

Summary of Public Comments Received on the Government of Canada’s Draft Screening Assessment Report and Risk Management Scope on Isoprene (78-79-5)

Formal comments made during the 60-day public comment period that took place from May 17, 2008 to July 16, 2008 on the draft screening assessment report and risk management scope on Isoprene, a substance included in Batch 2 of the substances to be addressed as part of the Chemicals Management Plan Challenge under the *Canadian Environmental Protection Act, 1999* (CEPA 1999), were provided by Lanxess, Dow Chemical Canada Inc., International Institute of Synthetic Rubber Producers, Inc. (IISRP).

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

- Validity of evidence
- Environmental impacts
- Economic considerations
- Weight of evidence and precautionary principle
- Effects on Human Health
- Risk Management

TOPIC	COMMENT	RESPONSE
Validity of Evidence	Exposure values were not greater than the critical threshold value (CTV) there is difficulty in recommending Risk Management actions.	Both cancer and non-cancer effects were considered in characterizing the risk from isoprene to human health. For non-cancer effects, the margin of exposure derived from the lowest inhalation effect value and the upper-bounding indoor air measurement in the screening assessment is considered potentially inadequate for the protection of human health when the uncertainties of both the exposure and hazard databases are taken into consideration. With regard to cancer, which was one of the critical effects of this screening assessment on isoprene, it is considered that there is a probability of harm at any level of exposure, as the mode of action for the induction of tumours has not been elucidated.
Environmental impacts	A certain baseline level of risk must already be incurred by the general population due to natural sources of exposure (endogenous, biogenic). Therefore any risk management of isoprene should target indoor air as it is a greater source of emissions.	The risk management action that can be taken to address exposure through indoor air is limited. We cannot control either endogenous or biogenic releases to indoor air. Health Canada’s Tobacco Control Directorate attempts to educate the public about the health risks of smoking in order to reduce exposure to toxicants released in cigarette smoke.

		While there may be a certain amount of risk incurred through exposure to naturally produced isoprene, it is nevertheless necessary to reduce exposure to the extent practicable when/where it can be controlled.
	The National Pollution Release Inventory (NPRI) threshold might not be adequate to capture the releases and disposal of various substances, including Isoprene and that the threshold should be re-evaluated considering the inherent toxicity nature of the substances.	Environment Canada will make a decision on whether or not to change the NPRI reporting thresholds. Changes to the Inventory may include the addition, modification or removal of substances as well as changes in the thresholds at which they must be reported. This will be discussed during the risk management phase of the CEPA process. For further details on NPRI, please see: http://www.ec.gc.ca/pdb/npri/npri_home_e.cfm .
Economic Considerations	Isoprene is an important constituent of butyl rubber, an essential component of modern tires. These manufacturing plants provide a valuable contribution to local communities employing hundreds of people.	The Government of Canada recognizes the economic importance of the butyl rubber manufacturing industry in Canada. The possible socio-economic impacts of risk management action are considered as part of their development.
Weight of evidence and precautionary principle	There were differences in conclusions on substances with similar magnitudes of margins of exposure and between isoprene and other similar substances. The screening assessments should include a discussion on why a margin of exposure may or may not be adequate. Also an explanation of how and when a precautionary approach is applied is necessary.	The determination of margins of exposure between conservatively selected critical effect levels and estimates of exposure may be incorporated in assessment of whether or not a substance is proposed to be “toxic” as defined in paragraph 64c of CEPA 1999. However, there is no absolute “cut off” for interpretation of this margin, but rather, determination of whether or not the margin is considered adequately protective is related to the dataset specific to a substance. Factors considered in interpretation of the margin of exposure include the uncertainties in the available information on exposure and hazard, the quality and quantity of the data, the nature or severity of the effect(s) considered critical in the assessment and other effects associated with exposure to the substance, the steepness of the exposure-response curve, information on differences in sensitivity between species and across the human population, etc. Consideration of these factors for various substances may account for the differing proposed conclusions for similar margins of exposure with respect to adequacy of the margin of exposure in each case.

	Due to differences in structure, biological response (tumour incidence, types; dose-response) and IARC classification between isoprene (CAS 78-79-5) and 1,3-butadiene (CAS 106-99-0), isoprene not be considered a high priority for human health under CEPA.	In this assessment of isoprene under the Challenge, consideration of the database on 1,3-butadiene (CAS 106-99-0) is appropriate in light of the similarity in chemical structure as well as the very similar profile of effects induced in experimental animals. While the epidemiological database for 1,3-butadiene (CAS 106-99-0) is not available for isoprene, there is believed to be sufficient reason to assume that, in light of the absence of information to the contrary, isoprene may also pose a carcinogenic risk to humans. In the absence of an elucidated mode of action for the various tumours induced by isoprene in laboratory species, the tumours cannot be dismissed as not being relevant to humans, and it cannot be precluded that tumours observed in experimental animals resulted from direct interaction with genetic material.
Effects on Human Health	Designating Isoprene as harmful under CEPA is inappropriate as it is found in nature and a natural concentration is present in the body. Since there is a threshold where isoprene can exist and be managed by the body a “safe” level of isoprene exposure should be established and used for analysis and potential risk management.	The contribution of natural versus anthropogenic isoprene to general exposure of the Canadian population is not known. Further comparative analyses of pharmacokinetic parameters (uptake of a substance, distribution and elimination from the body, etc.) and pharmacodynamic parameters (how the substance interacts with tissues in the body) of isoprene in vivo in various species would be required to determine the relative contribution of exogenous versus endogenous isoprene to observed effects in specific tissues. In addition, it is noteworthy that tumour induction by exogenous isoprene has been observed in experimental species which also produce the substance endogenously. The mode of action for induction of the different tumours induced by isoprene has not been fully elucidated; therefore, it has not been established that a threshold of exposure exists below which there is no probability of harm. Such analyses are beyond the scope of a screening assessment under the Challenge.
Risk Management	Industrial emissions should not be targeted for risk management when there are other sources that are important contributors to exposure. (ex. cigarette	Tobacco smoke, endogenous production, biogenic production by plants, and automobile emissions are all important sources of isoprene. Endogenous production and biogenic production by

	smoke, natural production in human body)	<p>plants are natural processes and are therefore not possible to control. Health Canada's Tobacco Control Program educates the public about the health risks of smoking, however it cannot control isoprene emitted in cigarette smoke as a result of the combustion process. In terms of emissions in automobile exhaust, the <i>On-Road Vehicle and Engine Emission Regulations</i>, the <i>Off-Road Compression-Ignition Engine Emission Regulations</i>, and the <i>Off-Road Small Spark-Ignition Engine Emission Regulations</i> (all under <i>CEPA 1999</i>) target Volatile Organic Compounds (VOCs) as a group and are likely to reduce isoprene emissions as they reduce those of other VOCs. Emissions from rubber manufacturing are a source of exposure to isoprene over which it is possible to exert some control; therefore, it is necessary to reduce this source of exposure to the extent practicable. The burden of risk management on industry will be considered in the development of risk management instruments. Action under CEPA to ensure the application of best available technology economically achievable (BATEA) for rubber manufacturing facilities emitting isoprene is being proposed. This will not penalize companies for actions already taken to reduce emissions, but will take these actions into account.</p>
	If it is deemed necessary to manage consumer products, a CEPA guideline for consumer products should be developed.	Based on available information, exposure to isoprene in consumer products appears to be negligible. Therefore consumer products will not be targeted for risk management.