

CARBON DISULFIDE

No comments were provided on the **environmental sections** of the CEPA PSL Assessment Report on Carbon Disulfide.

Comments on the **health-related sections** of the CEPA PSL Assessment Report on Carbon Disulfide were provided by

- Chemical Manufacturers Association, Arlington, Virginia.

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

Comment	Response
<p>In deriving the benchmark concentration (BMC), the limit that defines “abnormal” in the control population should be based on the one-percentile point of the control distribution, rather than on the five-percentile point employed in the draft report. In addition, a benchmark response level (BMR) of ten percent, rather than five percent, is more appropriate for determining the BMC for carbon disulfide.</p>	<p>As noted in the Assessment Report, there is no clear distinction between normal and adverse responses for the critical effect (reduced motor conduction velocity (MCV) of the peroneal nerve) and hence, the selection of cut-off values is necessarily arbitrary. The values for “abnormal” and BMR on which the BMC in the Assessment Report is based, were discussed extensively in a review of the Tolerable Concentration (TC) by an independent panel of scientific experts who agreed unanimously with the derivation of the BMC. The BMC derived in this manner is very similar to the lowest concentration that was without significant effect in the critical study. Also, though not selected for this reason and not strictly comparable, there is no compelling reason to deviate in this case from the use of a 5% BMR which is consistent with that for other Priority Substances.</p> <p>The principal reason of the reviewer for suggesting use of the alternate values in deriving the BMC appears to be that the resulting concentration is associated with an estimated mean peroneal MCV that is near the lower end of normal. However, a reduction of this magnitude would be expected to produce abnormally low conduction velocities in a considerable proportion of individuals, as a consequence of the wide range of peroneal MCV in unexposed populations.</p>
<p>The use of an uncertainty factor of 10 to account for variation in sensitivity among individuals is unduly conservative; the lack of metabolic activation of carbon disulfide as a precursor to toxicity and the demonstrated mechanism of action of carbon disulfide</p>	<p>As was noted in the Assessment Report, available data are insufficient to replace this component of the uncertainty factor with a data-derived value. Knowledge concerning the respective contributions of the parent compound and oxidative metabolites to the</p>

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<p>in inducing nerve conductivity effects (i.e., protein cross-linking in the axon) suggest no reason to expect differences in sensitivity among individuals.</p>	<p>critical effect is inadequate, and the metabolism of carbon disulfide is not fully known, particularly in humans. In addition, there are potential sensitive subpopulations that would not have been included in the occupational epidemiological studies on which the assessment is based, including the elderly and diabetics. These issues were discussed extensively in a review of the TC by an independent panel of scientific experts who agreed unanimously with the uncertainty factors employed in derivation of the TC.</p>
<p>In calculating the TC, it is preferable to adjust the BMC by ratio of the ventilatory volume over the workshift to that over 24 hours (rather than by the duration of the workshift), to take account of the fact that the ventilatory volume is typically greater among workers.</p>	<p>Because inhaled carbon disulfide rapidly approaches steady state, it is considered more appropriate to adjust by duration than by the ventilation volume. This issue was discussed in a review of the TC by an independent panel of scientific experts who agreed unanimously with this method of adjusting for discontinuous exposure in deriving the TC.</p>
<p>The formula for M for excess risk was incorrectly stated in the draft Assessment Report, though the reported values of M used to calculate the BMC were correct.</p>	<p>The formula has been corrected.</p>