EPA SCIENTIFIC ADVISORY COMMITTEE ON CHEMICALS
CHARGE TO THE PANEL – CARBON TETRACHLORIDE

As amended by the Frank R. Lautenberg Chemical Safety for the 21st Century Act on June 22, 2016, the Toxic Substances Control Act (TSCA), requires the U.S. Environmental Protection Agency (EPA) to conduct risk evaluations on existing chemicals. In December of 2016, EPA published a list of the initial ten chemical substances that are the subject of the Agency's chemical risk evaluation process (81 FR 91927), as required by TSCA. Carbon tetrachloride is one of the first ten chemical substances to undergo a peer review by the Scientific Advisory Committee on Chemicals (SACC). In response to this requirement, EPA has prepared and published a draft risk evaluation for carbon tetrachloride. EPA has solicited comments from the public on the draft and will incorporate them as appropriate, along with comments from the peer reviewers, into the final risk evaluation.

The focus of this meeting is to conduct the peer review of the Agency's draft risk evaluation of carbon tetrachloride and associated supplemental materials. At the end of the peer review process, EPA will use the reviewers' comments/recommendations, as well as the public comments, to finalize the carbon tetrachloride draft risk evaluation.

This draft risk evaluation contains the following components:

- Discussion of chemistry and physical-chemical properties
- Characterization of uses/sources
- Environmental fate and transport assessment
- Environmental exposure assessment
- Human health hazard assessment
- Environmental hazard assessment
- Risk characterization
- Risk determination
- Detailed description of the systematic review process developed by the Office of Pollution Prevention and Toxics to search, screen, and evaluate scientific literature for use in the risk evaluation process.

CHARGE QUESTIONS:

Systematic Review (Section 1.5 of the Draft Risk Evaluation):

The Toxic Substances Control Act (TSCA) requires that EPA use data and/or information in a manner consistent with the "best available science" and that EPA base decisions on the "weight of the scientific evidence". The EPA's Final Rule, *Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act* (82 FR 33726), defines ''best available science'' as science that is reliable and unbiased. This involves the use of supporting studies conducted in accordance with sound and objective science practices, including, when available, peer reviewed science and supporting studies and data collected by accepted methods or best available methods (if the reliability of the method and the nature of the decision justifies use of the data). The Final Rule also defines the "weight of the scientific evidence" as a systematic

review method, applied in a manner suited to the nature of the evidence or decision, that uses a pre-established protocol to comprehensively, objectively, transparently, and consistently identify and evaluate each stream of evidence, including the strengths, limitations, and relevance of each study and to integrate evidence as necessary and appropriate based upon strengths, limitations, and relevance.

To meet these scientific standards, EPA applied systematic review approaches and methods to support the carbon tetrachloride draft risk evaluation. Information on the approaches and/or methods is described in the draft risk evaluation as well as the following documents:

- *Strategy for Conducting Literature Searches for Carbon Tetrachloride: Supplemental File for the TSCA Scope Document*, (EPA-HQ-OPPT-2016-0733)
- *Carbon tetrachloride (CASRN 56-23-5) Bibliography: Supplemental File for the TSCA Scope Document*,(EPA-HQ-OPPT-2016-0733)
- *Carbon Tetrachloride Problem Formulation* (EPA-HQ-OPPT-2016-0733)
- *Application of Systematic Review in TSCA Risk Evaluations*

EPA has solicited peer review and public feedback on systematic review approaches and methods for prior evaluations. A general question on these approaches is not included in this charge; however, EPA will accept comment on the systematic review approaches used for this evaluation if provided.

1. Environmental Fate and Exposure (Sections 2.1 and 2.2 of the Draft Risk Evaluation):

The environmental fate of carbon tetrachloride is characterized by partitioning to the atmosphere, surface water and groundwater. Carbon tetrachloride in surface water is expected to volatilize and diffuse upwardly in the troposphere, with a half-life greater than 330 years. Ultimate diffusion to the stratosphere leads to photodegradation. Carbon tetrachloride has a low bioaccumulation potential and when in groundwater is expected to anaerobically biodegrade. EPA did not further analyze the environmental fate of carbon tetrachloride as indicated by the conceptual models in the problem formulation.

1.1 Please comment on the data, approaches and/or methods used to characterize exposure to aquatic receptors.

2. Environmental Hazard and Risk Characterization (Sections 3.1 and 4.1 of the Draft Risk Evaluation):

An analysis of potential risk to aquatic species indicates that expected environmental concentrations are below hazard thresholds for aquatic species. In addition, a qualitative consideration of physical-chemical properties and the conditions of use in this assessment indicate that risks to sediment-dwelling invertebrate species are not expected.

2.1 EPA determined that there are no environmental risks of concern to aquatic species

based on an assessment of risk using environmental hazard data, Probabilistic Dilution Model (PDM) within E-FAST, Discharge Monitoring Reports (DMR) data, fate information, and physical/chemical properties. Please comment on whether the information presented supports the analysis in the draft environmental hazard section (Section 3.1) and the findings outlined in the draft risk characterization section (Section 4.1).

3. Occupational Exposure and Releases (Section 2.4 of the Draft Risk Evaluation):

Workers and occupational non-users may be exposed to carbon tetrachloride when performing activities associated with conditions of use including, but not limited to:

- Connecting/disconnecting transfer lines used to unload carbon tetrachloride containers into storage or reaction vessels;
- Cleaning and maintaining equipment;
- Sampling chemical formulations containing carbon tetrachloride for quality control;
- Repackaging products containing carbon tetrachloride;
- Handling, transporting and disposing wastes containing carbon tetrachloride;
- Performing other work activities in or near areas where carbon tetrachloride is used.

3.1 Please comment on the reasonableness of the characterization of occupational exposure for workers and occupational non-users. What other additional information, if any, should be considered?

EPA distinguishes between workers (users) and occupational non-users (ONUs) to acknowledge that different tasks and activities are associated with different levels of exposures and thus risk in the same workplace. EPA assumes that area air monitoring is an appropriate surrogate for ONUs' exposure. In the absence of ambient air monitoring data, EPA assumes that the central tendency of personal breathing zone (PBZ) monitoring data is a good surrogate for ONU exposures because the agency rarely has PBZ monitoring data for ONUs.

3.2 Please comment on the scientific validity and transparency of EPA's approach and the assumptions EPA used to characterize exposure for ONUs. Please also comment on the uncertainties related to the assumptions used to characterize exposures for ONUs.

Workplace inhalation exposure concentrations to carbon tetrachloride were estimated for adults using a combination of monitoring data and modeled exposure air concentrations. For dermal exposures, EPA modeled exposures for workers using parameters such as exposed skin surface areas, body weight, and glove protection factors, if applicable. EPA used literature sources for estimating many of these occupational exposure parameters and generic assumptions when data were not available.

3.3 Please comment on the approaches and assumptions used and provide any specific suggestions or recommendations for alternative approaches, models or information that should be considered by the Agency for improving the workplace exposure assessment. More specifically, if other sources of monitoring data are available to estimate air concentrations for worker exposures, please provide specific citations.

3.4 Please comment on assumptions used in the absence of specific exposure information (e.g., dermal surface area assumptions: high-end values, which represents two full hands in contact with a liquid: 890 cm^2 (mean for females),1070 cm^2 (mean for males); central tendency values, which is half of two full hands (equivalent to one full hand) in contact with a liquid and represents only the palm-side of both hands exposed to a liquid: 445 cm^2 (females), 535 cm^2 (males)).

3.5 Please comment on EPA's approach to characterizing the strengths, limitations and overall confidence for each occupational exposure scenarios presented in Section 2.4.1. Please comment on the appropriateness of these confidence ratings for each scenario. Please also comment on EPA's approach to characterizing the uncertainties summarized in Section 4.4.1.

4. Human Health Effects (Section 3.2 of the Draft Risk Evaluation):

EPA evaluated human health hazards as follows:

- Reviewed reasonably available human health hazard data and determined whether specific subgroups may have greater susceptibility to carbon tetrachloride hazard(s) than the general population;
- Conducted hazard identification (the qualitative process of identifying non-cancer and cancer endpoints) and dose-response assessment (the quantitative relationship between hazard and exposure) for all identified human health hazard endpoints;
- Derived points of departure (PODs) where appropriate;
- Adjusted the PODs as appropriate to conform to the specific exposure scenarios evaluated (e.g., adjust for duration of exposure);
- Considered the route(s) of exposure (inhalation, dermal), available route-to-route extrapolation approaches, and the available approaches to correlate internal and external exposures to integrate the exposure and hazard assessments;
- Evaluated the weight of the scientific evidence based on the available human health hazard data for carbon tetrachloride.

4.1 Please comment on the reasonableness of the evaluation of human health hazards. Are there any additional carbon tetrachloride specific data and/or other information that should be considered?

EPA used a linear low-dose extrapolation for evaluating potential cancer risks from chronic exposures to carbon tetrachloride.

4.2 Please comment on the appropriateness of using a linear low-dose extrapolation versus a non-linear or threshold approach for assessing low exposures based on the cancer mode of action information presented in Section 3.2 and Appendix K

There are a limited number of quantitative studies on the absorption and systemic toxicity of carbon tetrachloride by the dermal route. Therefore, PODs for dermal exposures are based on (1) use of one unacceptable study and one acceptable study with similar dosing regimens in a weight of evidence

approach, (2) estimation of dermal absorption over time of exposure; (3) estimation of evaporation losses for non-occluded exposures and (4) extrapolation of dermal POD from inhalation POD (for chronic exposures).

4.3 Please comment on the appropriateness of the approaches used for generating PODs for dermal exposures, including the process/equation for extrapolating the cancer slope factor (CSF) and POD for chronic dermal exposures (dermal HED).

5. Risk Characterization (Section 4 of the Draft Risk Evaluation):

EPA calculated human health risks for acute and chronic exposures. For non-cancer effects EPA used a margin of exposure (MOE), which is the ratio of the hazard value to the exposure to calculate human health risks. Using an acute non-cancer POD, EPA evaluated potential acute risks for workers for certain scenarios. A benchmark MOE of 10 was used with the acute POD based on central nervous system (CNS) effects. For chronic occupational risks, EPA used a POD for liver effects as the basis of the chronic non-cancer MOE calculations. A benchmark MOE of 30 was used to interpret chronic risks for workers. An Inhalation unit risk (IUR) for adrenal gland tumors was used to evaluate potential chronic risks to cancer endpoints for worker exposure scenarios. The risk characterization also provides a discussion of the uncertainties surrounding the risk calculations.

5.1 Please comment on whether the information presented supports the finding outlined in the draft risk characterization section. If not, please suggest alternative approaches or information that could be used to further develop risk estimates within the context of the requirements stated in EPA's Final Rule, Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act (82 FR 33726).

5.2 Please comment on the characterization of uncertainties and assumptions including whether EPA has presented a clear explanation of underlying assumptions, and accurate contextualization of uncertainties. Please provide information on additional uncertainties and assumptions that EPA has not adequately presented.

5.3 Please comment on the validity of specific confidence summaries presented in section 4.5.

5.4 Please comment on the objectivity of the underlying data used to support the risk characterization and the sensitivity of the agency's conclusions to analytic assumptions made.

5.5 Please comment on any other aspect of the human health risk characterization that has not been mentioned above.

The Frank R. Lautenberg Chemical Safety for the 21st Century Act (2016; amended TSCA (TSCA §§ 6b[4a]) requires that "potentially exposed or susceptible subpopulations" (PESS) be considered in the risk evaluation process.

5.6 Please comment on whether the risk evaluation has adequately addressed potentially exposed or susceptible subpopulations.

5.7 Please comment on whether the risk evaluation document has adequately described the uncertainties and data limitations associated with the methodologies used to assess the human health risks. Please comment on whether this information is presented in a clear and transparent manner.

EPA characterization of human health risk from inhalation exposure to workers includes estimates of risk for respirator use. These estimates are calculated by multiplying the high end and central tendency MOE or extra cancer risk estimates without respirator use by the respirator assigned protection factors (APFs) of 10, 25 and 50 (air-supplied respirators). EPA did not assume occupational non users (ONUs) or consumers used personal protective equipment in the risk estimation process.

5.8 Please comment on whether EPA has adequately, clearly, and appropriately presented the reasoning, approach, assumptions, and uncertainties for characterizing risk to workers using PPE.

6. Content and Organization:

EPA's Final Rule, *Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act* (82 FR 33726) stipulates the process by which EPA is to complete risk evaluations under the Frank R. Lautenberg Chemical Safety for the 21st Century Act. To that end, EPA has completed a draft risk evaluation for carbon tetrachloride.

As part of this risk evaluation for carbon tetrachloride, EPA evaluated potential environmental and occupational exposures. The evaluation considered reasonably available information, including manufacture, use, and release information, and physical-chemical characteristics. It is important that the information presented in the risk evaluation and accompanying documents is clear and concise and describes the process in a scientifically credible manner.

To increase the quality and credibility of scientific information disseminated by EPA, EPA uses the peer review process specifically as a tool for determining fitness of scientific information for the intended purpose. The questions below are intended to guide the peer reviewers toward determining if EPA collected, used and disseminated information that is 'fit for purpose' based on utility (the data's utility for its intended users and for its intended purpose), integrity (the data's security), and objectivity (whether the disseminated information is accurate, reliable, and unbiased as a matter of presentation and substance). The peer reviewers' critical focus should pertain to recommendations of the technical information's usefulness for intended users and the public.

6.1 Please provide suggestions for improving the clarity of the information presented.

6.2 Are the data used to support the risk characterization presented in an objective and balanced manner? If not, please provide some specific recommendations to improve risk evaluation in this area.

6.3 Is the quality of the data used in the risk characterization appropriate for the purposes of the evaluation? If not, please provide specific examples and recommendations that may include additional data that EPA could consider in their assessment.

6.4 Are the uncertainties and assumptions underlying the risk assessment transparently documented? If not, which uncertainties and assumptions could benefit from additional contextualization and/or clarification?

6.5 What additional analyses might provide useful insight into the sensitivity of the agency's conclusions to analytic assumptions, including but not limited to the assumptions mentioned in sections 2, 3, 4, and 5 of this charge?