

Analysis of Batch 8 Challenge Substance Draft Assessment and Management Reports

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Introduction

On January 30, 2010 the federal government published the draft screening assessments for the eighth batch of the Industry Challenge of the Chemicals Management Plan. At this time, draft assessments were published for 14 substances and draft risk management scope documents for 4 substances. All of the above documents can be found at <http://www.chemicalsubstanceschimiques.gc.ca>.

Members of the public have until **March 31, 2010** to submit comments and feedback on the risk assessments for all 14 substances; the risk management proposals for the 4 substances that are proposed to be designated as “toxic” and added to the List of Toxic Substances in Schedule 1 of CEPA 1999. There was a proposal to apply the Significant New Activity (SNAc) provisions to 4 of the chemicals.

It is hoped that the information presented will help civil society organizations and their members to prepare comments on the government’s proposals and advocate for the sound management of these chemicals. All data, unless otherwise indicated, comes from the assessment and risk management scope reports.

Potential Chemicals of Interest to Northern Communities

Note that in the assessment, the following symbols are used to identify chemicals that may be of possible concern to northern communities. As a result of these concerns that are not often explicitly cited within the government assessments, the following symbols are being used by Environmental Defence to flag chemicals of potential interest on the basis of the information contained within the assessments:

- * May have long range transport ability in air on the basis of its persistence in this media
- ◆ May be used in oil, mining, or forestry operations on the basis of information presented

The flagged chemicals within this document are:

- ◆DTBSBP (CAS 17540-75-9) – used in the petrochemical sector
- *2-Nitropropane (CAS 79-46-9) – LRTP of 12 969 km based on the TaPL3 model and as presented in the original substance profile on the Challenge website
- ◆*2-Nitrotoluene (CAS 88-72-2) – used in the petrochemical industry in other jurisdictions, LRTP of 3198 km based on the TaPL3 model and as presented in the original substance profile on the Challenge website
- ◆NTA (CAS 139-13-9) – used in pulp and paper processing and oil extraction
- ◆Zinc BDBP (CAS 2215-35-2) – used in the petroleum sector
- ◆PTPTT (CAS 75768-65-9) – companies reported importing it appear to include those in the oil and gas industry
- *Benzene, 1,3,5-tribromo- (CAS 626-39-1) – LRTP of 5219 km based on the TaPL3 model and as presented in the original substance profile on the Challenge website
- *Nitromethane (CAS 75-52-5) - LRTP of 11 711 km based on the TaPL3 model and as presented in the original substance profile on the Challenge website

Our Priority Setting Criteria

For Batches 1-3, priority identification was only done at time of the final report. However, after some thought and consultation, attempting to assist NGOs wade through the large volume of information at the draft stage when risk assessment submissions are primarily considered was deemed most relevant. We have therefore identified priorities to help facilitate the ease with which NGOs tackle the draft data.

It is important to acknowledge that the line between high, medium, and low priorities is not always clear and that because and different organizations have different interests, it remains at the discretion of the reader to identify individual/organizational priorities. Criteria used to sort priorities by Environmental Defence are as follows:

- Designation as persistent, bioaccumulative, and/or inherently toxic;
- Volume of use and estimated level of exposure;
- Types of exposure (pathways);
- Quantity & quality of evidence for toxicity;
- Essentiality of the uses; and
- Availability of alternatives.

Batch 8 Challenge Substances Summary

Chemical	Uses	Volume (2006)	Categorization	CEPA "Toxic"	Basis	RM Focus	Priority for Action
♦DTBSBP (CAS 17540-75-9)	Plastics (e.g., PVC, polyurethane), brake fluids, ink resins, and the petrochemical sector	Medium	PBiT and thought to be in Canadian commerce	Yes	PBiT and in commerce	Virtual elimination, eliminating release in industrial effluents and/or prohibiting use in products	High (PBiT, in commerce, possible health concerns)
MAPBAP acetate (CAS 72102-55-7)	Dye mainly in the production of paper products	Medium	PBiT and thought to be in Canadian commerce	Yes	Persistent and RQs considered inadequate	Limiting levels in dye products and/or industrial releases, notification of changes in use	High (can cause ecological harm, possible health effects)
*2-Nitropropane (CAS 79-46-9)	Chemical intermediate, resins manufacture, explosives/propellants , fuels, rubbers, inks, adhesives, coatings	Low	IARC Group 2B carcinogen EC Category 2 carcinogen US NTP	Yes	Non-threshold carcinogen	Notification of changes in use, delisting from the food additives table	High (genotoxic, limited risk management)
♦*2-Nitrotoluene (CAS 88-72-2)	Mostly in the making of explosives, may also be used in petrochemical industry	Low	EC Category 2 carcinogen EC Category 2 genotoxin	Yes	Non-threshold carcinogen	Notification of changes in use	High (genotoxic, limited risk management)
♦NTA (CAS 139-13-9)	Cleaning products, pulp and paper processing, oil extraction, boiler water treatment, pesticides, personal care products	Low-Medium or High*	IARC Group 2B carcinogen US NTP	No	Not a danger to human life or health - adequate MOEs	NA	High (some low MOEs, reliance on 1970's data for exposure)
Butylated hydroxyanisole (CAS 25013-16-5)	Foods, animal feeds, pharmaceutical products, natural health products, personal care products, pesticides, cleaners	Low-Medium	IARC Group 2B carcinogen US NTP	No	Not a danger to human life or health - adequate MOEs	NA	High (some low MOEs, cumulative exposures not considered in MOE calculations)

Chemical	Uses	Volume (2006)	Categorization	CEPA "Toxic"	Basis	RM Focus	Priority for Action
♦Zinc BDBP (CAS 2215-35-2)	Crude petroleum, petroleum product manufacturing sectors	Medium-High	PBiT and thought to be in Canadian commerce	No	Not bioaccumulative and aquatic RQs considered adequate	NA	High (RQs just less than and greater than 1)
♦PTPTT (CAS 75768-65-9)	Used in the making a class of synthetic rubbers used in industrial applications	Low	PBiT and thought to be in Canadian commerce	No	Not bioaccumulative and aquatic RQs considered adequate	NA	Medium (early conclusion on ecological harm, possible health effects)
*Benzene, 1,3,5-tribromo- (CAS 626-39-1)	Solvent, motor oil, chemical manufacturing	Very Low	PBiT and thought to be in Canadian commerce	No	PBiT, but not in commerce	SNAc provisions under subsection 81(3) of CEPA	Medium (PBiT, but not in commerce)
Benzene, 1,2,3,4-tetrachloro-5,6-dimethoxy- (CAS 944-61-6)	Chemical manufacturing	Very Low	PBiT and thought to be in Canadian commerce	No	PBiT, but not in commerce	SNAc provisions under subsection 81(3) of CEPA	Medium (PBiT, but not in commerce)
Phosphonic acid, [[3,5-bis(1,1-dimethylethyl)-4-... (2:1) (CAS 65140-91-2)	Plastics, synthetic fibers, elastomers, adhesives, waxes and oils	Very Low	PBiT and thought to be in Canadian commerce	No	PBiT, but not in commerce	SNAc provisions under subsection 81(3) of CEPA	Medium (PBiT, but not in commerce)
Fatty acids, C6-C19-branched, zinc salts (CAS 68551-44-0)	Chemical manufacturing, in coal tar, wood, and ethanol sectors	Very Low	PBiT and thought to be in Canadian commerce	No	PBiT, but not in commerce	SNAc provisions under subsection 81(3) of CEPA	Medium (PBiT, but not in commerce)
*Nitromethane (CAS 75-52-5)	Fuels, chemical manufacturing, dry cleaning, dental manufacturing, adhesive remover	Low	IARC Group 2B carcinogen US NTP	No	Not a danger to human life or health - adequate MOEs	NA	Medium (need improved exposure estimates)

Chemical	Uses	Volume (2006)	Categorization	CEPA "Toxic"	Basis	RM Focus	Priority for Action
Benzenepropanoic acid ester (CAS 70331-94-1)	PVC (CPVC) products which have wide application, including piping, wire and cable insulation	Low	PBiT and thought to be in Canadian commerce	No	Not bioaccumulative and aquatic RQs considered adequate	NA	Low

*if salts are included and as per a different source

Volume Scale

Very Low	None reported
Low	100 - 1000 kg
Low-Medium	1 000 -10 000 kg
Medium	10 000 – 100 000 kg
Medium-High	100 000 - 1 000 000 kg
High	1 000 000 – 10 000 000 kg
Very High	> 10 000 000 kg

HIGH PRIORITIES

◆Phenol, 2,6-bis(1,1-dimethylethyl)-4-(1-methylpropyl)- (DTBSBP) CAS No. 17540-75-9

Category	Assessment
PBiT and believed to be in commerce in Canada.	Proposed that "DTBSBP meets one or more of the criteria set out in section 64 of the Canadian Environmental Protection Act, 199.9"

Manufacture & Use

DTBSBP is not naturally produced in the environment. No manufacture was reported for 2006, but 16 686 kg was imported into Canada by five companies. There is just one known global manufacturer of this substance, the SI Group in the United States. The amount imported within consumer products was not reported. It is a US and OECD HPV chemical and an EU LPV chemical. It is also on the Oslo-Paris (OSPAR) Commission's list of substances of possible concern. In Canada, it is used in plastics product manufacturing and brake fluid. Other use information collected via Section 71 notice was considered confidential. Additional information suggests that it is used in the polyvinyl chloride (PVC), ink resin, and petrochemical industries. It may be used in PVC films for wrapping meat and produce and is used at 0.1% wt in brake fluid. It is replacing the antioxidant butylated hydroxytoluene (BHT) in several non-food applications (e.g., foam industry).

Releases

No company reported air, water, or soil release, but some reported transfers (less than 100 kg in total) in non-hazardous waste to an off-site waste management facility. Using the Mass Flow Tool and the imported amount in 2006, it was estimated that the majority of DTBSBP (54.3%) would end up in waste disposal sites. There was no information on its release from the waste management sites. Another 38% is likely to go to recycling, 3.7% to wastewater (mostly because of industrial uses), 1.7% to incineration, 1.7% to export, 0.4% to air, and 0.2% to paved/unpaved surfaces. "The plastics products industry sector is estimated to account for the largest total losses."

Environmental Concerns

Modelling suggests DTBSBP will primarily partition into the media to which it is released. It is slightly volatile and 74% of it will remain in air if released there. While it is unlikely to volatilize much from water surfaces, it does have a high affinity for solids and will mostly partition into sediments if released there. It also has high affinity for soil. It is expected to be undissociated in water bodies at environmentally relevant pH (6–9). Two analogues with sufficient structural similarity are used in the assessment: 2,4,6-tri-tert-butylphenol (CAS 732-26-3) and 2,6-di-tert-butyl-4-ethylphenol (CAS 4130-42-1).

Fugacity models using empirical and analogue modeled data predict that DTBSBP will reside in air if released to air, with small amounts partitioning into the remaining environmental mediums. However, the modeled potential for persistence in air reveals that atmospheric oxidation will rapidly take place, and results in a half life in air of 0.26 days (<2 days). It is therefore

considered not persistence within the atmosphere. TaPL3 modelling suggests that the maximum distance traveled in air by 63% of the substance is low (131 km) and this is supported by the long-range transport potential as calculated using the OECD model (278 km). Thus, it was concluded that it is unlikely to “be transported over long distances in the atmosphere”. In addition to its log Kow value of 6.1, empirical data for the above analogues suggest that it will bioaccumulate (CAS 732-26-3 BCFs from 4320–23 200; CAS 4130-42-1 BCFs from 930 – 5060), as does modelled data for the above analogues (CAS 732-26-3 BCF 14 050 and BAF 324 700; CAS 4130-42-1 BCF 3119 and BAF7534). CAS 732-26-3 (analyzed in Batch 2 – proposed “toxic”) is the most structurally similar analogue. Modelled data for DTBSBP also suggest it bioaccumulates (median BCF = 22 387, median BAF = 870 963). The bioaccumulation decision is supported. A weight-of-evidence approach also suggests that it “causes harm to aquatic organisms following short-term (acute) and longer-term (chronic) exposure at relatively low concentrations (i.e., acute LC/EC50 ≤ 1.0 mg/L and/or chronic LC/EC50 or NOEC ≤ 0.1 mg/L).” This is based on modelled data for DTBSBP where all but one result evidenced this, and empirical data for CAS 732-26-3 where most results evidenced this. There was no empirical data for the other analogue. Only ecological effects in water were investigated.

Ecological Risk

There is no Canadian environmental data and PECs, PNECs, and RQs were not calculated. However, given its importation volume, use patterns suggesting the possibility of widespread and point-source releases, as well as persistence, bioaccumulation potential, and high potential for toxicity to aquatic organisms, it was concluded that DTBSBP “may be entering the environment under conditions that may have harmful long-term ecological effects”.

Health Concerns

A health assessment was also conducted. Human exposure is predicted to mostly occur via inhalation from consumer products. Using the NOEL for non-neoplastic effects of 30 ppm (1.5 mg/kg-bw per day) for the analogue CAS 732-26-3 via oral exposure as there are no inhalation exposure health effects data, as well as the upper-bounding estimate of daily intake (toddlers, foam-filled furniture, 8.72×10^{-4} mg/kg-bw per day), a MOE of 1720 was derived. The MOE for exposure via meat packaging (estimated probable daily intake of 0.0581 µg/kg-bw) was approximately 25 800. Exposure via PVC or plastic hoses used in the food industry was not calculated because it was considered negligible-low. Dermal exposure to foam was also considered negligible. No attention was paid to vulnerable populations

Risk Management

The government proposes to recommend DTBSBP’s addition to the List of Toxic Substances. The risk management scope document further suggests that risk management will be focused on virtual elimination, eliminating release in industrial effluents and/or prohibiting use in products made, imported, used, sold, or offered for sale.

Recommendations

1. DTBSBP should be designated as “toxic” in Canada given its persistence, bioaccumulation, and inherent toxicity, as well as relatively low MOE for inhalation from consumer products.
2. While the structural similarity of the analogues is considered high, the physical and chemical property data, at the very least, should be measured as these values would provide more reliable model input than the analogue data.
3. The amount imported within consumer products needs to be elucidated.
4. The lack of information on environmental concentrations in Canada is concerning in light of its persistence, bioaccumulation, and likely fate and should be addressed. This is particularly concerning given the volume imported for industrial purposes alone. Accurate concentration data is also needed to fully evaluate its effects.
5. There is no calculation of off-site releases to the environment from industrial or consumer product waste disposal, even though partitioning into water and sediment from this source is possible. Because of this, release results, although considered conservative, should be interpreted cautiously.
6. The lack of exposure, experimental, or predicted-effects data for non-aquatic organisms in sediment and soil is of concern, due to the chemical’s ability to partition into soil and sediment. A PEC for media other than water should be calculated, particularly since it is persistent in other mediums.
7. Since DTBSBP is persistent, further investigations on the biodegradation process are required. Biodegradation may lead to the formation of metabolites that may have toxic properties.
8. Chronic studies on the effects of DTBSBP exposure in various species are required to fully evaluate the impact of it in organisms and the environment. Empirical data with regards to its possible health effects in humans should be gathered.
9. Exposure assessments should be more comprehensive and consider the cumulative exposure via various consumer products.
10. Attention needs to be paid to determining vulnerable population exposures (e.g., occupational groups).

Methylium, [4-(dimethylamino)phenyl]bis[4-(ethylamino)-3-methylphenyl]-, acetate (MAPBAP acetate) CAS No. 72102-55-7

Category	Assessment
PBiT and believed to be in commerce in Canada.	Proposed that "MAPBAP acetate meets one or more of the criteria set out in section 64 of the <i>Canadian Environmental Protection Act, 1999</i> ".

Manufacture & Use

MAPBAP acetate is not naturally produced in the environment. It was not manufactured in Canada in 2006, but 10 001 - 100 000 kg was imported and used. This is greater than the amount imported in 2005. It may also be imported in manufactured items or in quantities below the 100 kg reporting threshold. It is reportedly used as a paper dye, with another use being considered confidential.

Releases

No company reported air, water, soil release, or transfers to waste management facilities. Using the Mass Flow Tool and 100 000 kg/year use it was estimated that the majority of MAPBAP acetate (41%) would end up in recycling. Another 39.5% is likely to go to landfills, 18.3% to wastewater, and 1.2% to incineration. There was no information on its release from the waste management sites. Although levels in imported products were not numerically considered, it was stated that "quantities sent for waste management would be higher if importation of these items were taken into consideration."

Environmental Concerns

MAPBAP acetate is a solid and its modelled vapour pressure suggests it will not volatilize from soil. It will also remain in sediment if released there. . If released to water, it will remain there given its high water solubility. It will ionize in water bodies at environmentally relevant pH, yielding a reactive carbocation and will likely react with anionic material in the water.

Modelled data suggests that it is persistent in water, soil, and sediment as 6 of 7 models suggest a water half-life > 182 days. Slow biodegradation is supported by findings that dyes are essentially non-biodegradable under aerobic conditions. Analogues were not used since they did not have suitable experimental data. The conclusion that it meets persistence criteria in water, soil, and sediment is supported. According to the original substance profile on the Challenge website, LRTP was expected to be moderate (444 km) based on the TaPL3 model. Although its modelled log Kow value of 6.9 suggests that it will bioaccumulate, modelled data using read-across data suggests it does not meet the bioaccumulation criteria. Three models produced a BAF of 1.015 L/kg, a BCF of 1.015 L/kg and a BCF of 65 L/kg, all considering metabolism. Only one analogue (Malachite Green (CAS 569-64-2) with unknown % structural similarity) had experimental data; its BCF was 36 - 91 L/kg. Ionic dyes were considered to have a very low bioaccumulation potential in other assessments. A weight-of-evidence approach also suggests that "MAPBAP acetate is potentially highly hazardous to aquatic organisms (acute LC/EC50 ≤ 1.0 mg/L)". The conclusion is supported. This is based on modelled data of MAPBAP acetate and empirical evidence for two analogues (Malachite Green (CAS 569-64-2) and Basic Violet 3

(CAS 548-62-9). Of 4 empirical studies, 3 had LC50s < 0.332 mg/L and of the 4 modelled data, 4 had LC/EC502 < 0.608 mg/L. Only ecological effects in water were investigated.

Ecological Risk

Since there is no Canadian environmental concentration data, models were used to estimate water concentrations. PECs ranging from 0.001 mg/L to 0.03 mg/L in water due to industrial use were calculated for 11 industrial sites. Within the estimation, it was assumed that 1000 to 10 000 kg/year was used at each site, 23.3% was lost to water during processing and container cleaning, and 3.4% was removed by STPs. A dilution factor of 10 was also applied. Releases due to consumer use of paper products were not calculated.

The RQs “ranged from 0.9 to 32.8 and exceeded 1 at 10 of the 11 industrial sites”. They were calculated using the above PECs and a PNEC of 0.001 mg/L (divided the analogue CAS 548-62-9’s LC50 of 0.1 mg/L for medaka fish by 100 to account for species variations and long-term effects). It was not stated why they chose to use this LC50 value. It was concluded that “MAPBAP acetate could be causing ecological harm in Canada.”

Health Concerns

General population exposure to MAPBAP acetate from environmental media and consumer products is expected to be negligible. That being said, estimated total daily intake from environmental media (mainly soil ingestion) was 0.01 µg/kg-bw per day (children 0.5 to 4 years) and estimated oral acute intake from paper ingestion was of 0.067 mg/kg-bw per event. Predications for carcinogenicity and genotoxicity were mixed, resulting in concerns over modelled carcinogenicity (6 positives and 4 negatives), genotoxicity (6 positives and 7 negatives), developmental (2 positive and 18 negatives and 10 NR), and reproductive toxicity (1 positive and 12 NR). There are also concerns given empirical data for similar triarylamine substances. For example, gentian violet (CAS 548-62-9) is an EC Category 2 carcinogen and malachite green (CAS 569-64-2) is an EC Category 3 reproductive toxin. Thus, the potential for carcinogenicity, genotoxicity and developmental toxicity should not be precluded.

Risk Management

The government proposes to recommend MAPBAP acetate’s addition to the List of Toxic Substances. The risk management scope document further suggests that risk management will be focused on limiting levels in dye products and/or industrial releases, and requiring federal government notification of changes in use pattern.

Recommendations

1. MAPBAP acetate should be designated as “toxic” in Canada given its persistence and non-conservative RQs that are considered to not be adequately protective.
2. Its carcinogenicity, genotoxicity, and reproductive toxicity should be further investigated since current data suggest that these health outcomes might be associated with this chemical.

3. Experimental data should be used to determine MAPBAP acetate's physical-chemical properties and bioaccumulation potential. Particularly with regard to the former, these values would at least provide more reliable model input than the analogue data.
4. The lack of information on environmental concentrations in Canada is concerning in light of its likely fate and should be addressed. The amount imported within consumer products also needs to be elucidated given use of this substance in other countries. The assessment would be more robust if this information was included.
5. There is no calculation of off-site releases to the environment from industrial or consumer product waste disposal, even though a significant proportion will go to waste disposal, and even though partitioning into water and sediment from this source is possible.
6. Considering it may potentially be discharged to soil from the disposal of products that degrade and from biosludge, toxicity data for soil organisms should be obtained. This is of particular importance since it has been shown that dyes strongly adsorb to wastewater treatment plant sludge and particulates. Toxicity data for sediment dwelling organisms should be also investigated.
7. Since MAPBAP acetate is persistent and ionizes in water further investigations on the biodegradation and ionization process are required. Both may lead to the formation of metabolites that may have toxic properties.

*Propane, 2-nitro- (2-Nitropropane) CAS No. 79-46-9

Category	Assessment
Considered to pose an intermediate potential for exposure of individuals in Canada and had been classified by other agencies on the basis of carcinogenicity.	Proposed that “2-nitrotoluene meets one or more of the criteria set out in section 64 of CEPA 1999”.

Manufacture & Use

Submitted information suggests that 2-nitropropane was not manufactured in Canada above the reporting threshold in 2006, but 100 - 1000 kg was imported. 270 kg was imported by a hazardous waste management company. “However, 2-nitropropane may be entering Canada in formulated products including inks, paints, adhesives, varnishes, polymers, and synthetic materials (NTP 2005) that may not be captured under section 71 reports.” It is a US HPV chemical with many uses, including a solvent in inks, paints (mostly industrial/commercial), and adhesives. It is also used to dissolve various resins, including those lining beverage cans, as well as in explosives, propellants, fuels, rubbers, traffic markings, marine coatings, paint and varnish removers, dyes, insecticides, and pharmaceutical manufacturing (where it is marketed under SYNTHATANE™ NP 200). It is approved for food packaging adhesive use in the US, and while no use in Canadian food packaging has been reported for at least 10 years, it is permitted in vegetable oil processing. It is prohibited in EC cosmetics. Canada-specific use information was not presented.

Releases

2-Nitropropane is not manufactured in reportable quantities in Canada. There were no domestic NPRI releases reported between 1997 and 2007 (most recent data available) and no releases were reported in response to Section 71. Other sources suggest 10.5 kg (23 lbs) in 2001 and 11.4 kg (25 lbs) in 2002 were released into air in the Great Lakes region from Ontario. The amount transferred to landfill, aside from that imported by a hazardous waste management company is unknown.

It will primarily reside in the environmental compartment (air, water, or soil) to which it is released. The conclusion that it is persistent in air, water, soil, and sediment (based on empirical and modelled data) is supported. The conclusion that it does not meet bioaccumulation criteria and that it “is not expected to cause harm to aquatic organisms at relatively low concentrations” is also supported. Its LRTP was not mentioned, but as per the original substance profile on the Challenge website, LRTP was expected to be high (12 969 km) based on the TaPL3 model. No suitable ecological effects studies were found for 2-nitropropane in media other than water despite its release to and persistence in air. A PEC of 0.0007 mg/L was calculated for water alone assuming that the total quantity is used by a single industrial facility, 5% loss to sewers, and 10 fold STP dilution capacity. A PNEC of 0.94 mg/L was derived from the modelled EC50 for alga of 94 mg/L/100 to account for uncertainties. The 94 mg/L was the lowest LC50/EC50. The resulting RQ was 0.07.

Human Exposure

In terms of environment, general population exposure was predicted to be 1.95 ng/m³ (air) and 1.22 ng/L (water). This was based on no releases being reported to NPRI, no releases being reported via Section 71, and the approximately 10 kg released in Ontario. As support, US data showed that 99.7% of ambient air concentration estimates were < 1 ng/m³ and that drinking water is not likely a significant exposure source. In terms of food, the mean daily intake via vegetable fats and oils was estimated to range from 0.0023 (70+ years) - 0.0078 µg/kg/day (6-8 years). In terms of smoking, intake was estimated to 0.21 (15-19 years) - 0.25 µg/kg/day (adults). There was no exposure scenario for food packaging (no Canadian uses reported for the past 10 years), pharmaceuticals, paints (use apparently largely eliminated), or other products. No particular attention was paid to vulnerable populations.

Health Concerns

2-Nitropropane has been classified as a Group 2B carcinogen by IARC and a Category 2 carcinogen by the EC. The US NTP concluded that “2-nitropropane is reasonably anticipated to be a human carcinogen”.

Its critical effect is carcinogenicity as increased incidences of liver tumours were observed in experimental animals from various studies. To expand, it has induced benign and malignant liver tumours in rats in a 16 week oral study (40 mg/kg-bw per day); metastases were also observed in the lungs of some of the animals. It also caused multiple hepatocellular carcinomas in rats (755 mg/m³) via inhalation over 6 months and initiated action in rats’ livers via intraperitoneal injection or inhalation in the presence of a promoter.

Available evidence led an IARC working group to conclude that 2-nitropropane “is mutagenic in a wide variety of *in vitro* and *in vivo* systems by a direct action”. There is much evidence to support this claim as it has been shown to induce gene mutations in hamster and rat cells, cause chromosomal aberration and induction of sister chromatid exchanges in human cells, and induce unscheduled DNA synthesis in human, rat, and mouse cells. Genotoxicity mechanisms in the rat appear to be relevant to human cells.

2-Nitropropane is also associated with non-cancer effects. Increased hepatic lipid peroxidation, oxidative DNA damage and cell proliferation in the liver of rats was observed in a 2-week, oral exposure study (LOAEL 26 mg/kg-bw per day). Slight elevation in liver weights was observed in a 4-week, oral exposure study (17 mg/kg-bw per day in male rats). Slightly increased focal vacuolization of the cytoplasm of hepatocytes and focal areas of hepatocellular nodules were observed in a 22-month inhalation study (LOAEL 91 mg/m³). Severe adverse liver effects were also observed in a 6-month inhalation study (130 mg/m³). Other effects at various doses were observed. The only developmental toxicity study found that intraperitoneal injection (170 mg/kg-bw per day) reduced pre- or post- implantation survival and foetal body weight or length.

The results of epidemiological studies were mixed. However, occupational inhalation was associated with severe headaches in those least exposed (73 mg/m³ daily) and anorexia, nausea, vomiting, and diarrhea in those most intimately exposed (164 mg/m³ daily). Furthermore, construction workers exhibited adverse effects after applying epoxy resin coating. Fatalities were reported in this and another case study where four workers using it, and likely other solvents, died 6 - 10 days later.

Using an oral exposure LOAEL of 26 mg/kg-bw per day (hepatic lipid peroxidation, oxidative DNA damage and cell proliferation in the liver) and estimated intake from vegetable fats and oils (children 6 to 8 years), an MOE of 3.3×10^6 was derived. No additional MOEs were calculated.

Risk Management

The government proposes to recommend its addition to the List of Toxic Substances. The risk management scope document further suggests that risk management will be focused on “a requirement for notification of the federal government regarding any potential changes in the use-pattern for 2-nitropropane and a requirement that 2-nitropropane be delisted from the food additives table, Division 16 (Food Additives) of the Food and Drug Regulations”.

Recommendations

1. Given its potential carcinogenicity, genotoxicity, and various non-cancer effects, 2-nitropropane should be designated as “toxic” under CEPA, 1999.
2. Concentrations within Canadian environmental media and specific imported consumer products (e.g., pharmaceuticals, paints) should be established. There is concern that an absence of definitively knowing the consumer products in which it may be an impurity could result in risk management that will not address population exposure to this substance via all relevant sources.
3. Exposure estimates need to be more thorough using information derived through environmental and consumer product monitoring.
4. Releases and disposal of 2-nitropropane (e.g., that through facility disposal and product disposal) should be examined and subject to further research since there is no data available on it.
5. Suitable ecological effects studies should be found for 2-nitropropane in soil, given its persistence here, and air, given that it may be persistent in this media.
6. Inhalation studies for carcinogenicity (which is highly relevant in light of potential population exposure) are needed to ensure that all risks are addressed and managed appropriately.
7. Attention needs to be paid to determining vulnerable population exposures (e.g., occupational groups).
8. The risk management focus needs to be expanded to address the volume already in commerce and its potential presence as an impurity in various products.

◆*Benzene, 1-methyl-2-nitro- (2-Nitrotoluene) CAS No. 88-72-2

Category	Assessment
Considered to pose an intermediate potential for exposure of individuals in Canada and had been classified by other agencies on the basis of carcinogenicity and genotoxicity.	Proposed that “2-nitrotoluene meets one or more of the criteria set out in section 64 of CEPA 1999”.

Manufacture & Use

2-Nitrotoluene does not occur naturally in the environment. Submitted information suggests that it was not manufactured in Canada above the reporting threshold in 2006, but 100 - 1000 kg was imported. Production and importation have been decreasing since the 1980's, but it remains recognized as an OECD and US HPV chemical. Submitted information also reveals that most is used to manufacture explosives in Canada. Other uses in Canada are likely industrial as it may be used as an “intermediate in the manufacture of agricultural and rubber chemicals, petrochemicals, colorants, pesticides and pharmaceuticals” elsewhere. It is not registered for pesticides in Canada.

Releases

According to the assessment, one Canadian facility involved in explosives production reported no releases to water or soil, and that releases to air were not detected. No other release information, waste disposal or otherwise, was reported.

It will primarily reside in the environmental compartment (air, water, or soil) to which it is released. The conclusion that it is persistent in water, soil, and sediment (based on empirical and modelled data) is supported. The conclusion that it does not meet bioaccumulation criteria and that it “typically exhibits moderate hazard to aquatic organisms” is also supported. No suitable ecological effects studies were found for 2-nitrotoluene in media other than water and sediment. Its LRTP was not mentioned by the assessors, but as per the original substance profile, LRTP was expected to be high (3198 km) based on the TaPL3 model.

A PEC of 0.006 mg/L was calculated for water alone assuming that the total quantity is used by a single industrial facility, 5% loss to sewers, 0% STP removal rate, and receiving water flow of 34 560 m³/day. A PNEC of 0.054 mg/L was derived from the empirical LC50 for *Daphnia* of 5.4 mg/L/100 to account for uncertainties. The 5.4 mg/L was the lowest empirical LC50/EC50. The resulting RQ was 0.11.

Human Exposure

General population exposure is expected to be negligible. Exposure via environmental media was not calculated, but anticipated to be negligible because modelled environmental concentrations were anticipated to be negligible. It is not expected to be found in food and beverages. Other consumer products are also not expected to be a source of exposure. However, it was acknowledged that it may be present in imported pharmaceuticals, and possibly art materials. No particular attention was paid to vulnerable populations.

Health Concerns

2-Nitrotoluene is a Category 2 carcinogen according to the EC and it is “reasonably anticipated to be a human carcinogen” by the US NTP. These decisions are based on 2-year cancer bioassays by the US NTP that showed “clear evidence of carcinogenic activity” in rats and mice of both sexes. Prior to the publication of NTP studies, IARC classified it as a Group 3 carcinogen. It is also classified as a Category 2 mutagen by the EC based on demonstrated genotoxicity in multiple *in vitro* and *in vivo* assays.

In terms of its carcinogenicity, “increased tumours were reported in multiple tissues, such as the mesothelium, skin, mammary gland, liver or lungs, in rats exposed in the diet”. Reduced survival rates were also reported. Tumours in the circulatory system, large intestine, and liver were reported in mice exposed via the dietary route. Survival was also reduced in high-dose female mice. Dermal exposure weakly initiated skin tumours in mice. No inhalation carcinogenicity bioassays or epidemiological studies have been identified.

2-Nitrotoluene has been shown to be genotoxic with information strongly suggesting that observed tumours are due to direct interaction with genetic material. To expand, the EC has concluded that it is a somatic cell mutagen with the potential to cause mutations in germ cells. It has also been clastogenic in human peripheral lymphocytes and caused DNA damage in mammalian cell lines. Notably, “clastogenic effects were observed in workers occupationally exposed to nitrotoluenes”.

2-Nitrotoluene has also been associated with a range of non-cancer effects in experimental animals, including the induction of adverse effects “in the lungs, liver, spleen, bone marrow and the hematopoietic system” of rodents following “chronic, subchronic and short-term oral exposures”. The lowest LOEL for chronic exposures of 25 mg/kg-bw per day (lesions in the liver, bone marrow, spleen and lungs, changes to testes cells), the lowest LOEL for subchronic exposures was 89 mg/kg-bw per day (lesions in the kidneys and spleen), and the lowest LOEL for short-term exposure was 90 mg/kg-bw per day (lesions in the hematopoietic system and spleen). MOEs were not calculated since general population exposure is expected to be negligible and because tumours were observed at these doses.

Risk Management

The government proposes to recommend its addition to the List of Toxic Substances. The risk management scope document further suggests that risk management will be focused on “a requirement for notification of the federal government regarding any potential changes in the use-pattern for 2-nitrotoluene so that the potential for exposure to the Canadian population does not substantially increase.”

Recommendations

1. Given its potential carcinogenicity, genotoxicity, and various non-cancer effects, 2-nitrotoluene should be designated as “toxic” under CEPA, 1999.
2. Concentrations within Canadian environmental media and specific imported consumer products (e.g., pharmaceuticals) should be established. There is concern that an absence of definitively knowing the consumer products in which it may be an impurity could result in risk management that will not address population exposure to this substance via all relevant sources.

3. Releases and disposal of 2-nitrotoluene (e.g., that through facility disposal and product disposal) should be examined and subject to further research since there is no data available on it. Relying on a single industry report is of concern.
4. The products of 2-nitrotoluene's degradation (2-methyl-6-nitrophenol and 2-methyl-4-nitrophenol) should be evaluated, given that findings in this regard would help draw conclusions on its persistence and bioaccumulation.
5. Suitable ecological effects studies should be found for 2-nitrotoluene in soil, given its persistence here.
6. Inhalation studies for carcinogenicity (which is highly relevant in light of potential population exposure) are needed to ensure that all risks are addressed and managed appropriately.
7. Attention needs to be paid to determining vulnerable population exposures (e.g., occupational groups).
8. The risk management focus needs to be expanded to address the volume already in commerce and its potential presence as an impurity in various products.

◆Glycine, N,N-bis(carboxymethyl)- (Nitrilotriacetic acid) CAS No. 139-13-9

Category	Assessment
Considered to pose an intermediate potential for exposure of individuals in Canada and is considered to pose a high hazard to human health.	Proposed that "isophorone does not meet the criteria set out in section 64 of CEPA 1999".

Manufacture and Use

NTA does not naturally occur in the environment. As per submitted information for 2006, it was not manufactured above the reporting threshold, but 1000 - 10 000 kg was imported. However, another source reported that 3.9 million kg of NTA (including its salts) was imported into Canada in 2006. In Canada, it is reportedly used in "institutional and industrial cleaning products, vehicle cleaners, asphalt paving, fertilizers, photographic developer solutions and descaling products for oil extraction and mining activities". It may also be used to treat boiler water, and in pulp and paper processing. Institutional and industrial cleaning products constitute the largest Canadian use. Globally, it is used as a water softener for various industrial applications. Its salt Na₃NTA (CAS 5064-31-3) is used in industrial and institutional cleaners, industrial water softener, pesticides, and personal care products. NTA is a known impurity (max of 0.1% by weight) in ethylenediaminetetraacetic acid (EDTA) and its salts (edentates). The latter are used in household cleaners, cosmetics, foods, agricultural products, pharmaceuticals, industrial processes, and heavy metal poisoning treatment.

Releases

According to Section 71 responses, no companies released NTA to air or land in 2006, but 1000 - 10 000 kg was released to water and 145 - 14 500 kg was sent to off-site waste management as hazardous or recycled waste. NPRI data suggests that on-site releases were 177 kg and off-site disposals were 5800 kg (sent to STPs) in 2006. Nothing was further delineated, although its environmental presence was stated as being predominantly due to sewage water release. Air releases were reported up until 2004.

Modelling suggests that it will remain in water if released there, but in soil if released to air or soil. Water was the focus of the assessment, which is considered reasonable since it appears unlikely to partition into sediment. The conclusion that NTA is not persistent in air, water, soil, or sediment is supported. LRTP was not reported here or in the original substance profile. Biodegradation models for NTA and its low log K_{ow} support a lack of bioaccumulation potential. Empirical data suggests neither it nor Na₃NTA is highly hazardous to aquatic organisms.

Water concentrations were available for Canadian receiving water and effluent during the 1970's, but a PEC was calculated and used instead. With a PEC of 0.05 mg/L (lower than 1970's data) and a PNEC of 0.5 mg/L, the RQ was 0.1.

Human Exposure

The primary source of exposure to the general population is through drinking. For environmental media, the upper-bounding estimates of intake from drinking water ranged from 0.41 µg/kg body weight (kg-bw) per day (12–19 years) - 2.18 µg/kg-bw per day (formula-fed infants 0–6 months).

This was based on the maximum drinking water concentration measured in Canada in the 1970's (20.4 µg/L). The Guidelines for Canadian Drinking Water Quality permit up to 400 µg/L. Exposure estimates via food were not calculated (even though it may be found in paper packaging), but considered negligible. In terms of frequently used personal care products, maximum dermal absorption of NTA was predicted to be 0.0197 mg/kg-bw per day, but inhalation was predicted to be negligible (with the exception of aerosols). In terms of occasionally used personally care products, total highest dermal exposure to Na₃NTA from a single consumer product was 0.00656 mg/kg-bw day.

Health Concerns

NTA and its sodium salts are classified as Group 2B carcinogens by IARC. Na₃NTA has been classified as a Category 3 carcinogen by the EC, NTA is “reasonably anticipated to be a human carcinogen” by the US NTP, and NTA is classified in Group IIIB (“possibly carcinogenic to humans”) by the Guidelines for Canadian Drinking Water Quality.

NTA's critical effect is considered carcinogenicity, with incidences of urinary system tumours being seen in a dose-related manner. In this regard, the lowest oral LOAEL for Na₃NTA was 100 mg/kg-bw per day (70 mg/kg-bw per day as NTA) because of changes to kidney and urinary system cells (short-term) and renal adenomas and adenocarcinomas (long-term). Marginal increases in hyperplastic and dysplastic have been observed at 10 mg/kg-bw per day. No chronic dermal toxicity studies were found, but short-term dermal studies were. In the latter, the highest doses resulted in NOAELs of 50 mg/kg-bw per day as Na₃NTA (35 mg/kg-bw per day as NTA) with the conservatively predicted NTA chronic dermal exposure of 0.0197 mg/kg-bw per day.

Mode of tumours induction has not been elucidated, but it is not considered to be genotoxic according to the assessors. IARC has concluded that “nitrilotriacetic acid and its sodium salts were not genotoxic in experimental systems *in vivo*, except that the acid induced aneuploidy in mouse germ cells. Neither the acid nor its salts were genotoxic in mammalian cells *in vitro* and they were not mutagenic to bacteria.” In a draft risk assessment, the European Union claimed that “there is no plausible evidence for *in vivo* mutagenicity of NTA and its sodium salts”.

NTA and Na₃NTA induced non-neoplastic lesions mainly in the kidneys, ureters and urinary bladders of experimental animals, with adverse lesions at dose levels causing tumours. Thus, non-neoplastic MOEs were not calculated.

The following MOEs were calculated:

- 32 000 for oral exposure (oral carcinogenicity LOAEL of 100 mg/kg-bw per day as Na₃NTA, 70 mg/kg-bw per day as NTA) and maximum general population exposure via the oral route (2.18 µg/kg-bw per day as NTA)
- 35 500 for dermal exposure (dermal carcinogenicity LOAEL of 1000 mg/kg-bw per day as Na₃NTA, 700 mg/kg-bw per day as NTA derived from oral LOAEL of 100 mg/kg-bw per day/10% for dermal absorption) and dermal exposure via frequently used personal care products (0.0197 mg/kg-bw per day)
- 3200 and 3550 for oral and dermal exposure (oral marginal increase of hyperplasia and dysplasia f LOEL of 10 mg/kg-bw per day as Na₃NTA, 7 mg/kg-bw per day as NTA) and unknown exposure predictions

- 1770 for subchronic dermal exposure (NOAEL 50 mg/kg-bw per day as Na₃NTA, 35 mg/kg-bw per day as NTA) and dermal exposure via frequently used personal care products (0.0197 mg/kg-bw per day)
- 900 for long-term dermal exposure (using hypothetical chronic NOAEL of 25 mg/kg-bw per day as Na₃NTA, 17.5 mg/kg-bw per day as NTA) and unknown exposure predictions

Risk Management

None proposed since the chemical is not proposed to be designated as “toxic”.

Recommendations

1. Given its potential for carcinogenicity, non-elucidated mode of action, low MOE for long-term dermal exposure, relatively low MOE for oral and dermal exposures, and reliance on 1970’s water concentrations to make these predictions, the precautionary approach should be justifiable and NTA should be proposed as “toxic” under CEPA, 1999 on the basis of precaution.
2. The discrepancy between reported import volumes should be remedied, particularly since there is such a substantial difference.
3. Recent concentrations in water, drinking water, and soil from various Canadian locations should be established. Relying on water levels from the 1970’s to determine exposure is not considered appropriate.
4. Contribution of NTA concentration in environmental media from waste-disposal and other release sources needs to be established. The fate of the 5800 kg of off-site disposals should be considered. The disposal of consumer products containing NTA also needs to be considered.
5. Long-term inhalation, dermal absorption, and oral studies for carcinogenicity (which is highly relevant in light of population exposure) and its non-cancer effects are particularly needed to ensure that all risks are addressed and managed appropriately. The dermal data set specifically needs strengthening.
6. Attention needs to be paid to determining vulnerable population exposures (e.g., occupation groups via manufacturing processes and industrial uses)

Phenol, (1,1-dimethylethyl)-4-methoxy- (Butylated hydroxyanisole) CAS No. 25013-16-5

Category	Assessment
Considered to present an intermediate potential for exposure of individuals in Canada and was considered to present a high hazard to human health.	Proposed that "BHA does not meet the criteria set out in section 64 of CEPA 1999".

Manufacture & Use

While BHA was not manufactured above the reporting threshold in Canada in 2006, 100 -1000 kg was imported and 1000 - 10 000 kg was used. It is a US EPA HPV chemical. BHA has many allowed uses, including use as an antioxidant in Canadian foods according to the *Food and Drug Regulations*. It was reportedly used in various foods to increase shelf-life (e.g., fats, oils, salad dressings, snack foods, gum) in 2006. In Canada, it is also reportedly used as a stabilizer in a few plastics intended for direct food contact, is a List 2 formulant in pesticide products (concentrations range from 0.000 04% to 1%), is allowed in "pharmaceutical products, natural health products and veterinary products manufactured in Canada", and is a "constituent of personal care products, such as deodorants, shampoos and body lotions". In the US, it is allowed in food, pesticides, cosmetics (where it "is listed among the most frequently used cosmetic ingredients"), animal feeds, rubber/petroleum products, and pharmaceutical preparations.

Releases

There was no release information. Modelling suggests that it will stay in water if released there, but will partition to soil if released to soil or air. In water, it will not dissociate.

The conclusion that it is not persistent in air, water, and soil, but it is in sediment is supported. LRTP was not stated, but is expected to be low (74 km) based on the TaPL3 model as per the original substance profile. Experimental and modelled evidence support a low bioaccumulation potential, but experimental data supports it being "moderately to highly hazardous to aquatic organisms" LC50/EC50 from 0.21 mg/L - 35 mg/L). Notably, "BHA is suspected to be a weak endocrine disrupting compound" that "stimulates both the transcriptional activity of the human estrogen receptor and the growth of breast cancer cells at concentrations of 2–3 mg/L and above."

Releases to water alone were calculated, even though BHA also partitions into soil. An RQ of 0.13 for consumer use was calculated for water given a PEC of 1.3×10^{-3} mg/L (highest reported STP effluent concentration in the US) and a 0.01 mg/L PNEC (based on LC50 of 1 mg/L for rainbow trout/100; however, the lowest EC50 was for bacterium). Additional RQs of 0.066 - 0.49 for consumer use was calculated for water given a PEC of 0.000 66 - 0.0049 mg/L (using the MegaFlush tool) and a 0.01 mg/L PNEC. An RQ of 0.028 was calculated for industrial release using a PEC of 2.8×10^{-4} mg/L (using the MegaFlush tool, 5-site release assumption, and different STP removal rates than the consumer product scenario) and a 0.01 mg/L PNEC.

Human Exposure

There is no Canadian water concentration data. The maximum daily intake from drinking water was predicted to be 0.02 µg/kg-bw per day (formula-fed infants) based on the maximum

concentration of 0.2 µg/L found in the 1999–2000 US Geological Survey. Exposure via any other environmental media was not calculated. In terms of food, mean intakes ranged from 0.023 - 0.095 mg/kg-bw per day based on approximately 40 food categories and assumptions. Maximum food intakes were not calculated. In terms of consumer products, maximum intakes ranged from 0.01 (men-5 products) - 0.07 mg/kg-bw per day (children 6 months to <5 years-2 products). The means ranged from 0.004 (infants-1 product) - 0.02 mg/kg-bw per day (women and children 6 months to 12 years-4 products). No particular attention was paid to vulnerable populations beyond children.

Health Concerns

BHA has been classified as an IARC Group 2B carcinogen and is “reasonably anticipated to be a carcinogen” according to the US NTP. Its mode of tumor induction in animals is not relevant to humans according to IARC.

The critical effect following oral dosing was forestomach carcinogenesis. The NOEL for forestomach hyperplasia in rats was 55 mg/kg-bw per day while the NOAEL for tumor formation was equivalent to 230 mg/kg-bw per day. There is no analogous forestomach in humans or other mammalian, non-rodent species. Short-term studies of species without forestomachs did not evidence “the extensive proliferative response in analogous tissues”. However, the LOEL based on liver weight increases and histopathological changes in these species was 54 mg/kg-bw per day. Studies of effects for dermal dosing were limited, but did not indicate pre-cancer lesions. One study reported an absence of toxicity up to a dose level of 10 - 15 mg/kg-bw per day for 30 weeks. Due to various limitations, oral endpoints were used to characterize dermal risk.

While the weight of evidence may suggest that BHA is not genotoxic, the “results of *in vitro* chromosomal aberration assays showed consistently positive results” and results from “*in vitro* chromosomal aberration studies with TBHQ were positive”. TBHQ is the principal oxidative metabolite of BHA and another antioxidant food additive.

In terms of non-cancer effects, oral dosing also caused changes in endocrine measures (thyroid gland, sex hormones, adrenal gland) with the increased clearance of hormones appearing secondary to enhanced liver enzyme activity due to BHA. The LOEL for non-cancer effects was found to be 50 mg/kg-bw per day in the pig “based on increased thyroid and liver weights without effects on reproductive/developmental parameters”. In rats, an LOEL of 100 mg/kg-bw per day was found for endocrine effects (thyroid cell changed, decrease in serum testosterone concentrations).

Using the above data various MOEs were calculated as follows. Cumulative MOES due to drinking water intake, food, and consumer products were not calculated. Firstly, using a NOAEL of 230 mg/kg-bw per day for oral dosing and tumour formation, MOES were:

- 2400 for oral intake and the highest mean BHA exposure (0.095 mg/kg-bw per day 4- to 8-year-old children via food)
- 57 500 and 11 500 for mean intake via personal care products for infants (0.004 mg/kg-bw per day), and women and children 6 months to 12 years (0.02 mg/kg-bw per day)
- 23 000 and 3300 for maximum intake via personal care products for men (0.01 mg/kg-bw per day) and children aged 6 months to <5 years (0.07 mg/kg-bw per day)

Using a LOEL of 50 mg/kg-bw per day for oral dosing and increased liver and thyroid weights, MOEs were:

- >500 for oral intake and the highest mean BHA exposure (0.095 mg/kg-bw per day 4- to 8-year-old children via food)
- 12 500 and 2500 using for mean intake via personal care products for infants (0.004 mg/kg-bw per day), and women and children 6 months to 12 years (0.02 mg/kg-bw per day)
- 5000 and 700 for maximum intake via personal care products for men (0.01 mg/kg-bw per day) and children aged 6 months to <5 years (0.07 mg/kg-bw per day)

Risk Management

None proposed since the chemical is not proposed to be designated as “toxic”. It is on the Ingredient Disclosure List (concentration 1% by weight) of the Hazardous Products Act.

Recommendations

1. Given its potential for carcinogenicity, endocrine disruption, as well as some MOEs for non-cancer and carcinogenic effects, BHA should be proposed as “toxic” under CEPA, 1999 on the basis of precaution.
2. Calculate MOEs for cumulative BHA exposure via environmental, food, and consumer products. Maximum values, as opposed to mean values, should be used within the assessment. This would be consistent with the methodology of other assessments.
3. Concentrations in water, drinking water, and soil from various Canadian locations should be established. Relying on levels found in the United States to determine exposure is not considered appropriate for Canada.
4. Contribution of BHA in the environment from waste-disposal and other release sources needs to be established. The lack of BHA release in Canada given its quantity is use is of concern.
5. Consumer product exposures should be further investigated given the limited number of products considered within the current assessment. For example, it is known that shaving gel available on Canadian shelves contains BHA¹, but these were not considered within the assessment.
6. Long-term inhalation, dermal absorption, and oral studies for carcinogenicity (which is highly relevant in light of population exposure) and its non-cancer effects are particularly needed to ensure that all risks are addressed and managed appropriately. The dermal and inhalation data set specifically need strengthening.
7. Attention needs to be paid to determining vulnerable population exposures (e.g., occupation groups via manufacturing processes and industrial uses).

¹ Environmental Defence used the Cosmetics Database to identify products that contain BHA. Certain identified shaving gels were subsequently found on Canadian store shelves.

◆Zinc, bis[O,O-bis(1,3-dimethylbutyl) phosphorodithioato-S,S']-, (T-4)- (zinc BDBP) CAS No. 2215-35-2

Categorization	Assessment
PBiT and believed to be in commerce in Canada.	Proposed that “zinc BDBP does not meet any of the criteria set out in section 64 of the <i>Canadian Environmental Protection Act, 1999.</i> ”

Manufacture & Use

Information submitted under Section 71 indicates that in 2006, zinc BDBP was not manufactured in Canada. However, “two companies reported importing between 100 000 and 1 000 000 kg”. This is greater than the amount reported imported in 2005. It may also enter the country in industrial or consumer products containing it. It is not naturally produced in the environment, and is an International Council of Chemical Associations, OECD, and US HPV chemical. Companies importing it are primarily engaged in the petroleum refinement and product manufacturing, as well as chemical product manufacturing. Elsewhere, it is used in lubricants for automotive applications. Both the US EPA and the EC have requested data on the substance in effort to conduct risk assessments.

Releases

No releases were reported for 2006. Using the Mass Flow Tool, 84.2% was predicted to be chemically transformed. It was also predicted that 11.7 % would go to recycling, 1.9% to wastewater, 1.1% to landfill, 0.9% to paved/unpaved surfaces, and 0.2% to incineration. None was predicted to go to air. There was no information on the release of zinc BDBP from the recycling or waste management sites. Releases from imported consumer products were not calculated.

Environmental Concerns

Zinc BDBP is considered to be non-volatile, as its modelled and experimental vapour pressures are low. If released to air or soil, it will primarily partition into the latter. It is also not soluble in water, but has a high affinity for solids; therefore, it is expected to primarily partition into particulate and likely end up in sediments if released to water. It is expected to be undissociated in water bodies at environmentally relevant pH (6–9). Using analogue data (% structural similarity of analogue not reported), modelled data (4/5 models showed it to be persistent in water), and knowledge that it contains two structural features associated slow biodegradation, it was concluded to be persistent in water, soil, and sediment. This conclusion is supported. LRTP was not reported, but expected to be low (17 km) based on the TaPL3 model as presented in the original substance profile on the Challenge website.

Two models were used to predict bioaccumulation, both leading to the conclusion that it is not bioaccumulative according to the regulations. The US EPA also considers all chemicals within the dialkyldithiophosphate group to have low bioaccumulation potential. However, the log Kow of 12.32 suggests that this substance may indeed have the potential to bioaccumulate. The Arnot and Gobas model is a reliable prediction model used to assess the bioaccumulation potential of substances having a log Kow value greater than 4, and is thought to provide the most reliable

prediction of bioaccumulation potential. However, due to zinc BDBP's high log Kow value of 12.32, this model could not be used for assessment, as its log Kow value falls outside of the domain of the model, which can only assess chemicals with a log Kow value up to 9. The bioaccumulation potential of Zinc BDBP were then determined by the OASIS and BCFWIN models, as the model contains some chemicals of structural comparability within its domain. These models indicate that zinc BDBP is expected to have low bioaccumulation potential.

Experimental and modelled evidence also suggests that it can harm aquatic organisms at relatively low concentrations. There were no ecological effects studies found for non-water media.

Ecological Risk

There is no Canadian environmental concentration data, and thus models were used. Using the 5th percentile of a Species Sensitivity Distribution (SSD), whereby it was assumed that the SSD reflects the most toxic zinc dialkyldithiophosphate category member substances, the acute PNEC was determined to be 0.17 mg/L. It apparently derives a lower PNEC than other models, but "does not meet the requirements of a type A guideline (CCME 2007)". A factor of 10 was applied to give a chronic PNEC of 0.017 mg/L. This is below zinc BDBP's predicted solubility. Note however, that there some toxicological risk assessors state that the PNEC should be set at 1/1000 of the limit of solubility when there is no toxicological data; this would therefore result in PNECs ranging from 0.0000305 to 0.0158 mg/L.

Using Environment Canada's IGETA tool, a PEC of 0.0153 mg/L in water due to industrial use was calculated. This was based on conservative assumptions regarding the quantities of chemical used (100 000 kg/year by a single facility), 0.31% loss to sewer, and 57.3% STP removal rate. Using Environment Canada's Mega Flush tool, a PEC of 0 to 0.038 mg/L in water due to down-the-drain releases from consumer product use was calculated. This was based on assumptions regarding quantities of the chemical in consumer products (1 000 000 kg/year), 2.5% loss to sewer, and 0% STP removal rate. Releases to other compartments were not delineated and "quantities sent to sewer could be significantly larger than the amount estimated".

The RQ for industrial discharges was calculated to be 0.9012, using the PEC of 0.0153 mg/L and chronic PNEC of 0.017 mg/L. The consumer release scenario tool predicted that PECs do not exceed the PNEC in 99.7% of water bodies receiving wastewater; however, if we consider the remaining 0.3% the RQ value for consumer product discharges is 2.2 using the PEC of 0.038 mg/L and chronic PNEC of 0.017 mg/L. The assessment then concluded that "zinc BDBP does not have the potential to cause ecological harm in Canada", although this is not considered appropriate given that not all RQs are <1. Furthermore, RQs for sediment were considered the same as in the aquatic compartment. Due to the range of RQs calculated and the amount of uncertainty involved in the calculations (overall environmental concentration and toxicological effects data) of RQs, there may be potential for zinc BDBP to cause ecological harm in Canada.

Health Concerns

A brief health assessment was also conducted, with the use of a LOEL of 884 mg/kg-bw/day (rabbits, dermal exposure) and an estimated maximum total daily in the magnitude of 10^{-3} $\mu\text{g}/\text{kg-bw}/\text{day}$. The result was a MOE in the order of magnitude of 10^8 . The dermal exposure pathway was determined to be the primary route of exposure for consumers. Using a dermal exposure for

consumer products (motor oil) of 0.858 mg/kg-bw, the MOE was 1030. The health assessment was not comprehensive enough to draw conclusions from. It also avoided using a LOAEL of 50 mg/kg-bw/day (oral toxicity), which showed moderate toxicity, and a LOAEL of 100 mg/kg-bw/day (reproductive, developmental and systemic effects) in establishing the MOEs. No attention was paid to vulnerable populations.

Risk Management

None proposed since the chemical is not proposed to be designated as “toxic”.

Recommendations

1. Zinc BDBP should be designated as “toxic” in Canada given that the highest calculated RQ for consumer product use is well-above 1 and the RQ for industrial use is relatively close to 1. Thus, it should be considered a substance that “is 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”.
2. The lack of information on environmental concentrations in Canada is concerning in light of its likely fate and should be addressed. This is particularly concerning given the volume imported for industrial purposes alone. Accurate concentration data is needed to fully evaluate its effects.
3. There is no calculation of off-site releases to the environment from industrial or consumer product waste disposal, even though partitioning into water and sediment from this source is possible. Because of this, release results, although considered conservative, should be interpreted cautiously.
4. The lack of exposure, experimental, or predicted-effects data for non-aquatic organisms in sediment and soil is of concern, due to the chemical’s ability to partition into soil and sediment. A PEC for media other than water should be calculated, particularly since it is persistent in other mediums. **The ongoing characterizing of risk within the aquatic compartment alone is considered unacceptable.**
5. Since zinc BDBP is persistent, further investigations on the biodegradation process are required. Biodegradation may lead to the formation of metabolites that may have toxic properties.
6. Chronic studies on the effects of zinc BPDP exposure in various species are required to fully evaluate the impact of it in organisms and the environment.
7. Cumulative effects from other zinc dialkyldithiophosphates with similar uses should be considered in subsequent assessments. Health effects of these compounds, including zinc BDBP should be further investigated in such an assessment.

MEDIUM PRIORITIES

◆Phosphonium, triphenyl(phenylmethyl)-, salt with 4,4'-[2,2,2-trifluoro-1-(trifluoromethyl)ethylidene]bis[phenol] (1:1) (PTPTT) CAS No. 75768-65-9

Category	Assessment
PBiT and believed to be in commerce in Canada.	Proposed that "PTPTT does not meet any of the criteria set out in section 64 of the <i>Canadian Environmental Protection Act, 1999</i> ".

Manufacture & Use

PTPTT and its dissociation acetate are not naturally produced in the environment. In 2006, no PTPTT was manufactured in Canada above the reporting thresholds, but 100 - 1000 kg was imported in fluoroelastomer precompounds. This was less than the reported amount imported in 2005, although it was anticipated that the upper limit of 2005 (100 000 kg) did not accurately reflect the quantity used. Use and import has reportedly been relatively stable. Definite uses were not reported, but companies importing it appear to be in the automotive, chemical manufacturing, and oil and gas industries. Literature suggests that it is a catalyst present in low concentrations ($\leq 5\%$) in uncured fluoroelastomers precompounds used in rubber processing. This class of rubber may be used for "O-ring seals in fuel, lubricant and hydraulic systems, valves seals and valve liners, firewall, shaft and tire valve stem seals, fuel hoses and fuel injectors O-rings, fuel tanks, diaphragms and gaskets in multiple industries, notably the aerospace and automotive industry." In the US, it is approved for use in making rubber that may contact food.

Releases

Releases are "likely to be very small" although no quantification of releases to air, water, soil release, or transfers to waste management facilities was made within the assessment. Using the Mass Flow Tool, it was estimated that the majority of PTPTT (99.8%) would be chemically transformed during industrial processing. Only 0.1 % was predicted to go to wastewater and only 0.1% was anticipated to go to landfills. There was no information on its release from landfills. Levels in imported products (e.g., food from the US) were not numerically considered.

Environmental Concerns

PTPTT is expected to completely and rapidly dissociate into its BTP cation and BPAF anion upon release into the aquatic environment; therefore, analysis focused on the dissociation products, BTP and BPAF. It is suggested that the majority (>90%) of BPAF will be converted to its neutral form in environmentally relevant water bodies. It will mostly remain in water if released there (a small portion may partition into sediment because of its electrostatic charge), but it will mostly partition into soil if released elsewhere. If released to that soil or air, it will mostly partition into soil as because of its cationic character and low vapour pressure.

Persistence was calculated using the dissociation chemicals BTP and BPAF, as greater than 90% of PTPTT will degrade into these compounds. This approach is considered reasonable. Using modelled data they are both considered persistent in water, soil, and sediment, a conclusion which is supported. Overall, 2 of 5 BTP models and 4 of 5 BPAF models showed the substances

to meet the persistence criteria. LRTP was not reported, but expected to be moderate (305 km) based on the TaPL3 model as in the original substance profile on the Challenge website.

Only one log Kow value was > 5 for BTP. None were > 5 for BPAF. Modelled data showed that neither BTP (ionic form) nor BPAF (neutral form) had BCFs or BAFs >5000 L/kg when correcting for metabolic rate. The highest was a BAF of 3981 L/kg for BPAF and the lowest was a BCF/BAF of 21.13 L/kg for BTP. The use of the ionic and neutral forms was appropriate. The conclusion that these ions do not meet the bioaccumulation criteria is considered appropriate.

Experimental evidence suggests that “the neutral form of BPAF causes harm to aquatic organisms at relatively low concentrations (acute LC/EC50 ≤ 1.0 mg/L).” This is supported considering 3 of 4 studies suggested a LC/EC50 ≤ 1 mg/L. Modelled data suggests that the ionic form of BTP may be less hazardous.

In non-water compartments, BTP may be able to accumulate in “the cytoplasm or mitochondria of mammalian cells where it will likely be persistent and has the potential bind to DNA”. It is also important to note that bisphenol A (BPA) is a BPAF analogue, and the endocrine-disrupting activities of BPAF along with BPA and 17 related compounds have been examined; results suggest that BPAF has greater estrogenic activity than BPA and significantly inhibits androgen activity. Thus, there is evidence that that BPAF causes endocrine disruption and this creates concerns about its release to water, affinity for sediment, and possibility of being applied to agricultural lands.

Ecological Risk

There is no Canadian environmental concentration data, and thus models were used to estimate water concentrations. PECs of 5.94×10^{-5} mg/L for BTP and 5.64×10^{-5} mg/L for BPAF were calculated. These were based on use of the maximum amount of PTPTT imported (1000 kg/yr), use at a single industrial facility, 0.1% loss to wastewater, 0% STP removal rate, and dissociation into 513 kg BTP and 487 kg BPAF. RQs ranged from 9.4×10^{-4} for BTP using a PNEC of 0.063 mg/L (daphnid chronic toxicity value of 6.36 mg/L for daphnid/100) - 0.3613 for BPAF using a PNEC of 1.56×10^{-4} mg/L (experimental toxicity value of 0.156 for algae/1000 “to account for interspecies and intraspecies variability in sensitivity, laboratory to field and endocrine disrupting potential”). The use of a PNEC of 1.56×10^{-4} mg/L is considered appropriate at this point in time since results from the aforementioned studies suggest BPAF estrogenic activity EC50 of 1.68×10^{-2} mg/L. However, this does not negate the fact that further investigation regarding the possible low-dose effects are needed to inform this risk assessment.

Health Concerns

A brief health assessment was also conducted, but MOEs were not calculated. Exposure to the general population is expected to be negligible given the limited amount of PTPTT imported into Canada and the low residual levels in consumer products (i.e., food). Predictions for carcinogenicity, genotoxicity, developmental toxicity and reproductive toxicity were stated as being predominantly negative. Those of BPAF were not mentioned in this context.

Risk Management

None proposed since the chemical is not proposed to be designated as “toxic”.

Recommendations

1. The decision on whether or not PTPTT is “toxic” should be delayed until further experimental data regarding its toxicity to aquatic and mammalian species is made. Considering it may potentially be discharged to soil from the disposal of products that degrade and from biosludge, an improved toxicity assessment for soil organisms should be obtained. Toxicity data for sediment dwelling organisms should be also investigated. There is much concern about its potential to bind to DNA and its greater estrogenic activity than BPA, as substance which has been proposed “toxic” for its ecological effects in Canada.
2. Population exposure needs to be further investigated and a more thorough investigation of its carcinogenicity, genotoxicity, and reproductive toxicity potential in humans should be conducted since current data suggest that these outcomes might be associated with this chemical.
3. Experimental data should be used to determine PTPTT’s, BTP’s, and BPAF’s physical-chemical properties as these values would at least provide more reliable model input and a better understanding of their states in environmentally relevant states. Water solubility of BPAF, octanol-water partition coefficients, and carbon-water partition coefficient would increase the assessment’s certainty.
4. The lack of information on environmental concentrations in Canada is concerning in light of its likely fate and should be addressed. The amount imported within consumer products also needs to be elucidated given use of this substance in other countries. The assessment would be more robust if this information was included.
5. There is no calculation of off-site releases to the environment from industrial or consumer product waste disposal, even though a significant proportion will go to waste disposal and even though partitioning into water and sediment from this source is possible.

***Benzene, 1,3,5-tribromo- CAS No. 626-39-1**

Benzene, 1,2,3,4-tetrachloro-5,6-dimethoxy- CAS No. 944-61-6

Phosphonic acid, [[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]methyl]-, monoethyl ester, calcium salt (2:1) CAS No. 65140-91-2

Fatty acids, C6-C19-branched, zinc salts CAS No. 68551-44-0

Categorization	Assessment
PBiT and believed to be in commerce in Canada.	Proposed that “these substances do not meet the definition of toxic as set out in section 64 of CEPA 1999”, but are recommended for SNAC provisions.

Manufacture & Use

There were no reports of import or manufacture of these chemicals above the 100 kg threshold in 2006. In Canada, they could be used as a colorants, pigments, stains, dyes, and inks for textiles and plastics.

Releases

Given reports on their levels in commerce, exposure is expected to be low.

Environmental Concerns and Ecological Risk

Responses to government notices and questionnaires revealed no new information on the PBiT properties of the substances, and thus the categorization decisions remain unchanged. They are thus considered highly hazardous to aquatic organisms, persistent, and bioaccumulative. LRTPs range from low – high (CAS CAS 626-39-1) according to the original substance profiles.

Risk Management

Their hazardous properties mean there is concern that new activities could lead to the substances meeting the criteria set out in section 64 of the Act. Thus, the application of SNAC provisions under subsection 81(3) of the Act are proposed. These are supposed to ensure that “new manufacture, import or use of these substances in quantities greater than 100 kg/year is notified and will undergo ecological and human health risk assessments” prior to market introduction.

Recommendations

1. Given their PBiT properties and concern that future activities may lead to these substances meeting the criteria for “toxic” under CEPA, application of SNAC is recommended.
2. Re-evaluation of this assessment under the SNAC program is necessary.

*Methane, nitro- (Nitromethane) CAS No. 75-52-5

Categorization	Assessment
Considered to present an intermediate potential for exposure of individuals in Canada and had been classified on the basis of carcinogenicity.	Proposed that "nitromethane does not meet the criteria set out in section 64 of CEPA 1999".

Manufacture & Use

While nitromethane was not manufactured above the reporting threshold in Canada in 2006, 100 -1000 kg was imported alone, in a mixture, or in products. Total use was also in this range. In Canada, it may be used in solvents for vapour degreasing, adhesive removal, dental applications, and in fuel for drag racing cars and model cars, boats, etc.. It has also been found in two professional use cosmetic products (gel eyelash adhesive, false nail remover) listed in the Cosmetic Notification System database. One registered pesticide no longer for sale and with a registration that expires August 1, 2011 contains nitromethane as a List 2 formulant. It may also be used as an intermediate in the making of some pharmaceutical products and thus may be in these products as an impurity. Elsewhere, it may be used in cleaners, rocket fuel, explosives, aerosol can linings, and agricultural fumigants. It may be released via vehicle exhaust, cigarette smoke, soil fumigants, and fungi.

Releases

For 2006, there was no release information to the environment reported, but less than 100 kg was transferred to hazardous waste facilities. Modelling suggests it will primarily remain in the compartment to which it is released. The conclusion that it is persistent in air (based on empirical data showing a half-life of 82 days), water, soil, and sediment (primarily based on empirical data using a 5.1% BOD as 5 of 6 models suggest biodegradation is fast) is supported. LRTP was not stated, but is expected to be high (11 711 km) based on the TaPL3 model as per the original substance profile. Experimental and modelled evidence support a low bioaccumulation potential and low ability to cause harm to aquatic organisms at relatively low concentrations.

Releases to water alone were calculated. An RQ of 0.0009 for industrial use was calculated given a PEC of 0.0026 mg/L (using the IGETA tool, total quantity used by a single facility, 5% loss to sewers, 10 fold STP dilution capacity) and a PNEC of 2.78 mg/L (using lone empirical LC50 of 278 mg/L for the fathead minnow/100 to account for species variability in sensitivity and long-term no-effects). RQs for air were not calculated despite an earlier statement that "most releases would probably be to air". Releases due to consumer product use were not calculated.

Human Exposure

There is no Canadian concentration data. Using empirical data from elsewhere, the maximum daily intake from environmental media and food was 6.1 µg/kg-bw per day for (0.5 and 4 years); air being the predominant exposure source (using ambient air concentration of 10.0 µg/m³ from Brazil, 1996-1997) with other media only contributing 0.090 µg/kg-bw per day to the maximum total intake (levels in soil and water were considered to be negligible/non-applicable, a maximum concentration of 1.4 µg/L was "assumed to be the concentration of nitromethane for 3 of 12 food categories"). It has been qualitatively detected at unspecified concentrations in breast milk and drinking water. In terms of consumer products, inhalation was considered the main exposure

route as it is not readily absorbed. Exposure estimates were only calculated for one of the two personal care products; the inhalation time-weighted average event exposure of 13 mg/m³ was determined for false nail remover (use frequency of 17 events/year, well-mixed room, inapplicable model, concentration of 25% by weight). Exposure via eyelash adhesive remover (concentration of 100% by weight) was not calculated because exposure was anticipated to be lower than the false-nail remover scenario (less used, less exposure duration). Exposure via adhesive remover, industrial solvents for removing flux, dental crowns, dry cleaning were not calculated for various reasons. That for the refilling of model engines was considered negligible. Data from an occupational study (showing a maximum 8-hour time-weighted average air concentration of 50 mg/m³ at a headlight manufacturing facility) was not used to estimate exposure. No attention was paid to vulnerable population exposures beyond children.

Health Concerns

Nitromethane has been classified as an IARC Group 2B carcinogen and is “reasonably anticipated to be a human carcinogen” by the US NTP.

Carcinogenicity is considered nitromethane’s critical effect. This is based on clear evidence of carcinogenic activity in a certain strain of mice and in female rats and chronic inhalation exposure shows “significantly increased incidences of benign and malignant tumours at multiple sites in both sexes of mice and in the mammary glands of female rats”. Of the studies, the lowest dose with effects was 470 mg/ m³. The mode of action for carcinogenicity has not been elucidated, but it has been hypothesized that “reactive radicals may be involved...because nitromethane metabolism yields intermediate superoxide radicals, hydrogen peroxide, nitrite, formaldehyde and/or acetone”. It is also possible “that the parent molecule promotes tumour growth through a direct effect on the cell”.

It was not shown to be genotoxic in *in vitro* or *in vivo* assays; “however, at the two highest concentrations tested and without S9 activation, nitromethane caused morphological transformation of Syrian hamster embryo cells”.

In terms of non-cancer effects, nitromethane has been associated with reduced body weight, nasal congestion at high acute exposure levels (LOEC 2495 mg/m³). At even higher levels unresponsiveness and lethality were observed. Liver effects (increased liver weights) following short term inhalation or oral exposure were seen (LOEC 235 mg/m³). Hyaline droplet formation in the respiratory epithelium and increased kidney weights were seen at a subchronic inhalation (LOEC 235 mg/m³). Liver impairment occurred in both rats and rabbits exposed for 2 months via drinking water (LOEC 23.5 mg/kg-bw per day). The LOAEC for reproductive effects is ≤ 938 mg/m³ based on a study showing increased in estrous cycle length at this dose and greater. In occupational studies, severe toxic effects (neurotoxicity) from inhalation exposure to nitromethane were seen at 1996 mg/m³ for 1 hour, with symptoms of illness being seen at 1248 mg/m³.

The calculated MOEs were as follows. Neither exposures via other consumer products nor cumulative exposure to consumer products and environmental media were considered.

- 23 500 (maximum air concentration of 10.0 µg/m³, lowest LOEC of 235 mg/m³ for hyaline droplet formation and increased absolute and relative kidney weights)
- 93 800 (maximum air concentration of 10.0 µg/m³, subchronic LOAEC of 938 mg/m³ for more adverse effects, including neurotoxicity in rats)

- 100 (off gasing of 13 mg/m³ from false nail remover, acute inhalation rat LOEC of 2495)
- 200 (off gasing of 13 mg/m³ from false nail remover, acute inhalation human LOEC of 1248 mg/m³)

Risk Management

None proposed since the chemical is not proposed to be designated as “toxic”.

Recommendations

1. Given its carcinogenicity and concern that new activities could lead to nitromethane meeting the criteria set out in section 64 of the Act, subjection of nitromethane to the SNAC provisions specified under subsection 81(3) of the Act should be thoughtfully considered.
2. Any re-evaluation of this assessment should fill current data gaps:
 - a. Studies using multiple doses and multiple, human-relevant species that address long-term inhalation exposure.
 - b. Studies further elucidating the toxicokinetics and metabolism of nitromethane and its metabolites in multiple species.
 - c. Studies that reliably determine the concentration in Canadian environmental media.
 - d. Studies that more accurately determine the population’s exposure via consumer products. While there is substantial concern over the low MOEs for false nail removal, it is acknowledge that the general population is not likely to be exposed via this and that exposure in the hazard studies was for a longer duration than the potential exposure period within this scenario.
 - e. Studies investigating occupational exposures (particularly, carcinogenic effects following chronic low dose exposure) and other vulnerable population exposures.

LOW PRIORITIES

Benzenepropanoic acid, 3,5-bis(1,1-dimethylethyl)-4-hydroxy-, (1,2-dioxo-1,2-ethanediyl)bis(imino-2,1-ethanediyl) ester (Benzenepropanoic acid ester) CAS No. 70331-94-1

Categorization	Assessment
PBiT and believed to be in commerce in Canada.	Proposed that "benzenepropanoic acid ester does not meet any of the criteria set out in section 64 of the <i>Canadian Environmental Protection Act, 1999</i> ".

Manufacture & Use

Benzenepropanoic acid ester is not naturally produced in the environment. In 2006, a total of 153 kg was imported, but there was no information on whether or not it was manufactured here during that year. In 2005, there were no reports of manufacture. It is an EU LPV. 2006 imports were contained in chlorinated polyvinyl chloride (CPVC) powder used in sheet, profile, and extrusion/injection molding. Most of it was sold to a maker of plastic piping. It may also be used to stabilize other types of plastics. It is not known to be used in consumer products, but CPVC products are used in mass transit, aerospace, fenestration, heating/ventilation/air conditioning, pool and spa, electrical components, irrigation, and mining industries. Health Canada has not received any submissions regarding its use in plastics used for food packaging since 1982.

Releases

No company reported air, water, soil releases, or transfers to waste management facilities. Using the Mass Flow Tool and the imported amount in 2006, it was estimated that the majority of benzenepropanoic acid ester (89.2%) would end up in waste disposal sites. There was no information on its release from the waste management sites, although such is not expected given the substance's affinity for soil and sediment. Another 4% is likely to go to wastewater, 4% to recycling, and 2.8% to incineration. Although levels in imported products were not numerically considered, it was stated that "quantities released to the environment and sent for waste management would be higher if importation of these items were taken into consideration."

Environmental Concerns

Benzenepropanoic acid ester is considered to be non-volatile, as its modelled and experimental vapour pressures are low. It is also expected to have high adsorptivity to soil. Thus, if released to air or soil, it will primarily partition into the latter. Given its high estimated log K_{oc}, it will strongly adsorb to sediment when released into water. The portion partitioning to water bodies at environmentally relevant pH (6–9) will remain undissociated.

Modelled data suggests that it is persistent in water, soil, and sediment. Modelled and empirical analogue data (using two ester analogues with empirical data that "are similar to approximately half of the dimer benzenepropanoic acid ester") suggests that it will not hydrolyze and biodegrade rapidly. LRTP was not noted, but was predicted to be moderate (477 km) in the original substance profile on the Challenge website based on the TaPL3 model.

Although its log Kow value of 6.68 suggests that it will bioaccumulate, modelled data suggest it does not meet the bioaccumulation criteria. The Arnot-Gobas model produced a BAF of 0.98 L/kg and a BCF of 0.95 L/kg, while two additional models produced two BCFs (6.7 L/kg and 300 L/kg). Analogue data was not used to support or refute the conclusion that it is not bioaccumulative.

A weight-of-evidence approach suggested that it can “cause harm to aquatic organisms at relatively low concentrations”. This is based on modelled and empirical evidence for the two analogues. All but one value derived from the modelled data for benzenepropanoic acid ester support this conclusion, as do most of the analogues empirical evidence which included a LOEL of 0.00018 mg/L for algae for one of the two analogues. The conclusion is supported. Only ecological effects in water were investigated.

Ecological Risk

There is no Canadian environmental concentration data, and thus models were used to estimate water concentrations. Using Environment Canada’s Industrial Generic Exposure Tool – Aquatic (IGETA), a PEC of 2.1×10^{-6} mg/L in water due to industrial use was calculated. This was based on conservative assumptions regarding the quantities of chemical used (153 kg/year by a single facility), a sewer loss of 0.055%, and STP removal rate of 78.7%. Releases due to use of consumer products were not calculated, but anticipated to be disperse and low.

The RQ for industrial discharges was calculated to be 0.1, using the PEC of 2.1×10^{-6} mg/L and a PNEC of 0.000018 mg/L (divided the LOEL of 0.00018 mg/L for algae by 10 to account for species variations). It was concluded that “benzenepropanoic acid ester has low potential to cause ecological harm to aquatic organisms in Canada.”

Health Concerns

A brief health assessment was also conducted. Human exposure is predicted to mostly occur via food from packaging migration. Using the oral exposure LOEL for liver effects of 2000 ppm (60 mg/kg-bw per day) for the analogue CAS 732-26-3 and the estimated probable daily intake (PDI) of 20 µg/kg-bw from food packaging, the MOE was 3000. No attention was paid to vulnerable populations

Risk Management

None proposed since the chemical is not proposed to be designated as “toxic”.

Recommendations

1. Reduce reliance on modelled and analogue data, particularly in terms of benzenepropanoic acid ester’s physical and chemical properties as these values would at least provide more reliable model input than the analogue data. Increased reliance should also be given to experimental (empirical) data for the rate of degradation in anaerobic sediments, the degree to which degradation occurs, and bioaccumulation potential.
2. Verify conclusions on bioaccumulation using experimental data, or at the very least, analogue data.

3. The lack of information on environmental concentrations in Canada is concerning in light of their likely fate and should be addressed. The amount imported within consumer products also needs to be elucidated given use of this substance in other countries. Although end uses in such products would be incredibly small, release quantities would be higher and the assessment more robust if this information was included.
4. There is no calculation of off-site releases to the environment from industrial or consumer product waste disposal, even though waste disposal is where most of it will end up, and even though partitioning into water and sediment from this source is possible.
5. Considering it may potentially be discharged to soil from the disposal of products that degrade and from biosludge, toxicity data for soil organisms should be obtained. This is of particular importance since it has been shown that dyes strongly adsorb to wastewater treatment plant sludge and particulates. Toxicity data for sediment dwelling organisms should be also investigated.
6. Since benzenepropanoic acid ester is persistent, further investigations on the biodegradation process are required. Biodegradation may lead to the formation of metabolites that may have toxic properties.

Appendix A- Glossary of Abbreviations

CEPA	Canadian Environmental Protection Act, 1999
EC/EU	European Commission/European Union
IARC	International Agency for Research on Cancer
HVIC	High volume industrial chemical (Australia)
HPV	High production volume chemical – those reported to be produced or imported at levels greater than 1,000 tonnes per year in at least one Organization for Economic Co-operation and Development (OECD) member country or levels greater than 1 million pounds or more per year in the U.S.
MOE	Margin of exposure - the ratio between levels causing effects and levels of human exposure
LOAEL	Lowest-observed-adverse-effect level - lowest concentration which causes an adverse effect
LOEC	Lowest-observed-effect-concentration - lowest concentration which causes an effect
PBiT	Persistent, bioaccumulative, and inherently toxic
PMRA	Pest Management Regulatory Agency
RQ	Risk quotient - the ratio between the levels below which exposure is not expected to have an effect (PNEC) and the predicted environment levels (PEC)
SNAc	Significant New Activity provisions under subsection 81(3) of CEPA
TSL	Toxic Substances List (Schedule 1 of CEPA, 1999)
US EPA	US Environmental Protection Agency
US NTP	US National Toxicology Program
LRTP	Long-range transport potential - as per the TaPL3 model, > 2000 km = high LRTP, 700 – 2000 km = moderate LRTP, < 700 km = low LRTP
PEC	Predicted environmental concentration
PNEC	Predicted no-effect concentration - the predicted concentration below which exposure to a substance is not expected to cause adverse effects
NOAEL	No-observed-adverse-effect-level – the concentration at which there is no adverse effect
NOEC/NOEL	No-observed-effect-concentration, no-observed-effect-level – the concentration at which there is no effect

Appendix B- Glossary of International Classifications

<i>Carcinogenicity</i>	
IARC Group 1	Carcinogenic to humans
IARC Group 2A	Probably carcinogenic to humans
IARC Group 2B	Possibly carcinogenic to humans
IARC Group 3	Not classifiable as to its carcinogenicity to humans
IARC Group 4	Probably not carcinogenic to humans
US EPA Group A	Carcinogenic to humans
US EPA Group B	Likely to be carcinogenic to humans
US EPA Group C	Suggestive evidence of carcinogenic potential
US EPA Group D	Inadequate information to assess carcinogenic potential
US EPA Group E	Not likely to be carcinogenic to humans
US NTP	Reasonably anticipated to be a human carcinogen
EC Category 1	Substance known to be carcinogenic to man
EC Category 2	Regarded as if carcinogenic to humans
EC Category 3	Causes concern for humans owing to possible carcinogenic effects
<i>Reproductive toxicity</i>	
EC Category 1	May impair fertility - human evidence
EC Category 2	May impair fertility - animal evidence
EC Category 3	Possible risk of impaired fertility
<i>Developmental toxicity</i>	
EC Category 1	May cause harm to the unborn child - human evidence
EC Category 2	May cause harm to the unborn child - animal evidence
EC Category 3	Possible risk of harm to the unborn child