In 2020, 6PPD-quinone (6PPD-q) was identified as a chemical that is fatal to coho salmon in urbanized areas of the Puget Sound in Washington State (Tian et al. 2021 [X8BRFG3P] Tian, Zhenyu, Haoqi Zhao, Katherine T. Peter, et al. 2021. “A Ubiquitous Tire Rubber–Derived Chemical Induces Acute Mortality in Coho Salmon.” Report. Science 371 (6525): 185–89. https://doi.org/10.1126/science.abd6951.). Since its discovery, 6PPD-q has been found to be acutely toxic to brook, rainbow/steelhead, lake trout, and coastal cutthroat trout, which are important ecological and recreational species throughout the United States (Nair et al. 2023 [9V5ES4MI] Nair, Pranav, Jianxian Sun, Linna Xie, et al. 2023. “In Process: Synthesis and Toxicity Evaluation of Tire Rubber–Derived Quinones.” Preprint. Chemistry, June 20. https://doi.org/10.26434/chemrxiv-2023-pmxvc. Brinkmann et al. 2022 [QN6HYEV7] Brinkmann, Markus, David Montgomery, Summer Selinger, et al. 2022. “Acute Toxicity of the Tire Rubber–Derived Chemical 6PPD-Quinone to Four Fishes of Commercial, Cultural, and Ecological Importance.” Environmental Science & Technology Letters, March 2, acs.estlett.2c00050. https://doi.org/10.1021/acs.estlett.2c00050. Roberts et al. 2024 [FMG8VP7Y] Roberts, Catherine, Junyi Lin, Evan Kohlman, et al. 2024. “Acute and Sub-Chronic Toxicity of 6PPD-Quinone to Early-Life Stage Lake Trout (Salvelinus namaycush).” Preprint, bioRxiv, April 3. https://doi.org/10.1101/2024.03.26.586843. Di et al. 2022 [BLEFEP7S] Di, Shanshan, Zhenzhen Liu, Huiyu Zhao, et al. 2022. “Chiral Perspective Evaluations: Enantioselective Hydrolysis of 6PPD and 6PPD-Quinone in Water and Enantioselective Toxicity to Gobiocypris Rarus and Oncorhynchus Mykiss.” Environment International 166 (August): 107374. https://doi.org/10.1016/j.envint.2022.107374.). Studies have shown that 6PPD-q is not lethal to several other aquatic species, including, but not limited to Atlantic and sockeye salmon (Foldvik et al. 2022 [LQWXZHJA] Foldvik, Anders, Fedor Kryuchkov, Roar Sandodden, and Silvio Uhlig. 2022. “Acute Toxicity Testing of the Tire Rubber–Derived Chemical 6PPD-Quinone on Atlantic Salmon (Salmo Salar) and Brown Trout (Salmo Trutta).” Environmental Toxicology and Chemistry 41 (12): 3041–45. https://doi.org/10.1002/etc.5487. Greer et al. 2023 [P6RF5UFR] Greer, Justin B., Ellie M. Dalsky, Rachael F. Lane, and John D. Hansen. 2023. “Establishing an In Vitro Model to Assess the Toxicity of 6PPD-Quinone and Other Tire Wear Transformation Products.” Environmental Science & Technology Letters, ahead of print, May 2. https://doi.org/10.1021/acs.estlett.3c00196.).

6PPD-q is now recognized as a global contaminant (Tian et al. 2022 [BICQHLBC] Tian, Zhenyu, Melissa Gonzalez, Craig A. Rideout, et al. 2022. “6PPD-Quinone: Revised Toxicity Assessment and Quantification with a Commercial Standard.” Environmental Science & Technology Letters, January 11, acs.estlett.1c00910. https://doi.org/10.1021/acs.estlett.1c00910.). To put 6PPD-q toxicity into context, in June 2024, the United States Environmental Protection Agency (USEPA) issued non-regulatory and non-binding screening levels for 6PPD-q that provide information to states and tribes for their water quality protection programs. These screening levels are intended to serve as values that are protective of aquatic life, including sensitive species like coho salmon. USEPA set the screening level for 6PPD-q at 11 nanograms per liter (ng/L), or 11 parts per trillion, for acute (1-hour) exposure.

Mammalian studies have found that 6PPD-q can pass through the placenta to a fetal mouse (Zhao et al. 2023 [GZZX9DMJ] Zhao, Haoqi Nina, Sydney P. Thomas, Mark J. Zylka, Pieter C. Dorrestein, and Wenxin Hu. 2023. “Urine Excretion, Organ Distribution, and Placental Transfer of 6PPD and 6PPD-Quinone in Mice and Potential Developmental Toxicity through Nuclear Receptor Pathways.” Environmental Science & Technology 57 (36): 13429–38. https://doi.org/10.1021/acs.est.3c05026.), damage rodent liver and other organs (He et al. 2023 [6MPWVZGE] He, Wenmiao, Aihua Gu, and Dayong Wang. 2023. “Four-Week Repeated Exposure to Tire-Derived 6-PPD Quinone Causes Multiple Organ Injury in Male BALB/c Mice.” Science of the

Total Environment 894 (October): 164842. https://doi.org/10.1016/j.scitotenv.2023.164842.), and primarily distribute in mice adipose tissue (Zhang et al. 2024 [BZQEGEXI] Zhang, Jing, Guodong Cao, Wei Wang, et al. 2024. “Stable Isotope-Assisted Mass Spectrometry Reveals in Vivo Distribution, Metabolism, and Excretion of Tire Rubber-Derived 6PPD-Quinone in Mice.” Science of the Total Environment 912 (February): 169291. https://doi.org/10.1016/j.scitotenv.2023.169291.). Data on human toxicity is lacking for 6PPD-q; however, human biomonitoring has measured 6PPD-q in human urine (Du et al. 2022 [DWFYR89F] Du, Bibai, Bowen Liang, Yi Li, Mingjie Shen, Liang-Ying Liu, and Lixi Zeng. 2022. “First Report on the Occurrence of N-(1,3-Dimethylbutyl)-N′-Phenyl-p-Phenylenediamine (6PPD) and 6PPD-Quinone as Pervasive Pollutants in Human Urine from South China.” Environmental Science & Technology Letters, ahead of print, November 21. World.

https://doi.org/10.1021/acs.estlett.2c00821.), serum (Zhang et al. 2024 [BZQEGEXI] Zhang, Jing, Guodong Cao, Wei Wang, et al. 2024. “Stable Isotope-Assisted Mass Spectrometry Reveals in Vivo Distribution, Metabolism, and Excretion of Tire Rubber-Derived 6PPD-Quinone in Mice.” Science of the Total Environment 912 (February): 169291.

https://doi.org/10.1016/j.scitotenv.2023.169291.), and cerebrospinal fluid (CSF) (Fang et al. 2024 [2L4QI2CG] Fang, Jiacheng, Xiaoxiao Wang, Guodong Cao, et al. 2024. “6PPD-Quinone Exposure Induces Neuronal Mitochondrial Dysfunction to Exacerbate Lewy Neurites Formation Induced by α-Synuclein Preformed Fibrils Seeding.” Journal of Hazardous Materials 465 (March): 133312. https://doi.org/10.1016/j.jhazmat.2023.133312.).

6PPD-q is a transformation product of N-(1,3-dimethylbutyl)-N’-phenyl-p-phenylenediamine (6PPD), the primary anti-degradant added to tires and used to prevent premature weathering and degradation of the rubber from sunlight, oxygen, and ozone damage (Hu et al. 2022 [ZYXPMXFA] Hu, Ximin, Haoqi Nina Zhao, Zhenyu Tian, Katherine T. Peter, Michael C. Dodd, and Edward P. Kolodziej. 2022. “Transformation Product Formation upon Heterogeneous Ozonation of the Tire Rubber Antioxidant 6PPD (N-(1,3-Dimethylbutyl)-N′-Phenyl-p-Phenylenediamine).” Environmental Science & Technology Letters, ahead of print, April 12. https://doi.org/10.1021/acs.estlett.2c00187. Santoso et al. 2007 [GZL3D5KN] Santoso, M., U. Giese, and R. H. Schuster. 2007. Investigations on Initial Stage of Aging of Tire Rubbers by Chemiluminescence Spectroscopy. 80: 762–76.

https://hero.epa.gov/hero/index.cfm/reference/details/reference_id/5714930. Rossomme et al. 2023 [AXGUT6MJ] Rossomme, Elliot, William M. Hart-Cooper, William J. Orts, Colleen M. McMahan, and Martin Head-Gordon. 2023. “Computational Studies of Rubber Ozonation Explain the Effectiveness of 6PPD as an Antidegradant and the Mechanism of Its Quinone Formation.” Environmental Science & Technology, March 24, acs.est.2c08717. https://doi.org/10.1021/acs.est.2c08717.). 6PPD serves an essential safety function in tires by guaranteeing a tire’s integrity and supports driver and passenger safety. 6PPD-q pollution primarily comes from tires containing 6PPD, although other products containing 6PPD may also be sources of 6PPD-q. A well-established route of exposure to 6PPD-q for coho salmon is via roadway runoff transported by stormwater into surface water (Tian et al. 2021 [X8BRFG3P] Tian, Zhenyu, Haoqi Zhao, Katherine T. Peter, et al. 2021. “A Ubiquitous Tire Rubber–Derived Chemical Induces Acute Mortality in Coho Salmon.” Report. Science 371 (6525): 185–89.

https://doi.org/10.1126/science.abd6951. Tian et al. 2022 [BICQHLBC] Tian, Zhenyu, Melissa Gonzalez, Craig A. Rideout, et al. 2022. “6PPD-Quinone: Revised Toxicity Assessment and Quantification with a Commercial Standard.” Environmental Science & Technology Letters, January 11, acs.estlett.1c00910. https://doi.org/10.1021/acs.estlett.1c00910.). Tire and road wear particles (TRWP) containing 6PPD, which can transform to 6PPD-q in the environment (USEPA 2023 [E43MRZ92] USEPA. 2023. “6PPD-Quinone.” Overviews and Factsheets. August 9. https://www.epa.gov/chemical-research/6ppd-quinone.), are nearly ubiquitous in the urban environment (Wagner et al. 2018 [4UCJI65Q] Wagner, Stephan, Thorsten Hüffer, Philipp Klöckner, Maren Wehrhahn, Thilo Hofmann, and Thorsten Reemtsma. 2018. “Tire Wear Particles in the Aquatic Environment — A Review on Generation, Analysis, Occurrence, Fate and Effects.” Water Research 139 (August): 83–100.

https://doi.org/10.1016/j.watres.2018.03.051. Kole et al. 2017 [NZZMY6WC] Kole, Pieter Jan, Ansje J. Löhr, Frank G. A. J. Van Belleghem, and Ad M. J. Ragas. 2017. “Wear and Tear of Tyres: A Stealthy Source of Microplastics in the Environment.” International Journal of Environmental Research and Public Health 14 (10): 1265. https://doi.org/10.3390/ijerph14101265.). These TRWP are transported throughout the environment. Research is ongoing to understand transport and the fate of the chemicals.

Removing 6PPD from tires is an identified long-term solution to preventing 6PPD-q pollution. Tire manufacturers, chemical manufacturers, and governments are working to find a safer alternative to 6PPD in tires. The alternative must continue to ensure compliance with Federal Motor Vehicle Safety Standards and other consumer, vehicle, and tire-manufacturer requirements while also meeting hazard criteria that aim to avoid regrettable chemical substitutions and minimize the potential for an alternative that is also highly toxic.

This Interstate Technology and Regulatory Council (ITRC) team convened in January 2023 to provide information to state, tribal, and municipal agencies that may need to learn more about 6PPD and 6PPD-q to pursue their own policies and regulations regarding these chemicals. These agencies include the following:

- departments of transportation and urban planning agencies
- water quality, air quality, and resource agencies
- fish and wildlife departments
- solid waste agencies
- departments of health
- drinking water and wastewater treatment plants
- agencies seeking chemical alternatives

Because 6PPD and 6PPD-q are so tightly linked by fate and transport—and possibly toxicity and hazard—this document discusses both chemicals. In each section, we will explain what is known and unknown about the linkage between the chemicals.

The information provided in this document is current as of March 2024 (with a few exceptions of updated information). Given the active research in this topic, additional studies have been published since the completion of this document. While the intent of this document is to present the most salient and recently available information on 6PPD and 6PPD-q, interested readers are encouraged to search the scientific literature for newly available information. During preparation of this document, the synonym 6PPD-q was consistently and uniformly used throughout. This ITRC Team is aware that some state and federal agencies are in the process of phasing out the 6PPD-q synonym in favor of 6PPD-quinone, 6PPDQ, or 6PPD-Q.

In September 2023, this ITRC team published a focus sheet entitled ***What We Know: 6PPD and 6PPD-quinone***. This focus sheet offered a first look and overview of 6PPD and 6PPD-q using available information through July 2023. This ITRC team also anticipates recording an interactive outreach session where each section of the team's final work product is discussed. Please visit the ITRC Training website in early 2025 to access this recording.

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