

Unified Parkinson's Advocacy Council

American Parkinson Disease
Association

Brian Grant Foundation

CurePSP

Dallas Area Parkinson Society

Davis Phinney Foundation

Friends of Parkinson's

Hawai'i Parkinson Association

Houston Area Parkinson Society

Lewy Body Dementia Association

Michigan Parkinson Foundation

MISSION MSA

Northwest Parkinson's Foundation

Parkinson Association
of Alabama

Parkinson Association
of Central Florida

Parkinson Association
of Northern California

Parkinson Association of
the Carolinas

Parkinson Association of
the Rockies

Parkinson & Movement Disorder
Alliance

Parkinson's Foundation

Parkinson's Resources of Oregon

Parkinson Foundation Western
Pennsylvania

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Power for Parkinson's

Power Over Parkinson's

Wisconsin Parkinson Association

The Michael J. Fox Foundation
for Parkinson's Research

The Unified Parkinson's Advocacy
Council (UPAC) is managed by **The
Michael J. Fox Foundation for
Parkinson's Research**

Ted Thompson, Senior Vice President
of Public Policy | 202-638-4101

April 1, 2024

Michal Freedhoff, PhD
Assistant Administrator,
Office of Chemical Safety and Pollution Prevention
U.S. Environmental Protection Agency
1200 Pennsylvania Ave.
Washington, DC 20460

Re: Docket (EPA-HQ-OPP-2011-0855)

Dr. Freedhoff:

An estimated more than 1 million Americans live with Parkinson's disease, with many more family members, friends and caregivers indirectly impacted by the disease. Approximately 90,000 Americans are diagnosed with the disease each year. Parkinson's disease is estimated to cost the economy over \$52 billion per year in both direct healthcare and indirect costs. Parkinson's disease is the world's fastest growing neurological disease, and projections estimate that over 1.5 million Americans will be diagnosed by 2037, with a corresponding economic burden of nearly \$80 billion. As symptoms worsen, patients must often leave their jobs, and in the later stages of the disease patients require great amounts of specialized care [1]. Only about a quarter of Parkinson's disease cases can be linked to potentially causative genetic mutations, implicating environmental exposures as a major contributing factor to the disease [2].

Exposure to paraquat has been linked to an increased risk of developing Parkinson's disease for decades, and The Michael J. Fox Foundation for Parkinson's Research has been sent personal stories from people with Parkinson's who recalled exposure to paraquat in their earlier days. One patient who now requires 24-hour care, must use a walker or wheelchair and is suffering from cognitive difficulties, recalls spraying paraquat on the family farm where he grew up. Another patient, who needed their spouse to write down their story, also used paraquat extensively on their farm and has now developed dementia in addition to their advanced Parkinson's disease. A former farm worker who sprayed paraquat for three summers as a teenager developed Parkinson's at the early age of 37, forcing them to retire from a promising career and severely disrupting the prime of their life.

There are numerous other stories of those who worked on farms in their youth, and recall working with paraquat, who have now developed

Parkinson's disease, and have family members who have developed the disease as well. There are a few stories of people in their formative years merely living near crops or fields doused in paraquat who have ended up developing Parkinson's. The long lag between the recalled exposures and the development of



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disease in these stories is unsurprising, as it is well accepted that the disease pathology of Parkinson's can be underway for decades prior to its clinical diagnosis [3].

While the stories above are anecdotal, the link between Parkinson's disease and paraquat has been identified and replicated across numerous epidemiologic studies. These studies have looked at different groups of people and utilized varied analysis methods, and far outnumber the number of studies finding no association between exposure to the herbicide and the risk of developing the disease. Observational studies have found that occupational and/or ambient exposure to paraquat is associated with an increased rate of Parkinson's disease [4-9]. A set of complementary studies also have identified that paraquat exposure may interact with known genetic and non-genetic risk factors for Parkinson's disease, resulting in even larger increased risk of developing Parkinson's disease in some cases [10-14].

While the epidemiological studies have identified an association between paraquat and Parkinson's disease, dozens of laboratory animal studies have repeatedly demonstrated that the exposure of animals to paraquat results in behavioral manifestations and pathology that are clear analogues of those seen in people with Parkinson's disease. Paraquat exposure so reliably induces Parkinson's disease-like phenotypes in multiple species that it is utilized to model the disease to aid in the study of disease mechanisms and therapeutic approaches [15-19]. Cellular experiments have identified multiple Parkinson's disease-relevant cellular pathways that are negatively impacted by paraquat [20].

The weight of the evidence of paraquat's harmful effects was sufficient for regulators in the European Union to ban the use of paraquat over 15 years ago. The evidence linking paraquat to Parkinson's disease has only increased in the intervening years, yet this is still somehow not enough for the United States Environmental Protection Agency (EPA) to protect its citizens from this chemical, which has many toxic effects beyond its links to Parkinson's disease.

The Michael J. Fox Foundation for Parkinson's Research provided over 40 additional studies that had been generated between 2018 and early 2023 to EPA months prior to their review deadline, providing further epidemiological, animal model and mechanistic data on the links between paraquat and Parkinson's disease. However, EPA declined to review these studies prior to issuing their interim decision without providing a clear rationale. Another example of the EPA's flawed evaluation process is the usage of a single study utilizing administration of liquid paraquat directly into the noses of rats to claim that inhalation of paraquat does not result in appreciable brain levels of paraquat, while disregarding a more recent study demonstrating that treating rats to an occupationally relevant exposure (in a whole body inhalation chamber for four hours per day, five days per week for five weeks) shows paraquat accumulating in the brain, including in the regions of the brain affected in Parkinson's disease [21, 22].

EPA has determined that paraquat is "unlikely" to pose a Parkinson's disease risk from its current approved uses yet has arrived at this conclusion by what appears to be an incomplete evaluation process. EPA has similarly failed to adequately assess paraquat's cancer risk, along with disregarding the real-world routes by which many people could feasibly be exposed to the herbicide. Finally, in a continuing theme, the EPA's opaque risk-benefit calculation for restricting the use of paraquat has the appearance of emphasizing the burden on "growers," and not the potential harms to U.S. citizens and the environment (See comments from Earthjustice for more detail).

The Unified Parkinson's Advocacy Council implores EPA to reconsider its interim registration review decision and revisit the flawed evaluation which greatly minimizes the risks posed to the U.S. population by the continued use of paraquat. This evaluation process, as outlined above, also failed to adequately evaluate the economic burden of the disease in its cost/benefit analysis. Removing paraquat from the

environment in which millions of people live and work should help reduce the future incidence of Parkinson's disease in the United States. Nearly 70 other countries, including China, with the world's second largest population, have taken this step with no discernable impact on agriculture production. It is long past time for the U.S. to ban paraquat.

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