ACRYLONITRILE

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

1. Saskatchewan Environment and Resource Management, Regina, Saskatchewan
2. Environmental Control, Rubber Division, Bayer Inc., Sarnia, Ontario
3. Industry Co-ordinating Group, Burlington, Ontario

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

Comment (source)	Response
Saskatchewan Environment agrees with the finding of acrylonitrile as CEPA "toxic" under clause 11(c). However, because of the limited use of acrylonitrile in Canada, the department would suggest that the considerations suggested for follow-up action be evaluated in terms of overall priority in comparison with other CEPA toxic substances, prior to commencing the suggested actions.(1)	Comment does not pertain to report itself. Suggestion will be passed on to risk managers.
Data provided by company taken out of context. Maximum predicted emission rates from stacks have never been achieved. Discharge from each stack is not continuous and discharges from stacks cannot be summed. Maximum predicted concentration of 9.3 $\mu g/m^3$ occurred for five 30 minute periods during 1998. Review of data by Ont Min of Env indicate the model may over predict actual concentrations by two orders of magnitude. (2)	Modify text section 2.3.2.1 (p. 12) to reflect additional caveats.
Misinterpretation of data. Clarify that "Of six determinations, acrylonitrile was not detected. If acrylonitrile is present in ambient air downwind of the plant, then the value is less than 52.9 $\mu g/m^3$ and is based on the lower detection of the analytical methods and the duration over which the sample was taken.(2)	Modify text in Section 3.3.1 (p. 13) to reflect additional caveat.
Data used in report is out of date. Use release values reported to NPRI. Bayer's release to air in 1996, 1997 and 1998 were 8.55, 5.19 and 4.95 tonnes, respectively.(2)	Cutoff for data acquisition was April 1998, as noted in the introduction of the assessment report. NPRI data for reporting year 1997 and 1998 were not available at the time of writing the assessment report. EC assessor sent an inquiry to the NPRI office - the 1997 and 1998 reports were not available as of Sept 1999.
Company that supplies data should be issued a draft report for comment prior to public release, in order to correct errors or misunderstandings.(2)	Environment Canada supplied draft environmental assessment reports and supporting document to commentor (Dec. 1997, Feb. 1998). Consolidated assessment (Health and Environment) report was not available for review prior to public release.

Comment (source)	Response
Selection of terrestrial inhalation CTV as LOEL of 55 mg/m^3 (effect on decrease in maternal absolute body weight) (Saillenfait *et al*. 1993) may be an adverse effect, but not a significant toxic effect. NOEL of 26.4 mg/m^3 and NOEL of 44 mg/m^3 could also be selected.(3)	Maintain CTV using LOEL with SF 100 = ENEV of 0.55 mg/m^3. Using the NOEL with SF of 10 would yield ENEV of either 2.6 mg/m^3 or 4.4 mg/m^3. Tier 1 assessment is hyperconservative, as reflected in the ENEV = 0.55 mg/m^3. No change to endpoint.

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Comments on the **health-related sections** of the CEPA PSL Draft Assessment Report on acrylonitrile were provided by:

- Bayer Inc., Sarnia, Ontario
- Industry Coordinating Group for CEPA, Burlington, Ontario
- Indiana University School of Medicine, Indianapolis

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
Lack of agreement with the conclusion that the available data indicate a direct interaction with genetic material as the most likely mode of induction of tumours.	The Synopsis will be modified to reflect the more detailed conclusion in the assessment report which indicates that: "Available data are insufficient to support a consensus view on a plausible mode of action for induction of tumours by acrylonitrile by other than direct interaction with genetic material" (Section 3.4, Proposed Conclusions). The full basis for this conclusion is specified in considerable detail in the assessment report and supporting documentation and was based on consideration of all identified data, including that considered admissible (i.e., for which full study reports were available prior to the end of the peer review period) from mechanistic studies in the U.S. graciously provided by members of the Industry Coordinating Group and their nominees in the first stage of external review of supporting documentation. (Every effort is made during the early stages of review to identify relevant data, through interface with those most likely to be familiar with recently completed studies). This information was fully considered not only by senior staff within Health Canada but by an independent panel of scientific experts who unanimously agreed with the above-mentioned conclusion and in an international exercise on methodology for cancer risk assessment.

Comment	Response
Reliance on data in rats in the face of a robust occupational database for acrylonitrile. Submission of a recent publication on this aspect by Collins and Strother (1999).	This aspect was fully discussed during review by an independent panel of scientific experts who unanimously agreed with the weighting of the data on carcinogenicity in animals for both the Hazard Evaluation and Exposure-Response Analyses. As discussed in the assessment report, the limitations of the negative epidemiological data and lack of information on mode of action of the tumours preclude meaningful weighting of the epidemiological data in these areas. To address these limitations, considerable additional data to address potential mode of action across species and increased sensitivity of the epidemiological analyses are required. The conclusion of Collins and Strother (1999) that: "Because of the rarity of CNS cancer in humans, and the lack of causal mechanisms of these tumors in rats, a more definitive conclusion will have to await additional experimental and observational data" is consistent with these conclusions of the assessment.
Nature of the data on mutagenicity in splenic T-cells need to be qualified.	The reference will be modified to: (Walker and Walker, 1997; abstract). As indicated in the current text, however, (in footnote No. 4) the description was based on "additional information ... provided by the authors." This study does not bear directly on the hazard characterization or dose-response analyses.
Clarification requested on limitations of liquid scintillation counting to determine unscheduled DNA synthesis.	The techniques of liquid scintillation counting versus autoradiography are discussed in more detail in the supporting documentation. As indicated in the Introduction to the draft assessment report, copies of the supporting documentation are available on request.
When reporting mutagenicity of urine from ACN-exposed rats and mice, it should be noted that there were no reports of cancer of the urinary tract in chronic assays.	In the section on genotoxicity, carcinogenicity is not addressed. In the section on carcinogenicity where there were no increases in tumour incidence, this is noted.
Request to omit last two sentences of Section 2.4.3.5.2.	This conclusion is based on consideration of inconsistencies of the available data and resulting lack of fulfillment of criteria for weight of evidence for the postulated mode of action of induction of tumours by oxidative damage based on expert opinion of an external peer review panel that included several genetic toxicologists..
Should be mentioned that increased levels of 8-oxodeoxyguanosine detected in the anterior portion of the brain correspond with the location of glioma formation in the rat brain	This is addressed in Section 2.4.3.8.2 of the Assessment Report.

Comment	Response
Additional references provided, relating to oxidative stress.	Oxidative stress was addressed in some detail in the section on toxicokinetics and mode of action. That discussion addressed two of the recent publications (as abstracts) submitted during the public comment phase. Other articles (including one still in press) were not published until after the cut-off date for consideration of new data but are unlikely to add significantly to the weight of evidence for mode of action, as assessed by an external peer review panel and in an international exercise on methodology for cancer risk. Nevertheless, the existence of relevant studies ongoing at the end of the assessment that might have implications for other assessments, when completed, was acknowledged in the assessment report.
Editorial error noted in Section 3.3.4 (Human health risk characterization)	Correction made to the table number (changed to 5 instead of 7)
Request for basis for designation of low, moderate and high priority for further action in Section 3.3.4	The basis for these designations (Health Canada, 1994 - "Human Health Risk Assessment for Priority Substances") is referenced on page 49 and included in the bibliography. As indicated in the Introduction of the Assessment Report, copies of this document can be accessed at http://www.hc-sc.gc.ca/ehp/ehd/bch/env_contaminants/psap/psap.htm