UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

Faye Graul, Executive Director
Halogenated Solvents Industry Alliance, Inc. - HSIA
3033 Wilson Boulevard, Suite 700
Arlington, VA 22201

Dear Ms. Graul:

This letter is the response to the Request for Correction received by the U.S. Environmental Protection Agency on October 6, 2015, which was assigned RFC #16001 for tracking purposes. In the RFC, the HSIA cites both the "objectivity" and "utility" criteria of the EPA's *Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated by the Environmental Protection Agency (IQG)*,[1] and requests corrections to the following EPA document disseminated by the Office of Pollution Prevention and Toxics:

> TSCA Work Plan for Chemical Assessment for Trichloroethylene (TCE); Degreasing, Spot Cleaning and Arts & Craft Uses (June 2014) (#740-R1-4002).[2]

Summary of the Request

The HSIA RFC provides various reasons for requesting the correction of the TSCA Work Plan Chemical Assessment for TCE to ensure that it meets data quality requirements before relying on it as the basis for any regulation of TCE. Most of these reasons are based on HSIA's opinion that the *Johnson et al. (2003) study* does not meet the Information Quality Act criteria for objectivity, utility or reproducibility. To support this statement in the RFC, HSIA discusses the deficiencies of the *Johnson et al. (2003) study*, including the results of an HSIA-sponsored critical review that indicates *Johnson et al.* does not provide "substantive or consistent epidemiologic evidence of a causal relationship between TCE exposure and congenital heart defects." HSIA's assertions and comments on the *Johnson et al. (2003) study* and the strength of the evidence supporting TCE-induced fetal cardiac malformations are not new.

Although this RFC raises the same concerns about the *Johnson et al. (2003) study* that were expressed in the RFC #14001 involving the EPA document "Toxicological Review of Trichloroethylene (CAS No. 79-01-6) in Support of Summary Information on the Integrated Risk Assessment System (IRIS)," HSIA states that this request is separate and distinct from RFC #14001, which was denied in March 2015,[3] and a subsequent request for reconsideration that was denied on February 26, 2016.[4] This RFC involves the OPPT Risk Assessment, which HSIA says goes beyond what was done for IRIS and "expressly relies on

[1] https://www.epa.gov/sites/production/files/2015-08/documents/epa-info-quality-guidelines.pdf.
[2] https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/tsca-work-plan-chemical-risk-assessment.
[3] http://www.epa.gov/sites/production/files/2015-09/documents/14001-response.pdf.
[4] https://www.epa.gov/sites/production/files/2016-03/documents/14001a-response.pdf.

hazard values derived directly from *Johnson et al.* (2003) to estimate acute risk." HSIA asserts that these extremely low values result in MOE values below 10 for almost all the occupational and residential exposure scenarios examined, and concludes that because the *Johnson et al. (2003) study* is flawed it should not be the basis for the toxicological value that is expected to serve as the basis for regulation under TSCA.

To address its information quality concerns, the HSIA states that the EPA should revise the TSCA Work Plan Chemical Assessment for TCE before relying on it as the basis for regulation.

The EPA Response to HSIA's Assertions

In this response, the EPA is addressing the following topics raised in the HSIA RFC:

- Use of the *Johnson et al. (2003) study* in risk estimation.
- Assertion that the TCE Work Plan risk assessment is a screening level assessment and thus cannot be used in a regulatory determination
- Classification consistency with the EPA's guidelines for evaluating carcinogens.
- Peer review consistency with the EPA's peer review guidance.
- Rulemakings initiated under TSCA to address the risks identified.

Use of the *Johnson et al. (2003) study* in risk estimation.

As noted in the HSIA RFC, the agency has already responded to a separately submitted RFC regarding the inclusion of the *Johnson et al. (2003) study* in its risk assessments, and although the HSIA RFC states that it is not asking for those issues to be reconsidered, this RFC raises those very same issues again. Since the EPA has already addressed the issues raised regarding the use of the *Johnson et al. (2003) study* in its "Toxicological Review of Trichloroethylene (CAS No. 79-01-6)," the information provided in those responses applies here as well.

The information presented in the TCE work plan risk assessment meets the EPA IQG standards of objectivity and utility. As indicated in the TSCA Work Plan Chemical Assessment on TCE, the EPA's policy supports the use of developmental studies to evaluate the risks of acute exposures. This science-based policy is based on the presumption that a single exposure of a chemical at a critical window of fetal development may result in adverse effects, and is based on the EPA's 1991 Guidelines for Developmental Toxicity Risk Assessment (pg. 38) and 1996 Guidelines for Reproductive Toxicity Risk Assessment (pg. 83). The EPA reviewed multiple studies for suitability for acute risk estimation including a number of developmental studies of TCE exposure and additional studies of TCE metabolites administered developmentally (Appendix N). This is captured in the supporting documentation available in the docket (EPA-HQ-OPPT-2012-0723). Most of the acute occupational and residential scenarios show risks irrespective of the selected key study. Since adverse developmental endpoints were observed in multiple studies, including the *Johnson et al. (2003) study*, the EPA made the decision to use the most health protective endpoint (*i.e.*, fetal cardiac malformations, *Johnson et al. (2003) study*) representing the most sensitive human population, i.e., adult women of childbearing age (> 16 years) and their fetuses for the acute risk assessment.

TCE Work Plan risk assessment is not a screening level assessment and can be used in regulatory determination.

As indicated in the HSIA RFC, the OMB information quality assurance (IQA) guidelines discuss screening level risk assessments used in decision making. The EPA IQGs also mention screening level assessments and state that "the screening level assessments may not result in 'central estimates' of risk or upper and lower-bounds of risks." In the response to comments document issued for the TSCA Work Plan Chemical Assessment for TCE, the EPA made clear that based upon multiple characteristics, the

TCE Work Plan Chemical Assessment was not a screening level assessment (e.g., use of complex and robust PBPK modeling, exposure modelling using both near field and far field approaches, E-FAST modeling with sensitivity analysis, and inclusion of monitoring data obtained from OSHA). Note that the TCE Work Plan Chemical Assessment provides risk estimates for 50th, 95th and 99th percentile. The TCE risk assessment provides central tendency and upper and lower bounds of risk and those characteristics, along with others, demonstrate that the TCE risk assessment does not meet the definition of screening level assessments in the IQA guidelines.

Finally, regarding screening level assessments, the EPA IQGs state "Such screening assessments provide useful information that are sufficient for regulatory purposes in instances when more elaborate, quantitative assessments are unnecessary." Thus, the HSIA suggestion that a screening level assessments cannot inform risk management decisions is erroneous. Furthermore, this assertion is irrelevant to the TCE risk assessment, since it is clearly not a screening level assessment, but rather an elaborate, quantitative assessment as evidenced by the multiple uses, exposure scenarios and extensive risk quantification included in it.

Classification was consistent with the EPA's Guidelines for Carcinogen Risk Assessment.[5]
Regarding TCE's carcinogenicity, HSIA states that the "EPA's classification of TCE as 'Carcinogenic to Humans' is not supported by the evidence and cannot be justified under the 2005 [Cancer] Guidelines." The EPA's cancer classification documented in the Toxicological Review of TCE was the result of a systematic evaluation and integration of all of the available human, animal and mechanistic information on TCE's cancer potential. HSIA's information quality concerns on the cancer endpoint were addressed through the IRIS assessment development process which ensures a transparent, open and public process for developing chemical assessments.

This process consisted of several levels of peer review including agency review, science consultation on the draft assessment with other federal agencies and the Executive Office of the President, public comment, and external peer review by the EPA's Science Advisory Board (SAB) in 2002, scientific consultation by the U.S. National Academy of Sciences in 2006, external peer review of the revised draft assessment by the EPA's Science Advisory Board (SAB) in January 2011 followed by final internal agency review and the EPA-led science discussion on the final draft. The outcome of this rigorous process was a final Toxicological Review of TCE that meets our EPA IQG standards of objectivity, utility and reproducibility for both cancer and non-cancer dose-response assessments. EPA's assessment is further supported by the fact that International Agency for Research on Cancer (2014) concluded that there is ***sufficient evidence in humans for the carcinogenicity of TCE*** and classified it in Group 1.[6] Trichloroethylene causes cancer of the kidney. A positive association has been observed between exposure to trichloroethylene and non-Hodgkin lymphoma and liver cancer. Furthermore, the 12th report on carcinogens (RoC) by the National Toxicology Program also concluded that TCE exposure is ***reasonably anticipated to be a human carcinogen 2015***.[7] These additional recent peer reviews are consistent with the EPA's classification: ***TCE is carcinogenic to humans by all routes of exposures based upon strong epidemiological and animal evidence***.

Peer review was consistent with the EPA's peer review guidance.
With respect to the peer review of the draft TSCA Work Plan Chemical Assessment for TCE, the peer review was consistent with the EPA's guidelines for influential scientific information and highly influential scientific assessments as outlined in EPA's Peer Review Handbook. Prior to conducting a

[5] https://www.epa.gov/risk/guidelines-carcinogen-risk-assessment.
[6] http://monographs.iarc.fr/ENG/Monographs/vol106/mono106-001.pdf.
[7] http://ntp.niehs.nih.gov/pubhealth/roc/candidates/tce.html.

panel peer review, the EPA posted the peer review plan of the TSCA Work Plan Chemical Assessment for TCE.[8] The EPA tasked an external independent contractor, Science Consulting Group (SCG), to assemble a panel of experts to evaluate the draft TCE TSCA risk assessment report for specific uses of TCE. SCG evaluated 27 candidates that were nominated through the public process as peer reviewers by the February 8, 2013, deadline established in the January 9, 2013, **Federal Register** notice. SCG also evaluated over 100 additional experts with expertise identified in the public notice through literature searches and service on previous peer review panels before submitting the proposed peer review panel members for final public comment. This proposed peer review panel was vetted by the contractor for conflict of interest and the appearance of bias according to the EPA's peer review guidance for conducting a peer review with an external contractor. A **Federal Register** notice was also published to publicly name the proposed peer panel members and their affiliations. The public had the opportunity to provide comments on the appearance of a conflict of interest or bias for any proposed peer review panel member. The comment period on the peer review panel membership closed on June 28, 2013.[9] Peer review charge questions were posted on the docket and the public was requested to provide input prior to the peer review meetings that took place on July 9, July 17 and August 21, 2013. Information about the peer review process is transparently documented in EPA-HQ-OPPT-2012-0723[10] and the contractor-run web site,[11] including public comments submitted by HSIA and other organizations, documents reviewed by peer review panel and final peer review report.

HSIA claims that the EPA ignored the comments from the peer review panel on various technical issues, including the use of the *Johnson et al. (2003) study*. The EPA's lack of agreement with a commenter should not be interpreted as a lack of consideration. The EPA did not ignore any of the peer review or public comments received. In fact, the draft TSCA Work Plan Chemical Assessment for TCE underwent significant revisions based on the peer review and public comments. The EPA posted in the docket the summary of external peer review and public comments and their disposition, including the response to comments on the screening level classification and those from Dr. Willhite on the *Johnson et al. (2003) study*.[12] The EPA did follow the peer review panel members' recommendations and updated the literature search for developmental toxicity database and performed further systematic review for TCE and relevant TCE metabolites. This additional analysis, performed in response to peer review recommendations is summarized in Appendix N of the June 2014 TSCA Work Plan Chemical Assessment for TCE and described also in response to comments document. Furthermore this additional systematic review was recently independently peer reviewed and published as part of a journal article.

Rulemakings initiated under TSCA to address risks identified.

To address the risks identified in the June 2014 TSCA Work Plan Chemical Assessment for TCE, the EPA promptly announced the initiation of several rulemakings under TSCA, including a significant new use rule under TSCA section 5(a)(2) and rulemaking proceedings under TSCA section 6. The rulemaking process provides clear opportunities for public review and comment on the agency's proposed action to address the risks identified, as well as all on the materials considered in the development of that action.

In fact, HSIA submitted comments on the proposed significant new use rule under TSCA section 5(a)(2) that was issued on August 7, 2015 (80 FR 47441), which proposed to designate the manufacture or processing of TCE for any use in a consumer product as a significant new use, with a proposed

[8] http://cfpub.epa.gov/si/si_public_pra_view.cfm?dirEntryID=245551.
[9] http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2012-0723-0023.
[10] http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2012-0723-0046.
[11] http://www.scgcorp.com/tcl2013/.
[12] http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2012-0723-0039.

exception for use of TCE in cleaners and solvent degreasers, film cleaners, hoof polishes, lubricants, mirror edge sealants, and pepper spray.[13] EPA received a total of four public comments on the proposal, including a comment from HSIA that stated the "final Work Plan Assessment for TCE (June 25, 2014) is deeply flawed and should not serve as the basis for regulation" and provided the same criticisms as those provided by the submitter in the RFC. On April 8, 2016 (81 FR 20535), the EPA issued a final significant new use rule to require notification to the EPA before certain new consumer uses of TCE begin or resume.[14] EPA's response to HSIA's comments on the proposed SNUR appears in Unit X. of the final rule. In summary, EPA believes that the commenter's specific concerns are not relevant to the "basis for regulation" for the SNUR. Under TSCA section 5(a)(2), EPA is neither required to determine that a particular new use of any chemical substances presents, nor even that it may present, an unreasonable risk to human health or the environment. Rather, EPA issues a SNUR for a particular new use of a substance if it has reason to anticipate that the use would raise significant questions related to potential exposure, so that it should have an opportunity to review the use before such use should occur. As discussed in Unit IV of the final rule, EPA based this judgment on a consideration of all relevant factors, including the specific factors identified in TSCA section 5(a)(2). The notification required by the final SNUR ensures that the EPA will review any effort to resume or begin certain new consumer uses of TCE and, if appropriate, take action to prohibit or limit those uses.

In addition, the EPA initiated a rulemaking proceeding under TSCA section 6, which provides authority for the EPA to ban or restrict the manufacture (including import), processing, distribution in commerce, and use of chemicals, as well as any manner or method of disposal. In this case, the EPA is determining whether the continued use of TCE in some commercial degreasing uses, as a spotting agent in dry cleaning, and in certain consumer products would pose an unreasonable risk to human health and the environment. [15] The public will have an opportunity to review and comment on the specific risk reduction approach proposed, as well as the information considered in developing the proposed rule. The EPA anticipates issuing the proposed rules addressing specific TCE uses in the fall of 2016.

Conclusion
The EPA, after careful review of the RFC submitted by HSIA, has concluded that the underlying information and conclusions presented in the TSCA Work Plan Chemical Assessment for TCE are consistent with the EPA's Information Quality Guidelines.

TSCA Work Plan for Chemical Assessments
Originally released in March 2012, the EPA's TSCA Work Plan for Chemical Assessments helps focus and direct the activities of the EPA existing chemicals program. Identification of a chemical on the TSCA Work Plan indicates only that the agency intends to consider it for assessment. The agency believes that identifying these chemicals early in the review process affords all interested parties the opportunity to bring additional relevant information on those chemicals to the agency's attention.

In preparing the TSCA Work Plan, the EPA provided several opportunities for stakeholder participation, including review and comment on the methodology the agency intended to use for the TSCA Work Plan. Comments received were considered and addressed. The agency also followed the EPA IQGs to ensure the utility, objectivity, and integrity of the information disseminated. The information provides specific references to the best available science and supporting studies, and is presented with applicable uncertainties and limitations discussed. The TSCA Work Plan is also formatted and designed with the

[13] https://www.gpo.gov/fdsys/pkg/FR-2015-08-07/pdf/2015-19348.pdf.
[14] https://www.regulations.gov/document?D=EPA-HQ-OPPT-2014-0697-0014.
[15] Listed in the EPA Annual Regulatory Plan and Semi-Annual Regulatory Agenda under RIN 2070-AK03. The eAgenda can be accessed at http://www.reginfo.gov.

intended audience in mind, and was distributed in a secure manner to protect the document from deliberate or accidental alteration.

Trichloroethylene (TCE); TSCA Work Plan Chemical Assessment

The EPA identified trichloroethylene for risk evaluation as part of its Work Plan for Chemical Assessment under TSCA.[16] TCE is used in industrial and commercial processes, and also has some limited uses in consumer products. In the June 2014 TSCA Work Plan Chemical Assessment for TCE, the EPA identified risks associated with commercial degreasing and some consumer uses.

The EPA provided opportunities for stakeholder participation, provided opportunity to comment on peer review plan and scope of the assessment, provided opportunity for public comment on draft risk assessment, conducted an independent external peer review, and post peer review of risk assessment. EPA also held an experts workshop on TCE alternatives and risk reduction approaches.[17] Comments received were carefully considered in revising the assessment and EPA's responses are publicly[18] available in a response to comment document. In preparing the TSCA Work Plan Chemical Assessment for TCE, the agency followed the EPA IQGs to ensure the utility, objectivity, and integrity of the information disseminated. The information provides specific references to the best available science and supporting studies, and is presented with applicable uncertainties and limitations discussed. The TSCA Work Plan Chemical Assessment for TCE is also formatted and designed with the intended audience in mind, and was distributed in a secure manner to protect the document from deliberate or accidental alteration.

TSCA Rulemakings Under Development

As indicated in section 8.5 of the EPA's IQGs, EPA believes that the thorough consideration provided by the public comment process serves the purposes of the Guidelines, provides an opportunity for correction of any information that is inconsistent with the Guidelines, and does not duplicate or interfere with the orderly conduct of the action. As such, when an information quality issue is raised on an EPA study, analysis or information that is disseminated with the draft or proposed action for public review and comment, EPA intends to address it in the context of the final agency action or information product.

In addition to the opportunities for public participation in the assessment of risks for TCE, the rulemaking process provides clear opportunities for public review and comment on the agency's proposed risk reduction regulations under TSCA, including review and comment of the materials considered in the development of that action. The agency reviews and considers all comments received related to each proposed rule, and, when the final rule is issued, provides the agency responses to the comments germane to each rulemaking. In fact, as indicated previously, the agency has already considered HSIA's quality issues raised about the TSCA Work Plan Chemical Assessment for TCE in the context of the rulemaking taken under TSCA section 5(a)(2).

Your Right To Appeal

If you are dissatisfied with this response, you may submit a Request for Reconsideration. The EPA requests that any such RFR be submitted within 90 days of the date of the EPA's response. If you choose to submit a RFR, please send a written request to the EPA Information Quality Guidelines Processing Staff via mail (Information Quality Guidelines Processing Staff, Mail Code 2811R, U.S. EPA,

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[16] TSCA Work Plan site https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/tsca-work-plan-chemical-risk-assessment.

[17] TCE expert workshop; https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/trichloroethylene-tce.

[18] public comments and responses to public comments and peer recommendations https://www.regulations.gov/document?D=EPA-HQ-OPPT-2014-0327-0001.

1200 Pennsylvania Avenue, NW, Washington, DC 20460); electronic mail (quality@epa.gov); or fax (202-565-2441). If you submit a RFR, please reference the request number assigned to the original Request for Correction (RFC #16001). Additional information about how to submit an RFR is listed on the EPA Information Quality Guidelines website at http://epa.gov/quality/informationguidelines/index.html.

Sincerely,

James J. Jones
Assistant Administrator

cc: Ann Dunkin, Chief Information Officer and
Assistant Administrator, Office of
Environmental Information
Vincia Holloman, Acting Director of
Enterprise Quality Management Division