12 291:3,13 292:16,25 295:17 304:7 306:18 318:3 324:3 326:14 327:4,6 344:3 355:22 359:7 367:7,14 421:7,13 447:12 448:18 449:16 450:25 454:23 470:2,17,24 472:12,22 473:4 474:9 475:9,17 482:2 483:8 485:4 487:1,25 488:5,24 490:19 491:24 492:8 493:4
objections 254:10 254:21 262:15 281:17 291:19 292:1,7 293:21 492:17
objective 292:23 309:4 475:7
obligation 279:11 283:20 488:19 490:7,13
obligations 463:7
observation 282:15
observe 382:10
observed 302:21 333:23 338:13 350:10 361:1 363:12 390:5,12 394:1,5 407:24 412:25 425:17 428:25 446:6,20 455:10,12 456:1
observing 352:18
obtain 475:7
obtained 338:24 350:17 380:15 451:11
obviously 303:25 398:10 437:15,23 489:3
occasion 264:23 351:7,10 353:17 356:21 363:17
occasionally 266:14 471:18
occupational 274:21
occupy 481:11
occur 271:5 384:23 423:11
occurred 379:25 381:9,15 471:25
occurrences 346:6
occurs 271:7 294:15
october 248:19 343:3
odds 275:2,3,7,8 275:12,13,21
offer 321:8 322:2 322:4,20,24 323:10 346:21
offering 308:15 440:5,6
officer 266:24
offices 245:16
official 476:15
oh 322:6 342:23 343:15 357:24
okay 253:10 255:20 256:12 257:6,14,25 258:22 259:21 267:17,22 268:10 268:23 271:4,9,24 272:3,20 273:18 278:25 280:9 282:4 284:4 285:2 285:9,12 286:11 287:10,21 288:6 290:10,24 291:6

292:10,19 293:24
294:11,24 295:6
296:19 297:3,4,18
298:4,8,11 300:25
301:17,18 302:21
303:5 304:13,19
305:7,11,19 307:5
307:8,24,25 308:5
310:10,15,18
313:7,14 314:15
316:11,16 317:2,9
317:20 318:7
319:10,14 320:5
321:2 324:13
325:1,12 326:12
326:17 327:1,13
327:16,19 329:2
329:15,20 331:5
332:9,12 333:1,4
333:10,14,18,22
334:3,18 335:16
335:20,23 336:4,8
336:21 337:6,10
337:19,22 338:5
339:13 340:18
341:9,12,25 342:5
342:13,16 343:6
343:17 344:17,21
345:14 346:1,17
346:24 347:3,10
347:24 348:8,11
348:15,20,24
349:15 350:7
351:6,15 352:4
353:15,23 354:4,9
356:14,18 357:2
357:11,20 358:11
358:16,23 359:5
359:11 363:6
364:1,8,14,17
366:2,2,7 367:4,13
368:12 369:14,15
370:19 371:8,21
372:10,20 373:3
373:10,22 377:8
377:19 378:8,15
378:20 379:19
380:11 381:1
382:5,15 383:3,8
383:17,21 384:22
385:4 389:14,16
389:25 390:11,24
391:2,23 392:22
393:7 395:2,13
397:7,13,23 398:1
400:4,9,11 401:11
402:4,20 403:3,16
404:20,20,23
406:5,8,9 408:24
410:4,15,20,23
412:16 413:2
414:23 415:4,11
415:19,20 416:8
418:6 420:6
422:19 423:3,25
424:6,16 425:6,23
426:16 427:1
428:21 430:1,7,25
431:4,14 432:10
434:9 436:13
438:3,13 439:19
439:24 441:4,13
441:20 442:21,25
443:17,22 444:5
444:12,14 448:9
448:15,23 453:14
453:22 454:2,22
455:21 456:10,17
457:3,9 460:5,6,15
461:18 462:8
463:23 464:8,13
464:14,20,25
465:3,15,23 466:2
468:11 469:7,18
470:8 472:25
473:3 474:22
475:25 476:25
477:11,20 478:13
480:9,11 481:3,16
481:18,25 483:2
483:13,16,24
484:13 485:9
487:11,22 488:3
490:11 491:1
492:21,24

old 272:17,22
273:14,18 355:17
437:24

older 269:24 270:8
273:7 355:10

olfactory 258:25
259:3

omitted 448:25

omitting 449:8

once 334:4 429:3

ones 286:1 303:24
368:18 429:10
467:4

ongoing 253:24
490:6,13

onset 252:23,24
269:20,22 271:2,3
271:7 272:23

onwards 479:8

open 291:9 304:14
304:23 305:13

openness 291:10

operandi 477:7

operation 373:1
470:19

operations 469:18

opinion 266:16,17
278:6,10 282:15
284:23 287:3
289:1 311:25
379:12

opinions 284:20
285:2

opportunity
344:25 493:12,14

opposed 368:17

opposite 321:24

optical 334:23
335:18 336:10
337:20 340:18

option 382:7
385:19

options 249:3
378:9 385:2,6,9,14

oral 300:10,13
446:16

order 251:13
260:11 261:8
265:13 327:24
347:18 350:8
366:13,25 377:7
424:25 426:5
463:11 466:13

orders 387:5

organ 285:19

organism 285:19
285:23

organization
265:12 266:23
276:6 303:21
309:13 431:7
463:4,17 466:4
478:1,6 484:12

organizations
267:5 479:16

organized 320:18

originated 258:8

orlet 246:20

outcome 293:12
330:14 466:17
494:17
outcomes 272:22
outline 258:24
outside 312:18
315:18 327:21
364:9 410:21
466:8 471:16,18
472:18 474:19
475:3 481:9,14,17
481:23 488:22
overall 253:17
264:24 408:16
448:1,20 454:25
459:1 465:12
471:13 489:4
override 313:7
oversight 468:23
468:24 478:16
owing 299:2 390:6
owns 485:3
oxydative 255:8

p

p 246:1,1
p.m. 493:21
pa 248:10
pacific 469:19
470:13 484:18
pack 421:19
page 247:3 248:3
299:17,24 305:21
306:8 307:9,18
317:10 318:12
319:12 328:10
329:21,22 337:24
338:19 340:2,4
349:16 352:13,13
352:14,17 354:1,7
361:12 372:14,14
372:16 378:8,11
383:21 390:2
393:15 402:2,19
409:4 414:25
416:12 424:10
425:6 428:21
434:6 445:8,10,12
445:13,16,19
451:3 453:15,18
494:5,6 496:4,7,10
496:13,16,19
pages 297:2
414:21 494:5
paid 293:10
442:13 443:7,21
pan 303:13 305:13
panel 444:15
446:19 455:7
paper 278:21
380:9 388:11,15
389:1
papers 384:21
405:19 441:10
468:18
paracetamol
421:19,20,23
paragraph 371:9
374:16 395:2
396:21 411:18
425:10 428:21
433:6
paragraphs 354:8
paralegal 246:23
parallelling 450:4
parameter 264:18
parameters
340:14 446:13
paraquat 248:9,12
248:14,17 249:11
249:13,18,21,24
253:11,14,19,25
254:13,20 255:2,7
255:16 259:8,22
259:23 260:9,16
260:20,25 261:13
262:22 263:10,16
263:19 264:11
265:17,24 266:1
267:13,14 268:15
268:24 270:14,17
270:20,22 271:5
272:4,18,21 277:1
277:11 278:1,21
279:15,19,25
280:11,20 284:12
284:13 287:23
290:4 295:2,7,15
295:21 297:9
298:9,22 299:2,9
299:18 300:10,13
302:2,22 303:8
306:16 307:10,15
307:23 308:22,24
309:19 311:23
312:4,16,23
315:17,22 316:10
316:18,24 318:18
318:25 319:21
320:1,6 323:17,21
324:14,15,20
325:12,14 326:19
327:20,22 328:4,7
328:11,16,21,25
329:5,7,11,16
330:2,7,11 331:8,9
331:13,22 333:16
333:24 334:4,9
336:9 339:23
343:7,21 347:15
347:21,24 349:21
350:10 351:8,11
351:21 353:9
359:25 360:1,10
361:5,15,23,25
362:13 365:23
369:19 370:7,18
372:4 373:6,15,23
374:3,5,9,11,24
375:12,13,15
378:16,21 379:21
381:3,9,14 382:7,8
382:17 384:9,17
385:2,9,13,14
388:6,24 389:12
389:19 391:6,15
391:16 392:8,11
393:3,10,18,22
394:2,6 395:6,14
395:18 396:2
397:1 400:12
401:20 402:23
403:12,20,24
405:1 406:23
407:7,25 408:15
408:15,22 409:12
409:23 410:12,16
410:24 411:20,25
412:7,13 413:9
415:15 416:9,19
417:15 418:8,10
418:12,13,18,19
419:2,11,12,16,22
420:1,23 421:1,3
422:3 423:18,19
425:13,21 428:17
429:2,3 431:5
432:6,14,19,24
433:4,20 439:5
440:13 441:21
444:12,16,21
446:2,13,21
450:24 451:20,24
452:3 453:7 455:9
456:13,19 457:4

459:2 460:21 464:1,10,18,21,23 464:25 465:9,11 465:20,25 467:5 468:4,9,11,23,25 471:6,14 472:21 473:19 474:7,8 476:16,16,21,22 477:11,17,20,25 478:4,7,9,10 481:19,21 483:13 483:14 484:19 485:10,15,19 487:5,17,24 488:4 488:16 489:8,12 489:16,25 490:7 490:13,18,24 491:3,9,10,16 492:7 493:3

paraquat's 375:7 427:18 432:3

paraquat.com 416:14,15 428:16

pardon 392:20

park 331:10,20 360:4

parkinson's 248:10,12,14 249:1,13,18,21 251:19,20 252:1,3 252:8,12,19,23,24 253:12,20 255:21 256:7 258:5 259:4 259:8 261:14 262:8,14 263:10 264:5,10 269:9,11 269:19,22,23 270:1,5,13,17,22 271:7,21 273:11 273:11 274:2,6,17 274:22 275:3,14 277:18 293:19 297:9 298:10 302:3,9 303:9 307:11 323:17,22 324:15 328:5,7,11 328:16 329:5,24 350:18 355:6 370:25 372:11 381:21 385:12 410:1,12,16 412:7 417:25 418:13,18 418:22 419:12,16 420:10,15,24 421:11,25 422:3 423:18 445:9,21 446:2 451:12,14 451:19 452:3 464:18 471:15 474:8

parkinsonian 319:22

parkinsonism 249:25 444:21 446:7 451:14,20 451:24 453:7

pars 349:24 361:7 427:6 428:17 429:1 434:12

part 262:10 264:3 270:22 282:13 289:5 298:21 331:22 337:24 338:23 346:22 347:1,24 350:3 360:10 361:21 381:21 384:8 389:2,15 401:13 421:24 426:6 429:25 435:15 443:6 450:10 452:10 461:12,13 463:9 471:2 473:17,22 476:15 476:20 477:2,7 480:2 481:23 484:2 493:19

participated 489:15

particular 255:12 258:4 264:2 301:15 309:6,10 316:25 344:8,24 411:14 415:2 438:18 473:21 476:5

particularly 252:22 253:18 277:5 438:18 465:25 474:1,24

parties 422:15 494:14,16

partition 306:25

parts 294:4,18 436:11 469:16,17 474:2

party 263:8,13 417:12 429:9

pass 258:7 287:10 287:15 290:2

passage 394:18

passed 258:9 273:19

patent 248:5,7 257:7 258:1,2,4,10 258:19

path 358:19

pathological 252:13 264:4 331:11 377:12,16 384:15 436:22

pathologist 440:11

pathologists 389:4 389:6 436:20 439:13 442:8,8

pathology 259:4 262:10 264:4 277:18 381:21

patients 381:22

pay 442:12

paying 443:6

pd 446:7

pecuniary 442:22

peer 295:19 317:11,14,22 344:10 353:18 363:4 407:4 439:3 443:5,13

pennsylvania 246:14

people 252:13,21 252:23 253:3 256:10 266:4,25 267:12 268:2 269:23 272:4,23 274:2,16 277:20 289:25 293:10,13 300:16 303:1,15 303:24 308:25 310:23 312:1 320:19 326:6 335:23 344:15 345:18 366:16 374:13 399:19 405:7 410:21 411:6,8,9 413:16 413:19 416:4,6 417:4,19 421:3 424:10 436:3,14 438:10 440:25 442:12,21,22,25 442:25 443:14 447:10 449:4

473:20,23,23,24 473:24,25 477:15 477:15,17,20,23 478:3 481:9,10,14 481:22 482:12 483:7 488:18,20
perceive 304:12
perceived 312:5 312:17 315:18
percent 351:12,13 352:4,7,17,18
percentage 274:16
perfectly 276:9 473:5
perform 264:20
performed 268:23 268:24 333:21
period 267:19 285:20,21 358:8 413:4 467:21,21 481:24,24
peripheral 294:15
peritoneal 277:11 278:1 390:15,16 446:14
peritoneally 349:25
permanent 391:18 394:23
permission 485:25
person 257:14 266:4 282:16 284:20 297:25 302:12,13 411:4,4 417:2 461:9 479:10
personal 365:2 456:25 457:3 470:5
personally 268:11 285:10 288:24 364:18,20,23 367:8,12
personnel 289:12
perspective 441:24
pervasive 293:19
pesticide 281:23 282:14 284:8 286:18 429:16 434:19 444:15
pesticides 274:10 303:19,22 304:1,1 306:3,17
phase 332:15
phased 450:24
phil 424:12
philip 245:15 246:24 247:4 251:1,5,8 359:19 422:23 494:4 495:5 496:2,24 497:2,4,12
philosophy 288:5 289:22
physical 294:13 299:3
physiological 278:8
picture 399:14
pieces 380:9
pigmented 382:6 412:12
pilt 267:15,16 465:18,18 466:1 481:17
place 280:17 479:2
plaintiff 246:3
plaintiff's 330:23 347:8 359:23 378:4 406:3 444:1
plaintiffs 245:6 420:12
plan 309:25
plausibility 253:14
plausible 253:16 255:1,13 324:9,10
play 252:11 435:21
plaza 246:4,19
please 256:16 257:2 301:10 317:21 318:8 323:16 328:3 329:2 340:1,6,11 354:5,6 370:14,19 384:6 402:7 406:9 409:2 411:13 412:2 415:9,19 422:20 426:8 430:5,8 444:3 452:19 459:25 461:12 487:12
pm 493:19
point 253:22 257:19 262:5 268:8 276:16 286:22 288:22 293:2 295:5 308:8 310:18,23 311:25 321:14 327:25 333:9 336:9 337:15,16 338:7,7 339:19,19 345:1 369:7,11 370:5 371:8 375:2 382:5 385:21,25 386:15 399:1 405:8 407:11 413:20,25 414:7,12 430:22 440:16 441:9 447:19 448:4 454:25 466:19 470:3 493:15
points 357:5 369:11 393:13 460:15
poisoning 256:3
polar 299:4
portion 255:3 334:11 427:19
portions 309:10
portray 305:17
pose 421:4
position 253:10,13 253:24 254:16,24 265:8 273:8 276:25 278:16 288:21 289:5 303:16 309:18 311:2,3 324:20 326:13 388:12 389:22 427:15 428:3,6,18 431:6 432:2,6 451:25 452:4 453:10,11 470:1 484:6
positioned 386:23
positive 312:6 351:10 401:5 406:22 407:19 436:21,25
possibility 330:5 339:5 357:5 361:25 387:23 400:16 423:8 425:19 432:24 447:4 487:20
possible 264:24 265:16 292:10 303:23 329:19 330:14 366:19

410:1 439:13 458:23 482:16 492:1
possibly 374:13 442:2 482:4
post 390:18 397:10
potential 255:10 255:11 260:23 261:8 269:8 279:4 280:10 292:13 369:21 384:24 385:13 390:3 392:23 393:17 413:10 419:22 427:18 430:12 432:4 451:13 473:7 475:5 482:18,25 483:5 485:11 488:4,7,10 489:25
potentially 261:14 275:22 276:4 278:25 296:1 338:21 380:22 382:20 426:1 434:1 462:21 463:3 464:6 466:6 466:11,22 467:24 469:8 480:14 481:5 482:1,11,14 482:22 483:3
powerpoint 248:11,14 249:23 297:20 318:19,20 318:21 319:14 328:4 444:7 445:17
powerpoints 472:10,11,14
pq 249:3,15,16 310:20,21 311:16 311:22 338:13 339:22 340:8 378:9 380:14,18 381:4 383:23 390:6 445:9,21 451:11
practice 261:17 320:13 345:16 424:3,23 461:1 462:6
pre 377:14
precautionary 424:20
preceded 308:22
preceding 352:12 352:13,16 419:13
precious 292:5
precise 465:16
precisely 252:17 334:12
predecessors 463:4
predisposition 271:3,17 274:3
preliminary 293:7
prep 438:3
preparation 336:23,25 337:4 379:21 435:23
prepared 313:14 367:20 424:17,24 425:3 435:18
presence 274:8,10 328:19
present 246:23 326:7 340:14 350:12 362:12 371:2 397:11 407:23 414:17 446:24
presentation 248:9,11,14,17 249:10,12,23 297:8,12,20,20 298:8,22 299:1,10 300:15,18 301:12 301:14,16 303:7 315:14 318:16,19 318:19,21 319:7 319:15 322:11 325:20 328:4,6 329:21 343:2 344:15,17 409:5 410:6,7,15 411:2,3 415:25 444:7,14 446:25 447:18 486:19,24 487:13
presentations 326:6 331:23 456:18 457:8,13 458:6 471:23 472:1,4
presented 249:25 298:9,21 371:5 445:25 448:23
presenter 343:14 343:15
presenters 297:19 297:22
presenting 448:1 448:19
pressures 303:8 307:10
presumably 300:16 436:13
pretty 475:13
prevent 291:24
previous 289:11 323:4 350:4 355:9 355:14 356:21 362:8,10 363:17 394:1 395:4 401:19 402:22 418:19 430:11,14 446:21
previously 254:12 285:16 347:14 350:15
prf 288:23 289:10 289:24 290:6,17 290:18,23 296:11 382:16,19,25 383:4 399:7,13,19 405:3,4,5 463:6,21 463:23 466:9,11 466:17,19 467:11 467:13,15,22,23 478:13,15,19 479:6,11,12,13 480:9,10,12,15,17 480:21 481:15 489:17 491:4
prfs 383:17
primarily 475:4
primary 284:13
principal 332:4 343:11 346:11 360:6
principles 424:22 441:24
printed 248:11,14 249:23 345:12 415:12
prior 285:15 379:11 399:5 408:12 453:1 458:3
private 472:19
privileged 422:17
prize 335:8,13,14 335:20,21 341:6

367:1
probably 270:2 324:10 351:3 369:8 384:5 392:20 439:18 447:21 492:23
problem 437:22
problems 293:14
procedures 255:25 344:9
proceed 288:2,12
process 256:21 266:13 289:24 292:20,22 306:2,4 306:20 320:25 339:14 359:1 374:23 375:11 401:13 404:19,21 459:12 467:22,23 479:2,8 480:12 481:2
processes 270:9
prodromal 259:5
produce 339:3 418:22 446:5
produced 291:2 297:5 302:1 338:8 431:1
produces 294:13
producing 259:7 447:10
product 249:17,20 254:20,20 259:19 260:4,6,19,19,21 261:9 262:1 265:9 283:21 286:19,20 298:2,5 309:13 323:23,25 330:7 372:3,4 375:21 417:19,20 421:10 423:6,21 424:1,25 426:24 427:5,16 427:21,21,23 428:2,6 431:7 432:3 434:6 443:8 448:13 460:21 463:16,20,21 466:3,12 469:5,7 475:5 478:25 482:14,23 483:2,7 490:6,12
production 387:20
products 259:22 282:2 292:11 308:20,25 309:2,6 309:10 324:13,14 469:1 482:21
professionalism 367:2
professionals 428:11
professor 376:9
profits 324:1
proforma 405:20
program 268:17 312:21 313:1 331:23 347:25 360:11 404:11 430:19 431:24 457:5 465:25 474:10 488:8
progress 326:25 474:14 475:2
progression 474:7
progressive 293:19
project 268:20
prominent 374:15
promise 366:8
promote 303:22 328:20
prone 270:10
pronounce 352:24 384:3
pronounced 353:1 442:5
pronunciation 353:3
proper 461:1
properly 293:4 376:12
properties 253:14 299:4
property 491:15
proportion 251:24 449:5
proposal 262:13 367:8
propose 294:7 400:15
proposed 399:12
proposing 265:15
prosecution 282:5
protected 422:17
protection 245:8 275:24 277:6 281:24 296:13 357:12 363:11 397:18 411:10 429:14 434:17 470:11 495:4 496:1 497:1
protective 251:13 252:16
protein 252:5 381:19
proteins 264:8
protocol 436:14
protocols 436:15
prove 286:16 305:25 375:12
proven 255:13 338:10
provide 385:15 486:1
provided 416:16 455:4
provides 282:22
prs 466:10
prudent 404:7 425:20 433:2,18
public 291:9,24 293:17 310:2 346:24 347:1 362:20 363:7 374:4 413:21,23 414:6,7 416:17,24 429:20 434:22 435:24 474:16 483:7 490:8,14 491:8 492:6 493:2 497:19
public's 459:10
publication 325:3 325:24 344:10 370:10,15 389:2 389:15 474:14
publications 248:13 295:18 302:2 308:20 309:1 325:8 352:6 352:18 353:20 440:25
publicly 278:11 308:14 346:2,20
publish 318:1 356:18 363:3 397:7,10 429:19
published 268:6 278:11 309:2 316:17 317:5 318:5 320:7

325:17 341:15,21 342:7,13,15 344:6 344:12,14 353:9 353:12 370:1,6 373:24 384:21 388:11 395:23 404:2 433:7 439:3 450:5,8 457:12,17 474:12 487:5
publishing 407:3
purpose 294:24 326:12 349:16,19 350:3,4 360:24 372:10 393:8,14 437:6
purposes 396:17 401:15 425:5 426:2 431:2 434:2 437:1
pushed 458:22
put 267:21 288:7 290:16 310:3 366:15 367:8 369:3 375:18 376:1 414:5 415:22 428:4 436:1,7 447:24 454:14,22 469:4 472:25 474:16
putting 339:9 408:18 430:16

q

qualification 419:20
qualifications 285:25
qualified 284:23
qualifier 293:1
qualify 393:10 419:18 432:5 454:15 491:25
qualifying 393:25
qualitatively 426:1 434:1
quality 293:3,6 320:16
quantitative 335:5
quantitatively 253:9
quantum 254:8
question 264:10 277:3 278:5 287:13 289:11 290:8 297:13 301:10 307:3 311:9,14,17,18 313:24 314:5,6,7,8 314:9,9,12,13,23 315:3 317:20 320:12 321:5 323:13,15 326:3 327:7 334:19 341:23 345:22 349:13 368:21 369:5 373:10,12 373:12 376:20 380:24 383:11 387:9,16 389:8,10 396:9 402:5 417:18,18 418:7,9 439:20 440:4,5 445:9,21 451:9,17 452:23 457:7,14 459:4,6 484:20 487:12 491:20
questioning 422:12,16 456:23 493:13
questions 251:9 257:5 294:9,25 296:10 313:10,15 315:6 324:22 368:14 409:4 417:5,16 445:2,6 445:25 451:4,10 452:20 453:16 470:5 486:5
quicker 260:12
quit 259:7
quite 267:18 280:13 290:11 310:7 316:7 322:7 389:22 436:1 481:24
quoted 286:14
quotes 347:7
quoting 281:25 303:8 307:10,22

r

r 245:5 246:1 496:3,3
r&d 266:5 268:22
radio 299:18
ragan 246:16 495:1
ragan.naresh 246:16 495:2
raised 324:22
raising 286:18
range 296:23 378:5 406:13
ranged 271:10
ranking 265:11
rat 385:18,19 388:18,21 413:5
ratio 275:2,3,7,13 275:21
ratios 275:9,12
rats 384:10,17,23
raw 461:1
reach 254:9 418:21 428:17 449:21
reached 355:20 439:3
reaching 322:13
reaction 448:15
read 251:11 257:3 274:1,24 287:1,22 290:13 304:16 317:20 322:17 327:1 331:5 336:23,25 337:2,9 337:10,25 338:17 340:6 345:22 348:5 354:5,10 370:22 373:3,7 379:3,5 402:5 415:15 425:10,24 426:19 428:22 432:10 433:6 441:2 451:8,21 459:25 460:2,4 495:9 497:5
readily 260:11 299:5,13
reading 288:19 314:14 329:12 340:10 401:24 418:23,24 435:20 466:15
readings 442:15
reads 425:23 426:8 433:24
ready 251:14 406:6
real 276:9 277:1 296:1 386:24 423:9,12,13 424:21 425:20 433:3,19 441:25 442:5 479:20 494:3

reality 447:15
realized 323:24 324:14
really 269:16 270:7 304:5,5 366:17 388:4 389:9 420:6 426:14 427:23 442:5
realm 474:22
reason 277:15 335:16 339:1 357:7,10 377:5 383:3 398:24 404:7,9 440:20 474:24 475:15 490:23 495:11 496:6,9,12,15,18 496:21
reasonable 339:5 400:14 447:13 482:4
reasonably 286:15
reasoning 383:5
reasons 277:15 341:5 373:5,14 400:17 433:15
recall 263:1,2,12 264:21 310:13 411:3 475:18
receipt 495:18
receive 284:21
received 343:20 376:4 474:19
recognize 287:5 335:22 430:18
recognized 336:5 367:1
recognizes 367:2
recommendation 265:21 296:12 401:11 405:23 480:18 481:4 489:22
recommendations 265:20 289:17 405:17 463:19 466:16 489:18
recommended 347:20 399:19 404:7,9 459:19
record 251:6,11 256:24 263:23 266:19 277:10 296:2,4,7,11 301:8 313:1 322:18 337:9 338:18 340:6 359:13,15 359:17 368:3,19 368:20 370:14,22 377:21,24 378:18 393:14 397:25 399:8,13,17,23 413:17 414:2 415:3,21,22 422:6 422:9,11,18,19,21 425:10 430:8 451:8 462:14,17 480:3 493:10,19 494:9
recorded 494:7
recover 394:17
red 483:4
redirect 292:5 369:4,11 493:11 493:12,14
redox 255:8
reduced 352:17 387:7
reducing 259:22
reduction 302:24 334:10,13 338:11 351:8,12,13 352:4 352:7,19 362:15 362:19 428:25
reductions 300:12
refer 297:16 342:8 427:22 442:21
referable 275:22 276:4 278:25 279:4 382:21 462:21 463:3 466:11,22,24 467:24 481:5 482:1,11
reference 303:12 342:23 352:12 378:12 409:11 426:3,4,10,12,20 426:21,23 427:1,5 427:7,8,11 430:12 434:3 445:12 455:21 456:12 476:7
referenced 278:21 298:22 302:23 321:13 326:18 401:4 429:11 495:6
references 297:1 302:6 316:14 352:21 362:22 416:21 429:10 446:15
referred 267:15 281:10,14 316:23 368:16 370:16 429:6 433:5
referring 265:25 308:22 342:19 345:7 368:3,17 389:21 423:14,15 441:7 455:18 476:6 480:19
refers 279:4 299:18 328:24 329:24 340:21 352:10 353:21 411:24
refined 354:22
reflect 431:15
refresh 415:5
refute 308:15 310:1 322:19,24 323:9
regard 286:16 459:21
regarding 291:22 325:13 372:11 375:7 378:16 456:19 478:7
regardless 262:6
regimen 429:3
regimens 309:20
region 251:21,23 255:12 335:3 406:12 409:25 420:2 429:2
regions 371:15 467:14 470:12 474:5
registering 306:3
registrant 282:5,9 284:9,13,21,22 286:13,15
registrants 281:23 284:6
registration 286:19,20 305:10 485:25 488:20
registrations 284:8
regularly 424:17

regulated 285:4
regulation 283:22 286:12 466:14 490:7,13
regulations 284:5 284:24 285:12,13 404:3
regulator 444:15
regulators 488:23 489:1
regulatory 266:5 279:10,12 280:11 280:19,21 324:23 364:5,8,14 365:4,6 365:18 397:17 405:14 429:17 434:20 451:4 456:12 459:9 462:3,5,10 467:25 478:7,16,23 480:14 481:6 486:14 487:23 488:3,14 489:8,12 490:1,8
reinforce 375:2
reiterate 306:19
rejected 290:5,11
relate 381:3 465:5
related 252:1 425:21 433:4,20 465:8 479:20
relating 282:13
relationship 249:24 270:21 442:23 444:20 446:1 451:23 452:2 453:6 471:11
relative 285:16 494:13,15
relatively 337:2 412:14 436:3
relevance 385:12 386:1,6 387:25 413:11 415:1 458:15
relevant 262:10 277:1 284:6,18 285:3 286:5 287:21 385:18 387:2 414:22 426:2 431:25 434:2
reliability 408:12
reliable 418:17
reliance 337:1
rely 441:11
remains 425:19 432:24
remarkable 274:25
remember 255:4 263:3,4 276:10 303:13 310:15 356:20 399:6 414:17 419:7 431:11 449:15 460:20 462:21 463:16 465:13,18 476:1 478:18 484:14,16
remembering 463:5
remind 342:15
repair 270:9
repeat 284:1 287:13 316:17,22 317:4 322:4 331:5 355:23 373:10 396:1,9 413:1 439:21 440:6 458:25 487:12 491:20
repeatability 325:18
repeatable 277:21 309:17 310:5 320:10,11 321:4 321:19,25
repeated 261:12 295:25 356:1 375:23 420:25
repeating 320:22
replicability 389:23
replicable 253:23 320:17 327:24 330:10 362:4 398:22 414:9,10
replicate 273:9 276:9,17 334:1 339:23 340:8 347:21 353:13 389:3 396:9,12 413:9 432:18 457:16,18 458:7
replicated 351:24 353:15 373:23 388:12 404:25 412:19 455:8 457:10 458:3
replicates 362:5
replicating 411:19
replication 320:14 374:6
report 248:15,21 248:23 249:5,8 267:10 279:11 281:2,23 284:6 288:1,3,11,13 289:3,21 290:4 296:17 331:3,5,14 332:7,21 333:10 338:25 340:21 344:22 345:8,10 346:17,19 347:11 348:2,12,24 349:8 349:11 358:8,13 363:19,23,25 364:2 373:3 382:23 390:25 392:16 397:21,23 398:1 399:3,4,20 400:9 403:16,17 403:20,23 404:23 405:23 429:5 441:13 443:8 481:6 489:7,11,16 489:25 490:9
reportable 285:14 286:5,13 358:10
reported 268:11 276:2 280:11 285:5 289:17 315:20 331:9 336:9 338:13 340:15 346:7,10 348:12 351:17,20 352:4 356:24 360:1,19 362:20 363:14,15,20 365:9,21 370:11 380:13 383:23 384:16 389:11,14 392:15 395:23 398:12,13,14,25 398:25 399:25 400:2,13 401:1 403:3,4 404:1 405:18 413:10 432:18,25 433:2 433:19 434:11 436:19 454:6

478:23,25 487:23 488:3
reporter 245:18 251:7 317:22 345:23 384:5 487:13 494:1,3
reporting 279:8 280:14 281:9 303:5 338:25 339:7 459:21 468:6
reports 267:10 282:10 332:12 337:20 348:15 349:1 350:13 353:23 354:17 356:13 360:20,24 361:5,13 362:11 362:19 399:5 406:10,21 412:11 442:16 460:7 461:20,24 462:7 468:6 472:6,8,9,19
represent 297:4 343:13 457:15 475:4
representation 282:25
representative 367:20
reproduce 317:6 322:12 323:14 396:18 454:6
reproducibility 333:15 350:9
reproducible 295:13 308:14 322:19,23 323:3 386:24 453:20,24 459:2 475:7
request 486:6
requested 284:22
require 254:8 266:10 279:8 284:5 285:12 404:4
required 280:11 282:10 287:21 340:10,13 458:13 463:11 482:16 483:5 490:17 497:13
requirement 280:16 281:10,11
requirements 280:14 288:19
requires 281:22
rereviewing 486:18
research 248:12 248:15,21,23 249:5,8 254:13 256:22 264:24 265:16,22 266:2 268:20 270:12 274:13 277:19 292:19,22,23 298:15 302:1 308:3 312:21 313:1 316:13 317:4,5 319:21 320:1 323:18 325:12 327:20 328:15,25 331:3 331:22 345:18 347:11,24 350:19 360:11 373:4,13 376:3 383:13 406:16 410:16 417:6 430:19 431:24 454:1 456:20 457:5,22 458:7 461:24 465:25 469:7,8 474:16 479:15 487:8 488:8
researcher 340:24
researchers 263:22 295:18 309:14 316:23 325:13,16 339:10 341:15,21 353:8 362:23 376:15,24 377:3 388:6 395:23 396:2,13 396:15,19 398:4 413:22 427:10 438:23 439:2 450:5 454:19 488:15
reservation 344:23
reservations 345:14,20,23 346:9,10,17
reserve 369:10
reserving 422:15
resource 416:16
respect 260:25 263:10 278:16 354:2 427:18 432:3 478:15
responds 451:15
response 324:21 432:23 446:4 451:7,8,15
responses 450:16
responsibilities 372:5 476:20
responsibility 279:9 287:2 288:25 309:6 374:20 375:6 470:23 471:13
responsible 288:2 288:12 289:23 405:6 423:7 425:1 439:10 459:9 465:12 470:19
rest 279:1 472:10 473:14
restate 413:15
rested 393:12
restricted 429:22 434:24
result 350:17 351:8,11 356:6 361:9 362:5 366:22 389:11 407:12 412:14 435:2 438:16 469:2 475:8
resulted 268:5 334:9 361:5
resulting 451:20
results 251:25 292:10 320:20,22 321:9,17 322:12 322:13 323:14 342:7,13 346:13 351:2 352:16 353:23 355:19 356:2,18 357:3,9 361:4,14,23 362:14 363:3,6 365:18,21 366:14 373:20 378:16,21 379:13 380:21 384:22 388:5 389:18 391:9 395:4 396:1 397:7 401:1,5,17,18 402:10,21 406:25

407:17,18 408:5 428:12 435:14 436:5,9,16 439:4,6 439:10,15 441:14 443:1 450:3,4,14 451:11 453:20,23 454:6,19 458:4 464:4 489:11
resume 251:14
retained 284:21 285:3 475:4
retired 372:9
return 495:13,17
reverse 395:1
reversibility 392:9 392:23 393:17
reversible 394:25
review 317:11,14 317:23 379:11 431:21 495:7
reviewed 295:19 344:10 353:18 363:4 407:4 439:3 443:5,13
reviewer 332:7 348:13 360:13
reward 335:23
rfiorillo 246:8
right 255:18 257:7 257:10,17 267:16 269:2 270:14,17 270:24,25 271:12 271:14 272:2,3,16 272:17 273:20,24 274:5 275:14 276:12 278:11 279:11 281:11 282:8 283:10,18 283:22 284:14 285:25 286:20 289:7,20 290:15 293:16 295:12 296:15 297:15,22 298:23 299:16,22 300:3,10,23 301:5 301:17,22 302:4 302:14 303:24 304:3,6,13,25 305:4,14 306:11 306:12 307:2,12 307:23 308:7,11 308:17 309:23 310:2,16,22,24,25 312:2,11,15,20 314:14,24 315:12 315:20 316:5,19 317:2,19 319:1,4 320:13,24 321:10 322:7,14,15 323:6 323:16 324:16 325:22 326:1,8,13 327:12,19 328:8,9 329:9 331:15,20 331:25 332:10,20 332:24 333:19 335:9,15,18 336:6 336:11,17 337:4 339:4,7,17 340:16 341:12,19 344:2,7 344:21 345:12,12 345:13 347:3,16 347:17 350:25 351:1 352:8 353:3 353:6 355:4,8 356:5,11 357:17 357:25 360:4,11 360:22 362:3,11 362:23 364:20 367:4,19 368:10 369:10 371:19,22 372:20 373:22 375:1,4,9 376:15 379:9,23 381:10 382:11 383:20 388:21 389:16 391:6,14 392:12 392:14,18 393:1 394:20,24 395:8 398:14 399:12 400:4 402:10,12 403:1,2,7,8 407:9 407:17 408:5,10 408:16,21 409:8 409:18,19 410:2 410:17 411:16 412:5,8 413:12,14 413:24 414:10,12 415:18,23 416:7 416:12 417:12 418:2,4 419:4,21 427:3 429:7 430:21,25 431:9 431:21,22 436:8 436:11 439:8 441:23,23 443:23 444:17 445:6,20 446:2,7 447:23 448:2 449:1,8 450:23 454:3,22 458:20 460:2,11 461:9,21 462:8,13 464:11 465:6,24 466:3 467:8,10 468:18 471:20 472:3 473:18,18 477:3,5 479:22 480:15 481:13,16 481:20 484:5,7 487:19 491:18
rights 248:7 258:20 422:15
rim 469:19 484:18
rise 274:17
risk 252:19 253:4 269:5,8,11,25 270:2 282:1 374:22,24 375:13 375:15,20 386:17 387:11 388:1,2 389:19 421:4 423:8 424:5,23 425:2 426:6 485:19
risks 284:7,19 285:4 490:24
river 295:6,12,16 295:22 350:1
robust 324:20 453:23
rodent 412:25 413:10
role 252:7,11,13 262:13,17 263:9 265:4 328:16 371:24 375:18 460:20
roles 265:9 481:11
ros 461:9,16,17,18 461:23
rosemarie 246:8
rough 315:1 484:22
round 294:9 356:2
route 259:1 277:4 277:21 278:7,16 278:22 285:22 385:24 425:14 432:15
routes 261:19
row 396:12
rule 254:22 286:24 345:18

rules 287:11,16,22
rumblings 418:2
run 320:18
rutgers 302:7

s

s 246:1 247:1,1 331:17 496:3
sacrifice 391:15
sacrificed 393:13 394:3
safe 261:1 305:25 327:22 418:8
safety 249:17,20 260:6 265:9 291:24 298:2,5 309:13 325:14 328:17 330:10 416:19 418:10 423:6,11,22 424:1 424:25 426:6,24 427:5,16,21,22,23 428:2,6 431:7 432:3,9 434:7 463:17,20,21 466:3,12 478:7
sake 296:11
sale 253:25 254:20 324:1 475:5 488:19 490:6,12
sales 330:8 421:12 469:5 470:6
samples 391:6
sampling 337:15 337:16 338:7,7 339:19,19
samson 461:12,13 461:14
san 246:10 248:19 343:3
sat 265:25
save 260:21
saw 359:4 363:19 363:19,21,22,23 363:23 386:14 460:9,25 487:7
saying 253:1 289:14,16 303:3 304:24 312:18,19 312:25 315:11 322:3,11 339:11 369:13 380:4,8 388:4 397:13 421:2,17 435:13 438:6,8 439:11 442:8,10,17 473:8 475:21 478:17 491:25
says 283:13 298:14 299:7,8 300:14 301:24 303:19 306:1,23 306:23 307:2,4,9 308:18 309:24 310:19,22 312:3,9 312:10,13,14 314:22,25 316:16 319:18 321:3,7,23 321:24 322:1 323:8,20 324:24 324:25 325:2,19 325:22 326:4 327:1,2,11,12 328:10,14,18,22 328:23 329:3,4,6 331:17 334:12 337:8,18,24 340:17 343:20,25 344:4 350:7,16 362:18 371:7,9 374:17 378:8 379:2,4 380:11 381:1 382:5,15,24 383:22 385:5 386:15 387:9,15 389:1 390:1,11 391:1 395:3 396:23 397:6 401:18,23 407:22 411:14,18 412:10 412:18,21,23 413:7 416:13 419:5 425:6 426:20 442:4 445:20 446:12 453:4,8,9,18 460:13 461:11,16 461:18,23
scared 421:20
scenario 260:17
scheme 282:24
schmidt 417:3
schoenberger 246:9
science 270:15,16 290:25 291:8 308:23 309:6 320:14,16 326:24 356:24 431:6 443:15 448:20 464:21,25 465:20 471:6,23 473:20 474:7 475:1,1,16 476:17 477:8,9,9 477:12,18 478:11 493:6
sciences 465:17 466:1
scientific 253:21 280:19 291:17,23 292:4,10,19,22 308:9 319:20 320:13,24,25 324:21 325:3,24 326:5 328:20 329:7,16 335:22 336:2 345:16 347:2 353:16 356:21 366:14,25 374:4,14,21 375:3 375:7,11,20 383:20 395:24 397:11 414:4 418:17 429:9 472:6 475:8 490:9 490:14,17 491:7 492:1,5 493:2
scientifically 324:20 409:22 438:15
scientifics 326:21
scientist 262:1 298:15 335:8 346:25 366:12,21 367:5,9,17 408:6 435:5 447:23 475:6 479:10
scientist's 352:25
scientists 263:11 264:22 265:3,11 265:17 270:20 271:15 291:1,2 300:16 301:13,15 309:5,8,9 325:8 326:7,22 351:25 377:10 380:6 442:20 472:20 473:15 479:16 481:22 488:22 490:16
scope 254:1 255:22 259:10 267:2 269:13 272:10 278:4

279:18 280:1 283:23 291:3 324:3 367:14 421:13 423:25 448:18 450:25 456:22 468:14 470:2,17 475:9 485:4 487:25 488:5 490:19
script 287:1
se 256:8
search 366:13
sec 290:17 469:2 469:10 490:3
second 273:13 308:13 329:3,6 347:15,23 348:7 352:24 355:18 356:2,19 359:14 372:16 374:17 378:11 385:25 390:1 428:21,21 451:17
secrecy 291:22
section 281:10,22 282:4 283:10 285:13 286:14 298:17 360:24 361:4 390:1 401:17 402:11 407:21,22 415:2
sections 282:8 436:7
secure 265:13
see 253:21 261:18 261:18 262:7,8 275:9 277:17,20 279:2 294:8 295:24 297:14 300:3 303:10 304:3 314:22,25 315:1 316:14 317:9 318:22,23 318:24 319:8,12 321:16 325:5 327:1,23 329:2,22 330:25 336:19 337:8 338:2,15 339:15 340:5 341:9,11 343:23 352:11,14 353:24 367:25 370:16 373:21 378:5,13 383:25 387:4,16 387:23 389:3,5 390:1,9,22 397:3 406:19 407:12 413:5 418:14 423:10 424:6,10 425:8 436:23 437:4,19,21 438:19 442:3,5 445:23 452:13 453:16 465:4 478:21 493:8
seeing 263:3,4 310:9 406:25 419:10 470:3,4,6
seek 264:19 266:8 268:9 307:15 317:11,14,22
seeking 307:20,23
seen 256:19,20 262:9 264:9 274:11 310:12 321:17,18,21 330:4 336:21,24 357:2 363:25 378:17 383:11 396:5,6 398:18,18 400:2 405:25 408:14,21 457:11 457:16 474:10
selective 328:21 409:15,23,24
selectively 421:1
sell 259:19,19 279:14 305:5,6 329:11 444:12 448:24 449:1 478:9 485:25 488:18
selling 259:7 283:21 323:25 374:24 448:13 487:16
sells 468:4
send 356:16 405:16,18 460:22 466:16
sends 460:17 461:6 479:11 483:3
senior 265:5,9,23 266:3,3,4,22 298:2 298:4
sense 267:11 294:22,23 346:19 346:20 425:4 468:24
sensitive 338:10 338:12 342:3 380:14 382:7 396:25 403:11
sensitivity 338:8 380:24 383:9,14 383:15
sent 401:5,8,15 405:21,22 431:15 460:23 461:3,8 463:19 480:14 495:14
sentence 338:2,17 338:18 374:17 428:23 433:17 452:17
separate 403:21 466:5,18
separately 415:12
september 248:22 249:19 348:16 392:18 427:16
sequence 348:9,10
series 302:1 349:1 392:7 406:10
serious 292:11 482:16
seriously 482:19 482:23 483:1
served 298:4 332:3,6
serves 399:12
set 339:13 340:14 393:14 414:2 463:9 466:12
seven 394:3
sex 285:22
share 366:8 429:13,16,20 434:16,19 490:14 490:17
shared 277:6 291:2
sharing 290:25 293:2,9
sheet 495:11
sheldon 461:9,16 461:17,18,23
shift 253:22
short 252:3 481:24
shorter 285:20,20
shorthand 275:25 388:2 494:7

show 285:17 447:5 451:19
showed 344:18 370:11 387:19
showing 277:18 314:10 398:23 419:14 436:6 437:14 439:4 450:9
shown 263:19 277:21 295:3 330:2 383:13 419:2,22 488:15
shows 257:9 313:1 343:11 352:16 399:9 413:18
shrinkage 390:6
sick 417:23 420:7
side 288:21 478:10 483:5
sign 251:12 495:12
signature 494:19
signed 494:20 495:20
significance 409:22 458:15 487:7
significant 251:24 275:7 334:13,16 344:2 351:8,12,17 361:6 362:14 383:15 394:8 426:25 441:17 467:21 469:8 470:15
silent 441:3
similar 253:4 265:8 278:11 285:15 336:13,15 351:22 394:15 401:5 467:16 477:14
simply 270:8 310:6 312:22 389:10 436:6
single 389:11,13 447:7 464:9
sir 258:23 261:15 296:24 311:4 312:13 315:5 318:17 319:12 321:23 325:20 330:25 342:20 354:7 357:23 359:23 361:20 378:3 379:6 387:21 392:4 396:21 400:7 406:4 423:1 449:2 453:15 455:19 468:22 490:5 493:9
sit 471:23
site 259:4
sitting 304:20 442:14,14 443:20
situation 301:6 305:16 430:24 473:6
six 272:16,21 273:7,14,18,22
sixteen 358:12 363:15
sixth 426:8,19
slechta 302:6 316:24 330:6 414:14 429:5
slide 308:2 320:5 321:13 330:16 411:14 412:2,7 447:6
slides 303:6 316:23 461:1
slightly 393:10 436:13
slow 374:22
small 312:5,17 315:17 334:9,12 338:20 419:23
smaller 268:2 449:5
smell 259:6
smith 246:24 249:1 264:19 265:7,17 370:24 371:3,21,22 372:11,21,23,24 373:4,13 378:21 379:11,12,19,25 380:3,5,7 390:4,24 391:3,14 406:22 411:7
society 248:18 291:17 292:14 343:2 345:5 356:23
software 337:12 354:14 355:2,10
sold 468:11,25 479:1 484:5,19 487:17
sole 440:20
solutions 495:23
somebody 323:7
somewhat 385:3 424:19
sorry 263:6 316:11 322:6,6 326:19 363:22 370:20 388:23 392:16 402:14 415:11
sort 265:15 275:9 294:7 345:17 391:19 401:14 407:3
sought 265:12
sound 291:4 298:6 308:9 319:20 336:2 374:3
sounds 482:4
source 362:25
south 469:18 470:14
span 273:16
speak 289:18 326:7 369:22 441:23 463:8
speaking 474:4,25
species 286:4,8 412:25 413:10
specific 264:17 266:14 270:13 284:7 288:18 309:4 313:21 315:5 369:22 371:11,14 377:17 383:24 401:16 405:19 418:21 439:9 462:7 474:6
specifically 262:24 280:18 292:14 309:12 318:4 331:4 333:9 334:23 337:5 365:14 370:13 396:4 409:4 423:14
specifics 251:22 439:20
speculate 290:7
speculative 358:25

spell 384:5
spoke 376:9 474:13
spoken 427:10
sponsor 293:10
sporadic 269:18 271:18
spring 326:18,20 327:12
st 245:2,17 246:5 246:19 313:12
stack 468:18
stage 254:9,23 271:24 337:14 355:9 425:20 433:2,18
stain 437:4
stained 435:19
staining 438:5
standard 320:15 323:1,2 424:3,23 491:23
standing 281:19
standpoint 270:6
start 251:10 269:20 271:19 426:16 463:11 464:8,15 493:1
started 260:2 272:18 392:14 438:20,22 465:15 477:12,12
starting 319:2 428:22 432:16 487:6
starts 273:12 296:23 300:3 308:7 338:18 425:15
state 313:7 406:19
stated 346:3 367:15 402:18
statement 278:11 282:21,25 283:6 292:2,15 303:16 320:9 365:24,25 384:20 415:3 420:17 422:2 428:16 447:9 452:5,25 457:24
statements 282:20 357:7 419:6
states 261:3 275:23 276:6 284:16 351:7 363:10 364:9 397:18 400:9 429:14 434:17 456:19 466:19 478:24 480:22
statistically 334:13,15 344:2 351:12,17 361:6 362:14 383:15 394:8
statute 282:21
stayed 394:20
stephen 246:6
steps 254:5
stereology 302:14 334:21,24 336:10 336:19 337:6,12 337:13 340:14,19 340:25 350:11,24 354:13,21 355:1 355:10,15 356:12 377:9,14 435:17 438:18
steve 251:10 281:16 311:9 313:3,22 368:2 391:24 422:6 426:13 452:15
stillery 246:6
stockholm 307:15 307:23
stomach 260:11
stop 310:8 313:3 313:22 421:23 452:15 479:22 480:13
straight 414:2 476:19
straightforward 280:13 414:2
strain 285:22 316:25 347:13 380:24 383:9,13 383:15 406:14 412:12 425:21 433:4,20
strains 380:14,17 381:9 382:7,9,14 382:17
strands 254:12
strategic 267:3
strategy 308:3 325:4,7,7,25 326:17,18,20 327:13,15 328:12 470:19
street 246:4,10
stress 408:18,19
striatal 300:12 333:23 349:22 361:16 393:20 395:7 401:22 402:25
striatum 302:24
strike 264:10 279:24 288:9 307:21 311:6
315:15,25 326:19 334:19 345:21 356:15 363:22 365:20 385:7 387:8 389:9 449:11 459:4 485:2 487:11
strikes 274:25
strong 254:23 265:21 271:3
stronger 400:12
strongly 389:22
structure 261:6,11 294:14 299:3
studied 366:20
studies 253:17,18 253:22 254:13 262:21 263:17,21 264:20 266:6 268:5,6,15,23 270:17 272:17 276:1,2,16 277:14 278:1 285:15,15 285:16 289:1 292:4,21 293:6,18 295:21 298:22 299:18 302:21 303:4,5 312:22 315:21,25 316:1,3 316:8,13,22 318:1 318:4 319:3,4 326:8 334:1 336:8 337:21 342:9 346:5 347:18,19 349:2 352:10,21 353:8 357:3 362:6 362:22 365:21 366:20 368:3,4,5,7 368:17 370:11 375:23 379:13 381:2,3,8 388:5

392:7 394:1 395:5 395:13 396:7,18 399:24 400:13 401:5,14,20 402:23 403:21,24 404:24 405:18,24 406:11 408:12 410:24 411:15,19 411:19,24 412:20 413:1,3 418:19 419:1 420:25 425:11 427:9,9,9 429:6,7,11 432:12 432:17,22 433:5 434:11 435:24 437:22,24 441:2 446:1,4,22 447:3 447:10 448:9,12 449:3,18 450:3,17 451:19 453:23 454:18 455:3,14 456:2,3 458:3,14 458:17 459:13 460:23,24 464:4 465:13 466:7 474:20,21 479:14 482:18 487:18 488:13

study 248:21,21 248:23 249:5,8,9 250:2 262:25 263:1,4,8 273:22 276:14 277:1 291:12 293:10,11 293:11 300:9 331:14,22 332:3,7 332:12,21 333:14 333:19,21 334:18 334:20 336:5,21 336:24 337:2 338:3 339:9,17 340:14,19 342:7,7 342:8,11,14 344:18,20,23 345:3 346:18 347:6,11,15,20,23 348:13,15,24 349:7,16,20 350:8 350:9,12,13,14 351:2,11 352:5 353:15,24 354:13 354:14,17 355:9 355:14 356:3,19 356:24,25 357:4,6 357:13,14,22 359:25 360:8,10 360:13,15,23,24 361:14 362:10,12 363:3,6,12,13 364:4 365:9,17 370:6,13,16 383:1 383:20 385:20 386:11 387:19 388:17,18 389:11 389:13 390:13,16 391:15 392:7,16 392:22 393:16 394:5,11,23 395:17,21 396:1 397:8,16,19 398:3 398:9,10 401:1,4,8 401:12,18,18 402:1,11,14,15,18 406:20,22 407:23 409:9,11 431:25 432:1 433:7 435:2 441:7,11 451:11 455:18,18 459:11 460:7 461:6

study's 347:21

stuff 283:14 375:24 420:7

sturgess 248:6,8 257:15 297:22,23 297:25 298:9,25 299:17 301:24 303:1 306:23 307:2 309:25 310:18 311:21 315:21 320:3 332:6,9 335:11 336:4 348:12 360:13 371:3,5 378:12,15 379:19 380:3,12 385:1,6,8 411:2,7 424:11 431:8 476:8

sturgess's 372:22

sub 426:11,22 427:1

subchapter 282:11

subgroups 464:10

subject 250:2 254:15 258:4 397:19 410:13 438:19 490:6,12 493:6

subjectively 491:17

subjects 367:21

submission 461:25 462:2,3

submit 286:13 480:24

submitted 282:15 285:16 458:17 462:4,9 466:21 480:4,7

submitting 288:8 307:5

subpopulation 396:25 403:11

subscribed 497:14

subsequently 265:18 305:3 370:1 385:17 391:20 441:9

subset 476:16

substance 273:5 351:10 451:13

substantia 251:22 253:15 255:3 258:12 295:7 302:23 309:22 333:17,24 334:11 344:19 349:24 352:8,19 356:13 361:1,7 362:16 371:12,17 377:11 387:19 388:16 393:1,20 395:12 395:13 403:25 406:13 407:20 409:13,17 412:15 419:15,25 421:1 421:24 425:12 427:6,19 428:17 429:1 432:13 434:12 439:5 456:14 457:11 459:3

substantially 408:20

substitute 492:21 492:21

subtle 380:17

suddenly 358:11

sue 306:15

suffering 292:13

sufficient 407:10

sufficiently 419:11

suggest 277:22,23 277:25 278:6

330:4 343:18 371:13 380:16 395:14 409:12 412:11 421:23 450:11
suggested 277:8 278:2 390:3,24 391:3,3,14 400:16 406:16,22 492:10
suggesting 373:16 388:7 449:23 487:5
suggests 269:7 304:22 305:1 307:18 325:10 349:6 372:13 378:18 390:6 409:15 459:1
suing 305:22 306:10,20
suit 306:13,24
suite 246:4,19
summarize 279:2
summary 249:12 298:10 351:4 410:6 412:7 415:25 416:3 432:11
sunnyvale 302:10 335:17 355:7 356:16 366:24
superiors 365:22 365:22 366:3 367:23 369:18 372:22
supplied 417:13
suppliers 380:16
support 249:24 255:24 361:14,23 361:25 362:2 395:4,14,16 401:19 402:22 444:20 477:13
supportive 396:24 403:10
sure 298:6 300:18 341:17 348:22 363:25 364:7 366:17 373:9 377:3 387:22 397:12 401:10 414:4 422:8 443:13 446:23 464:16 479:2
surface 437:3
susceptibility 252:22 380:18
suspect 281:17 321:22
sweden 306:4
swedish 305:22 306:10
swiss 381:16 382:9
switzerland 469:14 483:14
sworn 251:2 497:14
symposium 344:7 344:12 397:11
symptoms 251:25 252:2,14 259:6 319:22 418:22 446:6,9
syng 248:10 249:15,16
syngenta 245:8 246:24 248:8,9,16 249:7 253:21 254:8 255:6,20 257:12,13,21 258:8,15,20 259:24 262:21 263:4 264:15 265:4,11 266:12 266:19,21,22 267:8,10,10 268:4 268:19,20,21,23 270:13 276:3 281:5,23 284:13 285:3,12 287:6,10 287:15,21 288:20 289:8 296:12,13 296:23 297:8 298:2,15,19 299:9 300:15,17 301:13 301:13,14 304:20 308:3,19 309:17 310:21 311:23 312:16,21,22 315:7,13,14,16,20 316:5,8,13 317:10 317:14,22 318:1 320:5 322:22 323:23 326:21 327:21,21 330:6 331:3,4,19,23 333:11 335:9 340:19 342:7,9,13 344:18,22 345:2,2 345:9 346:2,14 347:16,25 356:16 356:18,23 357:11 360:11 363:3,10 364:4 368:6 370:6 370:6 373:23 374:3 375:6 378:5 381:8,24 383:17 384:22 388:4 389:18 395:17,21 396:1 397:7,10,16 400:23 410:10,22 411:9,15 412:19 412:25 413:17 417:9,11,13 418:4 422:14 424:18 428:24 429:13,16 429:19,23 432:2 432:17 433:5 434:16 442:9,23 444:12 446:20 452:4 455:8,12 456:11,18 457:4,9 457:15 462:25 463:4 467:12 468:4,12,20 469:12 470:5,16 470:18,19 471:1,7 471:8 473:15,16 481:3,7,10,11,14 481:17 482:7 485:3,7,16,24 487:23 488:3 489:10,24 490:16 490:23 495:4 496:1 497:1
syngenta's 253:10 253:24 276:25 297:7 324:13 325:12 326:6 329:10 367:20 374:8 410:16 427:16 428:6 446:4 451:25 453:10,11 469:14
synuclein 252:4,5 252:7,11,17 262:14,17,22,24 263:9,12,15,20,24 264:2,7,12 381:4 381:15,17,18,20
system 248:18 288:7 294:2,4,15 294:17,19 331:12 337:12 338:21

339:1,10,11 343:8 344:23 425:19 433:1,10 435:3,11 441:23 461:15
systems 338:22 354:21

t

t 245:22 247:1 248:1 496:3,3
take 254:16 257:3 265:22 273:22 276:18 324:4 354:4,8 359:11 373:9 393:6 400:20 409:2 415:9 418:4 424:4 430:5 436:8,16 448:1,5 462:12 482:18 483:1
taken 254:6 288:23 290:12 296:6 330:10 359:16 377:22 383:6 422:10 450:12 454:20 460:19 462:16 494:6
talk 255:11 273:13 333:7 397:11 406:6 456:15 464:12 471:18,20 476:1 483:12
talked 272:14 299:18 316:9 333:7 399:7 413:3 459:12 465:9 471:6 478:13
talking 264:1 272:4 277:10 286:1 308:24 309:12 310:4 314:2 332:10 338:2 350:15 367:21 371:22 379:22 387:24 391:13 398:5 420:22 430:11 435:17 456:15 457:23 459:13 464:3 466:6 470:7 476:6 484:3 486:17 492:2
targeted 421:1
task 467:16
tasked 465:24
teaching 346:25
team 264:22 265:17,18,24 266:1,22 267:13 267:14 270:15,16 270:20 289:2 308:23 364:23 373:4,13 427:23 427:25 428:2,7 431:6,13 464:21 464:25 465:10,11 465:17,20 466:1 471:2,6,8,8,10,13 471:16 473:15,17 473:20 474:7 476:16,17,22,23 477:1,2,3,4,5,8,9,9 477:12,12,18,21 477:25 478:4,11 481:19,22,23
teams 470:22 471:10 476:18
teased 420:1,4
teaspoon 260:16
technical 249:17 249:20 298:1,2,4 335:25 345:19 423:22 427:15 428:19 433:15,15 435:6 438:22 476:16,22,23 477:12
technique 334:21 335:9 338:10 340:25 341:2,14 341:14,19,20 342:1,2 344:23 346:12,18,25 348:10 350:24 356:1,4 366:22,24 436:3 438:14,15 438:18
techniques 302:18 346:13 347:14 348:4 356:7 377:12,15,16
technology 320:19 336:13,14,15 357:8 376:5,6,7,11 376:14 377:9,10
teenage 273:24
teenager 273:19
teenagers 276:13
teens 274:2
tell 267:12 269:10 269:15 272:7 286:24 318:16 337:9 352:24 356:24 358:1,3 359:24 370:6,13 371:2 396:22 406:6 416:9 447:23 448:17 455:3 456:1 457:21 458:9 473:3,5,19 475:23 488:11
telling 278:3 303:1 389:6 400:1 421:5 440:22 447:10 472:20 475:16 488:10 489:4
tells 416:20
ten 469:11 486:17
tend 270:10 484:21
term 278:6 418:11 419:1 482:6,8
terminate 313:11
terminated 332:15 332:19 348:18,20 348:23 360:17
terminating 254:19
termination 392:17
terms 253:9 257:25 258:2 266:10 270:4,12 273:15,19,24 274:24 275:8 278:13 283:21 284:3 286:19 287:8 290:5 349:8 365:1,2 408:11,12 420:18 424:1 458:20 459:8 469:3 470:1,22 473:7,19 474:7,21 475:4
test 261:12 264:15 265:14 267:22 283:2 285:19,23 334:7 419:13,14 419:14 425:18 433:1,10 435:3,11 436:10,14,15 441:22

tested 276:8 338:8
testified 251:2
testify 367:21,23
testimony 494:4 494:10 495:9,18 497:8
testing 276:7 282:14 466:7 488:21
tests 263:15 268:9 375:17 454:16
textbook 294:7
th 338:11 407:19 436:21,25
thank 274:5 315:12 317:25 318:11 330:21 343:1 349:15 369:16 373:11 402:8 415:14 426:17 445:16 462:12
theories 291:11 391:8
theory 258:23
thereabouts 477:11
thick 436:6
thickness 438:20
thing 267:18 310:24 346:21 348:9 357:24 376:25 381:18 389:8 391:24 400:15 404:7 407:13 439:8 440:9,16,18 458:16,20 488:12
things 270:8 285:18 358:18 373:16 377:7 380:20,23 389:7 407:7 416:21 424:4 438:20 447:20 473:7 474:23 478:8 487:3
think 251:10 252:16 254:23 255:10 262:18 264:6,9 269:4,6,21 271:20 291:4 292:2 293:22 298:7 301:6 302:13 314:8 322:8,14 324:9 335:10,12,15,15 340:21 341:7,11 342:3 351:2 358:2 359:6,9 365:14 366:15 368:18 371:25 373:19 375:3 376:10,23 383:3 385:11 389:24 392:19 393:9 400:14 404:12,14 405:9 412:3 413:17 419:9 420:3,6,9,17 421:11 424:7 426:13,15 428:8 436:4,18 438:17 439:18 440:4,21 440:22 441:18 443:10,12 445:14 445:18 447:13,19 447:25 448:15 449:9,17 454:25 456:5,6,24 465:21 472:16,17 473:14 474:10,23 476:5 479:6 484:20,23 484:24 486:10,16 487:2 488:17,23 488:25 489:1 490:3 491:1 492:11,23
thinking 380:1 443:17 449:19 450:13 474:8
third 263:8,13 325:2 395:17,21 396:1,12 417:12 425:14 429:9 432:15
thiruchelvam 353:1,2,5
thomas 245:5
thought 303:17 335:24 357:23 431:24 437:25 478:5
thoughts 249:3 378:9
threat 329:15 374:8,12
threaten 330:7
threats 329:7,10 375:10
three 261:2 275:2 275:16,16 297:16 302:22 303:6,7 325:19 334:4 348:24 357:21 368:4 393:1,11 400:12 403:21,24 404:24 418:5 429:4
tillery 246:3,6,23 247:5 251:14,17 254:7,18,25 256:15,18 259:12 259:17 261:21,24 262:12,20 267:6 269:17 272:12 278:9,15 279:20 279:23 280:3,8 281:4,20,21 283:3 283:24 286:10,23 287:9,14,18 288:15 291:5,15 291:21 292:3,9,18 293:5,23 295:20 296:2,9,22 301:4 301:11 304:9 305:18 306:22 311:11,15,18,20 313:5,19,24 314:2 314:5,11,14,18,20 314:24 315:4 318:6,14 324:6 326:16 327:8 328:2 330:22 340:3 342:18 344:5 347:5 355:24 358:6,22 359:8,11,22 364:19,24 367:10 367:18 368:5,9,11 368:15,20,25 369:8,13,16,17 370:4 378:2 392:1 392:3 400:6 402:9 406:2 409:1 410:5 414:19 421:8,15 422:8,19,24 426:14,16,18 430:4 440:6,15 443:25 447:17 448:22 449:20 451:2 452:16,21 452:22 453:2 455:2 457:2 459:24 462:12,19

468:15,17,19 470:7,9,21 471:4 472:15,24 473:10 474:18 475:12,20 482:5 483:11 485:6 487:10 488:2,9 489:6 490:21 491:21 492:4,13,20 493:7 493:17
time 251:4 255:18 259:14 260:22 267:19 268:8,11 268:17,17 278:14 295:5 304:13,17 308:19 311:5,8,25 312:15 315:13,13 315:16,19,20,23 316:1,4,8 317:16 321:14 322:22 323:15 327:23 332:19 339:5 344:22 345:10 348:1 354:8 357:23 358:8,10 359:12 360:12 363:13 366:11 369:1,23,24 371:24 372:25 373:2,9 374:18 376:24 377:6 383:11 385:16 386:23 387:1,21 388:25 392:9,23 393:5,6,13,16 399:5 400:2 405:3 405:8,14 406:4 409:21 414:7,11 420:19 428:4 430:22,24 431:5 436:19 442:13 449:17,23 458:9 460:19 461:14 462:25 463:11 465:21 466:4 471:12,12 473:24 479:5 494:3 495:19
timeframe 495:8
times 275:16,18 287:21 290:4 307:20,22 347:2 379:23 459:16 489:2
timescale 395:1
tissue 285:19 294:17 355:13 356:11 390:5 391:6 437:24
tissues 438:21
title 283:7 331:5 343:6 370:22 372:13 379:2 392:8 430:11 444:19 476:15
titled 248:25
titles 250:2
today 251:3,7 279:1 310:13 311:2 367:22 433:13 448:9 451:25 452:5,6 453:10 477:25 487:17 493:16
today's 493:19
told 259:18 268:10 269:3 280:4 313:16,17 367:5 400:17 416:5 418:6 421:9 447:2 448:10 450:7,15 450:20 454:22 462:20 475:19 484:24 489:7,11 489:20
tolerated 432:20 446:16
top 307:9 329:3 352:11,14 378:8 398:8 411:13 415:16 445:8,20 453:16 463:12 477:24
topic 301:20 365:8 444:19,24 462:21 468:16,17
topics 468:15 470:6
total 338:9,23 347:19
totality 399:10 404:11 419:10 420:21
touch 279:3
toxic 304:1 406:15 406:15 407:7
toxicant 271:4 272:5,21
toxicity 249:11 294:4,12 295:24 339:23 340:8 350:11 361:16,19 371:11 380:14 383:23 395:7,10 397:2 401:22 402:25 403:13 406:23,24 407:10 408:1,12,16 409:14 485:14
toxicological 261:17 285:14 287:3 310:6 424:3 441:24
toxicologist 265:5 372:3 460:21
toxicology 265:6 272:25 276:1,1,16 298:17 319:16,19 319:25 323:18 360:3 372:1 386:11
traditional 271:15
training 355:3
transcribed 494:8
transcript 251:12 314:10 494:5,9 495:6,20 497:5,8
translate 273:14
transparency 293:14 326:23 413:25 458:13,19 478:6
transparent 413:18,21 416:4 418:6 420:17,18 443:11 458:21 459:8
travis 248:6 257:17 424:11 431:9 476:9,10
treat 482:21
treated 338:9 440:14 446:21 455:9
treatment 255:20 255:23,25 256:1,6 258:5,11 260:12 425:21 433:4,20 435:21 440:12 441:2 453:24 479:20
treatments 256:2 258:12

trial 315:7
trick 282:23
tried 255:20 260:4 260:9
trouble 366:23
true 264:6,9 279:13 292:2 293:18 316:7 322:14,15 345:25 353:17 382:2 413:4 419:6,8,9 472:2 475:11 494:9 497:8
truly 463:18 491:10
truth 421:22 454:22,24
truthful 490:7
try 313:6 314:19 314:20 347:20 380:20 464:9
trying 267:21 277:16 295:23 305:12 306:25 311:13 327:14,23 334:1 340:22 353:13 373:19 387:22 423:25 438:25 439:19,25 448:2 492:3
turn 283:17 321:2 323:16 411:13 412:2 445:8
turning 319:10
twentieth 245:1
twice 275:13 421:18 429:3
two 254:11 265:2 265:11 272:14,16 275:2 277:15 302:1 304:20 342:4 354:8 357:2 364:25 372:14 380:6 395:4 399:5 399:24 401:4,19 402:22 410:23 414:21,25 430:13 444:3 445:25 451:10 474:5 476:12 487:3
type 367:5 388:18 388:23
types 268:15 275:12 384:22
typical 258:19 271:2
typically 271:18 271:19 272:1,6,15 281:10
tyrosine 437:3,5

u

u 384:7,7
u.s. 246:4
uk 261:2 265:8 337:13
ultimate 329:13 329:15
ultimately 330:12
um 297:6 305:3 333:16 346:8 348:5 376:3 428:1 454:11 478:7
umbrella 467:12
uncertain 264:25
uncertainties 426:23
uncertainty 252:17
uncover 438:23
underlying 343:12
understand 257:25 258:25 275:10 281:22 294:20 303:18 315:11 321:13,19 322:16 323:5 355:25 356:8 366:5 369:14 404:11 416:17 443:3 463:14 464:9 493:9,11
understanding 251:18 252:10 258:24 272:25 275:20 288:18 290:22 315:9 328:16 374:21,22 375:3,7,12 376:5 406:20 431:3 434:25 482:10,13 485:13
understood 271:2 271:9 281:5 293:4 325:15 341:17 375:22
undertaken 266:7
undertook 319:4
undoubtedly 374:10
unethical 367:13 491:9,14
union 304:15 306:10,17 484:1
unit 340:25
united 245:17,19 261:3 275:23 276:6 284:16 363:10 364:9 397:18 400:9 429:14 434:17 456:19 466:19 478:24 480:22
university 384:8
unlawful 282:9,21
unnecessary 292:6
unreasonable 282:1 293:22 404:13,14 409:21 447:25 489:3
unreliable 438:16
unresponsive 288:9 311:7 345:21 387:8 389:9 449:12 459:5 487:11
unsure 262:17
update 248:12 430:10 456:19
updates 457:5,9
upregulation 263:19,24 264:1 268:25 381:18,20
ups 390:3
usage 419:2
usc 283:10
use 249:24 255:24 256:2,3 258:3,6 272:8 273:6,7 290:12 294:9,24 320:10 328:17,19 328:21 335:9 340:24 348:4 350:23 369:1 370:7 376:12,18 377:10,13 386:12 389:18 407:7 416:18,18,24 429:22 434:24 442:11 443:19 444:21 492:18 493:13
useful 399:13

users 259:23 261:9
uses 283:1,4 416:20
usual 427:12 461:20
usually 263:25
utility 258:5 260:23
utilization 437:7

v

v 245:7 495:4 496:1 497:1
v2 495:5 496:2,24 497:2,12
validate 411:20
validity 325:16
valine 384:12,13
values 338:8
variability 438:19 438:23 439:14
variety 382:8
various 309:20 431:18 438:20
venture 259:13 358:25
verbatim 494:9
verified 454:18
verify 264:16 495:9
veritext 246:24 251:8 495:14,23
veritext.com. 495:15
version 430:14
versus 357:8 440:13
vetting 291:11
victims 292:13
video 245:15 422:19
videographer 246:24 251:3,7 296:4,7 359:15,17 377:20,23 422:9 422:21 462:14,17 493:15,18
vietnam 484:15
view 254:17,19 264:23 277:6,9 305:9 315:19 328:21 330:10 482:13 489:2
viner 246:24 251:8
violates 282:6
virtually 415:1 436:9 439:4 450:4 469:17
visibility 478:18
visit 350:18 355:3
visited 302:15
vital 292:22
vivo 298:22 316:13,17 317:2 319:2 411:19
voluminous 414:20
voluntarily 305:10
volunteer 315:6
vomit 260:20
vulnerable 397:1 403:12 409:16

w

w 247:1
wait 358:2 404:14
walkup 246:9
walkuplawoffic... 246:12
want 262:5,7 273:21 275:9 290:7,8 313:12,20 314:5 315:6,9 341:9 342:21 347:7 352:11 358:17,19,25 359:10 365:22 368:19,20,24 369:5,6 375:21 402:5 404:17 414:24,25 415:2 416:7,9 417:20 443:13 460:2,4 464:8,8,12 475:1 475:15 483:6
wanted 259:19 261:12 278:25 304:25 341:17 366:3 367:24 369:18 373:4,13 376:23 379:16 389:8 414:1,4 445:5
wanting 414:15
wants 383:18
washington 246:15
water 274:6,9,12
way 252:14 254:23 260:24 262:23 264:16 268:1 273:4 277:12 288:2,12 293:3 294:17 310:3 313:12 324:5 336:15 344:2 358:25 366:15 367:16 369:3 380:2 385:23 388:2 391:9 400:2 408:19 428:5 435:7,18 437:14 438:15 442:9 443:2 468:24 470:15 482:24 489:14 494:16
ways 373:19 379:20
we've 263:12 330:23 406:3 457:22 477:14
website 418:5 422:3 428:16
webster 381:16 382:9
week 272:16 273:14,18 333:11 334:4 349:3 359:5 429:3 460:1,15
weekly 331:12 362:13 393:11,18
weeks 272:22 273:7,22,23 334:4 418:5 429:4
weight 334:7 448:21,23,24 449:2,2,5,18 450:11 452:7,8 454:25 459:1 487:9 489:4 492:2 492:9
went 442:1 486:4
wheelhouse 289:18
whilst 253:13
widely 265:10 354:20
willing 368:22 422:12
wise 478:5
wish 341:10 387:25 415:6 491:11
wistar 384:10

withdraw 311:18 348:7 453:1,3
withdrew 305:10 305:24 306:1
withhold 283:15 491:11
withholding 280:19 491:2,7 492:5 493:2
withstanding 285:15
witness 246:13 247:3 251:16 315:7 345:22 368:13 493:11 494:4 495:8,10,12 495:19
wondered 441:5
wonderful 488:12
word 253:7 258:3 290:11,11 320:10 387:15 426:15 430:16 438:13 442:11 443:19 447:7,14 452:12 452:13 492:19,21 492:22,24
words 252:14 261:25 287:1 310:25 322:3 335:6,23 386:12 394:17 408:18 433:16 449:8,15 482:21
work 252:18 253:5 257:13,19 258:8 318:25 326:24 330:6 336:2,5 340:23 384:8 388:11 396:13 435:9 456:15 474:10
worked 257:19 298:19 376:5
working 259:13 431:13 442:19
works 257:12 478:20
world 276:9 277:2 279:11 321:19 325:9 326:7,22 364:5 365:18 376:7,8 377:3 397:17 429:17 436:11 466:9 469:16,17,25 470:12 473:20,22 474:2
worried 420:6
write 304:23
writing 283:4 304:13 349:8 405:6
writings 405:19
written 304:17 322:8,9,15 324:5 325:10 349:2
wrong 258:7 323:7 356:25 357:4,6 438:3,5,6,7,8,12 452:11
wrote 304:24 359:2 385:22

x

x 247:1 248:1,1 390:17
xm7229 342:11 350:13 353:24 354:13 461:3
xm7258 248:21 354:19 361:1,14 395:5 401:20 402:23 429:5 461:3
xm7371 248:23 360:8 395:5 401:20 402:23 461:3
xm7480 249:5 392:12 401:2,18 461:3
xm7552 461:4
xm7570 249:8 461:4
xr7641 461:4

y

y 384:7
year 289:14,15 333:13 358:24 469:13
years 255:9 261:2 261:13 271:6 272:14,16 273:24 277:13 283:7 289:12 332:21 333:2 348:25 358:3,3,7,13 363:15 398:12 404:15 410:23 419:13 430:13,16 478:2 486:17 492:3
yesterday 251:11 252:9 272:14 298:1 299:12,19 302:12 376:10 463:1 465:9 474:13
young 272:9 276:22

z

zachary 248:8
zeiss 337:14
zeneca 289:8

Illinois Code of Civil Procedure

Article II, Part E

Rule 207, Signing and Filing Depositions

Signing and Filing Depositions

(a) Submission to Deponent; Changes; Signing. Unless signature is waived by the deponent, the officer shall instruct the deponent that if the testimony is transcribed the deponent will be afforded an opportunity to examine the deposition at the office of the officer or reporter, or elsewhere, by reasonable arrangement at the deponent's expense, and that corrections based on errors in reporting or transcription which the deponent desires to make will be entered upon the deposition with a statement by the deponent that the reporter erred in reporting or transcribing the answer or answers involved. The deponent may not otherwise change either the form or substance of his or her answers. The deponent shall provide the officer with an electronic or physical address to which notice is to be sent when the transcript is available for examination and signing. When the deposition is fully transcribed, the officer shall deliver to the deponent, at the address supplied,

notice that it is available and may be examined at a stated place at stated times, or pursuant to arrangement. After the deponent has examined the deposition, the officer shall enter upon it any changes the deponent desires to make, with the reasons the deponent gives for making them. If the deponent does not appear at the place specified in the notice within 28 days after the mailing of the notice, or within the same 28 days make other arrangements for examination of the deposition, or after examining the deposition refuses to sign it, or after it has been made available to the deponent by arrangement it remains unsigned for 28 days, the officer's certificate shall state the reason for the omission of the signature, including any reason given by the deponent for a refusal to sign. The deposition may then be used as fully as though signed, unless on a motion to suppress under Rule 211(d) the court holds that the reasons given by the deponent for a refusal to sign require rejection of the deposition in whole or in part.

(b) Certification, Filing, and Notice of Filing. (1) If the testimony is transcribed, the officer

shall certify within the deposition transcript that the deponent was duly sworn by the officer and that the deposition is a true record of the testimony given by the deponent. A deposition so certified requires no further proof of authenticity

(2) Deposition transcripts shall not be filed with the clerk of the court as a matter of course. The party filing a deposition shall promptly serve notice thereof on the other parties and shall file the transcript and any exhibits in the form and manner specified by local rule.

DISCLAIMER: THE FOREGOING CIVIL PROCEDURE RULES ARE PROVIDED FOR INFORMATIONAL PURPOSES ONLY. THE ABOVE RULES ARE CURRENT AS OF APRIL 1, 2019. PLEASE REFER TO THE APPLICABLE STATE RULES OF CIVIL PROCEDURE FOR UP-TO-DATE INFORMATION.

VERITEXT LEGAL SOLUTIONS
COMPANY CERTIFICATE AND DISCLOSURE STATEMENT

Veritext Legal Solutions represents that the foregoing transcript is a true, correct and complete transcript of the colloquies, questions and answers as submitted by the court reporter. Veritext Legal Solutions further represents that the attached exhibits, if any, are true, correct and complete documents as submitted by the court reporter and/or attorneys in relation to this deposition and that the documents were processed in accordance with our litigation support and production standards.

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