July 5, 2022

Mr. Joel Wolf
Chief
Risk Management Branch 1
Existing Chemicals Risk Management Division
US Environmental Protection Agency
1200 Pennsylvania Avenue
Washington, DC 20460

Re: Existing Chemical Exposure Limits for Occupational Use of Trichloroethylene

Mr. Wolf:

The American Chemistry Council's Trichloroethylene (TCE) Panel was dismayed at the Agency's decision to post a memo outlining the derivation of an existing chemical exposure limit (ECEL) based on developmental toxicity in the docket for risk management of TCE under the Toxic Substances Control Act (TSCA).[1] The decision runs counter to the Agency's own conclusions and the recommendations from the Agency's Scientific Advisory Committee on Chemicals (SACC) on the Risk Evaluation for TCE and to the National Academies of Science, Engineering and Medicine's (NASEM) subsequent review of the systematic review process used for evaluating TCE under TSCA Section 6. The results reported in the 2003 publication by Johnson *et al.* that are the basis for the Agency's alternative ECEL have not been duplicated in three separate studies and have been the subject of numerous critiques in the peer reviewed literature. The findings were rejected by a National Research Council (NRC) committee convened by EPA in 2006, moreover, and the study was considered to be of "low confidence" by the majority of EPA scientists who reviewed it in 2014. The Agency's continued disregard of the best available science and the advice of its own peer reviewers violates the scientific standards mandated in TSCA Section 26.

Among the charge questions developed by the Agency for the SACC's review of the draft Risk Evaluation for TCE was a specific request to comment on the "weight of evidence (WOE) analysis approach and conclusions for [fetal heart malformations]." In response, the majority of the 27 standing and ad hoc members of the Committee agreed that the limited evidence for heart malformations should not be used for the purposes of quantifying risks. In its report to the Agency, the SACC identified a number of concerns with the draft Evaluation's analysis of the

[1] Second existing chemical exposure limit (ECEL) for occupational use of trichloroethylene. Memo to Joel Wolf from Keith Jacobs. March 31, 2022. EPA-HQ-OPPT-2020-0642-0025.

health endpoint, noting that the scoring of results for cardiac effects was "overly simplistic, difficult to understand, and problematic in its value judgments and net result."[2] Importantly, the SACC recommended that the Agency "revise and expand" its justification for not using fetal heart malformations for its risk determination, but did not challenge the decision to use another health endpoint.

The subsequent review of the final TCE Risk Evaluation by the NASEM committee reviewing the TSCA systematic review process revealed that the problems identified by the SACC had not been corrected. The committee concluded that the lack of a documented process to explain deviations from standard practice greatly impacts the transparency of the evidence integration for heart defects. In particular, the committee noted that the use of two different methods within the evidence integration step (mathematical average, semi-qualitative grouping) is troubling and "runs completely counter" to published Agency guidance. The committee also noted that the evaluation of the cardiac endpoint conflated aspects of three important systematic review elements – an evaluation of the individual studies, consideration of the body of evidence, and the level of confidence in a recommendation or determination of causation.

The concerns expressed by the SACC and NASEM committees are similar to those voiced by the NRC committee reviewing the draft assessment of TCE for the Integrated Risk Information System (IRIS) in 2006. The Committee noted that -

> the rodent studies showing trichloroethylene-induced cardiac teratogenesis at low doses were performed by investigators from a single institution. Also noted were the unusually flat dose-response curves in the low-dose studies from these investigators. . . Thus, the animal data are inconsistent, and the apparent species differences have not been addressed.[3]

The NRC committee concluded that "[t]he results need to be replicated in another laboratory to clarify the dose-response relationship."[4] Yet, despite the absence of cardiac defects in two subsequent laboratory studies – an inhalation study published later in 2006 and a drinking water study in 2020 – EPA continues to cite the findings of the single study group. The Agency's changing rationales for its conclusions are not credible – ranging from differences in exposure route to genetic drift to the inferiority of the Agency's approved dissection method.

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2 TSCA Science Advisory Committee on Chemicals. Meeting Minutes and Final Report No. 2020-4 (2020). EPA-HQ-OPPT-2019-0500-0111

3 NRC. Assessing the Human Health Risks of Trichloroethylene: Key Scientific Issues. Washington, DC: The National Academies Press (2006), at 171.

4 Ibid, at 5.

Publication of a second ECEL based on this study which has been roundly criticized, not duplicated in other labs, and rejected by the Agency's own advisory groups, demonstrates a blatant disregard for the weight of the scientific evidence and a clear bias on the part of the Agency. The alternative ECEL document should be removed from the docket and the Agency's analysis of risk management options should be based on the conclusions for acute immunosuppression and chronic autoimmunity which are supported by "the best available science and weight of scientific evidence."[5] Given EPA's continuing failure to conduct an objective review of the evidence for cardiac defects, moreover, any further review of the cardiac endpoint must be conducted by an independent group of the appropriate experts to ensure the credibility of such a review.

Sincerely,

Steve Risotto

Stephen P. Risotto
Senior Director

cc: Jeff Morris, ECRAD
Sheila Healy, ECRAD Risk Assessment Branch 5
Keith Jacobs, ECRAD Risk Assessment Branch 5

[5] USEPA. Risk Evaluation for Trichloroethylene (CASRN: 79-01-6). Document #740R18008 (November 2020), at 33.