PHENOL

Comments on the **environmental sections** of the CEPA PSL Draft Assessment Report on Phenol were provided by:

1. Private citizen
2. Chemical Manufacturers Association, Arlington, Virginia, U.S.A.

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

Comment[(source)]	Response
The assessment should have better addressed phenolic compounds. The assessment document recognizes that the largest source of these is the pulp, paper and wood industries. The 'pure phenol' as defined by the assessment is only a fraction of the release from these sources.[(1)]	We agree that "pure phenol" is only a fraction of phenolics. However, the PSL2 Expert Panel identified "pure phenol" as the priority substance. The assessment, therefore, focused on "pure phenol".
The NPRI, ARET and Section 16 inventories underestimate the release of phenols by the pulp, paper and wood industry.[(1)]	That data are the best estimates of releases of phenol/total phenolics that exist in Canada.
The assessment modelling assumes phenol is released alone into more or less clean air. This is not the case. Phenols are released along with many other VOCs, particulate and combustion source pollutants such as reduced sulfur and sulfur dioxides. The breakdown, distribution and ultimate fate of phenols is significantly modified by these factors.[(1)]	Given that a local type model was used to estimate concentrations near the industry, it is doubtful that other contaminants will have a significant impact on the distribution and fate of phenol. In addition, the predicted concentrations near the industry were higher than those measured at other sites in Canada. Based on this, we believe that the predicted concentrations are acceptable to conduct our conservative assessment. The ISCST3 model is one of the best model to predict the concentrations and fate of single substances near point sources. We have not identified any other good model that can take into account the interactions of other contaminants when determining the distribution and fate of single substances.
The comments above are based on measurements of phenols (4-aap) in water and sediment in Powell River at levels greater than the water and soil criteria listed in the assessment document table 22. These media are not downstream but rather are downwind of the pulp and paper mill which is the source.[(1)]	No supporting evidence was provided to clarify this comment.
Assessment should not rely on the Birge *et al.* 1979 rainbow trout study as it did not follow the standard protocol for acute toxicity testing on rainbow trout.[(2)]	There is no requirement in CEPA or in the guidance manual for ecological risk assessments of priority substances that only toxicity data from standard tests be used in the assessments. As long as the test meets

Comment[(source)]	Response
	certain quality assurance criteria (e.g., acceptable control mortality, limited losses of test compound during testing, acceptable pH and dissolved oxygen levels, etc.), the data may be used in the assessment. We disagree with the CMA assertion that exposing the eggs for 23 days prior to hatching somehow disqualifies the test data from being used in the phenol assessment. Where there are continuous releases of phenol from industrial or municipal wastewater outfalls, it is likely that fish eggs will be exposed prior to hatching. Thus, the test simulates a realistic exposure scenario in freshwater streams and rivers in Canada. Because eggs are an important stage in the life history of fish, we see no reason to disqualify this study.
Assessment should not rely on the Birge *et al.* 1979 study did not report individual mortality data for the control vessels or the vessels with test material. All the "observed " mortality was seen in eggs that did not hatch.[(2)]	Rejecting toxicity data because results of each replicate were not reported is too stringent a criterion — most published toxicity data would end up being rejected if such a criterion were to be adopted. The fact that most or all of the mortality occurred in the eggs rather than post hatch does not nullify the test results. In our opinion, this result indicates that rainbow trout eggs are more sensitive to phenol exposure than are other life stages. Because fish eggs are likely exposed to phenol in the Canadian environment, we see no reason to reject this study. Mortality at any early life stage has the potential to cause adverse effects at the population level.

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Comments (which were quite similar) on the **health-related sections** of the CEPA PSL Assessment Report on Phenol were provided by:

- Nonprescription Drug Manufacturers Association of Canada, Ottawa, Ontario
- Chemical Manufacturers Association, Arlington, Virginia.

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

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
The draft Assessment Report contains an error in the Tolerable Intake (TI) calculation.	This wordprocessing conversion error, in which µg in the units was inadvertently converted to mg throughout the report, has been corrected. This did not affect the calculated ratio of the TI to various exposure estimates, used in the human health risk characterization, which was correct.
In comparing exposure to the TI, the incremental exposure due to industrial activity should be considered alone, not the endogenous phenol detected in foods.	The presence of phenol in foods is a combined result of both natural and anthropogenic sources. It is not necessary in this case to distinguish the contribution from these two types of sources, since the compound is not considered to be "toxic" under Section 11. Even if the compound had been considered to be "toxic" under Section 11, such considerations would not be considered in the assessment but rather in the separate, subsequent risk management (strategic options) phase.
The decreased foetal body weight reported at the high dose in the rat developmental toxicity study of Jones-Price et al. (1983), on which the TI is based, in part, is considered questionable.	While the Jones-Price study was considered as part of the weight of evidence for critical effects, its results did not contribute directly to the quantitative derivation of the TI, i.e., the TI was based on a completely different study.

Comment	Response
The discussion of the pharmacokinetics of phenol and its metabolite hydroquinone should be revised to indicate that hydroquinone is a minor metabolite of phenol, and to discuss the conclusions of a recent comprehensive review of the toxicology of hydroquinone by DeCaprio (1999).	The assessment report indicated that only a small percentage of absorbed phenol is metabolized to hydroquinone, and that a smaller fraction of absorbed phenol is metabolized to hydroquinone in humans than in rats. While published after the cut-off date, the review by DeCaprio would not affect the assessment, since the issue of the toxicity of hydroquinone is not central to the conclusions of the PSL assessment for phenol.
The TI is incorrectly based on a short-term rat study, rather than using the much higher no observed effect levels in the long-term and developmental studies. The draft assessment is also based on unduly conservative uncertainty factors that fail to take into account the rapid metabolism and elimination of phenol. A threshold model for toxicity, based on the saturable metabolism of phenol, should be considered. It is also suggested that the conclusion that intake of phenol from use of certain nonprescription drug products can exceed the TI should be revised in view of these considerations and the fact that there are pharmacokinetic differences between the bolus dose used in the rat gavage study and human usage patterns of phenol-containing drugs.	The limitations of the longer term studies preclude their use in the development of a meaningful TI. As indicated in the assessment report, "There are not recent studies in which a wide range of effects has been examined following short-term or subchronic ingestion of phenol". These aspects were discussed extensively in a review of the TI by an independent panel of scientific experts who agreed unanimously with both the choice of the critical study selected for the exposure-response analyses, as well as the uncertainty factors employed in derivation of the TI. Quantitative data are not available to justify use of less than default values for inter- and intra-species variation for the uncertainty factor. Moreover, in view of the acknowledged conservative nature of the TI, no additional factor was incorporated to address lack of an adequate study on reproductive effects. Uncertainties in relation to all of the aspects mentioned by the reviewer were delineated in the assessment report (this includes administration of a bolus dose within saturable range of metabolism). Indeed, one respondent noted that "...Health Canada has done an excellent job with respect to placing their derived TI in the proper perspective with the appropriate caveats...".
It is hoped that the TI will be re-evaluated in light of new data from several recent studies in rats, including developmental, neurotoxicological, and two-generation reproduction studies.	These studies were released after the cut-off date. Nevertheless, the existence of these studies and priority for their consideration, when available, with respect to their implications for other assessments was acknowledged in the assessment report.

Comment	Response
It is premature to draw inferences concerning the systemic exposure to phenol from nonprescription drugs. It is likely inappropriate to present daily phenol exposure as an accumulation of doses of nonprescription drugs taken over a 24-hour period, since phenol is typically given in a divided dose, and is readily metabolized and excreted in humans. Further, most such products are indicated for short-term use and are not taken on a chronic basis.	Estimating exposure over a 24-hour period is done for all exposure media, in order to compare these estimates to a TI on the same time scale; this is also the same time scale on which the directions for use of nonprescription drugs are typically based. Though most nonprescription drugs are indicated for short-term use, there is no indication of significant variation in the levels that induce critical effects in studies that are of short- versus long-term duration, and this is supported by the fact that phenol is rapidly metabolized and excreted; this information is indicated in the assessment report. Moreover, as recommended in the report, appropriate authorities under the Food and Drugs Act (Therapeutic Products Programme - TPP) have considered the need for and completed a review of phenol in nonprescription drug products. Dr. Brian Foster, Office of Science, TPP, Health Canada (613-957-3506) can be contacted for additional information.
It is agreed that appropriate authorities under the Food and Drugs Act (Therapeutic Products Programme) should determine whether a review of phenol in nonprescription drug products is needed. If needed, this should consider the new toxicity studies, the unique pattern of consumer usage of these products, the rapid metabolism and excretion of phenol associated with divided doses, and the therapeutic benefits of these products.	A review of phenol in nonprescription drug products has been completed by staff of the Therapeutic Products Programme at Health Canada. Dr. Brian Foster, Office of Science, TPP, Health Canada (613-957-3506) can be contacted for additional information.
The Synopsis of the draft Assessment Report should emphasize the overly conservative nature of the data, assumptions, and modelling used in the assessment.	The Synopsis is a brief summary of the information considered critical for the determination of “toxic” presented in a ‘‘lay context”. Details on the conservative treatment of the uncertainties are presented in the body of the assessment report.