

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, <i>Oncorhynchus kisutch</i>	251	µg/L	24h	Mortality	(Tian et al. 2021)
6PPD	Fish	Japanese medaka, <i>Oryzias latipes</i>	28	µg/L	96h	Mortality	(Japan Ministry of the Environment 2018)
6PPD	Fish	Japanese medaka, <i>Oryzias latipes</i>	< 107	µg/L	96h	Mortality	(Hiki et al. 2021)
6PPD	Fish	Rainbow trout, <i>Oncorhynchus mykiss</i>	> 50	µg/L	96h	Mortality	(Nair et al. 2023)**
6PPD	Fish	Zebrafish, <i>Danio rerio</i>	442.62	µg/L	96h	Mortality	(Varshney et al. 2022)
6PPD	Fish	Zebrafish, <i>Danio rerio</i>	2,200	µg/L	96h	Mortality	(Peng et al. 2022)
6PPD	Fish	Zebrafish, <i>Danio rerio</i>	737	µg/L	96h	Mortality	(Fang et al. 2023)
6PPD	Fish	Zebrafish, <i>Danio rerio</i>	>137	µg/L	96h	Mortality	(Hiki et al. 2021)
6PPD	Invertebrate	Amphipod, <i>Hyalella azteca</i>	250	µg/L	96h	Mortality	(Prosser, Bartlett, et al. 2017)
6PPD	Invertebrate	Fatmucket mussel, <i>Lampsilis siliquoidea</i>	439	µg/L	48h	Viability	(Prosser, Gillis, et al. 2017)
6PPD	Invertebrate	Water flea, <i>Daphnia magna</i>	230	µg/L	48h	Mortality	(Japan Ministry of the Environment 2018)
6PPD	Invertebrate	Water flea, <i>Daphnia magna</i>	< 138	µg/L	48h	Mortality	(Hiki et al. 2021)
6PPD	Invertebrate	Wavy-rayed lampmussel, <i>Lampsilis fasciola</i>	137	µg/L	48h	Viability	(Prosser, Gillis, et al. 2017)
6PPD	Plant/algae	Algae, <i>Selenastrum capricornutum</i>	600	µg/L	96h	Cell number	(Monsanto Company 1978, as cited in OECD 2004)
6PPD-q	Fish	Arctic char, <i>Salvelinus alpinus</i>	> 14.2	µg/L	96h	Mortality	(Brinkmann et al. 2022)
6PPD-q	Fish	Atlantic salmon, <i>Salmo salar</i>	> 12.16	µg/L	48h	Mortality	(Foldvik et al. 2022)
6PPD-q	Fish	Brook trout fingerlings, <i>Salvelinus fontinalis</i>	0.5	µg/L	24h	Mortality	(Philibert et al. 2024)
6PPD-q	Fish	Brook trout fry, <i>Salvelinus fontinalis</i>	0.2	µg/L	24h	Mortality	(Philibert et al. 2024)
6PPD-q	Fish	Brook trout, <i>Salvelinus fontinalis</i>	0.59	µg/L	24h	Mortality	(Brinkmann et al. 2022)
6PPD-q	Fish	Brown trout, <i>Salmo trutta</i>	> 12.16	µg/L	48h	Mortality	(Foldvik et al. 2022)
6PPD-q	Fish	Chinese rare minnow, <i>Gobiocypris rarus</i>	> 500	µg/L	96h	Mortality	(Di et al. 2022)
6PPD-q	Fish	Chinook salmon, <i>Oncorhynchus tshawytscha</i>	> 2.5	µg/L	24h	Mortality	(Montgomery et al. 2023)
6PPD-q	Fish	Chinook salmon, <i>Oncorhynchus tshawytscha</i>	> 67.307	µg/L	24h	Mortality	(Lo et al. 2023)
6PPD-q	Fish	Chinook salmon, <i>Oncorhynchus tshawytscha</i>	82.1	µg/L	24h	Mortality	(Greer et al. 2023)
6PPD-q	Fish	Coho salmon, <i>Oncorhynchus kisutch</i>	0.041	µg/L	24h	Mortality	(Lo et al. 2023)
6PPD-q	Fish	Coho salmon, <i>Oncorhynchus kisutch</i>	0.0804	µg/L	24h	Mortality	(Greer et al. 2023)
6PPD-q	Fish	Coho salmon, <i>Oncorhynchus kisutch</i>	0.095	µg/L	24h	Mortality	(Tian et al. 2022)
6PPD-q	Fish	Fathead minnow, <i>Pimephales promelas</i>	>9.65	µg/L	96h	Mortality	(Anderson-Bain et al. 2023)
6PPD-q	Fish	Japanese medaka, <i>Oryzias latipes</i>	> 34	µg/L	96h	Mortality	(Hiki et al. 2021)
6PPD-q	Fish	Lake trout, <i>Salvelinus namaycush</i>	0.5	µg/L	24h	Mortality	(Roberts et al. 2024)**
6PPD-q	Fish	Lake trout, <i>Salvelinus namaycush</i>	0.51	µg/L	96h	Mortality	(Roberts et al. 2024)**
6PPD-q	Fish	Masu salmon, <i>Oncorhynchus masou masou</i>	> 3.5	µg/L	96h	Mortality	(Hiki and Yamamoto 2022)
6PPD-q	Fish	Pink salmon, <i>Oncorhynchus gorbuscha</i>	> 12.8	µg/L	48h	Mortality	(Foldvik et al. 2024)
6PPD-q	Fish	Pink Salmon, <i>Oncorhynchus gorbuscha</i>	>12.8	µg/L	48h	Mortality	(Foldvik et al. 2024)
6PPD-q	Fish	Rainbow trout, <i>Oncorhynchus mykiss</i>	0.64	µg/L	96h	Mortality	(Nair et al. 2023)**
6PPD-q	Fish	Rainbow trout, <i>Oncorhynchus mykiss</i>	1	µg/L	96h	Mortality	(Brinkmann et al. 2022)
6PPD-q	Fish	Rainbow trout, <i>Oncorhynchus mykiss</i>	2.26	µg/L	96h	Mortality	(Di et al. 2022)
6PPD-q	Fish	Sockeye salmon, <i>Oncorhynchus nerka</i>	> 50	µg/L	24h	Mortality	(Greer et al. 2023)
6PPD-q	Fish	Southern Asian dolly varden, <i>Salvelinus curilus</i>	> 3.8	µg/L	96h	Mortality	(Hiki and Yamamoto 2022)
6PPD-q	Fish	Westslope cutthroat trout, <i>Oncorhynchus clarkii lewisi</i>	>10	µg/L	24h	Mortality	(Montgomery et al. 2023)

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Chemical	Receptor (general)	Receptor (specific)	Benchmark Value (LC ₅₀ or EC ₅₀)	Units	Duration	Endpoint	Reference
6PPD-q	Fish	White spotted char, <i>Salvelinus leucomaenoides pluvius</i>	0.51	µg/L	96h	Mortality	(Hiki and Yamamoto 2022)
6PPD-q	Fish	White sturgeon, <i>Acipenser transmontanus</i>	> 12.7	µg/L	96h	Mortality	(Brinkmann et al. 2022)
6PPD-q	Fish	Zebrafish, <i>Danio rerio</i>	> 54	µg/L	96h	Mortality	(Hiki et al. 2021)
6PPD-q	Fish	Zebrafish, <i>Danio rerio</i>	132.92	µg/L	96h	Mortality	(Varshney et al. 2022)
6PPD-q	Fish	Zebrafish, <i>Danio rerio</i>	> 1,000	µg/L	12h	Mortality	(Ji et al. 2022)
6PPD-q	Invertebrate	Amphipod, <i>Hyalella azteca</i>	> 43	µg/L	96h	Mortality	(Hiki et al. 2021)
6PPD-q	Invertebrate	Freshwater rotifer, <i>Brachionus calyciflorus</i>	> 10,000	µg/L	NR	Mortality	(Klauschies and Isanta-Navarro 2022)
6PPD-q	Invertebrate	Marine amphipod, <i>Parhyale hawaiiensis</i>	> 500	µg/L	96h	Mortality	(Botelho et al. 2023)
6PPD-q	Invertebrate	Marine rotifer, <i>Brachionus koreanus</i>	> 1,000	µg/L	24h	Mortality	(Maji et al. 2023)
6PPD-q	Invertebrate	Mayfly, <i>Hexagenia</i> spp.	>53.4	µg/L	4d	Mortality	(Prosser, Salole, and Hang 2023)
6PPD-q	Invertebrate	Mayfly, <i>Hexagenia</i> spp.	>232	µg/L	4d	Mortality	(Prosser, Salole, and Hang 2023)
6PPD-q	Invertebrate	Washboard mussel, <i>Megalonaia nervosa</i>	>11.4	µg/L	8d	Mortality	(Prosser, Salole, and Hang 2023)
6PPD-q	Invertebrate	Washboard mussel, <i>Megalonaia nervosa</i>	>17.9	µg/L	8d	Mortality	(Prosser, Salole, and Hang 2023)
6PPD-q	Invertebrate	Water flea, <i>Daphnia magna</i>	> 46	µg/L	48h	Mortality	(Hiki et al. 2021)
6PPD-q	Plant/algae	Algae, <i>Chlamydomonas reinhardtii</i>	0.84 (LOEC)	µM	72h	Relative growth rate	(Wu et al. 2023)

Notes: **=Citation is pre-proof, presentation, or non-peer-reviewed articles 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 leucomaenoides 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.

- Klausches, 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 Dithiobisbenzylidene (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/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 Siriyappagounder, 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>.