Electronically Filed
Kahalah A. Clay
Circuit Clerk
Cassie Voelkel
17L0517
St. Clair County
3/15/2021 7:07 PM
12581464

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

DIANA HOFFMANN, et al.,

Plaintiffs,

v.

SYNGENTA CROP PROTECTION, LLC, et al.,

Defendants.

No. 17-L-517

FILED UNDER SEAL

PLAINTIFFS' MOTION FOR LEAVE TO FILE AMENDED COMPLAINT TO INCLUDE PRAYER FOR PUNITIVE DAMAGES

Come now Plaintiffs, by their attorneys, and pursuant to 735 ILCS 5/2-604.1, move the Court for leave to file an amended complaint that includes a prayer for relief seeking punitive damages against all Defendants on all counts asserted Jerry Mills, Ronald Niebruegge and Carroll Rowan.[1] In support of this motion, Plaintiffs state:

In this case, four Illinois farmers allege that long-term, low-dose exposure to paraquat-containing pesticides manufactured and distributed by Defendants caused them to develop Parkinson's disease. Plaintiffs' complaint asserts claims for strict liability (design defect/failure to warn), negligence, breach of implied warranty and violation of the Illinois Consumer Fraud &

[1] Freemon Schmidt recently passed away. Punitive damages are not recoverable in wrongful death actions. *Mattyasovszky v. W. Towns Bus Co.*, 61 Ill. 2d 31 (1975). The married Plaintiffs' wives also assert claims for loss of consortium. Punitive damages are also not recoverable on consortium claims. *Hammond v. N. Am. Asbestos Corp.*, 97 Ill. 2d 195, 211–12 (1983).

Deceptive Business Practices Act ("IFCA"). Punitive damages are available in product liability cases,[2] as well as under ICFA.[3]

In pertinent part, 735 ILCS 5/2-604.1 requires a plaintiff wishing to seek punitive damages in product liability/negligence cases involving bodily injuries to obtain pre-trial leave to amend his complaint to include a prayer for such relief. Leave should be granted where the plaintiff establishes a "reasonable likelihood of proving facts at trial sufficient to support an award of punitive damages."[4] The evidentiary material is viewed in the light most favorable to the plaintiff.[5]

Generally, punitive damages may be awarded "when torts are committed with fraud, actual malice, deliberate violence or oppression, or when the defendant acts willfully, or with such gross negligence as to indicate a wanton disregard of the rights of others."[6] Recognizing that the human qualities of "malice" and "willfulness" are difficult to ascribe to corporate entities and that manufacturers' decisions regarding the production and marketing of goods affect public safety, scholars have identified two characteristics of corporate misconduct that will serve as the basis for an award of punitive damages in products cases:

> The first is the manufacturer's lack of concern for the public safety, a spirit of utter indifference to whether the product might cause unnecessary injuries. The second characteristic is the flagrancy of this indifference as reflected by the extent of the manufacturer's awareness of the danger and its excessiveness, the over-all magnitude of the danger to the public, the ease of reducing the risk, and the

---

[2] *Townsend v. Sears, Roebuck & Co.*, 227 Ill. 2d 147, 156 (2007).

[3] *See* 815 ILCS 505/10a (allowing the court to award economic damages "or any other relief which the court deems proper" and specifically disallowing punitive damages in cases involving car dealers).

[4] 735 ILCS 5/2-604.1.

[5] *See Stcjkovich v. Monadnock Bldg.*, 281 Ill. App. 3d 733, 744 (1st Dist. 1996).

[6] *Kelsay v. Motorola, Inc.*, 74 Ill. 2d 172, 186 (1978).

> motives and other circumstances attending the manufacturer's failure to reduce the risk.[7]

In short, "[p]unitive damages may be assessed against the manufacturer of a product injuring the plaintiff if the injury is attributable to conduct that reflects a flagrant indifference to the public safety."[8] In product liability cases, the goal is to deter "manufacturers from placing dangerously defective products into the stream of commerce by making this unprofitable to an unpredictable degree."[9]

Here, the evidence will show that Defendants acted in flagrant indifference to the public safety and the Plaintiffs' health, prioritizing profits over safety. Plaintiffs incorporate by reference the attached evidentiary materials in support of this motion: Statement of Facts (Ex. A, with its supporting exhibits); the expert reports of Julie K. Andersen (Ex. B), Beate Ritz (Ex. C), John Timothy Greenamyre (Ex. D), William A. Farone (Ex. E), William C. Mobley (Ex. F), Terrence J. Collins (Ex. G), David Michaels (Ex. H) and Michael J. Kalsher (Ex. I), the declaration of former Syngenta scientist Jon R. Heylings (Statement of Facts, Ex. 28) and examples of relevant meeting minutes from the Board of Directors of Syngenta AG and the Syngenta Executive Committee (collectively, Ex. J). In summary, the evidence adduced at trial will prove:

---

[7] *Moore v. Remington Arms Co., Inc.*, 100 Ill. App. 3d 1102, 1114–15 (4th Dist. 1981) (quoting David G. Owen, *Punitive Damages in Products Liab. Litig.*, 74 Mich. L. Rev. 1257, 1367 (1976)). *See also Collins v. Interroyal Corp.*, 126 Ill. App. 3d 244, 256 (1st Dist. 1984) ("The essential elements of wilful and wanton conduct in a product liability case include knowledge of the defect, knowledge or notice that the defect was likely to cause injury and failure to warn of or remedy a known defect or take some other affirmative action to avoid the injury.").

[8] *Moore,* 100 Ill. App. 3d at 1115 (quoting Owen, *supra*).

[9] *Id.* at 1113.

- That paraquat is a neurotoxin, exposure to even small amounts of which can lead to the development of a horrible, incurable, debilitating, progressive condition known as Parkinson's disease that stems from a lack of dopamine production in the brain.[10]
- That occupational users of Defendants' paraquat-based herbicides would necessarily be exposed to the toxin in small amounts regardless of how careful they were in handling the product and that, when so exposed, paraquat would eventually end up in their brains. That when in the brain, paraquat targets and kills the sensitive neurons responsible for producing dopamine through a chemical reaction called redox cycling – the same reaction that makes paraquat deadly to all living cells.[11]
- That, by their own admission, Defendants knew many of these facts before their paraquat products were ever marketed in the U.S. and knew (certainly by the late 90s) that independent scientists had made a direct connection between paraquat exposure and the development of parkinsonian symptoms.[12]

---

[10] *See* Statement of Facts and supporting exhibits (specifically, sections titled "Paraquat and Redox Cycling" and "Parkinson's Disease and Paraquat"); *see also* expert reports of Andersen, Ritz and Greenamyre.

[11] *See* Statement of Facts and supporting exhibits (specifically, sections titled "Paraquat and Redox Cycling"; "How Paraquat Enters the Human Body/Brain and Defendants' Knowledge Thereof"; and "Occupational Exposure to Paraquat and the Use of Personal Protective Equipment, Defendants' Knowledge Thereof and Studies Related Thereto").

[12] *See* Statement of Facts and supporting exhibits (specifically sections titled "Defendants' Early Knowledge of Paraquat's Neurotoxicity"; "How Paraquat Enters the Human Body/Brain and Defendants' Knowledge Thereof"; and "Occupational Exposure to Paraquat and the Use of Personal Protective Equipment, Defendants' Knowledge Thereof and Studies Related Thereto").

- That, to the extent Defendants did not "know" any of these facts, it was due solely to their own willful ignorance, because a reasonable chemical manufacturer should and would have recognized obvious red flags pointing to paraquat's neurotoxicity and conducted testing to determine the extent of risk under exposure circumstances relevant to the users of their products. That, by their own admission, Defendants had the means and wherewithal to conduct such tests to determine paraquat's long-term neurotoxic risk since the 1960s, but they did not, instead consistently and flagrantly ignoring obvious indicators of paraquat's neurotoxicity for over 35 years.[13]
- That Defendants were very cognizant of their lack of knowledge and studies related to paraquat's long-term risks, but failed to do anything to rectify their lack of knowledge, instead focusing their research efforts almost exclusively on paraquat's obvious acute toxicity for the first 35 years they sold it.[14]
- That Chevron, as the primary registrant of paraquat in the U.S. at the time, secured paraquat's original registration through the use of fraudulent studies conducted by Industrial Bio-Test Laboratories ("IBT"). That while officials eventually discovered the fraud, criminally prosecuted IBT executives and forced

[13] *See* Statement of Facts and supporting exhibits (specifically, sections titled "Defendants' Ability and Efforts to Study Paraquat's Neurotoxicity"; and "Defendants' Ability and Efforts to Conduct Epidemiology Studies"). *See also* expert reports of Farone, Mobley and Collins.

[14] *See* Statement of Facts and supporting exhibits (specifically, sections titled "Defendants' Ability and Efforts to Study Paraquat's Neurotoxicity"; and "Defendants' Ability and Efforts to Conduct Epidemiology Studies"). *See also* expert reports of Farone, Mobley and Collins.

Chevron to replace the studies with valid ones in the 80s, Chevron realized the studies were problematic as early as 1966 and did nothing about it.[15]

- That Syngenta and Chevron knew paraquat was also acutely toxic because of its propensity to redox cycle – the same property that makes it a neurotoxin. That, faced with a rising death toll from acute poisoning incidents, in the early 1980s Syngenta and Chevron added an emetic to the paraquat formulation, ostensibly to induce vomiting in persons who ingested the product quickly enough to ensure they would not absorb a lethal dose of the poison. That Syngenta and Chevron did so knowing the emetic concentration was insufficient to have the desired effect, showing they simply did not care if their product killed people – whether by acute poisoning or slowly by neurotoxic injury from long-term, low-dose exposure.[16]
- That once it could no longer plausibly ignore the issue (because, again, independent scientists began publishing studies irrefutably drawing a direct connection between paraquat and Parkinson's disease in the late 90s), Syngenta developed and implemented a strategic influencing campaign, not just to conceal the truth, but rather to deliberately distort the scientific picture as to the relationship between paraquat and Parkinson's disease (by discrediting unfavorable studies and the scientists who published them, burying the results of

[15] *See* Statement of Facts and supporting exhibits (specifically, section titled "IBT Scandal and Defendants' Knowledge Thereof").

[16] *See* Statement of Facts and supporting exhibits (specifically, section titled "Paraquat's Acute Toxicity/Emetic"). *See also* expert report of Michaels and Heylings Declaration.

unfavorable internal research and publicly touting only those studies that were favorable to their position) to publicly create doubt as to whether paraquat is neurotoxic.[17]

- That, rather than publicly acknowledging the truth (that long-term, low dose exposure to paraquat causes neurotoxic damage that can result in Parkinson's disease), Defendants continue to deny that fact to this day, depriving users of the ability to make informed choices as to how best to protect themselves from exposure or whether to use Defendants' products at all.[18]
- That Syngenta knew all of this was unethical and in violation of its own corporate Code of Conduct.[19]
- That the top brass at Syngenta was fully aware of and complicit in the foregoing conduct.[20]
- That Growmark made no attempt to research/investigate the science regarding the link between paraquat and Parkinson's disease and admittedly does not care if

---

[17] *See* Statement of Facts and supporting exhibits (specifically, sections titled "Syngenta's Internal Studies to Examine Paraquat's Link to Parkinson's Disease Since 2003 and Communications Regarding Same"; "Nonhuman Primate Studies and Communications Regarding Same"; and "Efforts to Influence the Composition of the EPA's Science Advisory Panel"). *See also* expert report of Michaels.

[18] *See* Statement of Facts and supporting exhibits (specifically, section titled "Defendants' Warnings - On the Label or Otherwise - Regarding the Dangers of Paraquat"). *See also* expert report of Kalsher.

[19] *See* Statement of Facts and supporting exhibits (specifically, section titled "Corporate Ethics and Honest Communications with the Public").

[20] *See* SAG and SEC board meeting minutes.

paraquat causes Parkinson's disease and will continue to sell it as long as its EPA-registered – the very definition of gross indifference to the safety of others.[21]

- That Defendants' continuing denial of the link between paraquat and Parkinson's disease, utter refusal to take steps to reduce the danger, and complete unwillingness to accept responsibility for injuries caused by their products shows corporate complicity by ratification.[22]

In short, given the evidence summarized above (and attached hereto) and the horrific nature of the injuries suffered by Plaintiffs and countless other farmers and pesticide applicators in Illinois as a result of Defendants' misconduct, there is *more* than a reasonable likelihood that Plaintiffs will be able to prove Defendants acted willfully, wantonly and in flagrant disregard and/or indifference to public safety and their customers' health and wellbeing. Courts have upheld punitive damage awards in similar circumstances.[23] Defendants should be punished for their reprehensible conduct to deter them and others from acting similarly in the future.

---

[21] *See* Statement of Facts and supporting exhibits (specifically, section titled "Defendants' Ability and Efforts to Study Paraquat's Neurotoxicity").

[22] *See Stcjkovich*, 281 Ill. App. 3d at 745 (affirming denial of leave to add punitive damage prayer in case where there was no evidence that manufacturer of elevator that injured the plaintiff "deliberately refused to attempt repairs on the elevator or that it placed the elevator back in service knowing both the cause of its stoppages and that the cause had not been remedied").

[23] *E.g.*, *Lipke v. Celotex Corp.*, 153 Ill. App. 3d 498, 506 (1st Dist. 1987) (evidence that there was literature regarding the dangers of asbestos publicly available by the 1920s, that defendant had actual knowledge of the dangers of asbestos by the 1950s/60s and failed to warn or otherwise remedy was sufficient to support award of punitive damages); *Collins*, 126 Ill. App. 3d at 257 (upholding award of punitive damages where evidence showed corporate defendant had knowledge of the defect and that it could injure people, yet "made no attempt to take steps to remedy the defect or to issue warnings."); *Proctor v. Davis*, 291 Ill. App. 3d 265, 285–86 (1st Dist. 1997) (holding evidence that defendant "not only knew of the adverse effects of periocular use of [drug], but promoted and developed this off-label use through financial and technical assistance to doctors" was sufficient to justify the imposition of punitive damages). *See also In re Roundup Products Liab. Litig.*, 385 F. Supp. 3d 1042, 1046 (N.D. Cal. 2019) (under California law, upholding jury award of punitive damages against manufacturer of pesticide

WHEREFORE, Plaintiffs request leave to file an amended complaint to add a prayer for punitive damages against all Defendants on all Counts asserted by Jerry Mills, Ronald Niebruegge and Carroll Rowan.

Respectfully submitted,

KOREIN TILLERY, LLC, Attorneys for Plaintiffs

BY: /s/ Stephen M. Tillery
Stephen M. Tillery, #2834995, stillery@koreintillery.com
John C. Craig, #6206733, jcraig@koreintillery.com
Rosemarie Fiorillo, #6315964, rfiorillo@koreintillery.com
Robert L. King, #6209033, rking@koreintillery.com
John A. Libra, #36286721, jlibra@koreintillery.com
One U.S. Bank Plaza
505 N. 7th Street, Suite 3600
St. Louis, MO 63101
Telephone: (314) 241-4844
Facsimile: (314) 241-3525

---

where "evidence easily supported a conclusion that Monsanto was more concerned with tamping down safety inquiries and manipulating public opinion than it was with ensuring its product is safe."); *Johnson v. Monsanto Co.*, 52 Cal. App. 5th 434, 456, 266 Cal. Rptr. 3d 111, 130 (2020), *as modified on denial of reh'g* (Aug. 18, 2020), *review denied* (Oct. 21, 2020) (under California law, substantial evidence supported award of punitive damages where "Monsanto and its employees discounted legitimate questions surrounding glyphosate's genotoxic effect, failed to conduct adequate studies, surreptitiously contributed to and promoted articles reporting on glyphosate's safety, and lobbied regulators to conclude that glyphosate is safe."); *Taylor v. Mentor Worldwide LLC*, 940 F.3d 582, 598 (11th Cir. 2019) (under Florida law, record sufficient to support punitive damages where evidence showed defendant "(1) did not conduct sufficient product testing, including tests as to degradation despite it being well known that heat and pressure cause polypropylene to degrade, (2) knew of the relatively high rate of complications associated with ObTape but nonetheless concealed or materially understated those risks, and (3) ignored warnings from both Mentor employees and physicians outside of the company.").

EXHIBIT A
FILED UNDER SEAL

STATEMENT OF FACTS

Paraquat and Redox Cycling

Paraquat is a man-made chemical. Botham: 42; Patterson: 131.

Paraquat was first synthesized in the late 1800s. Patterson: 131.

Paraquat kills by causing "oxidative stress." Botham: 212-13.

Redox cycling is paraquat's mode of action. Botham: 83-84; 213.

Science has known of paraquat's high propensity to redox cycle since 1933. Botham: 214; Patterson: 152.

"Redox" refers to reduction and oxidation -- a type of chemical reaction between molecules. Botham: 62-63, 75; Patterson: 157.

In the first step of the redox cycle, paraquat dication (PQ++) is reduced (gains an electron) to form a free radical monocation (PQ+). Botham: 71-72; Patterson: 153, 154, 157.

This chemical reaction occurs very readily and very quickly in the presence of a suitable reagent. Botham: 71; Patterson: 153, 160.

Assuming the presence of molecular oxygen, during the second step of the redox cycle, the paraquat free radical monocation (PQ+) oxidizes or loses an electron to the oxygen molecule. Botham: 75-76; Patterson: 154-58.

This second redox reaction also generates a free radical, reactive oxygen species (or "ROS") called superoxide or superoxide radical. Botham: 59, 76; Patterson: 158-59.

The production of superoxide begins a cascade of reactions that creates other free radicals like hydrogen peroxide and hydroxyl radical. Botham: 89; Patterson: 170.

Free radicals like ROS interfere with the cellular function necessary to life and are toxic to cells. Botham: 59, 90, 213; Patterson: 170-71; Campbell: 28.

When paraquat gets into cells, it generates ROS that can cause damage to the cell. Botham: 212-214, 724.

The second redox reaction also returns the paraquat molecule to its original (PQ++) state, allowing the cycle to repeat. Botham: 78, 89; Patterson: 161, 169-70; Campbell: 28-29.

This chemical reaction also occurs very readily and very quickly. Botham: 77; Patterson: 160.

It is consistent with paraquat's mode of action that a single molecule of paraquat could trigger the production of countless molecules of superoxide. Botham: 214.

The cumulative effect of redox cycling is called oxidative stress. Guo J-D, Zhao X, Li Y, Li G-R, Liu, X-L (2018) Damage to dopaminergic neurons by oxidative stress in Parkinson's disease (Review) *International Journal of Molecular Medicine* 41:1817-1825.

Redox cycling can occur in any oxygen rich environment with an active blood supply. Botham: 160-61.

Paraquat readily redox cycles in the presence of molecular oxygen, which is plentiful in all living cells. Botham: 213.

Paraquat is particularly effective and does more damage in oxygen-rich environments. Campbell: 20-21.

The brain generates an enormous amount of oxygen. Botham: 161.

Nicotinamide adenine dinucleotide or "NAD" is a molecule found in all living cells. Botham: 87, 93; Patterson: 176.

NADPH can donate an electron to an acceptor. Botham: 94; Patterson: 176-77.

Paraquat is an efficient acceptor of electrons in animal cells. Botham: 94; Patterson: 177.

The redox potential certainly exists in the NADPH oxidase in the microglia of the human midbrain. Botham: 95.

Glutathione, or "GSH," is an antioxidant found in all life forms that helps mitigate damage from ROS. Botham: 96; *see also* Patterson: 178.
In stealing an electron from GSH, paraquat depletes the cell's natural antioxidant protection while also continuously producing more superoxide. Botham: 96.

If the conditions for redox cycling exist and paraquat can reach a target cell, then toxicity would be assumed to occur in animal cells. Patterson: 171.

Growmark knows that paraquat redox cycles. Powell: 147.

Imperial Chemical Industries ("ICI") discovered paraquat's herbicidal properties in 1955. Botham: 48, 584; *see also* Patterson: 131-32.

ICI applied for and obtained a British patent for the use of paraquat as an herbicide in 1956. Botham: 50-51; Patterson: 141; Ouzts: 39-40.

ICI began marketing a formulated paraquat product outside the U.S. in 1962. Ouzts: 39; *see also* Botham: 96.

ICI applied for and obtained a U.S. patent for the use of paraquat as an herbicide in 1961. Botham: 49; Patterson: 139-40; Ouzts: 39-40.

By agreement with ICI, California Chemical Company, later known as Chevron Chemical Company, was licensed to formulate, sell and distribute paraquat products in the U.S. and did so beginning in 1965. Patterson: 60, 62-63, 82, 387; Ouzts: 40.

Chevron was paraquat's primary registrant in the U.S. from 1965 to 1986. Patterson: 102-03.

Since 1965, Syngenta or its corporate predecessors have been, either by themselves or in cooperation with Chevron, the registrant for paraquat in the U.S. Botham: 904.

Syngenta is the primary registrant of paraquat now. Botham: 284.

In 1965, Chevron began selling a formulated paraquat product in the U.S. under the brand name Ortho paraquat. *See* Botham: 96-98; Patterson: 282; Ouzts: 39.

Chevron formulated Ortho paraquat using paraquat active ingredients manufactured by and purchased from ICI. Patterson: 282-83, 396.

Chevron was the exclusive distributor of paraquat products in the U.S. until 1982 when ICI began distributing paraquat in the U.S. itself. Patterson: 63-4, 300-01, 391-92, 407-08.

Beginning in 1982, Chevron helped ICI get Gramoxone registered, formulated Gramoxone products for ICI at its plant in California, and received royalties for the sale of those products. Patterson: 397, 399-400, 402, 426, 445.

From 1965 until at least 1982, there was no company other than Chevron or ICI selling paraquat products in the U.S. Patterson: 426-28, 445-46.

Chevron cancelled its registration and stopped distributing paraquat in the U.S. in 1986. Patterson: 112.

ICI and Chevron mutually agreed to advise each other of technical information regarding paraquat, including product toxicology and safety, at least twice a year, and meet at least once a year regarding paraquat issues. Patterson: 66-68, 71-72, 73-74, 283, 319.

ICI and Chevron met frequently to discuss paraquat and shared information and scientific studies to keep each other fully informed about any development regarding paraquat. Patterson: 435-436.

ICI and Chevron shared the costs of studies performed relating to paraquat. Patterson: 476-7.

How Paraquat Enters the Human Body/Brain and Defendants' Knowledge Thereof

It is possible for paraquat to enter the human body via absorption through the skin/epithelial tissue, via inhalation, and via the digestive tract when ingested, even when small droplets are swallowed. Botham: 204-06, 219.

In 1965, Chevron and ICI were aware that inhaling droplets or spray mist of paraquat would cause nose bleeds. Patterson: 539-540.

The addition of non-ionic surfactants to paraquat formulated products increases dermal absorption. Botham: 1233.

If there is greater dermal absorption, there is the potential that more paraquat will end up in the bloodstream. Botham: 1233-34.

If a high enough dose of paraquat is absorbed through the skin, inhaled, or ingested, it will get into the bloodstream. Patterson: 592-597, 635.

Once paraquat has entered the body by any means, it can enter the circulating bloodstream. Botham: 206, 1228-30.

Syngenta maintains a website, paraquat.com, to provide information on paraquat to the public and particularly farmers, growers and other users of paraquat. Botham: 416-17, 1136-37.

From at least 2008 on, paraquat.com stated that the reason paraquat is not a Parkinson's disease concern for farmers is because it does not "readily" or "easily" cross the blood brain barrier. Botham: 112-13, 418-19, 1163-64.

Through the years, had a farmer called and asked if paraquat could get into his brain via spraying operations, Syngenta's answer would be that paraquat does not cross the blood brain barrier. Ouzts 09-28-20: 83-84.

The blood brain barrier is a semi-permeable border of cells that prevents some substances in the circulating blood from non-selectively crossing into the extracellular fluid of the central nervous system where the neurons reside. Botham: 109-10; Patterson: 188-89.

The blood brain barrier system selectively allows some molecules to pass through by passive diffusion; others can cross only if carried by an active transporter. Botham: 110-12; Patterson: 189-90.

By 1974, ICI knew paraquat could cross cell membranes by active transport. Botham: 176, 207; *see also* Patterson: 275-277.

Paraquat crosses the blood brain barrier. Botham: 124-25.

The permeability of the blood brain barrier varies based on the condition of the organism and over time. Patterson: 190.

The blood brain barrier tends to become more permeable and less effective in the presence of inflammation/infection. Botham: 115-7; Patterson: 196, 197.

Central nervous system barriers are more leaky/vulnerable in the very young and the old. Botham: 1251.

Several parts of the brain are not protected by blood brain barrier. Botham: 117-19, 123; Patterson: 197.

Paraquat can also enter the brain via the olfactory bulb, cerebral spinal fluid and the enteric nervous system. Botham: 137-8.

The olfactory bulb lies directly behind the nose in the human brain and is not protected by the blood brain barrier. Botham: 117-18, 120-21; Patterson: 200.

When toxins are inhaled through the nose, they can directly enter the brain through the olfactory bulb. Botham: 118, 121, 207-8; Campbell: 119.

Injection is the most accurate way to measure the amount of a chemical you are dosing to a subject animal. Botham: 1216-17; *see also* Patterson: 619-626.

Starting in 1969, ICI and Chevron knew that laboratory studies detected measurable amounts of paraquat in animal brains after the animals were exposed to the chemical by various routes (dermal, oral and i.p. injection). Botham: 158-59, 163, 166, 179-80; Patterson: 265-67, 269-70, 272.

No matter what the route of exposure, paraquat will get into the brain. Botham: 1230-32.

From 1968 on, ICI knew from numerous post mortem examinations of people who had died from acute paraquat poisoning, both conducted internally and in the published literature, that paraquat was found in their brains. *See* autopsy reports, collected at the Bates ranges listed in Exhibit 19; *see also* Patterson: 316, 321-22, 326-27.

In 1968, ICI scientists knew that swallowing a relatively small amount of paraquat would result in paraquat entering the brain. Botham: 563, 568; *see also* Botham: 154-55.

From at least 1974 on, Chevron knew from numerous post mortem examinations of people who had died from acute paraquat poisoning, both conducted internally and in the published literature, that paraquat was found in their brains. *See* autopsy reports, collected at the Bates ranges listed in Exhibit 19; *see also* Patterson: 322-323, 326-31, 333-35.

By April 2009, Syngenta knew that once paraquat got into the brain, there was no metabolic breakdown of the chemical. Botham: 1244

Once paraquat is in the brain, it stays in there "a long time." Botham: 1246.

Growmark never asked Syngenta if paraquat could enter the human brain. Powell: 152.

Defendants' Early Knowledge of Paraquat's Neurotoxicity

Chevron "very closely" monitored the scientific literature relating to paraquat, including independent literature in the public domain. Patterson: 192.

If an article came out affecting paraquat, whether written by Chevron, ICI or anyone else, Chevron scientists read it. Patterson: 192-3.

Syngenta expects its scientists having responsibility for a product or a particular area of science to monitor and be aware of the appropriate literature. Botham: 309.

Before they put paraquat on the market, ICI and Chevron knew that paraquat has a very high potential to participate in redox reactions and produce ROS in the presence of a suitable reductant and oxygen. Botham: 70, 79, 86-87; Patterson: 152, 166-67, 270-71; *see also* Campbell: 28.

Before they put paraquat on the market, ICI and Chevron knew that paraquat was an effective herbicide because of its redox properties. Botham: 90-91; Patterson: 90, 94-95, 97.

Paraquat is also toxic to animals, including humans, and kills their cells in the same way as it does plants – oxidative stress due to redox cycling. Botham: 91, 212-13.

ICI has known since the 1960's that paraquat is toxic to both plant and animal cells because of oxidative stress. Botham: 214-15.

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. Botham: 294.

The brain is a part of the central nervous system. Patterson: 261.

By October 1958, ICI knew that paraquat had a toxicity affecting the central nervous system. Botham: 585-87.

Even prior to the time paraquat was marketed in the U.S., animals exposed to paraquat in lab studies exhibited behaviors that could be clinical signs of central nervous system effects. Patterson: 235-37, 241, 244, 246-48, 249-55, 260-61; Botham: 145, 149-50, 239-40.

By the time paraquat was sold in the U.K. in 1962 and in the U.S. in 1965, ICI should have known that paraquat had the potential to redox cycle in any human tissue including the brain, and theoretically, especially in oxygen-rich sections of the brain. Botham: 100, 174.

From 1968 on, ICI and Chevron knew from numerous post mortem examinations of people who had died from acute paraquat poisoning that there were histopathological changes and signs of damage to various areas of the brain. *See* autopsy reports, collected at the Bates ranges listed in Exhibit 19; *see also* Botham: 202-03; Patterson: 295, 313-14, 336-37.

From 1969 on, ICI and Chevron knew that the brains of animals dosed with paraquat showed signs of damage. Patterson: 260-61.

ICI concluded in a 1969 study that paraquat was a "hit and run" compound with delayed toxic effects, meaning the chemical causes immediate damage the consequences of which are not apparent until later. Botham: 151-52; Patterson: 255.

Paraquat accumulates in the central nervous system. Botham: 1246-47.

Paraquat can accumulate in the brain. Botham: 581, 1246.

Paraquat is not broken down or metabolized by the central nervous system. Botham: 1244.

Paraquat is excreted unchanged, indicating it is not metabolized. Patterson 01-22-21: 78.

Chevron has known that paraquat is not metabolized in the human body since the mid to late 60s. Patterson 01-22-21: 78.

Parkinson's Disease and Paraquat

Parkinson's disease is a progressive neurodegenerative disorder of the central nervous system primarily affecting the motor system. Botham: 208-09, 251-2.

The substantia nigra pars compacta is a part of the midbrain that controls dopamine production. Botham: 121-22, 576; Dixon: 186-89; Campbell: 31; Patterson: 337.

In 2008, paraquat.com stated that paraquat "does not reach the specific location in the brain necessary to produce Parkinson's symptoms," *i.e.*, the substantia nigra pars compacta. Botham: 418-9, 428.

That statement is not consistent with a 2008 internal Syngenta technical evaluation, stating that a number of labs, including Syngenta's own labs, have "observed a reduction in neuronal cell counts in dopaminergic neurons in the substantia nigra pars compacta brain region following paraquat administration." Botham: 428-29.

Dopamine is a neurotransmitter or a chemical messenger that helps transmit signals throughout the nervous system, which is critical to the brain's control of motor function. Botham: 122, 210; Dixon: 186-89.

Dopaminergic neurons express an enzyme called tyrosine hydroxylase, or "TH," on their cell surface that the cell needs to produce dopamine. Botham: 436-37.

The selective degeneration and death of dopaminergic neurons in the substantia nigra pars compacta is one of the primary pathophysiological hallmarks of Parkinson's disease. Botham: 210, 251-52, 421-22; Dixon: 187-9; Patterson: 227.

Once dopaminergic neurons die, they are not replaced. Botham: 211.

When enough dopaminergic neurons have died, dopamine production falls below the level necessary for the brain to control motor function, resulting in the symptoms of Parkinson's disease. Botham: 211, 251-52, 577; *see also* Patterson: 337.

There is no cure for Parkinson's disease; current treatments do not halt the progress of the disease. Botham: 210.

Only about 15% of Parkinson's disease cases are linked to a genetic mutation. https://www.parkinson.org/understanding-parkinsons/causes/genetics; Bandres-Ciga S, Diez-Fairen M, Singleton AB. (2020) Genetics of Parkinson's disease: and introspection of its journey towards precision medicine. *Neurobiology of Disease* 137:104782.

In 1982, seven young heroin users in California suddenly began exhibiting the symptoms of advanced Parkinson's disease. Langston, The MPTP Story, Journal of Parkinson's Disease 7 (2017): S11-S19, found at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5345642/pdf/jpd-7-jpd179006.pdf

Researchers determined the common link was they had all injected a neurotoxin called 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine, or "MPTP," made by a backroom chemist in a botched attempt to create a synthetic opioid. *Id.*

The discovery of the neurotoxic effects of MPTP was a breakthrough in Parkinson's disease research, because it allowed researchers to rapidly induce parkinsonism in animals in the laboratory to study the disease's physiology and treatment. *Id.*

In the 1980's, scientists made a possible connection between paraquat and Parkinson's disease due to the similarity between paraquat and the toxic metabolite of MPTP, which differ only by one methyl group. *Id.*

Since then, scientists have used paraquat in laboratories to create animal models of human Parkinson's disease to study the disease. Botham: 216.

Dopaminergic neurons are particularly susceptible to oxidative stress. Botham: 211.

The redox properties of paraquat that make it toxic to plant and animal cells also give it the potential to be toxic to dopaminergic neurons. Botham: 216.

Independent studies have shown that paraquat creates oxidative stress that kills dopaminergic neurons and causes other pathophysiology consistent with human Parkinson's disease. Botham: 216-17.

Independent studies have found a statistically significant loss of dopaminergic neurons in the substantia nigra of lab animals exposed to paraquat via various routes. Botham: 295, 352-53, 362; *see also* Dixon: 126-27.

The presence of Lewy bodies and Lewy neurites in the remaining neurons of the substantia nigra pars compacta is another pathophysiological hallmark of Parkinson's disease. Botham: 211, 264, 381; *see also* Patterson: 228, 231.

This Lewy pathology consists primarily of a build-up of insoluble clumps of a protein called alpha-synuclein. Botham: 211, 264; *see also* Patterson: 228, 231.

Independent researchers have found that paraquat causes upregulation, or an increase in the quantity of, alpha-synuclein in lab animals. Botham: 263-64.

Syngenta has known for 15 years that paraquat causes upregulation of alpha-synuclein. Botham: 1016.

In 2007, Syngenta knew that the Parkinson's Institute had reported that the build-up of alpha-synuclein was shown to destroy dopamine-producing neurons. Botham: 805.

Syngenta's Internal Studies to Examine Paraquat's Link to Parkinson's Disease Since 2003 and Communications Regarding Same

Replication is the hallmark of quality science; if the results are repeated at different labs time and again, it becomes more or less an established fact. Botham: 320-21.

In 2003, a Syngenta scientist named Louise Marks conducted an in-house study to see if she could replicate the findings of the independent studies that paraquat caused loss of dopaminergic neurons in the mouse brains. Dixon: 211; Botham: 317, 332-34.

Syngenta viewed such studies as a "threat" to paraquat. Botham: 655, 657.

If the loss of dopaminergic neurons were a consistent and reproducible finding, that would make paraquat neurotoxic, at least to the lab animals involved. Botham: 295.

In her first study, Marks found no statistically significant dopaminergic neuron loss using a manual stereology counting method. Botham: 334-35, 337-340.

Marks recognized in the report of the study that her manual methodology could be "deemed less accurate than the automated systems available and this may explain in part the differences in the total cell counts obtained." Botham: 338-39.

In 2003, Marks was nominated for a company award recognizing scientific achievement because she was the first scientist at Syngenta to use the optical fractionator method of stereology. Botham: 335-36.

In 2004, Syngenta developed "management tactics" to counter the "threat" of the independent studies, which tactics included: developing a database of neurotoxicity studies to support the continued regulatory approval of paraquat; "to [m]onitor, understand and influence ongoing academic PD research and manage the impact on paraquat registrations by putting published findings in context of the use of paraquat as an herbicide," to "[s]upport regulatory authorities in dismissing the hypothesis that paraquat is a risk factor for Parkinson's Disease in humans," and to "[c]reate an international scientific consensus against the hypothesis that paraquat is a risk factor for Parkinson's disease in humans." Botham: 658-62.

The results of the first Marks study were presented at the annual meeting for the Society of Neuroscience in October 2004. Botham: 343-44.

Following a visit to the Parkinson's Institute and discussions with Dino Di Monte, an expert in the field of neuroscience and stereology, Dr. Marks conducted three additional studies from September 2003 to September 2005 using the techniques she learned from Di Monte, which she described as "one of the most widely used and accurate stereology systems currently available." Botham: 302, 349-54, 359-62, 392-96; Dixon: 151-2.

The three later Marks studies reproduced the findings of the independent studies. Botham: 396.

In the three later studies using the automated stereology technique, Marks consistently found that paraquat causes a statistically significant loss of dopaminergic neurons in the substantia nigra in the i.p. mouse model. Botham: 395, 1145; Dixon: 223, 246-47.

Marks used her original manual stereology method to re-examine brain tissue obtained from lab animals during the later studies and came up with the same result (no statistically significant loss of neurons) as the first study. Botham: 356-57.

Marks concluded that the discrepancy between the results of her first study and the latter three studies was thus due to the difference in stereology methods, software and hardware. Botham: 354; Dixon: 150-52.

Syngenta has no reason to dispute her conclusion. Botham: 357.

The latter three Marks studies "point to the possibility" that the results of the first Marks study were wrong. Botham: 357.

Marks concluded that paraquat selectively targets vulnerable or sensitive subpopulations of dopaminergic neurons in the substantia nigra. Botham: 396-97, 403, 420-21.

One of the Marks studies also showed that paraquat caused an upregulation of alpha-synuclein. Botham: 1217-18.

In 2006, Marks conducted a fifth study to determine whether the results of the prior three studies, a loss of dopamine neurons in the substantia nigra, could be attributed to general toxicity due to dosing any compound at high levels as opposed to any neurotoxic effect of paraquat. She concluded the results of the prior studies could not be attributed to general toxicity, making it more likely the results of the prior studies were due to paraquat. Botham: 406-08.

Syngenta has not identified any flaw in the Marks studies and does not claim that anything she did was "wrong." Botham: 437-9, 1157.

Marks issued final reports regarding all of these studies in 2007. Botham: 332, 348-49.

Syngenta has never published the Marks studies confirming that paraquat caused loss of dopaminergic neurons in the substantia nigra. Botham: 318, 363, 1143.

Syngenta never published the results of the studies. Botham: 1452, 1448-50.

Growmark was never advised of the results of the Marks studies. Powell: 118.

Growmark would still sell the product even had it known about the results of the Marks studies. Powell: 116.

Syngenta knew that if the same neurotoxicity study was done again, the mice would show the same results. Botham: 1460.

If different laboratories at different times using different mice come back with the same results, it establishes the premise of the study. Botham: 1460.

In June 2006, Syngenta completed a 90-day rat feeding neurotoxicity study, the Chivers study, as required by EPA guidelines. Botham: 1441-42.

This was the first time Syngenta had been asked by the EPA to do a study that focused specifically on neurotoxicity. Botham: 1442.

In June 2006, Syngenta knew the results of the paraquat neurotoxicity studies performed by Dr. Marks. Botham: 1443-44.

In May 1998, the EPA published guidelines for neurotoxicity risk assessment in the Federal Register, and Syngenta would have been aware of them at that time. Botham: 1445-46.

Those guidelines assume that the most sensitive animal species will be used to assess human risk and that there is a non-linear dose response relationship for neurotoxicants. Botham: 1447-48.

At the time it submitted the rat study required by the guidelines in 2006, Syngenta knew from the Marks studies that the C57 black mouse was sensitive to paraquat exposure and consistently showed dopaminergic cell loss in the midbrain following exposure. Botham: 1448.

In 2006, Dr. Marks performed a paraquat neurotoxicity study in rats that failed to find the same loss of dopaminergic neurons she had found in mice, leading her to conclude that "this finding suggests the effects observed may be species and/or strain specific." Botham: 1454-55.

Dr. Marks' rat study involved the same strain of rat Syngenta used in the 2006 rat guideline study submitted to the EPA. Botham: 1455.

The rat guideline study was a feeding study. Ingestion results in less uptake in the bloodstream, and there is a greater potential for a higher concentration of paraquat in the bloodstream if i.p. injection is used. Botham: 1472-76.

It would have been possible that the researchers might have got a positive result in the rat had they used the i.p. injection method, but they did not do so because "this test was being done in accordance with EPA guidelines" and the "relevance of the route to possible human exposure is important; hence, the use of the oral dietary route." Botham: 1484-85.

"Under normal circumstances, you wouldn't expect an applicator to be exposed to paraquat... through the oral route.... normally speaking, that would not be relevant for an operator." Botham: 1486-87.

Dr. Marks used i.p. injection, not dietary intake, in her rat study. Botham: 1489-90.

The rat guideline study measured various neurotoxicological endpoints, but it did not measure the loss of dopaminergic neurons in the substantia nigra, did not measure the levels of dopamine/dopamine metabolites in the striatum, and did not investigate whether there was an upregulation of alpha-synuclein. Botham: 1478-79.

A trained stereologist, Louise Marks, was available in Syngenta's laboratory at the time the Chivers rat study was done. Botham: 1481-82.

The rat guideline study used animals that were the age equivalent of a human child or pre-teen at the start of dosing and about mid to late-20s at the end of the 90 day study. Botham: 1492-93.

The average age of onset of Parkinson's disease in humans is about 65 years, not age 20. Botham: 1493.

There was nothing preventing Syngenta from using older animals in its non-guideline studies. Botham: 1495.

Syngenta also conducted an acute neurotoxicity guideline study in rats in which rats were administered various oral doses of paraquat and observed for 14 days. Botham: 1502-03.

The study showed no treatment related effects at the various doses. Botham: 1503-04.

The study did not measure loss of dopaminergic neurons in the substantia nigra, or the levels of dopamine/dopamine metabolites in the striatum, or investigate whether there was an upregulation of alpha-synuclein in the rats. Botham: 1504.

The 14-day study doesn't tell us anything about the long-term effects of chronic low dose exposure to paraquat. Botham: 1504-05.

In 2011, Dr. Jeffrey Brent, working as a paid consultant to Syngenta, published a study titled, "Systematic Review of Parkinsonian Syndromes in Short- and Long-Term Survivors of Paraquat Poisoning." Botham: 1510-13.

Syngenta used a database of paraquat poisoning incidents to supply information to Dr. Brent to conduct the study. Botham: 1519, 1531-34.

The study would not allow one to rule out the possibility that paraquat could cause Parkinson's disease because it looked at clinical signs in a relatively short period after acute poisoning and didn't take into account latency. Botham: 1514.

The study was not intended to tell us anything about chronic low dose occupational exposure to paraquat. Botham: 1516.

The study was focused on parkinsonism, not Parkinson's disease, and the two are different. Botham: 1512.

The study was premised on the idea that, given the close structural similarity between MPTP and paraquat, if paraquat does cause Parkinson's disease, it would be expected to do so in a manner similar to MPTP and rapid onset parkinsonism should therefore occur following high dose paraquat exposure. Botham: 1517-19

The most significant finding of the study was that high doses of paraquat do not cause parkinsonism in the same way as MPTP. Botham: 1555.

The study authors stated, "[t]he paradigm on which this experimental approach rests assumes that if paraquat were a cause of [Parkinson's disease], it would act in a manner similar to that of MPTP. However, it is possible that paraquat works by a completely different mechanism. If that is the case, the model of acute high-dose exposures may not be relevant." Botham: 1524-25 .

Paraquat and MPTP differ in their ability to cross membranes. Botham: 1517.

Paraquat and MPP+ differ in terms of their transporter receptor binding. Botham: 1526.

While MPP+ and paraquat may look similar and be similar chemically, they do not behave in the same way. Botham: 1528.

There is evidence that shows despite the structural similarity between the two chemicals, paraquat exerts its effect on dopamine neurons in a manner different than MPTP. Botham: 1528-29.

High dose paraquat poisoning would have to kill 60-80% of the dopamine neurons quickly to cause the motor symptoms of Parkinson's disease. Botham: 1530

The patients in the Brent study averaged 22 years of age. Botham: 1544.

The longest post poisoning follow-up was ten years. Botham: 1544.

Syngenta scientist Charles Breckenridge published a study in 2013 that examined the effect of dosing mice with paraquat by i.p. injection. Botham: 1565.

Tyrosine hydroxylase, or "TH", is the key enzyme in the production of dopamine from dopaminergic neurons. Without TH+, the ability to produce dopamine is compromised. Botham: 1565-66.

Cells that produce dopamine have the TH enzyme in them. Botham: 1566.

Independent labs worldwide have shown that paraquat causes a loss of TH+ neurons in the substantia nigra. Botham: 1570.

The Breckenridge study confirmed that at 15 mg/kg, paraquat killed more TH+ neurons than the control MPTP. Botham: 1571.

In a study published in 2014, Syngenta scientist Daniel Minnema reported the results of a 13-week dietary study he had conducted in mice. Botham: 1586-87.

The mice used in the Minnema study were young; in human terms, in their 20s. Botham: 1587-88.

The study found no loss of dopamine or its metabolites and no loss of dopaminergic neurons in the brains of the paraquat treated mice. Botham: 1587.

The study also stated, referencing the Breckenridge study, "[o]ur IP studies using neuropathology, stereology and specific stains for glial activation have failed to replicate previously published findings, even with doses of PQ approaching the maximum tolerated dose…" Botham: 1589.

The Marks studies were not mentioned in the Minnema study. Botham: 1590-97.

According to Dr. Richard Smeyne (Syngenta's own retained stereology expert), the stereologist who did the cell count in both the Breckenridge and Minnema studies was not using the correct procedure and thus counted twice as many cells as actually existed. Botham: 1608, 1617-18.

Getting the cell count right is fundamental and essential to the validity of the study. If the cell count is too high, it will cause the study to underreport brain cell loss due to paraquat exposure. Botham: 1608.

In 2012, before he was a Syngenta consultant, Dr. Richard Smeyne published a study confirming several facts well established in the scientific literature – that paraquat acts as a redox cycling agent to induce formation of free radicals and when administered to mice induces the cardinal symptoms of Parkinson's disease, including the loss of TH+ neurons in the substantia nigra. Botham: 1640-41.

In Dr. Smeyne's study, he found that mice treated with paraquat lost about 50% of the neurons in their substantia nigra compared with untreated animals. Botham: 1642.

After the publication of his 2012 study, Dr. Smeyne was hired as a consultant by Syngenta, tasked with designing experiments to determine whether paraquat was neurotoxic in the C57 mouse. Botham: 1644.

The study used two different stereology methods – 2D and 3D – with Dr. Smeyne's lab using the 2D technology and the same stereologist who performed the stereology for Breckenridge and Minnema using 3D. Botham: 1647.

In 2016, Dr. Smeyne published the results of a study designed to determine whether paraquat treatment caused mice to have an immune response to paraquat, measured by microglial activation. Botham: 1648-49.

Microglial cells are immune cells found in the brain and the spinal cord and are the first responders to defend the central nervous system. Botham: 1650.

Microglial activation is a way of confirming there is genuine pathology, i.e., that cell death is occurring. Botham: 1649-50.

If there is microglial activation, there is a toxin or a damaged cell to dispose of. Botham: 1650-51.

The death of a dopaminergic neuron would signal the activation of microglial cell. Botham: 1651.

Microglial activation is seen because the cells change shape – when at rest they have a small round center with tentacles and when activated they withdraw their tentacles and are more of a larger orb than the resting cell. Botham: 1651.

The study reported that paraquat treatment did not result in microglial activation or loss of dopaminergic neurons. Botham: 1649.

Had the study found microglial activation, it would have increased the likelihood that paraquat was causing the death of dopaminergic neurons. Botham: 1652.

Dr. Smeyne reread the slides to confirm or validate the original assessment of the number of activated microglia performed by another scientist on the team and found that the paraquat treated mice had activated microglia. Botham: 1666-67.

The 2016 study report stated that it used a two-tailed test, because it was assumed that it was equally likely that microglia would be activated by cell death or by a direct cytotoxic effect (the toxin itself killing the microglia). Botham: 1652-53.

There is no evidence that paraquat has a direct cytotoxic effect on microglia. Botham: 1653, 1673.

The test would be one-tailed rather than two-tailed if paraquat doesn't kill microglia directly. Botham: 1673.

Both of the stereologists' microglial counts were statistically significant on the one-tail test. Botham: 1670-71.

Only the two-tailed count was reported. Smeyne RJ, Breckenridge CB, Beck M, Jiao Y, Butt MT, Wolf JC, et al. (2016) Assessment of the Effects of MPTP and Paraquat on Dopaminergic Neurons and Microglia in the Substantia Nigra Pars Compacta of C57BL/6 Mice.PLoS ONE 11(10): e0164094. doi:10.1371/journal.pone.0164094.

"Break the codes" means the data was unblinded and the researcher would be able to see which tissue was treatment and which was control. Botham: 1662.

The results of the Marks studies were never mentioned on paraquat.com. Botham: 1152.

Nonhuman Primate Studies and Communications Regarding Same

Nonhuman primates are more relevant to study Parkinson's disease in humans because they are genetically more similar to human beings. Botham: 738-39; Dixon: 347-48.

In April 2009, Dr. Dino Di Monte presented preliminary results of studies he conducted with paraquat in squirrel monkeys to Syngenta. Botham: 744-45.

Dr. Di Monte reported that the squirrel monkeys were substantially more sensitive to paraquat's toxicity than mice, and that alpha-synuclein was upregulated in the paraquat-treated monkeys. Botham: 747-48; Dixon: 352-54.

Dr. Di Monte also concluded that paraquat treatment reduced the number of neurons that contained both TH+ and neuromelanin, and increased the number of neurons containing only neuromelanin. Dixon: 362-63.

At the time, Syngenta knew that the upregulation of alpha-synuclein is a hallmark of Parkinson's disease. *See* Botham: 748, 1016-7.

In September 2010, Syngenta analyzed brain tissue samples from the squirrel monkeys used in Di Monte's study and found the presence of paraquat. Botham: 822-23, 1752.

The study report, authored by William Ray (a Syngenta analytical chemist), was titled "Analysis of Brain Samples from Paraquat-Exposed Squirrel Monkeys for Residues of Paraquat, Final Report" and is dated 2011. Botham: 1750-51.

Syngenta found paraquat residue in 12 out of the 15 samples. Botham: 1752; Dixon: 388.

Analyzed samples of the tissue from the monkeys' frontal cortex region showed the paraquat concentration did not measurably decline between samples taken two and eight weeks after a fixed program of paraquat dosing. Botham: 826.

The squirrel monkey model is more relevant to man than the mouse model, due to genetic relatedness. Botham: 818-19.

Dr. Di Monte has never published the results of his squirrel monkey studies. Botham: 785, 870.

Dr. Di Monte was at one time an external consultant to Syngenta. Botham: 737.

Dr. Di Monte was an external member of the Paraquat Health Sciences Team at Syngenta. Dixon: 339, 342.

The "brain findings" were the upregulation of alpha-synuclein and the reduction in the ratio of neurons containing TH+ and neuromelanin to neurons containing only neuromelanin. Dixon: 371.

The Stevens study was conducted by a number of scientists either currently or formerly employed by Syngenta as well as two scientists from Ramboll (a consulting company). Botham: 1707-09.

The Ramboll scientists are experts in "PBPK" modeling, or the mathematics that go into estimating the kinetics and distribution of chemicals. Botham: 1709.

The study is titled "Paraquat Pharmacokinetics in Primates and Extrapolation to Humans" and is expected to be published in 2021. Botham: 1710.

Radio-labeled paraquat was administered by intravenous infusion in two doses. Botham: 1714.

There was no pathological analysis of any of the monkeys' organs. Botham: 1715.

After the monkeys were euthanized, their skin was removed. The skin and the remainder of the carcass, including the brain, were put into separate blenders. 10% of the radio-labeled paraquat was found in the carcass. Botham: 1715-16, 1719.

The brain was not separately analyzed and was blended along with the rest of the carcass. Botham: 1719.

82.9% of the paraquat was found in the animals' excreta. Botham: 1716.

That number was calculated by Syngenta scientists, not the independent lab assisting in the study. Botham: 1716-17.

7.1% of the paraquat is unaccounted for. Botham: 1717-18.

The study cannot tell us the specific concentration of paraquat in the monkeys' brains. Botham: 1720.

Nothing prevented the study scientists from removing the brains and actually measuring the amount of radio-labeled paraquat in the brains. Botham: 1723.

Instead of directly measuring the amount of paraquat in the monkeys' brains, the scientists "estimated the amount… with mathematical models." Botham: 1722-24.

They used rodent data to essentially confirm or "validate" the findings of their modeling of concentrations in particular organs. Botham: 1726-27, 1729-30.

The studies relied upon to build the mathematical model are listed in the "parallel" study titled "Paraquat Pharmacokinetics in Rats, Mouse and Dog," also conducted by former/current Syngenta scientists and scientists from Ramboll and pending publication. Botham: 1731-33, 1735.

None of the studies on which they relied used monkey data – only rodents and dogs. Botham: 1748-49.

The scientists from Ramboll were the ones who predominantly created the actual modeling/formula. Botham: 1745.

The Ramboll scientists had regular discussions with Stevens and Travis as the model was being built. Botham: 1746.

Although Syngenta had the data from their own paraquat residue analysis of brain tissue from Di Monte's squirrel monkeys, they did not use it in creating the model for the Stevens study. Botham: 1753.

Defendants' Ability and Efforts to Study Paraquat's Neurotoxicity

1965, there was technology available to do a behavioral study using animals exposed to paraquat for different periods of time, at different doses and by different methods of exposure to investigate whether paraquat caused detectable central nervous system effects. Botham: 623.

In 1965, there was technology available to detect paraquat in the brain tissue of test animals exposed to it. Botham: 624.

In 1965, the technology was available to analyze brain tissue samples from test animals and persons poisoned by paraquat to see if paraquat was present. Patterson 695; *see also* Botham: 624.

In 1965, nonhuman primate studies were feasible. Botham: 626-27; Patterson 697.

In 1965, inhalation studies were feasible. Patterson: 697.

In 1965, lifetime animal tests were feasible. Patterson: 697.

In 1965, the technology existed to investigate whether exposure to paraquat caused any detectable central nervous system effects. Botham: 623.

Even in the 1960s, 2D and 3D stereology techniques existed that would have allowed researchers to count dopaminergic brain cells in the lab, and nothing prevented Syngenta from buying the necessary equipment and hiring a trained stereologist to do so. Botham: 1819.

The same is true of Chevron. Botham: 1820.

So in theory and from a technological standpoint, nothing prevented either company from conducting the same studies that Louise Marks conducted in the early 2000s much earlier. Botham: 1820-21.

In 1965, neurotoxicity would have been available as an endpoint to evaluate in repeat-dose and acute studies of pesticides. Patterson: 657-58.

In 1965, histopathology was available. Patterson: 658.

Toxicologists make judgments as to whether effects seen in animal studies are relevant to humans and, if so, whether it is "the right thing or not to do to market or sell a product." That standard applied in 1965 and applies today. Botham: 555-56.

Nothing in the state of the scientific or technical knowledge prevented Chevron from determining whether paraquat was neurotoxic in 1965. Patterson: 694.

In 1974, ICI and Chevron were aware there was "no experimental evidence to support the contention that there is no chronic effect from continual exposure to [paraquat] spray mist at subacute levels." Botham: 187-88; Patterson: 286-87.

In 1974, neither ICI nor Chevron had done any long-term study of the effects of inhaling paraquat mist. Botham: 188-89; Dixon: 417-19; Patterson: 289.

In 1975, neither ICI nor Chevron had done any long-term studies on the effects of paraquat. Botham: 542; Patterson: 305.

Without such a long term study, a reasonable scientist could not conclude that paraquat causes no long term effects. Botham: 542.

In 1976, scientists employed by ICI and Chevron recognized that the available animal toxicology studies regarding paraquat were "old" and some were "poorly done." Botham: 198; Patterson 01-22-21: 100-01.

Between 1965 and 2003, ICI/Zeneca/Syngenta is not aware of either it or Chevron conducting any neurotoxicity study on paraquat besides a 24-hour rat study conducted by Zeneca in 1995. Botham: 529-30.

A long-term, low-dose study in non-human primates could be used to investigate an applicator's exposure to paraquat, but there is no evidence that either ICI or Chevron have done those studies. Botham: 193, 542-43.

Had either ICI or Chevron wanted to perform a study of chronic exposure, either or both of them could have done long-term study in non-human primates to determine the central nervous system effects. Botham: 542-43, 558.

ICI and Chevron could have done a long-term study on non-human primates when they learned that paraquat got into the brain of humans on ingestion. Botham: 558-59.

In 1975, it was feasible that ICI could have done a non-human primate study in its pharmaceutical division, but it did not. Botham: 192, 199.

ICI could have hired an outside lab to conduct non-human primate studies if it did not have the facilities to do them in-house. Botham: 192.

Syngenta is doing its first non-human primate study now (the Stevens study). Botham: 128-30, 132.

Syngenta has conducted no studies on what amount of paraquat can get into the substantia nigra. Botham: 419-20.

Syngenta has never done any studies to investigate how much brain damage could occur from exposure to paraquat when used as directed. Botham: 156.

Syngenta has never done any studies to determine how much smaller of a dose of paraquat than a "very large dose" would cause brain damage. Botham: 156.

Syngenta has never conducted a study on paraquat's role in the misfolding of alpha-synuclein. Botham: 262-64.

Syngenta has never undertaken a study of alpha-synuclein with respect to paraquat. Botham: 748-49.

Syngenta has never done specific studies to measure alpha-synuclein as a reaction to paraquat. Botham: 734-35.

Syngenta has never done any research to explore the hypothesis that well water causes PD. Botham: 274.

Syngenta has never undertaken any studies longer than 90 days for the observation of specific neurotoxicity end points. Botham: 1443.

Syngenta has never conducted a long-term neurotoxicity study of paraquat where an evaluation of cellular loss in the substantia nigra of the test animal was made. Botham: 1625-26.

There is no record of any paraquat neurotoxicity study being done by Chevron pre-market. Patterson: 125, 658-59.

Chevron did not conduct its own investigation into paraquat's mode of action in animal cells prior to 1965. Patterson: 130.

Chevron did not conduct its own investigation into paraquat's toxicity to mammals or any other animal species prior to 1965. Patterson: 130.

ICI performed all of the premarket toxicological studies on paraquat; Chevron did not conduct any. Patterson: 54, 128, 655.

By agreement in 1964, ICI was to develop and furnish to Chevron the toxicology needed to meet the requirements for obtaining registration of paraquat for sale in the U.S. Patterson: 53.

ICI provided Chevron with the toxicology information to support the U.S. registration of paraquat. Patterson: 53, 83.

In 1965, Chevron relied on ICI to provide the toxicology information regarding paraquat. Patterson: 125-26; Patterson: 653.

ICI bore the primary responsibility of providing toxicological information regarding paraquat and provided multiple studies for Chevron to review and assess. Patterson: 485.

The "compendium" of studies submitted to the EPA in 1987 to support registration of paraquat states that from 1969 to 1976, ICI "handled" the studies and that Chevron was "minimally involved." Patterson: 105-08.

Nothing prevented Chevron from doing its own toxicology studies. Patterson: 290.

Chevron's labs were modern, state of the art and capable of handling most scientific analysis. Patterson: 119.

Chevron never conducted any chronic, meaning one-year or two-year, studies regarding paraquat, nor did it have any conducted for them. Patterson: 110-11.

Chevron never conducted a chronic study of the subacute effects of spray mist of paraquat. Patterson: 289-90.

Chevron never did any specific chronic inhalation studies itself. Patterson: 727-28.

Chevron has never conducted any non-human primate studies. Patterson: 119.

Chevron never conducted a study to determine whether paraquat accumulates in a primate brain. Patterson: 559.

Chevron never conducted a study to determine whether paraquat could get into the human brain. Patterson: 631-32.

Chevron never conducted any studies designed to directly measure whether paraquat passes through the blood brain barrier of humans or any other animal. Patterson: 630-32.

Chevron never conducted a study on paraquat distribution in the brain to evaluate the permeability of the blood brain barrier. Patterson: 195.

Chevron never conducted any studies to investigate how much brain damage could occur from exposure to paraquat. Patterson: 262.

Chevron never conducted a study to try to determine how much smaller the dose of paraquat would have to be than a "very high dose" in order to avoid brain damage. Patterson: 262.

Chevron never conducted studies to prove or disprove the theory that signs of central nervous system effects exhibited by lab animals exposed to paraquat were due to general, systemic toxicity versus neurotoxicity from paraquat. Patterson: 273-74.

Chevron never conducted a specific neurotoxicity study of paraquat. Patterson: 235, 274.

Chevron never conducted any research regarding paraquat's role in the alpha-synuclein misfolding process. Patterson: 229-31.

Growmark does not have and never has had any research laboratories. Powell: 34.

Growmark deals with applied science, but not research science. Powell: 74.

Growmark is not aware of any medical or scientific studies investigating the health effects or safety of paraquat. Powell: 74, 104-05.

Growmark has never asked Syngenta or Chevron for any such studies. Powell: 97, 111.

Growmark has never asked Syngenta for studies proving paraquat is safe to use. Powell: 97-98.

Growmark relies on Syngenta and Chevron to assess the studies. Powell: 108.

Growmark relies on third parties, like Syngenta, to assess the threats to human health from paraquat products. Powell: 93.

Growmark relies on third parties, like Syngenta and Chevron, to assess whether there is an association between exposure to paraquat and any neurological disease, like Parkinson's disease. Powell: 111.

As long as it is an EPA-approved product with a current label, Growmark would sell the product. Powell: 97.

If Growmark learned that paraquat caused Parkinson's disease, it would continue to sell the product if it were still a registered product. Powell: 159.

Growmark believes its obligation to learn about the potential health effects of paraquat extends only to what is stated on the product's label. Powell: 78-79, 108.

Growmark does not believe its role is to learn about paraquat's neurotoxicity, but rather relies on EPA approval of the product and on the product's registrants to provide accurate and honest information to the EPA. Powell: 75-76, 94, 110.

Growmark has no knowledge of and has done no investigation into neurotoxicity of paraquat. Powell: 161.

Growmark has never asked Syngenta for studies regarding paraquat's potential neurotoxicity and does not know if they exist. Powell: 110.

Growmark was not aware that paraquat is regarded as the most probable environmental toxicant for Parkinson's disease in the U.S. Powell: 120.

Growmark never asked Syngenta or Chevron about whether there were any long-term effects to farmers from paraquat exposure. Powell: 154.

Defendants' Ability and Efforts to Conduct Epidemiology Studies

It is Syngenta's position that only human epidemiological evidence can lead to a definitive conclusion about causality. Botham: 453.

In 1975, scientists employed by ICI and Chevron recognized the need for a "critical epidemiology study" and a "long term toxicity study using sprays on animals." Botham: 189-90; Patterson: 292-93.

In 1975, an ICI scientist suggested in correspondence to Chevron that a study be conducted in which a large cohort group exposed to paraquat over a long period would be medically followed for several years, but Syngenta is not aware of any such study being done. Botham: 550.

In 1975, ICI stated in correspondence to Chevron that it had never followed up on a case of a person who recovered from paraquat poisoning for more than a few weeks. Patterson: 304; Botham: 539-40.

At any time between 1965 and 1986, Chevron could have designed an epidemiological study that monitored paraquat users long term to determine paraquat's effect on their health. Patterson: 698.

The 1981 Howard study of 27 spraymen was conducted because ICI was concerned about the long-term health hazards of occupational exposure to paraquat spray mist. Botham: 1692-93, 1695-96.

All of the participants in the study were male and all the spraymen averaged 3-5 years of spraying, which the study defined as "long-term." Botham: 1698.

Spraymen were defined as those who sprayed pesticides a minimum of 1,000 hours, but the study acknowledges that because the men sprayed a number of herbicides, they did not know how much paraquat was sprayed in those 1,000 hours. Botham: 1698-99.

16 out of the 27 spraymen in the study's test group were under the age of 34. Botham: 1701.

"Selection bias" in epidemiology means you are not necessarily selecting a full cross section of the population, for example. Botham: 1703.

The Howard study was not intended to focus on Parkinson's disease or any specific neurotoxicity endpoint. Botham: 1705.

The Howard study was not designed and does not directly inform us on anything concerning the neurotoxic effects of long-term paraquat spraying. Botham: 1706.

It was not the intention of the Howard study to tell us anything about long-term exposure to paraquat potentially causing Parkinson's disease. Botham: 1706-07.

Many epidemiological studies have found an association between paraquat exposure and Parkinson's disease, including multiple studies finding a 2- to 5-fold or greater increase in the risk of Parkinson's disease in populations with occupational exposure to paraquat, compared to those without such exposure. Botham: 217-18.

In 2011, Syngenta published its first epidemiological study on the relationship between paraquat and Parkinson's disease, using workers from its own plants employed in the paraquat production process. Campbell: 128, 132.

Growmark is not aware of epidemiological studies showing a higher incidence of Parkinson's disease among persons who live or work in geographic areas where paraquat is used and has never researched whether such studies exist. Powell: 100-01.

Growmark relies on Syngenta to conduct epidemiological studies, but does not know what studies Syngenta has conducted and has never asked for them. Powell: 102.

Occupational Exposure to Paraquat and the Use of Personal Protective Equipment, Defendants' Knowledge Thereof and Studies Related Thereto

Environmentally relevant routes of exposure to paraquat by human users are dermal, inhalation and ingestion. Botham: 1223-24.

ICI and Chevron knew before they ever put paraquat on the market that people who mixed, loaded and applied paraquat and those nearby when it was applied would be exposed to the chemical. Botham: 156, 203-04.

Growmark knows that people who mix, load and apply paraquat and those nearby when it was applied could be exposed to the chemical. Powell: 146.

ICI knew that paraquat users/nearby bystanders would be exposed to spray drift, contact with plants, during maintenance of equipment and during the process of mixing, loading and spraying. Botham: 203-04.

A worker using paraquat as contemplated by Syngenta and who is out spraying it in his farm fields is going to get some amount of paraquat in his brain. Botham: 1009.

In 1969, an ICI scientist named Swann published the results of two exposure studies (field trials conducted in Malaysia in 1965 and 1967) designed to examine the average conditions of spraying by agricultural workers in the real world. The 1965 study observed the fact that workers generally wore "light clothing" due to weather conditions and that the estates on which they worked did not typically provide "more elaborate protective clothing." Ouzts: 53-60; *see also* Patterson: 588-90.

In the 1967 study, the study subjects were divided into four groups, with one group wearing their normal clothing during the spraying process and the other three groups wearing one of the

following combinations of protective equipment: boots and gloves, gloves and mask, boots and mask. Ouzts: 53-60; Patterson: 600-01.

A small amount of paraquat was detected in every worker's urine at some point during the 12-week spraying period. Ouzts: 53-60; Patterson: 601-02.

In 1974, Chevron and ICI were aware of concerns by California regulators of "possible long term chronic effects of workers licking small quantities of paraquat daily from their lips and/or breathing in low doses via small droplets from spray mist." Botham: 186-87; Patterson: 284-85.

Another paraquat exposure study commissioned by ICI and Chevron in 1980 reported that agricultural workers in real world situations regularly come into contact with paraquat by touching contaminated spraying equipment with their bare hands. Ouzts: 67-71.

Paraquat residues were detected in the urine of nine out of the nineteen spray operators and one of the seven carriers in the 1980 study. Ouzts: 71-72, 75; Patterson: 611-12.

In 1995, Zeneca commissioned a study of workers in pecan orchards in the U.S. to understand their exposure based on their application methods. Part of the study observed what the workers wore during spraying after being told to wear the normal attire they would use for their application methods. Slightly more than half of the workers did not wear gloves and only four wore face shields. Ouzts: 87-94.

They were not following label-recommended instructions for the use of personal protective equipment (or "PPE"). Ouzts: 93-94.

The study report included photos of the workers taken during the study. Three photos showed study subjects mixing paraquat with no PPE; one photo showed a man securing the lid on a container of paraquat with his bare hands (no gloves); and another shows a man rinsing out a container of paraquat with his bare hands (no gloves). Ouzts: 94-97.

The study report also included written observations about worker behavior, including bare hands touching contaminated equipment; hands not being washed during the exposure period; making phone calls in the middle of spraying operations; smoking cigarettes during the exposure period; splashing paraquat onto clothing; and eating lunch while on the tractor spraying. Ouzts: 101-05.

In an occupational exposure study published in 1996, Costa Rican banana workers were observed touching contaminated equipment with their bare hands; clearing spray nozzles by blowing them out; eating, drinking, smoking and biting their nails without washing their hands; and not showering immediately after work. Ouzts: 107-09.

In a 1997 study commissioned by Zeneca of workers in Spanish citrus orchards, while the researchers noted "minor deviations" from the label recommended PPE, the workers were required as a condition of the study to wear face shields and gloves while mixing and loading

paraquat. Paraquat was detected in the urine of eighteen of the twenty study subjects. Ouzts: 111-17.

A "respirator" means a dust/mist filter, not a gas mask. Dixon: 493-94.

By the mid-1990's, Syngenta was aware that it was likely small amounts of paraquat would get into the brains of paraquat users doing their jobs. Botham: 1157.

In a 2007 Syngenta-sponsored study, workers were instructed to wear what they normally would during spraying operations. Two of the workers did not wear gloves; six did not wear respirators. Observations of worker behavior included paraquat splashes on worker coveralls, shoes and sprayer; windows left open in tractor cab and heavy smell inside cab; workers touching contaminated equipment with bare hands; and a worker walking onto a treated plot. Ouzts: 128-38.

Study subject 102, who wore Tyvek-type coveralls, rubber gloves and respiratory protective equipment while working with paraquat, showed detectable levels of paraquat in his urine. Ouzts: 142-45.

Study subject 109, who wore a respirator and a working coverall while working with paraquat, showed detectable levels of paraquat in his urine. Ouzts: 143-45.

In another 2007 exposure study sponsored by Syngenta France, fifteen experienced agricultural workers were observed applying paraquat according to their "habitual or typical" work practices, or "as is." Some wore gloves; others did not. Some wore boots; others wore heavy work shoes or sports shoes. "Most" wore shorts and t-shirts, leaving lower legs and forearms uncovered. Only one wore a respirator. Ouzts: 145-50.

Observations included workers touching paraquat contaminated equipment with their bare hands; workers touching their faces with contaminated gloves; paraquat splattering; workers walking onto treated weeds; workers drinking water from a bottle with contaminated gloved hand; and a worker answering a phone call while spraying and on rest. Ouzts: 150-52.

Another "as is" exposure study from 2007 sponsored by Syngenta France observed inconsistent use of PPE, with many workers not wearing gloves or respirators while handling paraquat; workers handling contaminated equipment with their bare hands; and workers spraying in front of them and walking through paraquat-treated areas. Ouzts: 154-66.

Two of the four workers who wore respiratory equipment had paraquat in their urine. Ouzts: 169-71.

Another 2007 study sponsored by Syngenta France observed inconsistent use of PPE, with many workers not wearing gloves and only one wearing a respirator while handling paraquat; workers handling contaminated equipment or weeds with their bare hands; workers spraying their boots/shoes and themselves with paraquat; one worker using a mobile phone while spraying; and several workers walking through paraquat-treated areas. Ouzts: 174-84.

Study subject No. 9, who wore respiratory equipment, gloves, boots, trousers, shirt and a Tyvek overall, had detectable levels of paraquat in his urine. Ouzts: 184-85.

In the final 2007 occupational exposure study sponsored by Syngenta France, workers were instructed to use the PPE directed on the product label, and such equipment was provided to the subjects by Syngenta. Even wearing all of the PPE required by the label, ten of the fifteen subjects tested positive for paraquat in their urine. Ouzts: 187-97.

If paraquat is in the urine, it is being excreted by the kidneys, which means it is in the blood system. Ouzts: 59-60, 71-73, 171; Patterson: 591-92, 599-600.

All of these studies show "similar" or "consistent" trends in how farmer applicators use paraquat no matter in the world where they are located. Ouzts: 137, 152-53, 159, 165-66.

Syngenta has been aware since the 1960s that spray nozzles become clogged during paraquat spraying operations. Ouzts 09-28-20: 121-22.

Syngenta is aware of "some instances" where respirators were not worn by paraquat applicators and has been since the product was first on the market. Ouzts 09-28-20: 51-52.

Through its own studies, Syngenta has been aware since the mid-1960's that at least some percentage of paraquat applicators were not wearing respirators. Ouzts 09-28-20: 55, 144.

Syngenta has not undertaken studies to determine the percentage of paraquat users who wear rubber gloves. Ouzts 09-28-20: 68.

Syngenta has not undertaken studies to determine the percentage of paraquat users who wear respirators. Ouzts 09-28-20: 68.

Syngenta's position on the use of respirators has vacillated at times, sometimes taking the position with regulators that respirators were not required. Ouzts 9/28/20: 70, 71.

Chevron realized the fact that persons would not always wear the label-recommended PPE was a "potential issue." Patterson: 517.

In 1965, Chevron submitted a document to the U.S. Dept. of Agriculture observing that trained paraquat sprayers in El Salvador were not wearing any "specific protective clothing" and were "normally dressed." Patterson: 519-20.

Correspondence between Chevron and ICI indicates ICI was also aware of how paraquat products were actually being used in El Salvador in 1965. Patterson: 522-23.

1965 correspondence between Chevron and ICI discusses a field investigation in which it was observed that the workers wore gloves and goggles only when handling

paraquat concentrate and otherwise wore their ordinary work clothing when carrying out spraying operations. Two of the four men in the study spilled concentrate on their skin of their forearms during operations. Patterson: 525-26.

Chevron knew it was a possibility that to some extent there would be some individuals who would not follow the instructions on the label regarding the use of PPE, including that users would not always be wearing gloves. Patterson: 735-36.

Chevron participated in only one exposure study during the 21 years it sold paraquat in the U.S. Patterson: 535.

In all the years that paraquat's been applied, Growmark associates have never gone out and watched the farmers apply the product. Powell: 204.

Growmark has never done any investigation to determine whether there is strict adherence to the warning labels in the application of paraquat. Powell: 208.

Internal ICI correspondence from 1971 states, "one realizes only too well that farmers do not invariably follow label directions…" Dixon: 409-11.

Following three 1983 meetings of numerous ICI employees regarding efforts to increase paraquat sales in the Americas, ICI put together a document to be used as a handout to distributors to help them answer questions going forward. The Q&A section includes a question about the difference between normal use and recommended use that acknowledges "users will not always follow our recommendations. Misuse is a problem for all products." Ouzts: 77-82.

In that same document, another question asks, "What is normal exposure?" ICI's answer was that from the Malaysian study where paraquat was applied for "long periods (up to 13 years), spraymen did not wear anything like full protective clothing: in some cases they wore virtually no clothing at all. These people did not come to any harm and their health was perfectly normal." Ouzts: 82-83.

The spray method of application providing the most protection to users is via equipment with a closed cab and filtered air; the least protection is provided by backpack sprayers. Ouzts 09-28-20: 106-07.

Syngenta is aware that there is variability in the spraying equipment used in applying paraquat. Ouzts 09-28-20: 109.

Syngenta has never told users they should use a certain type of equipment when applying paraquat. Ouzts 09-28-20: 108-09.

Syngenta is aware that some farmers use open air tractors without enclosed cabs to spray paraquat. Ouzts 09-28-20: 76.

Syngenta has never warned users they should not use open air equipment to spray paraquat or that they should wear a respirator if they do. Ouzts 09-28-20: 110.

Syngenta is not aware of having told any paraquat user that wearing a respirator will protect against neurotoxicity. Ouzts 09-28-20: 59.

Knowing paraquat can be ingested in small amounts, Syngenta does not allow its workers to eat, drink or smoke in the work place. Campbell: 64; 101-02.

The manufacture of paraquat is an entirely closed process to make it impossible for plant workers to be exposed the chemical in the absence of deliberate contamination. Campbell: 64-65.

Syngenta employees involved in the paraquat manufacturing process are required to wear overalls/coveralls; steel toe, chemical resistant boots; safety glasses; rubber gloves and a hard hat. Campbell: 69, 93-94.

A face shield is also required for employees working in the formulation, filling, and packing process because that is the only time a worker would come in contact with paraquat. Campbell: 70.

At various times, Syngenta has required its employees involved in the manufacture of paraquat to wear respirators or respiratory protection. Campbell: 71, 74, 92.

Defendants' Warnings - On the Label or Otherwise - Regarding the Dangers of Paraquat

The registrant is responsible for submitting a label to the EPA that includes precautionary statements, warnings and directions. Dixon: 328-30.

A registrant can propose or request any language it wants included on the label to the EPA, and the EPA makes the final determination as to what is or is not allowed on the label. Dixon: 330-32.

The EPA's Office of Pesticide Programs does not conduct any testing or suggest label changes except as required by its mandate. Dixon: 332.

The EPA does not actually endorse a particular product for a particular use; the EPA simply registers products. Dixon: 334.

Chevron would have had more of a leading role in the creation/content of the label until the 80s, then ICI would have had the prominent role. Dixon: 398-99.

ICI objected to Chevron's proposal to add a skull and crossbones to the label in correspondence dated May 1966. Dixon: 401-03.

Defendants have changed the safety instructions and directions for the use of personal protective equipment on the labels of their products many times since 1965. *See generally*, product labels, collected at Bates ranges listed on Exhibit 20.

The overall hazards expressed on the labels were consistent from 1969 through 1986. Patterson: 717.

The 1968 Ortho Paraquat CL label does not instruct users to wear gloves or a respirator when spraying paraquat, there is no skull and crossbones on the label, the focus is on acute use injury, and there are no warnings of cumulative effects or potential neurotoxic effect. Dixon: 404, 406-07.

In 1974, ICI had a meeting with Chevron concerning proposed label changes. ICI's notes from that meeting indicate ICI believed a label warning about using goggles and a respirator while spraying might have repercussions on non-U.S. markets, but that it was unlikely they could persuade Chevron the precaution was unnecessary. Dixon: 413-16.

Chevron's notes from the meeting indicate that legal believed "there were many shortcomings in the label" and that toxicology believed "the lack of chronic inhalation toxicity information and epidemiological surveys were a definite weakness in properly evaluating the safety of paraquat use… but Dr. Fletcher of ICI "felt confident" a worker-hazard study then being conducted "would demonstrate that paraquat is safe and minimal amounts are absorbed by workers after prolonged usage." Dixon: 422-3.

The Chevron notes of the meeting also indicated that ICI stated "respirator and goggles need not be worn at all times when spraying paraquat." Dixon: 423-24.

The 1974 Ortho Paraquat CL label now requires the wearing of a full face shield (in addition to gloves and apron) when handling the concentrate and the wearing of "goggles and approved face mask capable of filtering spray droplets when spraying." It advises users to "avoid spray mist." Dixon: 424-26.

In 1981, an agricultural worker named Richard Ferebee sued Chevron (as the manufacturer of paraquat) alleging he developed pulmonary fibrosis due to occupational exposure to paraquat. *Ferebee v. Chevron Chem. Co.*, 552 F. Supp. 1293 (D.D.C. 1982), *aff'd*, 736 F.2d 1529 (D.C. Cir. 1984).

In response to the Ferebee lawsuit, Chevron proposed adding new warnings to the label, including that paraquat "may be harmful or fatal if absorbed through the skin or inhaled," and "…strictly follow all these rules as if your life depended on it." SYNG-PQ-13120362 (emphasis in original).

A 1983 "confidential" communication from ICI's G A Willis (Manager, Product Safety and Registration Group) regarding Chevron's proposed label changes indicated that although Willis was "not very happy" with the changes, they "do not alter the overall appearance of the label and

they are likely to go unnoticed by all but those who have a specific effort to compare the old and new texts in detail." *Id.*, *see also* Dixon: 439-43.

The same communication indicates ICI's objection to Chevron's lawyers' idea of circulating a letter to distributors drawing attention to the change , stating it would cause "immense problems" for both companies and "without such a letter the label changes would pass mainly unnoticed." The communication also indicates that Willis "would place a high priority in seeking to persuade [Chevron's senior level people] not to circulate any such note." Dixon 443-44.

The Gramoxone paraquat label contained a number of warnings, including, "Wash splashes from skin and eyes," "Remove and wash contaminated clothing," "ash before eating, smoking or drinking," "Wear full face shield, rubber gloves, and apron when handling or mixing concentrate," "Avoid working in spray mist. If there's a risk of exposure, wear goggles and a full face mask capable of filtering spray droplets," and "Wear waterproof footwear and clothing when spraying or when contacting vegetation wet with spray." Dixon: 427-35.

The warnings, as written, were not targeted to any neurotoxic effects. Dixon: 437, 460-61.

None were designed to warn against potential latent effects of paraquat. Dixon: 461.

They were designed to prevent acute, day-of-event worker exposure. Dixon: 460-61.

For the first time in 1986, the Gramoxone Super label included a new warning: "Keep all unprotected persons out of operating areas or vicinity where there might be danger of drift." Dixon: 456-57.

The intent of the respirator or dust mask requirement was to prevent the particles from creating nasal irritation/nosebleeds. Dixon: 459-60.

A Gramoxone Super brochure from the mid to late 80s that was designed to communicate information to users regarding the new product, states that when used according to label directions, the product "poses no undue risk to agricultural workers or neighboring individuals..." Dixon: 462-63, 467.

The brochure also states that its a "myth" that Gramoxone Super causes Parkinson's disease and that "There is absolutely no scientific evidence that Gramoxone Super can cause Parkinson's disease." Dixon: 468.

That is not Syngenta's position now. "There is evidence out there..." that "there is a potential for paraquat use to be associated with potential etiology of Parkinson's disease." Dixon: 469-70.

The brochure also states it's a "myth" that workers always had to wear special clothing to protect themselves from exposure to Gramoxone Super. The brochure stated it was a "fact" that "after mixing... diluted Gramoxone Super poses no serious risk to spray operators as a result of

absorption through the skin, though prolonged contact with skin can lead to irritation. Once mixed, only waterproof footwear and work clothing need to be worn." The brochure went on "it's a good idea to keep rubber gloves handy in the event that a nozzle or equipment adjustments are necessary." Dixon: 472-73.

The brochure states that the statement "paraquat accumulates in the body" is a myth, and that the "fact" is paraquat "is not stored or accumulated in body fat," and "paraquat that may have been absorbed in the blood is rapidly and effectively eliminated in the urine by the kidneys." Dixon: 473.

The Gramoxone Extra label from 1992 contains a new warning – users are to wear a NIOSH/MSHA-approved pesticide respirator when pouring, loading or mixing concentrate or when exposure to concentrate is possible. Dixon: 476.

The mask was not designed to guard against spray mist getting into the deep lung or passing into the bloodstream though the alveolar structures; the respirator requirements were addressing nasal irritation. Dixon: 481-82.

Nothing on the label suggests users should wear a respirator or gloves when spraying. Dixon: 482-83.

It was Syngenta's position in 1992 and remains its position today that respirators are not necessary for applicators because agricultural sprays do not produce droplets small enough to get into the deep lung. Dixon: 487-88.

It was Syngenta's position in 1992 that waterproof footwear, disposable suit/coveralls or long-sleeved shirt and pants and a wide brimmed hat were "adequate" protection and that the addition of protective eyewear, a respirator and chemical resistant gloves was "excessive." Dixon: 489.

In 1996 or 1997, Zeneca (a predecessor to Syngenta) removed the requirement of the dust/mist filtering mask from the label. Dixon: 496-97; Ouzts: 110.

There is no respirator requirement on the 1999 label. Dixon: 500-01.

In 2001, the EPA again required use of dust/mist filtering respirators by paraquat applicators and handlers, because the public literature reported that nosebleeds and other forms of respiratory irritation could occur without proper respiratory protection. Dixon: 501-02.

The respirator requirement has been on the label since 2001. Dixon: 501-04.

Syngenta does not now and never has mandated the use of a closed-cab during application; the use of a closed cab has been recommended on the labels since 2001, but is not mandated. Dixon: 514-15.

Syngenta's consistent position has been that inhalation exposure is not a relevant risk to workers, so it is Syngenta's position that applicators do not need to wear masks. Dixon: 520-21.

The requirement to wear a dust/mist filter was due to reported incidents of nosebleeds and upper respiratory irritation, not due to concerns over neurotoxicity. Dixon: 522-23.

Internal Syngenta emails from 2002 state, "we are steadfast in our resolve to get this dust/mist filter requirement off the label" and that Syngenta was working to have that requirement replaced with "directions more pertinent to reducing applicator exposure," for instance, avoiding contact with the nose by contaminated fingers. Dixon: 526.

In 2003, Syngenta released a Q&A document stating that under normal use, with "minor predictable deviations," the product is safe to users and bystanders and that the "operator does not need any special protective clothing." Dixon: 529.

The document goes on to state that "we advise normal work wear for spraying Gramoxone" and that the "skin is actually an excellent barrier to paraquat and the product has no vapor pressure to allow it to be inhaled." Dixon: 531.

The document also states, "There is no scientific or reliable epidemiological evidence to link paraquat with Parkinson's disease" and that "previous studies have demonstrated that paraquat does not cross the blood-brain barrier easily." Dixon: 537.

In a companion document, it is stated, "simple protection, provided by work clothes and boots, is sufficient." Dixon: 541.

Syngenta does not believe a face mask or dust/mist filter is warranted, but included it on the U.S. labels because the EPA mandated it. Dixon: 533.

Syngenta has not initiated any research to examine the effectiveness of its warnings or labels. Dixon: 546.

Syngenta has not undertaken studies to determine how users understand the labels. Ouzts 09-28-20: 65.

Syngenta has never done any analysis of how many people actually follow label directions or warnings. Dixon: 547.

Syngenta and Chevron have never specifically warned that there is any neurotoxic risk, including the risk of Parkinson's disease, associated with exposure to paraquat on the labels of their products or otherwise. *See* Patterson: 566, 718-19; *see also* Powell: 195; Dixon: 396-97, 437-38.

Syngenta never warned paraquat users that paraquat could get into their brains. Botham: 1162.

Paraquat.com never stated that paraquat will get into users' brains when used as anticipated. Botham: 1164.

Syngenta has never warned U.S. users about any long-term chronic effects from exposure to paraquat. Dixon: 438.

During the 20 years it sold paraquat products, Chevron had more information about paraquat's toxicity than its customers or the general public. Patterson 01-22-21: 80.

Chevron never warned users about any possible central nervous system effects from the use of paraquat. Patterson: 719-20.

Chevron never warned paraquat users that high doses of paraquat could cause brain damage. Patterson: 261-62.

Chevron never put a warning on its paraquat labels that its toxic effects are cumulative and delayed. Patterson: 557.

Growmark has never told its crop specialists to warn farmers who buy the product about paraquat's long-term health effects, or that paraquat is a neurotoxic hazard and could cause Parkinson's disease. Powell: 92-93.

Growmark never warned users that paraquat can cause brain damage. Powell: 153.

Growmark never warned users that exposure to paraquat can cause Parkinson's disease. Powell: 153.

Growmark never warned users that exposure to paraquat can cause neurotoxicity. Powell: 154.

Other than providing the product with the label on it, Growmark has never afforded any instruction or any other safety warning or safety-related information to farmers who buy paraquat. Powell: 211-12.

Paraquat's Acute Toxicity/Emetic

Paraquat is an acutely toxic or highly poisonous compound when ingested orally, even in small doses. Botham: 91-92, 1254-55; Ouzts: 24-25; Patterson: 174.

15 ml is the lowest dose of paraquat that could cause lethality in humans. Patterson 01-22-21: 123.

Diluting the paraquat product would make it less toxic. Botham: 1413.

There is no antidote to paraquat poisoning. Botham: 92, 1185; Patterson: 547-48.

The skull and crossbones (or poison) symbol was added to paraquat labels in the 1968-69 time period. Patterson: 543, 716-17.

A "high number" of people have died from acute paraquat poisoning by accidental and intentional ingestion since paraquat came on the market. Botham: 1257; *see also* Patterson: 174-75.

Emetics are compounds designed to induce vomiting in poisoning victims quickly enough to eliminate the poison from the body before the body absorbs a lethal dose. Botham: 1261-62, 1778; Patterson: 40.

Between 1968 and 1972, ICI's pharmaceuticals division was attempting to develop a compound called "PP796" as a drug for the treatment of asthma and undertook clinical trials. Patterson 01-22-21: 132.

That effort was abandoned in 1973 when it became clear following human clinical trials conducted by ICI scientist Dr. P.F.C. Bayliss that PP796 "had a variety of unpleasant side effects (nausea, vomiting, dizziness, flushing) at low doses," appeared to induce angina pectoris in two patients in later stages, and because "no beneficial effect [was] seen in the pilot studies." SYNG-PQ-14420786_R at 5.

PP796 was also known as ICI 63197. Patterson 01-22-21: 161-2.

Around the same time, Chevron and ICI became concerned that regulators would take action against paraquat's registration due to the rising number of deaths from acute paraquat poisoning and thus considered adding an emetic to formulated paraquat products. SYNG-PQ-02508147; SYNG-PQ-01843764.

ICI assigned Dr. Michael Rose to head a study group for this purpose in January 1976. SYNG-PQ-02450112.

On February 9, 1976, Dr. Rose issued a report from the study group, which had considered a number of known emetics, including PP796. SYNG-PQ-02450023.

PP796 was described as "a potent, centrally acting emetic, causing vomiting in man with oral doses of the order of 5mg." SYNG-PQ-02450023.

A March 1976 ICI memo outlined a program to obtain EPA clearance for the use of PP796 as an emetic in paraquat products by 1977. SYNG-PQ-02450073

The Bayliss data was the only clinical trial human data available regarding PP796. Patterson 01-22-21: 185-86.

The entirety of the human data on PP796 is the Bayliss clinical data included in Rose's assessment/report. Patterson 01-22-21: 163-64.

The Rose report is based 100% on Bayliss's 1973 analysis of the human trials with PP796. Patterson 01-22-21: 231.

The Rose report was the only data provided to Chevron regarding the emetic. Patterson 01-22-21: 135.

The only human data Chevron had regarding PP796 was the 1973 results of the clinical trials authored by Dr. Bayliss. Patterson 01-22-21: 163-64.

Dr. Richard Cavalli was a Chevron toxicologist who was involved with paraquat at the time. Patterson: 29, 298.

He was the key toxicology contact at Chevron for ICI. Patterson: 78.

An internal Chevron document indicates that Dr. Cavalli believed "the survival rate of ingestion cases may not be significantly improved" by inclusion of the emetic as proposed. Patterson 01-22-21: 156-57.

Dr. Cavalli noted, "there are serious discrepancies between the actual data provided and what [ICI] has been telling us verbally." Patterson 01-22-21: 157.

In correspondence from August 1976, Dr. Cavalli noted that ICI had stated the recommended emetic concentration would produce emesis within 15 minutes in 80% of the people, but based on his review of the Bayliss data, the data did not support this statement and no one in the study vomited within 15 minutes. Patterson 01-22-21: 164-65, 175-77, 184-85.

Dr. Cavalli also noted that the dose recommended to be included in paraquat formulations was "significantly lower" than the dose found effective in dog and monkey and that the data did not support what ICI had told him – that PP796 was more active in humans. Patterson 01-22-21: 176-77.

Cavalli's opinion was that further human testing should be done to substantiate the effectiveness of Rose's recommended dose. Patterson 01-22-21: 179.

An October 1976 draft of the Rose report states that the recommended concentration of PP796 would induce vomiting in 70% of those ingesting a lethal dose of paraquat within an hour. Patterson 01-22-21: 184.

Between August and October 1976, ICI went from claiming the recommended emetic dose would produce vomiting in 80% of people within 15 minutes to 70% of people within an hour but there was no additional human data provided by ICI that would support that change. Patterson 01-22-21: 185.

Later in October 1976, Dr. Cavalli raised the issue with Dr. Rose, indicating his belief that the argument that 5mg of the emetic was an effective dose was "weak" and does not support the statement emesis will occur in 80% at 15 minutes, that the EPA would likely require "actual data" regarding the effectiveness of the dose recommended and that they conduct further human clinical trials. Patterson 01-22-21: 192-93.

Rose wrote back that the clinical data on PP796 was "certainly weak," but that they could not conduct the further human trials Dr. Cavalli suggested for ethical reasons. Patterson 01-22-21: 194.

In November 1976, Cavalli again wrote to Rose indicating the arguments were sufficient to send to the EPA with Chevron's first submission, but that the EPA may well request additional data demonstrating the dose/effect relationship of PP796 as an emetic in man. Patterson 01-22-21: 218.

A November 1976 internal memo between Chevron employees indicated that toxicology raised questions about the effectiveness of the recommended dose, but that "subsequent correspondence with [ICI] have confirmed that the recommended rate of the emetic agent represents as good a proposal as possible based on available information." Patterson 01-22-21: 219-20.

The data on which ICI estimated the amount of emetic that needed to be included in its paraquat products in order to be effective was "weak." Botham: 1403-04.

Dr. Cavalli, with input from his staff, recommended that the emetic concentration suggested by Dr. Rose be accepted as an adequate dose, but Chevron Chemical ultimately would have made the decision. Patterson 01-22-21: 136-37.

Chevron was completely independent and could do it thought was best. Chevron did not have to do what ICI told it to do. Patterson 01-22-21: 212.

A latter communication from ICI indicated that ICI's overseas companies would commence discussions with regulators with the objective of ensuring ICI's emetic (PP796) was the sole paraquat formulation allowed to be sold. Patterson: 1-22-21: 216-17.

ICI and Chevron began including an emetic in the Ortho paraquat sold in the U.S. in 1982 or 83. Patterson: 39-40; *see also* Dixon: 268.

PP796 is the only emetic ICI/Syngenta has ever used. Dixon: 282; Patterson 01-22-21: 162.

The paraquat concentrate came to Chevron from ICI with the emetic and stenching agent added, but Chevron diluted it with water to meet the product specifications and added a defoamer. Patterson 01-22-21: 49-51.

Chevron did not undertake any independent studies on PP796. Patterson 01-22-21: 117-18.

Chevron did not undertake any studies on any other emetic to be used in conjunction with paraquat either. Patterson 01-22-21: 118.

Chevron never did a human trial to estimate the level of emetic necessary to prevent someone who ingested the minimum lethal dose of paraquat from dying. Patterson 01-22-21: 130.

There is no regulatory reason why Chevron would have been restricted from suggesting that 3x Rose's recommended amount be included in formulated products. Patterson 01-22-21: 222-23.

The animal studies indicated that increasing the dosage of emetic would not be hazardous to the person ingesting it. Patterson 01-22-21: 238.

While the chemical added as an emetic has not changed, there have been changes to the level of emetic over the years and generally speaking, the emetic level has somewhat increased over time. Botham: 1789.

It is likely that increasing the dose of the emetic would increase the response. Patterson 01-22-21: 221.

From the 1980's through 2005, the emetic concentration in Gramoxone Max or comparable end-use products was .5 grams per liter. Dixon: 270-71, 273-74, 328.

The dose of emetic in formulated paraquat products is .107 mg/kg whereas the study referenced in the Rose report indicates the monkeys were dosed at 2 mg/kg or 20x higher. Patterson 01-22-21: 124-26.

In 2005, Gramoxone Max was replaced with Gramoxone Inteon, which included 1.5 grams of emetic per liter of end-use paraquat product. Dixon: 269-71, 274.

In addition to a 3x increase in the amount of emetic, Gramoxone Inteon also included an alginate and a purgative, all to try to improve the survivability of oral ingestion of the concentrated product. Dixon: 276.

The purgative was magnesium sulfate and it was designed to flush anything out that may have gotten into the small intestine. Dixon: 277.

Inteon was replaced by Gramoxone SL2.0 in 2011 or 12. Dixon: 277.

The only significant difference between Inteon and SL2.0 was the removal of the alginate. Dixon: 277-78.

The alginate was removed because the manufacturer went out of business and because studies in dogs showed the alginate did not help to reduce the concentration of paraquat in the blood. Dixon: 278.

The purgative may also have been removed then. Dixon: 281.

"CSF" are confidential statements of formula and are required to be submitted to the EPA to establish the contents of the formulations. Dixon: 272.

They tried to meet the emetic requirements in the Food and Agricultural Organization of the United Nations specifications. Dixon: 292.

Competing products may contain higher levels of emetic, for instance Parazone and Firestorm are believed to contain 2.5g per liter. Dixon: 295-96.

There are 20-25 different paraquat products on the market currently – "probably less than 30, but closer to 30 than 20." Dixon: 296, 448.

Since 2006, Syngenta's paraquat products have included nearly triple the emetic concentration or ratio of paraquat to emetic. Dixon: 32-37.

The amount was increased because it was believed that a higher emetic level would allow it to get to the brain faster, thus causing emesis faster. Dixon: 287.

According to a former Syngenta scientist named Jon Heylings, ICI knew in 1977 that the emetic concentration proposed for Defendants' paraquat products would be ineffective and that the concentration was based on falsified data. *See* Declaration of Jon R. Heylings, Ph.D. (and attached exhibits); *see also* Botham: 1392-93; Dixon: 31-32.

Heylings had raised the issue with Syngenta on more than one occasion, beginning in 1990 and also more recently in 2019. Botham: 1390-92.

Heylings' allegations have never made it into the public domain. Dixon: 46-48.

Since around 2003, Syngenta has maintained some kind of database tracking adverse health incidents resulting from paraquat exposure. Botham: 1774.

Prosar was the outsourced database that covered the Americas and North American incidents. Botham: 1782-3.

In America, in the event of an accident or incident with one of Syngenta's products, the container contains a telephone number that puts the caller in touch with Prosar. Botham: 1783.

The "AHI" or adverse health incident database was something similar for the rest of the world. Botham: 1784.

The information in that database was not necessarily gathered from callers, but rather came from a variety of sources – a global network of poison centers. Botham: 1785-86.

The AHI-Prosar report contains over 10,800 entries for adverse health incidents involving paraquat since 2003 – 20 years after the emetic was added. Botham: 1787.

Based on the AHI-Prosar report, over 3,500 persons died from their exposure to paraquat since 2003. Botham: 1799-800.

Syngenta is not legally allowed to sell paraquat in 70 countries around the world, including all member nations of the European Union and China. Syngenta's Response to Request to Admit Facts; *see also* Botham: 483-85, 1210-11.

Growmark was aware that foreign countries had banned paraquat, but never tried to find out why. Powell: 142-43. That is not Growmark's role. Powell: 143.

In the U.S., paraquat is a restricted use pesticide that can only be purchased and applied by licensed pesticide applicators. https://www.epa.gov/ingredients-used-pesticide-products/paraquat-dichloride.

Syngenta's Efforts to Influence the Composition of the EPA's Science Advisory Panel

A chemical company should not be involved in working behind the scenes to make sure certain people are not appointed to the EPA's Scientific Advisory Panel, or "SAP"; it would be inconsistent with Syngenta's Code of Conduct. Botham: 665-66.

Internal emails from 2005 show Syngenta employees discussing whether to try to use an agricultural trade association (CropLife America) to send information to the EPA against the nomination of a scientist involved in paraquat-Parkinson's disease research to the SAP on paraquat. Botham: 675-81.

A related email indicates that the matter should be handled "with care" in such a way that the comments could not be attributed to Syngenta and would submitted informally and not placed on the public docket and proposes specific language for CropLife America to use. Botham: 685-87.

CropLife America sent a letter to the EPA stating that the scientist was not an appropriate candidate for the panel, using language similar to what the Syngenta employee had proposed. Botham: 688-89.

When the EPA asked CropLife America for additional information on the scientist, CropLife America went back to Syngenta and asked for that information. Botham: 691.

Syngenta again suggested language for CropLife America to use in its response to the EPA's follow-up inquiry. Botham: 695.

In defeating the scientist's nomination to the SAP, Syngenta removed a "potential threat" to the continued sale of paraquat. Botham: 696.

When the same scientist was again nominated to the EPA's SAP in 2010, CropLife America opposed the nomination using language "very similar" to that drafted by a Syngenta employee. Botham: 700-04.

Corporate Ethics and Honest Communications with The Public

Companies who are in the business of manufacturing and distributing pesticides have a duty to act responsibly to ensure the health and safety of their products. Botham: 598.

Companies who are in the business of manufacturing and distributing pesticides have a duty to disclose lists of serious harm from their products to the consumers of their products. Botham: 599.

Companies who are in the business of manufacturing and distributing pesticides have a duty to conduct scientific research with the highest standards of professionalism and good science. Botham: 599.

Companies who are in the business of manufacturing and distributing pesticides have a duty to be transparent regarding their research findings and to publicly disclose research results of significance in an objective and accurate way. Botham: 599-600.

Companies who are in the business of manufacturing and distributing pesticides have a duty to communicate information concerning health, safety and toxicity in a timely and responsible manner. Botham: 600.

These general principles guiding corporate duties and responsibilities have remained constant from the first development of paraquat. Botham: 600.

Syngenta's Code of Conduct states, "We will investigate all credible reports of previously unknown short and long-term effects associated with the correct use of our products and take appropriate actions." Botham: 614.

Syngenta's Code of Conduct states, "We will publicly disclose research and development results of significance in an objective and accurate way." Botham: 614-15.

Syngenta's Code of Conduct states, "We will carefully identify hazards, assess risks associated with the use and alert users of consequences from misuse of a product on the product package, leaflet and label." Botham: 615.

Syngenta's Code of Conduct states, "Syngenta employees will apply the highest ethical and scientific standards and adopt robust processes and controls. They will be alert to wider societal concerns about technology and its impacts, as well as applying rigorous scientific risk assessment." Botham: 615-16.

Syngenta's Code of Conduct states, "Syngenta ensures the quality and state of its products and services by applying state of the art science and technology standards throughout a product life cycle and ensuring adequate training for our employees and customers." Botham: 616.

While not written down exactly as they have been in more recent times, these code principles have been applicable and present for the last forty years at Syngenta and its predecessor entities. Botham: 617.

Syngenta scientists are ethically required to share their scientific findings about paraquat. Botham: 490.

If paraquat is found to be neurotoxic, the "right thing" would be to make that known to users. Ouzts 09-28-20: 104-05.

Transparency in science is critical, especially for heavily used products and serious health effects. Botham: 291-93.

As good stewards, if a company has reason to believe its product has a potential health concern, it should do everything in its power to fully understand whether or not the concern is legitimate or real. Dixon: 326.

A good steward would do so regardless of whether a governmental agency required it. Dixon: 326.

It is not Growmark's role to suggest label changes. Powell: 167.

If Growmark learned that information regarding the hazards associated with the use of a product had not been disclosed, they would still continue to sell it so long as it was an EPA-registered product. Powell: 96.

If Syngenta has information that paraquat is a neurotoxin, it would be improper, unethical and dishonest to withhold that information from the public. Botham: 491-93.

An internal document from some time between 2004-2005 describing the research strategy "being followed" at Syngenta noted that they "avoided measuring [paraquat] levels in the brain, since the detection of any [paraquat] in the brain (no matter how small) will not be perceived externally in a positive light." Botham: 315; Dixon: 128-30.

Syngenta scientists were advised by counsel that they should run documents relating to paraquat and Parkinson's disease through the lawyers to assert attorney work product and attorney client privilege. Botham: 1104-06, 1191-93.

Syngenta was and is concerned about its ability to continue selling paraquat if a link between paraquat and Parkinson's disease is established. Botham: 324, 329, 374, 662.

Money does not justify concealing health risks of paraquat. Botham: 490.

IBT Scandal and Defendants' Knowledge Thereof

Industrial Bio-Test Laboratories ("IBT") was a contract research organization and animal testing facility that conducted studies of paraquat and other chemicals for Chevron. Patterson: 451; Patterson 11-16-20: 115.

From at least 1963 through 1975, members of IBT attended meetings between Chevron, ICI, and various regulators to discuss paraquat toxicity and regulatory testing. SYNG-PQ-02509504; CUSA-00089525-27; CUSA-00425333; *see also* Patterson 11-16-20: 29-30.

IBT conducted the chronic toxicity studies that Chevron submitted to the USDA in support of its original paraquat registration. Patterson 11-16-20: 24, 100-101; CUSA-00283893.

IBT also prepared study protocols, as directed by Chevron, to "soften" paraquat warning statements. SYNG-PQ-02509488.

In 1963, ICI scientists noticed "unusually high" mortality rates in IBT's chronic paraquat study in mice, which would "not satisfy the UK authorities." SYNG-PQ-02509489; SYNG-PQ-02509526.

IBT's founder, Joseph Calandra, assured ICI and Chevron he would place additional groups of mice in the study to "meet FDA and our requirements." SYNG-PQ-02509526.

In 1964, Calandra told ICI that he was unable to find a correlation between paraquat dose and paraquat residue in the urine of animals used in IBT's chronic dog study. SYNG-PQ-02509734.

ICI wrote back to Calandra, "puzzled" and "disturbed" by his comments, calling it "difficult to understand why dogs on such widely varying paraquat intakes (up to ten-fold) should show no difference in the levels of paraquat excretion." SYNG-PQ-02509732; SYNG-PQ-02509727.

In 1964, ICI suggested to Chevron that IBT conduct the subacute inhalation studies for paraquat, saying, "such experiments can be made to yield any result one chooses by manipulation of the particle size of the aerosol." SYNG-PQ-02509700.

After Chevron submitted IBT's inhalation study to the USDA in 1965, ICI realized that IBT's data underestimated the inhalation toxicity of paraquat. SYNG-PQ-02510034.

In 1966, J.N. Ospenson wrote an internal memorandum—"not intended for distribution other than within our own company"—revealing that Chevron's paraquat petition contained "a major error and several errors of omission, one of the errors of omission being an exceedingly serious one from the scientific point of view." CHEV-SJ0027442.

The exceedingly serious error was discovered when Chevron saw that IBT's paraquat residue recovery report was identical in every respect to the one submitted a year earlier, and that "no recovery studies had been made whatsoever with this year's test." *Id.*

Ospenson said this omission in some respects "negates the value of the entire project" and that it could render the entire test invalid. *Id.*

Handwriting at the top of this memorandum reveals that the test was ultimately cancelled because IBT could not develop satisfactory recovery data. *Id.*

Looking back at IBT's chronic studies in February 1976, Chevron scientists called them "poorly done," and "inadequate for a good defense" of paraquat, noting that one could not even tell what killed the animals in the studies. Patterson 11-16-20: 96-100, 108-10; CUSA-00189780.

Also in 1976, ICI's Central Toxicology Laboratory internally reviewed IBT's chronic paraquat study in the rat, calling part of IBT's report "ludicrous" and concluding it would not withstand critical scrutiny. CUSA-00161987.

In 1976, regulators began investigating IBT after the FDA and EPA discovered serious deficiencies in IBT tests conducted to support the registration of numerous drugs and pesticides. Patterson 11-16-20: 117-18.

The investigation of IBT led to criminal convictions for falsifying data, and the EPA ultimately determined 15 of the 17 paraquat studies IBT conducted for Chevron were invalid. Patterson 11-16-20: 129-30; Patterson 01-22-21: 59.

The studies that replaced the invalid IBT studies were also determined by the EPA to contain "insufficient data" to assess potential chronic health effects from paraquat. Patterson 11-16-20: 73-75, 129-30.

APPENDIX TO STATEMENT OF FACTS

Exhibit 1 – Vol. I, Video Deposition of Dr. Philip Botham, taken February 25, 2020, pages 1-244

Exhibit 2 – Vol. II, Continued Video Deposition of Dr. Philip Botham, taken February 26, 2020, pages 245-497

Exhibit 3 – Video Deposition of Dr. Clive Campbell, taken February 27, 2020

Exhibit 4 – Vol. I, Video Deposition of Timothy Patterson, Ph.D., taken March 4, 2020, pages 1-215

Exhibit 5 – Vol. II, Continued Video Deposition of Timothy Patterson, Ph.D., taken March 5, 2020, pages 216-360

Exhibit 6 – Video Deposition of David Powell, PhD, taken June 10, 2020

Exhibit 7 – Vol. III, Continued Video Deposition of Dr. Philip Botham, taken June 17, 2020, pages 498-834

Exhibit 8 – Vol. IV, Continued Video Deposition of Dr. Philip Botham, taken June 18, 2020, pages 835-1119

Exhibit 9 - Vol. V, Continued Video Deposition of Dr. Philip Botham, taken June 19, 2020, pages 1120-1420

Exhibit 10 – Vol. 1, Video Deposition of Clark Ouzts, taken June 22, 2020, pages 1-202

Exhibit 11 – Vol. III, Continued Video Deposition of Timothy Patterson, Ph.D., taken June 23, 2020, pages 361-569

Exhibit 12 – Vol. I, Video Deposition of Monty Dixon, taken June 24, 2020, pages 1-250

Exhibit 13 – Vol. IV, Continued Video Deposition of Timothy Patterson, Ph.D., taken June 25, 2020, pages 570-767

Exhibit 14 – Vol. II, Continued Video Deposition of Clark Ouzts, taken September 28, 2020, pages 1-287

Exhibit 15 – Vol. VI, Continued Video Deposition of Dr. Philip Botham, taken January 5, 2021, pages 1421-1683

Exhibit 16 – Vol. VII, Continued Video Deposition of Dr. Philip Botham, taken January 6, 2021, pages 1684-1827

Exhibit 17 – Vol. II, Continued Video Deposition of Monty Dixon, taken January 7, 2021, pages 251-557

Exhibit 18 – Vol. V, Continued Video Deposition of Timothy Patterson, Ph.D., taken January 22, 2021, pages 1-245

Exhibit 19 – Autopsy Reports, list of bates numbers

Exhibit 20 – Product Labels, list of bates numbers

Exhibit 21 - SYNG-PQ-13120361

Exhibit 22 - SYNG-PQ-14420786_R at 5

Exhibit 23 – SYNG-PQ-02508147

Exhibit 24 - SYNG-PQ-01843764

Exhibit 25 - SYNG-PQ-02450112

Exhibit 26 - SYNG-PQ-02450023

Exhibit 27 - SYNG-PQ-02450073

Exhibit 28 – Declaration of Jon R. Heylings, Ph.D., with attachments

Exhibit 29 – Syngenta's Objections and Response to Plaintiffs' First Request for Admission of Facts

Exhibit 30 - SYNG-PQ-02509504

Exhibit 31 - CUSA-00089525-27

Exhibit 32 - CUSA-00425333

Exhibit 33 - CUSA-00283893

Exhibit 34 - SYNG-PQ-02509488

Exhibit 35 - SYNG-PQ-02509489

Exhibit 36 - SYNG-PQ-02509526

Exhibit 37 - SYNG-PQ-02509734

Exhibit 38 - SYNG-PQ-02509732

Exhibit 39 - SYNG-PQ-02509727

Exhibit 40 - SYNG-PQ-02509700

Exhibit 41 - SYNG-PQ-02510034

Exhibit 42 - CHEV-SJ0027442

Exhibit 43 - CUSA-00189780

Exhibit 44 - CUSA-00161987

Exhibit 45 – Vol. VI, Video-Recorded Videoconference Deposition of Timothy Patterson, Ph.D., taken November 16, 2020, pages 1-227