THE MICHAEL J. FOX FOUNDATION
FOR PARKINSON'S RESEARCH

November 4, 2022

Pesticide Regulation Branch
Department of Pesticide Regulation
P.O. Box 4015
Sacramento, California 95812-4015
Registration.Comments@cdpr.ca.gov
Attn: Tulio Macedo

Dear Dr. Macedo:

On behalf of The Michael J. Fox Foundation for Parkinson's Research (MJFF), I write to you today to respectfully urge the Department of Pesticide Regulation to reevaluate use of the herbicide, paraquat dichloride, because of the significant adverse impacts of this product, particularly the scientific evidence of paraquat's links to Parkinson's disease (PD).

Parkinson's disease is a progressive, neurodegenerative disease and MJFF funds research towards prevention, treatment, and cures.

Parkinson's is a chronic, progressive neurological disorder with motor and non-motor symptoms. PD occurs when dopamine neurons that coordinate movement stop working or die. PD affects over 6.1 million people globally,[1] and over 1 million of those individuals are in the United States.[2] In California, it is estimated that over 115,000 people have Parkinson's.[3] The exact cause of PD is unknown, although research points to a combination of genetic and environmental factors.[4] Certain chemicals, such as nicotine and caffeine, have been found to protect dopaminergic neurons,[5] and others, such as paraquat, cause cell death due to oxidative stress.[6]

PD is the fastest-growing neurological disease in the world (by absolute prevalence).[7] In 2017, the disease cost Americans at least $52 billion each year[8] and, of that amount, at least $5.8 billion to Californians.[9] By 2037 – just 15 years from now – that total cost will balloon to $79 billion.[10] The financial impact and rising prevalence, however, can be alleviated through mitigations to prevent PD and providing additional federal funding directed at research for treatments and cures.

Parkinson's gradually worsens over time. Currently, there is no treatment to slow, stop, or reverse the progression of the disease, nor is there a cure. The treatment of patients diagnosed early with PD can aim to slow clinical progression, control motor and non-motor symptoms, maintain functioning in daily life activities, prevent motor complications, and minimize risk of side effects. The largest proportion of costs incurred in PD occur in the later stages of the disease.[11] Any strategy that would reduce or maintain PD symptoms in the earlier stages of the disease (i.e., fewer and less severe) would likely prove substantially beneficial toward limiting expenditures. From a patient quality-of-life perspective, much the same is true. Considering that the effect of PD on patient quality of life is one of the most severe of all chronic diseases, and because the most severe symptoms occur in more advanced disease, care management strategies aimed at early detection and treatment have the potential to improve the experience of living with PD.

The Michael J. Fox Foundation is leading the charge toward a world without Parkinson's disease. The Foundation is dedicated to finding a cure for Parkinson's disease through an aggressively funded research agenda and to ensuring the development of improved therapies for those living with Parkinson's today.

As the Foundation works toward treatments and cures for those currently living with Parkinson's and those yet

to be diagnosed, we seek to mitigate risks that trigger PD. Between 10% [12] and 27% [13] of PD cases have a predominant genetic link. This means that the majority of PD cases have an environment or gene-environmental interactions component.[14] Reducing environmental risks, such as paraquat, would decrease the number of Parkinson's cases and moves toward the vision of a world without PD.

Paraquat is used frequently in California.

Paraquat is a widely used [15] and non-selective herbicide.[16] Introduced in the 1960s,[17] it kills most green plant tissue on contact through inhibition of photosynthesis and can also desiccate crops.[18] Paraquat is used as an alternative for weeds resistant to glyphosate, an herbicide commonly known as "Roundup."[19] Usage is expected to grow due to increased glyphosate-resistant weeds in the food system and high profile glyphosate-related lawsuits.[20]

Paraquat is the fourth largest active ingredient herbicides used in California, with over one million acres treated for the most recent year available (2018).[21] Crops that are treated with paraquat in California included alfalfa, ("104,207 acres treated, an 8% increase"), almonds, cotton, pistachios (increased by 14% in acres treated), table and raisin grapes, walnut, and wine grapes.[22]

Research indicates that paraquat is linked to Parkinson's disease.

A recent amicus brief in support of litigation against the Environmental Protection Agency (EPA) over its decision to re-register paraquat by Dr. Timothy Greenamyre, Dr. Michael Okun, and Dr. Beate Ritz detail the evidence of paraquat and Parkinson's disease.[23] The brief outlines that "paraquat likely has a causal relationship with Parkinson's" through three main points: 1) "epidemiological studies demonstrate an association between paraquat and Parkinson's"; 2.) "paraquat exposure can cause Parkinson's-like symptoms in animal studies"; and 3.) "in vitro studies suggest a plausible mechanism for how paraquat can cause Parkinson's".[24] This brief is enclosed with this email because of the thoughtful arguments presented and the significant evidence presented in this body of work. MJFF is a petitioner in the suit against the EPA.

EPA recognizes the toxicity of paraquat and is working on re-register the process.

EPA's own website details specific instructions to "prevent severe injury or death" from paraquat ingestion, skin exposure, or eye exposure.[25] It even notes that "paraquat is highly toxic. One small sip can be fatal and there is no antidote."[26] While ingestion is a significantly different exposure route than low-dose chronic exposures that could lead to PD, the EPA's website acknowledges the inherent danger.

As a result of an Earthjustice lawsuit[27], EPA has petitioned for a voluntary remand of paraquat, allowing them to reconsider components of the rulemaking process that would have reregistered paraquat for fifteen years.[28]

For context, at least 50 other countries have banned paraquat.[29]

Recent reporting indicates that manufacturers of paraquat dichloride had knowledge of risks and created uncertainty.

In an October 2022 *The Guardian* article, reporters Carey Gilliam and Aliya Uteuova outline evidence that paraquat manufacturers created uncertainty around connections of adverse impacts out of a desire to protect sales.[30] In an egregious example, "Syngenta also created a website the company used to publicly dismiss concerns about links between paraquat and Parkinson's disease and provide positive product messaging. On that website, the company asserted that paraquat did not readily cross the blood-brain barrier, even when the company had evidence from animal and human data that paraquat accumulated in brain tissue. The company no longer uses that language on its website."[31]

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Symptoms of Parkinson's disease

The experience of living with Parkinson's over the course of a lifetime is unique to each person. No standard trajectory or path exists and, for many, this proves to be among the most challenging aspects of the disease.

Symptoms can include motor symptoms such as stiffness, slowness, resting tremors, walking problems, or difficulty with balance and coordination. Non-motor symptoms sometimes are called the "invisible" symptoms of Parkinson's because you cannot see them from the outside. These common symptoms affect almost every body system, occur any time in the course of disease and differ in severity from person to person. Non-motor symptoms can significantly impact quality of life for people with Parkinson's and their families and may include: autonomic dysfunction (constipation, low blood pressure, sexual problems, sweating problems, urine problems), mood and thinking changes (apathy, memory or thinking problems, mood disturbances, psychosis), and other physical changes (drooling, fatigue, pain, skin changes, sleep problems, smell loss, speech problems, swallowing problems, vision changes, weight changes).

Conclusion

Our founder, Michael J. Fox, stated about his Parkinson's disease diagnosis, "I had to build a new life when I was already pretty happy with the old one." While Michael J. Fox's Parkinson's is not believed to have been triggered by paraquat; today, you are in a unique position to help change lives and prevent more people from paraquat exposure that may cause them to develop Parkinson's disease and force them to build new lives.

We respectfully urge you and the Department of Pesticide Regulation to re-evaluate the use of paraquat in California. While MJFF's interest in banning paraquat dichloride is related to Parkinson's disease, there are many co-benefits of reduced paraquat use including other human health effects (such as dermal irritation, lung and kidney damage, and death from accidental or intentional ingestion)[32] and environmental health (such as paraquat absorbed into soil).[33]

Thank you for time and attention to this important matter and for allowing us this opportunity to share essential information on supporting the Parkinson's disease community. Please contact Dr. Megan May at mmay@michaeljfox.org should you have any questions or require further information.

Sincerely,

Ted Thompson, JD
Senior Vice President, Public Policy

Julia Worcester, JD
Director of State Government Relations

Enclosed: Amicus Brief

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