| Table 2-1. Summary of acute aquatic toxicity data for 6PPD and 6PPD‑q | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Chemical | Receptor (general) | Receptor (specific) | Benchmark Value  (LC50 or EC50) | Units | Duration | Endpoint | Reference |
| 6PPD | Fish | Coho salmon, *Oncorhynchus kisutch* | 251 | µg/L | 24h | Mortality | (Tian et al. 2021) |
| 6PPD | Fish | Japanese medaka, *Oryzias latipes* | 28 | µg/L | 96h | Mortality | (Japan Ministry of the Environment 2018) |
| 6PPD | Fish | Japanese medaka, *Oryzias latipes* | < 107 | µg/L | 96h | Mortality | (Hiki et al. 2021) |
| 6PPD | Fish | Rainbow trout, *Oncorhynchus mykiss* | > 50 | µg/L | 96h | Mortality | (Nair et al. 2023)\*\* |
| 6PPD | Fish | Zebrafish, *Danio rerio* | 442.62 | µg/L | 96h | Mortality | (Varshney et al. 2022) |
| 6PPD | Fish | Zebrafish, *Danio rerio* | 2,200 | µg/L | 96h | Mortality | (Peng et al. 2022) |
| 6PPD | Fish | Zebrafish, *Danio rerio* | 737 | µg/L | 96h | Mortality | (Fang et al. 2023) |
| 6PPD | Fish | Zebrafish, *Danio rerio* | >137 | µg/L | 96h | Mortality | (Hiki et al. 2021) |
| 6PPD | Invertebrate | Amphipod, *Hyalella azteca* | 250 | µg/L | 96h | Mortality | (Prosser, Bartlett, et al. 2017) |
| 6PPD | Invertebrate | Fatmucket mussel, *Lampsilis siliquoidea* | 439 | µg/L | 48h | Viability | (Prosser, Gillis, et al. 2017) |
| 6PPD | Invertebrate | Water flea, *Daphnia magna* | 230 | µg/L | 48h | Mortality | (Japan Ministry of the Environment 2018) |
| 6PPD | Invertebrate | Water flea, *Daphnia magna* | < 138 | µg/L | 48h | Mortality | (Hiki et al. 2021) |
| 6PPD | Invertebrate | Wavy-rayed lampmussel, *Lampsilis fasciola* | 137 | µg/L | 48h | Viability | (Prosser, Gillis, et al. 2017) |
| 6PPD | Plant/algae | Algae, *Selenastrum capricornutum* | 600 | µg/L | 96h | Cell number | (Monsanto Company 1978, as cited in OECD 2004) |
| 6PPD‑q | Fish | Arctic char, *Salvelinus alpinus* | > 14.2 | µg/L | 96h | Mortality | (Brinkmann et al. 2022) |
| 6PPD‑q | Fish | Atlantic salmon, *Salmo salar* | > 12.16 | µg/L | 48h | Mortality | (Foldvik et al. 2022) |
| 6PPD‑q | Fish | Brook trout fingerlings, *Salvelinus fontinalis* | 0.5 | µg/L | 24h | Mortality | (Philibert et al. 2024) |
| 6PPD‑q | Fish | Brook trout fry, *Salvelinus fontinalis* | 0.2 | µg/L | 24h | Mortality | (Philibert et al. 2024) |
| 6PPD‑q | Fish | Brook trout, *Salvelinus fontinalis* | 0.59 | µg/L | 24h | Mortality | (Brinkmann et al. 2022) |
| 6PPD‑q | Fish | Brown trout, *Salmo trutta* | > 12.16 | µg/L | 48h | Mortality | (Foldvik et al. 2022) |
| 6PPD‑q | Fish | Chinese rare minnow, *Gobiocypris rarus* | > 500 | µg/L | 96h | Mortality | (Di et al. 2022) |
| 6PPD‑q | Fish | Chinook salmon, *Oncorhynchus tshawytscha* | > 2.5 | µg/L | 24h | Mortality | (Montgomery et al. 2023) |
| 6PPD‑q | Fish | Chinook salmon, *Oncorhynchus tshawytscha* | > 67.307 | µg/L | 24h | Mortality | (Lo et al. 2023) |
| 6PPD‑q | Fish | Chinook salmon, *Oncorhynchus tshawytscha* | 82.1 | µg/L | 24h | Mortality | (Greer et al. 2023) |
| 6PPD‑q | Fish | Coho salmon, *Oncorhynchus kisutch* | 0.041 | µg/L | 24h | Mortality | (Lo et al. 2023) |
| 6PPD‑q | Fish | Coho salmon, *Oncorhynchus kisutch* | 0.0804 | µg/L | 24h | Mortality | (Greer et al. 2023) |
| 6PPD‑q | Fish | Coho salmon, *Oncorhynchus kisutch* | 0.095 | µg/L | 24h | Mortality | (Tian et al. 2022) |
| 6PPD‑q | Fish | Fathead minnow, *Pimephales promelas* | >9.65 | µg/L | 96h | Mortality | (Anderson-Bain et al. 2023) |
| 6PPD‑q | Fish | Japanese medaka, *Oryzias latipes* | > 34 | µg/L | 96h | Mortality | (Hiki et al. 2021) |
| 6PPD‑q | Fish | Lake trout, *Salvelinus namaycush* | 0.5 | µg/L | 24h | Mortality | (Roberts et al. 2024)\*\* |
| 6PPD‑q | Fish | Lake trout, *Salvelinus namaycush* | 0.51 | µg/L | 96h | Mortality | (Roberts et al. 2024)\*\* |
| 6PPD‑q | Fish | Masu salmon, *Oncorhynchus masou masou* | > 3.5 | µg/L | 96h | Mortality | (Hiki and Yamamoto 2022) |
| 6PPD‑q | Fish | Pink salmon, *Oncorhynchus gorbuscha* | > 12.8 | µg/L | 48h | Mortality | (Foldvik et al. 2024) |
| 6PPD‑q | Fish | Pink Salmon, *Oncorhynchus gorbuscha* | >12.8 | µg/L | 48h | Mortality | (Foldvik et al. 2024) |
| 6PPD‑q | Fish | Rainbow trout, *Oncorhynchus mykiss* | 0.64 | µg/L | 96h | Mortality | (Nair et al. 2023) \*\* |
| 6PPD‑q | Fish | Rainbow trout, *Oncorhynchus mykiss* | 1 | µg/L | 96h | Mortality | (Brinkmann et al. 2022) |
| 6PPD‑q | Fish | Rainbow trout, *Oncorhynchus mykiss* | 2.26 | µg/L | 96h | Mortality | (Di et al. 2022) |
| 6PPD‑q | Fish | Sockeye salmon, *Oncorhynchus nerka* | > 50 | µg/L | 24h | Mortality | (Greer et al. 2023) |
| 6PPD‑q | Fish | Southern Asian dolly varden, *Salvelinus curilus* | > 3.8 | µg/L | 96h | Mortality | (Hiki and Yamamoto 2022) |
| 6PPD‑q | Fish | Westslope cutthroat trout, *Oncorhynchus clarkii lewisi* | >10 | µg/L | 24h | Mortality | (Montgomery et al. 2023) |
| 6PPD‑q | Fish | White spotted char, *Salvelinus leucomaenis pluvius* | 0.51 | µg/L | 96h | Mortality | (Hiki and Yamamoto 2022) |
| 6PPD‑q | Fish | White sturgeon, *Acipenser transmontanus* | > 12.7 | µg/L | 96h | Mortality | (Brinkmann et al. 2022) |
| 6PPD‑q | Fish | Zebrafish, *Danio rerio* | > 54 | µg/L | 96h | Mortality | (Hiki et al. 2021) |
| 6PPD‑q | Fish | Zebrafish, *Danio rerio* | 132.92 | µg/L | 96h | Mortality | (Varshney et al. 2022) |
| 6PPD‑q | Fish | Zebrafish, *Danio rerio* | > 1,000 | µg/L | 12h | Mortality | (Ji et al. 2022) |
| 6PPD‑q | Invertebrate | Amphipod, *Hyalella azteca* | > 43 | µg/L | 96h | Mortality | (Hiki et al. 2021) |
| 6PPD‑q | Invertebrate | Freshwater rotifer, *Brachionus calyciflorus* | > 10,000 | µg/L | NR | Mortality | (Klauschies and Isanta-Navarro 2022) |
| 6PPD‑q | Invertebrate | Marine amphipod, *Parhyale hawaiensis* | > 500 | µg/L | 96h | Mortality | (Botelho et al. 2023) |
| 6PPD‑q | Invertebrate | Marine rotifer, *Brachionus koreanus* | > 1,000 | µg/L | 24h | Mortality | (Maji et al. 2023) |
| 6PPD‑q | Invertebrate | Mayfly, *Hexagenia* spp. | >53.4 | µg/L | 4d | Mortality | (Prosser, Salole, and Hang 2023) |
| 6PPD‑q | Invertebrate | Mayfly, *Hexagenia* spp. | >232 | µg/L | 4d | Mortality | (Prosser, Salole, and Hang 2023) |
| 6PPD‑q | Invertebrate | Washboard mussel, *Megalonaias nervosa* | >11.4 | µg/L | 8d | Mortality | (Prosser, Salole, and Hang 2023) |
| 6PPD‑q | Invertebrate | Washboard mussel, *Megalonaias nervosa* | >17.9 | µg/L | 8d | Mortality | (Prosser, Salole, and Hang 2023) |
| 6PPD‑q | Invertebrate | Water flea, *Daphnia magna* | > 46 | µg/L | 48h | Mortality | (Hiki et al. 2021) |
| 6PPD‑q | Plant/algae | Algae, *Chlamydomonas reinhardtii* | 0.84(LOEC) | uM | 72h | Relative growth rate | (Wu et al. 2023) |

Notes: \*\*=Citation is pre-proof, presentation, or non-peer-reviewed article; µg/L=micrograms per liter; d=days, dw=dry weight, h=hours, LOEC=lowest observed effect concentration; kg=kilogram, mg=milligram

**References**

Anderson-Bain, Katherine, Catherine Roberts, Evan Kohlman, Xiaowen Ji, Alper J. Alcaraz, Justin Miller, Tabitha Gangur-Powell, et al. 2023. “Apical and Mechanistic Effects of 6PPD-Quinone on Different Life-Stages of the Fathead Minnow (*Pimephales Promelas*).” *Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology* 271 (September):109697. https://doi.org/10.1016/j.cbpc.2023.109697.

Botelho, Marina Tenório, Gabriely Groto Militão, Markus Brinkmann, and Gisela de Aragão Umbuzeiro. 2023. “Toxicity and Mutagenicity Studies of 6PPD-Quinone in a Marine Invertebrate Species and Bacteria.” *Environmental and Molecular Mutagenesis* 64 (6): 335–41. https://doi.org/10.1002/em.22560.

Brinkmann, Markus, David Montgomery, Summer Selinger, Justin G. P. Miller, Eric Stock, Alper James Alcaraz, Jonathan K. Challis, 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, acs.estlett.2c00050. https://doi.org/10.1021/acs.estlett.2c00050.

Di, Shanshan, Zhenzhen Liu, Huiyu Zhao, Ying Li, Peipei Qi, Zhiwei Wang, Hao Xu, Yuanxiang Jin, and Xinquan Wang. 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.

Fang, Chanlin, Liya Fang, Shanshan Di, Yundong Yu, Xinquan Wang, Caihong Wang, and Yuanxiang Jin. 2023. “Characterization of N-(1,3-Dimethylbutyl)-*N′*-Phenyl-*p*-Phenylenediamine (6PPD)-Induced Cardiotoxicity in Larval Zebrafish (*Danio Rerio*).” *Science of the Total Environment* 882 (July):163595. https://doi.org/10.1016/j.scitotenv.2023.163595.

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.

Foldvik, Anders, Fedor Kryuchkov, Eva Ulvan, Roar Sandodden, and Elii Kvingedal. 2024. “Acute Toxicity Testing of Pink Salmon (*Oncorhynchus gorbuscha*) with the Tire Rubber–Derived Chemical 6PPD‐Quinone.” *Environmental Toxicology and Chemistry*. https://doi.org/10.1002/etc.5875.

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*, May. https://doi.org/10.1021/acs.estlett.3c00196.

Hiki, Kyoshiro, Kenta Asahina, Kota Kato, Takahiro Yamagishi, Ryo Omagari, Yuichi Iwasaki, Haruna Watanabe, and Hiroshi Yamamoto. 2021. “Acute Toxicity of a Tire Rubber–Derived Chemical, 6PPD Quinone, to Freshwater Fish and Crustacean Species.” *Environmental Science & Technology Letters* 8 (9): 779–84. https://doi.org/10.1021/acs.estlett.1c00453.

Hiki, Kyoshiro, and Hiroshi Yamamoto. 2022. “The Tire-Derived Chemical 6PPD-Quinone Is Lethally Toxic to the White-Spotted Char *Salvelinus leucomaenis pluvius* but Not to Two Other Salmonid Species.” *Environmental Science & Technology Letters* 9 (12): 1050–55. https://doi.org/10.1021/acs.estlett.2c00683.

Japan Ministry of the Environment. 2018. “Results of Aquatic Toxicity Tests of Chemicals Conducted by Ministry of the Environment in Japan (March 2018).” Tokyo, Japan: Japan Ministry of the Environment. https://www.env.go.jp/en/chemi/sesaku/aquatic\_Mar\_2018.pdf.

Ji, Jiawen, Jinze Huang, Niannian Cao, Xianghong Hao, Yanhua Wu, Yongqiang Ma, Dong An, Sen Pang, and Xuefeng Li. 2022. “Multiview Behavior and Neurotransmitter Analysis of Zebrafish Dyskinesia Induced by 6PPD and Its Metabolites.” *Science of the Total Environment* 838:156013.

Klauschies, Toni, and Jana Isanta-Navarro. 2022. “The Joint Effects of Salt and 6PPD Contamination on a Freshwater Herbivore.” *Science of the Total Environment* 829 (July):154675. https://doi.org/10.1016/j.scitotenv.2022.154675.

Lo, Bonnie P., Vicki L. Marlatt, Xiangjun Liao, Sofya Reger, Carys Gallilee, Andrew R.S. Ross, and Tanya M. Brown. 2023. “Acute Toxicity of 6PPD‐Quinone to Early Life Stage Juvenile Chinook (*Oncorhynchus tshawytscha*) and Coho (*Oncorhynchus kisutch*) Salmon.” *Environmental Toxicology and Chemistry* 42 (4): 815–22. https://doi.org/10.1002/etc.5568.

Maji, Usha Jyoti, Kyuhyeong Kim, In-Cheol Yeo, Kyu-Young Shim, and Chang-Bum Jeong. 2023. “Toxicological Effects of Tire Rubber–Derived 6PPD-Quinone, a Species-Specific Toxicant, and Dithiobisbenzanilide (DTBBA) in the Marine Rotifer *Brachionus koreanus*.” *Marine Pollution Bulletin* 192 (July):115002. https://doi.org/10.1016/j.marpolbul.2023.115002.

Monsanto Company. 1978. “Acute Toxicity of Santoflex 13 (BN-78-1384316) to the Freshwater Alga *Selenastrum capricornutum*.” Unpublished study No. BN-78-362.

Montgomery, David, Xiaowen Ji, Jenna Cantin, Danielle Philibert, Garrett Foster, Summer Selinger, Niteesh Jain, et al. 2023. “Not Yet Peer Reviewed: Toxicokinetic Characterization of the Inter-Species Differences in 6PPD-Quinone Toxicity Across Seven Fish Species: Metabolite Identification and Semi-Quantification.” bioRxiv. https://doi.org/10.1101/2023.08.18.553920.

Nair, Pranav, Jianxian Sun, Linna Xie, Lisa Kennedy, Derek Kozakiewicz, Sonya Kleywegt, Chunyan Hao, et al. 2023. “In Process: Synthesis and Toxicity Evaluation of Tire Rubber–Derived Quinones.” Preprint. Chemistry. https://doi.org/10.26434/chemrxiv-2023-pmxvc.

OECD. 2004. “SIDS Initial Assessment Report for N-(1,3-Dimethylbutyl)-N´-Phenyl-1,4-Phenylenediamine (6PPD), Organisation for Economic Co-Operation and Development (OECD).” https://hpvchemicals.oecd.org/UI/handler.axd?id=5e1a446c-5969-479c-9270-7ced8726952e.

Peng, Weijuan, Chunsheng Liu, Daqing Chen, Xinbin Duan, and Liqiao Zhong. 2022. “Exposure to N-(1,3-Dimethylbutyl)-N’-Phenyl-p-Phenylenediamine (6PPD) Affects the Growth and Development of Zebrafish Embryos/Larvae.” *Ecotoxicology and Environmental Safety* 232 (113221). https://doi.org/doi.org/10.1016/j.ecoenv.2022.113221.

Philibert, Danielle, Ryan S. Stanton, Christine Tang, Naomi L. Stock, Tillmann Benfey, Michael Pirrung, and Benjamin de Jourdan. 2024. “The Lethal and Sublethal Impacts of Two Tire Rubber–Derived Chemicals on Brook Trout (*Salvelinus fontinalis*) Fry and Fingerlings.” *Chemosphere*, May. https://doi.org/10.1016/j.chemosphere.2024.142319.

Prosser, R. S., A. J. Bartlett, D. Milani, E. A. M. Holman, H. Ikert, D. Schissler, J. Toito, J. L. Parrott, P. L. Gillis, and V. K. Balakrishnan. 2017. “Variation in the Toxicity of Sediment-Associated Substituted Phenylamine Antioxidants to an Epibenthic (Hyalella Azteca) and Endobenthic (Tubifex Tubifex) Invertebrate.” *Chemosphere* 181 (August):250–58. https://doi.org/10.1016/j.chemosphere.2017.04.066.

Prosser, R. S., J. Salole, and S. Hang. 2023. “Toxicity of 6PPD-Quinone to Four Freshwater Invertebrate Species.” *Environmental Pollution*, September, 122512. https://doi.org/10.1016/j.envpol.2023.122512.

Prosser, R.S., P.L. Gillis, E.A.M. Holman, D. Schissler, H. Ikert, J. Toito, E. Gilroy, et al. 2017. “Effect of Substituted Phenylamine Antioxidants on Three Life Stages of the Freshwater Mussel *Lampsilis Siliquoidea*.” *Environmental Pollution* 229 (October):281–89. https://doi.org/10.1016/j.envpol.2017.05.086.

Roberts, Catherine, Junyi Lin, Evan Kohlman, Niteesh Jain, Mawuli Amekor, Alper James Alcaraz, Natacha Hogan, Markus Hecker, and Markus Brinkmann. 2024. “Acute and Sub-Chronic Toxicity of 6PPD-Quinone to Early-Life Stage Lake Trout (*Salvelinus namaycush*).” bioRxiv. https://doi.org/10.1101/2024.03.26.586843.

Tian, Zhenyu, Melissa Gonzalez, Craig A. Rideout, Haoqi Nina Zhao, Ximin Hu, Jill Wetzel, Emma Mudrock, C. Andrew James, Jenifer K. McIntyre, and Edward P. Kolodziej. 2022. “6PPD-Quinone: Revised Toxicity Assessment and Quantification with a Commercial Standard.” *Environmental Science & Technology Letters*, January, acs.estlett.1c00910. https://doi.org/10.1021/acs.estlett.1c00910.

Tian, Zhenyu, Haoqi Zhao, Katherine T. Peter, Melissa Gonzalez, Jill Wetzel, Christopher Wu, Ximin Hu, et al. 2021. “A Ubiquitous Tire Rubber–Derived Chemical Induces Acute Mortality in Coho Salmon.” *Science* 371 (6525): 185–89. https://doi.org/10.1126/science.abd6951.

Varshney, Shubham, Adnan H. Gora, Prabhugouda Siriyappagouder, Viswanath Kiron, and Pål A. Olsvik. 2022. “Toxicological Effects of 6PPD and 6PPD Quinone in Zebrafish Larvae.” *Journal of Hazardous Materials* 424 (February):127623. https://doi.org/10.1016/j.jhazmat.2021.127623.

Wu, Jiabin, Guodong Cao, Feng Zhang, and Zongwei Cai. 2023. “A New Toxicity Mechanism of *N-*(1,3-Dimethylbutyl)-*N′*-Phenyl-*p-*Phenylenediamine Quinone: Formation of DNA Adducts in Mammalian Cells and Aqueous Organisms.” *Science of the Total Environment* 866 (March):161373. https://doi.org/10.1016/j.scitotenv.2022.161373.