OPPT Charge to External Peer Reviewers for the review of the TSCA Workplan Chemical Risk Assessment of TCE

June 2013

OPPT focused its risk assessment on three specific uses of TCE: as a spray degreaser by workers in small commercial facilities, as a spray degreaser by consumers (hobbyists), and as a clear protective coating spray (an art/crafts use) by consumers (hobbyists). For all uses, only the inhalation route of exposure was evaluated, and risk estimates for individuals physically near the user of the TCE product (but not using it; called either bystanders or non-users) were also calculated.

General Question on the Risk Assessment Document

Issue 1. This risk assessment is divided into three chapters with six appendices and three supplemental documents. The first two chapters describe the scoping exercise EPA used and background information on TCE that sets the stage for the information available and used in the risk assessment. Chapter 3 includes the exposure, hazard assessment and risk characterization and a section on uncertainties for each of the three uses of TCE which are the focus of this risk assessment. The risk assessment is intended to provide a clear and transparent summary of the Agency's analysis.

> **Question 1-1:** Please comment on whether the characterization provides a clear and logical summary of EPA's analysis. Please provide specific suggestions for improving the document.

> **Question 1-2:** Please comment on whether appropriate background information is provided and accurately characterized. Please provide any other significant literature, reports, or data that would be useful to complete this characterization.

Questions on the Exposure Assessment

Issue 2. Workplace exposure estimates were developed for adults using spray degreasers in small commercial settings. These scenarios represent small businesses that use degreaser products on equipment regularly, but not all day during the course of their job. An example would be a garage/car mechanic business. Readily available data from sources such as the National Emissions Inventory (NEI), Toxics Release Inventory (TRI), and National Occupational Exposure Survey (NOES), other literature sources and assumptions were used to develop the workplace exposure assessment.

> **Question 2-1:** Please comment on the approach 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, including estimations for bystander/non-users (e.g., women of childbearing age).

Issue 3. Exposure estimates were developed for two different consumer uses: a degreasing product and a clear protective coating spray product. Both products are aerosol sprays and appear to be available for sale and use by consumers/hobbyists in the US. There were no reliable data regarding the hobbyist scenarios, so OPPT estimated hobbyist exposures using a standard exposure assessment modeling approach (the Consumer Exposure Module [CEM] of the Exposure and Fate Assessment Screening Tool, or E-FAST).

> **Question 3-1:** Please comment on the approach used and provide any specific suggestions or recommendations for alternative approaches, models, or information (*e.g.*, information on duration and number of user events) that could be considered by the agency in developing the exposure assumptions and estimates for the hobbyist degreaser and clear protective coating spray uses, and for the bystander/non-users (e.g., children, women of childbearing age).

Questions on the Hazard Assessment

Issue 4. Information on the inherent hazards of TCE has been well-characterized. There are six major domains of adverse effects (primarily in animal models) following exposure to TCE: non-cancer effects on the liver, kidney, nervous system, immune system, reproductive (predominantly male) toxicity, and developmental toxicity; as well as cancer effects on the liver, kidney and the immune system (Non-Hodgkins Lymphoma, or NHL). TCE metabolism is extensive in mammalian systems and different metabolites are likely to be responsible for different toxicity. The 2011 US EPA Integrated Risk Information System (IRIS) assessment for TCE reviewed many human and animal studies. There were 32 endpoints/27studies identified as "candidates" for developing the reference concentration (called the RfC) - these included both inhalation and oral studies. Physiologically-based pharmacokinetic (PBPK) modeling was used by the IRIS program to derive different HEC (*i.e.,* human equivalent concentration) values. OPPT reports all of these values, but focused on using only the 12 inhalation studies. Rather than use a single value to represent hazard, OPPT used the lowest lower bound HEC_{99} – the 99th percentile predicted HEC concentration -- for the effect of concern for each target organ. Furthermore, OPPT distinguished between effects that may occur following acute exposure (*i.e.,* neurotoxicity and developmental toxicity) versus those that may occur following chronic exposures (*i.e.,* liver, kidney, immunotoxicity, and male reproductive toxicity and cancer).

> **Question 4-1:** Please comment on the strengths and weaknesses of evaluating different endpoints based on exposure durations (*i*.e., acute versus chronic).

> **Question 4-2:** Please comment on the strengths and weaknesses of using multiple values for each type of adverse effect.

> **Question 4-3:** PBPK modeling was employed in the 2011 IRIS assessment for route-to-route extrapolation to develop a corresponding inhalation value from oral studies, some of which involved endpoints not studied or reported in inhalation studies. OPPT supports the approach used in the IRIS assessment. However, OPPT did not use PBPK-derived human-equivalent concentrations from oral studies in the current draft risk assessment,

because OPPT focused on a narrow set of TCE consumer uses (e.g., degreasing and arts/crafts uses) that are subject to TSCA and therefore, OPPT's draft risk assessment relied only on inhalation exposure studies that directly mimicked inhalation exposure use scenarios for both adults and developmental lifestages. Please comment on whether the 2011 IRIS assessment's PBPK-derived inhalation values from oral studies should be used in the final OPPT risk assessment.

Questions on the Risk Assessment

Issue 5. A margin of exposure (MOE) approach was used to evaluate potential non-cancer risk and the IRIS inhalation unit risk (IUR) was used to evaluate potential cancer risk. The small commercial degreaser workplace risk estimate assumed chronic (daily) inhalation exposures to TCE. The consumer use of both the degreaser spray and the clear protective coating spray used in the arts/crafts field risk estimates assumed only intermittent (acute) inhalation exposures to TCE. As part of the risk characterization, there is a discussion of the uncertainties surrounding the risk calculations.

Question 5-1: Please comment on the strengths and weaknesses of the MOE approach used to estimate the chronic, non-cancer risk for the workplace exposures; including non-users.

Question 5-2: Please comment on the strengths and weaknesses of the MOE approach used to estimate the acute risk to consumers; including non-users (e.g., children, women of childbearing age). Specifically, please comment on the decision to limit the analysis to acute exposures without residual concern between events (*i.e.,* once/week for users of the clear protective coating spray, and twice/month for degreaser users).

Question 5-3: Please comment on the use of a uniform benchmark MOE of 30 rather than a benchmark MOE equal to the composite Uncertainty Factors for each study as identified in the 2011 US EPA IRIS assessment for TCE.

Question 5-4: Please comment on whether the document has adequately described the uncertainties and data limitations in the methodology used to assess risks to allow the EPA to reduce risks to human health from TCE. Please comment on whether this information is presented in a transparent manner.