1,3-BUTADIENE

Comments on the **environmental sections** of the CEPA PSL Draft Assessment Report on 1,3-Butadiene were provided by:

1. Emulsion Polymers Council, Inc.
2. Health, Environment and Safety, Bayer Inc.
3. Canadian Petroleum Products Institute
4. International Institute of Synthetic Rubber Producers, Inc.
5. Vehicle Environmental and Energy Programs, DaimlerChrysler Canada Inc.
6. Nova Chemicals Corporation

Comments and responses are summarized below by Environment Canada. (All were based on the English version of the report).

Comment[(source)]	**Response**
Concerns were expressed with regards to the determination that 1,3-butadiene is toxic based on its danger to the environment on which human health depends, due to its potential to contribute to the formation of ground-level ozone and photochemical smog. The approach used to assess the contribution of 1,3-butadiene to ground-level ozone formation is not consistent with that described in the Environment Canada Guidance Manual for Environmental Assessments of Priority Substances (March 1997). The criteria for concluding whether 1,3-butadiene is CEPA-toxic under Paragraph 64(b) should be explicitly stated. Without such criteria, industry is not in a position to assess the strength of the conclusion. Environment Canada should engage stakeholders in the appropriate update of the guidelines prior to implementation. (1) (3) (4) (6)	As noted in the Environment Canada Guidance Manual for Environmental Assessments of Priority Substances (March 1997), "the manual is intended to provide guidance only, not strict rules, to allow for the flexibility required to assess different types of substances and for developments in experience and science." Since the preparation of the Guidance Manual, understanding of reactions leading to the formation of ground-level ozone and photochemical smog has continued to progress, as have databases of concentrations of volatile organic compounds in Canada, allowing the estimation of relative contributions of such compounds to ozone formation. The text of the Assessment Report has been revised to provide a discussion of the reactivity of 1,3-butadiene which leads to its contribution to ozone formation, followed by a presentation of the relative importance of 1,3-butadiene to this process in Canada. Given the many on-going refinements to the assessment process for priority substances under both Paragraphs 64(a) and 64(b) of CEPA, stakeholders will be engaged to review and discuss all these assessment approaches after the current round of PSL2 assessments.
1,3-Butadiene may not be a significant contributor	1,3-Butadiene is very reactive in the presence of

Comment[(source)]	Response
to the formation of ground-level ozone given that it is not persistent and that it ranked 60th of 117 species sorted by mixing ratio; it represents 0.9% of the total VOC reactivity for a ranking of 26th as a contributor to the formation of ground-level ozone. (1) (2) (3) (4) (6)	hydroxyl radicals, yielding a high photochemical ozone creation potential (407 for 1,3-butadiene, relative to 100 for the reference compound ethene). Because of this high reactivity, its contribution to ozone formation is greatest near sources of release. As 1,3-butadiene is transformed in air, it yields compounds such as formaldehyde which are also active in the formation of ozone. Thus, although the current concentrations of 1,3-butadiene in Canada result in its ranking as 26th as contributor, it is in fact one of the more reactive VOCs and has a high potential for contribution to ozone formation. The text of the Assessment Report has been revised to provide a discussion of the reactivity of 1,3-butadiene which leads to its contribution to ozone formation.
Given that natural sources constitute 49.3% of total emissions of 1,3-butadiene in Canada, anthropogenic sources may contribute less than 0.5% of total VOC reactivity with regards to formation of ground-level ozone. (1)	While VOCs from natural sources (i.e., forest fires) may be important contributors to local formation of ground-level ozone during fires, forest fires are sporadic and local events. 1,3-Butadiene is not persistent, with an atmospheric half-life of hours. As such, its widespread presence in urban areas can be more closely associated with continuous anthropogenic sources rather than with forest fires. Forest fires would therefore not be expected to be major contributors to urban concentrations of 1,3-butadiene and to the resulting contribution to the formation of ground-level ozone by 1,3-butadiene in urban centres. The text of the Assessment Report has been modified to discuss the contribution of forest fires to urban concentrations of 1,3-butadiene.
The report should outline where concentrations of 1,3-butadiene are highest and present a more detailed accounting of 1,3-butadiene emissions inventory from all sources and future forecasts to help guide appropriate risk management actions if required. (5)	Very good or reasonable data are available for concentrations of 1,3-butadiene in ambient air in urban areas and near industrial sources, respectively. These are presented in the Assessment Report, with more detailed information in the supporting document. The Assessment Report recognizes the need to obtain more data on concentrations and sources in indoor air.

Comment[(source)]	Response
	The Assessment Report provides estimates for releases from all key sources in Canada, recognizing the uncertainty as it relates to estimates for combustion sources such as forest fires; more information is provided in a supporting document which can serve in discussions by risk managers. With regards to future projections, possible changes to releases from the automotive sector are of key interest - see below.
Vehicle exhaust estimates in the report have been based on estimates from historical models that neglect current and agreed changes in vehicle technology and fuel composition. Data were submitted indicating how reductions in releases are associated with current emission control technology (Tier 1) and the more stringent technology (low emission vehicle) that is to enter the market in the next few years. Similarly, changes to gasoline composition such as lower sulphur and distillation temperature and removal of MMT would reduce emissions of 1,3-butadiene; since 1,3-butadiene has a high reactivity with regards to formation of ground-level ozone, the adoption of the U.S. EPA National Low Emission Vehicle program vehicle emission requirements would result in indirect control of 1,3-butadiene and account for its ozone formation potential. (4) (5) One note of caution was expressed that controls to reduce emissions may not always be effective in reducing environmental levels, and that better understanding of uncertainties in emissions and source apportionment should parallel if not precede the development of control measures. (4)	The Assessment Report simply provides an overall estimate of releases from on-road vehicles, as calculated by the National Pollutants Release Inventory. Given the complexity of this issue, it is not proposed that it be dealt with in the Assessment Report. A statement has been added to the Assessment Report noting that the estimates are based on modelling and that current and planned changes to emission technology equipment and gasoline formulation will affect emissions. Environment Canada recognizes the importance of evolving control technologies and gasoline composition with regards to emissions and to any possible risk management actions, and looks forward to continued input and discussions with the automotive industry. Potential changes in emissions of 1,3-butadiene from vehicles must be discussed in the context of reductions of all VOCs and other pollutants from such sources. This matter will be referred to risk managers for further consideration.
For the characterization of risks to terrestrial organisms exposed to 1,3-butadiene in air, the hyperconservative quotient uses an Estimated Exposure Value of 28 $\mu g/m^3$, which is the highest outdoor ambient concentration recorded in Canada. A similar calculation should also be provided for a range of concentrations down to the typical ambient level of 1 $\mu g/m^3$. (5)	As described in Section 3.1 of the Assessment Report, if a hyperconservative quotient is less than 1, it can safely be assumed that the substance does not pose a significant risk for that assessment endpoint, and there is no need to pursue the analysis further. Since 1,3-butadiene was determined not to pose a significant risk to terrestrial biota even when considering the highest concentrations likely encountered in ambient air in

Comment[(source)]	Response
	Canada, exposure to lower concentrations will obviously pose a lower risk. The current text was not revised.

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Comments on the **health-related sections** of the CEPA PSL Assessment Report on 1,3-butadiene were provided by:

- Canadian Petroleum Products Institute, Ottawa, Ontario
- DaimlerChrylser Canada, Inc., Windsor, Ontario
- DuPont Canada, Inc., Kingston, Ontario.

Comments were also received from: International Institute of Synthetic Rubber Producers, Houston, Texas; Bayer, Inc., Sarnia, Ontario; and, NOVA Chemicals Corporation after the closing date of the public comment period. However, no issues additional to those raised in previous submissions were identified in these late comments.

To ensure transparency and defensibility of the health assessments, a cut-off date for consideration of new data is specified. In addition, the process for assessing the risks to human health includes several stages of internal and external review to ensure both quality and transparency. Addition of new data beyond the cut-off date, even if it was certain that these were the only new relevant data, would require an additional round of both internal and external reviews. This is impractical given the legally mandated time limits for completing these assessments. Such data are flagged for consideration in the SOP or a subsequent re-assessment.

Comment	Response
New data were identified which were considered to be relevant to the assessment of 1,3-butadiene, including a re-assessment of the exposure of the cohort of styrene-butadiene rubber workers in the critical epidemiological study.	This research was completed after the cut-off date for consideration of data; in addition, most of the identified studies have not yet been published. Moreover, if the estimates of exposure for workers in the critical cohort study were increased by the magnitude indicated by recent additional exposure estimates cited in submitted comments, there would be little impact on the priority for investigation of options to reduce exposure. Indeed, the resulting values for Exposure-Potency Indices would still be considered to be in the "high" category.
Suggestions were made for revision of presentation of technical data for various studies	Suggestions were considered and incorporated, where they were verifiable in the peer reviewed published literature and did not conflict with revisions introduced in response to comments received during the earlier, extensive technical review.
It was suggested that the text describing the	Since the references for the studies cited in the

Comment	Response
available database for *in vivo* genotoxicity include references.	section of the text concerning *in vivo* genotoxicity are presented in the table included in the document, it was not considered necessary to repeat them in the text. In addition, because of the large number of relevant references, this format has generally been preferred by reviewers of CEPA Priority Substances Health Assessments.
The "high" priority for investigation of options to reduce human exposure presented in the Assessment Report was questioned. In addition, the values used to categorize this priority for strategic options analysis differ from those used in other PSL assessments.	The determination of the priority for analysis of options to reduce population exposure to 1,3-butadiene was based on assessment of data available before April, 1998. With respect to the values assigned to the categories of priority, in the case of 1,3-butadiene, the Exposure-Potency Index was based on a TC_{01} (i.e., the concentration associated with a 1% increase in cancer in the critical study), as compared to the TC_{05} that was used for other substances, due to the nature of the exposure-response in the critical study. This value was considered more appropriate by the Final Review Panel, since it fell within the range of the majority of the observed data. The priority for investigation of options to reduce exposure was, however, based on the same criteria for exposure potency indices as for all other Priority Substances.
It was requested that a section be added to the Assessment Report in which the risk to health associated with exposure to 1,3-butadiene be put into context with other issues.	This is beyond the scope of Priority Substances assessments, the objective of which is to establish priorities for control on the basis of the scientific database, relative to other chemical contaminants in the general environment.
The presentation of the positive and negative results of the epidemiological data was considered unbalanced.	This comment was raised in an earlier round of technical review by industrial experts (but not others). Revisions introduced following this earlier stage were considered by an external final review panel who concluded that presentation was well balanced and addressed well the comments received in the earlier stages of peer review.
The evidence for an association between exposure to butadiene and lymphomas and	The conclusion that "butadiene is considered highly likely to be carcinogenic in humans"

Comment	Response
leukaemia should be considered separately in the evaluation of the consistency of the epidemiological database, as concluded by the US EPA Science Advisory Board.	presented in the assessment report was based on the weight of evidence for leukaemia in epidemiological studies, along with the evidence for genotoxicity and carcinogenicity in experimental animals as well as the limited data of genotoxic effects in exposed workers.
The model chosen to describe the exposure-response relationship does not reflect a plausible underlying biological mechanism.	Available data are inadequate as a basis for development of a biologically-based case-specific model for exposure-response for butadiene. Existing physiologically-based pharmacokinetic models are also inadequate, for reasons outlined in the report. As a result, the model chosen was that which best fit the observed data.-Uncertainties associated with the carcinogenic potencies derived for this substance are discussed in the report.
The differences in cancer response in rats, mice and humans should be more comprehensively considered.	Available data are inadequate to assess the likelihood of site concordance of tumours between animals and humans for butadiene. Moreover, the power to detect increases of tumours observed in bioassays in animal species in epidemiological studies is limited. Hence, the observation of the reviewer that "None of these tumors in the rat, or those in the mouse have been found to be elevated in any human study to date" is not germane to assessment of the weight of evidence of the carcinogenicity of 1.3-butadiene. The exposure-response for tumour induction in experimental species was also characterized primarily for comparison with the estimate of carcinogenic potency developed on the basis of epidemiological data
The rationale presented in the assessment report for not incorporating interspecies scaling between humans and animals in derivation of cancer potency estimates based on data in experimental animals (i.e., that similar exposures would result in equivalent toxicity across species since a steady state is reached during prolonged exposure) was questioned on the basis that differences in metabolism to reactive epoxides have been	While there appear to be species differences in the formation of putatively active metabolites of butadiene, available kinetic data are inadequate to address cross-species dosimetry for the epoxides. Hence, the most reasonable default is use of parent chemical dosimetry. Distribution to tissues for a volatile hydrocarbon, such as butadiene, is expected to be similar across species. Thus, interspecies scaling for exposure to the parent butadiene,

Comment	Response
noted across species.	based on differences in inhalation to body weight ratios of body surface areas, was not considered appropriate by the Final Review Panel.
The leukaemia response observed in the critical epidemiological study was likely influenced by co-exposure to other substances.	As discussed in the Assessment Report, data are inadequate for consideration of the contribution of exposure to other substances) to mortality due to leukaemia in the study population. (Exceptions were styrene and benzene, which were determined not to be associated with leukaemia by the authors of the critical study).
The conclusions of the Assessment Report differ from those of the International Agency for Research on Cancer and the U.S. Environmental Protection Agency's Science Advisory Board.	Conclusions of IARC and the Science Advisory Board (SAB) of the U.S. EPA concerning weight of evidence of carcinogenicity reflects a consensus evaluation of a particular panel of experts based on review of the data against IARC or EPA criteria, respectively. It should be noted that conclusions of the SAB may or may not be accepted in subsequent review by the U.S. EPA. Consensus of the IARC panel of experts or the SAB of the U.S. EPA on the classification of the weight of evidence for the carcinogenicity of butadiene was also not readily acquired. Outcome of CEPA assessments reflects consistent evaluation by Health Canada of the weight of evidence for carcinogenicity against specified criteria taking into account considerable technical input from external contributors.
Some epidemiological studies included in the Assessment Report were considered to be uninformative (e.g., the case-control study in styrene butadiene rubber workers and studies in tire manufacturing workers).	The text of the Assessment Report has been modified to emphasize the contribution of the case-control study in styrene butadiene rubber workers (i.e., independent verification of exposure-response in a subset of the larger cohort study. Discussion of the investigations in tire manufacturing workers has been deleted.