

Summary of Public Comments received on the Challenge substance 1,4-Dioxane (CAS 123-91-1) Draft Screening Assessment Report for Batch 7

Comments on the draft screening assessment report for 1,4-Dioxane to be addressed as part of the Chemicals Management Plan Challenge were provided by International Institute of Concern for Public Health (IICPH), Dow Chemical Canada Inc., Chemical Sensitivities Manitoba and Canadian Environmental Law Association, Inuit Tapiriit Kanatami (ITK).

A summary of comments and responses is included below, organized by topic:

- Human hazard assessment
- Human exposure assessment
- Human risk characterization
- Food and Product Safety
- Environmental and ecological assessment
- Peer Review
- Risk Management

TOPIC	COMMENT	RESPONSE
Human hazard assessment	The similarity in metabolic pathway in humans and experimental animals indicates the human relevance of 1,4-dioxane carcinogenicity.	The screening assessment acknowledges the potential relevance of carcinogenicity of 1,4-dioxane in animal studies to humans .
	There is a lack of toxicity data for all routes of exposure as well as information on reproductive toxicity.	For 1,4-dioxane, chronic toxicity data is available for all routes of exposure. An additional chronic inhalation study became available during the public comment period and has been included in the assessment report. Some data on reproductive toxicity is available. Gaps in the health effects database have been acknowledged in the screening assessment and were taken into consideration when determining the adequacy of the margins of exposure.
	There is no clearly defined rationale for the existence of a threshold for the carcinogenicity of 1,4-dioxane.	Information regarding genotoxicity, and conclusions of other agencies, indicate that 1,4-dioxane is not likely to be genotoxic. Non-linear toxicokinetics of 1,4-dioxane have been observed in rats, and the existence of a threshold dose for toxicity and

		carcinogenicity was suggested. Therefore a threshold approach is used to characterize risk to human health. The text in the screening assessment on risk characterization has been modified to provide increased clarity.
	Eye and nose irritation from exposure to low levels of 1,4-dioxane should be addressed more substantially to gain a better understanding of the impacts from this chemical.	Levels of 1,4-dioxane in indoor air and potential exposure from use of hair dye is compared to levels resulting in eye and nose irritation in humans in the screening assessment. The margins of exposure are considered adequate. Similarly, other exposure scenarios resulted in lower exposure estimates and a concern for irritation was therefore not identified.
	Statements regarding the carcinogenicity of 1,4-dioxane do not reconcile with statements regarding its lack of genotoxic potential and should be further explained. The draft assessment concluded that 1,4-dioxane is not CEPA toxic, which apparently dismisses the carcinogenicity categorization by other bodies.	The carcinogenic potential of 1,4-dioxane is well recognized in the screening assessment. The carcinogenicity classification for 1,4-dioxane by international agencies has been taken into consideration in the screening assessment and identified as a critical effect of 1,4-dioxane. However, available information indicates that 1,4-dioxane is not a genotoxic substance and therefore a threshold approach is used for risk characterization for both cancer and non-cancer effects.
	The government should seek additional data on inhalation exposure route using section 71(1)(c) of CEPA.	Exposure to 1,4-dioxane via inhalation has been recognized as one of the sources of exposure for the general Canadian population and the level of inhalation exposure has been taken into consideration in the risk characterization. Also, there are acute, short-term, sub-chronic and long term toxicity studies available for 1,4-dioxane via the inhalation route of exposure. An additional chronic inhalation study became available during the public comment period and has been included in the screening assessment report.
	Data and conclusions of other agencies suggest that 1,4-dioxane is not likely a mutagen. However positive results for chromosomal aberrations in occupationally exposed workers and positive results for effects on deoxyribonucleic acid were observed.	The collective evidence indicates that 1,4-dioxane is not a mutagen. With respect to the study involving occupationally exposed individuals, these individuals were also exposed to other chemicals, some mutagenic, and the positive results cannot be attributed to 1,4-dioxane. Hazard information obtained from occupational settings, in particular data from epidemiological investigations, is considered in the screening assessments. The information developed through

		the Chemicals Management Plan may be used to inform decisions concerning additional actions to minimize exposure to workers. The Government of Canada is working to communicate results to appropriate occupational health and safety groups.
Human exposure assessment	The use of limits of detection, maximum specification or maximum permitted levels of use, 100 % inhalation absorption and no recognition of volatility and low boiling point all lead to an extreme or very conservative exposure analysis. The government is strongly urged to provide a rationale on the adoption of these conservative assumptions which will reduce the required margin of exposure for what is acceptable.	A tiered approach to characterize exposure was used as part of the screening assessment process. This involves starting with an upper-bounding conservative exposure analysis and refining, where data permits, as necessary. Screening assessments outline confidence in the exposure assessments, and highlight areas of uncertainty. These considerations are then taken into account when determining the adequacy of the margins of exposure.
	The assessment is limited by the various assumptions used in consumer product exposure, specifically the assumption of 90% and 10 % availability for inhalation and dermal exposure respectively.	The assumption of 90% and 10 % availability for inhalation and dermal exposure respectively is based on substance-specific considerations including volatility and experimental data indicating that when added to a lotion-like material, 90 % of 1, 4-dioxane evaporates in 15 minutes.
	The assessment should expand to consider vulnerable populations such as children, pregnant women, aboriginal communities, individuals with low income and chemical sensitivities.	The Challenge screening assessments are based on consideration of the available data. The various conservative exposure scenarios used are considered to be protective of vulnerable populations in Canada and do incorporate specific exposure estimates for Canadians of different ages. However, if information is available which suggests that a specific sub-population would be particularly vulnerable, this information would be considered in the assessment. In this assessment, it was recognized that use of personal care products is more prevalent by women than men, and this is reflected in the screening assessment. Personal care product exposure scenarios were also specifically developed for children in this assessment.
	The focus of assessment targets mainly chemicals and not residues. However, if a chemical is found as a residue, priority must be placed on the source of the residue as well as the process. A more	Upper-bounding estimates of exposure were calculated based on levels found in products or the environment, regardless of the source, and includes those present as a residual remaining from the ethoxylation process.

	comprehensive investigation on the ethoxylation process in the assessment is warranted.	
	The assessment is limited (i.e. exposure is underestimated) by the low number of personal care and household product modeled.	A variety of personal care products were considered in estimating exposure; however, a smaller number of products contribute most significantly to exposure based on the frequency of their use, amount of product used per application, type of application (e.g. stay-on products) or the concentration of residual 1,4-dioxane present in the product. For household products, although residual 1,4-dioxane was present in some household products, dishwashing detergent was selected to represent an upper-bound estimate of exposure from use of a household product based on measured levels of residual 1,4-dioxane; direct nature of the exposure; and the frequency and duration of use of the product. Use of maximum 1,4-dioxane concentrations in products and conservative assumptions in exposure modelling increase confidence that the exposure estimates are upper-bounding estimates.
	Cumulative and long term exposure to 1,4-dioxane should be analyzed for personal care products used over a lifetime.	Aggregated product exposures were assumed to occur over a lifetime when the comparison to results from long-term animal studies was conducted.
	Only personal care product exposure estimates for women and children were presented. Furthermore a different weight was used for women in the dishwashing liquid scenario.	Exposure from personal care products was estimated for women, men, and children. However, after analysis, it was apparent that because of factors such as product use and frequency of use, women had the highest potential exposure to 1,4-dioxane. Therefore the assessment report focuses on exposure estimates derived for women and children. The assessment report documents this analysis. In the final assessment report, a common body weight is used for both the personal care product scenario and for the dishwashing

		liquid scenario.
	Why is 1,4-dioxane used and found in baby products?	1,4-dioxane is not an intentional ingredient in personal care products. In fact, it is present on Health Canada's Cosmetic Ingredient "Hotlist"; which prohibits its intentional use as an ingredient in cosmetics. Rather, it is formed unintentionally during the ethoxylation manufacturing process and may be present as a residual.
	The use of non Canadian data in the consumer product modeling was not adequately justified in the assessment.	Canadian data was used where available. Non-Canadian data is also considered relevant to characterizing exposure to Canadians. A number of the products in the surveys are also available on the Canadian market and there is no indication that the source of residual 1,4-dioxane in the products was different in the countries from which the data was obtained. This rationale has been added to the screening assessment report.
	Concentrations in environmental media need to be established within Canada. For water, relying on not finding 1,4-dioxane in municipally treated water from the Great Lakes region, can not be extrapolated to calculate exposure across Canada.	All soil, air and water data used to estimate exposure are Canadian. For drinking water, 1, 4-dioxane was monitored in the Great Lakes region where it would likely be at the highest levels given the high manufacturing activity in this area. In this study 1, 4-dioxane was not detected; however it may be present at a lower concentration than was measured in the study. Therefore it was considered a conservative approach to use the detection limit.
	The Government should investigate if 1,4-dioxane is found naturally in food or from contamination by ethoxylated food additives and pesticides.	The margins of exposure to 1,4-dioxane estimated for food are considered adequately protective of human health due to the volatile nature of this compound in general, and in consideration of the conservative estimates of exposure that were utilized for the potential carry-over of 1,4-dioxane in foods through its possible presence as an impurity in substances that come into contact with food. Therefore, actual levels of 1,4-dioxane in food are expected to be very low.
	It is difficult to decipher amounts of dioxane manufactured, used and imported because they are provided in a range.	In order to protect confidential business information (CBI) ranges are used to report on manufacturing, use and import volumes.
	Reporting releases of 1,4-dioxane to the NPRI	Any party (person, government or organization) in Canada may

	should be reviewed to examine whether the threshold for reporting is appropriate. Discrepancies between releases stated by NPRI and the US TRI should be explained. Use patterns in other countries should be compared with that in the US and Canada.	submit a proposal to Environment Canada for changes to the National Pollutant Release Inventory (NPRI) program. Changes to the substance list result from the NPRI Consultations process and may include the addition, modification or removal of substances as well as changes in the thresholds at which they must be reported. Reporting requirements under the US Toxics Release Inventory differ from the NPRI. Therefore there will be differences in releases reported under the two programs.
	Suggest tabulating, in the uses section, the impurity concentrations of 1,4-dioxane in various applications (cosmetics, pharmaceuticals, detergents, food additives etc) to give perspective against the actual concentrations used in exposure estimates.	A tabulation of the residual levels of 1,4-dioxane in personal care products was tabulated in the exposure section. Further tabulation was not done as measured residual levels of 1,4-dioxane were only available for selected applications (personal care products, detergents) while other levels were maximum residual limits allowed in the products.
	There was no consideration for exposure to 1,4-dioxane via breast milk despite one model indicating it may be present in breast milk.	Additional information has been added to the screening assessment on potential for exposure via breast milk
Human risk characterization	There is concern that the lower limit margins of exposure for environmental and consumer product exposure and levels at which no tumors or adverse effects are observed are relatively small.	All estimated margins of exposure (MOEs) were considered to be adequately protective of human health. Although margins of exposure for the acute use of hair dyes were smaller than for other uses of personal care products and for environmental media, a very conservative approach was utilized in the assessment of this scenario. The exposure levels from use of hair dyes were likely over-estimated and the acute inhalation effects, such as eye or nose irritations, were observed under 4-6 hours inhalation exposure, which is a much longer period of time compared to the actual household hair dye use scenarios. Also, the toxicity values used in this case are from humans.
Food and Product Safety	Although 1,4-dioxane is listed on the Cosmetic Ingredient Hotlist, there are no restrictions for this chemical when unintentionally formed (residue). A strengthening in the approach of how residues in products are addressed is needed.	The compound 1,4-dioxane cannot be deliberately added to cosmetic products for sale in Canada. However, it may still be present in small amounts in some cosmetics as it is formed as a by-product during the manufacturing processes of certain

		ingredients such as detergents and foaming agents. Health Canada will periodically survey cosmetics to confirm that levels in these products are minimal.
	There should be an effort for the food product industry to find alternatives to polysorbate products and polyethylene glycol.	1,4-Dioxane is present as an impurity in food additives and is not intentionally added to food. Furthermore, the estimated 1,4-dioxane exposures in food, that may result from carry-over due to its potential presence as an impurity in certain food additives are considered an overestimate because losses due to its volatility and food processing considerations were not accounted for. As indicated in footnote 3 and 4 (of Appendix 2), actual use levels of the permitted polysorbates and polyethylene glycol may be lower than the maximums assumed for this assessment, as well, alternate, permitted food additives may be in use for foods in which provision exists for those alternate food additives. Finally, although a food additive is permitted for use in a food, it does not necessarily mean that it is used in that food (manufacturers' discretion). Therefore, the margins of exposure estimated for food from the use of certain food additives that may contain 1,4-dioxane as an impurity, are considered adequately protective of human health.
Environmental and ecological assessment	Conflicting data from model predictions have been presented in the assessment, therefore it is suggested to provide rationale related to the data selection and ultimately the conclusion.	The assessment report will be revised to clarify the rationale data selection.
	The bioaccumulation conclusion needs to be re-examined, because the conclusion was proposed based on limited information for the water compartment.	Indeed there are few experimentally measured Bio-Concentration Factors (BCF) for aquatic organisms. However considering the physical and chemical properties together with the experimentally measured BCFs and model predictions, there is sufficient evidence to conclude with confidence that the substance is not bioaccumulative. The conclusion statements in the assessment will be revised.
	To assess the impact of 1,4-dioxane as released in	The Mega Flush release scenario will be added in the report,

	water, a more substantial consideration of receiving waters and the effectiveness of the treatment processes are required, with emphasis on the fact that the effectiveness of treatment plants varies within Canada.	which simulates the substance released in wastewater (from consumer uses).
	The presence of 1,4-dioxane in municipal waste, which could end up in sludge, has not been addressed in the draft assessment. In order to understand the full impact of this chemical, the consideration of the waste stream should represent an important source of potential exposure.	Given its chemical properties, very little of 1,4-dioxane would be expected to be present in sludge. Thus exposures in soil associated with application of sewage treatment plant sludge to agricultural land are expected to be very low.
Peer Review	For transparency and acceptability in the regulated community, a full peer review should incorporate global expertise regardless of their position in the spectrum of stakeholders in order to meet scientific standards.	The draft assessments as part of the Chemical Management Plan Challenge were all reviewed by external reviewers before their publication. Technical expertise is the main criteria for identifying suitable individuals, who may come from academia, industry, consulting firms, or other government jurisdictions. All comments provided by peer reviewers were taken into consideration.
Risk Management	What is the basis for adding 1,4-dioxane to the DSL inventory update or for it being subject to further monitoring and research?	This follow-up activity was recommended to assist in the verification that levels of exposure do not increase. Health Canada will periodically survey personal care products to confirm that levels in these products remain low. .
	A more precautionary approach for 1,4-dioxane assessment is required with the result of a CEPA toxic designation.	Conservative assumptions were used throughout the assessment in order to be protective of human health. On the basis of the adequacy of the margins between conservative estimates of exposure to 1,4-dioxane and critical effect levels in experimental animals, it is concluded that 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.