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Screening Assessment

Substances Identified as Being of Low Concern Using the Ecological Risk Classification of Inorganic Substances and Three Human Health Science Approaches

Environment and Climate Change Canada
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Synopsis

Pursuant to sections 68 or 74 of the *Canadian Environmental Protection Act, 1999* (CEPA), the Minister of the Environment and the Minister of Health have conducted a screening assessment of 21 substances. These substances were identified as priorities for assessment as they met categorization criteria under subsection 73(1) of CEPA or were considered a priority on the basis of other human health concerns. The Chemical Abstracts Service Registry Numbers (CAS RN[1]) and their *Domestic Substances List* (DSL) names are listed in the table below.

Substances assessed using the ecological risk classification of inorganic substances and one of three human health science approaches

CAS RN	DSL name
409-21-2	Silicon carbide (SiC)
513-77-9	Carbonic acid, barium salt (1:1)
1313-27-5[a]	Molybdenum oxide (MoO_3)
1317-33-5	Molybdenum sulfide (MoS_2)
1345-24-0	C.I. Pigment Red 109
7440-31-5	Tin
7440-41-7	Beryllium
7553-56-2	Iodine
7681-11-0	Potassium iodide (KI)
7681-82-5	Sodium iodide (NaI)
7722-84-1	Hydrogen peroxide (H_2O_2)
7727-18-6	Vanadium, trichlorooxo-
7727-43-7	Sulfuric acid, barium salt (1:1)
7789-20-0	Water-d_2
10361-37-2	Barium chloride ($BaCl_2$)
11099-11-9	Vanadium oxide
12713-03-0[b]	Umber
17194-00-2	Barium hydroxide ($Ba(OH)_2$)

[1] The Chemical Abstracts Service Registry Number (CAS RN) is the property of the American Chemical Society, and any use or redistribution, except as required in supporting regulatory requirements and/or for reports to the Government of Canada when the information and the reports are required by law or administrative policy, is not permitted without the prior written permission of the American Chemical Society.

CAS RN	DSL name
20461-54-5	Iodide
51274-00-1	C.I. Pigment Yellow 42
63325-16-6	Mercury, diiodobis(5-iodo-2-pyridinamine)-, dihydriodide

[a] This substance was not identified under subsection 73(1) of CEPA but was included in this assessment as it was considered a priority on the basis of human health concerns.
[b] This CAS RN is a UVCB (unknown or variable composition, complex reaction products, or biological materials).

The 21 substances in this assessment were evaluated for ecological risk and human health risk using four different science approaches (i.e., one ecological and three human health). This screening assessment concludes on those substances that were identified as having a low likelihood of causing harm to human health and the environment based on these streamlined approaches.

The ecological risks of the substances in this assessment were characterized using the Ecological Risk Classification of Inorganic Substances (ERC-I). The ERC-I is a risk-based approach that employs multiple metrics for both hazard and exposure, with weighted consideration of multiple lines of evidence for determining risk classification. Hazard characterization in ERC-I included a survey of past predicted no-effect concentrations (PNEC) and water quality guidelines, and the derivation of new PNEC values when required. Exposure profiling considered two approaches: predictive modelling using a generic near-field exposure model for each substance, and an analysis of measured concentrations collected by federal and provincial water quality monitoring programs using these concentrations as a conservative indicator of exposure for individual substances. Modelled and measured predicted environmental concentrations (PECs) were compared to PNECs, and multiple statistical metrics were computed and compared to decision criteria to classify the potential to cause harm to the environment. The ERC-I identified the 21 substances in this assessment as having low ecological concern.

The human health risks of the substances in this assessment were characterized using one of three science approaches: Biomonitoring-based Approach 1, Biomonitoring-based Approach 2, or the Low Human Health Hazard Potential Approach. Biomonitoring-based Approach 1 is a qualitative science approach used to identify substances with limited exposure based on substances or moieties measured in the Canadian population at very low frequencies. Biomonitoring-based Approach 2 compares human biomonitoring data (exposure) against biomonitoring guidance values (health effects), such as biomonitoring equivalents (BEs), to identify substances with low concern for human health. The Low Human Health Hazard Potential approach is used to identify substances with low inherent repeated-dose toxicity.

When the results of ERC-I and the three human health science approaches are considered together, a subset of 21 substances are identified as being of low concern to both human health and the environment. Additional substances are identified by the science approach documents as being either of low concern to the environment or to

human health, but not to both. Conclusions on these additional substances will be made in other assessments.

Considering all available lines of evidence presented in this screening assessment, there is low risk of harm to the environment from the 21 substances in this assessment. It is concluded that these substances do not meet the criteria under paragraphs 64(*a*) or (*b*) of CEPA as they are not entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity or that constitute or may constitute a danger to the environment on which life depends.

On the basis of the information presented in this screening assessment, it is concluded that the 21 substances in this assessment do not meet the criteria under paragraph 64(*c*) of CEPA as they are not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

It is therefore concluded that these 21 substances do not meet any of the criteria set out in section 64 of CEPA.

Table of Contents

1. Introduction

Pursuant to sections 68 or 74 of the *Canadian Environmental Protection Act, 1999* (CEPA) (Canada 1999), the Minister of the Environment and the Minister of Health have conducted a screening assessment of 21 substances to determine whether these substances present or may present a risk to the environment or to human health. The substances were identified as priorities for assessment as they met categorization criteria under subsection 73(1) of CEPA or were considered a priority on the basis of other human health concerns (ECCC, HC [modified 2017]).

The 21 substances in this assessment were evaluated for ecological risk and human health risk using four different science approaches. The four science approaches, Ecological Risk Classification of Inorganic Substances (ERC-I) (ECCC [modified 2018]), Biomonitoring-based Approach 1 (HC 2016a), Biomonitoring-based Approach 2 (HC 2016b), and Substances with Low Human Health Hazard Potential approach (HC 2019), were published between 2016 and 2018, inclusively. This screening assessment concludes on 21 substances that were identified as having a low likelihood of causing harm to both human health and the environment through these approaches.

The ecological risks of the substances in this assessment were characterized using the ERC-I (ECCC [modified 2018]). The ERC-I is a risk-based approach that employs multiple metrics for both hazard and exposure, with weighted consideration of multiple lines of evidence for determining risk classification. Hazard characterization in ERC-I included a survey of past predicted no-effect concentrations (PNEC) and water quality guidelines, or the derivation of a new PNEC value when required. Exposure profiling considered two approaches: predictive modelling using a generic near-field exposure model for each substance and an analysis of measured concentrations collected by federal and provincial water quality monitoring programs using metal concentrations as a conservative indicator of exposure for individual substances. Modelled and measured predicted environmental concentrations (PECs) were compared to PNECs, and multiple statistical metrics were computed and compared to decision criteria to classify the potential for causing harm to the environment.

The human health risks of the substances in this assessment were characterized using one of three science approaches: Biomonitoring-based Approach 1, Biomonitoring-based Approach 2, or the Low Human Health Hazard Potential approach. Biomonitoring-based Approach 1 is a qualitative science approach used to identify substances with limited exposure based on substances or moieties measured in the Canadian population at very low frequencies. Biomonitoring-based Approach 2 compares human biomonitoring data (exposure) against biomonitoring guidance values (health effects), such as biomonitoring equivalents (BEs), to identify substances with low concern for human health. The Low Human Health Hazard Potential approach is used to identify substances with low inherent repeated-dose toxicity.

This screening assessment was prepared by staff in the CEPA Risk Assessment Program at Health Canada and Environment and Climate Change Canada and incorporates input from other programs within these departments. The ecological portion of this assessment is based on the ERC-I science approach document (published May 12, 2018), which was externally peer-reviewed and subject to a 60-day public comment period. The health portion of this assessment is based on the Biomonitoring-based Approach 1 science approach document (published September 3, 2016), the Biomonitoring-based Approach 2 science approach document (published December 9, 2016), and the Substances with Low Human Health Hazard Potential science approach document (published December 16, 2017), which were each subject to a 60-day public comment period. Additionally, several of these science approach documents were externally peer-reviewed. External peer-review comments were received on the Biomonitoring-based Approach 2 science approach document, on the Substances with Low Human Health Hazard Potential science approach document and on the technical portions of the ERC-I science approach document. Public comments were received on the ERC-I science approach document, the Biomonitoring Approach 2 science approach document and the Low Human Health Hazard Potential science approach document and an updated Low Human Health Hazard Potential science approach document was published (March 2019). Additionally, the draft of this screening assessment (published April 13, 2019) was subject to a 60-day public comment period. While external comments were taken into consideration, the final content and outcome of the screening assessment remain the responsibility of Health Canada and Environment and Climate Change Canada.

This screening assessment focuses on information critical to determining whether substances meet the criteria as set out in section 64 of CEPA by examining scientific information and incorporating a weight of evidence approach and precaution.[2] The screening assessment presents the critical information and considerations on which the conclusions are based.

[2]A determination of whether one or more of the criteria of section 64 of CEPA are met is based on an assessment of potential risks to the environment and/or to human health associated with exposures in the general environment. For humans, this includes, but is not limited to, exposures from ambient and indoor air, drinking water, foodstuffs, and products available to consumers. A conclusion under CEPA is not relevant to, nor does it preclude, an assessment against the hazard criteria specified in the *Hazardous Products Regulations*, which are part of the regulatory framework for the Workplace Hazardous Materials Information System for products intended for workplace use. Similarly, a conclusion based on the criteria contained in section 64 of CEPA does not preclude actions being taken under other sections of CEPA or other acts.

2. Approach

2.1 Potential to cause ecological harm

The ecological risks of substances in this assessment were characterized using the ERC-I (ECCC [modified 2018]). The ERC-I is a risk-based approach that employs multiple metrics for both hazard and exposure, with weighted consideration of multiple lines of evidence for determining risk classification. A summary of the approach is outlined below; the approach is described in detail in the ERC-I science approach document (ECCC [modified 2018]).

Hazard characterization in ERC-I included a survey of past domestic and international assessment predicted no-effect concentrations (PNEC) and water quality guidelines. When no suitable existing PNEC or water quality guideline was found, hazard endpoint data were collected from multiple sources including comprehensive literature searches for specific groups, targeted searches of the ECOTOX database (2016) and European Chemicals Agency (ECHA) registration dossiers (2016). In the absence of more recent information, the assumptions used in the 2006 categorization of the DSL were also considered (ECCC, HC [modified 2017]). Dependent on data availability, either a species sensitivity distribution (SSD) or an assessment factor (AF) approach was taken to derive a new PNEC value.

Exposure profiling considered two approaches: predictive modelling using a generic near-field exposure model and an analysis of measured concentrations collected by federal and provincial water quality monitoring programs. The generic near-field exposure model used Canadian import and manufacture volumes and associated use information of the substances collected from surveys issued pursuant to CEPA section 71 (Environment Canada 2009; Environment Canada 2013). As an additional line of evidence, and to address substances where CEPA section 71 survey information was unavailable, trade merchandise import data were obtained for relevant harmonized system (HS) codes (CBSA 2016). Additionally, third-party market research reports were used to complement data from other sources and to fill gaps for substances not included to date in a CEPA section 71 survey. Volume data from surveys issued pursuant to CEPA section 71, CBSA, and market research were used in a conservative near-field exposure scenario similar to that used in previous rapid screening approaches (EC, HC 2013; EC, HC 2014; ECCC, HC 2016) and as further detailed in ECCC [modified 2018] to generate PECs.

In addition to using import, manufacture, and use information to model releases to the aquatic environment, reported releases data were also available from the National Pollutant Release Inventory (NPRI) for certain substances or groups of substances. NPRI data for groups of substances (e.g., vanadium, except when in an alloy, and its compounds) were conservatively considered applicable to the subsets of CAS RNs that are remaining priorities. A similar near-field risk-based evaluation was performed using

NPRI reported release data for the last five years available at the time of preparation (2011 to 2015).

Water quality monitoring data for surface fresh waters were collected for each substance or group of substances, where available, from multiple federal and provincial programs and repositories covering a number of ecoregions in Canada, as described in ECCC [modified 2018]. Measured concentrations were obtained for the period 2005 to 2015. For some substance groups, measured concentrations in waterbodies exposed to metal mining activities and corresponding reference waterbodies were available from Environmental Effects Monitoring (EEM) studies conducted under the *Metals Mining Effluent Regulations* (MMER).

Modelled and measured PECs were compared to PNECs, and statistical metrics considering both the frequency and magnitude of exceedances were computed and compared to decision criteria to classify the potential for ecological risk of substances. Critical data and considerations used to create substance-specific ecological profiles and classifications associated with ecological risk, as well as identification of potential need for tracking of future use patterns, are presented in ECCC [modified 2018]. The ERC-I classifications specific to these 21 substances are presented in Table A-2.

2.2 Potential to cause harm to human health

The human health risks of the substances in this assessment were characterized using one of the three human health based approaches: the Biomonitoring-based Approach 1 (HC 2016a), the Biomonitoring-based Approach 2 (HC 2016b), and the Low Human Health Hazard Potential approach (HC 2019).

Biomonitoring-based Approach 1

This science approach is a qualitative biomonitoring-based approach to identify substances of low concern for human health which were identified as priorities for assessment as they met categorization criteria under subsection 73(1) of CEPA.

This biomonitoring-based approach considers available Canadian and U.S. biomonitoring data based on the analysis of the substance or moiety in whole blood, serum, and/or urine. Total concentrations of a substance (or moiety) in blood or urine may provide a biologically-relevant, integrated measure of exposures that may occur across multiple routes (e.g., oral, dermal and inhalation) and sources (including environmental media, diet, and frequent or daily use products to which they were exposed). When biomonitoring data indicate that general population exposure is limited or unlikely, substances or moieties are considered to be of low concern with respect to human health. To determine if exposure is limited or unlikely, a number of metrics are taken into consideration, including the prevalence of exposure across the population

(substances or moieties with limited biomarker[3] detection frequency in the population are considered to have limited exposure), the magnitude of the biomarker concentration (if detected at the upper tails of the exposure distribution), the toxicokinetic properties of the substance or moiety, and the use pattern of the substance.

Uncertainties associated with this approach have been outlined in the science approach document (HC 2016a). Critical data and considerations used in the Biomonitoring-based Approach 1 are presented in the science approach document (HC 2016a). The magnitude and prevalence of exposure (based on biomonitoring data) for the substances addressed by this approach are summarized in Table A-3.

Biomonitoring-based Approach 2

This science approach incorporates biomonitoring data from large population level biomonitoring programs with a human biomonitoring guidance value (e.g., biomonitoring equivalents (BEs), German human biomonitoring values) to identify substances of low concern for human health.

Similar to Biomonitoring-based Approach 1, Biomonitoring-based Approach 2 considers available Canadian and U.S. biomonitoring data based on the analysis of the substance or moiety in whole blood, serum, and/or urine. Total concentrations of a substance in blood or urine may provide a biologically relevant, integrated measure of exposures that may occur across multiple routes (e.g., oral, dermal and inhalation) and sources (including environmental media, diet, and frequent or daily use products to which they were exposed). The Biomonitoring-based Approach 2 also incorporates health effects data relevant to humans in the assessment of risk. Human biomonitoring reference values are typically derived from existing health-based exposure guidance values such as a reference dose (RfD) or Tolerable Daily Intake (TDI) and/or pharmacokinetic data. In some cases, the human biomonitoring guidance values are based on human studies or epidemiology data.

A thorough review of available toxicokinetic data is an integral part of the Biomonitoring-based Approach 2. This approach is only recommended for use if the biomarker (chemical concentration in whole blood, plasma, serum or urine) is considered adequate to quantify the exposure in the general population.

If exposures (on the basis of biomonitoring data from large-scale studies) are below the human biomonitoring guidance value (on the basis of an RfD, TDI or other critical health

[3] A biomarker of exposure is the chemical or its metabolite or the product of an interaction between a chemical and some target molecule or cell that is measured in a compartment in an organism (NRC 2006), e.g., a metal moiety measured in blood or urine.

effects), then the substance or metal moiety is considered to be of low concern with respect to human health at current levels of exposure.

Uncertainties associated with this approach have been outlined in the science approach document (HC 2016b).

The BE values or human biomonitoring values (HBM-I) do not represent diagnostic criteria for health assessment at the individual level, but they are useful tools to interpret population-level biomonitoring data. The BE values should only be used for the interpretation of exposure in the general population and should not be used for occupational exposure or for individuals (LaKind et al. 2008). The HBM-I value can be used in the interpretation of exposure in the general population (Angerer et al. 2011).

Critical data and considerations used in the Biomonitoring-based Approach 2 are presented in the science approach document (HC 2016b). The biomonitoring data and human biomonitoring guidance values for the substances addressed by this approach are summarized in Table A-4. In addition, critical data and considerations used for five iodine-containing substances are presented in Hays et al. (2018).

Substances with Low Human Health Hazard Potential

This approach is a hazard based screening approach that considers available toxicological data based on human and/or animal studies (HC 2019). It focuses on the inherent toxicity of a substance. When toxicological data shows that health effects are unlikely up to the limit dose of 1000 mg/kg-bw/day (by the oral or dermal route as defined by the OECD), or are limited to recoverable or localized effects above 100 mg/kg-bw/day, in repeated-dose studies of high quality and sufficient duration, the substances or moieties are considered to be of low concern with respect to human health. The relevant route of exposure and high hazard flags (i.e., potential for carcinogenicity, mutagenicity/genotoxicity, and reproductive/developmental toxicity) are considered in the process as well.

Substances are first screened regarding the potential for carcinogenicity, mutagenicity/genotoxicity, and reproductive/developmental (CMR) toxicity. This includes assessment of all health effects of a given substance based on a weight of evidence approach and taking into account the totality of the findings including structure-activity relationship, knowledge of mode of action, toxicokinetics and the acknowledgement of limitations of the available data. It also includes a requirement for adequate repeated-dose studies relevant to the primary route of exposure as part of this approach. Only substances not identified as having carcinogenic, genotoxic or reproductive/developmental toxic properties are considered candidates for the low hazard-based approach, and are considered further. Following that, an assessment of the dose level at which health effects are observed is conducted and characterization of the severity or seriousness of those effects is addressed. If there are no health effects documented up to 1000 mg/kg-bw/day, or health effects between 100 and 1000 mg/kg

bw/day are limited to site of contact effects, considered reversible, compensatory effects and not serious in nature, the substance is considered as having low concern for human health and no further risk characterization is warranted.

Uncertainties associated with this approach have been outlined in the science approach document (HC 2019).

Critical data and considerations used in the Low Human Health Hazard Potential approach are presented in the science approach document (HC 2019). The decision points and supporting data for the substances addressed by this approach are summarized in Table A-5. In addition, critical data and considerations used for two iron-containing substances are presented in Appendix B.

3. Summary of screening assessment results

Combining the results from ERC-I and the three streamlined human health approaches, 21 substances were identified to be of low concern for both human health and ecological risk and are listed in Table A-1. Given the low ecological and human health concern associated with these 21 substances, there is low risk of harm to organisms and the broader integrity of the environment from these substances and the potential risk to human health is considered to be low.

While exposures of the general population to these 21 substances are not of concern at current levels, three substances (silicon carbide CAS RN 409-21-2, molybdenum oxide CAS RN 1313-27-5, and beryllium CAS RN 7440-41-7) are considered to have a health effect of concern on the basis of their potential for carcinogenicity if exposure were to increase (see Table A-6 for further details).

Additional substances were identified by the science approach documents as having either a low ecological or low human health concern, but not both. Conclusions on these additional substances will be made in other screening assessments conducted under section 68 or 74 of CEPA.

4. Conclusion

Considering all available lines of evidence presented in this screening assessment, there is low risk of harm to the environment from the 21 substances in this assessment. It is concluded that these substances do not meet the criteria under paragraphs 64(*a*) or (*b*) of CEPA as they are not entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity or that constitute or may constitute a danger to the environment on which life depends.

On the basis of the information presented in this screening assessment, it is concluded that the 21 substances in this assessment do not meet the criteria under paragraph 64(*c*) of CEPA as they are not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

It is therefore concluded that these 21 substances do not meet any of the criteria set out in section 64 of CEPA.

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Appendix A. ERC-I and streamlined human health approaches for substances addressed in this screening assessment

Table A-1. List of substances and approaches used in this screening assessment

CAS RN	DSL name	Ecological approach	Human health approach
409-21-2	Silicon carbide (SiC)	ERC-I	Low Human Health Hazard Potential
513-77-9	Carbonic acid, barium salt (1:1)	ERC-I	Biomonitoring-based Approach 2
1313-27-5[a]	Molybdenum oxide (MoO_3)	ERC-I	Biomonitoring-based Approach 2
1317-33-5	Molybdenum sulfide (MoS_2)	ERC-I	Biomonitoring-based Approach 2
1345-24-0	C.I. Pigment Red 109	ERC-I	Biomonitoring-based Approach 2
7440-31-5	Tin	ERC-I	Biomonitoring-based Approach 2
7440-41-7	Beryllium	ERC-I	Biomonitoring-based Approach 1
7553-56-2	Iodine	ERC-I	Biomonitoring-based Approach 2
7681-11-0	Potassium iodide (KI)	ERC-I	Biomonitoring-based Approach 2
7681-82-5	Sodium iodide (NaI)	ERC-I	Biomonitoring-based Approach 2
7722-84-1	Hydrogen peroxide (H_2O_2)	ERC-I	Low Human Health Hazard Potential
7727-18-6	Vanadium, trichlorooxo-	ERC-I	Biomonitoring-based Approach 1
7727-43-7	Sulfuric acid, barium salt (1:1)	ERC-I	Biomonitoring-based Approach 2
7789-20-0	Water-d_2	ERC-I	Low Human Health Hazard Potential
10361-37-2	Barium chloride ($BaCl_2$)	ERC-I	Biomonitoring-based Approach 2
11099-11-9	Vanadium oxide	ERC-I	Biomonitoring-based Approach 1
12713-03-0[b]	Umber	ERC-I	Low Human Health Hazard Potential
17194-00-2	Barium hydroxide ($Ba(OH)_2$)	ERC-I	Biomonitoring-based Approach 2
20461-54-5	Iodide	ERC-I	Biomonitoring-based Approach 2
51274-00-1	C.I. Pigment Yellow 42	ERC-I	Low Human Health Hazard Potential
63325-16-6	Mercury, diiodobis(5-iodo-2-pyridinamine)-, dihydriodide	ERC-I	Biomonitoring-based Approach 2

[a] Post-categorization human health concern

[b] This CAS RN is a UVCB (unknown or variable composition, complex reaction products, or biological materials).

Table A-2. ERC-I classifications for the 21 substances addressed in this screening assessment

CAS RN	DSL name	ERC-I Predictive Modelling Ranking	ERC-I Water Quality Monitoring Ranking	Overall ERC-I Classification
409-21-2	Silicon carbide (SiC)	Low	N/A	Low
513-77-9	Carbonic acid, barium salt (1:1)	Low	Low	Low
1313-27-5[a]	Molybdenum oxide (MoO_3)	Low	Low	Low
1317-33-5	Molybdenum sulfide (MoS_2)	Low	Low	Low
1345-24-0	C.I. Pigment Red 109	Low	Low	Low
7440-31-5	Tin	Low	Low	Low
7440-41-7	Beryllium	Moderate	Low	Low
7553-56-2	Iodine	Low	N/A	Low
7681-11-0	Potassium iodide (KI)	Low	N/A	Low
7681-82-5	Sodium iodide (NaI)	Low	N/A	Low
7722-84-1	Hydrogen peroxide (H_2O_2)	Low	N/A	Low
7727-18-6	Vanadium, trichlorooxo-	Low	Low	Low
7727-43-7	Sulfuric acid, barium salt (1:1)	Low	Low	Low
7789-20-0	Water-d_2	Low	N/A	Low
10361-37-2	Barium chloride ($BaCl_2$)	Low	Low	Low
11099-11-9	Vanadium oxide	Low	Low	Low
12713-03-0	Umber	Low	N/A	Low
17194-00-2	Barium hydroxide ($Ba(OH)_2$)	Low	Low	Low
20461-54-5	Iodide	Low	N/A	Low
51274-00-1	C.I. Pigment Yellow 42	Low	N/A	Low
63325-16-6	Mercury, diiodobis(5-iodo-2-pyridinamine)-, dihydriodide	Low	N/A	Low

Abbreviations: N/A, not applicable

[a] Post-categorization human health priority

Table A-3. Biomonitoring data for three substances addressed using the Biomonitoring-based Approach 1[a]

CAS RN	Moiety	Matrix	LOD (µg/L)	Magnitude: median, 95th percentile concentration	Prevalence: range of % detected
7440-41-7	Be	Whole Blood	0.45	ND, ND[b]	0
7440-41-7	Be	Serum	0.45	ND, ND[b]	0
7440-41-7	Be	Urine	0.004 – 0.45	ND, ND[b]	0.3 to ≤ 5[c]
7727-18-6 11099-11-9	V	Urine	0.1	ND, 0.24-0.35 µg/g creatinine	7.8-10.9

Abbreviations: LOD = limit of detection, ND = Not Detected
[a] HC 2016a
[b] 97.5th percentile
[c] 1988-1994 US data not included as it is not considered to be representative of current exposure

Table A-4. Biomonitoring data for 13 substances addressed using the Biomonitoring-based Approach 2[a]

CAS RN	Moiety	Matrix	Biomonitoring Guidance Value	Range of Median Concentration	Range of 95th percentile Concentration
513-77-9 7727-43-7 10361-37-2 17194-00-2	Ba	Urine	246 µg/g creatinine	1.17-2.18 µg/g creatinine[b]	5.54-7.10 µg/g creatinine[b]
1313-27-5 1317-33-5	Mo	Whole Blood	5.04-27.9 µg/L	0.59-1.25 µg/L	1.2-2.78 µg/L
1313-27-5 1317-33-5	Mo	Urine	1326-7516 µg/g creatinine	36-140 µg/g creatinine	94-490 µg/g creatinine
1345-24-0 7440-31-5	Sn	Urine	26 µg/g creatinine	0.45-0.89 µg/g creatinine[b]	2.80-7.91 µg/g creatinine[b]
7553-56-2 7681-11-0 7681-82-5 20461-54-5 63325-16-6	I	Urine	> 300 µg/L	122-232 µg/L	N/A

N/A= not applicable
[a] HC 2016b, Hays et al. 2018
[b] 1988-1994 US data not included as it is not considered to be representative of current exposure

Table A-5. Summary of hazard findings for five substances addressed using the Low Human Health Hazard Potential approach[a]

CAS RN	DSL name	CMR[b]	Decision point 1: Does the substance cause any health effects up to Limit Dose (1000 mg/kg bw/d)?	Decision point 2: Does the substance cause serious effects between 100 and 1000 mg/kg bw/d?
409-21-2	Silicon carbide (SiC)	Yes[c]	No	N/A
7722-84-1	Hydrogen peroxide (H_2O_2)	No	Yes	No, recoverable, indications of irritation at 76-785 mg/kg bw/day(FMC Corporation 1997; EU RAR 2003, as cited in HC 2019)
7789-20-0	Water-d_2	No	No	N/A
12713-03-0	Umber	No	No	N/A
51274-00-1	C.I. Pigment Yellow 42	No	No	N/A

Abbreviations: N/A= Not Applicable, CMR= Carcinogenicity, Mutagenicity, Reproductive/Developmental
[a] HC 2019, umber and C.I. Pigment Yellow 42 data presented in Appendix B
[b] Identified on the basis of classifications by other national or international agencies for carcinogenicity, genotoxicity, developmental toxicity or reproductive toxicity for the oral route of exposure which is considered to be most relevant for general population exposure
[c] Fibrous silicon carbide is a group 2B carcinogen according to IARC. Only non-fibrous sources are currently used in Canada, which does not increase cancer risk.

Table A-6. Substances with human health high hazards

CAS RN	DSL name	Human Health High Hazard[a]
409-21-2	Silicon carbide (SiC)	IARC group 2B carcinogen (fibrous silicon carbide). Only non-fibrous sources are currently used in Canada, which does not increase cancer risk.
1313-27-5[b]	Molybdenum oxide (MoO_3)	IARC Group 2B carcinogen, potential for increased risk of lung cancer in occupational groups exposed to molybdenum oxide through steel production.
7440-41-7	Beryllium	IARC Group 1 carcinogen, increased risk of lung cancer in occupational groups exposed to beryllium or beryllium compounds

[a] High health hazards were identified on the basis of classifications by other national or international agencies for carcinogenicity, genotoxicity, developmental or reproductive toxicity.
[b] Post-categorization human health concern

Appendix B. Results of the Low Human Health Hazard Potential approach for C.I. Pigment Yellow 42 and umber

Oral intake for the general Canadian population is expected to be the primary route of exposure to C.I. Pigment Yellow 42 (CAS RN 51274-00-1) and umber (CAS RN 12713-03-0). C.I. Pigment Yellow 42 is a hydrated iron (III) oxide with the formula $FeO_2H \cdot H_2O$, while umber is a UVCB, which contains iron (III) oxide as its major component (40% to 73%) (Fuller 1988). Due to limited empirical health effects data on C.I. Pigment Yellow 42 and umber, a read-across approach using data from the analogue iron oxide (CAS RN 1309-37-1) was used to inform the human health effects assessment of these substances. Iron oxide, a pigment consisting of Fe (III), is a suitable analogue as it contains iron in the same redox state as C.I. Pigment Yellow 42 and umber. The totality of the information indicates that iron oxide is negative for carcinogenicity, mutagenicity and reproductive/developmental toxicity up to the Limit Dose of 1000 mg/kg bw/day (JECFA 1980, 1983; IARC 1987; EFSA 2015). In repeated-dose studies, there were no health effects of concern below the Limit Dose of 1000 mg/kg bw/day (i.e., Decision point 1 based on the approach for Substances with Low Human Health Hazard Potential, HC 2019) (Yun et al. 2015). Therefore, based on the analogue iron oxide, C.I. Pigment Yellow 42 and umber are considered to be of low concern for human health according to the Low Human Health Hazard Potential approach.

Table B-1. Hazard summary for C.I. Pigment Yellow 42 and umber

Primary route of exposure	Oral
Read-across Rationale	Given limited substance-specific empirical data, a read-across approach was used, with iron oxide as the analogue for both substances. Iron oxide is a pigment consisting of Fe (III), iron in the same redox state as C.I. Pigment Yellow 42 and umber.
Carcinogenicity	Negative Study: 8 year oral administration of iron oxide colourant in diet in 10 dogs. The daily consumption was estimated at 428 mg/dog. No adverse effects were reported. (unpublished study from Carnation Co. 1967, as reported in JECFA 1983 and EFSA 2015) Study: 7 year oral administration of iron oxide in diet containing 1 900 mg/kg diet (475 mg/kg bw/day) of iron from iron oxide (equivalent to 0.27 % iron oxide) in cats. (unpublished study from Ralston Purina 1968, as reported in JECFA 1983 and EFSA 2015)

	Evidence suggesting lack of carcinogenicity for haematite (red iron oxide) and ferric oxide (unspecified compound) to animals, and inadequate evidence for carcinogenicity to humans. (IARC 1987)
Genotoxicity/Mutagenicity	Negative (EFSA 2015)[a]
Reproductive and Developmental Toxicity	No signs of reproductive toxicity were observed in 2 unpublished studies referenced by JECFA (1980, 1983) "rats consuming more than 50 mg/kg bw iron oxide for 8 generations showed no effects on reproduction" (JECFA 1980, 1983)
Repeated Dose Toxicity	NOAEL = 1000 mg/kg bw/day Study: 13-week oral feed study with Sprague-Dawley rats (n=12/sex/group) dosed at 250, 500 and 1000 mg Fe_2O_3 nanoparticles/kg bw/day. No clinical signs of toxicity or adverse effects on body weight, food consumption, haematological or serum biochemistry parameters, organ weights or histopathology. (Yun et al. 2015)
Recommendation and rationale for the recommendation	Oral intake for the general Canadian population is the primary route of exposure to C.I. Pigment Yellow 42 (CAS RN 51274-00-1) and umber (CAS RN 12713-03-0). Iron oxide was used as read-across for C.I Pigment Yellow 42 and umber. There was no health effect of concern for carcinogenicity, mutagenicity/genotoxicity, and reproductive/developmental toxicity up to the limit dose of 1000 mg/kg-bw/day (IARC 1987; JECFA 1980, 1983; EFSA 2015; Yun et al. 2015). Therefore, C.I Pigment Yellow 42 and umber are considered to be of low concern for human health.

[a] The EFSA panel concluded there was no concern with respect to systemic genotoxicity of orally administered red iron oxide. Although DNA strand breakages were observed in some studies in cultured mammalian cells in vitro, this was not confirmed in other in vitro studies. In addition, red iron oxide was negative for genotoxicity in a well-conducted in vivo study.