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# Policy recommendations for tire additive 6PPD and its derivative 6PPD-Q

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# Policy recommendations for tire additive 6PPD and its derivative 6PPD-Q.

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A capstone project in partial fulfillment of the requirements for the degree of Master of Arts in Marine Science at the Virginia Institute of Marine Science, William & Mary

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Policy Brief

Background	3
Distribution & Sources of 6PPD-Q	4
Water	.4
Soil & Sediment	.5
Dust	. 5
Atmosphere	.6
Humans	6
Toxicity	.7
Fishes	7
Invertebrates	.9
Mammalian Systems (Mice)	.9
Humans1	0
6PPD-Q Management through Statutory, Regulatory, and Policy Engagement1	0
Actions taken in the U.S 1	1
Policy Recommendations1	2
Recommendation #1: Replacement of 6PPD as a rubber antioxidant1	2
Recommendation #2: Prevent 6PPD-Q distribution in the environment1	3
Recommendation #3: Terminate recycling rubber in products with direct human contact 1	3
Lastly, the Precautionary Principle	4
References1	15

# Background

Around 3.1 billion tires are produced around the world annually<sup>1</sup>. The antioxidant additive, 6PPD (i.e., N-(1,3-dimethylbutyl)-N'-phenyl-p-phenylenediamine) is widely employed in passenger and commercial vehicle tires at 0.4-2% by mass to impede tire degradation<sup>2</sup>. Antioxidants are intended to migrate to tire surfaces and form protective films to prevent rubber oxidation. 6PPD is designed to react with oxidant species like ozone, intentionally forming chemical transformation products that can then escape from the tire and into the environment. 6PPD-Q (i.e., 2-anilino-5-[(4-methylpentan-2-yl)amino]cyclohexa-2,5-diene-1,4-dione) is one such transformation product.

After release and disbursement in the environment, 6PPD-Q is bioavailable to aquatic animals and mammals and acute exposure to 6PPD-Q can be lethal to some organisms. Additionally, exposure at environmentally relevant concentrations can induce neuro-, cardio-, intestinal, respiratory, and reproductive toxicity. 6PPD-Q was discovered to be the cause of massive coho salmon (*Oncorhynchus kisutch*) die-offs in the U.S. Pacific Northwest in 2021<sup>3</sup>. Following this discovery, many publications have further documented its toxicity to diverse organisms including fish, invertebrates, bacteria, and mice. The presence of 6PPD and 6PPD-Q have been reported in a variety of environmental matrices worldwide. The potential risks to human and environmental health posed by 6PPD-Q has only recently been investigated. There is, however, a deficiency of publications regarding policy and regulation of this chemical.

Despite its widespread detection, much is unknown about 6PPD-Q. Yet understudied is its toxicity to humans, species specific toxicity mechanisms of action, long-term exposure impacts, and sublethal and developmental toxicity endpoints. Its impact on other organisms and ecosystems, such as freshwater invertebrates, amphibians, and aquatic plants, also remains uncertain. More information regarding bioaccumulation and biotransformation are also needed. With so much being unknown about 6PPD-Q, it is important for responsible policies to be developed and implemented quickly. The benefit of enacting policies early outweighs any potential added costs of action.

Considering the decades of harm its use has likely caused, quick actions should be taken to reduce future impacts. Failure to implement policies in a timely manner regarding environmental pollution is too often the norm and it allows for much harm to come to the inhabitants of the natural environment – including humans. While it is too late to work proactively to prevent all releases of 6PPD and 6PPD-Q, it is imperative to put policies and other mechanisms in place to stem their release, protect sensitive populations, and to ensure the chemicals replacing 6PPD as rubber additives do not pose additional threats.

<sup>&</sup>lt;sup>1</sup> Stokstad, 2020

<sup>&</sup>lt;sup>2</sup> Tian et al., 2021

<sup>&</sup>lt;sup>3</sup> Ibid

# Distribution & Sources of 6PPD-Q

6PPD and 6PPD-Q are chemicals of concern, not only because of their toxicity, especially 6PPD-Q, but because of their global ubiquity. 6PPD and 6PPD-Q have been detected at levels that pose risks to living organisms<sup>4</sup>. 6PPD-Q is globally widespread in diverse environments. It has been detected in runoff and surface waters around the world<sup>5</sup>, in indoor dust<sup>6</sup>, atmospheric snow<sup>7</sup>, and in the urine of humans including pregnant women<sup>8</sup>.

A single 4-wheel vehicle can release up to 140-700g of 6PPD and 1.4-500g of 6PPD-Q during its lifetime<sup>9</sup>. In the USA alone, the estimated 6PPD-Q release from tire wear particles shed from tires during use is around 1,900 tons per year<sup>10</sup>. Other sources of 6PPD, and therefore 6PPD-Q, include rubber-related products like clothes, recreation facilities, sporting equipment, pipes, wires, conveyor belts, and cables<sup>11</sup>.

#### Water

6PPD and 6PPD-Q have been detected in roadway runoff in Seattle, WA; Los Angeles, CA; Hong Kong, China; and Saskatoon, Canada<sup>12</sup>. They have been found in the urban water system in South China<sup>13</sup> as well as in tunnel wash runoff, runoff from an artificial turf field, and a puddle on a country road in Norway<sup>14</sup>. Also, they are present in snowmelt in Saskatoon, Canada<sup>15</sup> and Leipzig, Germany<sup>16</sup>.

River water containing 6PPD and 6PPD-Q, likely as a result of being receptacles for urban roadway runoff, has been reported in the Don River and Highland Creek of the Greater Toronto area<sup>17</sup> and Cubberla Creek in Australia<sup>18</sup>.

Influent and effluent of wastewater treatment plants, especially following rain events or snowmelt which increase roadway runoff, contained 6PPD and 6PPD-Q in Toronto, Canada<sup>19</sup> and Leipzig, Germany<sup>20</sup>. Additionally, depending on wastewater treatment processes utilized, 6PPD-Q concentrations either increased or decreased from influent to effluent<sup>21</sup>.

<sup>10</sup> Hu et al., 2022

- <sup>12</sup> Tian et al., 2021; Cao et al., 2022; Challis et al., 2021; respectively
- <sup>13</sup> Zhang, H.-Y. et al., 2023
- <sup>14</sup> Kryuchkov et al., 2023
- <sup>15</sup> Challis et al., 2021
- <sup>16</sup> Seiwert et al., 2022

<sup>&</sup>lt;sup>4</sup> Nicomel & Li, 2023

<sup>&</sup>lt;sup>5</sup> e.g., Tian et al., 2023; Challis et al., 2021; Johannessen et al., 2021; Cao et al., 2022; Kryuchkov et al., 2023; Seiwert et al., 2022

<sup>&</sup>lt;sup>6</sup> Cao et al., 2022; Huang et al., 2021; Zhang, Z. et al., 2024; Zhang, Y. et al., 2022

<sup>&</sup>lt;sup>7</sup> Zhang, X. et al., 2024

<sup>&</sup>lt;sup>8</sup> Mao et al., 2024; Du et al., 2022; Zhao et al., 2023b

<sup>&</sup>lt;sup>9</sup> Johannessen et al., 2022

<sup>&</sup>lt;sup>11</sup> Huang et al 2021, Liang et al 2022, Zhang, Y. et al 2022; Zhang, Z. et al 2024

<sup>&</sup>lt;sup>17</sup> Johannessen et al., 2021, 2022

<sup>&</sup>lt;sup>18</sup> Rauert et al., 2022

<sup>&</sup>lt;sup>19</sup> Johannessen et al., 2021

<sup>&</sup>lt;sup>20</sup> Seiwert et al., 2022

<sup>&</sup>lt;sup>21</sup> Johannessen & Metcalfe, 2022

Notably, 6PPD-Q water concentrations in most studies were much higher than the coho salmon LC50, with the highest observed environmental concentration reaching 19 ug/L in Seattle, WA,<sup>22</sup> indicating widespread potential threats to aquatic organisms.

#### Soil & Sediment

In addition to roadside soils in Hong Kong<sup>23</sup>, 6PPD and 6PPD-Q were also found consistently present in riverine, estuarine, and coastal, and deep-sea sediments in and around the South China Sea<sup>24</sup>. Their presence in the soil indicates the possibility of plant contamination. Indeed, 6PPD-Q has been found to accumulate in the roots and leaves of market-bought lettuce<sup>25</sup>. 6PPD-Q accumulation in lettuce roots may be indicative of additional human exposure from root vegetables such as carrots and radishes.

#### Dust

Dust has been found to contain 6PPD and 6PPD-Q in a variety of environments. They were detected in road dust across China and Tokyo, Japan<sup>26</sup> and in dust from underground parking lots in Hong Kong<sup>27</sup> and Guangzhou, China<sup>28</sup>.

6PPD and 6PPD-Q has also been found in dust with high frequencies in indoor environments, e.g., vehicles in Hong Kong<sup>29</sup>, kindergartens in Shantou, China<sup>30</sup>, and bedrooms, residential air conditioners, shopping malls, and college dormitories in Guangzhou, China<sup>31</sup>. This indicates that additional rubber-related products like clothes, entertainment facilities, furniture, and electronic equipment could be 6PPD-Q sources. Road, house, and kindergarten dust from an area near a major e-waste recycling location in Guiyu, China was found to have significantly higher 6PPD-Q compared to a reference location<sup>32</sup>. Of note, in indoor environments, infants are expected to have higher exposure risk than children and adults due to their proximity to the ground, where dust settles<sup>33</sup> and their hand-to-mouth behaviors.

An important source of 6PPD and 6PPD-Q in dust is the use of recycled rubber. Recycled tires are used for sidewalks, fitness center floors, and playground surfaces<sup>34</sup>. Concentrations of 6PPD in outdoor rubber playground dust were found to be higher than living room dust collected in Beijing, China, indicating the release of these chemicals from rubber playgrounds<sup>35</sup>. Another

<sup>&</sup>lt;sup>22</sup> Tian et al., 2021

<sup>&</sup>lt;sup>23</sup> Cao et al., 2022

<sup>&</sup>lt;sup>24</sup> Zeng et al., 2023

<sup>&</sup>lt;sup>25</sup> Castan et al., 2022

<sup>&</sup>lt;sup>26</sup> Zhang, Y. et al., 2024; Hiki & Yamamoto 2022a; Deng et al., 2022; Huang et al., 2021

<sup>&</sup>lt;sup>27</sup> Cao et al., 2022

<sup>&</sup>lt;sup>28</sup> Huang et al., 2021

<sup>&</sup>lt;sup>29</sup> Cao et al., 2022; Huang et al., 2021

<sup>&</sup>lt;sup>30</sup> Zhang, Z. et al., 2024

<sup>&</sup>lt;sup>31</sup> Zhang, Y. et al., 2022

<sup>&</sup>lt;sup>32</sup> Zhang, Z. et al., 2024

<sup>&</sup>lt;sup>33</sup> Zhu, J. et al., 2024

<sup>&</sup>lt;sup>34</sup> Llompart et al., 2012

<sup>&</sup>lt;sup>35</sup> Liu et al., 2019

use of recycled tires is artificial turf fill. A single professional-sized sports field requires crumb rubber from 20,000 - 40,000 tires at initial installation, with additional crumb rubber granules required for replenishment as granules migrate or disintegrate during use<sup>36</sup>. As of 2017, the USA had an estimated 12,000 artificial turf fields made from around 10 million tires and around 17.5 million tires were used to cover children's playgrounds<sup>37</sup>.

#### Atmosphere

In the atmosphere, 6PPD-Q has been found in 81% of atmospheric particle samples (PM2.5) in six Chinese megacities<sup>38</sup>, in all airborne PM2.5 samples along a highway in Mississippi<sup>39</sup>, and in most air particle samples in Hong Kong<sup>40</sup>. Cumulative effects through frequent inhalation are a human health concern. Additionally, detection of 6PPD and 6PPD-Q in freshly fallen snow that did not reach the ground in seven urban areas in China is an indicator of their presence in the atmosphere<sup>41</sup>.

#### Humans

Perhaps most alarming of these findings may be that 6PPD and 6PPD-Q have commonly been detected in human cerebrospinal fluid, implying a tendency for them to accumulate in the human brain<sup>42</sup>. Additionally, they were found in human serum<sup>43</sup> and in most human urine samples, with the highest concentrations being in women and pregnant women<sup>44</sup>. Additionally, 6PPD and 6PPD-Q have been reported in several types of market-bought fish, indicating that they bioaccumulate and may biomagnify<sup>45</sup>. All of these studies indicate that humans and other terrestrial organisms are exposed and at risk, not just aquatic organisms.

An important aspect of human exposure is that certain populations will be more exposed and more at risk than others. Infants, as previously mentioned, are more highly exposed due to their proximity to the ground where dust settles and their hand-to-mouth behaviors. Athletes on artificial turf fields will also be more exposed. Finally, people with jobs near where tires are used will be more exposed including tire store and garage workers, NASCAR pit crews, aircraft carrier deck crews, truck drivers, and people who clean roads or work in road construction. These populations should be of particular concern and prioritization when producing protective policies.

<sup>&</sup>lt;sup>36</sup> Watterson, 2017

<sup>37</sup> Ibid

<sup>&</sup>lt;sup>38</sup> Zhang, Y. et al., 2022, 2024

<sup>&</sup>lt;sup>39</sup> Olubusoye et al., 2023

<sup>&</sup>lt;sup>40</sup> Cao et al., 2022

<sup>41</sup> Zhang, X. et al., 2024

<sup>&</sup>lt;sup>42</sup> Fang, J. et al., 2024

<sup>43</sup> Song et al., 2024

<sup>&</sup>lt;sup>44</sup> Mao et al., 2024; Du et al., 2022; Zhao et al., 2023b

<sup>&</sup>lt;sup>45</sup> Ji et al., 2022a

# Toxicity

A flurry of 6PPD-Q effects research has emerged following the initial discovery of its impact on coho salmon populations in the U.S. Pacific Northwest<sup>46</sup>.

#### Fishes

Research on coho salmon found that while the dose required for 50% lethality in test subjects (LC50) of 6PPD is 250 ug/L, 6PPD-Q is far more acutely toxic, with a LC50 of 0.095 ug/L in just 6 hours of exposure<sup>47</sup>. Juveniles are even more sensitive, with a LC50 of 0.041 ug/L<sup>48</sup>. Hypotheses for specific mechanisms leading to the high toxicity include disruption of the blood-brain barrier<sup>49</sup> and embryo growth inhibition<sup>50</sup>. Even road runoff diluted by 95% is still highly toxic to coho salmon<sup>51</sup>. Unfortunately, concentrations measured in salmon-bearing waterways are above LC50s for coho, suggesting potential for population-level consequences in urban waters<sup>52</sup>.

Following coho salmon, white spotted char, brook trout, and rainbow trout are considered the next most sensitive species; the white spotted char 24 h LC50 is 0.51 ug/L, the brook trout 24h LC50 is 0.59 ug/L, and rainbow trout 72h LC50 is 1.00 ug/L<sup>53</sup>. A relationship between neurotoxicity and acute lethality was observed in rainbow trout where the fish that died had significantly higher brain concentrations of 6PPD-Q than those that survived<sup>54</sup>.

In contrast, chinook and steelhead salmon appear less sensitive, but still experienced mortality and toxicity when exposed to diluted runoff and did not recover when transferred to uncontaminated water<sup>55</sup>. Furthermore, chinook juveniles are similarly less sensitive than coho juveniles to mortality, exhibiting more sublethal impacts than lethal<sup>56</sup>.

Paradoxically, other fish species, even those closely related to coho salmon, have drastically different responses to exposure. Sockeye salmon<sup>57</sup>, atlantic salmon and brown trout<sup>58</sup>, masu salmon<sup>59</sup>, white sturgeon and arctic char<sup>60</sup>, and japanese rice fish<sup>61</sup> were tolerant to much higher concentrations than coho salmon. However, sublethal toxicity endpoints still need to be explored in most species.

<sup>&</sup>lt;sup>46</sup> Tian et al., 2021

<sup>&</sup>lt;sup>47</sup> Tian et al., 2021, 2022

<sup>&</sup>lt;sup>48</sup> Lo et al., 2023

<sup>&</sup>lt;sup>49</sup> Blair et al., 2021

<sup>&</sup>lt;sup>50</sup> Greer et al., 2023b

<sup>&</sup>lt;sup>51</sup> French et al., 2022

<sup>&</sup>lt;sup>52</sup> Tian et al., 2021; Challis et al., 2021; Johannessen et al., 2021, 2022

<sup>&</sup>lt;sup>53</sup> Hiki & Yamamoto, 2022b; Brinkmann et al., 2022

<sup>&</sup>lt;sup>54</sup> Liao et al., 2023

<sup>&</sup>lt;sup>55</sup> French et al., 2023; Greer et al., 2023a

<sup>&</sup>lt;sup>56</sup> Lo et al., 2023

<sup>&</sup>lt;sup>57</sup> French et al., 2022; Greer et al., 2023a

<sup>&</sup>lt;sup>58</sup> Foldvik et al., 2022

<sup>&</sup>lt;sup>59</sup> Hiki & Yamamoto, 2022b

<sup>&</sup>lt;sup>60</sup> Brinkmann et al., 2022

<sup>61</sup> Hiki et al., 2021

Sublethal impacts are of broader concern as more species are impacted by sublethal rather than lethal concentrations. Fathead minnows, for example, were insensitive to 6PPD-Q induced acute mortality, but exhibited sublethal responses such as oxidative stress and disruption of the metabolism in their gills and livers<sup>62</sup>. Further, in zebrafish, acute lethal toxicity at high concentrations are not observed<sup>63</sup>, but multiple studies report sublethal impacts of concern. These include bioaccumulation and cardiotoxicity<sup>64</sup>, activity inhibition, loss of balance, and anxiety with symptoms similar to Huntinton's Disease in humans<sup>65</sup>, neurodevelopmental toxicity and disruption of the thyroid system<sup>66</sup>, altered central nervous system functioning<sup>67</sup>, affected metabolic pathways in the liver and intestine as well as impacted cellular processes associated with cholesterol metabolism and muscle tissue development<sup>68</sup>, and teratogenicity in embryos, inducing malformations, decreased heart rate, and impaired intestine development and function<sup>69</sup>. Additionally, co-exposure to chlorinated disinfection products, e.g., in wastewater treatment, enhances toxicity to embryos<sup>70</sup>.

The mechanism of acute lethality to salmonids remains unclear, though disruption of the blood-brain barrier and mitochondria are suspects<sup>71</sup>. Further studies have suggested that in sensitive species, acute lethality might be caused by uncoupling of mitochondrial respiration in gills<sup>72</sup>. Multiple studies observed sensitive species gasping and displaying increased ventilation rate, suggesting a possible impact on respiration<sup>73</sup>. A study within fish cells concluded that toxicity might be driven by a tissue-specific disruption of mitochondrial respiration, the most important generator of energy for cells<sup>74</sup>. Yet another study observed genotoxicity in which 6PPD-Q bonds with DNA and the resulting chemical was found to accumulate in gills and roe of market-bought capelins<sup>75</sup>. Evidence was also found that exposure in parental generations could cause toxicity to their offspring by direct transportation of 6PPD-Q in roe, as well as by the passing down of abnormal genetic information induced by DNA damage after exposure<sup>76</sup>. Tolerant species and life stages of fish have been shown to efficiently detoxify 6PPD-Q in their bodies prior to the onset of acute lethality<sup>77</sup>. The reason for the species specific toxicity and the mechanism of toxicity is a point of major research focus.

<sup>62</sup> Anderson-Bain et al., 2023

<sup>&</sup>lt;sup>63</sup> Hiki et al., 2021

<sup>64</sup> Fang, C. et al., 2023

<sup>&</sup>lt;sup>65</sup> Ji et al., 2022b

<sup>&</sup>lt;sup>66</sup> Peng et al., 2022

<sup>&</sup>lt;sup>67</sup> Ricarte et al., 2023

<sup>&</sup>lt;sup>68</sup> Varshney et al., 2024

<sup>69</sup> Zhang, S.-Y. et al., 2023

<sup>&</sup>lt;sup>70</sup> Jiao et al., 2024

<sup>&</sup>lt;sup>71</sup> Hiki & Yamamoto 2022b; Blair et al., 2020; Mahoney et al., 2022

<sup>&</sup>lt;sup>72</sup> Anderson-Bain et al., 2023

<sup>&</sup>lt;sup>73</sup> Lo et al., 2023; Brinkmann et al., 2022; Mahoney et al., 2022

<sup>&</sup>lt;sup>74</sup> Mahoney et al., 2022

<sup>&</sup>lt;sup>75</sup> Wu et al., 2023

<sup>76</sup> Ibid

<sup>77</sup> Montgomery et al., 2023

#### Invertebrates

Potentially the most studied organism with respect to 6PPD-Q toxicity is *Caenorhabditis elegans* (roundworms). Multiple sublethal impacts have been found in roundworms at environmentally relevant concentrations, including reduced dopamine content and changed dopamine-related behaviors<sup>78</sup>, neurotoxicity and neurodegeneration with resulting abnormal locomotion and sensory perception behaviors<sup>79</sup>, and shorter lifespan and healthspan due to altered insulin signaling<sup>80</sup>. Further, long-term exposure caused intestinal toxicity by affecting the intestinal barrier<sup>81</sup> and reduced reproductive capacity due to impaired gonad development and enhancement in DNA damage with an increase in expression of related genes<sup>82</sup>.

Other invertebrates with sensitivity to 6PPD-Q include mutagenicity in an amphipod<sup>83</sup>, inhibited survival in springtails following a 28-day chronic exposure<sup>84</sup>, and mortality in rotifers, cladocerans, washboard mussel, and file ramshorn snails at environmentally relevant concentrations<sup>85</sup>. Interestingly, in the rotifer *Brachionus calyciflorus*, 6PPD was found to be more harmful than 6PPD-Q and synergistic effects were observed with the addition of salt (NaCl)<sup>86</sup>.

Invertebrates have also shown species-specific responses to 6PPD-Q exposure. Those that appear tolerant to mortality at high concentrations include an amphipod (*H. azteca*), *Daphnia manga*, a species of rotifer (*Brachionus koreanus*), copepods, burrowing mayflies, and juvenile cladocerans<sup>87</sup>. Most of these studies reported on lethality, thus there is need for further investigation regarding sublethal impacts.

#### Mammalian Systems (Mice)

Both 6PPD and 6PPD-Q have been shown to be toxic to mice in a variety of ways. They bioaccumulate in the liver and may cause hepatotoxicity and metabolic disorders therein<sup>88</sup>. Also, environmentally relevant doses can disrupt intestinal barrier integrity<sup>89</sup>. Repeated exposure induced inflammation and fibrosis and multiorgan effects including accumulation in the liver and lung, lung function impairment, and alteration of liver, kidney, lung, spleen, testis, and brain activities<sup>90</sup>. Moreover, the liver has been found impacted in pregnant mice treated with 6PPD and 6PPD-Q, followed by the brain and placenta<sup>91</sup>. In the mice fetuses, detection of both chemicals in

<sup>&</sup>lt;sup>78</sup> Hua & Wang, 2023a

<sup>&</sup>lt;sup>79</sup> Hua et al., 2023a; Liu et al., 2024

<sup>&</sup>lt;sup>80</sup> Hua & Wang, 2023b

<sup>&</sup>lt;sup>81</sup> Hua et al., 2023c

<sup>82</sup> Hua et al., 2023b

<sup>&</sup>lt;sup>83</sup> Botelho et al., 2023

<sup>&</sup>lt;sup>84</sup> Xu et al., 2023

<sup>&</sup>lt;sup>85</sup> Li, J. et al., 2023; Prosser et al., 2023

<sup>&</sup>lt;sup>86</sup> Klauschies & Isanta-Navarro, 2022

<sup>&</sup>lt;sup>87</sup> Li, J. et al., 2023; Hiki et al., 2021; Maji et al., 2023; Prosser et al., 2023

<sup>88</sup> Fang, L. et al., 2023

<sup>89</sup> Yang et al., 2024

<sup>&</sup>lt;sup>90</sup> He et al., 2023, 2024

<sup>&</sup>lt;sup>91</sup> Zhao et al., 2023b

the bodies and brains demonstrates bioaccumulation, placental transfer, and blood-brain barrier permeation potentials<sup>92</sup>.

#### Humans

There are currently no literature reports on the safe concentration of 6PPD-Q for humans<sup>93</sup>. Given its widespread presence in various environmental matrices, humans have been extensively exposed to 6PPD-Q. Due to the wide distribution of 6PPD and 6PPD-Q in environmental media, entry into the human body may occur through multiple pathways, such as ingestion, inhalation, and skin contact. 6PPD and 6PPD-Q have been found in most human urine samples, with the highest levels in women and pregnant women<sup>94</sup>. Also, an in-vitro study found bioaccumulation of 6PPD-Q in human synthetic gastrointestinal fluids following ingestion of football field crumb rubber<sup>95</sup>. 6PPD-Q has been found in cerebrospinal fluid more frequently and at higher concentrations in those with Parkinson's Disease. This indicates it may be a risk factor for the disease and for neurotoxicity with a notable disruptive effect the mitochondrial respiration of neurons<sup>96</sup>. Additionally, exposure to these chemicals may increase the odds of prevalent secondary nonalcoholic fatty liver disease as well as inducing liver damage<sup>97</sup>. Further evidence of liver damage is indicated by the inhibited enzyme activity of liver microsomes with increased 6PPD-Q exposure, suggesting toxic effects on human liver tissue<sup>98</sup>. A higher daily intake of 6PPD-Q has also been associated with lower BMI and higher frequency of influenza and diarrhea in children<sup>99</sup>. Finally, 6PPD-Q in PM2.5 enhances the oxidative potential of PM2.5 by 15.6-42.2%, prompting DNA damage and oxidative stress<sup>100</sup>.

Luckily, 6PPD-Q has been predicted to not cause mutagenicity or carcinogenicity<sup>101</sup>. However there is no indication of lack of toxicity potential, especially because some metabolites of 6PPD-Q are predicted to have immunotoxic or mutagenic toxicity<sup>102</sup>.

# 6PPD-Q Management through Statutory, Regulatory, and Policy Engagement

States and the federal government are equipped to manage chemical pollutants such as 6PPD-Q through a variety of statutory and regulatory authorities. For instance, due to its extreme toxicity in select salmon species, 6PPD-Q has been listed as a priority toxic chemical by the Washington State Department of Ecology<sup>103</sup>. More research is certainly needed to fully

<sup>92</sup> Ibid

<sup>93</sup> Fang, J., et al 2024

<sup>&</sup>lt;sup>94</sup> Mao et al., 2024; Du et al., 2022

<sup>&</sup>lt;sup>95</sup> Armada et al., 2023

<sup>&</sup>lt;sup>96</sup> Fang, J. et al., 2024

<sup>&</sup>lt;sup>97</sup> Song et al., 2024

<sup>98</sup> Zhang, Y.-Y. et al., 2024

<sup>&</sup>lt;sup>99</sup> Zhang, Z. et al., 2024

<sup>&</sup>lt;sup>100</sup> Wang, W. et al., 2022

<sup>&</sup>lt;sup>101</sup> Yang et al., 2024

<sup>&</sup>lt;sup>102</sup> Zhang, Y.-Y. et al., 2024

<sup>&</sup>lt;sup>103</sup> Washington State Department of Ecology, 2022

understand the potential impacts of 6PPD and 6PPD-Q on the environment and human populations. However, what is currently known is enough to warrant implementation of policies.

6PPD has been listed as a high production volume chemical by the Organisation for Economic Co-operation and Development<sup>104</sup>. At the same time, 6PPD-Q is a proven toxicity concern to multiple fish species protected under the Endangered Species Act including some Coho and Chinook salmon, and steelhead trout populations<sup>105</sup>. 6PPD-Q is predicted to pose a calculated "high" ecological risk, and the human health risk prediction was unquantifiable as there is no published safe intake value<sup>106</sup>. There is clearly a gap between research and policy that needs to be closed. Indeed, many governments, including the U.S., permit crumb rubber as a means of recycling rubber tires while also opposing landfilling of tires because of concerns about leachates<sup>107</sup>.

According to the U.S. Environmental Protection Agency (EPA), chemicals that pose risks to children's health should be prioritized for assessment under the Toxic Substances Control Act (TSCA)<sup>108</sup>. While the impact of 6PPD-Q to children's health is unquantified, there are known high exposures from a multitude of matrices, proven uptake in the human body, and an association between exposure and multiple human health parameters including neurotoxicity, liver damage, and DNA damage. Further, higher daily intake of 6PPD-Q is associated with lower BMI and higher frequency of influenza and diarrhea in children. Enough is known to initiate the implementation of risk prevention policies.

#### Actions taken in the U.S.

In the U.S., federal policy draws from underlying statutes, like the Clean Water Act and the TSCA, and implementing regulations wherein federal agencies are allowed to implement rules adding specificity to ambiguous statute language. Beyond that, policy can add even more specificity regarding things like what chemicals to regulate, how to regulate, and what operational actions will be.

The U.S. EPA is one of the bodies working to regulate 6PPD and 6PPD-Q. Current statutory and regulatory actions being taken by the EPA include a broad suite of actions under multiple federal statutes<sup>109</sup>. Several of these actions fall under the TSCA. Section 6 of TSCA authorizes the EPA to address risks by restricting activities involving a chemical that poses an "unreasonable risk" to health or the environment<sup>110</sup>. These restrictions can range from minor tweaks to total prohibition of manufacturing, distribution, and/or use of the chemical. To determine which chemicals pose unreasonable risk, the EPA follows a detailed process to prioritize and evaluate the hazards of the more than 70,000 substances listed on the TSCA

<sup>&</sup>lt;sup>104</sup> OECD, 2004

<sup>&</sup>lt;sup>105</sup> NOAA Fisheries, https://www.fisheries.noaa.gov/species/pacific-salmon-and-steelhead/esa-protected-species

<sup>&</sup>lt;sup>106</sup> Zhang, H.-Y. et al., 2023

<sup>&</sup>lt;sup>107</sup> Watterson, 2017

<sup>&</sup>lt;sup>108</sup> U.S. EPA, 2014; Zhao et al., 2023b

<sup>&</sup>lt;sup>109</sup> U.S. EPA, https://www.epa.gov/chemical-research/6ppd-quinone

<sup>&</sup>lt;sup>110</sup> U.S. 40 CFR Part 710, https://www.ecfr.gov/current/title-40/part-710

Inventory<sup>111</sup>. The EPA has proposed 6PPD-Q as a potential candidate for risk evaluation and prioritization under TSCA Section 6<sup>112</sup>. Further, the EPA has a CompTox Dashboard<sup>113</sup> where data and information about over one million chemicals, including 6PPD<sup>114</sup>, is maintained. This data feeds into their regulation and management actions.

Before specific compliance regulations can be implemented, an approved analytical method to analyze the regulated chemical needs to be established. Without a method to measure chemical concentration in regulated media like streams or wastewater effluent, the EPA cannot ensure compliance to chemical limits. This is why a not-yet-approved draft method (Method 1634) was published for testing 6PPD-Q in surface water and stormwater<sup>115</sup>.

To speed action, on August 1, 2023 a petition was sent to the EPA from the Yurok Tribe, the Port Gamble S'Klallam Tribe, and the Puyallup Tribe of Indians asking for the prohibition of manufacture, processing, using, and distribution of 6PPD<sup>116</sup>. Three months following the petition, on November 2, 2023 the EPA granted the petition<sup>117</sup>. This commenced proceeding for proposed rulemaking<sup>118</sup>. Under the TSCA section 6, the EPA will decide what is needed to make regulation and then policy.

# Policy Recommendations

To be protective of the most sensitive species and designated waterbody use, 6PPD should be phased out of use in tires. Additionally, recycled tires should no longer be permitted for use in direct human contact purposes like playgrounds and artificial turf. Indeed, in September 2023 the European Union enacted a ban on the sale of products containing intentionally added microplastics, listing crumb rubber infill as such<sup>119</sup>. Furthermore, it has been recommended that risk thresholds be set as soon as feasible to reduce risk of exposure<sup>120</sup>.

#### Recommendation #1: Replacement of 6PPD as a rubber antioxidant

Safe and effective alternative antioxidants for use in tires and other elastomeric products should be developed. The replacement of 6PPD will be a challenge for the industry as rubber products are susceptible to degradation from reactive chemicals. Additionally, 6PPD is used

<sup>&</sup>lt;sup>111</sup> U.S. EPA, https://www.epa.gov/tsca-inventory

<sup>&</sup>lt;sup>112</sup> U.S. 89 Fed. Reg. 20918, https://www.federalregister.gov/d/2024-06303

<sup>&</sup>lt;sup>113</sup> U.S. EPA, https://comptox.epa.gov/dashboard/

<sup>&</sup>lt;sup>114</sup> U.S. EPA, https://comptox.epa.gov/dashboard/chemical/details/DTXSID9025114

<sup>&</sup>lt;sup>115</sup> U.S. EPA, 2023,

https://www.epa.gov/system/files/documents/2024-01/draft-method-1634-for-web-posting-1-23-24\_508.pdf <sup>116</sup> Earthjustice 2023,

https://www.epa.gov/system/files/documents/2023-08/TSCA%20Section%2021%20Petition%20to%20EPA%20re%206PPD%20in%20tires.pdf

<sup>&</sup>lt;sup>117</sup> U.S. EPA 2023,

 $https://www.epa.gov/system/files/documents/2023-11/pet-001845\_tsca-21\_petition\_6ppd\_decision\_letter\_esigned20\ 23.11.2.pdf$ 

<sup>&</sup>lt;sup>118</sup> U.S. 89 CFR 20918, https://www.federalregister.gov/d/2024-06303

<sup>&</sup>lt;sup>119</sup> Zuccaro et al., 2024

<sup>120</sup> Zhang, H.-Y. et al., 2023

globally in tires and without it, tires can fail within 100-1000 miles of running, posing safety risks<sup>121</sup>. However, the toxicity to aquatic organisms as well as mammals, including humans, warrants pressure on manufacturers and decision makers to find alternative solutions.

Natural antioxidants are diverse and include bamboo polyphenols, rosmarinic acid derivatives, and other plant-based flavonoid and phenol antioxidants<sup>122</sup>. Synthetic variants have been suggested as replacements in a recent report for the U.S. Tire Manufacturers Association<sup>123</sup> and others<sup>124</sup> including 7PPD, IPPD, CCRP, specialized graphine, TMQ, ethoxyquin. An important note is that the lack of information on the risk from transformation products of these chemicals may result in a similar unintended consequence as 6PPD-Q. Alternatives and their transformation products will need to be studied for their effects on fish and other animal species, including humans, before their widespread use.

#### Recommendation #2: Prevent 6PPD-Q distribution in the environment

Until a suitable replacement for 6PPD is found for the tire and rubber industry, best management practices are necessary to reduce impact on aquatic and terrestrial populations. These include source control strategies like regular roadside cleanup. More than 90% of the total load of 6PPD and its transformation products in roadside snow has been found in the particulate fraction of snow<sup>125</sup>. Thus, removing the particulate fraction of road runoff before its discharge into surface water would substantially reduce 6PPD and 6PPD-Q emissions. Additionally, bioretention technologies, green infrastructure, and stormwater filtration have been proven to be effective at filtering pollutants before entry into receiving waters<sup>126</sup>. These methods should also be implemented around artificial turf fields and playgrounds using recycled tire rubber. Other actions that can be taken include regular maintenance of roads to reduce tire wear, finding alternative routes to avoid excessive braking in trucks, rubber modified asphalt, and maintaining proper tire pressure<sup>127</sup>.

#### Recommendation #3: Terminate recycling rubber in products with direct human contact

Tires are often recycled after use, sometimes into products with direct human contact like artificial turf crumb rubber or playground flooring. With the harm that extended exposure may induce, this is an unnecessary risk. While disposal of tires remains an issue, recycling tires and other used rubber products into products with human contact should not be the solution. There have been several local actions by school boards or localities that prevent tires from being used

<sup>&</sup>lt;sup>121</sup> Bohara et al., 2024

<sup>122</sup> Ibid

<sup>123</sup> Gradient, 2024,

https://www.ustires.org/sites/default/files/2024-03/USTMA%20Consortium%206PPD%20AA%20Preliminary%20 Report\_3-25-24.pdf

<sup>&</sup>lt;sup>124</sup> Wang, W. et al., 2022; Jin et al., 2023

<sup>&</sup>lt;sup>125</sup> Seiwert et al., 2022

<sup>&</sup>lt;sup>126</sup> McIntyre et al., 2023

<sup>&</sup>lt;sup>127</sup> Washington State Department of Ecology, 2022

in artificial turf<sup>128</sup>. This is a great first step, however, piecemeal policy is not an efficient or sufficiently protective action. Therefore, a larger scale broad policy should be enacted.

### Lastly, the Precautionary Principle

Beyond 6PPD and 6PPD-Q, there should be more careful toxicological assessment for transformation and degradation products of all high production volume commercial chemicals subject to pervasive environmental discharge. Furthermore, environmental pollution regulation in the U.S. is almost entirely reactionary, with the underlying assumption being that absence of evidence of risk can be interpreted as absence of risk. Instead, the precautionary principle should be used in chemical management. The precautionary principle is an epistemological, philosophical, and legal approach to innovations with the potential for causing harm when extensive scientific knowledge on the matter is lacking. The definition contained in Principle 15 of the 1992 Rio Declaration<sup>129</sup> is widely recognized and provides practical guidance in the development and application of law:

"Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation."

The precautionary principle implies that there is a social responsibility to protect the environment and the public from exposure to harm when scientific investigation has found a plausible risk. If the precautionary principle was mobilized in environmental policy, so much time and money would be saved, and harm prevented. Therefore, there should be a policy of comprehensive preventative toxicity testing of chemicals, particularly high production volume chemicals, before production, distribution, and use.

<sup>&</sup>lt;sup>128</sup> Agrawal, 2023; Houghton, 2024

<sup>&</sup>lt;sup>129</sup> United Nations 1992,

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