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October 21, 2019

Ministry of Health, Labour and Welfare
Chemical Hazards Control Division
Industrial Safety and Health Department
Labour Standard Bureau

Dear Sir or Madam,

We greatly appreciate the opportunity to present to MHLW a summary of our comments on 1-bromopropane to EPA.

The American Chemistry Council (ACC) and Albemarle Corporation submitted separate comments to the US Environmental Protection Agency (EPA) regarding the TSCA Work Plan Chemical Draft Risk Assessment of 1-Bromopropane, Docket No. EPA-HQ-OPPT-2015-0084, May 9, 2016.

Albemarle's comments emphasized the following points (please see attachment for full Albemarle comment):

1. Recently, Dr. Bruce Ames wrote a brief article which will be published in an upcoming special edition of Toxicology and Research Application. The article describes the general problem of the high false positive rates inherent in the current protocols for testing the carcinogenicity of chemicals in rats and mice in chronic bioassays.

2. Albemarle has collaborated with outside experts in human pulmonary pathology to evaluate the applicability of lung tumors in mice toward predicting the potential pulmonary tumorigenicity in humans. In our opinion, expressed in a recently published peer-reviewed manuscript, mouse lung tumors represent a level of sensitivity to chemical carcinogenesis that is much higher than would be expected in humans based upon an extensive literature.

3. Ventilation and personal protective equipment play an important potential role in reducing exposure to 1-bromopropane. Albemarle conducted an occupational exposure study in an aerospace wiring assembly plant which employed two back to back vapor degreasers running 16 hours per day. In this high ventilation environment, exposure levels below the level of detection (< 0.2 ppm) were observed even for the machine operators. While the ventilation levels in this assembly facility were on the high end of the marketplace, these results demonstrate that ventilation in conjunction with the proper use of personal protective equipment can be used to significant effect in reducing exposure to 1-bromopropane or other chemicals.

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ACC made a number of comments and suggestions to improve the overall risk assessment of 1-bromopropane and ensure a scientifically rigorous approach to evaluate risks associated with this chemical (please see attachment for complete ACC comments). The key issues identified by ACC were the following:

1. The 1-bromopane risk assessment uses methods consistent with a screening-level risk assessment, not a refined risk assessment, which must be reflected in the conclusions in the draft assessment. EPA should work with industry to refine the draft 1-bromopropane draft risk assessment.
2. EPA's risk assessment fails to use "best science" approaches, which are critical to a scientifically defensible assessment. Failure to use best science approaches is a critical flaw in EPA's 1-bromopropane risk assessment.
3. A systematic review of study quality, relevance, and reliability is missing from the assessment and must be included in order to adequately review and evaluate EPA's decisions. A systematic evaluation of each study used is a necessary part of a scientifically defensible risk assessment.
4. The 1-bromopropane exposure assessment is outdated and does not reflect current exposures in occupational and consumer populations. ACC believes that EPA should work with industry to refine and update the 1-bromopropane exposure assessment.
5. EPA has failed to describe adequately the scientific basis for decisions made when applying benchmark dose modeling to reproductive and developmental toxicity datasets. The risk assessment should incorporate significant additional discussion and explanation of the benchmark dose modeling process used. Without a discussion of the details of the modeling, risk assessors cannot judge the validity of certain modeling outputs and decisions.
6. EPA has failed to consider its own guidance regarding developmental toxicity and relies on a study endpoint and dose where maternal toxicity was present. EPA has failed to discuss why this endpoint is appropriate in light of maternal toxicity. In addition, EPA has not articulated its consideration of study quality when selecting studies upon which to rely.
7. EPA has used very conservative benchmark dose modeling response levels without describing the rationale for the choices made. EPA indicates that it followed its own guidance, yet a review of the two documents cited reveals important differences between the recommendations contained in EPA's guidance and what EPA actually did in the 1-bromopropane risk assessment.
8. The genotoxicity discussion in the 1-bromopropane risk assessment is incomplete. A weight-of-evidence assessment, which includes all available data, indicates that genotoxicity is not the mode of action for tumor induction in rodents exposed for a lifetime to 1-bromopropane by whole body inhalation. ACC agrees with EPA statements in the draft 1-bromopropane assessment that a mode of action for cancer is not known, based on available data.
9. The female mouse lung tumor is not relevant for the 1-bromopropane human cancer risk assessment. EPA should refine the risk assessment to consider data related to this type of tumor as discussed at the 2014 EPA State-of-the-Science Workshop on Chemically-induced Mouse Lung Tumors.

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In ACC's concluding comments, the following recommendations were strongly urged to EPA:

1. Acknowledge that its assessment of 1-bromopropane is a screening-level assessment that should be refined to determine if unreasonable risks exist in the occupational and/or consumer applications that are the focus of the assessment;
2, Refine the 1-bromopropane assessment using "best science" approaches in all aspects of the assessment, i.e., benchmark dose modeling, non-cancer and cancer risk assessments, and the exposure component;
3. Conduct a systematic review of study quality, relevance, and reliability of each study used in the revised and refined assessment;
4. Refine the exposure assessment with current data and information in both occupational and consumer settings with the assistance of industry stakeholders;
5. In a refined assessment of 1-bromopropane, describe in adequate detail the scientific basis for decisions made when applying modeling to reproductive and developmental toxicity datasets;
6. Consider its own guidance regarding developmental toxicity and explain the endpoints relied upon for its conclusions; and
7. Consider all available data regarding genotoxicity and apply a weight-of-evidence approach in drawing conclusions from the data.

Please do not hesitate to contact me if further information would be helpful.

Best Regards,

Carr J Smith

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