United States
Consumer Product Safety Commission

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CPSC Staff Statement on University of Cincinnati Report "Final Report on Technical Support Activities for a Screening-Level Risk Assessment of Playground Surfaces"[1]

As part of the *Federal Research Action Plan on Recycled Tire Crumb Used on Playing Fields and Playgrounds* (FRAP),[2] the U.S. Consumer Product Safety Commission (CPSC) contracted with the Risk Science Center of the University of Cincinnati (UC) to support risk assessment for selected chemical substances potentially present in playground surfaces that are made with recycled tire rubber. The technical support activities under this task order focus on identification of toxicity reference values (TRVs) of selected chemicals, and selection of parameter values and exposure models for the exposure assessment.

The following report describes UC's findings and recommendations regarding the contracted tasks. The first part of the report includes UC's collection of available TRVs derived from authoritative sources for nine chemicals selected by CPSC staff as substances of concern that were recently detected in recycled tire rubber samples.[3] The nine chemicals are benzo(a)pyrene, hexavalent chromium, zinc, 4-methyl-2-pentanone, benzothiazole, lead, dibutyl phthalate, diethylhexyl phthalate, and 4-tert-octylphenol. UC staff identified acute, subchronic, and chronic TRVs, where available, for the oral, inhalation, and dermal routes. UC staff made recommendations for which values should be used in quantitative hazard and risk assessments of playground surfaces made of recycle tire rubber.

For the second part of the report, CPSC staff provided UC staff with 11 proposed exposure models that included five inhalation, three dermal, and four oral exposure scenarios. The UC team commented on the appropriateness of each model for the intended screening assessment,

[1] This statement was prepared by the CPSC staff, and the attached report was produced by the University of Cincinnati for CPSC staff. The statement and report have not been reviewed or approved by, and do not necessarily represent the views of, the Commission.
[2] https://www.epa.gov/sites/production/files/2016-02/documents/federal_research_action_plan_tirecrumb_final_2.pdf
[3] U.S. EPA and CDC/ATSDR. 2019. Synthetic Turf Field Recycled Tire Crumb Rubber Research Under the Federal Research Action Plan Final Report: Part 1 - Tire Crumb Characterization (Volumes 1 and 2). (EPA/600/R-19/051). United States Environmental Protection Agency, Centers for Disease Control and Prevention/Agency for Toxic Substances and Disease Registry.

each model's assumptions and limitations, and which variables have the greatest potential for uncertainty.

CPSC staff's screening-level risk assessment activities for tire rubber in playground surfaces are ongoing. These screening-level assessments will inform CPSC staff on the usefulness of the proposed models and may help staff to develop more comprehensive risk assessments of recycled tire rubber used in playground surfacing. Stakeholders can find updates on CPSC's FRAP-related activities at https://www.cpsc.gov/Safety-Education/Safety-Education-Centers/Crumb-Rubber-Safety-Information-Center.

Final Report on Technical Support Activities for a Screening-Level Risk Assessment of Playground Surfaces

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LIST OF ABBREVIATIONS

2MBZT 2-mercaptobenzothiazole
4-4-OP 4-tert-Octylphenol
AALM All Ages Lead Model
ACGIH American Conference of Governmental Industrial Hygienists
ADD average daily dose
ADI acceptable daily intake
AGD anogenital distance
ATSDR Agency for Toxic Substances and Disease Registry
BAP Benzo(a)pyrene
BLL blood lead level
BMCL benchmark concentration lower limit
BMR benchmark response
BZT benzothiazole
CDC Centers for Disease Control and Prevention
CHAP Chronic Hazard Advisory Panel
CMP Chemical Management Plan
CPSC United States Consumer Product Safety Commission
Cr(VI) hexavalent chromium
DBP dibutyl phthalate
DEHP diethylhexyl phthalate
DNEL derived no effect level
ECHA European Chemicals Agency
ERASSTRI European Risk Assessment Study on Synthetic Turf Rubber Infill
FDA Food and Drug Administration
FRAP federal research action plan
HI hazard index
HPVIS High Production Volume Information System
HQ hazard quotient
IARC International Agency for Research on Cancer
IEUBK Integrated Exposure Uptake Biokinetic Model for Lead in Children
IQ intelligence quotient
IRIS Integrated Risk Information System
IRL Interim Reference Level
IUR inhalation unit risk
JECFA Joint FAO/WHO Expert Committee on Food Additives
LOAEC lowest adverse effect concentration
LOAEL lowest observed adverse effect level
LOEL lowest observed effect level
LRGA Literature Review and Data Gaps Analysis
MDH Minnesota Department of Health
MIBK Methyl Isobutyl Ketone
MOA mode of action
MOE margin of exposure
MRL minimal risk level

NAAQS National Ambient Air Quality Standard
NHANES National Health and Nutrition Examination Survey
NOAEC no observed adverse effect concentration
NOAEL no observed adverse effect level
NTP National Toxicology Program
NYSDEC New York State Department of Environmental Conservation
OECD Organisation for Economic Co-operation and Development
OEHHA Office of Environmental Health Hazard Assessment
OEL occupational exposure limit
PAH Polycyclic aromatic hydrocarbons
Pb lead
PEAA potency estimates for antiandrogenicity
PM particulate matter
POD point of departure
PPARα peroxisome proliferator-activated receptor α
PPRTV Provisional Peer-Reviewed Toxicity Value
PTTDI Provisional Tolerable Total Dietary Intake
ReV reference value
RfC reference concentration
RfD reference dose
RIVM National Institute for Public Health and the Environment
SIDS Screening Information Dataset
SVOC semi volatile organic compounds
TCEQ Texas Commission on Environmental Quality
TRV toxicity reference values
TSP total suspended particulate
TTC threshold of toxicological concern
TURI Toxics Use Reduction Institute
U.S. EPA United States Environmental Protection Agency
UC University of Cincinnati
UF uncertainty factor
UF uncertainty factor
VOC volatile organic compound
WOCBA women of childbearing age
WOE weight of evidence
Zn zinc

Introduction

This document is the final report on the technical support activities completed by the University of Cincinnati (UC) for Task Order: 61320619F1011. The purpose of this task order was for UC to provide the U.S. Consumer Product Safety Commission (CPSC) with technical support for a screening-level risk assessment for targeted chemical substances potentially present in playground surfaces that are made with recycled tire rubber. The technical support activities under this task order focus on selection of toxicity values based on available toxicological data sources, and selection of parameter values for the exposure assessment based on available data sources. The screening assessment is intended to focus on playground surfaces made with rubber sourced from recycled tires and not on tire-crumb rubber athletic fields.

The Risk Science Center of UC conducted necessary research to provide documentation of information needed to complete a risk assessment but did not conduct the actual risk assessment. CPSC staff plans to use the results of the UC work to complete the remaining steps of a screening-level risk assessment. CPSC staff will complete the exposure assessment, risk characterization, and remaining discussion of background, uncertainties, and associated potential future data needs.

CPSC staff prioritized 298 chemicals present in the "Tire Crumb Rubber" list from U.S. Environmental Protection Agency (U.S. EPA) Chemicals Dashboard (https://comptox.epa.gov/dashboard/chemical_lists/TIRECRUMB) and identified nine chemical compounds that could potentially be present in rubberized playground surfaces for this task order (see Table 1). The Dashboard information was based on data contained within the 2016 *Federal Research Action Plan on Recycled Tire Crumb Used on Playing Fields and Playgrounds* (U.S. EPA, 2016a). The technical support activities for the screening-level risk assessment covered selected chemicals that could potentially be present in rubberized playground surfaces as specified by CPSC in Table 1 below.

Table 1: Chemical Compounds of Interest for Screening-Level Risk Assessment

CAS	Chemical Name	Chemical Abbreviation
95-16-9	Benzothiazole	BZT
7439-92-1	Lead	Pb
7440-66-6	Zinc	Zn
50-32-8	Benzo(a)pyrene	BAP
18540-29-9	Hexavalent Chromium (Cr^{6+})	Cr(VI)
84-74-2	Dibutyl Phthalate	DBP
117-81-7	Diethylhexyl Phthalate, also known as Di(2-ethylhexyl)phthalate	DEHP
140-66-9	4-tert-Octylphenol	4-t-OP
108-10-1	4-Methyl-2-pentanone (Methyl Isobutyl Ketone)	MIBK

CPSC staff provided UC with several data and information sources, some staff notes on existing toxicity reference values (TRVs), and a Draft Conceptual Exposure Framework document. These materials were reviewed and considered in performing the work for this task order, along with additional documents identified through literature and Internet searching (described below). This report describes the results of our technical support activities covering the following tasks:

- Identified TRVs from available sources for the nine substances listed in Table 1. Conducted a targeted literature survey from readily available hazard databases and completed assessments that reported toxicity reference values and compiled these values. Recommendations for most appropriate values are provided.
- Supplemented the TRVs identified for 4-tert-Octylphenol with a targeted literature survey to determine whether other relevant toxicity information that could be used to derive a TRV is available.
- Reviewed and commented on the Draft Conceptual Exposure Framework document prepared by CPSC staff to help identify a set of potential exposure models and prepared a spreadsheet to use to compile available chemical data by equation and parameter.
- Conducted literature and Internet searching for recycled crumb rubber assessments and data published since the 2016 Federal Research Action Plan (FRAP) on Recycled Tire Crumb Used on Playing Fields and Playgrounds report (U.S. EPA, 2016a). Screened the results to identify assessments that may contain relevant toxicity and/or exposure information.
- Extracted exposure parameter values from the identified assessments and FRAP reports (U.S. EPA, 2016a and U.S. EPA & CDC, 2019).
- Determined data availability for parameters for each exposure model and recommended best approaches and models, given the available data.

Toxicity Reference Values

Approach

We identified relevant TRVs[4] derived by authoritative sources for the nine chemicals listed in Table 1. To compile the TRVs we conducted a targeted literature survey from readily available databases (see Appendix A for sources). We also reviewed recent playground and artificial turf risk assessments for TRVs of interest. That is, we determined whether the assessment reported or derived TRVs for our chemicals of concern that had not already been identified from the literature survey. We identified available TRVs relevant to both chronic and less-than-chronic durations.

In this section, we present tables that summarize the identified TRVs for each chemical. For each TRV, we list the organization, the year of the assessment (to the degree that can be determined from the available documentation), the numerical value of the TRV, relevant key decision points for the TRV derivation (principal study, critical effect, point of departure, and uncertainty factors for noncancer TRVs; or cancer category, slope factor and unit risk for cancer assessments), and any additional explanation needed to understand the derivation. Where an assessment from the listed organization was not located, that is shown as – in the table. If an assessment exists, but specific data are not applicable (e.g., no quantitative cancer assessment per the organization's approach, or the data were insufficient to derive a TRV), that is shown as N/A in the table. N/A is also used in situations where the TRV was available, but documentation on the basis was not publicly available. The tables also note whether an age-dependent adjustment factor is applied. This is a factor unique to the U.S. EPA and applied only for chemicals shown to cause cancer via a mutagenic MOA (U.S. EPA, 2005a). Based on the compiled information and our best professional judgement, we recommend the most appropriate TRV to use in the screening risk assessment and provide a short rationale to support the choice of TRV, including a brief discussion of any substantive differences in TRV derivation across organizations. Key text related to recommendations is bolded. We also note if the TRV is not relevant to children (e.g., a reference dose [RfD] based on developmental toxicity resulting from maternal exposure may not be relevant to a child).

In cases where no TRVs were available for a given route and/or duration of interest, we considered approaches for modifying existing TRVs to fill the gap. If a TRV is available for the desired duration for a different route, we noted whether route-to-route extrapolation is appropriate. Extrapolation from a subchronic TRV to a chronic TRV could be considered where a subchronic TRV was available but not a chronic TRV. Similarly, if an acute TRV is desired, but no acute TRV is available from an authoritative source, one can consider using a chronic TRV, or an intermediate-duration TRV, if available, in a screening assessment.

This report provides TRV data and recommendations for the following chemicals:

- Benzo(a)pyrene (BAP) (CASRN 50-32-8)
- Hexavalent Chromium (Cr(VI)) (CASRN 18540-29-9)

[4] This is a generic term that includes, for example, reference dose (RfD) and acceptable daily intake (ADI), as well as the corresponding values for shorter durations and cancer potency estimates.

- Zinc (CASRN 7440-66-6)
- 4-Methyl-2-pentanone (MIBK) (CASRN 108-10-1)
- Benzothiazole (BZT) (CASRN 95-16-9)
- Lead (CASRN 7439-92-1)
- Dibutyl Phthalate (DBP) (CASRN 84-74-2)
- Diethylhexyl Phthalate (DEHP) (CASRN 117-81-7)
- 4-tert-Octylphenol (4-tOP) (CASRN 140-66-9)

Benzo(a)pyrene (CASRN 50-32-8)

Benzo(a)pyrene (BAP) TRVs are summarized in Tables 2 and 3. Cancer is the primary endpoint of concern following exposure to Benzo(a)pyrene (BAP) via the oral or inhalation route. Most organizations have characterized BAP with their highest cancer weight of evidence, carcinogenic to humans. **Inhalation unit risks (IURs) of 1.1 x 10^{-3} per µg/m^3 (OEHHA, 2009, 2015) and 6 x 10^{-4} per µg/m^3 (U.S. EPA, 2017) are within a factor of two; the California Environmental Protection Agency's *Office of Environmental Health Hazard Assessment* (*OEHHA*) value could be used in screening assessments, as the more conservative value**. Other organizations using quantitative approaches adopted either the OEHHA or U.S. EPA values. For the **oral route, the OEHHA (2010) drinking water assessment reported a cancer slope factor of 1.7 per mg/kg-day, and U.S. EPA (2017) calculated a lower slope factor of 1 per mg/kg-day**. This difference is well within the uncertainty of the methods. The OEHHA value could also be used as a more conservative approach for the oral route.

U.S. EPA (2017), Minnesota Department of Health (MDH, 2020a), and OEHHA (2010) derived separate noncancer limits for BAP. The U.S. EPA derived an **oral RfD of 3 x 10^{-4} mg/kg-day** based on developmental toxicity, and MDH (2020a) derived an essentially identical short-term RfD of 3.1 x 10^{-4} mg/kg-day from the same study. MDH (2020a) applied the short-term RfD for all durations, including short-term, subchronic, and chronic exposure. The study design involved exposure and testing of neonatal rat pups, and so the RfDs are relevant to children. OEHHA's oral noncancer TRV is higher but was developed prior to the publication of the principal study used by the other two organizations. U.S. EPA (2017) derived a **chronic inhalation reference concentration (RfC) of 2 x 10^{-6} mg/m^3 (2 x 10^{-3} µg/m^3)**. This could be used for a noncancer inhalation assessment, but the IUR would drive the inhalation assessment.

No dermal TRVs were located for BAP. A health-protective approach would be to extrapolate from the oral TRVs, accounting for differences in absorption. That is:

$$Dermal\ TRV\ \frac{mg}{kg}/day = \frac{Oral\ TRV\left(\frac{\frac{mg}{kg}}{day}\right) X\ oral\ bioavailability\ faction}{dermal\ bioavailability\ fraction}$$

Table 2. Benzo(a)pyrene Non-cancer Assessments

Organization (year)	TRV	Species	Critical Effect	Point of Departure	Uncertainty Factor	Principal Study
ATSDR (1995)	No oral or inhalation MRLs	N/A	N/A	N/A	N/A	N/A
U.S. EPA (2017)	Oral RfD: $3x10^{-4}$ mg/kg-day	Rat	Developmental toxicity (including developmental neurotoxicity)	BMDL(1SD) = 0.092 mg/kg-day	300 UFA = 10 UFH = 10 UFD = 3	Chen et al., 2012
U.S. EPA (2017)	Chronic Inhalation RfC: $2x10^{-6}$ mg/m^3	Rat	Decreased embryo/fetal survival	LOAEL = 25 µg/m^3 LOAEL(HEC) = $4.6x10^{-3}$ mg/m^3	3000 UFA = 3 UFH = 10 UFL = 10 UFD= 10	Archibong et al., 2002
OEHHA (2010)	ADD = 0.0017 mg/kg-day	Rat	Renal toxicity	LOAEL = 5 mg/kg=day	3000 UFH = 10 UFA = 10 UFL = 10 UFS = 10	Knuckles et al., 2001
PPRTV	--	--	--	--	--	--
Health Canada (1993a)	No TRV derived	N/A	N/A	N/A	N/A	N/A
TCEQ	--	--	--	--	--	--
MDH (Air Guidance Values)	--	--	--	--	--	--
MDH (Water Guidance Values) (MDH, 2020a)	Short term RfD: 0.00031 mg/kg-day	Rat	Functional test of neurological changes in neonatal rats (elevated maze)	BMDL(1SD) = 0.0917 mg/kg-day	300 UFA = 10 UFH = 10 UFD = 3	Chen, 2012
MDH (Water Guidance Values) (MDH, 2020a)	Short-term RfD of 0.00031 mg/kg-day applied to subchronic duration	N/A	N/A	N/A	N/A	N/A

Organization (year)	TRV	Species	Critical Effect	Point of Departure	Uncertainty Factor	Principal Study
MDH (Water Guidance Values) (MDH, 2020a)	Short-term RfD of 0.00031 mg/kg-day applied to chronic duration	N/A	N/A	N/A	N/A	N/A

TRV = toxicity reference value; ADD = not defined, but presumably acceptable daily dose; MRL = minimal risk level; N/A = not applicable; RfD = reference dose; RfC = reference concentration; BMDL = benchmark dose lower bound; SD = standard deviation; UFA – uncertainty factor animal; UFH = uncertainty factor human; UFD = uncertainty factor database; UFS = uncertainty factor subchronic to chronic; LOAEL = lowest observed adverse effect level; HEC = human equivalent concentration; UFL = uncertainty factor.

Table 3. Benzo(a)pyrene Cancer Assessments

Organization (year)	Weight of Evidence Characterization	Quantitative assessment	Extrapolation Method	ADAF
OEHHA (2009, 2015) Based on a 1993 assessment Hot spots program	Not available	Oral slope factor 12 per mg/kg-day Inhalation unit risk 1.1 x 10^{-3} per µg/m^3	Linearized multistage	N/A
OEHHA (2010) Drinking water program	Not available	Oral slope factor: 1.7 per mg/kg-day Oral slope factor: 2.9 per mg/kg-day after accounting for the ADAF	Time to tumor model with linear extrapolation from LED10	Yes
ECHA (2016)	May cause cancer (Category 1B)	N/A	N/A	N/A
U.S. EPA (2017) (oral)	Carcinogenic to humans (2005 guidelines)	Oral slope factor: 1 per mg/kg-day	Time-to-tumor dose-response model with linear extrapolation from the POD ($BMDL_{10}$(HED)) associated with 10% extra cancer risk.	Yes. EPA has concluded that benzo[a]pyrene is carcinogenic by a mutagenic mode of action.

Organization (year)	Weight of Evidence Characterization	Quantitative assessment	Extrapolation Method	ADAF
U.S. EPA (2017) (inhalation)	Carcinogenic to humans (2005 guidelines)	Inhalation unit risk: 6 x 10^{-4} per µg/m^3	Time-to-tumor dose-response model with linear extrapolation from the POD ($BMCL_{10}$(HED)) associated with 10% extra cancer risk.	Yes. EPA has concluded that benzo[a]pyrene is carcinogenic by a mutagenic mode of action.
PPRTV	--	--	--	--
IARC (2012)	There is sufficient evidence that benzo[a]pyrene is carcinogenic to humans (Group 1)	N/A	N/A	N/A
Health Canada (1993) (oral)	Probably Carcinogenic to Humans (Group II)	N/A	N/A	N/A
Health Canada (1993) (inhalation)	Probably Carcinogenic to Humans (Group II)	TD_{05}: 1.6 mg Cr(VI)/m^3	N/A	N/A
TCEQ	--	--	--	--
MDH (Air Guidance Values) (MDH, 2016)	Not available	Oral slope factor 1.7 per mg/kg-day Inhalation unit risk 1.1 x 10^{-3} per µg/m^3	Based on OEHHA (2010)	Yes
MDH (Water Guidance Values) (MDH, 2020a)	Carcinogenic to humans (U.S.EPA, 2017)	Slope factor: 1 per mg/kg-day	Based on U.S.EPA (2017)	Yes

ADAF = age-dependent adjustment factor; POD = point of departure; BMDL = benchmark dose lower limit; HED = human equivalent dose; LED = lower bound effective dose; BMCL = benchmark concentration lower limit; TD = tumorigenic dose.

Hexavalent Chromium (CASRN 18540-29-9)

Hexavalent Chromium TRVs are summarized in Tables 4 and 5. As reviewed by several organizations (IARC, 1990; Health Canada, 1993b; U.S. EPA, 1998; TCEQ, 2014), there are substantial data supporting the conclusion that hexavalent chromium is carcinogenic to humans via the inhalation route. Recent quantitative assessments calculated inhalation unit risks (IURs) of 0.012 – 0.0023 per µg/m^3 (U.S.EPA, 1998; TCEQ, 2014). Both organizations modeled the same study (Mancuso, 1975), and the differences reflect differences in the subtleties of the modeling. For the purposes of this CSPC screening assessment, the higher (more conservative) IUR could be used, and this decision could be revisited if predicted risks are of concern. Similar chronic **noncancer TRVs of 0.1 µg Cr(VI)/m^3, 0.2 µg Cr(VI)/m^3, and 0.22 µg Cr(VI)/m^3 were derived by U.S. EPA (1998), OEHHA (2008), and TCEQ (2014), respectively, based on related studies; the lower value of 0.1 µg Cr(VI)/m^3 could be used for a screening assessment**. Some organizations, such as Health Canada, do not derive noncancer TRVs if there is a cancer TRV that would drive the overall risk assessment.

Although oral exposure to hexavalent chromium caused cancer in rodents (NTP, 2008), recent assessments (Health Canada, 2016; TCEQ, 2016) have concluded that the weight of evidence supports a cytotoxic mode of action (MOA) for these tumors. Therefore, these assessments derived chronic oral TRVs based on hyperplasia, as a precursor to the tumors, and using a threshold approach. The U.S. EPA (1998) cancer assessment was prepared prior to the publication of the National Toxicology Program (NTP, 2008) study. Texas Commission on Environmental Quality (TCEQ, 2016) and Health Canada (2016) derived similar oral chronic TRVs of 0.0031 mg Cr(VI)/kg-day and 0.0022 mg Cr(VI)/kg-day, respectively; the differences related to differences in interspecies extrapolation and the choice of benchmark response (BMR) for the point of departure. The **lower chronic TRV of 0.0031 mg Cr(VI)/kg-day** is a reasonable conservative choice for a screening assessment, and is the same as U.S. EPA's TRV for noncancer effects based on a different study. The chronic oral TRV of 0.003 mg Cr(VI)/kg-day is preferred over the Agency for Toxic Substances and Disease Registry (ATSDR) (2012) value of 0.0009 mg Cr(VI)/kg-day, because TCEQ and Health Canada used internal dose metrics in their calculations, while ATSDR simply used an uncertainty factor for interspecies extrapolation. Use of internal dose metrics accounts for toxicokinetic differences between animals and humans more accurately than does the use of default uncertainty factors.

Less-than-chronic inhalation TRVs are available from several organizations. ATSDR (2012) derived an intermediate duration minimal risk level (MRL) of 0.3 µg Cr(VI)/m^3, TCEQ (2014) derived a 24-Hour acute inhalation reference value (ReV) of 1.3 µg Cr(VI)/m^3, and Minnesota Department of Health (MDH, 2002) derived a subchronic TRV of 1 µg Cr(VI)/m^3. ATSDR and TCEQ used the same study and related endpoints for their derivations, with some differences in the specifics of the modeling; the available documentation for Minnesota does not specify the basis for the TRV. The differences in how the TRVs are labeled for these groups relates to their specific methods guidance and the durations for which they derive TRVs. As a conservative choice for a screening assessment, a TRV of 0.3 µg Cr(VI)/m^3 could be used for durations of 1 day – 1 year.

The only less-than-chronic oral TRV for hexavalent chromium is the ATSDR (2012) intermediate oral MRL of 0.005 mg Cr(VI)/kg-day, which applies for an exposure of up to a year in duration. This TRV is appropriately slightly higher than the recommended chronic oral TRV.

No dermal TRVs were identified for hexavalent chromium, although it is noted that chromium is a dermal sensitizer. Route-to-route extrapolation would not be appropriate for a dermal cancer assessment, since both the oral and inhalation assessments are based on portal-of-entry effects.

Table 4. Hexavalent Chromium Non-Cancer Assessments

Organization (year)	TRV[5]	Species	Critical Effect	Point of Departure	Uncertainty Factor (UF)	Principal Study
ASTDR (2012)	Intermediate Inhalation MRL: 0.0003 mg Cr(VI)/m^3 (particulate Cr(VI) compounds)	Rat	Alterations in lactate dehydrogenase levels in bronchoalveolar lavage	BMCL(HEC) = 0.010 mg Cr(VI)/m^3	30 UFA = 3 UFH = 10	Glaser et al., 1990
ASTDR (2012)	Intermediate Oral MRL: 0.005 mg Cr(VI)/kg-day	Mouse	Microcytic, hypochromic anemia	BMDL(2SD) = 0.52 mg Cr(VI)/kg-day	100 UFA = 10 UFH = 10	NTP, 2008
ASTDR (2012)	Chronic Oral MRL: 0.0009 mg Cr(VI)/kg-day	Mouse	Diffuse epithelial hyperplasia of duodenum	BMDL10 = 0.09 mg Cr(VI)/kg-day LOAEL = 0.004 – 0.05 mg/kg/day	100 UFA = 10 UFH = 10	NTP, 2008
U.S. EPA (1998)	Chronic Oral RfD: $3x10^{-3}$ mg/kg-day	Rat	None Reported	NOAEL = 25 mg/L (2.5 mg/kg/day, adj) No LOAEL	300 UFA = 10 UFH = 10 UFS = 3 MF = 3[6]	MacKenzie et al., 1958
U.S. EPA (1998)	1 x 10^{-4} mg Cr(VI)/m^3 (particulates)	Rat	Lactate dehydrogenase in bronchoalveolar lavage fluid	BMCL10(HEC) = 3.4 x 10^{-2} mg/m^3	300 UFA = 3 UFS = 10 UFH = 10	Glaser et al., 1990 Malsch et al., 1994
PPRTV	--	--	--	--	--	--
Health Canada (2016)	0.0022 mg Cr(VI)/kg-day	N/A	Diffuse hyperplasia of small intestine as precursor to tumors	BMDL01(HED) = 0.054 mg Cr(VI)/kg-day	25 UFA = 2.5 UFH = 10	NTP, 2008

[5] Separate TRVs for chromic acid mists and dissolved Cr(VI) aerosols was not considered relevant to this assessment.
[6] Modifying factor to account for concerns raised by the study of Zhang and Li (1987)

Organization (year)	TRV[5]	Species	Critical Effect	Point of Departure	Uncertainty Factor (UF)	Principal Study
OEHHA (2008) (hot spot program)	Chronic REL: 0.0002 mg Cr(VI)/m^3 (soluble hexavalent chromium compounds other than chromic trioxide)	Rat	Bronchoalveolar hyperplasia	BMCL05 = 12.5 µg Cr(VI)/m^3 No NOAEL LOAEL = 50 µg Cr(VI)/m^3	100 UFH = 10 UFA = 3 UFS = 3	Glaser et al. 1990
TCEQ (2014)	24-Hour Acute inhalation ReV: 1.3 µg Cr(VI)/m^3	Rat	Increase in relative lung weight based on 30-day study	BMDL10(HEC) = 38.71 µg Cr(VI)/m^3	30 UFA = 3 UFH = 10 UFD = 1 Database quality = Medium-High	Glaser et al., 1990
TCEQ (2014)	Chronic inhalation ReV: 0.22 µg Cr(VI)/m^3	Rat	Increase in relative lung weight in 90-day study	NOAEL(HEC) = 60.25 µg Cr(VI)/m^3	270 UFA = 3 UFH = 10 UFS = 3 UFD = 3 Database quality = Medium-High	Glaser et al., 1986[7]
TCEQ (2016)	Chronic oral RfD: 0.0031 mg Cr(VI)/kg-day	Mouse	Cytotoxicity-induced regenerative hyperplasia as key precursor to cancer MOA	BMDL10 = 0.31 mg Cr(VI)/kg-day	100 UFA = 10 UFH = 10	NTP, 2008
MDH (Air Guidance Values) (MDH, 2002)	Subchronic Health Risk Value for Cr(VI) particulates: 1 µg Cr(VI)/m^3	N/A	Lower respiratory system Further details not provided	N/A	N/A	N/A

[7] Incorrectly cited in the TCEQ document in some places as Glaser et al. (1985)

Organization (year)	TRV[5]	Species	Critical Effect	Point of Departure	Uncertainty Factor (UF)	Principal Study
MDH (Water Guidance Values) (MDH, 1993)	Chronic Health Risk Limit: 100 ug/L	N/A	Basis and RfD not provided, aside from “no effects”	N/A	N/A	N/A

TRV = toxicity reference value; MRL = minimal risk level; RfD = reference dose; N/A = not applicable or not available (see Approach); REL = reference exposure level; BMCL = benchmark concentration lower limit; HEC = human equivalent concentration; UFA = uncertainty factor animal; UFH = uncertainty factor human; BMDL benchmark dose lower limit; HED = human equivalent dose; SD = standard deviation; LOAEL = lowest observed adverse effect level; NOAEL= no observed adverse effect level; UFS = uncertainty factor subchronic; MF = modifying factor; ReV = inhalation reference value; UFD = uncertainty factor database; MOA = mode of action.

Table 5. Hexavalent Chromium Cancer Assessments

Organization (year)	Weight of Evidence Characterization	Quantitative assessment	Extrapolation Method	ADAF
OEHHA (2020) Hot spots program	Not available	Oral slope factor: 0.42 per mg/kg-day Inhalation unit risk: 0.15 per $\mu g/m^3$	Not available	N/A
OEHHA (2011) Drinking water program	Not available	Oral slope factor: 0.5 per mg/kg-day	Modeled	Yes
U.S. EPA (1998) (inhalation)	Group A – known human carcinogen (1986 guidelines) Known human carcinogen by inhalation route (1996 proposed guidelines)	Inhalation unit risk: 1.2×10^{-2} per $\mu g/m^3$	Multistage, extra risk, direct modeling of human data	N/A
U.S. EPA (1998) (oral)	Group D - Carcinogenic potential cannot be determined (1986 guidelines)	N/A	N/A	N/A
IARC (1990)	Carcinogenic to humans (Group 1)	N/A	N/A	N/A
JECFA	--	--	--	--
JMPR	--	--	--	--
Health Canada (2016) (oral)	The MOA analysis supports hyperplasia as a key precursor event to tumour development and a threshold approach for the risk assessment for ingested Cr(VI).	See RfD calculation above	N/A	No
Health Canada (1993b) (inhalation)	Carcinogenic to humans (Group I)	TCO5: 6.6×10^{-4} mg $Cr(VI)/m^3$ Concentration for 1 in 100,000 risk level: 1.3×10^{-7} mg $Cr(VI)/m^3$	Direct modeling of epidemiology data TC05 is computed directly from the dose-response curve within or close to the experimental range	N/A

Organization (year)	Weight of Evidence Characterization	Quantitative assessment	Extrapolation Method	ADAF
TCEQ (2014)	Carcinogenic to humans via inhalation (at least at sufficiently high long-term doses)	Chronic ESL (nonthreshold-c)[8]: 0.0043 µg Cr(VI)/m^3 Inhalation unit risk factor 2.3 x 10^{-3} per µg Cr(VI)/m^3	Direct modeling of epidemiology data	No
TCEQ (2016)	"The WOE indicates that cytotoxicity-induced regenerative hyperplasia is indubitably the most scientifically well-supported MOA"	See RfD calculation above	N/A	No
MDH (Air Guidance Values) (MDH, 2002)	Additional documentation not available	HRV_{02} = 0.0008 ug/m^3 Corresponding to additional lifetime risk of 1 in 100,000	N/A	N/A
MDH (Water Guidance Values)	--	--	--	--

ADAF = age-dependent adjustment factor; N/A = not applicable or not available (see Approach); TC05 = tumorigenic concentration; RfD = reference dose; ESL = effects screening level; WOE = weight of evidence; MOA = mode of action; HRV = health risk value

[8] Based on a no significant risk level of 1 in 100,000 excess cancer risk, and applicable to all forms of Cr(VI) compounds (e.g., particulate, dissolved Cr(VI) – such as chromic acid mist)

Zinc (CASRN 7440-66-6)

Zinc TRVs are summarized in Tables 6 and 7. Zinc is an essential element, and so adverse health effects can result from both a deficiency and from over-exposure (ATSDR, 2005). Several different organizations have derived similar TRVs for zinc, based on generally similar points of departure (JECFA, 1982; U.S. EPA, 2005b; ATSDR, 2005; ECHA, 2020a). Although there are slight differences in the point of departure (POD) and whether the observed effects reflect a no observed adverse effect level (NOAEL) or a lowest observed adverse effect level (LOAEL), there is general consensus that the observed effects are of minimal severity; U.S. EPA (2005b) used a factor of 1 for LOAEL to NOAEL, even though the POD is identified as a LOAEL, based on the minimal severity. The European Chemicals Agency (ECHA, 2020a) TRV is higher than the other organizations, because it did not include an uncertainty factor (UF) for human variability. OEHHA (2007a) stated that there is no evidence to suggest that children are more sensitive than adults to zinc compounds.

In light of the general agreement of TRVs, **the recommended subchronic and chronic oral TRV for zinc is 0.3 mg Zn/kg-day**. As noted by ATSDR (2005) and U.S. EPA (2005b), the same TRV can apply for subchronic and chronic durations. No acute TRVs for zinc were located.

As noted by ECHA (2020a), it is reasonable to conduct a route-to-route extrapolation to the dermal and inhalation routes from the oral TRV based on the relative bioavailability and inhalation rates. First-pass metabolism is not of concern for an element such as zinc. Therefore, an approach analogous to that of ECHA was used, extrapolating from the oral TRV of 0.3 mg Zn/kg-day. Based on 20% oral bioavailability, 2% dermal bioavailability for soluble zinc compounds, and 0.2% bioavailability for slightly soluble/insoluble compounds, one can calculate **chronic dermal TRVs of 3 mg Zn/kg-day for soluble zinc compounds and 30 mg Zn/kg-day for insoluble zinc compounds**. Similarly, a chronic inhalation TRV can be calculated assuming 40% inhalation bioavailability for soluble zinc compounds, 0.2% for slightly soluble/insoluble compounds and a breathing volume of 20 m^3/day. The resulting **chronic inhalation TRV is 0.42 mg Zn/m^3 for soluble compounds and 0.84 mg Zn/m^3 for slightly soluble/insoluble compounds**.

Organizations that have evaluated the carcinogenicity of zinc have described the data as insufficient to assess the carcinogenicity of zinc compounds (U.S. EPA, 2005b; JECFA, 1982).

Table 6. Zinc Non-Cancer Assessments

Organization (year)	TRV	Species	Critical Effect	Point of Departure	Uncertainty Factor	Principal Study
ATSDR (2005)	Intermediate Oral MRL: 0.3mg Zn/kg-day[9] (15– 364 days)	Human	Decreases in erythrocyte superoxide dismutase (ESOD) and serum ferritin levels	NOAEL = 0.83 mg/kg/day	UFH = 3	Yadrick et al., 1989
ATSDR (2005)	Chronic Oral MRL: The intermediate oral MRL 0.3 mg Zn/kg-day has been accepted as the chronic oral MRL.	N/A	N/A	N/A	N/A	N/A
ATSDR (2005)	Inhalation MRLs not available	N/A	N/A	N/A	N/A	N/A
ECHA (2020a)[10]	General public oral DNEL (derived no effect level): 0.83 mg/kg-day (soluble or slightly soluble compounds)	Human	None	NOAEL = 50 mg Zn/day = 0.83 mg/kg-day for a 60 kg woman	1	Not provided
ECHA (2020a)	General public dermal DNEL (derived no effect level): 8.3 mg Zn/kg-day – soluble 83 mg Zn/kg-day - insoluble	Human	None	Derived from oral DNEL assuming 20% oral bioavailability	1	Not provided Assumed 2% dermal bioavailability for soluble, 0.2% for slightly soluble/insoluble compounds

[9] Assumes "healthy dietary levels of zinc and copper and represents the level of exposure above and beyond the normal diet that is believed to be without an appreciable risk of toxic response."

[10] First published March 2011, dossier last modified October 2020. From the zinc oxide dossier, but the DNELs are derived based on soluble zinc compounds

Organization (year)	TRV	Species	Critical Effect	Point of Departure	Uncertainty Factor	Principal Study
ECHA (2020a)	General public inhalation DNEL (derived no effect level): 1.25 mg Zn/m^3 – soluble, 2.5 mg Zn/m^3 – slightly soluble/insoluble	Human	None	Derived from oral DNEL assuming 20% oral bioavailability	1	Not provided Assumed 40% inhalation bioavailability for soluble, 0.2% for slightly soluble/insoluble compounds and accounted for breathing volume
U.S. EPA (2005b)	Chronic Oral RfD: 0.3 mg Zn/kg-day	Human	Decreases in erythrocyte Cu, Zn-superoxide dismutase (ESOD) activity in healthy volunteers	No NOAEL LOAEL = 0.91 mg/kg-day	UFH = 3	Yadrick et al., 1989; Fischer et al., 1984; Davis et al., 2000; Milne et al., 2001
PPRTV	--	--	--	--	--	--
JECFA (1982)	Provisional maximum tolerable daily intake: 0.3-1.0 mg Zn/kg-day	Human	Wide margin between nutritionally required amounts and toxic levels. Clinical study of up to 600 mg $ZnSO_4$ (200 mg Zn) in divided doses for several months with no adverse effects “provides a basis for the evaluation”	N/A	N/A	No single study identified.
Health Canada	--	--	--	--	--	--
TCEQ	--	--	--	--	--	--

Organization (year)	TRV	Species	Critical Effect	Point of Departure	Uncertainty Factor	Principal Study
MDH (Air Guidance Values)	--	--	--	--	--	--
MDH (Water Guidance Values) (MDH, 1994a)	Chronic Health Risk Limit: 2000 ug/L	N/A	Basis and RfD not provided, aside from “no effects”	N/A	N/A	N/A

TRV = toxicity reference value; MRL = minimal risk level; ESOD = erythrocyte superoxide dismutase; NOAEL = no observed adverse effect level; UFH = uncertainty factor human; DNEL = derived no effect level; N/A = not applicable or not available (see Approach); NOAEL = no observed adverse effect level; RfD = reference dose; LOAEL = lowest observed adverse effect level.

Table 7. Zinc Cancer Assessment

Organization (year)	Weight of Evidence Characterization	Quantitative assessment	Extrapolation Method	ADAF
U.S. EPA (2005b)	D (Not classifiable as to human carcinogenicity) Inadequate information to assess carcinogenic potential	N/A	N/A	N/A
IARC	--	--	--	--
JECFA (1982)	The available long-term studies are insufficient to assess carcinogenicity	N/A	N/A	N/A
JMPR	--	--	--	--
Health Canada	--	--	--	--
TCEQ	--	--	--	--
MDH (Air Guidance Values)	--	--	--	--
MDH (Water Guidance Values)	--	--	--	--

ADAF = age-dependent adjustment factor; N/A = not applicable or not available (see Approach);

Methyl Isobutyl Ketone (MIBK), 4-methyl-2-pentanone (CASRN 108-10-1)

Methyl Isobutyl Ketone (MIBK) TRVs are summarized in Tables 8 and 9. No quantitative assessments of MIBK carcinogenicity were identified. The International Agency for Research on Cancer (IARC, 2013) and Health Canada (2019) both considered MIBK positive/possibly carcinogenic to humans (Group 2B), while U.S. EPA (2003) concluded that the data are inadequate for an assessment of human carcinogenicity. Presumably, the reason for the discrepancy is that the U.S. EPA assessment was conducted prior to the publication of the 2-year inhalation bioassay of MIBK (NTP, 2007), which concluded that there was "some evidence" of MIBK carcinogenicity in male rats and mice of both sexes, and "equivocal evidence" of carcinogenic activity in female rats. Based on these results**, it is prudent to consider MIBK a possible carcinogen via the oral and inhalation routes**. Health Canada (2019) stated that MIBK is not considered genotoxic but did not conduct a full evaluation of the MOA.

Health Canada (2019) and ECHA (2020b) both identified similar effect levels in the chronic NTP (2007) study, but apparently differed with regard to the adversity at that level. Health Canada considered the concentration of 1843 mg/m^3 to be a lowest observed adverse effect concentration LOAEC, based on chronic nephropathy in female rats, while the ECHA derived no effect level (DNEL) derivation listed a concentration of 1847 mg/m^3 (450 ppm) as a no observed adverse effect concentration (NOAEC). It is not clear why ECHA did not consider 450 ppm to be a LOAEC, since chronic nephropathy was substantially and statistically significantly increased in female rats at that concentration. As reported in Schneider et al. (2020c), a $BMCL_{10}$ (benchmark concentration lower limit) calculated based on chronic nephropathy in female rats is 57 mg/m^3. The BMCL would be preferred over the LOAEC as a point of departure, but the choice of uncertainty factors would need to be reconsidered, since Schneider used a somewhat different uncertainty factor structure than typically used by CPSC. Health Canada used a margin of exposure (MOE) approach and so did not identify uncertainty factors. The U.S. EPA (2003) RfC of 3 mg/m^3 predated the NTP bioassay. In addition, it was based on effects to fetuses exposed *in utero*, and so relevance to child exposure is uncertain. The only less-than-chronic inhalation value is the short-term (14-day) inhalation POD of a NOAEC of 410 mg/m^3 identified by Health Canada, based on the data summarized by U.S. EPA (2003). As for the other Health Canada values, this POD was applied in an MOE approach.

There are no high-quality chronic oral studies for MIBK. ECHA (2020b) developed oral and dermal DNELs from the inhalation DNEL, but these values can be questioned, in light of the issues noted in the previous paragraph. Conversely, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) (1999) approach based on threshold of toxicological concern (TTC) could be used for screening but is a very conservative generic approach. Health Canada (2019) identified a POD of a lowest observed effect (LOEL)/NOAEL of 250 mg/kg-day for a 13-week study, as summarized by U.S. EPA (2003), and noted that this POD was supported by a LOAEL of 101 mg/kg-day calculated from the 2-year NTP study by route-to-route extrapolation. Health Canada also identified a POD of a LOAEL of 300 mg/kg-day for dermal exposure, supported by a LOEL/NOAEL of 250 mg/kg-day, extrapolated from oral data. All of these Health Canada assessments used a MOE approach, but this analysis could be extended to derive a TRV.

Table 8. MIBK Non-Cancer Assessments

Organization (year)	TRV	Species	Critical Effect	Point of Departure	Uncertainty Factor	Principal study
ASTDR	--	--	--	--	--	--
ECHA (2020b[11])	General public inhalation DNEL: 14.7 mg/m^3	Not reported	Not reported	83 mg/m^3 – OEL Supported by NOAEC of 1847 mg/m^3 in NTP (2007)	Additional UFs included to account for differences between occupational and general public exposure	Not reported
ECHA (2020b)	Oral DNEL 4.2 mg/kg-day	N/A	Derived from inhalation DNEL assuming that oral and inhalation absorption are both 100%	N/A	N/A	N/A
ECHA (2020b)	Dermal DNEL 4.2 mg/kg-day	N/A	Derived from inhalation DNEL assuming that dermal and inhalation absorption are both 100%	N/A	N/A	N/A
U.S. EPA (2003)	Chronic Oral RfD	N/A	Withdrawn on 03/01/91; effects in subchronic studies not clearly adverse	N/A	N/A	N/A

[11] ECHA dossier accessed February 4, 2021. First published 2011, last updated 2020. Inhalation DNEL based on a 15-minute exposure also available.

Organization (year)	TRV	Species	Critical Effect	Point of Departure	Uncertainty Factor	Principal study
U.S. EPA (2003)	Chronic Inhalation RfC: 3 mg/m^3	Mice/ Rats	Reduced fetal body weight, skeletal variations, and increased fetal death in mice, and skeletal variations in rats	NOAEL(HEC) = 1026 mg/m^3	300 UFA = 3 UFH = 10 UFD = 10	Tyl et al., 1987
PPRTV	--	--	--	--	--	--
JECFA (1999)	540 µg/day for class II = 7.7 µg/kg-day for a 70 kg person	N/A	N/A	N/A	N/A	Based on Cramer classes for TTC
Health Canada 2019)[12]	Short-term (14-day) inhalation	Rats and/or mice	Increased relative kidney weight and hyaline droplet-related tubular nephrosis	NOAEC = 410 mg/m^3	N/A	U.S. EPA, 2003
Health Canada (2019)	Repeated dose toxicity oral MOE subchronic	Rats	Hepatic and renal effects at 13 weeks; chronic nephropathy in females at 2 years	LOEL/NOAEL = 250 mg/kg-day (13 weeks) LOAEL = 101 mg/kg-day (2 years) extrapolated from inhalation	N/A	MAI, 1986, as cited in U.S. EPA, 2003; NTP, 2007

[12] In this screening assessment, Health Canada identified points of departure, but used a margin of exposure approach, rather than identifying uncertainty factors and a final TRV.

Organization (year)	TRV	Species	Critical Effect	Point of Departure	Uncertainty Factor	Principal study
Health Canada (2019)	Repeated dose toxicity inhalation MOE chronic	Rats and/or mice	Renal tubule hyperplasia and chronic nephropathy (female) and mineralization of renal papilla (male) at unspecified duration; chronic nephropathy in females at 2 years	LOAEC = 410 mg/m^3 (see 14-day) LOAEC = 1843 mg/m^3 (2 years)		U.S. EPA, 2003; NTP, 2007
Health Canada (2019)	Repeated dose toxicity dermal MOE subchronic	Rats	Morphological changes in several tissues for 4 months	LOAEL = 300 mg/kg-day LOEL/NOAEL = 250 mg/kg-day (from oral data)		Malysheva, 1988, as cited in NTP, 2007
IPCS (1990)	--	--	--	--	--	--
Schneider et al. (2020c)[13]	Reference value 2.3 mg/m^3 Also references Ad ho AG (2013) who derived Health hazard guideline value (RW II) 1 mg/m^3 Precautionary guide (no health effects assumed) of 0.1 mg/m^3	Rats	Progressive nephrotoxicity	BMCL10 = 57 mg/m^3	25 UFA = 2.5 UFH = 10	NTP, 2007
TCEQ	--	--	--	--	--	--
MDH (Air Guidance Values)	--	--	--	--	--	--

[13] Citing the German Working Group on Indoor Guidelines, Ad hoc AG (2013) [German, with English abstract].

Organization (year)	TRV	Species	Critical Effect	Point of Departure	Uncertainty Factor	Principal study
MDH (Water Guidance Values) (MDH, 1994b)	Chronic HRL_{94}: 300 ug/L	N/A	Liver system; Kidney system	N/A	N/A	N/A

TRV = toxicity reference value; DNEL = derived no effect level; OEL = occupational exposure limit; N/A = not applicable or not available (see Approach); NOAEC = no observed adverse effect concentration; RfD = reference dose; RfC = reference concentration; NOAEL = no observed adverse effect level; HEC = human equivalent concentration; UFA = uncertainty factor animal; UFH = uncertainty factor human; UFD = uncertainty factor database; TTC = threshold of toxicological concern; LOEL = lowest observed effect level; LOAEL = lowest adverse effect level; LOAEC = lowest observed adverse effect concentration; MOE = margin of exposure BMCL = benchmark concentration lower limit; RW II = action level, health effects cannot be excluded; UF = uncertainty factor; HRL = health risk limit.

Table 9. MIBK Cancer Assessments

Organization (year)	Weight of Evidence Characterization	Quantitative assessment	Extrapolation Method	ADAF
U.S. EPA (2003)	Data are inadequate for an assessment of human carcinogenic potential	N/A	N/A	N/A
IARC (2013)	Possibly carcinogenic to humans (Group 2B)	N/A	N/A	N/A
JECFA	--	--	--	--
JMPR	--	--	--	--
Health Canada (2019)	Positive (sic); Category 2 carcinogen according to the GHS	N/A	N/A Not considered genotoxic	N/A
TCEQ	--	--	--	--
MDH (Air Guidance Values)	--	--	--	--
MDH (Water Guidance Values)	--	--	--	--

ADAF = age-dependent adjustment factor; N/A = not applicable or not available (see Approach); GHS = globally harmonized system.

Benzothiazole (CASRN 95-16-9)

Benzothiazole TRVs are summarized in Tables 10 and 11. Limited data are available on benzothiazole (BZT). U.S. EPA (2004a) evaluated the data on benzothiazole and determined there were insufficient data for even a Provisional Peer-Reviewed Toxicity Value (PPRTV) for either the oral or inhalation routes, but it appears that the authors did not have access to an unpublished study (Morgareidge, 1971) used in other assessments.

Ginsberg[14] et al. (2011) conducted a toxicity assessment of BZT in support of a human health risk assessment of synthetic turf fields cushioned with crumb rubber. In light of the limited database for BZT, BZT data were supplemented with data for surrogate chemicals, in order to develop acute and chronic noncancer and cancer assessments for BZT.

There are no cancer bioassays conducted with BZT. As summarized by Ginsberg et al. (2011), BZT was tested in only one genotoxicity study, in which it produced a mutagenic response in one *S. typhimurium* strain in the presence of S9; it was not clear whether other strains were tested. The related chemical, 2-mercaptobenzothiazole (2MBZT), was negative for mutagenicity in *S. typhimurium*. 2MBZT was, however, positive in two mouse lymphoma assays (which detect point mutations and chromosome breaks) with S9, and it was positive for clastogenicity in a Chinese hamster ovary cell chromosome aberration test. However, 2MBZT was negative in the micronucleus test (an assay for clastogenicity) in two mouse strains. 2MBZT was positive for carcinogenicity in an NTP bioassay. IARC (2018) concluded that 2MBZT is probably carcinogenic to humans (Group 2A). IARC concluded that there was limited evidence in humans for the carcinogenicity of 2MBZT, based on a positive association between exposure to 2MBZT and cancer of the urinary bladder, and sufficient evidence in experimental animals.

Based on the structural similarity between BZT and 2MBZT, and supported by the single positive mutagenicity result with BZT, Ginsberg et al. (2011) considered BZT to be a possible carcinogen. Ginsberg et al. noted that BZT can be metabolized to form a hydroxylamine, which is of concern for bladder cancer, although they also noted metabolic differences between BZT and 2MBZT. They applied the 2MBZT cancer risk values calculated by Whittaker et al. (2004) to BZT. Ginsberg et al. (2011) did not provide a quantitative evaluation of the similarity between BZT and 2MBZT, but according to the CompTox Chemicals Dashboard, the score is 0.80. This means that the similarity can be considered weak but worth considering for read across. A score of 0.80 is the minimum similarity score for which the Dashboard provides structurally similar chemicals. Other cautions related to the read across relate to the additional functional group in MBZT, the differences in metabolism, and the different results in the *S. typhimurium* assay. Based on these considerations, it may be worth doing a more rigorous evaluation of potential analogs for any with existing TRVs or adequate data for deriving a TRV. Alternatively, it appears that 2MBZT would be a conservative basis for read across.

[14]Ginsberg's affiliation is listed as the Connecticut Dept of Public Health. A footnote states that "the article and underlying risk assessment report were reviewed by staff from the Connecticut Department of Public Health. The Connecticut Academy of Science and Engineering reviewed the underlying report and made formal recommendations (CASE June 15, 2020, report) that are reflected in (this – i.e., the published) article."

For 2MBZT, Whittaker et al. (2004) calculated an **oral cancer slope factor of 6.34 E-04 per mg/kg-day, which was applied directly to BZT**. Ginsberg and colleagues converted the **slope factor to an inhalation unit risk of 1.8 E-07 per µg/m^3**, based on a 70 kg adult breathing 20 m^3 of air/day.

There is one subchronic oral study of BZT, which was reviewed by JECFA (2003)[15], and further discussed by Ginsberg et al. (2011). In this unpublished study, the single dose level tested (5.1 mg/kg-day) was a NOAEL, based on a wide range of endpoints evaluated, but only limited reporting of the data. The New York State Department of Environmental Conservation (NYSDEC, 2009) and Ginsberg et al. (2011) both derived a chronic **RfD of 5 µg/kg-day** from this subchronic study. Ginsberg also noted that this screening-level RfD is consistent with the RfD of 14 µg/kg-day that could be extrapolated from the 2MBZT data using read-across from kidney effects reported in the 2-year NTP (1988) bioassay of 2MBZT.

Based on the approach of NYSDEC (2009), Ginsberg et al. (2011) calculated a chronic RfC by extrapolating from the RfD of 5 µg/kg-day. The resulting **RfC was 18 µg/m^3** (which would be rounded to 20 µg/m^3).

No dermal limit was located, but one could be calculated from the oral RfD.

Ginsberg et al. (2011) stated that BZT appears to be a skin allergen, a finding that is supported by the potential for 2MBZT to elicit contact dermatitis and sensitization in humans and rodents. Ginsberg et al. (2011) also suggested that BZT may be a nose and throat irritant, based on anecdotal reports from asphalt-rubber workers who experienced greater irritation when laying pavement containing rubber. Alternatively, other rubber ingredients may have contributed to the irritation.

[15] Year as reported by NYSDEC (2009).

Table 10. Benzothiazole Non-Cancer Assessments[1]

Organization (year)	TRV	Species	Critical Effect	Point of Departure	Uncertainty Factor (UF)	Principal Study
ATSDR	--	--	--	--	--	--
U.S. EPA (IRIS)	--	--	--	--	--	--
PPRTV (U.S. EPA, 2004a)	No subchronic or chronic oral RfD	N/A	N/A	N/A	N/A	Insufficient data to develop an RfD because no subchronic or chronic oral studies available
PPRTV (U.S. EPA, 2004a)	No subchronic or chronic Inhalation RfC	N/A	N/A	N/A	N/A	Insufficient data to develop an RfC because no subchronic or chronic inhalation studies available
Ginsberg et al. (2011)	Chronic RfD = 5 µg/kg-day	Rat	No adverse effects	NOAEL= 5.1 mg/kg-day No LOAEL	1000 10H 10A 10S	Morgareidge, 1971
Ginsberg et al. (2011)	Chronic RfD for BZT based on 2MBZT = 14 µg/kg-day	Rat	Kidney effects	NOAEL= 14 mg/kg-day	1000 10H 10A 10D data gaps and extrapolation across chemicals	NTP, 1988
Ginsberg et al. (2011); NYSDEC (2009)	Chronic RfC = 18 µg/m^3	Rat	No adverse effects	Extrapolated from RfD using 20 m^3/day for a 70 kg adult	N/A	N/A
NYSDEC (2009)	Chronic RfD = 5 µg/kg-day	Rat	No adverse effects	NOAEL= 5.1 mg/kg-day No LOAEL	1000 10H 10A 10S	Morgareidge, 1971

Organization (year)	TRV	Species	Critical Effect	Point of Departure	Uncertainty Factor (UF)	Principal Study
Health Canada[16]	--	--	--	--	--	--
JECFA (2003)	Margin of exposure approach	Rats	No adverse effects in a 90-day rat study	NOAEL= 5.1 mg/kg-day No LOAEL	N/A Margin of exposure	Morgareidge, 1971
TCEQ	--	--	--	--	--	--
MDH (Air Guidance Values)	--	--	--	--	--	--
MDH (Water Guidance Values)	--	--	--	--	--	--

TRV = toxicity reference value; RfD = reference dose; N/A = not applicable or not available (see Approach); RfC = reference concentration; RD50 = concentration resulting in a 50% decrease in respiratory rate; NOAEL = no observed adverse effect level; LOAEL = lowest observed adverse effect level; UFH = uncertainty factor human; UFA = uncertainty factor animal; UFS = uncertainty factor subchronic; BZT = benzothiazole; 2MBZT= 2-mercaptobenzothiazole

[1]Data related to 2MBZT is highlighted in gray.

[16]Health Canada's Chemical Management Plan (CMP) included a benzotriazoles and benzothiazoles group, but benzothiazole was not included among the listed group members, https://www.canada.ca/en/health-canada/services/chemical-substances/chemicals-management-plan-3-substances/benzotriazoles-benzothiazoles-group.html

Table 11. Benzothiazole Cancer Assessments[1]

Organization (year)	Weight of Evidence Characterization	Quantitative assessment	Extrapolation Method	ADAF
U.S. EPA	--	--	--	--
IARC – BZT	--	--	--	--
IARC (2018) 2MBZT	Probably carcinogenic to humans (2A)	N/A	N/A	N/A
TCEQ	--	--	--	--
PPRTV (U.S. EPA, 2004b)	--	--	--	--
Whittaker et al. (2004) – 2MBZT	N/A	6.34 E-04 per mg/kg-day	Linear from LED10	No
Ginsberg et al. (2011) BZT	Possible carcinogen	6.34 E-04 per mg/kg-day, extrapolated from 2MBZT	N/A	N/A
Ginsberg et al. (2011) BZT	Possible carcinogen	1.8 E-07 per µg/m^3, calculated from the oral value	N/A	N/A

ADAF = age-dependent adjustment factor; BZT = benzothiazole; N/A = not applicable or not available (see Approach); 2MBZT = 2-mercaptobenzothiazole; LED = lower bound effective dose

[1]Data related to 2MBZT is highlighted in gray

Lead (CASRN 7439-92-1)

Lead TRVs are summarized in Tables 12 and 13. Several organizations have conducted qualitative assessments of the carcinogenicity of lead, but no quantitative assessments are available. Each organization has its own language for the specific characterization, but the available qualitative assessments are consistent that the weight of evidence (WOE) supports the conclusion that inorganic lead is probably carcinogenic to humans (U.S. EPA, 1988a; IARC, 2006; NTP, 2016). Quantitative assessments are limited by the absence of good quantitative human data. As noted by U.S. EPA (1988a):

> Quantifying lead's cancer risk involves many uncertainties, some of which may be unique to lead. Age, health, nutritional state, body burden, and exposure duration influence the absorption, release, and excretion of lead. In addition, current knowledge of lead pharmacokinetics indicates that an estimate derived by standard procedures would not truly describe the potential risk. Thus, the Carcinogen Assessment Group recommends that a numerical estimate not be used.

OEHHA (2020) did provide quantitative cancer risk estimates for both the oral and inhalation route, but the basis was not available. Based on the U.S. EPA (1988a) assessment, the OEHHA values are likely associated with substantial uncertainty.

A large number of organizations have evaluated the noncancer toxicity of lead. Many of these assessments were specific to the oral route, but many others were based on an internal measure of lead dose (the blood lead level, or BLL), which theoretically could be converted to administered doses or exposure concentrations from the oral, inhalation, or dermal routes.

Noncancer assessments of lead differ from most noncancer assessments, because no threshold has been identified for health effects of lead. This has led to a variety of approaches for evaluating the health impact of lead exposure. Some organizations estimated a dose corresponding to a specified level of risk or change in intelligence quotient (IQ) (EFSA, 2010; JECFA, 2011; OEHHA, 2007b), or estimated a dose corresponding to a negligible concern (JECFA, 2011). In all cases, dose-response modeling was based on the meta-analysis of Lanphear et al. (2005), with several also considering the subsequent reanalysis Crump et al. (2013). Health Canada (2013) did not derive a reference level or other specific benchmark, but stated that health effects have been associated with BLLs as low as 1–2 µg/dL. Although the Health Canada assessment noted that there is uncertainty associated with effects observed at these levels, it stated that “it is considered appropriate to apply a conservative approach when characterizing risk,” and to implement further measures to reduce exposures. Finally, ATSDR (2020) and U.S. EPA (2004b) declined to derive a specific value, although the U.S. EPA uses the Integrated Exposure Uptake Biokinetic Model for Lead in Children (IEUBK) and All Ages Lead Model (AALM) for evaluating exposures to lead (U.S. EPA, 2019).

CPSC staff (K. Hatlelid, personal communication, 4/20/2021) stated that given the CPSC focus on implementing and enforcing statutory requirements for lead content in children’s products, rather than performing case-by-case product assessments, staff has not derived a lead TRV that takes into account the most current evidence for adverse effects of lead exposure. Instead, when needed, CPSC staff has applied the Food and Drug Administration (FDA)-derived interim reference level (IRL) of 3 µg/day derived by Flannery et al. (2020) for children under 6 years of

age in evaluations of possible consumer product hazards. Because this is the current CPSC staff approach, the basis of the FDA IRL is discussed in additional detail here.

Rather than basing the IRL on a population analysis of the dose-response analysis of *health effects*, Flannery et al. (2020) based their assessment on that of Centers for Disease Control and Prevention (CDC, 2020), which is itself based on the *population distribution of exposure*. Specifically, CDC updated its guidance in 2012 to specify a blood lead reference level of 5 µg/dL. This reference level is not a risk-based value. Rather, it is based on the highest 2.5% of BLL in U.S. children ages 1-5 years (based on National Health and Nutrition Examination Survey [NHANES] data) and is used to identify children who have been exposed to lead and require risk management.

Flannery et al. (2020) used the CDC blood lead reference value to calculate IRL that is designed to minimize the potential for adverse effects from dietary exposure to lead. The authors used the term IRL instead of FDA's more typical Provisional Tolerable Total Dietary Intake (PTTDI), recognizing that a safe exposure level for lead has not been identified, and therefore avoiding the term "tolerable."

Applying a conversion factor of 0.16 µg/dL per µg Pb per day to the reference level of 5 µg/dL, Flannery et al. (2020) calculated that the CDC blood lead reference level corresponds to a dietary intake for children of 30 µg/day. The same conversion factor was used for children 0-6 years of age and 7+ years of age, resulting in the same dietary intake on a µg/day basis. Use of the same conversion factor for both age ranges was a health-protective approach, in the absence of specific data for older children. For women of childbearing age (WOCBA), the conversion factor was 0.04 µg/dL per µg Pb per day, resulting in a dietary intake of 125 µg/day. Flannery et al. (2020) applied a UF of 10 to convert from the dietary intakes to IRLs, resulting in IRLs of 3 µg/day for children of all ages and 12.5 µg/day for WOCBA. The UF of 10 accounted for the wide variability in the relationship between dietary intake and BLL, which can be affected by the type of food consumed, nutritional status, the amount of lead ingested, and age. For example, the authors noted absorption varying from 3.5% to 54.3%, depending on the type of food ingested. The authors also noted that limiting exposure to below the IRL would minimize the effect of lead on systolic blood pressure and chronic kidney disease in adult females. The BLL corresponding to the IRLs is 0.5 µg/dL (i.e., 10-fold lower than the reference level of 5 µg/dL).

The use of the IRL from the Flannery et al. (2020) paper by CPSC staff as a benchmark is a reasonable and health-protective approach. The IRL can be used in standard risk assessment applications and is somewhat lower than the doses or BLLs considered to be of negligible concern by JECFA (2011). The IRL also has the advantage of being a child-specific value.

For an inhalation limit, one could use the National Ambient Air Quality Standard (NAAQS) primary standard of 0.15 µg/m^3. This value was re-affirmed in a 2016 review (U.S. EPA, 2016b), and is currently undergoing the standard NAAQS 5-year review. An Integrated Science Assessment (U.S. EPA, 2013) conducted a weight of evidence evaluation of the causal association between lead exposure and a number of different endpoints, but this assessment did not result in a specific qualitative or quantitative characterization. A caution about using the

NAAQS is that recent documentation did not specify the details of the derivation, but the primary NAAQS are based on human health and protection of sensitive populations. **Alternatively, the BLL corresponding to the IRL could be converted to an air concentration using the AALM. Similarly, the AALM could be used to calculate a dermal exposure corresponding to a BLL of 0.5 µg/dL.**

Table 12. Lead Non-Cancer Assessments

Organization (year)	TRV	Species	Critical Effect	Point of Departure	Uncertainty Factor	Principal study
ATSDR (2020)	Not derived because the lowest BLLs (≤5 µg/dL) are associated with serious adverse effects (declining cognitive function in children)	N/A	N/A	N/A	N/A	N/A
CDC (2020) First developed in 2012	Reference level for lead of 5 µg/dL BLL for intervention – corresponds to the 97.5th percentile of the population distribution of BLL for children in the US	Human	None – population distribution of exposure	N/A	N/A	N/A
EFSA (2010)	Reference point 1.2 µg/dL in blood (0.5 µg/kg-day) based on BMDL of 1% extra risk in children for full scale IQ	Human	Developmental neurotoxicity (decreased IQ) in children, cardiovascular effects (systolic blood pressure - SBP) and nephrotoxicity (decreased GFR) in adults	BMDL01 (1% extra risk) = 12 µg/L, (0.50 µg/kg-day)	Margin of exposure approach	Lanphear et al., 2005
Health Canada (2013)	No TRV derived, but noted that health effects have been associated with BLLs as low as 1–2 µg/dL	--	--	--	--	--
JECFA (2011)	Exposure below the level associated with a population decrease of 0.5 IQ points is considered negligible. 0.3 µg/kg-day[17]	Human	Decreased IQ	Modeled using bi-linear model	N/A	Lanphear et al., 2005
MDH (Air Guidance Values)	--	--	--	--	--	--

[17] Calculated by Flannery et al. (2020) to correspond to a BLL of about 0.8 µg/dL for a 16 kg child

Organization (year)	TRV	Species	Critical Effect	Point of Departure	Uncertainty Factor	Principal study
MDH (Water Guidance Values) (MDH, 2015a)	N/A; BLL of 5 µg/dL considered an elevated BLL, as a policy decision related to prevention rather than an assessment of risk	N/A	N/A	N/A	N/A	N/A
OEHHA (2007b)	Child-specific benchmark-change in blood lead concentration of 1 µg/dL, lower bound estimate of dose resulting in a decrease of 1 IQ point. Increased daily intake of 6 µg ingested soluble lead or 5 µg of inhaled lead	Human	Intellectual function – full-scale Wechlser IQ	Based on average IQ/blood lead slope over BLL range of <1 – 10 µg/dL. BMR = decrease of 1 IQ point	Used upper end of the 95% CI on the slope	Lanphear et al., 2005
TCEQ	--	--	--	--	--	--
U.S. FDA (Flannery et al., 2020)	3 µg/day for children 12.5 µg/day for women of childbearing age	Human	Neurodevelopmental	BLL of 5 µg/dL	10	Based on CDC, 2012[18], 2020 reference value of 5 µg/dL BLL
U.S. EPA (2004b) – IRIS	RfD not derived, based on adverse effects at BLL levels "so low as to be essentially without a threshold" and ongoing CDC re-evaluation.	--	--	--	--	--
U.S. EPA (2016b) - NAAQS	*NAAQS 0.15 µg/m^3 Rolling 3-month average, not to be exceeded*	*Human*	N/A	N/A	N/A	N/A

TRV = toxicity reference value; BLL = blood lead level; N/A = not applicable or not available (see Approach); BMDL = benchmark dose lower bound; IQ = intelligence quotient; SBP = systolic blood pressure; GFR = glomerular filtration rate; BMR = benchmark response; CI = confidence interval; RfD = reference dose; CDC = Centers for Disease Control and Prevention; NAAQS = national ambient air quality standard

[18]Developed in 2012, but no separate reference.

Table 13. Lead Cancer Assessments

Organization (year)	Weight of Evidence Characterization	Quantitative assessment	Extrapolation Method	ADAF
OEHHA (2020) Hot spots program	N/A	Oral slope factor: 0.0085 per mg/kg-day Inhalation unit risk: 1.2 x 10^{-5} per µg/m^3	Not available	N/A
IARC (2006)	Probably carcinogenic to humans (2B)	N/A	N/A	N/A
NTP (2016)	Reasonably anticipated to be human carcinogen (lead and lead compounds)	N/A	N/A	N/A
TCEQ	--	--	--	--
U.S. EPA (1988a) - IRIS	B2, probable human carcinogen	N/A	N/A	N/A

ADAF = age-dependent adjustment factor; N/A = not applicable or not available (see Approach)

Dibutyl Phthalate (DBP) (CASRN 84-74-2)

DBP TRVs are summarized in Tables 14 and 15. The toxicity literature on phthalates, including DBP, is extensive and complex. The report to the CPSC by the Chronic Hazard Advisory Panel on Phthalates and Phthalate Alternatives (CHAP, CPSC, 2014) stated:

> Although phthalates cause a wide range of toxicities, the most sensitive and most extensively studied is male developmental toxicity in the rat. Specifically, exposing pregnant dams to certain phthalates causes a syndrome indicative of androgen deficiency, referred to as the "phthalate syndrome" in rats. Exposure results in abnormalities of the developing male reproductive tract structures, the severity and prevalence of which depends on the dose. The phthalate syndrome is characterized by malformations of the epididymis, vas deferens, seminal vesicles, prostate, external genitalia (hypospadias), and by cryptorchidism (undescended testes) as well as by retention of nipples/areolae (sexually dimorphic structures in rodents) and demasculinization of the perineum, resulting in reduced anogenital distance (AGD). The highest incidence of reproductive tract malformations is observed at higher phthalate dose levels whereas, changes in AGD and nipple/areolae retention are frequently observed at lower phthalate dose levels. Furthermore, phthalates produce this developmental toxicity in male rodents with an age-dependent sensitivity, i.e., with fetuses being more sensitive than neonates, which are, in turn, more sensitive than pubertal and adult animals.

Based on this analysis, the CHAP focused on endpoints related to antiandrogenicity (i.e., phthalate syndrome effects). Points of departure were combined with UFs to calculate "potency estimates for antiandrogenicity (PEAAs)," using three different approaches ("cases"). In brief, case 1 was based on published PEAAs (Kortenkamp and Faust, 2010), case 2 was based on relative potency assumptions from Hannas et al. (2011), and case 3 was based on a *de novo* analysis of individual phthalates conducted by the CHAP. These PEAAs can be considered TRVs for the most sensitive endpoint. The **range of PEAAs for DBP was 0.05 to 0.5 mg/kg-day,** a range that the CHAP interpreted as providing information on the sensitivity of results to the assumptions used in their calculation.

The CHAP (CPSC, 2014) also briefly discussed the carcinogenic potential of phthalates. The report noted that "some phthalates are capable of producing carcinogenic effects, but these effects have been dismissed as not relevant to humans. In its evaluation of DEHP, the International Agency for Research on Cancer (IARC) considered that the induction of liver tumors in rodents by DEHP was mediated by peroxisome proliferator-activated receptor α (PPARα), a mechanism regarded as not relevant for humans (IARC, 2000). The CHAP report also noted that there are suggestions of a PPARα-independent mechanism that may be relevant to humans. The CHAP did not rule out the potential for phthalates to cause cancer via a MOA that may be relevant to humans, but noted considerable knowledge gaps with regard to a potential carcinogenicity MOA and chose to focus on male developmental toxicity in the rat, as the most sensitive and most extensively-studied endpoint.

No quantitative cancer assessments were located for DBP. The organizations with qualitative assessments (U.S. EPA, 1988b; Health Canada, 1992) considered DBP not classifiable as to

carcinogenicity. It is noted that a draft report is available for a new chronic study of DBP (NTP, 2021a). However, that study appears unlikely to result in a different conclusion. The draft report states that in the study, there was *equivocal evidence* of carcinogenic activity in male rats, and *no evidence* of carcinogenic activity in female rats or male or female mice.

In light of the complexity of the data and the number of varying acute and chronic TRVs, this text does not attempt to recommend final screening TRVs for DBP. Doing so would require a thorough review of the underlying studies for each assessment, the assessment rationale, and a review of the current literature on phthalates. Such a review is beyond the scope of this report. Instead, the text here focuses on characterizing the range of relevant TRVs and in comparing the basis for their derivation.

Acute oral TRVs have been derived by MDH (2015b) and ATSDR (2001). The ATSDR (2001) acute MRL used the same critical study and derived the same TRV as used by CPSC (2014) for the *de novo* PEAA. The MDH (2015b) acute TRV of 0.023 mg/kg-day is based on studies published after the ATSDR assessment (but prior to CPSC, 2014). The MDH value also considers additional areas of uncertainty in derivation of the acute TRV and is more conservative than the ATSDR value. However, the MDH (2015b) acute TRV of 0.023 mg/kg-day is smaller than both the lower bound of the range of PEAAs derived by CPSC (2014) and the chronic acceptable daily intake (ADI) derived by CPSC (2010a) discussed below. This is contrary to the expectation that acute TRVs should be comparable to or higher than chronic TRVs.

CPSC (2010a) derived a chronic ADI of 0.2 mg/kg-day. With the exception of the 1987 Integrated Risk Information System (IRIS) assessment (U.S. EPA, 1987a), all of the other chronic TRVs for DBP are lower than this chronic ADI. The lowest chronic TRV was the chronic oral DNEL of 0.007 mg/kg-day derived by ECHA (2013a). It is noted that CPSC (2010a) reviewed the Lee et al. (2004) study that is the principal study for the ECHA (2013a) assessment, but CPSC did not report the effects noted by ECHA as critical effects.

ECHA (2013a) derived inhalation and dermal DNELs for the general population from the oral DNEL. A similar approach could be used to derive the oral and inhalation TRVs for the screening assessment, once a choice has been made regarding the appropriate chronic oral TRV.

DBP is not irritating to the skin or eye and is not a skin sensitizer (OECD, 2001).

Table 14. DBP Non-Cancer Assessments

Organization (year)	TRV	Species	Critical Effect	Point of Departure	Uncertainty Factor (UF)	Principal Study
ATSDR (2001)	Acute Oral MRL: 0.5 mg/kg-day	Rat	Increased incidence of retained areolas and nipple in the male offspring of rats	NOAEL = 50 mg/kg-day	100 UFH = 10 UFA = 10	Mylchreest et al., 2000
CPSC (2014)	PEAAs ranging from 0.05 to 0.5 mg/kg-day Case 3 (de novo) presented here = 0.5 mg/kg-day See report for other cases	Rat	Increased nipple retention in male pups, increased male anogenital distance	NOAEL= 50 mg/kg-day	100 UFH = 10 UFA = 10	Mylchreest et al., 2000; Zhang et al., 2004
CPSC (2010a)	Chronic ADI = 0.2 mg/kg-day	Rats	Male infertility	NOAEL = 20 mg/kg-day	100 UFH = 10 UFA = 10	Mahood et al., 2007
ECHA (2013a)	Oral DNEL = 0.007 mg/kg-day Same for adults and children.	Rat	Delayed germ cell development in prepubertal rats and mammary gland changes (vacuolar degeneration and alveolar atrophy) in adult male rats exposed perinatally.	LOAEL = 2 mg/kg-day	300 UFA = 4 x 2.5 = 10 UFH = 10 UFL = 3	Lee et al., 2004
ECHA (2013a)	Dermal DNEL = 0.07 mg/kg-day Same for adults and children.	Rat	Same as for oral DNEL	LOAEL = 2 mg/kg-day 10% absorption Corrected LOAEL = 20 mg/kg-day	300 UFA = 4 x 2.5 = 10 UFH = 10 UFL = 3	Lee et al., 2004

Organization (year)	TRV	Species	Critical Effect	Point of Departure	Uncertainty Factor (UF)	Principal Study
ECHA (2013a)	Inhalation DNEC = 0.02 mg/m^3 Same for adults and children.	Rat	Same as for oral DNEL	LOAEL = 2 mg/kg-day Converted to LOAEC = 1.74 mg/m^3 based on respiratory volume/kg bw-day.	300 UFA = 4 x 2.5 = 10 UFH = 10 UFL = 3	Lee et al., 2004
U.S. EPA (1987a) - IRIS	Chronic Oral RfD = 0.1 mg/kg-day	Rat	Increased mortality	NOAEL = 125 mg/kg-day (0.25% of diet) LOAEL = 600 mg/kg-day (1.25% of diet)	1000 UFA = 10 UFS = 10 UFS, UFD = 10	Smith, 1953
U.S. EPA PPTRV	--	--	--	--	--	--
Health Canada (1992) (oral)	TDI = 0.063 mg/kg bw-day (more recent assessments used an MOE approach)	Mouse	Fetotoxic and teratogenic effects	NOEL = 62.5 mg/kg-day	1000 UFA = 10 UFH = 10 10 for severity of the effect at the LOAEL - i.e., teratogenicity, and for inadequacies of the database	Hamano et al., 1977
TCEQ	--	--	--	--	--	--
MDH (Air Guidance Values)	--	--	--	--	--	--

Organization (year)	TRV	Species	Critical Effect	Point of Departure	Uncertainty Factor (UF)	Principal Study
MDH (Water Guidance Values) (MDH, 2015b)	Acute RfD = 0.023 mg/kg-day	Sprague-Dawley rats	Decreased fetal testosterone, decreased testicular cell number and testes size	NOAEL = 10 mg/kg-day NOAEL(HED) = 2.3 mg/kg-day	100 UFA = 3 UFH = 10 UFD = 3 (additional study is warranted for potential thyroid and immunological effects)	Lehmann et al., 2004; Boekelheide et al., 2009
MDH (Water Guidance Values) (MDH, 2015b)	Short term RfD = 0.023 mg/kg-day	Sprague-Dawley rats	Decreased fetal testosterone, decreased testicular cell number and testes size	NOAEL = 10 mg/kg-day NOAEL(HED) = 2.3 mg/kg-day	100 UFA = 3 UFH = 10 UFD = 3 (additional study is warranted for potential thyroid and immunological effects)	Lehmann et al., 2004; Boekelheide et al., 2009
IPCS (1997)	Guidance value ADI= 0.066 mg/kg-day	Rats	Testicular and reproductive/developmental effects in continuous breeding study	LOAEL= 66 mg/kg-day	1000 UFA=10 UFH=10 UFL=10	NTP, 1995 (sic); Wine et al., 1997
JMPR	--	--	--	--	--	--
JECFA	--	--	--	--	--	--

TRV = toxicity reference value; MRL = minimal risk level; NOAEL = no observed adverse effect level; UFH = uncertainty factor human; UFA = uncertainty factor animal; PEAA = potency estimate for antiandrogenicity; ADI = acceptable daily intake; DNEL = derived no effect level; LOAEL = lowest observed adverse effect level; UFL = uncertainty factor LOAEL; DNEC = derived no effect concentration; LOAEC = lowest observed adverse effect concentration; RfD = reference dose; UFS = uncertainty factor subchronic to chronic; UFD = uncertainty factor database; TDI = tolerable daily intake; NOEL: = no observed effect level; MOE = margin of exposure; HED = human equivalent dose

Table 15. DBP Cancer Assessments

Organization (year)	Weight of Evidence Characterization	Quantitative assessment	Extrapolation Method	ADAF
U.S. EPA (1988b) - IRIS	D (Not classifiable as to human carcinogenicity)	N/A	N/A	N/A
IARC	--	--	--	--
JECFA	--	--	--	--
JMPR	--	--	--	--
Health Canada (oral and inhalation)	"Unclassifiable with respect to carcinogenicity in humans" (Group VI).	N/A	N/A	N/A
TCEQ	--	--	--	--

ADAF = age-dependent adjustment factor; N/A = not applicable or not available (see Approach)

Diethylhexyl Phthalate (DEHP) (CASRN 117-81-7)

DEHP TRVs are summarized in Tables 16 and 17. The toxicity literature on DEHP is even more extensive and complex than that for DBP. As noted in the summary for DBP, the CHAP report (CPSC, 2014) focused on endpoints related to antiandrogenicity, and derived PEAAs using three different approaches (cases). The **range of PEAAs for DEHP was 0.03 – 0.05 mg/kg-day,** much narrower than the range for DBP.

As discussed in the context of the DBP text, the CHAP (CPSC, 2014) noted that liver tumors related to (PPARα) are believed to occur via a MOA that is not relevant to humans. (See also CPSC, 2001; Klaunig et al., 2003). The report also noted uncertainties regarding the cancer MOA but stated that the phthalate syndrome effects are more sensitive than carcinogenicity. In its earlier DEHP assessment, CPSC (2010b) concluded that, although there is sufficient animal evidence for the designation of DEHP as a "probable carcinogen," the carcinogenic human relevance to humans is thought to be negligible. Based on the CHAP report, this conclusion may warrant revisiting to determine if DEHP-related tumors are all related to PPARα, but it appears that any changes in the carcinogenicity assessment would not drive the overall quantification. A draft report is available from a recent NTP study investigating age-related differences in cancer susceptibility to DEHP (NTP, 2021b). The draft report concluded that, under the conditions of the perinatal and postweaning study, as well as in the postweaning-only study, there was *clear evidence of carcinogenic activity* in male and female rats (mice were not tested). In addition to hepatocellular tumors, pancreatic tumors were observed consistently, along with several other tumors observed in various substudies (i.e., age/sex combinations).

Of the available cancer assessments for DEHP, most noted the MOA human relevance issue and differentiated between rodent carcinogenicity and human carcinogenic potential. IARC (2013) had a more conservative approach, considering DEHP "possibly carcinogenic to humans." Of the few organizations that applied a quantitative approach, OEHHA (2002) adjusted the slope factor down (lower potency) to reflect interspecies differences, while the IRIS assessment (U.S. EPA, 1988c) was developed prior to the MOA understanding related to PPARα.

In light of the complexity of the data and the number of varying acute and chronic TRVs, this text does not attempt to recommend final screening TRVs for DEHP. Doing so would require a thorough review of the underlying studies for each assessment, the assessment rationale, and a review of the current literature on phthalates. Such a review is beyond the scope of this report. Instead, the text here focuses on characterizing the range of relevant TRVs and in comparing the basis for their derivation.

CPSC (2010b) derived short-term, intermediate-term, and long-term TRVs for the general population of 0.1, 0.024, and 0.058 mg/kg-day, respectively. In addition, CPSC (2010b) developed an intermediate-term and long-term TRV for male reproduction of 0.037 and 0.0058 mg/kg-day, and a maternal exposure TRV of 0.011 mg/kg-day. Consistent with the understanding of the DEHP MOA, the most sensitive TRV overall developed by CPSC (2010b) was the long-term TRV for male reproduction of 0.0058 mg/kg-day. However, our review noted that the intermediate-term general population TRV developed by CPSC (2010b) is lower than

the long-term TRV for the general population, and is lower than the male reproduction TRV for the same duration. This observation is contrary to the general progression of lower TRVs for increasing duration. It also differs from the CHAP (CPSC, 2014) assessment in identifying the liver as more sensitive than the male reproductive tract for the intermediate duration, contrary to the current understanding of antiandrogenicity as the most sensitive endpoint. The apparent inconsistency regarding duration and the apparently evolving understanding of the critical effect do not appear to have been addressed in the CPSC (2010b) assessment.

A variety of other TRVs are available for DEHP. Acute oral TRVs were derived by ATSDR (2019) and MDH (2015c). Their acute TRVs differ by a factor of 10; the larger value (the MDH 2015c TRV of 0.029 mg/kg-day) is comparable to the CPSC (2010b) intermediate-term male reproductive TRV of 0.037 mg/kg-day; the ATSDR TRV is a factor of 10 lower, and not based directly on a male reproductive effect.

Chronic oral TRVs include several in the range of 0.02-0.05 mg/kg-day (ANSES, 2012; ECHA, 2013b; U.S. EPA, 1987b; Health Canada, 1994; MDH, 2015c). Many of these were based on male reproductive effects, but used a variety of different principal studies. These TRVs are in the range of the PEAAs developed by CPSC (2014), but about an order of magnitude larger than both the TRV for longer-term exposure based on male reproduction developed by CPSC (2010b) and the ATSDR (2019) intermediate-duration oral TRV.

ATSDR (2019) developed an intermediate duration inhalation TRV based on male and female reproductive effects in an inhalation study. The only other inhalation TRV (ECHA, 2013b) was a chronic TRV based on extrapolation from the corresponding oral TRV and was substantially larger than the ATSDR TRV. The difference may reflect route-to-route differences or differences in interpretation of the toxicity data by the two organizations.

ECHA (2013b) also derived a chronic dermal TRV from the chronic oral TRV. A similar approach could be used to develop a dermal TRV once a final oral value is determined.

As stated in OECD (2005), “(a)nimal studies performed to current guidelines have shown a slight skin and eye irritation after administration of DEHP, but DEHP is not corrosive to the skin or eyes. DEHP has not been found to induce skin sensitisation in animals.”

Table 16. DEHP Non-Cancer Assessments

Organization (year)	TRV	Species	Critical Effect	Point of Departure	Uncertainty Factor (UF)	Principal Study
ANSES (2012)	Chronic TRV = 0.05 mg/kg-day	Rat	Developmental abnormalities of the male reproductive organ	NOAEL = 5 mg/kg-day	100 UFH = 10 UFA = 10	Wolfe and Layton, 2003[19]; NTP, 2004
ATSDR (2019)	Provisional intermediate inhalation MRL = 0.0002 ppm (0.003 mg/m^3)	Rat	Altered reproductive system in developing males and females	LOAEL = 5 mg/m^3 (0.3 ppm) LOAEL(HEC) = 0.05 ppm	300 UFA = 3 UFH = 10 UFL = 10	Kurahashi et al., 2005; Ma et al., 2006
ATSDR (2019)	No chronic inhalation MRL (no chronic duration studies examining noncarcinogenic effects)	N/A	N/A	N/A	N/A	N/A
ATSDR (2019)	Provisional acute oral MRL = 0.003 mg/kg-day	Rat	Altered glucose homeostasis in adult offspring following fetal exposure	LOAEL = 1 mg/kg-day	300 UFH = 3 (F1 offspring exposed *in utero* considered a susceptible population) UFA = 10 UFL = 10	Rajesh and Balasubramanian, 2014
ATSDR (2019)	Provisional intermediate oral MRL = 0.0001 mg/kg-day	Mouse	Delayed meiotic progression of germ cells in GD 17.5 F1 fetuses; accelerated folliculogenesis in F1 and F2 PND 21 offspring	LOAEL = 0.04 mg/kg-day	300 UFH = 3 (study population (offspring) considered a susceptible population) UFA = 10 UFL = 10	Zhang et al., 2015

[19] Cited as Wolfe et al. (2003) by CPSC (2010b)

Organization (year)	TRV	Species	Critical Effect	Point of Departure	Uncertainty Factor (UF)	Principal Study
ATSDR (2019)	No chronic oral MRL - Not derived because candidate PODs from chronic studies are 2 orders of magnitude greater than the POD for the intermediate duration MRL	N/A	N/A	N/A	N/A	N/A
CPSC (2014)	PEAAs ranging from 0.03 to 0.05 mg/kg-day Case 3 (de novo) presented here = 0.05 mg/kg-day. See report for other cases	Rat	Increased reproductive organ abnormalities	NOAEL = 4.8 mg/kg-day	100 UFH=10 UFA=10	NTP study, cited as Foster et al., 2006; Supported by several other studies in a weight of evidence approach
CPSC (2010b)	Short-term exposure oral ADI= 0.1 mg/kg-day General population	Rat	Increase absolute and relative liver weight	NOAEL = 10 mg/kg-day	100 UFH=10 UFA=10	Dostal et al., 1987a, 1987b; ATSDR, 2002; ECB, 2008
CPSC (2010b)	Intermediate-term exposure oral ADI= 0.024 mg/kg-day General population	Rat	Increase relative liver weight	LOAEL = 24.0 mg/kg-day	1000 UFH=10 UFA=10 UFL=10	BIBRA, 1990; ECB, 2008
CPSC (2010b)	Long-term exposure oral ADI=0.058 mg/kg-day General Population	Rat	Increased absolute and relative liver weight and peroxisome proliferation in male rats	NOAEL = 5.8 mg/kg-day	100 UFH=10 UFA=10	David et al., 2000; Moore, 1996; ECB, 2008
CPSC (2010b)	Intermediate-term exposure oral ADI= 0.037 mg/kg-day. Male Reproduction	Rat	Induced mild vacuolation of Sertoli cells in the testes	NOAEL = 3.7 mg/kg-day	100 UFH=10 UFA=10	Poon et al., 1997; ECB, 2008

Organization (year)	TRV	Species	Critical Effect	Point of Departure	Uncertainty Factor (UF)	Principal Study
CPSC (2010b)	Long-term exposure oral ADI= 0.0058 mg/kg-day Male reproduction	Rat	Increased incidence of aspermatogenesis	LOAEL = 5.8 mg/kg-day	1000 UFH=10 UFA=10 UFL=10	David et al., 2000
CPSC (2010b)	Maternal exposure oral ADI= 0.011 mg/kg-day	Rat	Increased incidence of pups with phthalate syndrome (morphological and functional changes in reproductive organs)	LOAEL = 11 mg/kg-day	1000 UFH=10 UFA=10 UFL=10	Gray et al., 2009
ECHA (2013b)	Oral DNEL = 0.034 mg/kg/d Same for adults and children.	Rat	Testicular toxicity (small testes/epididymes/seminal vesicles and minimal testis atrophy) was observed in offspring.	NOAEL = 4.8 mg/kg-day NOAEL (corrected) = 3.36 mg/kg-day, adjusted for 70% oral absorption	100 UFA = 4 x 2.5 = 10 UFH: 10	Wolfe and Layton, 2003
ECHA (2013b)	Dermal DNEL = 0.672 mg/kg-day Same for adults and children. .	Rat	Same as for oral	NOAEL = 4.8 mg/kg-day NOAEL (corrected) = 67.2 mg/kg-day, adjusted for 5% dermal absorption	100 UFA = 4 x 2.5 = 10 UFH: 10	Wolfe and Layton, 2003

Organization (year)	TRV	Species	Critical Effect	Point of Departure	Uncertainty Factor (UF)	Principal Study
ECHA (2013b)	Inhalation DNEC = 0.16 mg/m^3 for adults 0.12 mg/m^3 for children	Rat	Same as for oral	NOAEL = 4.8 mg/kg-day NOAEC (corrected) = 3.90 mg/m^3 for adults NOAEC (corrected) = 2.92 mg/m^3 for children After adjustment for 75%/100% absorption (adults/children) and respiratory volume	100 UFA = 4 x 2.5 = 10 UFH: 10	Wolfe and Layton, 2003
U.S. EPA (1987b)	Chronic RfD = 0.02 mg/kg-day	Guinea pig	Increased relative liver weight	No NOAEL LOAEL = 19 mg/kg-day (0.04% of diet)	1000 UFH = 10 UFA = 10 UFS / UFL = 10 (duration between subchronic and chronic, and LOAEL minimally adverse)	Carpenter et al., 1953
PPRTV	--	--	--	--	--	--
Health Canada (1994) (oral)	TDI = 0.044 mg/kg-day	Mouse	Reproductive and developmental effects	NOEL = 44 mg/kg-day	1000 UFH = 10 UFA = 10 10 for potential teratogenicity	Wolkowski-Tyl et al., 1984
TCEQ	--	--	--	--	--	--
MDH (Air Guidance Values)	--	--	--	--	--	--

Organization (year)	TRV	Species	Critical Effect	Point of Departure	Uncertainty Factor (UF)	Principal Study
MDH (Water Guidance Values) (MDH, 2015c)	Acute RfD = 0.029 mg/kg-day	Rats	Male reproductive tract malformations (small testes, small epididymis, small cauda epididymis, small seminal vesicles)	BMDL = 3.8 mg/kg-day BMD(HED) = 0.874 mg/kg-day	30 UFH = 10 UFA = 3	Blystone et al., 2010
MDH (Water Guidance Values) (MDH, 2015c)	Short term RfD = 0.029 mg/kg-day	Rats	Same as for acute RfD	BMDL = 3.8 mg/kg-day BMD(HED) = 0.874 mg/kg-day)	30 UFH = 10 UFA = 3	Blystone et al., 2010
MDH (Water Guidance Values) (MDH, 2015c)	Subchronic RfD = 0.029 mg/kg-day	Rats	Same as for acute RfD	BMDL = 3.8 mg/kg-day BMD(HED) = 0.874 mg/kg-day)	30 UFH = 10 UFA = 3	Blystone et al., 2010
MDH (Water Guidance Values) (MDH, 2015c)	Chronic RfD same as subchronic RfD = 0.029 mg/kg-day	Sprague-Dawley rats	Same as for acute RfD	BMDL = 3.8 mg/kg-day BMD(HED) = 0.874 mg/kg-day)	30 UFH = 10 UFA = 3	Blystone et al., 2010
IPCS (1992)	No value derived	N/A	N/A	N/A	N/A	N/A
JMPR	--	--	--	--	--	--
JECFA (year NS)	No quantification	N/A	N/A	N/A	N/A	N/A
OEHHA (1997) Public Health Goal	RfD = 0.01 mg/kg-day (alternative calculation approach)	Mice	Reproductive or developmental toxicity	NOAEL = 14.2 mg/kg-day	1000 UFH = 10 UFA = 10 10 for developmental and reproductive endpoint	NTP, 1984

Organization (year)	TRV	Species	Critical Effect	Point of Departure	Uncertainty Factor (UF)	Principal Study
OEHHA (2005) Proposition 65	Maximum allowable dose level for oral exposure calculated for various groups	Rats	Aspermatogenesis	NOAEL = 5.8 mg/kg-day	1000 Specified by regulation for reproductive effect in males	David et al., 2000

TRV = toxicity reference values NOAEL = no observed adverse effect level; UFH = uncertainty factor human; UFA = uncertainty factor animal; MRL = minimal risk level; LOAEL = lowest observed adverse effect level; HEC = human equivalent concentration; UFL = uncertainty factor; N/A = not applicable or not available (see Approach); GD = gestational day; PND = post natal day; POD = point of departure; PEAA = potency estimates for antiandrogenicity; ADI = acceptable daily intake; LOAEL = lowest observed adverse effect level; DNEL = derived no effect level; DNEC = derived no effect concentration; NOAEC = no observed adverse effect concentration; RfD = reference dose; UFS = uncertainty factor subchronic to chronic; TDI = tolerable daily intake; NOEL = no observed effect level; BMDL = benchmark dose lower bound; BMD = benchmark dose; HED = human equivalent dose

Table 17. DEHP Cancer Assessments

Organization (year)	Weight of Evidence Characterization	Quantitative assessment	Extrapolation Method	ADAF
CPSC (2010b)	Sufficient animal evidence for the designation of DEHP as a “probable carcinogen.” The carcinogenic human relevance to humans, however, is thought to be negligible.	N/A	N/A	N/A
U.S. EPA (1988c) IRIS (oral) No estimate for inhalation exposure	B2 - probable human carcinogen	Oral slope factor = 1.4 x 10^{-2} per mg/kg-day Drinking water unit risk: 4 x 10^{-7} per µg/L	Linearized multistage procedure, extra risk	N/A
IARC (2013)	Possibly carcinogenic to humans (Group 2B)	N/A	N/A	N/A
JECFA (year NS)	DEHP is a hepatocarcinogen in rats and mice	N/A	N/A	N/A
JMPR	--	--	--	--
Health Canada (1994) (oral and inhalation)	"Unlikely to be carcinogenic to humans" (Group IV). However, the available database concerning effects of DEHP in primates and humans is not extensive and on this basis classification as "possibly carcinogenic to humans" might also be appropriate	N/A	N/A	N/A
OEHHA (2002) Proposition 65 NSRL	N/A	0.0022 per mg/kg-day Based on the relative expression levels of PPARα in humans compared to mice, potency reduced by 10x compared to mouse value Human data do not support route-specific differences in potency	Linearized multistage model Nonthreshold model used because a cellular receptor having endogenous ligands appears to be central to the hepatocarcinogenic effect in rodents	N/A

Organization (year)	Weight of Evidence Characterization	Quantitative assessment	Extrapolation Method	ADAF
OEHHA (1997) Public Health Goal	No overall assessment, but quotes U.S. EPA IRIS (1988c) and IARC (1982) conclusions	0.003 per mg/kg-day Nonlinear: 33.4 mg/kg-day / 1000 – 10 for severity, 10H, 10L = 0.03 mg/kg-day	Multistage model (using Tox_Risk) Or nonlinear approaches	N/A
OEHHA (2020) (Air toxics hot spots program)	N/A	Inhalation Unit Risk: 2.4 E-6 per $\mu g/m^3$ (Based on the oral slope factor of 0.0084 per mg/kg-day developed by CDHS, 1988)	Multistage model, converted from oral to inhalation route	N/A
TCEQ	--	--	--	--
MDH (Air Guidance Values)	--	--	--	--
MDH (Water Guidance Values) (MDH, 2015c)	Group B2, probable human carcinogen	Slope factor: 0.014 per mg/kg-day Source of slope factor: U.S. EPA (1993), further cited to U.S. EPA/IRIS	N/A	N/A

ADAF = age-dependent adjustment factor; N/A = not applicable or not available (see Approach); NSRL = No significant risk level; PPARα peroxisome proliferator-activated receptor α

4-tert-Octylphenol (CASRN 140-66-9)

4-tert-Octylphenol (4-t-OP) TRVs are summarized in Tables 18 and 19. No cancer assessments were located for 4-t-OP. Based on the literature reviewed, it appears that 4-t-OP has been tested in several subchronic studies of varying quality, but no chronic studies, and so a cancer assessment is not possible. 4-t-OP was negative in guideline-compliant bacterial gene mutation assays and a guideline-compliant *in vitro* chromosome aberration assay (OECD, 1995).

The only TRVs located for 4-t-OP were from MDH (2020b), based on the two-generation reproductive toxicity study of Tyl et al. (1999). MDH (2020b) **developed a short-term RfD of 0.17 mg/kg-day, a subchronic RfD of 0.17 mg/kg-day, and a chronic RfD of 0.051 mg/kg-day**. In all three cases, the low dose was a NOAEL, but the critical effects differed. For the short-term RfD the critical effects were decreased pup body weight and increased time to preputial separation, while the critical effects for the subchronic and chronic RfDs were decreased uterine weight and decreased adult body weight. The choice of different endpoints relates to the MDH methods, and that the purpose of the short-term RfD is to protect children, while the subchronic and chronic RfDs consider larger parts of the lifespan. Tyl et al. (1999) was a well-conducted guideline-compliant study that examined a wide range of endpoints. We concur that it is an appropriate basis for the oral TRVs.

Because 4-t-OP TRVs are available from only one organization, and these TRVs have not been cited in any assessment of exposure to recycled tire rubber that we reviewed, we conducted limited supplemental searching and review of the toxicity literature on 4-t-OP as an independent check on the MDH (2020b) assessment. We did note, however, that the MDH assessment is itself an update of a prior assessment (completed in 2015) and the MDH (2020b) assessment included more than three pages of references. This suggests that it reflects the current state of the science. Our limited literature review included a review of the studies provided by CPSC staff, unpublished data posted on the ECHA website, unpublished data posted on U.S. EPA's High Production Volume Information System (HPVIS) website, the OECD (1995) Screening Information Dataset (SIDS) dossier, as well as a cursory screen of PubMed search results. Studies conducted using a duration and design potentially appropriate for derivation of subchronic or chronic TRVs are summarized in Table 20. These data support the conclusion that the Tyl et al. (1999) study is an appropriate basis for the 4-t-OP oral TRVs.

Concerns have been raised about potential estrogenic effects of 4-t-OP, in part because of its structural similarity to nonylphenol, a known estrogenic chemical (reviewed by Tyl et al., 1999; ECHA, 2020c). However, as shown in Table 20, systemic toxicity consistently occurs at doses below doses causing effects on reproduction or other effects reflecting any hormonal disruption. This finding is consistent with the low *in vitro* estrogenic activity of 4-t-OP. For example, Laws et al. (2006) reported that the inhibitory concentration (IC 50) of 4-t-OP was 12.0 µM, compared to 0.00052 µM for 17 -β–Estradiol. This means that the estrogenic potency of 4-t-OP is several orders of magnitude lower than that of estradiol. Several of the studies provided by CPSC staff (Aydogan and Barlas, 2006; Blake and Boockfor, 1997; Boockfor and Blake, 1997; Mikkila et al., 2006; Yoshida et al., 2001) reported estrogenic effects of 4-t-OP, including adverse effects on male reproductive parameters. However, these studies were conducted using subcutaneous injection. Therefore, even though some estrogenic effects may have been seen at lower doses

than the LOAEL in the Tyl et al. (1999) study, the results cannot be translated directly to the oral route.

No dermal or inhalation TRVs were located. 4-t-OP is slightly irritating to the skin, highly irritating to the eyes, and may cause depigmentation of the skin, based on a subcutaneous injection study in mice (OECD, 1995).

A dermal TRV for systemic effects could be developed based on extrapolation from the oral TRV, ideally accounting for differences in absorption. Alternatively, assuming 100% dermal absorption is an appropriate conservative approach for a screening assessment, since dermal absorption is likely to be much lower than oral absorption. An inhalation TRV could also be extrapolated from the oral TRV. However, in light of the potentially irritating effects of 4-t-OP, consideration should be given to the potential for portal of entry effects on the respiratory tract; portal of entry effects from oral exposure are rare unless the chemical is corrosive, and are not generally a consideration in developing an oral TRV.

Table 18. 4-tert-Octylphenol Non-Cancer Assessments

Organization (year)	TRV	Species	Critical Effect	Point of Departure	Uncertainty Factor	Principal Study
ATSDR	--	--	--	--	--	--
IPCS	--	--	--	--	--	--
JECFA	--	--	--	--	--	--
JMPR	--	--	--	--	--	--
Health Canada	--	--	--	--	--	--
TCEQ	--	--	--	--	--	--
U.S. EPA	--	--	--	--	--	--
MDH (Air Guidance Values)	--	--	--	--	--	--
MDH (Water Guidance Values) (MDH, 2020b)	Short term Reference Dose: 0.17 mg/kg-day	Sprague-Dawley rats	Decreased pup body weight and increased time to preputial separation	NOAEL = 22 mg/kg-day NOAEL(HED) = 5.06 mg/kg-day (body weight scaling, dosimetric adjustment factor = 0.23) 2-generation study	30 UFA = 3 UFH = 10	Tyl et al., 1999
MDH (Water Guidance Values) (MDH, 2020b)	Subchronic Reference Dose = 0.17 mg/kg-day	Sprague-Dawley rats	Decreased uterine weight, decreased adult body weight	NOAEL = 22 mg/kg-day NOAEL(HED) = 5.06 mg/kg-day (body weight scaling, dosimetric adjustment factor = 0.23)	30 UFA = 3 UFH = 10	Tyl et al., 1999

Organization (year)	TRV	Species	Critical Effect	Point of Departure	Uncertainty Factor	Principal Study
MDH (Water Guidance Values) (MDH, 2020b)	Chronic Reference Dose = 0.051 mg/kg-day	Sprague-Dawley rats	Decreased uterine weight, decreased adult body weight	NOAEL = 22 mg/kg-day NOAEL(HED) = 5.06 mg/kg-day (body weight scaling, dosimetric adjustment factor = 0.23)	100 UFA = 3 UFH = 10 UFS = 3	Tyl et al., 1999

TRV = toxicity reference value; NOAEL = no observed adverse effect level; HED = human equivalent dose; UFA = uncertainty factor animal; UFH = uncertainty factor human, UFS = uncertainty factor subchronic

Table 19. 4-tert-Octylphenol Cancer Assessments

Organization (year)	Weight of Evidence Characterization	Quantitative assessment	Extrapolation Method	ADAF
IARC	--	--	--	--
NTP	--	--	--	--
TCEQ	--	--	--	--
U.S. EPA	--	--	--	--

ADAF = age-dependent adjustment factor

Table 20. Summary of Toxicity Studies Relevant to Derivation of 4-tert-Octylphenol RfD

Citation	Exposure scenario	Doses tested (mg/kg-day)	Observed effects*	NOAEL/LOAEL	Comments
Bian et al., 2006	**Male Sprague Dawley rats 30 days**	**Gavage with 0, 50, 150, or 450 mg/kg-day in corn oil**	**Damage to spermatogenic cells, decreased sperm numbers, decreased sperm motility**	**150/450**	**Short-term study**
Blake et al., 2004	**Male F344 rat Drinking water 4 months 6/dose/study**	**0, 10^{-9}, 10^{-7}, 10^{-5} M in drinking water 0, 0.000035, 0.0035, 0.35 mg/kg-day at beginning of study, 0, 0.00002, 0,0020, and 0.2 mg/kg-day at end**	**Increased tail abnormalities at all doses, dose-related No effect on body weight gain, hematocrit, reproductive organ weight, mean serum LH< FSH, testosterone, or sperm number**	**Statistical significance suggests 0.000035 mg/kg-day as a LOAEL, but lack of effect in other studies at higher doses raises questions.**	**Doses calculated by study authors Analyses done on 6 rats/dose sacrificed on successive days**
HRC, 1995, as reported by ECHA, 2020c	**Sprague Dawley Crl:CD rats Gavage in corn oil 12/sex/dose 2 weeks prior to mating, 2 weeks mating, through PND 4**	**0, 125, 250, 500 mg/kg-day**	**At 250 mg/kg-day: Decreased body weight gain, increased liver weight, cortical scarring of kidneys At 500 mg/kg-day: parental death decreased implantation rate, litter size, increased pre- and postnatal morality, reduced litter weight)**	**125/250 (systemic) 250/500 (reproductive/ developmental)**	**OECD 421 reproduction/developmental toxicity screening study**
Tyl et al., 1999	**CD (Sprague-Dawley) rats 2-gen repro**	**0, 0.2, 20, 200, 2000 ppm in diet**	**Decreased body weights in adults and during the latter portion of lactation in**	**200/2000 ppm 10.9 - 32.6/111 - 369 mg/kg-day**	**Conducted according to U.S. EPA OPPTS Guideline 870.3800 draft (1996)**

	30/sex/dose to yield at least 20 pregnant females at term/dose	Corresponding to 0.011-0.034, 1.05 - 3.3, 10.9 - 32.6, 111 - 369 mg/kg-day	offspring and minor body weight-related delays in acquisition of vaginal opening and preputial separation		0.2 ppm included to evaluate low-dose effects No reproductive effects
Bayer, 1982, as reported by Schenectady International, 2002; ECHA, 2020c	Wistar rats 90-day 20/sex/dose	0, 30, 300, 3000 ppm in diet, corresponding to 0, 2.2, 22.5, and 227.9 mg/kg-day (males)	Reduced body weight gain, reduced organ weights	300/3000 ppm 22.5/227.9 mg/kg-day (males) 24.9/248.6 mg/kg-day (females) (doses calculated by submitter)	Conducted according to OECD guideline 408; judged reliable with restrictions due to no ophthalmological examination, sensory reactivity not examined separately
Rohm and Haas, 1961, as reported by Schenectady International, 2002	Albino rat, 3 months, 15/sex/dose	0 or 5% in diet	No effect on growth, survival, food consumption, urinary excretion of glucose and protein, hematologic values, or organ to body weight ratios, and no pathologic lesions.	5% in diet/None ~4300 mg/kg-day, based on a food factor of 0.086	Not GLP

NOAEL = no observed adverse effect level; LOAEL = lowest observed adverse effect level; LH = luteinizing hormone; FSH = follicle stimulating hormone; PND = post natal day; GLP = good laboratory practice

*Observed effects with a focus on effects at the LOAEL

Toxicity Reference Value Summary for Use in Risk Assessment

The previous section identified relevant TRVs for the chemicals of interest, including noncancer and cancer TRVs and qualitative cancer assessments, where available. Acute, subchronic and chronic TRVs have been identified where available, for the oral, inhalation and dermal routes. Where appropriate, the potential for route-to-route extrapolation is noted. The availability of noncancer TRVs is noted in Table 21, and the availability of qualitative and quantitative cancer assessments is noted in Table 22. Tables 21 and 22 also include gray-shaded boxes that note where a TRV *could* be derived or extrapolated, either by route-to-route extrapolation, or by conservatively applying a longer duration TRV for a shorter duration (i.e., a chronic TRV for a subchronic duration, or a subchronic TRV for an acute duration). These potential extrapolations are suggested based only on first principles; we did not search for assessments that conducted such extrapolations. Additional considerations for uses of TRVs, particularly extrapolated ones, are also noted in footnotes to the tables.

Table 21. Summary of availability of noncancer TRVs[1]

Noncancer Assessment	Oral (mg/kg-day)			Inhalation (mg/m^3)			Dermal (mg/kg-day)		
	Acute	**Sub-chronic**	**Chronic**	**Acute**	**Sub-chronic**	**Chronic**	**Acute**	**Sub-chronic**	**Chronic**
Benzothiazole	X	X (MOE)	X	X	X	X (extrap) Possible irr	X sens	X sens	X sens
Lead[2]	X	X	X	X	X	X	X	X	X
Zinc	X	X	X	X	X	X	X	X	X
Benzo(a)pyrene	X	X (extrap)	X	X	X	X	X	X	X
Hexavalent Chromium (Cr(VI))	X	X	X	X	X	X	X sens	X sens	X sens
Dibutyl Phthalate	X	X	X	X	X	X (extrap)	X	X	X (extrap)
Diethylhexyl Phthalate	X	X (uncert)	X	X	X	X (extrap)	X Slight irr	X Slight irr	X (extrap) Slight irr
4-tert-Octylphenol	X	X	X	X Consider irr	X Consi-der irr	X Consider irr	X Slight irr, Possible depig	X Slight irr, Possible depig	X Slight irr, Possible depig
4-Methyl-2-pentanone (Methyl Isobutyl Ketone)	X	X	X (extrap)	X (MOE)	X (MOE)	X	X	X (extrap, MOE)	X (extrap)

[1]Gray background to the cell indicates that a value *could be* extrapolated for that chemical, duration and route

[2] Most lead TRVs are based on a concentration in blood, which is not duration-specific, and for which corresponding exposures can be modeled. There is also a subchronic inhalation TRV and a chronic oral value.

X = indicates that a value exists; Depig = depigmentation; Extrap = a TRV exists for that cell, but was developed by extrapolation across routes or applying TRV for one duration to another duration; Irr = irritant; MOE = margin of exposure; Sens = sensitizer; Uncert = inconsistencies noted in derived value, additional evaluation recommended

Table 22. Summary of availability of cancer assessments and TRVs[1]

Cancer Assessment	Oral		Inhalation		Dermal	
	Qualitative	Quantitative (mg/kg-day)	Qualitative	Quantitative (mg/m^3)	Qualitative	Quantitative (mg/kg-day)
Benzothiazole	X Read across	X Read across	X Read across, extrap	X Read across, extrap	X	X
Lead	X	X (uncert)	X (implied)	X (uncert)	X	X
Zinc	X	--	X	--	X	--
Benzo(a)pyrene	X	X	X	X	X	X
Hexavalent Chromium (Cr(VI))	X	X	X	X	--	--
Dibutyl Phthalate	X	--	X	--	X	--
Diethylhexyl Phthalate	X	X (uncert)	X (implied)	X (uncert)	X	--
4-tert-Octylphenol	--	--	--	--	--	--
4-Methyl-2-pentanone (Methyl Isobutyl Ketone)	X	--	X	--	X	--

[1]Gray background to the cell indicates that a value could be extrapolated for that chemical, duration and route

-- = No available data, and extrapolation not appropriate; X = indicates that a value exists; Extrap = A TRV exists for that cell, but was developed by extrapolation across durations or routes; Implied = No qualitative assessment was located, but a quantitative assessment was found, which implies a minimum qualitative assessment; Uncert = High uncertainty or other issues associated with the slope factor; recommendation is not to use

Exposure Parameters

Approach

We compiled exposure data to aid CPSC staff in estimating human exposure to the nine chemicals of interest from playground surfaces made with recycled tire crumb rubber. The types of data needed were identified in a draft conceptual exposure framework document, literature and Internet searches were used to identify publications and other sources of relevant information, and a spreadsheet was designed to capture relevant exposure parameter values for each route and exposure equation identified in the framework. The results section summarizes the available data for each of the exposure equations. A table summarizing the available data is provided for each model. An "X" indicates we found data for the model parameter (or a default or generic parameter value is available) and a "-" indicates we did not find relevant data in our sources.

Draft Conceptual Exposure Framework

CPSC staff provided a Draft Conceptual Exposure Framework for the UC team to review and to provide comments and suggestions on the conceptual model, exposure scenarios, and exposure equations. Our first round of comments focused on the appropriateness of each model for the intended screening assessment, its assumptions and limitations, and which variables have the greatest potential for uncertainty. We noted the need to define what is meant by acute and chronic exposures in the scenarios and to ensure consistency with duration of exposure associated with the toxicological benchmarks used for risk characterization. CPSC staff reviewed iterative comments and revised the document.

Sources from FRAP Reports

The FRAP project conducted an extensive literature review and prepared a Literature Review and Data Gaps Analysis (LRGA) document that included a spreadsheet which summarized available exposure data (U.S. EPA, 2016a). We reviewed the LRGA spreadsheet and FRAP reports (U.S. EPA 2016a, U.S. EPA and CDC/ATSDR, 2019) and extracted relevant data for exposure parameters on the chemicals of interest. Data from the following list of 20 publications were captured. Those that have playground data are italicized.

Bocca et al. 2009. Metals contained and leached from rubber granulates used in synthetic turf areas. Science of the total environment, 407(7), pp.2183-2190.

CalRecycle (California Department of Resources Recycling and Recovery). 2010. Tire-Derived Rubber Flooring Chemical Emissions Study: Laboratory Study Report. October.
CDPH (Connecticut Department of Public Health). 2010. Human Health Risk Assessment of Artificial Turf Fields Based Upon Results from Five Fields in Connecticut.

CDPH (Connecticut Department of Public Health). 2010. Human Health Risk Assessment of Artificial Turf Fields Based Upon Results from Five Fields in Connecticut. http://www.ct.gov/deep/lib/deep/artificialturf/dph_artificial_turf_report.pdf.

Celeiro et al. 2014. Investigation of PAH and other hazardous contaminant occurrence in recycled tyre rubber surfaces. Case-study: restaurant playground in an indoor shopping centre. International Journal of Environmental Analytical Chemistry, 94(12), pp.1264-1271.

Dye et al. 2006. Norwegian Pollution Control Authority. Measurement of Air Pollution in Indoor Artificial Turf Halls. Oslo, Norway: Norwegian Pollution Control Authority, Norwegian Institute for Air Research.

Gomes et al. 2010. Toxicological assessment of coated versus uncoated rubber granulates obtained from used tires for use in sport facilities. Journal of the Air & Waste Management Association, 60(6), pp.741-746.

Highsmith et al. 2009. A Scoping-Level Field Monitoring Study of Synthetic Turf Fields and Playgrounds. In National Exposure Research Laboratory. US Environmental Protection Agency.

Incorvia Mattina et al. 2007. Examination of crumb rubber produced from recycled tires. The Connecticut Agricultural Experiment Station, New Haven, CT.

Lioy and Weisel. 2011. Crumb Infill and Turf Characterization for Trace Elements and Organic Materials. Report prepared for NJDEP, Bureau of Recycling and Planning.

Llompart et al. 2013. Hazardous organic chemicals in rubber recycled tire playgrounds and pavers. Chemosphere, 90(2), pp.423-431.

Marsili et al. 2015. Release of polycyclic aromatic hydrocarbons and heavy metals from rubber crumb in synthetic turf fields: preliminary hazard assessment for athletes. Journal of Environmental & Analytical Toxicology, 5(2), p.1.

Menichini et al. 2011. Artificial-turf playing fields: Contents of metals, PAHs, PCBs, PCDDs and PCDFs, inhalation exposure to PAHs and related preliminary risk assessment. Science of the Total Environment, 409(23), pp.4950-4957.

Nilsson et al. 2008. Mapping, emissions and environmental and health assessment of chemical substances in artificial turf. Copenhagen, Denmark: Danish Environmental Protection Agency.

NIPH (Norwegian Institute of Public Health). 2006. Artificial turf pitches – an assessment of the health risks for football players Oslo, Norway.

OEHHA (Office of Environmental Health Hazard Assessment). 2007. Evaluation of Health Effects of Recycled Waste Tires in Playground and Track Products. Prepared for the California Integrated Waste Management Board.

Pavilonis et al. 2014. Bioaccessibility and Risk of Exposure to Metals and SVOCs in Artificial Turf Field Fill Materials and Fibers. Risk Analysis, 34: 44–55

Simcox et al. 2010. Artificial Turf Field Investigation in Connecticut. Final Report. Prepared for the Connecticut Department of Environmental Protection. Section of Occupational and Environmental Medicine, University of Connecticut Health Center, University of Connecticut (July 27, 2010).

U.S. EPA and CDC/ATSDR. 2019. Synthetic Turf Field Recycled Tire Crumb Rubber Research Under the Federal Research Action Plan Final Report: Part 1 - Tire Crumb Characterization (Volumes 1 and 2). (EPA/600/R-19/051). United States Environmental Protection Agency, Centers for Disease Control and Prevention/Agency for Toxic Substances and Disease Registry.

Vetrano and Ritter. 2009. Air quality survey of synthetic turf fields containing crumb rubber infill. Prepared for New York City Department of Health and Mental Hygiene. TRC Project, (153896).

Zhang et al. 2008. Hazardous chemicals in synthetic turf materials and their bioaccessibility in digestive fluids. Journal of exposure science & environmental epidemiology, 18(6), pp.600-607.

Literature Search

We conducted literature and internet searches to identify recent hazard, exposure, and risk assessments that have not previously been identified by CPSC or in the FRAP LRGA. While we initially planned to limit our searches to playgrounds, we included key words to also capture assessments of artificial turf fields. Search terms and databases used are described in Appendix B. We also reviewed the sources and URLs listed on the web page entitled "Government Organization Websites Related to the Use of Tire Crumb on Fields and Playgrounds" on the U.S. EPA FRAP website (https://www.epa.gov/chemical-research/government-organization-websites-related-use-tire-crumb-fields-and-playgrounds) to identify newer assessments or information published after 2016[20]. We screened the results of these searches to identify hazard, exposure, and risk assessments for playgrounds and artificial turf fields, and other relevant studies published since the FRAP report in 2016. In screening the search results, we identified references with quantitative information on the chemicals of interest and prioritized those that assessed rubberized playground surfaces. Some artificial tire crumb turf assessments and references were also included to fill data gaps.

Below we describe the 16 references we prioritized: eight playground specific assessments/studies and eight artificial turf assessments/studies. Note that five of the assessments did not have relevant data available for this project.

[20] We focused our search to publications from 2016 on because the 2016 FRAP report covered literature prior to this date.

Playground Specific Assessments and Publications with Data Relevant to Playground Surfaces (8), since 2016

Almansour, K. S., Arisco, N. J., Woo, M. K., Young, A. S., Adamkiewicz, G. & Hart, J. E. 2019. Playground lead levels in rubber, soil, sand, and mulch surfaces in Boston. PLoS One, 14, e0216156.

Measured lead levels from poured in place playground rubber surfacing, soil, sand, and wood mulch from 28 random playgrounds in Boston, Massachusetts. Evaluated the association between material type and lead concentrations, controlling for distance from major roadways, environmental justice neighborhood designation, presence of peeling paint at playground, and condition of the rubber surface. Relevant information was extracted from this assessment and included in the Exposure Parameter Spreadsheet.

Čakmak, D., Perović, V., Kresović, M., Pavlović, D., Pavlović, M., Mitrović, M. and Pavlović, P., 2020. Sources and a health risk assessment of potentially toxic elements in dust at children's playgrounds with artificial surfaces: A case study in Belgrade. Archives of environmental contamination and toxicology, 78(2), pp.190-205.

Measured concentrations of metals in dust samples from 15 playgrounds covered with artificial surfaces and adjacent soil samples to determine origin (atmospheric or surrounding soil) of elements found on playground surfaces and calculated direct oral, inhalation, and dermal exposures. However, the publication does not link the concentrations to type of playground surfaces and so we cannot know what data are relevant to recycled rubber playground surfaces. Nevertheless, this information was extracted to provide additional information about concentrations of metals in soil and dust at playgrounds. Relevant information was extracted from this assessment and included in the Exposure Parameter Spreadsheet.

California Office of Environmental Health Hazard Assessment (OEHHA) (ongoing).

Ongoing project to study human health effects from use of recycled tires in playground and synthetic turf products. OEHHA contracted with CalRecycle to conduct sampling, hazard identification, and to develop exposure scenarios. Work has not yet been published, but information (e.g., air concentration and skin wipe samples) is anticipated to be released in the near future.

Celeiro et al., 2021 Hazardous compounds in recreational and urban recycled surfaces made from crumb rubber. Compliance with current regulation and future perspectives. Science of the Total Environment, 755, p.142566.

Chemical characterization was conducted on crumb rubber samples from 40 synthetic turf fields, outdoor and indoor playgrounds, urban pavements, commercial tiles and granulates, and scrap tires. Playground specific concentration data were reported for several chemicals of interest (PAHs and phthalates)

Consumer Product Safety Commission. 2019. Survey of American Households: Child Interaction and Potential Exposure to Playground Surfacing Materials. September 15.

Results of national survey on children's behavior on playgrounds including frequency and duration of playground visits, dermal contact, clothing worn, hygiene practices, etc. Relevant information was extracted from this report and included in the Exposure Parameter Spreadsheet.

Huang et al., 2019. Children's exposure to phthalates in dust and soil in Southern Taiwan: A study following the phthalate incident in 2011. Science of the Total Environment, 696, 133685. Southern Taiwan.

Surface dust samples from playgrounds and running tracks in Taiwan were analyzed for phthalate esters (as well as dust concentrations of homes, elementary schools, and kindergartens). The authors estimated average daily intakes for dermal absorption and dust ingestion and evaluated cumulative exposure. Relevant information was extracted from this assessment and included in the Exposure Parameter Spreadsheet.

RIVM, 2016. Assessment of the product limit for PAHs in rubber articles. The case of shock-absorbing tiles. RIVM Report 2016-0184.

RIVM assessed risk (cancer only) from the current product limit for PAHs in rubber tiles made from recycled tires to evaluate whether the limit provides adequate protection. The assessment used the product limit concentration, but not actual measured concentrations from playgrounds. Dermal and oral (hand-to-mouth transfer from dermal contact) exposures were evaluated for a reasonable worst-case scenario for children 2-12 years. Relevant information was extracted from this assessment and included in the Exposure Parameter Spreadsheet.

Tarafdar, A., Oh, M.J., Nguyen-Phuong, Q. and Kwon, J.H., 2020. Profiling and potential cancer risk assessment on children exposed to PAHs in playground dust/soil: A comparative study on poured rubber surfaced and classical soil playgrounds in Seoul. Environmental geochemistry and health, pp.1-14.

Measured PAH concentrations in surface soils and in the dust on poured rubber playground surfaces (poured in place) from 14 children's parks in Seoul, Korea. Probabilistic estimates of lifetime cancer risk (direct ingestion, inhalation and dermal) using BAP potency equivalents. Relevant information was extracted from this assessment and included in the Exposure Parameter Spreadsheet.

Artificial Turf Assessments and Publications (8), since 2016

European Risk Assessment Study on Synthetic Turf Rubber Infill (ERASSTRI). 2020. (Published as Schneider et al., 2020 in three parts)

A Europe-wide human health risk assessment of outdoor synthetic turf fields made with recycled tire rubber granulate infill (Schneider et al., 2020a, 2020b, 2020c). The study was funded by industrial associations and companies involved in the supply chain for tire granulate. Exposure and risk were estimated for players and bystanders for oral, inhalation, and dermal routes. Relevant information was extracted from this assessment and included in the Exposure Parameter Spreadsheet.

European Chemicals Agency (ECHA). 2017. Annex XV Report an Evaluation of the Possible Health Risks of Recycled Rubber Granules Used as Infill in Synthetic Turf Sports Fields.

ECHA evaluated human health risk from substances in recycled rubber granules used as infill in outdoor artificial turf fields for players (including children), adult professional players, and workers installing or maintaining the fields. Dermal contact and ingestion were estimated, as well as inhalation of volatile organic compounds (VOCs) and dust. ECHA used both public and unpublished data on concentration of substances in rubber granules and data from evaporation and leaching studies. Relevant information was extracted from this assessment and included in the Exposure Parameter Spreadsheet.

Haering, S.A., 2015. Alexandria Health Department Crumb Rubber Review. September 16.

Reviewed the literature and concluded no evidence for health concern from the city's synthetic turf playing fields. The brief report included a list of references, but no specific data on exposure parameters or TRVs; therefore, no data were extracted.

Kromberg, J., 2020. Synthetic Turf Wars: A Crumb Rubber Human Health Risk Assessment (Thesis).

Honors college thesis that briefly discussed the literature and conducted a rudimentary human health risk assessment to calculate hazard quotients and a hazard index. No data were extracted from this document.

Massey, R., Pollard, L., Jacobs, M., Onasch, J. & Harari, H. 2020. Artificial Turf Infill: A Comparative Assessment of Chemical Contents. New Solut, 30, pp. 10-26.

A hazard-based alternatives assessment prepared by the Toxics Use Reduction Institute (TURI) comparing tire crumb and other alternative infill materials for artificial turf and play surfaces. Concentration data on the chemicals of interest, but with a small sample size. No data were extracted from this document. Related publications:

TURI. 2019. Athletic Playing Fields Choosing Safer Options for Health and the Environment. TURI Report #2018-002December 2018 (updated April 2019). Toxics Use Reduction Institute. UMass Lowell.

TURI 2018. Playground Surfacing Choosing Safer Materials for Children's Health and the Environment. TURI Report #2018-003December 2018. Describes the different types of playground surfaces but does not contain exposure or toxicity information for this project.

Peterson, M.K., Lemay, J.C., Shubin, S.P. and Prueitt, R.L., 2018. Comprehensive multipathway risk assessment of chemicals associated with recycled ("crumb") rubber in synthetic turf fields. Environmental Research, 160, pp.256-268.

Assessed risk from crumb rubber and natural turf fields with soils impacted by urban pollutions. Estimated risk for players and spectators, for a large list of contaminants, for oral, inhalation and dermal exposure routes. Supplemented values from the literature for

recycled rubber and air sampling data collected near synthetic turf fields, with data solicited from rubber recyclers and synthetic pitch installers. Relevant information was extracted from this assessment and included in the Exposure Parameter Spreadsheet.

RIVM (National Institute for Public Health and the Environment) 2017. Evaluation of health risks of playing sports on synthetic turf pitches with rubber granulate: Scientific background documents. RIVM Report 2017-0017. Peer review publication is Pronk et al. (2018).

The National Institute for Public Health and the Environment (RIVM) assessed human health risk of playing sports on synthetic turf fields that utilize rubber granulate infill. They analyzed rubber granulate infill (made from recycled tires) from 100 synthetic turf fields in The Netherlands to identify chemicals of interest and conducted migration studies (gastrointestinal fluid, sweat, and evaporation in hot weather. They estimated exposure for dermal contact, inhalation, and ingestion for players from 4 years to 50, performance and recreational players, field and goal keepers, and lifelong players. They also investigated the relationship between leukemia and lymphoma incidence and playing sports on synthetic turf with rubber granulates. Relevant information was extracted RIVM (2017) and included in the Exposure Parameter Spreadsheet.

RIVM, 2018. Environmental impact study on rubber granulate. RIVM Briefrapport 2018-0072.

In Dutch, could not find an English translation.

Other Data Sources with Exposure Parameter Values

Five additional data sources that provide information on non-chemical exposure parameters were included. These are model user guides, approach documents, and handbooks.

U.S. EPA. 2011. Exposure Factors Handbook.

U.S. EPA. 2017. Exposure Factors Handbook.

U.S. EPA. Consumer Exposure Model (CEM) 2.1.

U.S. EPA. Consolidated Human Activity Database (CHAD)

Wilson and Richardson. 2016. Estimation of dust ingestion rates in units of surface area per day using a mechanistic hand-to-mouth model, Human and Ecological Risk Assessment: An International Journal, 22:4, 874-881.

Playground Exposure Parameter Values Spreadsheet

We extracted relevant parameters for each of the equations identified in the Draft Conceptual Exposure Framework. Using the spreadsheet of Draft Framework equations, we first extracted

chemical specific parameter values from the FRAP LRGA spreadsheet that were relevant to playground exposures and the exposure equations. We then supplemented the FRAP data with data from the newer playground and artificial turf assessments and studies identified from the targeted literature search. Each entered value was verified by a second person to ensure that the information was entered accurately. A complete list of the 36 publications used to populate the spreadsheet is found in in Appendix C.

Based upon the initial playground specific data focus, we found little data specific to playgrounds in the FRAP LRGA spreadsheet for most of the equation parameters. For the inhalation models we only found data for Zn, Pb, and BAP. For the dermal models we only found data for Zn, BAP, DBP, and DEHP. For the oral models we only found data for Pb, Zn and BAP. Adding in data from the more recent playground and artificial turf assessments and publications provided additional data, but because there are few data for the nine target chemicals, we could not recommend specific parameter values for use in each of the models.

Results and Recommendations for Exposure Models

The Draft Conceptual Exposure Framework Document (v 6) identified 11 exposure models that could be considered for assessing exposure: five inhalation, three dermal, and four oral models. Below we present each model and the available data for that model, followed by recommendations for preferred models given the available data. The model parameters that were searched for in Subtasks 2 and 3 are provided in the model formulations below.

Based on the data extracted from the literature and assessments, a full set of specific chemical parameter data were not available for most of the models. Note that none of the assessments or publications included data for hexavalent chromium, only total chromium concentrations were reported. Data were found for all parameter values for the following models and chemicals:

- Inhalation Model 1 – Chromium (based on total chromium)
- Inhalation Model 2 – BAP (indoor and outdoor), chromium (outdoor), and lead (outdoor)
- Inhalation Model 3 – BAP (if concentration in particulate matter PM_{10} and $PM_{2.5}$ are used), as well as chromium and lead (if the total chemical concentration in tire crumb is used)
- Inhalation Model 4 – BAP, chromium, and lead
- Dermal Model 1 – BAP, as well as DBP, DHEP, MIBK and 4-tert-Octylphenol (if the solid phase diffusion is estimated)
- Dermal Model 2 - Zinc
- Dermal Model 3 – Zinc
- Oral Model 1 – BAP
- Oral Model 4 – BAP, chromium, and lead

Note that Inhalation Model 5, and the Oral Models 2 and 3 do not have a full set of parameter values for any of the chemicals.

Inhalation Models

Five inhalation models are considered. Both indoor and outdoor exposures are of interest and the chemicals of interest include VOCs, semi volatile organic compounds (SVOCs), and metals.

Inhalation Model 1

Equation 1 or 2 can be used to estimate an indoor air concentration by using an emission rate or emission factor coupled with an air exchange rate and room volume. These values are typically determined from chamber experiments. Equation 3 is then used to calculate a daily dose.

$$air\ concentration\ \frac{mg}{m3} = Emission\ factor\ (mg\ per\ gram\ per\ hour) * \left(\frac{M}{V}\right) * \left(\frac{1}{N}\right) \quad (1)$$

$$air\ concentration\ \frac{mg}{m3} = Emission\ factor\ (mg\ per\ m2\ per\ hour) * \left(\frac{A}{V}\right) * \left(\frac{1}{N}\right) \quad (2)$$

Where:

M = mass of tire crumb or tire mulch present on rubberized surface (g)

A = Area of rubberized playground surface (m^2)

N = air exchange (frequency per hr)

V = Volume of room (m^3)

$$Dose - \frac{mg}{kg}/day = \frac{A\left(\frac{mg}{m3}\right)X\ B\left(\frac{m3}{hr}\right)X\ C\left(\frac{hr}{day}\right)X\ D\ (fraction\ bioavailable)}{E\ (kg)} \quad (3)$$

Where:

A = chemical concentration in the air (time averaged) (mg/m^3)

B = inhalation rate (short-term) for higher activity level (m^3/hr)

C = hours spent on or near the field (hr/day)

D = fraction bioavailable (gastric)

E = body weight for age of interest (kg)

Table 23 summarizes the available data for the exposure parameters in Inhalation Model 1. Chromium was the only chemical that had data for all the parameter values. However, if one uses measured air chemical concentrations from chamber studies (ERASSTRI-1, CalRecycle) in Equation 3, then this would eliminate the need for Equation 1 or 2.

Table 23. Inhalation Model 1 – Emission from surface to room (Indoor)

Chemical	Surface Mass	Surface Area	Emission Factor	Air Ex-change Chamber	Volume Room or Chamber	Inhala-tion Rate	Duration on Play-ground	Fraction Bio-availble	Body Weight
Benzo(a)pyrene	X	X	-		-	X	X	X	X
Benzothiazole	X	X	X	X	X	X	X	-	X
Chromium	X	X	X	X	X	X	X	X	X
DBP	X	X	X	X	X	X	X	-	X
DEHP	X	X	-	-	-	X	X	-	X
Lead	X	X	-	-	-	X	X	X	X
MIBK	X	X	X	X	X	X	X	-	X
Zinc	X	X	-	-	-	X	X	-	X
4-tert-Octylphenol	X	X	-	-	-	X	X	-	X

Inhalation Model 2

Measured monitoring data for air concentrations near playground surfaces are used in Equation 4 to estimate a daily dose. Inhalation Model 2 (Equation 4), which can be used for either indoor or outdoor situations, is essentially the same model formulation as Inhalation Model 1 (Equation 3) except that measured monitoring data for air exposure concentrations are used instead of calculated values.

$$Dose - \frac{mg}{kg}/day = \frac{A\left(\frac{mg}{m3}\right)X\ B\left(\frac{m3}{hr}\right)X\ C\left(\frac{hr}{day}\right)X\ D\ (fraction\ bioavailable)}{E\ (kg)} \quad (4)$$

Where:

A = chemical concentration in the air (measured, varied by microenvironment) (mg/m^3)

B = inhalation rate (short-term) for higher activity level (m^3/hr)

C = hours spent on or near the playground and other microenvironments (hr/day)

D = fraction bioavailable (gastric)

E = body weight for age of interest (kg)

Table 24 summarizes the available model parameters for Inhalation Model 2. There is a complete set of model parameter input values for benzo(a)pyrene (indoor and outdoor), chromium (outdoor), and lead (outdoor). The only parameter missing for the other chemicals of interest is fraction bioavailable. One could assume the fraction bioavailable is equal to 1, which

would lead to a conservative estimate of the dose. One could also assume a bioavailable fraction equal to the ratio of the water leachable amount to the total amount, which would be more realistic.

Table 24. Inhalation Model 2 – Air Monitoring Data (Indoor and Outdoor)

Chemical	Chemical Air Concentration Outdoor	Chemical Air Concentration Indoor	Duration on Playground	Fraction Bioavailable	Body Weight
Benzo(a)pyrene	X	X	X	X	X
Benzothiazole	X	X	X	-	X
Chromium	X	-	X	X	X
DBP	X	X	X	-	X
DEHP	X	-	X	-	X
Lead	X	-	X	X	X
MIBK	X	X	X	-	X
Zinc	X	-	X	-	X
4-tert-Octylphenol	-	X	X	-	X

Inhalation Model 3

Equation 5 can be used to estimate the dose associated with inhalation of chemicals adhered to suspended particulates. This model is similar to Equation 4, except that the air chemical concentration is replaced with the air particulate chemical concentration.

$$Dose - \frac{mg}{kg}/day = \frac{A\left(\frac{mg}{m3}\right)X\ B(fraction\ chemical)X\ C\left(\frac{m3}{hr}\right)X\ D\left(\frac{hr}{day}\right)X\ E\ (fraction\ bioavailable)}{F\ (kg)} \quad (5)$$

Where:

Dose = Internal dose of chemical present in the body ((mg/kg)/day)

A = TSP (total suspended *particulate)* concentration in the air (mg/m^3)

B = fraction of chemical in TSP, convert from chemical concentration in tire crumb (mg/mg)

C = inhalation rate (short-term) for higher activity level (m^3/hr)

D = hours spent on or near the field (hr/day)

E = fraction bioavailable (gastric)

F = body weight for age of interest (kg)

Table 25 summarizes the available model parameters for input into Inhalation Model 3. While there is information available on the concentration of TSP (PM_{10} and $PM_{2.5}$) above playgrounds and artificial turf, there is no specific information of the fraction of chemical in the TSP. However, there is information on the chemical concentration in PM_{10} and $PM_{2.5}$ for BAP, DBP, and DEHP that could be used with the concentration of TSP to determine a fraction of chemical in TSP. Also, if one assumes that the TSP is entirely comprised of tire crumb, then the total chemical concentrations in tire crumb could be used to determine the fraction of chemical in TSP. The other model parameter with missing information is the fraction bioavailable. One could assume the fraction bioavailable is equal to 1, which would lead to a conservative estimate of the dose. Thus, there is a complete set of model parameters for BAP when the chemical fraction in TSP is used, as well as for Cr and Pb if the total chemical concentration in tire crumb is used in Inhalation Model 3.

Table 25. Inhalation Model 3 – Suspended Particulate Concentration (Indoor and Outdoor)

Chemical	TSP Air Concentration	Fraction Chemical in TSP	Inhalation Rate	Duration on Playground	Fraction Bioavailable (Gastric)	Body Weight
Benzo(a)pyrene	X	X	X	X	X	X
Benzothiazole	X	*	X	X	-	X
Chromium	X	*	X	X	X	X
DBP	X	X	X	X	-	X
DEHP	X	X	X	X	-	X
Lead	X	*	X	X	X	X
MIBK	X	*	X	X	-	X
Zinc	X	*	X	X	-	X
4-tert-Octylphenol	X	*	X	X	-	X

* Total chemical concentration in tire crumb is available.

Inhalation Model 4

Equation 6 is an alternate approach to estimate the dose from inhaling chemicals adhered to suspended particulates.

$$Dose - \frac{mg}{kg}/day = \frac{A\left(\frac{mg}{kg}\right)X\ B\left(\frac{kg}{m3}\right)X\ C\left(\frac{m3}{hr}\right)X\ D\left(\frac{hr}{day}\right)X\ E\ (fraction\ bioavailable)}{F\ (kg)} \quad (6)$$

Where:

A = Concentration of chemical in the tire crumb (mg/kg)

B = Particulate Emission Factor (kg/m^3)

C = inhalation rate (short-term) for higher activity level (m^3/hr)

D = hours spent on or near the field (hr/day)

E = fraction bioavailable (gastric)

F = body weight for age of interest (kg)

Table 26 summarizes the available model parameters for input into Inhalation Model 4. There is a full set of model input parameters available for BAP, chromium, and lead. In addition to information on the chemical concentration in tire crumb, chemical concentration in PM_{10} and $PM_{2.5}$ are available for benzo(a)pyrene, DBP, and DEHP. For those chemicals without fraction bioavailable information, one could also assume the fraction bioavailable is equal to 1. This assumption would make the estimate of dose conservative.

Table 26. Inhalation Model 4 – Particulate Emission Factor (Outdoor)

Chemical	Particulate Chemical Concentration	Particulate Emission Factor*	Inhalation Rate	Duration on Playground	Fraction Bioavailable (Gastric)	Body Weight
Benzo(a)pyrene	X	X	X	X	X	X
Benzothiazole	X	X	X	X	-	X
Chromium	X	X	X	X	X	X
DBP	X	X	X	X	-	X
DEHP	X	X	X	X	-	X
Lead	X	X	X	X	X	X
MIBK	X	X	X	X	-	X
Zinc	X	X	X	X	-	X
4-tert-Octylphenol	X	X	X	X	-	X

*Note the particulate emission factor is not chemical specific and has units of kg/m^3 [$(mg/m^3)/(mg/kg)$].

Inhalation Model 5

Equation 7 estimates the dose from volatilization that occurs due to both inherent physical chemical properties and environmental conditions (elevated temperatures).

$$Dose - \frac{mg}{kg}/day = \frac{A\left(\frac{mg}{kg}\right)X\ B\left(\frac{kg}{m3}\right)X\ C\ \left(\frac{m3}{hr}\right)X\ D\ \left(\frac{hr}{day}\right)X\ E\ (fraction\ bioavailable)}{E\ (kg)} \quad (7)$$

Where:

A = Concentration of chemical in the tire crumb (mg/kg)

B = Volatilization Factor (kg/m^3)

C = inhalation rate (short-term) for higher activity level (m^3/hr)

D = hours spent on or near the field (hr/day)

E = fraction bioavailable (gastric)

F = body weight for age of interest (kg)

Table 27 summarizes the available model parameters for input into Inhalation Model 5. None of the chemicals has a full set of input parameters because there is no information on the volatilization factor. Without this type of information, this model cannot be used to assess the chemical dose for inhalation. Note that Incorvia et al. (2007) reported vapor phase concentrations from laboratory experiments for benzothiazole (866.7 mg/mL-air per g crumb) and 4-tert-Octylphenol (21.6 ng/mL-air per g crumb) using crumb rubber, but they did not report the initial concentration in the crumb rubber. Thus, a volatilization factor could not be determined.

Table 27. Inhalation Model 5 – Volatilization Factor (Outdoor)

Chemical	Chemical Tire Crumb Concentration	Volatilization Factor*	Inhalation Rate	Duration on Playground	Fraction Bioavailable	Body Weight
Benzo(a)pyrene	X	-	X	X	X	X
Benzothiazole	X	-	X	X	-	X
Chromium	X	-	X	X	X	X
DBP	X	-	X	X	-	X
DEHP	X	-	X	X	-	X
Lead	X	-	X	X	X	X
MIBK	X	-	X	X	-	X
Zinc	X	-	X	X	-	X
4-tert-Octylphenol	X	-	X	X	-	X

*Note the volatilization factor has units of kg/m^3 [(mg/m^3)/(mg/kg)]

Inhalation Model Recommendation

Inhalation Model 2 would be the best model to use for assessing inhalation dose because all of the input parameter information is available, except for fraction bioavailable for some of the chemicals. Making an assumption on the bioavailable fraction would allow for this model to be used for all of the chemicals. Likewise, Inhalation Model 4 could be used for all of the chemicals if tire crumb concentrations are used, and an assumption is made for the bioavailable fraction.

Dermal Models

Three dermal models are considered for both indoor and outdoor estimates of exposure for the chemicals of interest.

Dermal Model 1

Equations 8 and 9 can be used to estimate dose associated with sustained dermal contact with a playground surface.

$$l = \left(\sqrt{2 \times D \times Dur}\right) \quad (8)$$

Where:

l = Average distance a diffusing molecule travels through rubberized playground material per a contact event (cm/event)

D = Solid phase diffusion coefficient of chemical (cm^2/s)

Dur = Duration of rubberized playground surface contact during one event (s)

$$ADD = \frac{C_{art} \times SA \times l \times FA \times FQ}{BW} \quad (9)$$

Where:

ADD = Potential Chronic Average Daily Dose ((mg/kg)/day)

C_{art} = Chemical concentration in rubberized playground surface (mg/cm^3)

l = Distance chemical diffuses through playground material over one contact event (cm/event)

SA = Surface area skin exposed (cm^2)

FA = Fraction absorbed (unitless)

FQ = frequency of contact, events per day

BW = Body weight (kg)

Table 28 summarizes the available model parameters for input into Dermal Model 1. Only benzo(a)pyrene has all of the input parameters available to run Dermal Model 1. The major parameter missing is the solid phase diffusion coefficient, followed by the fraction absorbed through the skin. However, if estimated solid phase diffusion coefficients are used, then DBP, DEHP, MIBK and 4-tert-Octylphenol would have a full complement of parameter values to run Dermal Model 1.

Table 28. Dermal Model 1 – Diffusion Approach (Indoor and Outdoor)

Chemical	Solid Phase Diffusion	Duration on Playground*	Chemical Tire Crumb Concentration	Skin Surface Area	Fraction Absorbed by Skin	Body Weight
Benzo(a)pyrene	X	X	X	X	X	X
Benzothiazole	**	X	X	X	-	X
Chromium	-	X	X	X	X	X
DBP	**	X	X	X	X	X
DEHP	**	X	X	X	X	X
Lead	-	X	X	X	X	X
MIBK	**	X	X	X	-	X
Zinc	-	X	X	X	X	X
4-tert-Octylphenol	**	X	X	X	-	X

*Contact time of exposed skin surface area
**Estimated

Dermal Model 2

Equation 10 can be used to estimate dermal transfer to the skin from several contacts over the course of a sustained event such as a playground visit.

$$ADD = \frac{Loading\ surface \times SA \times af \times AF \times FQ}{BW} \quad (10)$$

Where:

ADD = average daily dose ((mg/kg)/day)

Loading surface = Amount of chemical per rubberized surface area (mg/cm^2)

SA = surface area skin exposed (cm^2)

af = adherence factor of solids to the skin (per event)

AF = absorption fraction through skin

FQ = frequency of events per day

BW = body weight (kg)

Table 29 summarizes the available model parameters for input into Dermal Model 2. Only zinc has a full set of parameters need to run Dermal Model 2. The major parameter missing is the surface loading to skin. The absorption fraction by the skin is also missing for benzothiazole, MIBK, and 4-tert-Octyphenol

Table 29. Dermal Model 2 – Transfer from Surface to Skin (Indoor and Outdoor)

Chemical	Surface Loading	Surface Area of Skin	Adherence Factor Solid to Skin	Absorption Fraction of Skin	Events per Day	Body Weight
Benzo(a)pyrene	-	X	X	X	X	X
Benzothiazole	-	X	X	-	X	X
Chromium	-	X	X	X	X	X
DBP	-	X	X	X	X	X
DEHP	-	X	X	X	X	X
Lead	-	X	X	X	X	X
MIBK	-	X	X	-	X	X
Zinc	X	X	X	X	X	X
4-tert-Octylphenol	-	X	X	-	X	X

Dermal Model 3

Equation 11 is an approach to estimate dermal exposure by direct monitoring of the skin.

$$ADD = \frac{Loading\ skin \times SA \times AF \times FQ}{BW} \qquad (11)$$

Where:

ADD = average daily dose ((mg/kg)/day)

Loading skin = Amount of chemical per skin area (mg/cm^2 per event)

SA = surface area skin exposed (cm^2)

AF = absorption fraction through skin

FQ = frequency of events per day

BW = body weight (kg)

Table 30 summarizes the available model parameters for input into Dermal Model 3. Only zinc has all the parameters need to run Dermal Model 3. The major parameter missing is the surface loading to the skin. The absorption fraction of the skin is also missing for benzothiazole, MIBK, and 4-tert-Octyphenol.

Table 30. Dermal Model 3 – Direct Monitoring of Skin (Indoor and Outdoor)

Chemical	Surface Loading to Skin	Surface Area of Skin	Absorption Fraction of Skin	Body Weight
Benzo(a)pyrene	-	X	X	X
Benzothiazole	-	X	-	X
Chromium	-	X	X	X
DBP	-	X	X	X
DEHP	-	X	X	X
Lead	-	X	X	X
MIBK	-	X	-	X
Zinc	X	X	X	X
4-tert-Octylphenol	-	X	-	X

Dermal Model Recommendations

Dermal Model 3 would be the best model to use for estimating the average daily dose to skin because it is the simplest model to use with the least number of parameters. One just needs the surface loading to the skin and the dermal absorption fraction, along with skin surface area and body weight, to run this model. Assumptions could be made for dermal absorption.

Oral Models

Four oral models are considered for both indoor and outdoor estimates of exposure for the chemicals of interest.

Oral Model 1

Equation 12 estimates the average daily dose associated with ingestion of dust or soil adhered to rubberized playground surfaces. Note, indoor exposures are assumed to be associated with dust ingestion and outdoor exposures are assumed to be associated with soil ingestion.

$$ADD = \frac{C_{mg/kg} \times IR \times FA}{BW} \qquad (12)$$

Where:

ADD = average daily dose ((mg/kg)/day)

C = concentration of chemical in dust or soil on or near playgrounds (mg/kg)

IR = ingestion rate of dust or soil (kg/d)

FA = fraction of chemical absorbed (gastric) from dust or soil

BW = body weight (kg)

Table 31 summarizes the available model parameters for input into Oral Model 1. Benzo(a)pyrene is the only chemical that has a full set of parameter values. The major parameter values missing are the fraction bioavailable (gastric) of dust and the chemical concentration in the dust.

Table 31. Oral Model 1 – Ingestion of Rubberized Dust (Indoor and Outdoor)

Chemical	Chemical Dust Concentration	Ingestion Rate of Dust or Soil	Fraction Bioavailable (Gastric)	Body Weight
Benzo(a)pyrene	X	X	X	X
Benzothiazole	-	X	-	X
Chromium	-	X	X	X
DBP	X	X	-	X
DEHP	X	X	-	X
Lead	-	X	X	X
MIBK	-	X	-	X
Zinc	-	X	-	X
4-tert-Octylphenol	-	X	-	X

Oral Model 2

Equation 13 estimates ingestion of dust when a surface dust loading value is available.

$$ADD = \frac{(Load\ surf \times TEH * SA\ Hands * Frac\ Hand\ mouthed) * (ET * NR) * (1-(1-AF) * \frac{FQ}{NR})}{BW} \quad (13)$$

Where:

ADD = average daily dose ((mg/kg)/day)

Load surf = amount of chemical per area of playground surface (mg/cm^2)

TEH = transfer efficiency to hands

SA = surface area of hands (cm^2)

Frac Hand mouthed = fraction of hand mouthed

ET = exposure time at playground (hr/d)

NR = replenishment rate, intervals of hand touches to the surface per hour

AF = fraction absorbed to saliva

FQ = number of hand to mouth contacts in an hour

BW = body weight (kg)

Table 32 summarizes the available model parameters for input into Oral Model 2. None of the chemicals has a full set of model input parameters. The major parameter missing is the transfer efficiency of the chemicals to the hand. The other parameter missing for most of the chemicals is the chemical loading per surface area and the fraction of chemical absorbed into saliva.

Table 32. Model Oral 2 – Surface Loading from Ingestion of Dust (Indoor and Outdoor)

Chemical	Chemical Loading per Surface Area	Transfer Efficiency to Hands	Surface Area of Hands	Fraction of Hand Mouthed (Transfer Efficiency)	Exposure Time at Play-ground	Replenish Rate (Hand to Surface)	Fraction Absorbed into Saliva	Number Hand to Mouth Contacts	Body Weight
Benzo(a)pyrene	-	-	X	X	X	X	X	X	X
Benzothiazole	-	-	X	X	X	X	-	X	X
Chromium	-	-	X	X	X	X	X	X	X
DBP	-	-	X	X	X	X	-	X	X
DEHP	-	-	X	X	X	X	-	X	X
Lead		-	X	X	X	X	X	X	X
MIBK	-	-	X	X	X	X	X	X	X
Zinc	X	-	X	X	X	X	-	X	X
4-tert-Octylphenol	-	-	X	X	X	X	X	X	X

Oral Model 3

Equation 14 estimates exposure from mouthing larger pieces of rubberized playground material.

$$ADD\,\frac{mg}{kg}/day = \frac{\mathrm{MR}_{\frac{mg}{cm2}/hour} \times SA\ cm2\ X\ Dur\ hr/day}{BW\ kg} \qquad (14)$$

Where:

ADD = average daily dose ((mg/kg)/day)

MR = migration rate of chemical into saliva ((mg/cm^2)/hr)

SA = surface area mouthed (cm^2)

Dur = hours mouthing per day (hr/d)

BW = body weight (kg)

Table 33 summarizes the available model parameters for input into Oral Model 3 – Mouthing Playground Pieces. There are no data for migration rate to saliva. Therefore, this model cannot be run without key input data.

Table 33. Oral Model 3 – Mouthing of Playground Pieces (Indoor and Outdoor)

Chemical	Migration Rate to Saliva	Surface Area Mouthed	Duration of Mouthing	Body Weight
Benzo(a)pyrene	-	*	*	X
Benzothiazole	-	*	*	X
Chromium	-	*	*	X
DBP	-	*	*	X
DEHP	-	*	*	X
Lead	-	*	*	X
MIBK	-	*	*	X
Zinc	-	*	*	X
4-tert-Octylphenol	-	*	*	X

*Note the surface area of pieces mouthed and duration of mouthing could be assumed.

Oral Model 4

Under some circumstances, a child may unintentionally swallow a piece of rubberized mulch. This would be a one-time event that could be modeled as an acute exposure.

$$ADR\,\frac{mg}{kg}/event = \frac{\mathrm{A}\times\mathrm{B}\times AF}{BW} \qquad (15)$$

Where:

ADR = acute dose rate ((mg/kg)/event)

A = chemical concentration in tire crumb (mg/kg)

B = mass of rubberized mulch piece swallowed (kg)

AF = absorption fraction (gastric)

BW = Body weight (kg)

Table 34 summarizes the availability of model input parameters for Oral Model 4 – Swallowing Playground Pieces. There are sufficient input model parameters for BAP, chromium, and lead to run this model.

Table 34. Oral Model 4– Swallowing of Playground Pieces

Chemical	Rubberized Mulch Concentration	Mass of Mulch Swallowed	Absorption Fraction	Body Weight
Benzo(a)pyrene	X	X	X	X
Benzothiazole	X	X	-	X
Chromium	X	X	X	X
DBP	X	X	-	X
DEHP	X	X	-	X
Lead	X	X	X	X
MIBK	X	X	-	X
Zinc	X	X	-	X
4-tert-Octylphenol	X	X	-	X

Oral Model Recommendations

Only Oral Model 1 for BAP, and Oral Model 4 for BAP, chromium, and lead have full sets of model parameters. It should be noted that Oral Model 2 has promise for estimating the average daily dose from dust ingestion. Here a loading rate from the playground surface and the transfer of chemical to the hand are needed. The surface loading to skin, which is also needed for Dermal Model 1, could be used instead of multiplying the chemical loading per surface area by the transfer efficiency to the hand.

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Appendix A – TRV Search Strategy

CPSC has identified nine chemical compounds that are present in rubberized playground surfaces made from recycled tires (see Table 1 in report). For each of the chemicals in Table 1 we searched for and compiled information on TRVs. The following general strategy describes the approach used. Initial data source identification was based on the spreadsheet provided by CPSC as well as the file provided by CPSC on staff notes regarding toxicity of selected compounds, and CPSC assessments cited in the staff notes. We surveyed for updates using the following strategy:

- The following **secondary compilation of risk values** was surveyed for relevant TRVs:
    - ITER http://iter.tera.org/database.htm. This database contains TRVs from a large number of organizations, including details on the derivation and links to further information[21].
- The following **primary sources** of TRVs were reviewed for relevant TRVs, and key decision points were captured in a tabular form:
    - U.S. EPA IRIS https://www.epa.gov/iris. Chronic oral and inhalation values
    - ATSDR profiles https://www.atsdr.cdc.gov/toxprofiledocs/index.html. Includes acute, intermediate, and chronic oral and inhalation values
    - INCHEM http://www.inchem.org/#/search. Includes rapid access to several WHO databases – IPCS Environmental Health Criteria (EHC) monographs; IARC evaluations; JECFA monographs
    - Health Canada assessments were accessed through the ITER database when possible, and if not, by searching the internet for the chemical name and Health Canada.

- The following primary sources of TRVs were identified in our project plan as **supplementary sources** to be surveyed if adequate recent risk values were not identified in the initial group of primary sources. In addition, some of these databases can provide information on less-than-chronic TRVs. In general, we searched for ECHA and PPRTV values only. ECHA was a key reference, since it was used by many of the assessments identified in Task 3; ECHA was also an important source of unpublished studies for 4-tert-Octylphenol. PPRTV values were also surveyed, since these values include less-than-chronic values for chemicals on the U.S.EPA's IRIS database, as well as lower-quality (compared to IRIS) peer-reviewed assessments conducted according to the U.S. EPA's methods. The French (ANSES) assessment was also included for DEHP, because we were aware from previous work that it used a principal study not used by many other assessments. In addition, these sites were searched for

[21] Our initial project plan envisioned also using the U.S. EPA CompTox Dashboard to identify relevant TRVs. However, the dashboard contains a broad mix of TRVs for different durations (as short as 1 hour) and quality, and so it was more effective to go directly to websites for relevant organizations, as described in the rest of this appendix.

benzothiazole:

- ECHA -European Chemicals Agency https://echa.europa.eu/information-on-chemicals for DNELS
- U.S. EPA Provisional Peer-Reviewed Toxicity Values (PPRTVs) https://www.epa.gov/pprtv. Includes chronic and subchronic inhalation and oral values; less detailed and less review than IRIS assessments https://www.epa.gov/pprtv/provisional-peer-reviewed-toxicity-values-pprtvs-assessments
- EFSA - European food safety authority https://www.efsa.europa.eu/
- NICNAS - Australian Department of Health National Industrial Chemicals Notification and Assessment Scheme https://www.industrialchemicals.gov.au/chemical-information/search-assessments
- ANSES – French agency for food, environment and occupational health and safety https://www.anses.fr/en/content/list-toxicity-reference-values-trvs-established-anses
- Danish EPA https://eng.mst.dk/chemicals/
- RIVM -Dutch national institute of public health and the environment https://www.rivm.nl/en

- In addition to any less-than-chronic TRVs identified in the above sources, the following sources were searched for **less-than-chronic TRVs**:
  - RAIS - Risk Assessment Information System https://rais.ornl.gov/. Compilation of risk values from numerous sources. HEAST data on RAIS were not further pursued, due to their low quality and limited documentation.
  - Minnesota Department of Health, Minnesota Air Guidance Values https://www.health.state.mn.us/communities/environment/risk/guidance/air/table.html
  - Minnesota Department of Health, Minnesota Water Guidance Values https://www.health.state.mn.us/communities/environment/risk/guidance/gw/table.html. Concentrations in water for different durations and ages – and corresponding RfD development.
  - California EPA Inhalation Reference Exposure Levels (RELs) https://oehha.ca.gov/air/general-info/oehha-acute-8-hour-and-chronic-reference-exposure-level-rel-summary
  - Texas Commission on Environmental Quality (TCEQ) inhalation values https://www.tceq.texas.gov/toxicology/dsd/final

In addition, risk assessments of surfaces made of recycled tire crumb rubber were reviewed to identify the TRVs used in those assessments.

Additional supplemental searching was conducted for 4-tert-Octylphenol and benzothiazole, since limited TRV information was available for these.

For 4-tert-Octylphenol, this additional searching consisted of reviewing the data posted on the following two websites:

- ECHA website https://echa.europa.eu/
- U.S. EPA TSCA/Challenge website https://iaspub.epa.gov/oppthpv/public_search.html_page
- In addition, PubMed was searched for articles on 4-tert-Octylphenol. Because a very recent assessment by MDH was located, and no additional useful toxicity studies were identified on the ECHA or U.S. EPA websites, a cursory screen was conducted of the PubMed hits, but no further searching was conducted for 4-tert-Octylphenol.

Similarly, it was noted that the Ginsberg et al. (2011) paper summarized an assessment conducted by the Connecticut Department of Public Health and was itself based on an assessment by the New York Department of Environmental Conservation.

For benzothiazole, additional searching included:

- PubMed was searched for publications similar to or citing the Ginsberg article. Further searching was not conducted for, because the existing TRVs were considered appropriate in light of the available data.

Appendix B – Literature Search Strategy

Several search strategies were employed to identify more recent crumb tire hazard, exposure, and risk assessments published since the FRAP report (2016 to present) and more recent data on tire crumb and other potentially useful data on exposure (no date limit). Searches were conducted using Web of Science, PubMed, and Google Scholar with no date cut offs (a second Google Scholar search was limited to 2016 to present).

1. **Web of Science on November 9, 2020 - 58 results**

TOPIC: (("crumb rubber*" OR "tire crumb*" OR "unitary surface*" OR "loose fill*" OR "poured-in-place" OR "PIP" OR "bonded rubber*" OR "rubber mulch*" OR "recycled tire*")) AND
TOPIC: ((field* OR infill* OR turf* OR playground* OR "play area*" OR "play surface*")) AND
TOPIC: (("exposure assessment*" OR "risk assessment*" OR "exposure characterization*" OR "risk characterization*" OR toxic* OR exposure*))
Timespan: 1965-present. Indexes: SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI

2. **PubMed on November 9, 2020 – 57 results**

("crumb rubber*" OR "tire crumb*" OR "unitary surface*" OR "loose fill*" OR "poured-in-place" OR "PIP" OR "bonded rubber*" OR "rubber mulch*" OR "recycled tire*") AND (field* OR infill* OR turf* OR playground* OR "play area*" OR "play surface*") AND ("exposure assessment*" OR "risk assessment*" OR "exposure characterization*" OR "risk characterization*" OR toxic* OR exposure*)
Years: 1981-present

3. **Google Scholar – November 5, 2020 – 107 potentially relevant results**

("crumb rubber" OR "tire crumb") AND (field* OR infill* OR turf* OR playground* OR "play area*" OR "play surface*") AND ("exposure assessment*" OR "risk assessment*" OR "exposure characterization*" OR "risk characterization*" OR toxic* OR exposure*).
Date: 2016-present

The first 150 entries were screened manually with this question in mind –"Does this reference contain any potentially useful information to assist with quantifying exposures, hazards, or human health risks or rubberized playground surfaces?", and 107 potentially relevant were saved. Note that the actual search string was truncated as it was longer than what Google Scholar allows. A second Google Scholar search was done to remedy this limitation (see 4 below).

These first three searches were combined into a single Endnote library and duplicates were removed. The result was 95 references.

4. **Google Scholar – November 9, 2020 - 151 potentially relevant**

CPSC staff performed a second search of Google Scholar using a shorter search string.

("crumb rubber" OR "tire crumb" OR "rubber mulch" OR "bonded rubber") AND (field* OR infill* OR turf* OR playground* OR "play area*" OR "play surface*") AND ("exposure assessment*" OR "risk assessment*" OR exposure* OR toxic)

The search was split into four batches (no cut-off to 2012, 2013-2017, 2018-2019, and 2020) and the Publish or Perish tool was used to extract citations from Google Scholar. Results were screened with this question in mind –"Does this reference contain any potentially useful information to assist with quantifying exposures, hazards, or human health risks or rubberized playground surfaces?". A total of 151 potentially relevant references were identified.
Date: No date cut off

Results from the four literature searches were combined into one list and 52 duplicates were removed (n=194). The remainder were screened to remove 36 references that were abstracts from conference proceedings, in languages other than English, duplicates, or had no pdf available. Those remaining were then screened with the following question in mind – “Does this reference contain any potentially useful information to assist with quantifying exposures, hazards, or human health risks of rubberized playground surfaces?” and 51 more references were screened out (n=107).

For exposure data the remaining references were screened as follows:

- Is this reference prioritized for extraction because quantitative information supporting the framework document is present for chemicals of interest? MUST ANSWER YES
- Is this reference prioritized for extraction because it is an assessment for rubberized playgrounds (YES), rubber turf fields (SOMEWHAT), or neither rubberized playgrounds or turf fields (NO)? CAN BE YES OR SOMEWHAT

Following this more detailed screening, 11 new publications were identified that contained relevant information that was extracted and included in the exposure parameter spreadsheet.

For toxicity data we identified those assessments that contained toxicity information or TRVs on the chemicals of interest. We then reviewed each reference to determine if it reported or derived TRVs for our chemicals of interest from a source other than those already identified from authoritative sources described in Appendix A.

Appendix C – Exposure Parameter Spreadsheet References

As discussed in the Exposure Approach discussion, data were extracted from publications identified from a number of sources. Twenty were from the FRAP reports, 11 were from the literature search, and five were other data sources with generic exposure parameters.

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