Chemical Management Plan Batch 7 Challenge Substances Submission

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November 2, 2009

Ottawa, Canada

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Submission - Batch 7 Challenge Substances

November 4, 2009
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Re: Comments on draft screening assessments, and where applicable, the accompanying risk management scope for specific Batch 7 substances (Canada Gazette Part I, Vol. 143 No. 36 September 5, 2009).

Detailed comments are given for two substances, namely

- 2-Butanone, oxime (butanone oxime) CAS No**.** 96-29-7
- 1,4-Dioxane CAS No. 123-91-1

Introductory Remarks

ITK's participation in the Chemical Management Program (CMP) has, among other avenues, included the Stakeholder Advisory Council and the CMP Civil Society Capacity Building Project. ITK has also been following the Challenge Program and to date, has made submissions on a select number of substances in Batches 4, 5 and 6.

As in its previous submissions, ITK continues to emphasize that fundamental principles, including the precautionary principle, pollution prevention, and consideration for vulnerable populations, are essential components of the assessments and risk management strategies.

ITK is mainly concerned about the harm these substances might cause to Inuit people and their environment as a result of the substances' potential for long-range transport and their inclusion in products and processes that may be used by Inuit. While the comments submitted by ITK cover a broad range of issues on these chemicals, they are also channelled through an "Inuit lens" which includes;

- Waste disposal - releases to the environment resulting from waste disposal methods and wastewater/sewage treatment methods (e g., incineration, landfill, etc.);
- Resource extraction activities – releases to the environment from the use of chemicals in these activities;
- Food - chemicals ingested either due to consumption off the land or due to consumption of commercially bought foods;
- Chemicals found in personal use products, pharmaceuticals, house-cleaning materials and other products likely to be used in the household (lubricants, etc.) and in industrial products (disposed via land fill sites – e.g., computer/machine components);and
- Long-range atmospheric transport - chemicals released into the environment that may reach Inuit lands via this route.

A. Batch 7 – Overview

The draft screening assessments for batch 7 substances have proposed that three out of the fourteen substances meet the criteria for toxicity under the *Canadian Environmental Protection Act 1999* (CEPA 1999), because they may be entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health. One of these substances, butanone oxime, is of particular interest to ITK as it has been identified as having potential for long-range transport.

For the five substances (pigments and dyes) that are persistent, bioaccumulative and inherently toxic (PB iT) in Batch 7, the assessments have recommended that they be subject to Significant new Activity (SNAc) provisions under Section 81(3) of CEPA 1999. The rationale for this is that they are but not presently are not in commerce in Canada and not entering the environment, but could potentially pose harm if they re-enter commerce in Canada.

The remaining batch 7 substances were not considered to meet the criteria for toxicity under CEPA 1999. Four of these are dyes (but not PBiT). The other two substances, 1-4 dioxane and Isophorone, are categorized as Category 3 carcinogens by the European Union (i.e., substances which cause concern for humans, owing to possible carcinogenic effects) and similarly by other agencies.

An unfortunate element of the screening assessment process is that it does not account for cumulative or long-term exposure. Many batch 7 substances are pigments and dyes and are found in numerous commonly-used products in the household (paints, etc.).

Even though some of these substances may no longer be in commerce, they are likely still in products being used or in products that have been disposed of in some manner, such as incineration. It is also likely that these products are used in communities, and possibly isolated northern communities, where social conditions and considerations could result in the use of products that are no longer on the market in urbanized communities in Canada, which is naturally of concern to ITK.

In all its submissions, ITK has stressed that any substance that is a known, suspected or potential carcinogen be designated toxic under CEPA 1999, and consequently appropriate measures are required to restrict and/or ban the use and importation of this substance or products containing it. The same concern holds for substances that are known or suspected genotoxins, mutagens, reproductive and developmental toxins.

ITK is duly concerned that two substances with possible carcinogenic effects (1-4 Dioxane and Isophorone) have not been proposed toxic.

For its submission on Batch 7, ITK is providing comments specifically on the draft assessment of 1-4 dioxane, in anticipation that the issues raised will be considered in the final screening assessment. The concerns ITK has regarding Isophorone are similar in nature.

Case 1: 2-Butanone, oxime (butanone oxime)

Part 1

a. Overview – Draft Screening Assessment and Conclusions

Under the categorization exercise, butanone oxime was identified as posing the greatest potential for exposure of individuals in Canada. It has been classified by other agencies on the basis of its carcinogenicity and thereby designated a high priority substance under the Challenge Program. While it met the ecological categorization criteria for persistence, it did not meet the criteria for bioaccumulation potential or inherent toxicity to aquatic organisms. Therefore, the focus of the screening assessment for butanone oxime relates primarily to human health risks.

On the basis of the potential inadequacy of the margins between estimated exposures to butanone oxime and critical effect levels, the assessors propose that butanone oxime meets the criterion for toxicity under section 64(c) of CEPA 1999, that is, it may be entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health. Butanone oxime has been proposed for addition to the List of Toxic Substances, Schedule 1, CEPA 1999.

Based on the available information, the draft screening assessment finds that butanone oxime does not have an immediate or long-term harmful effect on the environment or its biological diversity, or that constitute or may constitute a danger to the environment on which life depends and thus does not meet the criteria for toxicity under sections 64(a) and 64(b).

In addition, while butanone oxime meets the criteria for persistence in air, but not in any other media, the assessors conclude that it does not meet the bioaccumulation criteria as set out in the *Persistence and Bioaccumulation Regulations,* 2000.[1]

ITK's comments on butanone oxime include a summary of its uses as they may be pertinent to Inuit. The comments summarize aspects of the draft screening assessment that relate to the exposure pathway, health aspects and other issues of concern. As well, ITK is commenting on the risk management scope document.

ITK is particularly interested in the impacts that butanone oxime may have in Inuit communities due to its potential for long-range transport.

b. Manufacturing and Uses

Since butanone oxime is not a naturally occurring substance, its presence in the environment results directly from human activity. Butanone oxime is widely used in numerous diverse products and processes, such as,

- The formulation of alkyd paints, varnishes, stains and coatings for both industrial and

[1] *Canadian Environmental Protection Act: Persistence and Bioaccumulation Regulations*, P.C. 2000-348, 23 March 2000, SOR/2000-107. http://www.gazette.gc.ca/archives/p2/2000/2000-03-29/html/sor-dors107-eng.html

- In Canada, butanone oxime has been reported in a number of pesticide products (for example, wood preservatives and antifouling marine paints), as well as in some adhesives, silicone sealants, printing inks and artist paints.
- It is used as a corrosion inhibitor in industrial boilers and water treatment systems and serves as a blocking agent in the manufacturing process of urethane polymers.[2]

While butanone oxime is found in some printing inks used in the manufacture of food packaging materials, the assessors indicate that there is no direct contact of butanone oxime with food.

Butanone oxime is considered a high production volume chemical (HPV) by the Organisation for Economic Co-operation and Development (OECD), the US EPA and the European Commission (EC). Worldwide production is estimated at between 10 000 and 20 000 tonnes per year.

While butanone oxime was not manufactured by any company in Canada in 2006, imports of the substance into Canada above the reporting threshold of 100 kg were approximately 500 000 kg in the same year and nearly 120 000 kg (reporting threshold of 1000 kg) was used that year. Both import and use amounts are considerable for the Canadian market.[3]

The use of butanone oxime in cosmetics is prohibited in Denmark and in the United Kingdom. In Canada, no current use in cosmetics has been notified. Further, butanone oxime is subject to the *Pest Control Products Act* and is categorized as a List 2 Formulant on the Pest Management Regulatory Agency (PMRA) List of Formulants (published on June 28, 2007). [4]

c. Releases

The high volume of butanone oxime imported into Canada, together with its diversity of use in a variety of consumer products, indicate potential for widespread release into the Canadian environment. However, there are few data on the release and fate of butanone oxime in environmental media in Canada or elsewhere, as noted by the assessors.

While there were no reports of any significant industrial releases of butanone oxime in 2006, the Canadian Chemical Producers' Association reported the release of 356 kg to the environment in 2007. [5] It should be noted that the National Pollutant Release Inventory (NPRI) does not require reporting of releases of butanone oxime.

d. Persistence and Bioaccumulation

Based on the empirical and modelled data, butanone oxime meets the persistence criterion in air (half-life in air ≥2 days), but not for water, soil or sediment as set out in the *Persistence and Bioaccumulation Regulations*.

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[2] Draft Screening CAS 96-29-7, September 2009 - p.8,9

[3] The amounts used were determined through information submitted by industry under section 71 of CEPA 1999

[4] Risk Management Scope Document for butanone oxime September 2009, p.4. A List 2 designation elevates the priority for reassessment within the PMRA.
http://www.ec.gc.ca/substances/ese/eng/challenge/batch7/batch7_96-29-7_rm_en.pdf

[5] Draft Screening Assessment for butanone oxime p.9

On the basis of modelled data, butanone oxime is expected to have a moderate long-range transport potential, that is, the maximum distance travelled by 63% of butanone oxime is 1376 km.[6] Experimental data "suggest" a low potential to bioaccumulate.

e. Ecotoxicity

The toxicity data indicate that butanone oxime has a moderate potential to be toxic to algae and a low potential for most other aquatic organisms. If released to water, butanone oxime is expected to remain mainly within water. Considering the low hydrolysis rate of butanone oxime, the assessment indicates that hydrolysis products are not expected to pose a threat to the ecosystem. The assessment concludes that butanone oxime is unlikely to be causing ecological harm in Canada, noting "this conclusion was reached despite the conservative assumptions that were made in response to uncertainties encountered in the assessment."[7]

f. Human Health Concerns

Carcinogenicity was considered in the health effects assessment for butanone oxime, as the substance had been classified as a Category 3 carcinogen (*causes concern for humans owing to possible carcinogenic effects*) by the European Commission (EC). The EC suggests that butanone oxime may cause cancer in male rats and mice via metabolism to a carcinogenic agent, but have not indicated whether carcinogenicity was due to threshold mechanisms.

Increased incidences of liver tumours have been observed in animal lifetime studies, as well as an increased incidence of mammary gland tumours in female rats. However, these incidences were observed only at mid- and/or high concentrations of butanone oxime. Therefore, the assessment used a threshold approach to assess risk to human health.

Although the mode of induction of tumours is not fully elucidated, the assessment views that tumours observed are not considered to have resulted from direct interaction with genetic material, indicating that butanone oxime is not likely to be genotoxic.

While the majority of assays (including oral and inhalation assays) have suggested it is not mutagenic, other assays have suggested otherwise.[8] In addition to its carcinogenic effects, butanone oxime has been shown to cause dose-related increases in liver hypertrophy and necrosis in rodents via inhalation, and olfactory epithelium degeneration in the nasal passageway. It has also been shown to cause effects in the spleen, blood, and testes at differing doses.

Animal studies show that butanone oxime is rapidly absorbed from the gastrointestinal tract, undergoes widespread uptake, distributes over the entire body, is extensively metabolized and does not accumulate in tissues. Excretion of butanone oxime and its metabolites occurs in the urine and bile or as volatiles in expired air.[9]

While exposure of the "general population" to butanone oxime is considered to be most likely from the use of consumer products, mainly alkyd paint products, uncertainty is associated with

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[6] Ibid p.11,12 Characteristic travel distances of >2000 km as representing high long-range transport potential, 700–2000 km as moderate and <700 km as low.

[7] Ibid p.19

[8] Mutagen: a physical or chemical agent that changes the genetic material (usually DNA) of an organism and thus increases the frequency of mutations. A genotoxin is capable of causing damage to DNA.

[9] Draft Assessment p.19

the use of non-Canadian-specific default assumptions in the modelled consumer product exposure scenarios.

Part 2

Summary of Issues – Draft Assessment

Numerous deficiencies, contradictions and data gaps noted in the draft assessment, for example;

Manufacture and Use:
The difference between the amount imported (500 000 kg) and used (120 000 kg) in one year is substantial. The different thresholds under Section 71 CEPA 1999 for reporting import amounts (100 kg) versus use (1 000 kg), may be a contributing factor but this cannot be assumed. An explanation is needed to account for this.

Releases:
Overall, the amounts of butanone oxime released to air, water, and land, or the amounts disposed of from industrial process, or consumer products use are virtually unknown.

ITK notes that no environmental monitoring data was available. Furthermore, butanone oxime is not reported to the NPRI and there are no other mandatory reporting requirements that would determine releases to the environment or disposal amounts. Yet the assessment expects that the total industrial releases of butanone oxime are low, and that the most significant releases of butanone oxime are expected to take place at the consumer use stage. Without any solid information and data about releases, such expectations are unfounded.

Persistence:
(i) Long-range transport: Butanone oxime persists in air and there are strong indications that it could travel well beyond 1000 km. This is of particular concern to ITK. But there is no further indication of interest to explore the impact of long-range transport, the likelihood of travelling to the far north and the impact of its deposition.

(ii) The report notes that uncertainties exist regarding the conclusion for persistence in water, soil and sediment. Very limited empirical data was available to estimate approximate half-lives in these media and some models were contradictory. Despite that, the assessors conclude that "the weight of evidence, considering both the empirical and modelled data, indicates that this substance does not meet the persistence criteria for water, soil or sediment." [10]

Ecotoxicity:
The report notes that **e**xposures near point sources are expected to be highest in the aquatic compartment, and aquatic organisms are expected to be among the most sensitive to this substance. However, no toxicity data were found for the organisms in the soil or sediment compartments. Furthermore, the significance of soil and sediments as important media of exposure is not well addressed by the effects data available.

ITK finds the information on ecotoxicity confusing and deficient and questions how any conclusions can be drawn based on the above somewhat contradictory statements above, for example.

[10] Ibid p.14

Human Health:
The draft screening assessment of butanone oxime, as noted by the assessors, does not include a full analysis of the mode of induction of effects, including cancer. Only limited information is available concerning the potential toxicity of butanone oxime following oral and dermal exposure. Other significant gaps and deficiencies identified in the assessment include:

- Lack of reproductive and developmental toxicity studies based on inhalation exposure;
- Lack of chronic toxicity/carcinogenicity studies based on oral exposure;
- Limited *in vivo* genotoxicity data and a lack of dermal studies for several endpoints except for acute exposures;
- No clinical human toxicity or epidemiological studies were identified.
- There are inherent uncertainties in the interpretation of intraspecies and interspecies variation.[11]
- Modeling was only conducted for only six products and cumulative exposures were not taken into account.
- The assessors indicate that there is no direct contact of butanone oxime with food, despite it being found in some printing inks used in the manufacture of food packaging materials. No evidence is available to support this supposition.

These gaps and uncertainties are very limiting to interpreting the biological significance of the effects of exposure to butanone oxime from environmental media and food in Canada. As a result, the margins of exposure, at least for the so-called general population, are not protective.

Thresholds for Exposure:
Another important matter concerns the potential assumption that there is a threshold for observing carcinogenic effects from exposure to butanone oxime. ITK strongly recommends that a precautionary approach be taken, particularly in light of the lack of the gaps and uncertainties, and adopt a "non-threshold" approach for this substance. Furthermore, one cannot look at its exposure in isolation, considering the numerous other potential carcinogens to which the population is exposed.

Populations – General and Vulnerable:
Typically, assessments have looked at the exposure and intake of the "general populations", including infants and children. But as stated in the draft assessment, "due to the lack of empirical data on concentrations in several media, estimates of daily intake for the "general population" were not derived." [12]

And once again, there is absolutely no mention, let alone consideration, for the range of vulnerable populations that are potentially exposed to this substance. This includes young children, pregnant women, First Nations, Métis and Inuit peoples and disadvantaged, isolated communities. As well, no attention is paid to occupational exposures.

Substitution:
There is no indication that efforts will be made to pursue substitution with safer alternatives were examined.

[11] Ibid p.21
[12] Ibid p.15

Part 3

Comment on Proposed Risk Management Scope

The government proposes to recommend the addition of butanone oxime to the List of Toxic Substances in Schedule 1. If the final screening assessment report concludes that butanone oxime meets the criteria under section 64 of CEPA 1999, options for risk management would focus on "reducing the amounts of butanone oxime to which the general population will be exposed during the application of consumer products containing butanone oxime, including alkyd paints, primers, varnishes and stains." It is also proposing to add butanone oxime to the *Environmental Emergencies Regulations*.[13]

ITK finds this scope limiting in that it addresses only the "general population" and only specific consumer products. It does not even consider long-range transport effects.

Certainly the numerous data gaps and deficiencies that have been detailed in its submission need to be acknowledged and addressed to ensure that risk management actions are effective in protecting human health for all populations.

Some of these gaps that need to be filled include:

i. Concentrations within Canadian environmental media, specific consumer products, and food should be established. Furthermore the "significance of soil and sediments as important media of exposure is not well addressed by the effects data available".

ii. Releases and disposal of butanone oxime (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. That no significant releases were reported, aside from industry data, is of concern given its persistence and air and toxicity to humans.

iii. More experimental data regarding its carcinogenicity should be acquired for chronic exposures beyond inhalation.

iv. Data gaps pertaining to reproductive and developmental toxicity via inhalation, *in vivo* genotoxicity, and non-carcinogenic effects via dermal exposures should be filled.

v. Attention needs to be paid to determining vulnerable population exposures given the processing and use of this chemical.

vi. The assumption that there is no exposure through food must be tested – as this substance is found in some printing inks used in the manufacture of food packaging materials.

vii. Efforts should be made to seek potential substitution with safer alternatives.

viii. Releases of butanone oxime to all environmental should be reported (via the NPRI) at an appropriate threshold.

[13] Risk management Scope Document for butanone oxime September 2009, http://www.ec.gc.ca/substances/ese/eng/challenge/batch7/batch7_96-29-7_rm_en.pdf

ix. The amount of butanone oxime imported annually and used should be examined to fill in any inconsistencies.

The main issues that ITK would want to see addressed in the final assessment and in the risk management include:

- Vulnerable populations, including children, who are potentially exposed through the use of products containing butanone oxime and from potential leaching;
- Given that butanone oxime has the potential for long-range transport, the ensuing impacts on receiving communities, likely northern communities, need to be examined.
- The impact of the disposal of products containing butanone oxime and potential releases from disposal methods, whether through incineration, or in other wastestreams; and
- The potential for contamination of food through food packaging materials containing butanone oxime.
- A re-examination of the ecotoxicity effects of butanone oxime, as the draft assessment was lacking in appropriate data. This would include re-assessing the findings on bioaccumulation.
- Reporting and monitoring environmental releases through an appropriate public reporting system (e.g., NPRI).

Case 2: 1,4-Dioxane CAS No. 123-91-1

Part 1: Overview

ITK is very concerned about the conclusions formulated in the draft screening assessment. Accordingly, the assessors have proposed that 1,4-dioxane does not have or may not have an immediate or long-term harmful effect on the environment or its biological diversity or that constitute or may constitute a danger to the environment on which life depends.

Further, 1,4-dioxane is not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health, based on adequacy of the margins of exposure.

The consequent proposal is that 1,4-dioxane does not meet any of the criteria in section 64 of CEPA 1999. As a result, no risk management scope has been prepared.

While 1,4-dioxane does meet the criteria for persistence (in water, soil and sediment), it does not meet the criteria for bioaccumulation potential as set out in the *Persistence and Bioaccumulation Regulations.*

Several agencies have classified 1,4-dioxane as a carcinogen. For example, it is has been classified as a Group 2B carcinogen by the International Agency for Research on Cancer (IARC) (possibly carcinogenic to humans); a Category 3 carcinogen by the EC (possible carcinogenic effects); a Group B2 (Probably Carcinogenic to Humans) by the US EPA; and is "reasonably anticipated to be a human carcinogen" by the US National Toxicology Program (NTP).

So it begs the question as to how the draft assessment could have arrived at its proposed recommendation, and apparently dismisses the carcinogenicity categorization by other bodies.

The findings of the draft assessment are not definitive nor are they sufficiently compelling to determine that 1,4-dioxane is not CEPA-toxic.

ITK is strongly urging the government to re-consider the recommendations of the draft assessment, particularly, given the prolific use of 1,4-dioxane, and especially in products used by women and applied to children.

The following sections highlight aspects of the draft screening assessment, including uses, exposure and health effects, and includes comments in each section, as deemed necessary and appropriate.

Part 2: Draft Screening Assessment for 1-4-Dioxiane – Review and Issues

a. Manufacture & Use

1-4-Dioxiane has a broad and diverse range of uses in products and processes. Historically, it was used predominantly as a stabilizer for 1,1,1-trichloroethane. This function has been phased out due to controls placed on 1,1,1-trichlorethane use under the Montreal Protocol.

Currently, 1,4-dioxane is used extensively as a solvent for pharmaceutical processing and research and development, and as an analytical reagent for laboratory use in Canada. It is used as a carrier solvent in the manufacture of pharmaceuticals, veterinary drugs and natural health products. 1,4-Dioxane is also a component of industrial agents used as corrosion inhibitors, antioxidants and heavy equipment degreasers.

Residual 1,4-dioxane is formed during the production of ethoxylated substances that are used in a variety of applications (e.g., cosmetics, detergents, food packaging, agricultural products and industrial processes). In Canada, ethoxylated substances containing 1,4-dioxane as a by-product are produced and used as surfactants, emulsifiers, wetting agents and foaming agents in various industries.

1,4-Dioxane is also found as an impurity in 168 pest control products with food and/or non-food uses; solvents used in making food packaging materials; and polysorbates 80, 65 and 60 and polyethylene glycol.

No natural source of 1,4-dioxane have been identified. However, limited data indicate that it is a natural constituent in some food items. It is not known whether this occurrence results from natural production or contamination, as 1,4-dioxane is known to be an impurity in ethoxylated food additives and pesticides. [14]

In Canada, 10 000 -100 000 kg was manufactured, 10 000 - 100 000 kg was imported, and the same amount was used in 2006.

1,4-Dioxane is listed on the Cosmetic Ingredient “Hotlist”, in which its intentional use as an ingredient in cosmetics is prohibited, but its presence as an impurity is not listed.

b. Releases to the Environment

Information submitted by industry under the Section 71 notice of CEPA 1999 indicate that 10 000 - 100 000 kg of 1,4-dioxane was released, the majority to water and air, into the environment

[14] Draft Screening assessment 1,4-Dioxane CAS RN 123-91-1 September 2009 pp.4 - 6

in 2006. According to reports to the National Pollutant Release Inventory (NPRI) for 2006, 13 800 kg was released to air and 6 500 kg was released to water, and none reported to land.

In addition, information obtained under Section 71 reveal that 71 100 - 1000 kg was transferred to hazardous waste facilities and less than 100 kg was transferred to non-hazardous waste facilities.

In the US, 56 000 kg was released to air, 22 000 kg to water and 64 000 kg were released by underground injection in 2006. [15] The emissions to air and water in Canada are more than one-quarter of the reported US figures, which could indicate a relatively wide use in Canada.

- The disparity in releases of 1,4-dioxane via underground injection in the US and no reported land releases in Canada requires explanation.
- Use patterns in other countries should be compared with that in the US and Canada.
- Limitations from thresholds and criteria for industries required to report 1,4-dioxane to the NPRI may result in an incomplete picture of releases of adequately.

c. Persistence and Bioaccumulation

1,4-Dioxane resides primarily in the environmental compartment (air, water, or soil) to which it is released. It is not considered persistent in air, but is in water, soil, and sediment. It is anticipated to have low LRT potential for long-range transport, given the maximum distance travelled by 63% of the substance is 95 km. The assessors indicate that it is unlikely to bioaccumulate or harm aquatic organisms at low concentrations. [16]

- The conclusion regarding bioaccumulation needs to be re-examined as it relies only on limited aquatic information.

d. Human Exposure

The principal routes of exposure to 1,4-dioxane for the general population are expected to be from the general environment, food, and the use of consumer products. The highest upper-bounding estimate from ambient air (Canadian data), indoor air (Canadian data), soil (Canadian data) and drinking water (using the detection limit from a Canadian study from water from a municipal water treatment plant in the Great Lakes region where 1,4-dioxane was not found) was 1.26 μg/kg-bw per day for formula-fed infants <6 months. No other Canadian water testing was identified.

Drinking water is considered to be the major exposure source, for the "general population", while indoor air was the second largest. An exposure estimate via food most generally (using Japanese data suggesting 1,4-dioxane in several food groups) was not included because of potential differences in 1,4-dioxane water content between Canada and Japan, differing food additive provisions, etc. However, the maximum exposure via food additives using Canadian information was 0.335 μg/kg-bw per day for children 1 - 4 years.[17]

- Inhalation and dermal exposure via consumer products was acknowledged, but only exposure estimates for female adults (weighing 69 kg) and 0- to 6-month-old child

[15] Ibid p.6
[16] Ibid p.9
[17] Ibid p.12-14

exposures were presented. Interestingly, dishwasher detergent levels referred to women weighing 75 kg.

- This assessment is very limited by the low number of products that were examined (e.g., 5 adult products, 3 child products), even though it is known that 25% of all women use at least 15 products daily (many of which may contain 1,4-dioxane), various assumptions (90% of 1,4-dioxane is available for inhalation and 10% available for dermal uptake), and modelling reliance.[18]
- The list of personal care products containing 1,4-dioxane includes baby shampoos, skin moisturizers, body wash and lotions. ITK questions how or why such a substances is used and found in products for babies. This is very disturbing.[19]
- There was no consideration for exposures via other consumer products (e.g., detergents) and breast milk, despite one model indicating it might be found here. Vulnerable populations, beyond children within the "general population" are not addressed. Neither is occupational exposure.
- What constitutes a "general population" must be clearly delineated. In fact, the term itself, excludes many from various backgrounds who may not be necessarily considered "vulnerable".
- Given that these personal care products are used over a lifetime, cumulative and long-term exposure to 1,4-dioxane from such products and other types of products and uses need consideration, even if difficult to ascertain..
- Efforts should be made to determine whether the occurrence of 1,4-dioxane in food results from natural production or contamination by ethoxylated food additives and pesticides.
- There is no testing of 1,4-dioxane in drinking water in Canada.

e. Health Concerns

The carcinogen classifications for 1,4-Dioxane are based on "hepatocellular adenomas and carcinomas in mice, tumours of the nasal cavity, liver subcutaneous tissues, mammary gland and peritoneal mesotheliomas in rats and tumours of the liver and gallbladder in guinea pigs orally exposed to 1,4-dioxane". Some of these effects were observed when exposed via drinking water at a very low concentration.

The only available chronic inhalation study did not demonstrate carcinogenicity or other adverse effects. Dermal exposure did not induce tumours in mice unless another chemical was administered prior to application (then tumours in lung, kidney, spleen and liver were observed).

The Danish Cancer Registry data showed significantly higher than expected rates of incidence ratios for liver tumours in male workers exposed to 1,4-dioxane and other chemicals in occupational settings "and an increase in liver cancer incidence of 50% was identified in one workplace where only 1,4-dioxane was used". Its critical effect is considered tumorigenesis (that is, formation or production of tumours) following oral exposure.

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[18] Environmental Working Group. www.cosmeticsdatabase.com/research/whythismatters.php September 15, 2009.
[19] Draft Screening Assessment .14, Table 7a, p. 16 Table 7c

- Data and conclusions of other agencies suggest it is not a likely a mutagen, although potential modes of action have not been fully elucidated. Although "all tests for mutagenicity were negative", significantly increased chromosomal aberrations were seen in workers exposed to various mutagens, including 1,4-dioxane. It was also "positive in some assays…for effects on deoxyribonucleic acid (DNA)", typically at "higher doses or following prolonged exposure and often in the presence of cytotoxicity".
- The assessors conclude that there is a threshold for carcinogenicity, although their reasoning for this is not clear. It appears to be that this threshold exists whereby 1,4-dioxane promotes tumours at doses where its oxidation to its metabolites becomes saturated. However, the assessors later state that "there is uncertainty in the mechanism of tumorigenesis". Similar metabolic pathways between humans and animals have been found.
- Other systemic effects (e.g., central nervous, respiratory and blood systems and stomach) via oral, dermal and inhalation have also been seen. Reproductive and immunological effects were also observed in mice. But there are limitations to studies on these effects. Some of these limitations are highlighted in the next section.

f. Uncertainties in Evaluation of Risk to Human Health

As the draft screening report notes in this section[20]:

"There is some uncertainty in estimating intake from food sources, as Canadian monitoring data on the levels of 1,4-dioxane in foods were unavailable and as a result were not included in the overall intake estimate."

"There is some uncertainty due to the limited information on the presence or concentrations of the substance in consumer products available in Canada."

"There is uncertainty regarding the mechanism of 1,4-dioxane-induced tumorigenesis, as data on dose–response and temporal progression with which to characterize and/or identify the key events in the processes of 1,4-dioxane-induced tumour formation of different types and thus support any of the hypothesized carcinogenic modes of action are insufficient, inconsistent or not available."

"As well, there is uncertainty with respect to the human relevance of 1,4-dioxane carcinogenicity, as epidemiological investigations have not provided conclusive evidence."

"There are no sufficient data to preclude the distribution of 1,4-dioxane to the nasal tissue by systemic circulation via oral exposure".

"As to the non-neoplastic effects, there are some uncertainties concerning the critical exposure levels associated with these effects via inhalation or dermal exposure to 1,4-dioxane, as the dermal dataset is limited and there are inconsistent results obtained from 13-week and 2-year inhalation studies".

"As well, data on reproductive toxicity associated with 1,4-dioxane exposure are limited, as there is no multigenerational study available."

[20] Ibid p. 23

In light of such uncertainties, ITK is both puzzled and perturbed that the assessors proposed that 1,4-dioxane is not toxic under CEPA 1999. This is surely a case where the precautionary principle needs to be applied.

g. Recommendations

i. Given its carcinogenicity, "uncertainty regarding the mechanism of 1,4-dioxane-induced tumorigenesis", and relatively small, lower-limit MOEs for environmental and consumer product exposure and levels at where no tumours or adverse effects are observed, 1,4-dioxane should be designated as "toxic" under CEPA, 1999.

ii. Further, given that "data on dose–response and temporal progression with which to characterize and/or identify the key events in the processes of 1,4-dioxane-induced tumour formation of different types…are insufficient, inconsistent or not available" a precautionary approach is justified.

iii. Concentrations in water, drinking water, and soil from various Canadian locations should be established. Relying on its non-detection in municipally treated water from the Great Lakes region to calculate exposure cannot be extrapolated across Canada.

iv. Contribution of 1,4-dioxane concentration in environmental media from waste-disposal and exposures via additional sources (e.g., food, considering its use in pest control products, and that it may be found in breast milk were. were not included in intake estimates and should be included.

v. Consumer product exposures should be further investigated given the limited number of products, and users, considered within the current assessment; current values are likely underestimated.

vi. Reporting releases of 1,4-dioxane to the NPRI should be reviewed to examine whether the threshold for reporting is appropriate.

vii. 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.

viii. Attention needs to be paid to determining vulnerable population exposures. This includes infants and children, pregnant women, communities with cultural differences via food update, First Nations, Métis, and Inuit peoples.

ix. Further, occupational exposure through manufacturing processes, personal care employees and industrial uses needs consideration.

Summary Comments

As noted in reviewing the results of assessments on other substances under the Challenge Program, ITK has found the noted limitations a challenge to relating concerns about these substances and their potential effect on vulnerable populations, northern communities in general, and specifically to Inuit in Canada.

For this particular batch, ITK has expressed its concern on the findings of the draft assessment for 1,4-dioxane. ITK urges the government to re-examine the proposed conclusion of the assessors that it is not toxic under CEPA 1999. This matter speaks to the need to apply the precautionary principle, and in this case, where the degree of uncertainty is paramount.

Further, ITK is requesting that more information needs to be gathered over the impact of long-range potential of butanone oxime, which could be a concern for Inuit communities.

While ITK intends to stay involved in the Challenge Program and will continue to make submissions on the various batches as they are released, ITK is greatly concerned as to how or whether the many issues raised in these submission and others are being addressed so that the assessments and proposed risk management strategies, where applicable, be made more meaningful to Inuit.