



TOXICOLOGICAL REVIEW

OF

TRICHLOROETHYLENE

CHAPTER 1

(CAS No. 79-01-6)

**In Support of Summary Information on the
Integrated Risk Information System (IRIS)**

September 2011

1. INTRODUCTION

This document presents background information and justification for the Integrated Risk Information System (IRIS) Summary of the hazard and dose-response assessment of trichloroethylene (TCE). IRIS Summaries may include oral reference dose (RfD) and inhalation reference concentration (RfC) values for chronic and other exposure durations, and a carcinogenicity assessment.

The RfD and RfC, if derived, provide quantitative information for use in risk assessments for health effects known or assumed to be produced through a nonlinear (presumed threshold) mode of action. The RfD (expressed in units of mg/kg-day) is defined as an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. The inhalation RfC (expressed in units of ppm or $\mu\text{g}/\text{m}^3$) is analogous to the oral RfD, but provides a continuous inhalation exposure estimate. The inhalation RfC considers toxic effects for both the respiratory system (portal-of-entry) and for effects peripheral to the respiratory system (extrarespiratory or systemic effects). Reference values are generally derived for chronic exposures (up to a lifetime), but may also be derived for acute (≤ 24 hours), short-term (>24 hours up to 30 days), and subchronic (>30 days up to 10% of lifetime) exposure durations, all of which are derived based on an assumption of continuous exposure throughout the duration specified. Unless specified otherwise, the RfD and RfC are derived for chronic exposure duration.

The carcinogenicity assessment provides information on the carcinogenic hazard potential of the substance in question and quantitative estimates of risk from oral and inhalation exposure may be derived. The information includes a weight-of-evidence judgment of the likelihood that the agent is a human carcinogen and the conditions under which the carcinogenic effects may be expressed. Quantitative risk estimates may be derived from the application of a low-dose extrapolation procedure. If derived, the oral slope factor is a plausible upper bound on the estimate of risk per mg/kg-day of oral exposure. Similarly, an inhalation unit risk is a plausible upper bound on the estimate of risk per ppm or $\mu\text{g}/\text{m}^3$ in air breathed.

Development of these hazard identification and dose-response assessments for TCE has followed the general guidelines for risk assessment as set forth by the National Research Council (1983). U.S. Environmental Protection Agency (U.S. EPA) Guidelines and Risk Assessment Forum Technical Panel Reports that may have been used in the development of this assessment include the following: EPA Guidelines and Risk Assessment Forum technical panel reports that may have been used in the development of this assessment include the following: *Guidelines for the Health Risk Assessment of Chemical Mixtures* (U.S. EPA, 1986b), *Guidelines for Mutagenicity Risk Assessment* (U.S. EPA, 1986a), *Recommendations for and Documentation of Biological Values for Use in Risk Assessment* (U.S. EPA, 1988), *Guidelines for Developmental*

Toxicity Risk Assessment ([U.S. EPA, 1991](#)), *Interim Policy for Particle Size and Limit Concentration Issues in Inhalation Toxicity* ([U.S. EPA, 1994b](#)), *Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry* ([U.S. EPA, 1994a](#)), *Use of the Benchmark Dose Approach in Health Risk Assessment* ([U.S. EPA, 1995a](#)), *Guidelines for Reproductive Toxicity Risk Assessment* ([U.S. EPA, 1996](#)), *Guidelines for Neurotoxicity Risk Assessment* ([U.S. EPA, 1998a](#)), *Science Policy Council Handbook: Risk Characterization* ([U.S. EPA, 2000a](#)), *Benchmark Dose Technical Guidance Document* ([U.S. EPA, 2000b](#)), *Supplementary Guidance for Conducting Health Risk Assessment of Chemical Mixtures* ([U.S. EPA, 2000c](#)), *A Review of the Reference Dose and Reference Concentration Processes* ([U.S. EPA, 2002b](#)), *Guidelines for Carcinogen Risk Assessment* ([U.S. EPA, 2005b](#)), *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens* ([U.S. EPA, 2005e](#)), *Science Policy Council Handbook: Peer Review* ([U.S. EPA, 2006b](#)), and *A Framework for Assessing Health Risks of Environmental Exposures to Children* ([U.S. EPA, 2006a](#)).

The literature search strategy employed for this compound was based on the chemical name, Chemical Abstracts Service Registry Number (CASRN), and multiple common synonyms. Any pertinent scientific information submitted by the public to the IRIS Submission Desk was also considered in the development of this document. Primary, peer-reviewed literature identified through December 2010 was included where that literature was determined to be critical to the assessment. The relevant literature included publications on trichloroethylene which were identified through Toxicology Literature Online (TOXLINE), the U.S. National Library of Medicine's MEDLINE, the Toxic Substance Control Act Test Submission Database (TSCATS), the Registry of Toxic Effects of Chemical Substances (RTECS), the Chemical Carcinogenesis Research Information System (CCRIS), the Developmental and Reproductive Toxicology/Environmental Teratology Information Center (DART/ETIC), the Environmental Mutagens Information Center (EMIC) and Environmental Mutagen Information Center Backfile (EMICBACK) databases, the Hazardous Substances Data Bank (HSDB), the Genetic Toxicology Data Bank (GENE-TOX), Chemical abstracts, and Current Contents. Other information, including health assessments developed by other organizations, review articles, and independent analyses of the health effects data were retrieved and may be included in the assessment where appropriate. It should be noted that references have been added to the Toxicological Review after the external peer review in response to peer reviewer's comments and for the sake of completeness. These references have not changed the overall qualitative and quantitative conclusions.

In addition to using peer-reviewed, published scientific literature, the preparation of this toxicological review considered the advice to EPA from a 2002 SAB peer review report ([SAB, 2002](#)), a 2006 NRC consultation report ([NRC, 2006](#)), and a 2011 SAB peer review report ([SAB, 2011](#)), as well as comments from the public and other federal Agencies (weblinks).