Summary of External Peer Review and Public Comments and Disposition

This document summarizes the public and external peer review comments that the EPA's Office of Pollution Prevention and Toxics (OPPT) received for the draft work plan risk assessment for trichloroethylene (TCE). It also provides EPA/OPPT's response to the comments received from the public and the peer review panel.

EPA/OPPT appreciates the valuable input provided by the public and peer review panel. The input resulted in substantial revisions to the risk assessment.

Peer review charge questions[1] are used to categorize the peer review and public comments into specific issues related to five main themes.

- General Issues on the Risk Assessment Document
- Occupational Exposure Assessment
- Consumer Exposure Assessment
- Hazard and Dose-Response Assessments
- Risk Characterization

A separate section called *Other Public Comments* organizes the response to those public comments that are unrelated to the main themes listed above.

[1] These are the questions that EPA/OPPT submitted to the panel to guide the peer review process.

General Issues on the Risk Assessment Document

Charge 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.

Charge 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.

#	Summary of Peer Review and Public Comments for Specific Issues Related to Charge Questions 1-1 and 1-2	EPA/OPPT Response
1	Document is not clear about the purpose of the risk assessment. The document would be substantially improved if a clear statement was made regarding the audience and utility of the report.	EPA/OPPT has made significant revisions to the TCE risk assessment to improve the clarity of the assessment. In addition, the purpose and audience have been described in *section 1.1* of the final TCE OPPT risk assessment.
2	EPA/OPPT did not assess dermal exposure to TCE for occupational and residential scenarios; why is dermal exposure considered less significant than inhalation exposure? By not including dermal exposure in the exposure assessment, exposure is likely to be underestimated.	EPA/OPPT recognizes that dermal exposure to highly volatile materials such as TCE can occur. However, based on the physical-chemical properties of TCE and the scenarios described in this assessment, EPA/OPPT believes that inhalation is the main exposure pathway for this risk assessment. This assessment may underestimate total exposures resulting from the uses of TCE due to this assumption. Thus, we agree this assessment likely underestimates risks resulting from the uses of TCE being assessed. As stated in *Section 1.3.2* of the final risk assessment, recent modeled and experimental work supports the assumption that inhalation is the predominant exposure pathway. The dermal model described by Tibaldi et al. (2014) estimates that about 1% of TCE on the skin will be absorbed into the epidermis with the other 99% evaporating. Also, an experimental comparison of dermal to vapor exposure found that TCE and hexane had the least dermal absorption amongst a set of volatile solvents. The ratio of dermal to respiratory intake was found to be 0.1 % for TCE (Kezic et al., 2000). ***Citations*:** Kezic, S., A. C. Monster, J. Kruse, and M. M. Verberk. 2000. *Skin Absorption of Some Vaporous Solvents in Volunteers*. International Archives of Occupational and Environmental Health, 73(6), 415-422. Tibaldi, R., W. ten Berge, and D. Drolet. 2014. *Dermal Absorption of Chemicals: Estimation by Ih Skinperm*. J Occup Environ Hyg, 11(1), 19-31.

3	Can EPA/OPPT clarify why it did not include the use of TCE as a spotting agent in its assessment?	Based on additional information provided during peer review, EPA/OPPT has revised its original assessment to include the use of TCE as a spotting agent at dry cleaning facilities. The exposure assessment for the spotting use can be found in the *occupational section 2.4* of the final TCE OPPT risk assessment and in Appendix H. EPA/OPPT did not identify TCE-based spot cleaners used in consumer products (Section 2.5.1). It is possible that members of the general public could obtain products intended for commercial use, but these activities are not included in the final TCE risk assessment.
4	For the commercial degreasing scenario, EPA's discussion regarding comparison of National Emissions Inventory (NEI) and Toxics Release Inventory (TRI) data was somewhat confusing. Can this be further clarified?	EPA/OPPT has further clarified its comparison of NEI and TRI data. In particular, the final risk assessment includes illustrations that provide an overview of EPA/OPPT's assessment for the commercial degreasing scenario. These revisions and illustrations can be found in *section 2.3, Figure 2-1, and Appendices E and F* of the final TCE OPPT risk assessment.
5	EPA did not cite the correct publication for the two-zone mass balance model. In addition, EPA did not reference the publication provided by Dr. Jayjock regarding the validity of the two-zone mass balance model. This publication adds strong support for using the two-zone model to estimate occupational exposures from commercial degreasing. Including this reference will strongly strengthen EPA's case for using such a model to infer exposures. Also, this reference supports that EPA/OPPT's assessment is more than a screening level assessment.	The risk assessment has been updated to cite the correct publication (Keil, C. B. et al., 2009) for the two-zone mass balance model. In addition, EPA/OPPT updated its risk assessment to reference the publication provided by Dr. Jayjock during peer review. ***Citation*:** Keil, C. B., C. E. Simmons, and A. T. Renee. 2009. *Mathematical Models for Estimating Occupational Exposure to Chemicals* (2nd ed.) American Industrial Hygiene Association (AIHA).
6	In Appendix D, a paragraph had a missing notation for the Free Surface Area (FSA), thus causing confusion for readers.	The risk assessment has been updated to address the issue with the missing notation for the Free Surface Area (FSA). Please note that Appendix D in the draft risk assessment corresponds to Appendix G in the final risk assessment.
7	EPA/OPPT did not reference monitoring data to validate its exposure estimates resulting from the use of TCE in commercial degreasing processes. How can one have confidence in EPA/OPPT's estimates for occupational exposures?	In collaboration with the Occupational Safety and Health Administration (OSHA), relevant monitoring data specific to TCE from site surveys were identified and incorporated into the final risk assessment in *section 2.3.3 and Figure 2.2.* OSHA's data and EPA's assessment of it is included in the supplementary file: "OSHA IMIS TCE SAMPLES_062314v1.xlsx".

8	EPA/OPPT used a steady-state assumption in estimating airborne exposure concentrations resulting from commercial degreasing operations. This is problematic and perhaps simplistic for these scenarios.	In the revised risk assessment, EPA/OPPT used a transient (non-steady state) mass balance model to estimate airborne exposure concentrations that result from commercial degreasing processes.
9	There does not seem to be an exhaustive effort made to find all existing appropriate literature for the various sections of the risk assessment.	Additional references submitted to EPA/OPPT as part of the peer review process were incorporated if they were relevant to the assessment. Additional references were included relevant to the weight-of-evidence (WOE) analysis supporting the hazard/dose-response assessment (Section 2.6) and the WOE analysis for fetal cardiac malformations (Appendix N). Please see the *Reference* section for the complete list of references used in the final risk assessment.
10	EPA/OPPT should improve the transparency and readability of Table F-1 and Table 3-19. Table F-1 listed the hazard values as reported in the IRIS assessment. Table 3-19 listed the hazard values used in the OPPT risk assessment.	EPA/OPPT has made significant changes to the hazard information presented in Table F-1 and Table 3-19 of the draft TCE OPPT risk assessment. In the final assessment, the information can be found in *Table 2-18 and Appendix L*. Table 2-19 lists the lowest hazard values for different effects domains that the OPPT assessment used to estimate risks. Table 2-19 contains the following information: exposure duration for risk analysis (acute vs. chronic), target organ/system, species, route of exposure, range of doses or concentrations, duration, point of departure (POD), effect, human equivalent concentrations (HEC) at the 50^{th}, 95^{th} and 99^{th} percentiles, uncertainty factors used as the benchmark margin of exposure and the reference citation. Appendix L contains the complete list of oral and inhalation studies that the U.S. EPA's Integrated Risk Information System (IRIS) program deemed suitable for non-cancer dose-response analysis.
11	Peer review comments suggested that the EPA's Office of Pesticides (OPP) may have empirical data that could improve the TCE work plan risk assessment. Particularly, indoor monitoring data for inert chemicals in consumer pesticides might provide useful information for the TCE risk assessment, provided that the monitoring data were for chemical substances with similar physical-chemical properties.	EPA/OPPT in collaboration with the Office of Pesticide programs (OPP) searched OPP's Pesticide Inert database. No exposure data that would be relevant or indoor monitoring data on TCE or surrogate chemical were found. OPP confirmed our lack of results and the improbability of finding the type of information that was suggested to us by the peer reviewers. Even if data were found within EPA/ OPP, it is highly likely that it is confidential business information if it was submitted by a company as part of a pesticide registration under the pesticide laws, and therefore not usable in a public risk assessment. Given these circumstances, EPA/OPPT believes that this effort would not provide useful surrogate data for refining the OPPT risk assessment.

12	One of the peer reviewers stated that while Section A. Physical and Chemical Properties of TCE and Section C. Production Volume and General Information on Uses seemed appropriate, Section B. Environmental Fate did not seem to be necessary or relevant to an assessment focused on inhalation of TCE from industrial or consumer products?	The environmental fate of a substance (i.e., its transport and transformation in the environment) can mitigate or enhance its exposure to humans or the environment. In the initial steps of assessing the potential risk of a substance, its environmental fate is considered in conjunction with its release patterns and its physical-chemical properties to provide an understanding of how its behavior after release may impact exposure. The discussion of the environmental fate of TCE was used to help focus the assessment on the appropriate exposure routes (inhalation) and pathways (volatilization to air). However, EPA/OPPT agrees with the peer reviewer that the full discussion of the environmental fate of TCE is not necessary to include in the main document. The full discussion of the environmental fate of TCE has been moved to *Appendix C*.
13	One of the peer reviewers requested clarification of the terms "low" and "moderate" in the conclusion of the fate discussion below to make it less open to interpretation: "Based on the experimental evidence and environmental fate data available, TCE is expected to have low bioaccumulation potential and moderate persistence."	In the Environmental Fate Section, EPA/OPPT addressed only bioaccumulation/bioconcentration in aquatic organisms and environmental persistence. The peer reviewer appeared to interpret bioaccumulation potential and persistence to refer to human bioaccumulation and half-life in humans rather than bioaccumulation in aquatic organisms and environmental persistence as it was intended. EPA/OPPT agrees that the language used in the concluding statement needs further clarification and made the following change: "*Based on the experimental evidence and environmental fate data available, TCE is expected to have low bioaccumulation potential in aquatic organisms (bioconcentration/bioaccumulation factor less than 1000) and moderate persistence in the environment (environmental half-life of greater than two months but less than six months)* ."The revised text is found in *Appendix C*.

Occupational Exposure Assessment

Charge 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).

#	Summary of Peer Review and Public Comments for Specific Issues Related to Charge Question 2-1	EPA/OPPT Response
14	EPA/OPPT did not reference monitoring data to validate its exposure estimates resulting from the use of TCE in commercial degreasing processes. EPA's risk assessment contains little actual data on exposure at small commercial shops on which to base a robust analysis. If EPA/OPPT is going to distinguish facilities based on their size, then more representative data needs to be obtained before finalized the risk assessment. EPA/OPPT seems to indicate that its exposure estimates for workers at commercial degreasing facilities are similar to measured values; but EPA does not provide any monitoring data in its risk assessment. It is important to know what TCE workplace exposure data are available; EPA/OPPT should include this data in the risk assessment. EPA/OPPT should gather or identify monitoring data for TCE exposures resulting from activities that are of concern; exposure assumptions and models are no substitute for exposure data. At a minimum, EPA should solicit and welcome peer review of the TCE risk assessment from the Consumer Product Safety Commission (CPSC) and the National Institute for Occupational Safety and Health (NIOSH). EPA/OPPT did not use monitoring data to estimate workplace exposures for the commercial degreasing scenario. Instead, EPA chose to estimate workplace exposures based on calculating an emission rate from degreasing operations. Further, EPA cites Walden et al. (1989) and incorrectly states	In collaboration with OSHA, relevant monitoring data specific to TCE was identified. This additional information has been incorporated into the risk assessment in *section 2.3.3 and Figure 2.2*. OSHA's data and EPA's assessment of it is included in the supplementary file: "OSHA IMIS TCE SAMPLES_062314v1.xlsx". The National Emissions Inventory (NEI) contains data for nonpoint sources. Traditionally, small commercial facilities have been represented as nonpoint sources; EPA/OPPT has used data for nonpoint sources to represent small commercial facilities. The publication from Wadden et al. (1989) reported a total emission of 27.29 grams of TCE per minute from an open top degreaser. Since local exhaust ventilation (LEV) was used, only 2.57 grams of TCE per minute (or 9.5% of the total emission) were reported as escaping into the workplace. Based on these data, EPA/OPPT assumed that if no LEV were used, then the total emission of 27.29 grams of TCE per minute could potentially be released into the workplace. ***Citation:*** Wadden, R. A., P. A. Scheff, and J. E. Franke. 1989. *Emission Factors for Trichloroethylene Vapor Degreasers*. American Industrial Hygiene Association Journal, 50(9), 496-500.

	that the emission rate ranged from 2.57 to 27.29 grams of TCE per minute. The data from Walden et al. (1989) are for environmental emissions that are released externally; only 9.5% of the value is emission escaping into the workplace. EPA should not assume environmental emissions that are released externally can be used to estimate workplace exposures.	
15	For the commercial degreasing scenario, it is not clear whether EPA/OPPT is using the most currently available data to estimate the number of workers exposed. It seems EPA is using data from the 1970s or 1980s. Releases of TCE have decreased substantially since that time. Also, workplace practices and industrial hygiene standards have improved. Thus, it is likely that EPA is overestimating the number of workers and non-users exposed. EPA/OPPT estimates the number of workers and non-users at commercial degreasing facilities as 7,415 and 17,796, respectively. But EPA/OPPT does not appear to provide any explanation for how these estimates were obtained.	EPA/OPPT has updated the risk assessment with additional information to further clarify how the number of workers and non-users was estimated (see *section 2.3.3* and *Appendix F* of the revised risk assessment). By using more recent data from the 2008 NEI and EPA's 2006 risk assessment for the halogenated solvent cleaning source category (EPA, 2006d) to estimate the number of facilities (1,746), EPA/OPPT's estimate likely captures the downward trend in the number of facilities using TCE for degreasing and provides an adequate order of magnitude estimate. More recent and relevant survey data were not identified for the purposes of comparison. EPA/OPPT estimated the number of workers and non-users potentially exposed to TCE based on: (1) a National Occupational Exposure Survey (NOES) from the 1980s; (2) EPA's draft generic scenario on vapor degreasing (EPA, 2001a); and (3) the number of small degreasing facilities as determined from the 2008 National Emissions Inventory (NEI) and EPA's 2006 risk assessment for the halogenated solvent cleaning source category (EPA, 2006d). ***Citation:*** EPA (U.S. Environmental Protection Agency). 2001a. *Draft Generic Scenario- Use of Vapor Degreasers*. Office of Pollution Prevention and Toxics, Chemical Engineering Branch, Washington, DC. EPA (U.S. Environmental Protection Agency). 2006d. *Risk Assessment for the Halogenated Solvent Cleaning Source Category Web Site*. Washington, DC. http://yosemite.epa.gov/ee/epa/ria.nsf/vwRef/A.2006.10?OpenDocument (accessed on November 8, 2012).

16	EPA's draft risk assessment does not consider the impacts of the Halogenated Solvent Cleaning National Emission Standard for Hazardous Air Pollutants (NESHAP), which EPA finalized in 2007. This standard limits emissions from open-top degreasers.	EPA/OPPT updated its risk assessment to take NESHAP emission limits into account (see *section 2.3.3, Table 2-8, and Appendix E* of the final risk assessment).
17	The overall methodology EPA/OPPT used to estimate emissions of TCE from commercial degreasing operations is complex and convoluted.	EPA/OPPT has clarified its comparison of NEI and TRI data. In particular, the revised risk assessment includes illustrations that provide an overview of EPA/OPPT's assessment for the commercial degreasing scenario (see *section 2.3.3, Figure 2-1, and Appendix E* of the final risk assessment).
18	We downloaded the file "Facility-Level by Pollutant" at EPA's 2008 NEI website. The total TCE emissions were 4,088,000 lb across 2,378 facilities, which are close, but slightly less, than the total provided by EPA (4,340,000 lb). Later in the discussion there is a reference made to only including emissions from facilities in one of 78 North American Industry Classification Scheme (NAICS) codes. When we only include the 78 NAICS codes, the emissions in the "Facility-Level by Pollutant" are reduced to 2,734,000 lb across 373 facilities. It is not clear where EPA is getting the 186 TCE point sources and 1,779 nonpoint sources. It is possible that some of the non-point sources are not in the facility file, but it seems that some of them must be since there are more facilities with the 78 NAICS codes than the 186 quoted by EPA.	EPA/OPPT has updated its assessment to further clarify which National Emissions Inventory (NEI) data were used (see *section 2.3.3 and Appendix E* of the final risk assessment). In brief, EPA/OPPT used point and nonpoint source data from the 2008 NEI. These data were filtered, for example, by pollutant name, source classification codes (SCC), etc. After filtering the data, the number of point source (large) facilities was estimated to be 154. Based on EPA's 2006 risk assessment for the halogenated solvent cleaning source category (EPA, 2006d), the total number of degreasing facilities was expected to be approximately 1,900. The number of small commercial degreasing facilities was estimated to be 1,746 (1,900 total facilities minus 154 large facilities). ***Citation:*** EPA (U.S. Environmental Protection Agency). 2006d. *Risk Assessment for the Halogenated Solvent Cleaning Source Category Web Site*. Washington, DC. http://yosemite.epa.gov/ee/epa/ria.nsf/vwRef/A.2006.10?OpenDocument (accessed on November 8, 2012).
19	For the commercial degreasing scenario, EPA/OPPT provides no indication on the relative prevalence of local exhaust ventilation (LEV). EPA/OPPT should describe how the local exhaust ventilation (LEV) affects the generation rate.	EPA/OPPT has adopted a scenario-based approach for its exposure assessment. Thus, exposure scenarios with and without LEV have been assessed. However, the relative prevalence of LEV is not known to EPA. Based on information presented in (Wadden et al., 1989), EPA/OPPT assumed that LEV can have an effectiveness of up to 90%. For scenarios in which LEV is assumed to be present, the generation rate is reduced by 90% (also see *section 2.3.3 and Appendix E* of the final risk assessment).

		Citation: Wadden, R. A., P. A. Scheff, and J. E. Franke. 1989. *Emission Factors for Trichloroethylene Vapor Degreasers*. American Industrial Hygiene Association Journal, 50(9), 496-500.
20	EPA/OPPT assumed that small commercial degreasing facilities operate for 2 hours (hrs) a day. This is a critical parameter; the basis for this should be fully described.	The basis for this assumption is information included in EPA's draft generic scenario on vapor degreasing (EPA, 2001a). This draft scenario contains general facility estimates, such as days of operation, and hours of operation. The assumption is described in *section 2.3.3* of the final risk assessment. Please note that EPA/OPPT did not locate further data about facility and operating parameters.
21	The free surface area (FSA) value in Table D-1 is listed as 180 square feet. However, based on equation (5) in Appendix D, the FSA should be 340 square feet. It appears that EPA used the correct value of 340 square feet in its calculations, but mistakenly listed the value as 180 square feet in the document.	The listed FSA value has been updated to 340 square feet (see *Appendix G and Table G-1* of the revised risk assessment).
22	EPA/OPPT should use different methods to assess workplace exposures. For example, Drs. Jayjock and Driver both mentioned using the Nicas model.	In the final assessment, EPA/OPPT used the Nicas model (two-zone NF/FF mass balance model) that Drs. Jayjock and Driver referred to; this model was used to assess workplace exposures (see *sections 2.3.3 and 2.4.2, and Appendices F and G* of the revised risk assessment).
23	An understanding of actual work place practices and the proportion of workers experiencing near field exposures is imperative. EPA/OPPT should use a sensitivity analysis of some type to ascertain the important parameters in the model used for worker exposure.	In collaboration with OSHA, relevant monitoring data specific to TCE was identified and used in the assessment. A comparison between the OSHA's monitoring data and the modeled results showed that the EPA's exposure estimates were in-line with data from OSHA. This additional information has been incorporated into the risk assessment (see *section 2.3.3 and Figure 2-2* of the final risk assessment). EPA/OPPT agrees that work place practices information can further refine the exposure assessment. However, such information was not readily available and no such information was submitted to EPA/OPPT during the review and comment period. EPA/OPPT agrees that performing a sensitivity analysis can, in some, but not all instances, produce useful and actionable insights. In this instance, EPA/OPPT has

		adopted a scenario-based approach for its exposure assessment. The estimates from this approach likely capture actual exposure levels as evidenced by OSHA data.
24	It is not intuitive why the number of machines found at a large facility (which logically might be expected to have more than one machine) can be translated to small nonpoint sources (which logically might be expected to have only one machine/facility). Clarification on this point would be appreciated.	In this assessment, EPA/OPPT assumed one degreasing unit per facility for small commercial operations because smaller facilities were expected to have less degreasing units per facility than larger ones. Large facilities were estimated to have 1.2 degreasing units per facility (see *section 2.3.3* of the final risk assessment).
25	For the commercial degreasing scenario, I found the inhalation model choice, model inputs and treatment of the industrial inhalation scenario to be well done with the possible exception of the "typical ventilation" rate. The only questionable variable in my opinion is the use of 3,000 cubic feet per minute (cfm) as the "typical value" for general ventilation in an industrial room. My experience has been that industrial rooms without special exhaust will be ventilated in a range of 2 to 5 air changes per hr.	Based on this input and additional published sources, EPA/OPPT has adjusted its range for the air exchange parameter to 2 to 15 air exchanges per hr for its scenario-based exposure assessment (see *Appendix G and Table G-1* of the final risk assessment).

Consumer Exposure Assessment

Charge 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).

#	Summary of Peer Review and Public Comments for Specific Issues Related to Charge Question 3-1	EPA/OPPT Response
26	Panelists and the general public commented on the use of the Consumer Exposure Model (CEM) to calculate exposures for the consumer use scenarios. Some commenters felt that the Multi- Chamber Concentration and Exposure Model (MCCEM) or other models (e.g., Nicas2) should be used as well. Some commenters also suggested the use of probabilistic methods (e.g. Monte Carlo).	In the final assessment, EPA/OPPT retained the current consumer exposure model to estimate exposure levels for the residential scenarios. The available data for TCE did not support the use of MCCEM or other higher tier models. Those models rely on more complex input data to generate human exposure. It should be noted that many of the inhalation models use similar calculation engines to generate exposure concentrations. For example, one of the main properties distinguishing MCCEM from CEM is the ability to enter data from chamber studies into MCCEM to replace the empirical model used to generate evaporation rates in CEM. Running additional models without the satisfactory input data, when many use similar 2 box models for the calculation engines, will not yield significant improvements to the consumer exposure assessment. Models like Nicas2 that include personal breathing zone calculation would likely increase the exposure to consumers by accounting for the higher air concentrations near users of aerosol products. This added level of detail may be important for assessments where further refinement of exposure is needed, but in this assessment risk exists without the more refined Nicas model for consumers. Given the current uncertainty in the input parameters and how closely they may correspond to real user behavior, appropriate input distributions are not available for probabilistic exposure modeling.

27	Panelists and the general public commented on the absence of indoor monitoring data within the consumer exposure assessment.	EPA/OPPT did not find monitoring studies related to the use of consumer products containing TCE. Indoor air concentrations have been added to the final risk assessment in *section 2.5.4.2* and a list of references and concentrations is in the supplemental material entitled "*Literature Review of Measured TCE Concentrations in Indoor Air"*. The only studies found were those related to TCE exposures from vapor intrusion or studies related to general household levels of volatile organic compounds (VOCs). These studies are not expected to represent the concentrations that may result due to the use of products containing TCE under the scope of this assessment.
28	Panelists and the general public suggested describing the consumer exposure assessment as screening level. A Panelist recommended using the Westat survey data to provide further information on consumer behavior patterns and the collection of mass used during product use data.	The exposure assessment is not a theoretical bounding assessment or a worst case assessment. Collection of new data or measurements is outside the scope of the workplan assessment process. The TCE assessment did not use the screening level parameters that are set as the defaults in the EFAST2 modeling software. A hypothetical scenario was created based on professional judgment due to a lack of consumer use data for the products in the assessment. EPA/OPPT has not found a quantitative source of consumer use information for these products. The values chosen for the hypothetical consumer use behavior patterns were meant to be high end, but the household parameters used in the modeling were set to mean or median values e.g. air exchange rate. The Westat survey data have been added to the final assessment in *Appendix I*.

29	The public commented on the back calculation used to generate 24-hr time averaged exposure numbers for the consumer exposure portion of the exposure assessment. One reviewer seemed to think the assessment was based on a single peak value from the CEM run.	The CEM module calculates potential acute dose rates (ADRs) for the occupants of the simulated home. This dose rate involves summing the doses from multiple small intervals which are based on the concentration of the chemical in the home and the breathing rate and body mass of the user or a bystander. The back calculation removed the parameters describing the physical characteristics of the users in different age groups (e.g. breathing rate and body weight) from the acute dose rate and converted it to the mean concentration experienced by either the user or a bystander over a 24-hr time period. The CEM output also discusses a peak concentration for the 24-hr time period, but this value was not used in the risk assessment because it only describes a single 10-second interval within the entire simulation and is mainly meant for doing model diagnostics. Additional information about the conversion of ADRs to air concentrations (ppm) is found in *Appendix J*.
30	Peer reviewers and the public submitted comments expressing confusion regarding how CEM calculated emission rates of TCE and on how mixtures of chemicals may affect the evaporation rates. Commenters expressed a desire for further transparency on the model parameter selection within EFAST in the main body of the document.	In the absence of measured data for emission of TCE in residential settings or chamber studies for the selected products, EPA/OPPT used an empirical model to estimate the evaporation rates of solvents from a surface. The emission rate is based on an exponential decay model and is not constant during the period of use or the 24-hr period used to calculate the air concentration the occupants are exposed to. Further explanation for this calculation, the effects of mixtures, and information on the model parameters in general has been added in the exposure *section 2.5* and *Appendix I*.
31	Commenters were unsure of the meaning of some fate parameters and the need for a fate section.	The persistence and bioaccumulation scores were based on aquatic considerations and were mainly present as part of the justification for not performing an ecological assessment. An overview of the environmental fate and releases of TCE can be found in the main body of the document, particularly *section 2.2*. The rest of the information has been moved to *Appendix C*.
32	Peer reviewers requested further information on the peer review of the CEM model.	EPA/OPPT has posted the peer review documentation for the CEM model at http://www.epa.gov/oppt/exposure/pubs/efastqa.htm.
33	Peer reviewers requested that the technical presentation be more contiguous within the main body of the document.	More information on the exposure assessment has been moved from the supplementary documents to the main body of the risk assessment, in particular in *section 2.5.3*.

34	Public and peer reviewers requested the collection of experimental data to increase the certainty of the exposure assessment. Requested data included mass of TCE emitted during use, chamber study data, personal breathing zone monitoring, and indoor air measurements to validate user and bystander exposures.	Data collection requests are outside the scope of OPPT Workplan chemical assessment process, which rely on data and models that are currently available. EPA/OPPT requested that outside parties submit data that would inform workplan chemical risk assessments with the agency, but the agency has not received data that would augment the TCE consumer exposure assessment.
35	A peer reviewer suggested expanding the age level for users of the TCE consumer products.	EPA/OPPT believes that users of these products will generally be adults, however it is possible that teenagers or younger children may be users or be in the same room with the user while engaging in arts and crafts projects or degreasing. The current exposure assessment can be expanded to all potential user age levels by using the indoor air concentrations estimates for the user of the products. Data are not available for any consumer use patterns, so the current estimated indoor air concentrations would be applied to any age user.
36	Peer reviewers suggested that CEM undergo model validation	CEM has undergone a peer review and some limited validation.
37	Peer reviewers requested that a sensitivity analysis be performed for the exposure assessment.	The mass of product used per event would be a highly sensitive parameter based on professional judgments created through repeated use of CEM. However when weighing the relative importance of other parameters, it is important to remember that all of the consumer behavior pattern input parameters for the consumer behavior are hypothetical. This could lead a full sensitivity analysis to incorrectly identify certain parameters as being more important than they would be if survey data were available for these uses. For example, the current assumption is that the user spends 2 hrs in the room of use (i.e., a utility room). This parameter choice leads to a relative decrease in the importance of the emission rate of TCE to the room air since a slower rate would still lead to exposure of all of the emitted TCE. Thus, a sensitivity analysis of the current parameters would perhaps falsely indicate that the emission rate from the surface of use was relatively unimportant. Further consumer behavior pattern information would be needed before a sensitivity analysis would be useful, and such information has not been identified by EPA.

38	A panel member commented that the model runs may have not correctly used the data from the most recent exposure factors handbook for the weight and breathing rates of the members of different age groups.	The default exposure values cited in the EFAST2 documentation and used in the publically available model preceded those recently published in the EPA's 2011 Exposure Factors Handbook (EFH). EPA/OPPT did not use the default values in EFAST2, but instead relied on the exposure values published in EPA's 2011 EFH. This has been clarified *in section 2.5.3 and in Appendix I*.
39	A panelist commented that product compositions would vary over time leading to inaccurate chronic exposure calculations.	The chronic exposure numbers are generated by default in CEM but they were not used in the TCE risk assessment. They are only included for completeness since they are generated by CEM for all model runs.
40	Peer reviewers asked for a determination of the exposed population from these consumer products.	EPA/OPPT did not find exposed population data nor receive data during the public comment period for the draft TCE risk assessment that would help address this point. The workplan assessments are based on available data. This information would not affect the calculated exposure concentrations for users and bystanders.

Hazard and Dose-Response Assessments

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

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

Charge 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 life stages. 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.

#	Summary of Peer Review and Public Comments for Specific Issues Related to Charge Questions 4-1, 4-2 and 4-3	EPA/OPPT Response
41	It was suggested that EPA/OPPT needed to conduct a systematic evaluation of the quality of each toxicological study used in the TCE risk assessment. The final TCE OPPT risk assessment should have a discussion of the study quality criteria used in the study evaluation, as well as a discussion of the strengths and limitations of the studies selected as the basis for hazard values. Some peer reviewers and public commenters criticized EPA/OPPT for using studies that had deficiencies and were not used in the IRIS' non-cancer dose-response assessment for deriving candidate RfCs. Some peer reviewers and public commenters suggested that the selection of the hazard value should be based on the "best" study that represents the health effects domain (or endpoint) based on the assessment of study integrity/quality. This "best" study should be selected instead of using a range of hazard values within a specific endpoint.	The final TCE risk assessment relies on the non-cancer and cancer assessments that were published in the latest Toxicological Review for TCE prepared by the U.S. EPA's Integrated Risk Information System (IRIS) in 2011 [also referred as *the TCE IRIS assessment*]. The U.S. EPA's IRIS assessment represents the latest hazard/dose-response analysis for TCE that EPA has completed to date. The TCE IRIS assessments used a systematic weight-of-evidence (WOE) approach, the latest scientific information and physiologically-based pharmacokinetic modeling (PBPK) to develop hazard and dose-response assessments for TCE's carcinogenic and non-carcinogenic health effects resulting from lifetime oral or inhalation exposure. The strengths and limitations of the data set for cancer and non-cancer effects can be found in the TCE IRIS assessment. Development of TCE's hazard and dose-response assessments considered the principles set forth by the various risk assessment guidelines issued by the National Research Council and the U.S. EPA (see *Appendix K* of the final TCE risk assessment). Primary, peer-reviewed literature identified through December 2010 was also included where that literature was determined to be critical to the assessment.

	One peer reviewer recommended reviewing the data set available for each endpoint and determining whether the data are adequate to describe the qualitative and dose-response elements of the endpoint.	The TCE IRIS assessment identified the most suitable non-cancer studies for dose-response analysis by health effects domain (i.e., liver toxicity, kidney toxicity, neurotoxicity, immunotoxicity, reproductive toxicity, and developmental toxicity). A list of these studies are found in *Appendix L* of the final TCE OPPT risk assessment. EPA/OPPT relied on the studies with the lowest hazard values (i.e., human equivalent concentration or HECs) to estimate acute or chronic non-cancer risks for the specific TCE uses (see section *2.6.1.2.2 and Table 2-18* in the final TCE OPPT assessment).
42	The draft risk assessment did not provide information about how the PBPK modeling was used to develop the non-cancer hazard values (i.e., HECs).	EPA/OPPT added new language in the risk assessment explaining the PBPK modeling approach and HEC derivation. The information is presented in *sections 2.6.1.2.2 and 2.6.1.4*. A comprehensive discussion of the TCE PBPK model can be found in the TCE IRIS assessment.
43	EPA/OPPT should use both inhalation and oral studies that the TCE IRIS assessment evaluated when deriving the inhalation RfC. The TCE IRIS assessment used physiologically-based pharmacokinetic (PBPK) modeling to do route-to-route extrapolation.	The final TCE OPPT risk assessment used the oral and inhalation studies that the TCE IRIS assessment evaluated in the non-cancer dose-response analysis. EPA/OPPT relied on the point of departures (PODs) that the TCE IRIS assessment identified for the most suitable studies for dose-response analysis. The PODs were categorized by health effects domains (i.e., liver toxicity, kidney toxicity, neurotoxicity, immunotoxicity, reproductive toxicity, and developmental toxicity). These studies are listed in *Appendix L* of the final TCE OPPT risk assessment. The studies with the lowest hazard values (i.e., human equivalent concentration or HECs) were used to estimate acute or chronic non-cancer risks for the specific TCE uses (see *section 2.6.1.2.2 and Table 2-18* in the final TCE OPPT assessment).
44	Some panelists and public commenters indicated that the developmental toxicity studies cannot be used to derive hazard values for single exposures. The developmental toxicity studies reported adverse effects that resulted from repeated exposures to TCE and thus they should not be used to estimate acute risks. In addition, there were also public and peer review comments objecting to the use of the developmental toxicity studies by Johnson et al. (2003, 2005) for estimating acute or chronic non-cancer risks due to methodological and replicability issues.	EPA/OPPT used developmental toxicity data to evaluate the non-cancer risks of acute exposures based on EPA's long standing policy that a single exposure within a critical window of development may induce developmental effects, as discussed in the EPA's Guidelines for Developmental Toxicity Risk Assessment (http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=23162). EPA/OPPT acknowledges that this is a health-protective policy that may overestimate the acute risks. Developmental effects, including fetal cardiac defects, may occur following maternal exposure to TCE. Chick embryo and oral developmental studies, including those reported by the Johnson et al. studies (see list of references below), have reported cardiac malformations after exposure to TCE. The

		incidence of congenital cardiac malformation has been replicated in several studies from the same laboratory group and has been shown to be TCE-related. Moreover, studies with TCE metabolites have also induced cardiac defects in developmental oral toxicity studies. A recent erratum (Johnson, 2014) and subsequent evaluation of the developmental toxicity data reaffirmed that the Johnson et al. studies are adequate to use in hazard identification and dose-response assessment (Appendix N). As explained in the TCE IRIS assessment, while the Johnson et al. studies have limitations, there is insufficient reason to dismiss their findings, especially when the findings are analyzed in combination with human, animal and mechanistic evidence. A summary of the weight of evidence supporting TCE-related fetal cardiac defects is provided in *section 2.6.2.3.6* and Appendix N of the final TCE OPPT risk assessment. The comprehensive WOE evaluation of the developmental toxicity data, including fetal cardiac teratogenesis, is discussed in the TCE IRIS assessment and expanded in this assessment (Appendix N). Thus, EPA/OPPT has incorporated the Johnson et al. studies in the final risk assessment (*see Tables 2-18, 2-31 to 2-35; sections 2.7.2 and 2.7.3.2*). **Citations**: Dawson, B., P. Johnson, S. Goldberg, and J. Ulreich. 1990. *Cardiac Teratogenesis of Trichloroethylene and Dichloroethylene in a Mammalian Model*. Journal of the American College of Cardiology, 16(5), 1304-1309. (as cited in EPA, 2011e). Dawson, B., P. Johnson, S. Goldberg, and J. Ulreich. 1993. *Cardiac Teratogenesis of Halogenated Hydrocarbon-Contaminated Drinking Water*. Journal of the American College of Cardiology, 21(6), 1466-1472. (as cited in EPA, 2011e). Johnson, P., S. Goldberg, S. Mays, and B. Dawson. 2005. *Correction: Threshold of Trichloroethylene Contamination in Maternal Drinking Waters Affecting Fetal Heart Development in the Rat*. Environmental Health Perspectives, 113, A18. (as cited in EPA, 2011e). Johnson, P. D. 2014. *Erratum: Erratum for Johnson Et Al. [Environ Health Perspect 113: A18 (2005)]*. Environmental Health Perspectives, 10.1289/ehp.122-A94.

		Johnson, P. D., S. J. Goldberg, M. Z. Mays, and B. V. Dawson. 2003. *Threshold of Trichloroethylene Contamination in Maternal Drinking Waters Affecting Fetal Heart Development in the Rat*. Environmental Health Perspectives, 111(3), 289-292. (as cited in EPA, 2011e).
45	PBPK-derived HECs from developmental toxicity studies should not be used in the OPPT's risk assessment of TCE. The TCE PBPK model does not model pregnancy or gestation and as such the internal doses are based on dose-metrics that are not considering developmental effects in the fetus. Typically the placenta is expected to lower exposure to the fetus by 2 to 10-fold. Since a key concern is developmental toxicity, that should be considered. Comparison of benchmarks derived from oral and inhalation routes can provide useful insight.	The TCE PBPK model did not incorporate a pregnancy compartment in the model to estimate the internal dose of TCE in the developing fetus. The maternal dose metric was used as surrogate for the fetal internal dose. This assumption has been noted in *section 2.6.1.4* and *Table 2-23* of the final TCE OPPT risk assessment. Also, the uncertainties related to using maternal dose-metrics for the developing fetus have been discussed in *section 2.8.2.2* of the TCE OPPT risk assessment.
46	EPA/OPPT inappropriately uses the Healy et al. (1982) study for the acute inhalation exposures, as the Healy et al study does not report dose-response data.	The TCE IRIS assessment identified Healy et al. (1987) as one of the critical developmental toxicity studies (see *Appendix L* of the final TCE OPPT risk assessment). Among all of the developmental toxicity studies listed in *Appendix L,* EPA/OPPT selected the study reporting the lowest hazard value (i.e., HEC), which in this case was the Johnson et al. (2003) study and not *Healy et al. 1982*.
47	Peer reviewers noted that the Forand et al. (2012) study was cited in the EPA's presentation to the TCE peer review panel as a supporting study for the association between TCE exposure and fetal cardiac malformations in humans. Two panelists requested to review the study. One of the reviewers requested to do a review by an independent scientist.	The Forand et al., (2012) is a small retrospective cohort study of 1,440 live births among New York residents in a TCE contaminated area via vapor intrusion. The study provides evidence for an association between maternal exposure to TCE and cardiac defects. The study observed an elevated risk estimate for cardiac defects (adjusted rate ratios of 2.15; 95% confidence interval: 1.27 - 3.62) and conotruncal defects compared to no exposure (adjusted rate ration of 4.91; 95% confidence internal: 1.58 - 15.24). EPA conducted an internal review of the Forand et al. study and concluded that the study findings were consistent with other human epidemiological data that have observed cardiac malformations in children exposed prenatally to TCE. EPA/OPPT incorporated a brief summary of the study and its findings in *section 2.6.2.3.6* of the final TCE OPPT risk assessment. *Section 2.6.2.3.6* also provides a summary of the human data supporting the effects in the heart following prenatal exposure to TCE as well as a summary of the weight-of-evidence analysis supporting the association between TCE exposure and fetal cardiac

		teratogenesis. Appendix N contains the weight-of-evidence analysis for fetal cardiac malformations following TCE exposure. **Citation:** Forand, SP; Lewis-Michl, EL; Gomez, MI. (2012). Adverse birth outcomes and maternal exposure to trichloroethylene and tetrachloroethylene through soil vapor intrusion in New York State. Environ Health Perspect 120: 616-621.
48	The selection of the HEC_{99} for the dose-response assessment is overly conservative. EPA/OPPT should explore using another HEC at a different percentile. Several panelists indicated that the document did not articulate why the HEC_{99} was the best choice compared to other values at different percentiles. The panelists also could not understand the uncertainty around the chosen HEC and the appropriateness of the lower bound 99th percentile across the various dose-response relationships considered.	EPA/OPPT used the HEC_{50}, HEC_{95} or HEC_{99} estimates reported in the TCE IRIS assessment, which represent the 50th, 95th or 95th percentile of the combined uncertainty and variability distribution of human internal doses, respectively. The HEC_{50} was interpreted as being the concentration of TCE in air for which there is 50% likelihood that a randomly selected individual will have an internal dose less than or equal to the internal dose POD (idPOD) from the rodent study. The HEC_{95} and HEC_{99} were interpreted as being the concentrations of TCE in air for which there is 95% and 99% likelihood, respectively, that a randomly selected individual will have an internal dose less than or equal to the idPOD derived from the rodent study. The TCE IRIS assessment preferred the HEC_{99} for the non-cancer dose-response analysis because the HEC_{99} was interpreted to be protective for a sensitive individual. EPA/OPPT supported the interpretation of the HEC_{99} as expressed in the TCE IRIS assessment. Hence, HEC_{99}-based risk estimates are favored in this assessment over those estimated from the HEC_{50} and HEC_{95} values. Despite this preference, the OPPT's risk assessment also includes risk estimates based on the HEC_{50} and HEC_{95} values to provide a sense of the difference between the median, the 95% and 99% confidence bound for the combined uncertainty and variability. Calculations of $HEC_{50/95}$ and $HEC_{50/99}$ ratios generally showed a 2-3 fold difference for the various studies identified in Table 2-18. The exception was the study reporting kidney effects (NTP, 1998) that showed higher $HEC_{50/95}$ and $HEC_{50/99}$ ratios (i.e., 5-9-fold) due to uncertainties in the rodent internal dose estimates. In contrast, HEC_{95} values were similar to HEC_{99} values with $HEC_{95/99}$ ratios showing a 1.3-1.5 fold difference. *Section 2.6.1.4* describes the range of HEC percentiles used in the TCE OPPT risk assessment as well as the ratio comparison among the HECs at specific percentile values. *Sections 2.7.2 and 2.7.3.2* present the acute and chronic non-cancer risk estimates, respectively, for the range of HEC percentiles.

		Citation: NTP (National Toxicology Program). 1988. *Toxicology and Carcinogenesis Studies of Trichloroethylene (CAS No. 79-01-6) in Four Strains of Rats (ACI, August, Marshall, Osborne-Mendel--Gavage Studies)*. U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, Research Triangle Park, NC. (as cited in EPA, 2011e).
49	HEC_{99} values are questionable since they are 2 to 10,000-fold lower than the corresponding POD value. When the difference between the benchmark from an animal study and the HEC_{99} is >100 it suggests that additional UFs are not necessary. Moreover, differences of 1000-fold or more call into question the underlying assumptions that produced these hypothetical differences. For example, when endpoints are similar (neurotoxicity or reproductive toxicity) for animals and humans, the ratio of POD to HEC are < 100-fold between species. So what underlying assumptions make the ratio of BMDL to HEC_{99} > 10,000 for kidney effects?	EPA/OPPT disagrees with the way the HEC_{99} values were compared with the animal POD values. The TCE PBPK model predicted human equivalent concentration (HEC) that would be expected to induce the same magnitude of toxic effect as the experimental animal species concentration based on internal dose metrics at the target tissue. On the other hand, the animal POD is the external air concentration of TCE obtained from the animal study that marks the beginning of a low-dose extrapolation in the non-cancer dose-response analysis. Thus, it is not appropriate to compare the animal POD with the HECs at different percentiles because the HECs are based on measures of internal dose extrapolated from rodent to humans, whereas the animal POD is only based on the external air concentration.
50	EPA/OPPT inappropriately used the HEC_{99} to support excluding dermal exposures. Several panelists criticized that the HEC "can provide a counterweight to not considering dermal exposure."	EPA/OPPT deleted this argument from the final risk assessment. Also, note that the PBPK model for TCE lacks a dermal compartment that would facilitate dermal risk estimation via route-to-route extrapolation or aggregate risk of dermal and inhalation exposures.
51	Neurotoxic endpoints should be used when evaluating the chronic risks at the workplace setting. The occupational risks were assessed using renal, immune and reproductive endpoints. Neurotoxicity was not included.	EPA/OPPT agrees with this comment. Inclusion of the neurotoxicity endpoint for chronic non-cancer risk estimation is presented in *section 2.7.3.2*. EPA/OPPT also considered other endpoints (i.e., developmental toxicity, kidney, immunotoxicity, reproductive toxicity, liver toxicity) when assessing the occupational non-cancer risks of TCE exposures.
52	EPA/OPPT incorrectly described TCE as a "probable human carcinogen".	EPA/OPPT agrees with this comment. The U.S. EPA's IRIS program has classified TCE as a human carcinogen by all routes. The correct classification appears in *sections 1.3.4* and *2.6.1.2.1* of the final TCE OPPT risk assessment.
53	EPA/OPPT did not provide empirical data supporting the assumption that minimal buildup of TCE would be expected	This assumption was supported by PBPK simulations presented in Tables 2-24 and 2-25. In these simulations, the TCE PBPK model was used to estimate HECs at the 50th and 99th percentile for the cardiac malformation endpoint under

	in humans exposed to TCE in an intermittent basis based on product usage assumptions.	chronic (steady-state) or intermittent (occupational) exposure to TCE under different exposure durations (i.e., 1 day, 3 weeks, 9 months, chronic). The 1-day HEC at the 50th and 99th percentile did not show significant variation when compared to the HECs for the other exposure durations (i.e., 3 weeks and 9 months) under continuous and intermitted exposures to TCE. Thus, the results from the PBPK simulations showed that the assumption (i.e., no substantial buildup of TCE in the body between exposure events) is reasonable to use in the final TCE OPPT risk assessment. This explanation has been incorporated in *section 2.6.1.4* of the final risk assessment.
54	EPA/OPPT did not discuss the physiological TCE levels associated with the acute exposures assessed in the document.	The TCE PBPK model can be used to estimate the internal doses of TCE ("physiological TCE levels) associated with the acute exposures of TCE uses within the scope of the OPPT risk assessment. The model already integrated the internal doses when calculating the 24-hr human equivalent concentrations (HECs) for specific health effects domains. EPA/OPPT used the 24 hr-HECs (HEC_{50}, HEC_{95}, or HEC_{99}) for developmental effects to estimate acute risks by comparing the HECs with the acute exposure concentrations estimated in the consumer exposure assessment (i.e., 24-hr exposure levels).
55	EPA/OPPT incorrectly adjusted the exposure duration and frequency for the hazard values. This resulted in hazard values that did not match the exposure of the persons for whom the assessment was being conducted. Selection of the appropriate time-averaging period, relevant to each endpoint selected from reliable studies is critically important for deciding what exposure (absorbed dose) metric should be used for risk estimate derivation. For example, the POD hazard values were adjusted in the IRIS program to continuous exposure (i.e., 24-hr HECs). Thus, worker exposure estimates need to be adjusted from 8-hr to 24-hr estimates. For chronic risks, the daily exposure should be put into an annual (chronic) average exposure and compared to the chronic hazard benchmark. Also, neurotoxicity and developmental toxicity endpoints may, or may not be appropriate for comparison to acute /	EPA/OPPT used 24-hr exposure estimates to estimate acute or chronic risks and made time adjustments to the exposure estimates, when necessary, to match them with the 24-hr HECs. For instance, the 8-hr worker exposure estimates were adjusted to 24 hrs for acute exposures. Average daily concentrations (ADCs) or lifetime average daily concentrations (LADCs) were estimated and used for the non-cancer or cancer chronic risk calculations, respectively. Note that the consumer exposure estimates for TCE were not adjusted because they were expressed as 24-hr time averaged indoor air concentrations. *Sections 2.3.3 and 2.4.2* of the final TCE OPPT risk assessment present the equations that were used to adjust the worker estimates to 24-hrs. The final TCE OPPT risk assessment considered the body of developmental toxicity data, including the recent developmental neurotoxicity studies (Blossom et al. 2012 and 2013), but only estimated acute risks for developmental effects based on the cardiac defect findings reported by the Johnson studies (see comment #44). Acute risks for neurotoxic effects as reported by Arito et al. (1994) were dropped in the final assessment because the neurotoxicity inhalation study did not involve an acute/short-term exposure to TCE. For instance, Arito et al. (1994) exposed rats to TCE for 8 hrs/ day, 5 days per week for 6 weeks.

	peak potential inhalation exposure/dose estimates, depending on the time to effect.	Although developmental toxicity studies are of a repeat-dose nature, EPA's policy is that a single exposure within a critical window of development may induce developmental effects. EPA/OPPT acknowledges that this is a health-protective policy that may overestimate the acute risks. See comment #44 for further information about the selection of fetal cardiac defects as the preferred endpoint for the acute risk estimates. **Citations:** Arito, H., M. Takahashi, and T. Ishikawa. 1994. Effect of Subchronic Inhalation Exposure to Low-Level Trichloroethylene on Heart Rate and Wakefulness-Sleep in Freely Moving Rats. Sangyo Igaku/Japanese Journal of Industrial Health (Japan), 36(1), 1-8. (as cited in 2011 TCE IRIS assessment). Blossom, S. J., S. Melnyk, C. A. Cooney, K. M. Gilbert, and S. J. James. 2012. Postnatal Exposure to Trichloroethylene Alters Glutathione Redox Homeostasis, Methylation Potential, and Neurotrophin Expression in the Mouse Hippocampus. Neurotoxicology, 33(6), 1518-1527. Blossom, S. J., C. A. Cooney, S. B. Melnyk, J. L. Rau, C. J. Swearingen, and W. D. Wessinger. 2013. Metabolic Changes and DNA Hypomethylation in Cerebellum Are Associated with Behavioral Alterations in Mice Exposed to Trichloroethylene Postnatally. Toxicology and Applied Pharmacology, 269(3), 263-269. Johnson, P. D., S. J. Goldberg, M. Z. Mays, and B. V. Dawson. 2003. Threshold of Trichloroethylene Contamination in Maternal Drinking Waters Affecting Fetal Heart Development in the Rat. Environmental Health Perspectives, 111(3), 289-292. (as cited in 2011 TCE IRIS assessment).

Risk Characterization

Charge 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.

Charge 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).

Charge 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.

#	Summary of Peer Review and Public Comments for Specific Issues Related to Charge Questions 5-1, 5-2, and 5-3	EPA/OPPT Response
56	Some peer reviewers and public commenters suggested using the endpoint/study-specific uncertainty factors (UFs) reported in the TCE IRIS assessment as the benchmark MOE. Some peer review and public comments noted that the UFs associated with the PBPK-derived HEC_{99} were not appropriate. One reviewer said that the UFs associated with the PBPK-derived HEC_{99} must be revised for acute exposures.	EPA/OPPT revised the benchmark MOEs to reflect the endpoint/study-specific UFs identified in the IRIS assessment for the PBPK-derived hazard values associated with specific non-cancer effects domains. Table 2-18 shows the endpoint/study-specific UFs by study/effects domain that EPA/OPPT used as benchmark MOEs for the acute and chronic non-cancer risk calculations.
57	EPA/OPPT provided an inadequate explanation for not using the RfC values and hazard quotients (HQ) calculations in the EPA/OPPT draft risk assessment for TCE.	EPA/OPPT used margin of exposures (MOEs) to present a range of risk estimates for different adverse endpoints identified to be relevant for different exposure scenarios. For this reason, MOEs were selected over a single HQ risk estimate based on the inhalation RfC. The IRIS RfC is generally applicable for chronic exposures, although can be used for less-than-chronic exposure under certain circumstances. This issue was discussed in *section 2.6.1.2.2* of the TCE OPPT risk assessment.
58	EPA/OPPT used a risk metric (i.e., MOEs) that did not account for differences that occur in susceptibility between humans and animals nor within animals or humans.	The differences between human and animals or within animal or humans were captured in the UFs that were used as the benchmark MOE. Depending on the study/endpoint, a variety of UFs were used (*Section 2.7.1*): • Interspecies UF • Intraspecies UF

		• Subchronic to chronic UF • LOAEL to NOAEL UF;
59	Peer review and public comments criticized the cancer risk level of 1 x 10^{-5} that the assessment used to interpret the cancer risks and suggested to use 1 x 10^{-4}.	EPA/OPPT reported the occupational cancer risks for three benchmark levels for different scenarios and uses: 1 x 10^{-4}, 1 x 10^{-5}, and 1 x 10^{-6} (see *section 2.7.3.1* and *Figures 2-6 and 2-7*).
60	The MOE approach does not quantitatively characterize the uncertainty in the estimated risk. The fact that the MOE is reduced to the use of two numbers, the hazard value and the exposure value, regardless of how they were obtained, does not provide a quantitative assessment of how much we can rely on that estimated risk. This issue could be addressed, by incorporating in the MOE a metric to characterize the uncertainty in the hazard value and/or the exposure value, for instance calculating the MOE with different possible values of both, the hazard and the exposure, under different scenarios to understand the impact in the obtained MOE. An empirical variance of the MOE would explain how variable the MOE would be, and sensitivity analysis would explain how sensitive the MOE is to how the exposure and the hazard are obtained under different scenarios of interest. Comparing the MOE to just a benchmark number, 30 in this case, is questionable, in particular when there is no assessment of the variability and uncertainty in the MOE.	The comment is implying that EPA/OPPT should conduct a probabilistic risk assessment. EPA/OPPT focused on feasible refinements to the exposure and hazard/dose-response assessment based on the available data and resources. Thus, a probabilistic risk assessment was not developed. The final risk assessment estimates non-cancer risks for various health effects endpoints based on the PBPK-derived hazard values (HEC_{50}, HEC_{95}, HEC_{99}). These HECs captured the 50th, 95th or 95th percentile of the combined uncertainty and variability distribution of human internal doses, respectively. See *comment #48*

Charge 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.

#	Summary of Peer Review and Public Comments for Specific Issues Related to Charge Question 5-4	EPA/OPPT Response
61	How can one have confidence in EPA's estimates for occupational exposures? EPA did not reference monitoring data to validate its exposure estimates resulting from the use of TCE in commercial degreasing processes.	In collaboration with OSHA, relevant monitoring data specific to TCE was identified. EPA/OPPT incorporated this additional information in section 2.3.3 of the final risk assessment.
62	EPA/OPPT has not adequately described data limitations and uncertainties associated to the exposure, hazard/dose response, and risk characterization assessments. In	EPA/OPPT has expanded upon and further refined the Uncertainty and Data Limitations section. See *section 2.8* of the final TCE OPPT risk assessment.

	addition, variability and uncertainty were treated the same in some of the discussion in the Uncertainty section.	

Other Public Comments		
#	**Summary of Other Public Comments**	**EPA/OPPT Response**
63	Public commenters indicated that EPA is adequately regulating TCE under the Clean Air Act (CAA). Does that pertain to the exposure scenarios described in the assessment?	Appendix B of the final risk assessment provides a summary of the regulatory history of TCE in the U.S. EPA, including regulations under CAA. The National Emission Standards for Hazardous Air Pollutants (NESHAP) are an example of such regulation under CAA. OPPT's risk assessment took NESHAP emission limits into account and characterized human health risks for specific TCE uses covered under the Toxic Substances Control Act (TSCA).
64	It was stated that the assessment was based on exposure data that predated regulations on vapor degreasing. Is this true? If so, how would more recent values affect the risk assessment?	EPA/OPPT's exposure assessment for vapor degreasing was based on recent data from the 2008 National Emissions Inventory (NEI) and the 2012 Toxics Release Inventory (TRI). Further, EPA/OPPT updated its risk assessment to take NESHAP emission limits into account.
65	Some public comments criticized EPA/OPPT for using modeled rather than measured exposure data.	EPA/OPPT acknowledges that it is not always possible to use only measured data for the purposes of risk assessment and that validated models can also be used for the purposes of estimating potential exposures.