

Summary of Public Comments Received on the Government of Canada’s Draft Screening Assessment Reports for n-Hexane (CAS 110-54-3)

Comments on the draft screening assessment reports for n-Hexane to be addressed as part of the Chemicals Management Plan Challenge were provided by Learning Disabilities Association of Canada.

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

- Risk Management
- Future Notifications
- Toxicity
- Exposure

TOPIC	COMMENT	RESPONSE
Risk Management	Risk management action should be taken for n-Hexane because of its production volume, high import into Canada, and its classification as a reproductive toxicant by international bodies.	Based on the analysis of relevant information, exposure from n-hexane is below the level at which critical health effects are likely. As a result, n-hexane has not been found to meet the criteria of section 64 (c) of the <i>Canadian Environmental Protection Act, 1999</i> , and risk management is not required.
	n-Hexane should be subjected to the Significant New Activity provisions of CEPA.	The assessment report concluded that the critical health effects from exposure to n-hexane would result from exposures to high levels over long periods of time. Measurements of n-hexane in both indoor and ambient air, which would be the source of long-term exposures, were not at levels that would pose a risk to human health. Further, the assessment concluded that exposure from the broad range of identified uses of n-hexane in products in the screening assessment would not pose a risk to human health, as they are intermittent. Given the extensive range of existing uses, and the large volumes of n-hexane currently in commerce, it considered unlikely that any new use could significantly change the existing exposure profile.
Uses	n-Hexane has a wide variety of uses. Exposure to humans comes from a variety of sources such as an additive in food, in food processing, and in skin moisturizers. No Canadian data was identified for	Indoor air represented the predominant contribution to the total estimated daily intake of n-hexane for the general population. n-Hexane is a listed food additive in Canada which is permitted for use as a carrier or extraction solvent (Health Canada 2006). The

	<p>these or other media (drinking water, soil, and food) other than air. However the screening assessment did not consider these media to be significant contributors to exposure “based on the physical and chemical properties of this substance”.</p>	<p>daily intake of n-hexane from food was estimated to contribute only 1.95% of total intake in the two age groups of highest consumption. Exposure of n-hexane via drinking water and soil were modelled and found not to contribute significantly, which agrees with physical chemical properties (high volatility and low water solubility) of this substance.</p> <p>In regards to skin moisturizers, there was only one notification to Health Canada (CNS 2008) for use of <i>n</i>-hexane in skin moisturizers and it reported a concentration level of < 1%. This skin moisturizer contained hexane/alcohol/flower extract where the combined concentration of n-hexane and alcohol was < 1%, and thus the actual concentration of n-hexane may be well below this level. Therefore, no exposure estimate was considered necessary for this product.</p>
	<p>The estimation of the cumulative exposure to n-hexane through consumer products should be required due to the diverse uses of n-hexane from these products, and concentrations of n-hexane in environmental media in Canada should be obtained.</p>	<p>The assessment considers that the indoor air concentrations do capture exposure from the diverse uses of n-hexane and that aggregate exposure from multiple sources is taken into consideration. Cumulative exposure was also not considered appropriate due to the fact that the types of products identified were either infrequent use or short-term (< 240 min) use.</p>
Toxicity	<p>There is not sufficient information on the toxicity endpoint of concern (neurotoxicity) because studies designed to predict effects in the developing nervous system were not available.</p>	<p>As stated in the screening assessment, there is sufficient information to address the endpoint of concern (neurotoxicity) based on inhalation exposure, including human studies which measured neurotoxicity. The limited developmental endpoints cited in the screening assessment accounts for lack of a developmental neurotoxicity study. The recent assessment of n-hexane by the US EPA, already cited in the screening assessment, stated that there was lack of a developmental neurotoxicity study, including lack of the same studies mentioned above, and also stated a medium confidence in the database. Their conclusions are consistent with the conclusions of the screening assessment conducted under the Chemicals Management Plan.</p>
	<p>The Government of Canada should re-evaluate the</p>	<p>The information on the exposure to the general population and</p>

	Margins of Exposure (MOEs) and request submission of a developmental neurotoxicity study.	toxicological endpoints have not changed as no new information was received through public comments. Therefore, the MOEs do not require re-evaluation. As n-hexane has not been proposed as a compound subject to Significant New Activity provisions, there is currently no requirement for additional studies.
	The decreased fetal weight observed in rat and mice toxicity studies should be considered as a predictor of adverse effects on development after birth.	The lowest effect level determined in the one oral developmental toxicity study was based on decreased fetal weights. The lowest effect level determined from 5 inhalation developmental toxicity studies was based on resorptions which occurred at a concentration lower than the concentrations at which decreased fetal weights were observed. Thus, the screening assessment has already accounted for possible developmental effects due to decreased fetal weights.
	Why are the effect levels from occupational epidemiology studies not used to establish a margin of exposure?	Epidemiology studies may be used to characterize the critical effects and routes of exposure. However, the epidemiology studies reported in the screening assessment are not as robust as the animal studies because effects from co-exposure to several other substances could not be separated from effects due to n-hexane exposure. This is already clarified in the screening assessment. However, the following text will be added: "...and due to other confounding factors inherent in epidemiology studies."
Exposure	The n-hexane assessment should be considered in terms of cumulative hazard with other solvents/hydrocarbons.	n-Hexane is often present in co-occurrence with other substances. The potential hazard due to combined exposures to n-hexane with other solvents/hydrocarbons is not considered in the screening assessment. This approach is consistent with the screening assessments for other substances listed under the Challenge program.