Report on Carcinogens: Webinar on Trichloroethylene (TCE) Human Cancer Studies on Exposure to TCE: Methods Used to Assess Exposure and Cancer Outcome.

March 17, 2014 9:00 a.m. to 1 p.m EDT
# Trichloroethylene (TCE) Webinar Agenda

<table>
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<th>Session</th>
<th>Presenter/Author</th>
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<tr>
<td>Welcome and Introduction: Mary Wolfe/Ruth Lunn, NTP</td>
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<td>Webinar Agenda and Logistics: Cheryl Siegel Scott, U.S. EPA</td>
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<td>Seminar Presentations: Cheryl Siegel Scott</td>
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<tr>
<td>• Methods Used to Assess TCE Exposure Levels, Duration, and Probability in Epidemiologic Studies.</td>
<td>Patricia Stewart, PhD, Stewart Exposure Assessments, LLC</td>
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<td>• Methods Used to Classify Cancer Outcomes – Specifically Lymphohematopoietic Cancers.</td>
<td>Bernard D. Goldstein, MD, Professor Emeritus, University of Pittsburgh</td>
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<td>• Use of Exposure and Outcome Assessments in the Epidemiologic Studies.</td>
<td>Mark Purdue, PhD, National Cancer Institute</td>
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<td>Discussion: Neela Guha, International Agency for Research on Cancer</td>
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<td>• Topic-Specific Questions</td>
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<td>• Public-Initiated Questions</td>
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<td>Draft Protocol for Preparing the Draft RoC Monograph on TCE: Ruth Lunn</td>
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<td>Next Steps/Closing Remarks: Ruth Lunn/Mary Wolfe</td>
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The cancer evaluation for TCE is captured in the draft RoC monograph

- Draft RoC monograph consists of two parts:
  - Cancer evaluation component.
  - Substance profile [proposed for the RoC]: Preliminary listing recommendation and key scientific evidence.

- Cancer evaluation component for TCE*:
  - Focuses on specific cancers: non-Hodgkin lymphoma (and hematopoietic related cancers), kidney, and liver.
  - Assesses the level of evidence of carcinogenicity from human cancer studies
  - Evaluates the evidence from mechanistic and other relevant data.
  - Accepts the current RoC listing’s conclusions of carcinogenicity from studies in experimental animals and significant U.S. exposure.
  - Integrates the overall body of evidence and reaches a preliminary listing recommendation for the RoC.
  - Organized by cancer site rather than topic (usual convention).

* Outlined in concept document.
Draft RoC protocol for TCE: Overview

- Discusses methods to prepare the draft RoC monograph on TCE.
- Consists of four parts:
  - Part A: Preliminary outline of the cancer evaluation component.
  - Part B: Methods for evaluating the human cancer studies.
  - Part C: Methods for evaluating other relevant and mechanistic data.
  - Part D: Methods for updating exposure information in the draft substance profile.

## Part A: Preliminary outline of cancer evaluation component

<table>
<thead>
<tr>
<th>ADME/Toxicokinetics</th>
<th>Summary of data on absorption, distribution, and excretion</th>
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<tr>
<td></td>
<td>More detailed discussion on metabolism</td>
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<td>Relevant biological effects</td>
<td>Genetic and related effects</td>
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<td>Immune effects</td>
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<td>Assessments: 3 cancer sites</td>
<td>Human cancer assessment</td>
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<td>Evaluation of mechanistic and related data</td>
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<td>Final Conclusions</td>
<td>Preliminary level of evidence: Human cancer studies</td>
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<td>Preliminary listing recommendation</td>
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<td>Appendices</td>
<td>Literature search strategy</td>
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<td>Human cancer studies: Study description/quality evaluation</td>
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<td></td>
<td>Evidence-based tables: Genetic and related effects</td>
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<tr>
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<td>Evidence-based tables: Immune effects</td>
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Part B: Evaluation of human cancer studies

**Selection of studies**
- Inclusion
  - Three cancer sites
  - TCE specific risk estimate
  - Peer-reviewed
- Exclusion
  - Dry Cleaners
  - Geographical studies

**Systematic data extraction**
- Appendix tables:
  - Population and study characteristics
- Results:
  - Evidence based tables for each cancer site

**Evaluation of study quality**
- Potential for selection bias
- Potential for information bias
- Potential for confounding
- Other factors
- Analytical methods

**Cancer assessment**
- Individual studies
- Integration across studies
Part B, Section 3: Approach for evaluating study quality and its impact on the study’s findings

- Key questions and/or guidelines used to evaluate the following aspects of a study:
  - Potential for selection and information bias.
    - If there is a potential bias, would it likely lead to an overestimate or underestimate of the risk estimate, or is the direction of the bias unknown?
    - Webinar will inform the evaluation of information biases.
  - Quality of the methods to consider confounding.
  - Other factors related to a study’s ability to inform the cancer evaluation, such as exposure level, duration and range, length of follow-up, statistical power, and analytical methods.

- Approaches for evaluating impact of confounding in individual studies or across studies.

- The potential for bias or confounding is used to help interpret the study’s findings and does not necessarily mean that the study should be disregarded.
Parts C & D: Mechanistic, other relevant data, and exposure sections

• Mechanistic and other relevant data: Cancer evaluation component.
  – Identifies key questions for each section.
  – Outlines the methods for identifying and selecting literature for each section.
    • Literature search strategy.
    • Exclusion/inclusion questions.
  – Discusses the approach for writing the different sections, including the use of authoritative reviews and primary literature.
  – Identifies the proposed modes of action for each cancer site.

• Exposure: Substance profile.
  – Identifies the literature search strategy, sources of exposure information, and types of information to be updated in the profile.
Trichloroethylene

Status: Candidate Substance

- Background
  - CAS # 79-01-6
  - Halogenated alkene used mainly as an intermediate for hydrofluorocarbon production (67%) and as a degreaser for metal parts (30%). It is a major ingredient in many consumer products and has been found in food and drinking water, and the environment (ambient air, ground and tap water).
  - Currently listed as *Reasonably Anticipated to be a Human Carcinogen* in the 12th RoC.

- RoC documents related to the scientific review of trichloroethylene
  - Federal Register Notice (January 19, 2012) requesting public comment on nominated substances
  - Revised Concept Document (December 31, 2013)
  - **Protocol: Methods for preparing the draft RoC monograph on TCE** (December 31, 2013)
  - Preliminary literature search and identified citations
  - Draft RoC Monograph
  - Final RoC Monograph

- Public Comments

- Meetings, Webinars and Listening Sessions
  - Federal Register Notice (Nov. 12, 2013) - requesting nominations of speakers for a proposed TCE webinar
  - Webinar (March 17, 2014) - “Human Cancer Studies on Exposure to Trichloroethylene (TCE): Methods Used to Assess Exposure and Cancer Outcomes”

- **INPUT – provide information** (such as citations or new studies, scientific issues, nomination of experts, or comment on RoC documents)

NTP will communicate via the NTP list serve (http://ntp.niehs.nih.gov/go/getnews) when new information is added or current information is updated on this page.