

Office of the Report on Carcinogens (RoC)

RoC Update and Report on the Peer Review of the RoC Monograph on Trichloroethylene

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NTP Board of Scientific Counselors
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Background information: RoC

National Academy of Sciences reviews of styrene and formaldehyde

13th RoC

Current evaluations

Report on the peer review of Draft RoC Monograph on Trichloroethylene



The RoC is congressionally mandated

- Public Health Service Act, Section 301(b)(4) (1978, amended 1993)
 - Directs Secretary, Health and Human Services (HHS) to publish a list of carcinogens
- Identifies substances that pose a cancer hazard for people in the United States
 - Lists substances as “*known*” or “*reasonably anticipated human carcinogens*”
- NTP prepares the RoC for the Secretary, HHS
- Each edition of the report is cumulative



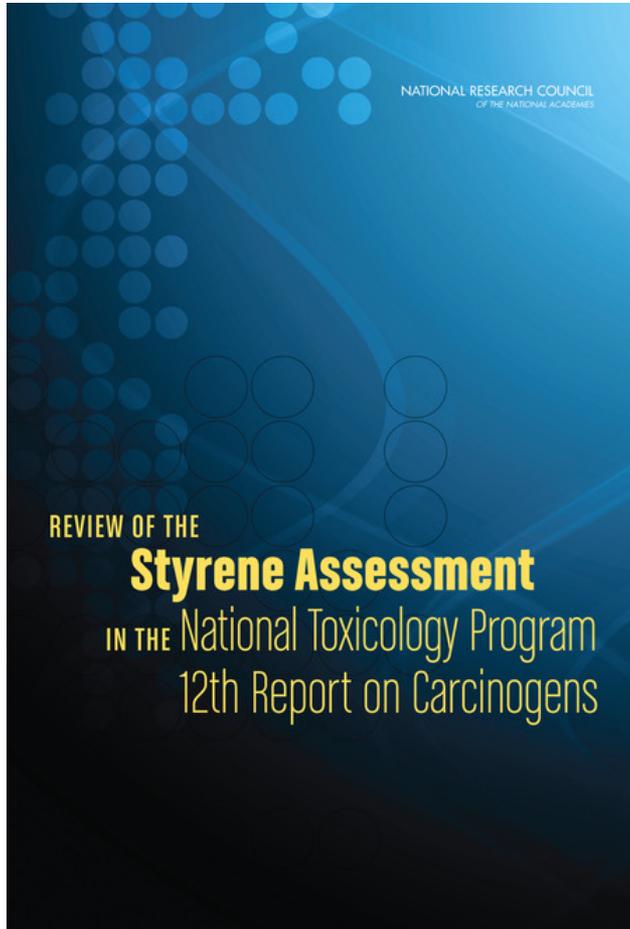


National Academy of Sciences (NAS) Reviews

- Congress directed HHS to fund NAS to independently review the NTP formaldehyde and styrene assessments and listings in the 12th RoC
- Each National Research Council committee conducted two activities
 - Peer review of the RoC listings
 - Independent assessment of the literature for each chemical (including literature published after 12th RoC release)
- The NRC Reports for both reviews were released in summer
 - Styrene: July 2014
 - Formaldehyde: August 2014



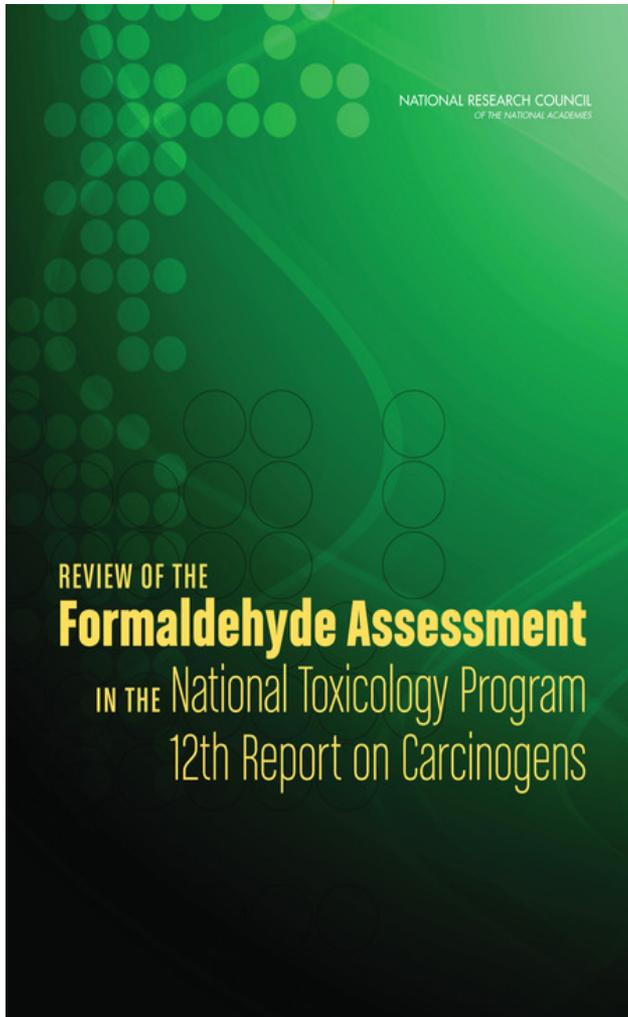
Endorsed listing of styrene as *reasonably anticipated to be a human carcinogen* in the 12th RoC



- Limited but credible evidence from studies in humans
- Sufficient evidence from studies in experimental animals
- Convincing “relevant information” in mechanistic studies that observed DNA damage in human cells that had been exposed to styrene



Endorsed listing of formaldehyde as *known to be a human carcinogen* in the 12th RoC



- Sufficient evidence from studies in humans
 - Nasopharyngeal cancer
 - Sinonasal cancer
 - Myeloid leukemia
- Sufficient evidence from studies in experimental animals
- “Convincing relevant information” that formaldehyde induces mechanistic events associated with the development of cancer in humans



Process for preparation of the RoC

Nomination and Selection of Candidate Substances

Invite nominations to the RoC

↓

Interagency review
Public comment

↓

Develop draft concept documents for substances proposed for evaluation

↓

Public comment

↓

Review of draft concept documents by NTP Board of Scientific Counselors* (public meeting, public comment)

↓

NTP Director

↓

Select candidate substances

Scientific Evaluation of Candidate Substances

Prepare draft RoC Monograph for a candidate substance (initiate cancer evaluation component)

↓

External scientific input, as needed (e.g., consultants, *ad hoc* presentations, expert panels*)

↓

Public input (e.g., listening session, comment)

↓

Interagency input (complete cancer evaluation component and prepare draft substance profile)

↓

Interagency review

↓

Complete draft RoC Monograph

Public Release and Peer Review of Draft RoC Monographs

Release draft RoC Monograph

↓

Public comment

↓

Peer review of draft RoC Monograph by NTP Peer-Review Panel* (public meeting, public comment, peer-review report)

↓

Present information regarding the peer review and revised draft RoC Monograph to NTP Board of Scientific Counselors (public meeting, public comment)

↓

NTP Director

↓

Finalize RoC Monograph (cancer evaluation component and substance profile)

HHS Approval and Release of Latest Edition of the RoC

Submit recommended listing status for newly reviewed candidate substances

↓

NTP Executive Committee

↓

Approval of listing status by Secretary, HHS (transmit latest edition of RoC to Congress and release to the public)

Key

HHS = Health and Human Services
NTP = National Toxicology Program
RoC = Report on Carcinogens
* Federally chartered advisory groups

RoC Update



- Released October 2014
- 243 Listings, 4 newly reviewed
- Released in electronic format only (website)
 - 45 Media outlets carried news of the release
 - 80,000 visits



New listings



1-Bromopropane

- *Reasonably anticipated to be a human carcinogen*
- Used as a cleaning solvent and in spray adhesives
- No current Federal regulations



Cumene

- *Reasonably anticipated to be a human carcinogen*
- Environmental pollutant: Found in fuel products
- Used to make acetone and phenol



Pentachlorophenol and By-products of Its Synthesis

- *Reasonably anticipated to be a human carcinogen*
- Exposure associated with increased risk of non-Hodgkin lymphoma
- Wood preservative used to treat utility poles

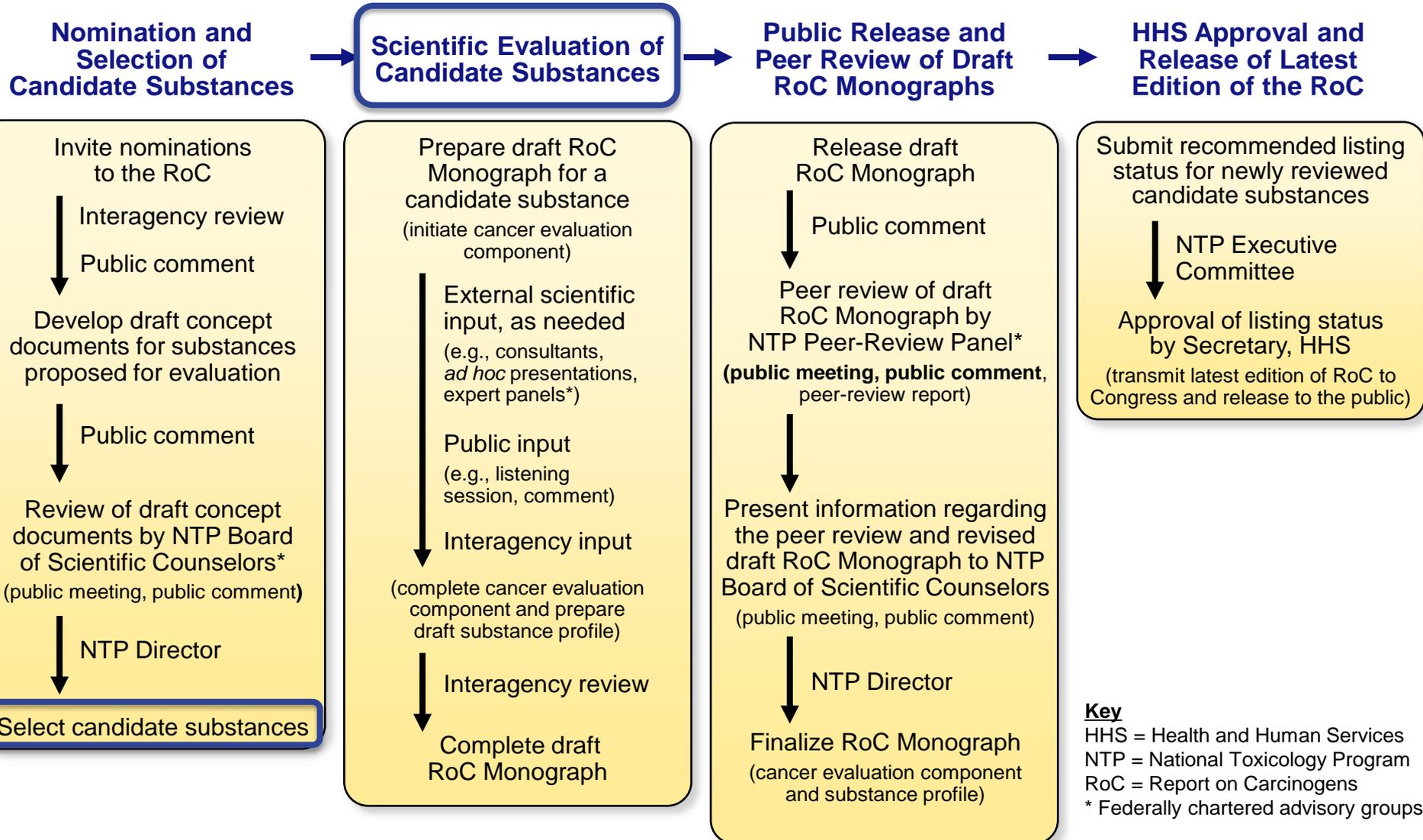


ortho-Toluidine

- *Known to be a human carcinogen*
- Exposure causes urinary bladder cancer
- Used to make dyes, rubber chemicals, and herbicides



New candidate substances





Evaluations in progress



Cobalt and certain cobalt compounds

- Informational group provided input on scope of review



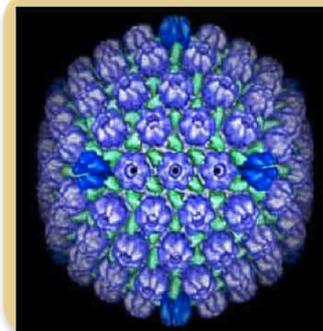
Goldenseal root powder

- Evaluation will consider scientific issues raised by the NTP BSC



Shift work at night, light at night, and circadian disruption

- Coordinating initial steps with OHAT



Five selected viruses

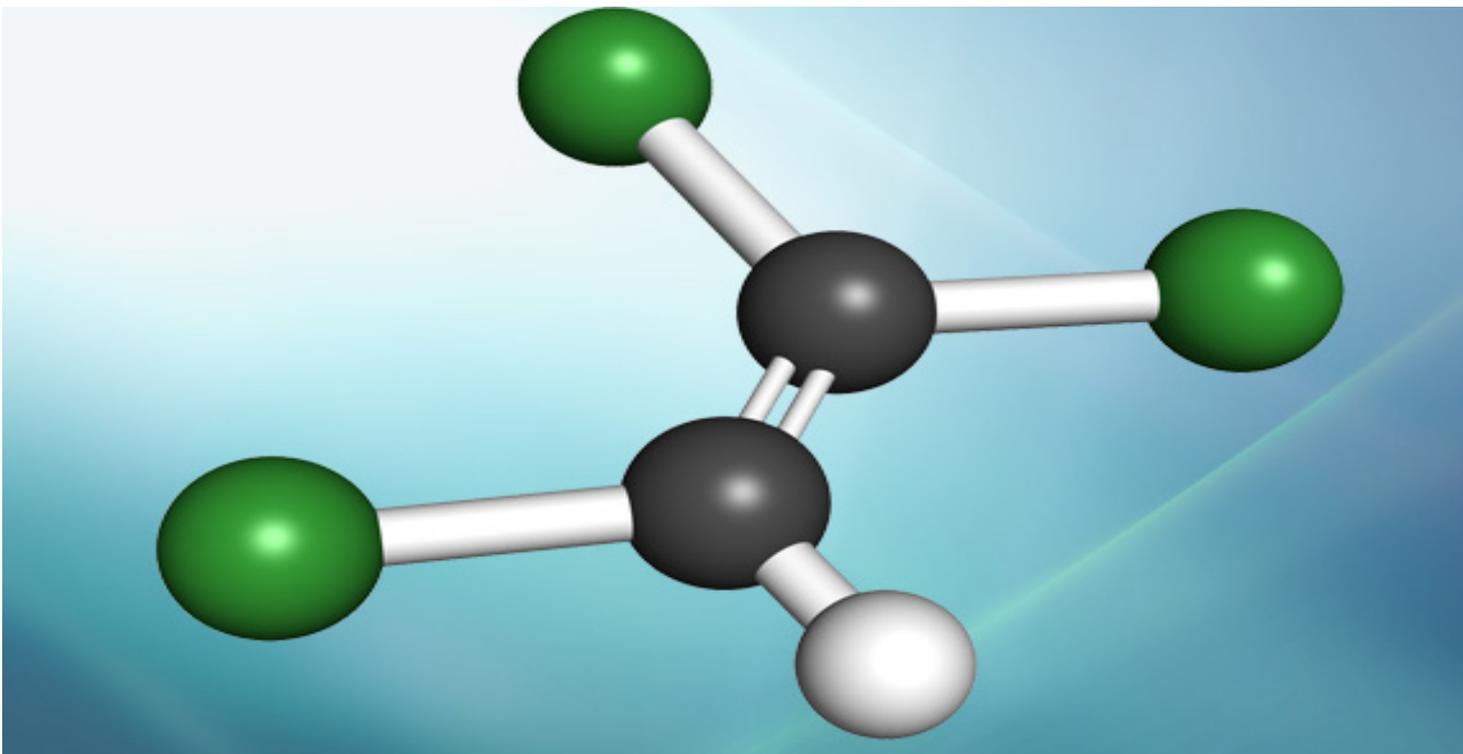
- Epstein-Barr virus
- Kaposi sarcoma-associated herpesvirus
- Human immunodeficiency virus
- Human T-cell lymphotropic virus type 1 (HTLV-1)
- Merkel-cell polyomavirus

Questions



Draft RoC Monograph on Trichloroethylene

NTP Peer-Review Meeting: August 12, 2014

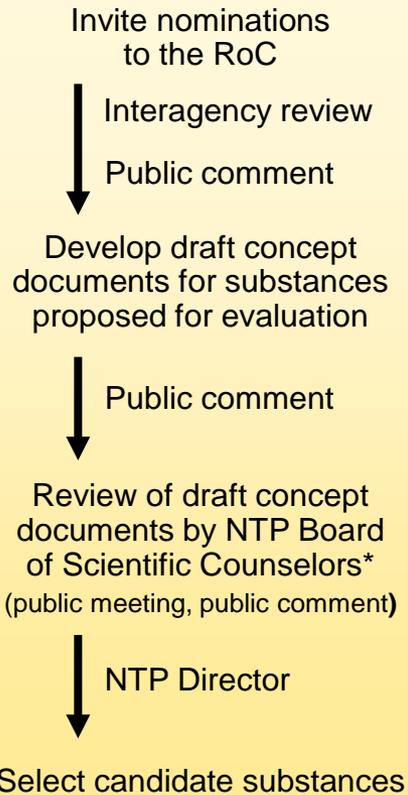


Objective: To provide the NTP Board of Scientific Counselors (BSC) with information regarding the peer review of draft RoC Monograph for Trichloroethylene (TCE)

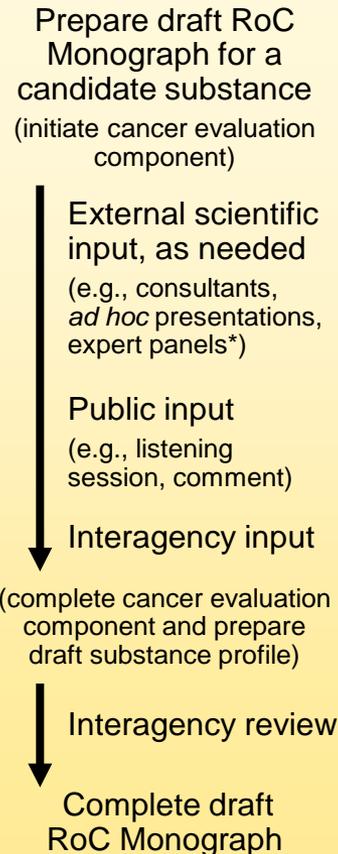


Scientific Review Completed for One Substance

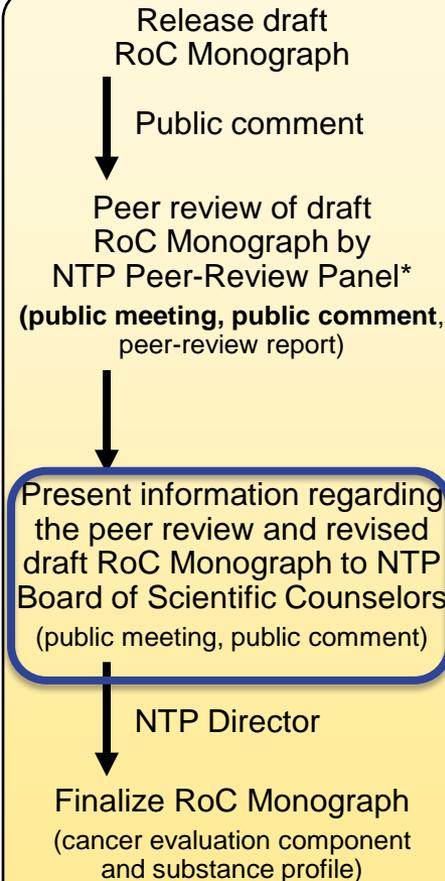
Nomination and Selection of Candidate Substances



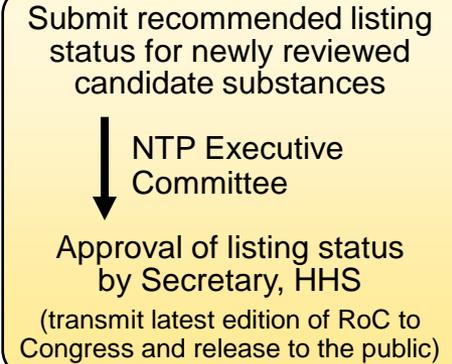
Scientific Evaluation of Candidate Substances



Public Release and Peer Review of Draft RoC Monographs



HHS Approval and Release of Latest Edition of the RoC



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Background and rationale for evaluation

- TCE is a chlorinated alkene used primarily as a metal degreaser in the past; recent use is mainly for hydrofluorocarbon production
 - TCE is also ubiquitous in the atmosphere, soil, ground, surface and drinking water, and in food
- Currently listed in the RoC as *reasonably anticipated to be a human carcinogen*
- Adequate database of human cancer studies published since the last RoC review

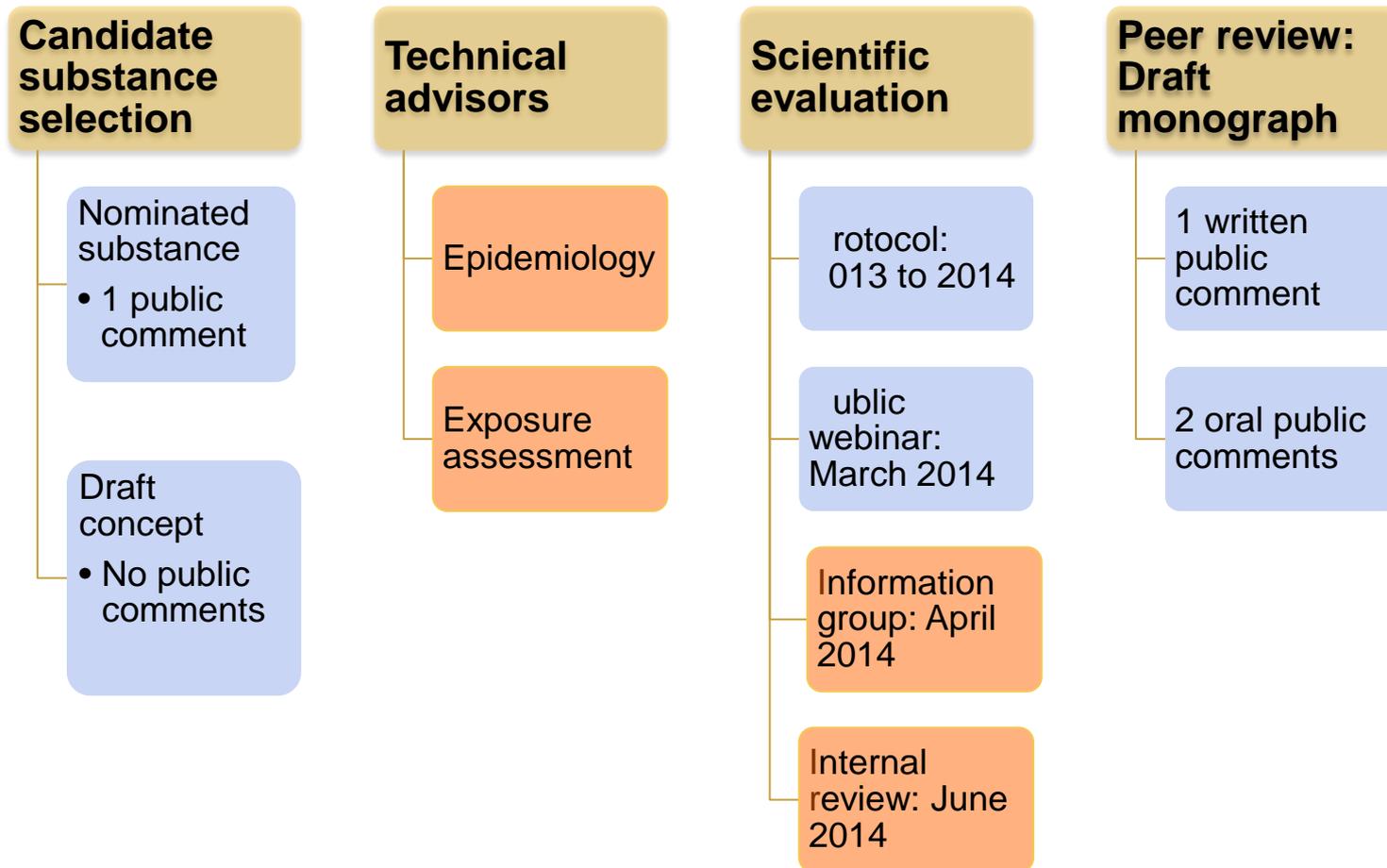


RoC Monograph on TCE

- Focused on three cancer sites: Kidney, liver, and non-Hodgkin lymphoma (NHL) and related subtypes
 - Identified by authoritative reviews as cancers of interest.
 - Tissue site concordance in experimental animals.
- Evidence in experimental animals
 - No new studies identified that would question the RoC conclusion of sufficient evidence.
 - Cancer findings included in the mechanistic evaluation but no reevaluation of the level of evidence.



Scientific input and public comments



Time was set aside at the peer-review meeting to discuss scientific issues raised in the public comments.



TCE Peer-Review Panel

Member	Affiliation
David A. Eastmond, PhD (Chair)	University of California, Riverside
Sarah J. Blossom, PhD	Arkansas Children's Hospital Research Institute
Kenneth P. Cantor, PhD, MPH	KP Cantor Environmental, LLC
John M Cullen, PhD, VMD, DACVP, FIATP	North Carolina State University
George R. Douglas, PhD	George R. Douglas Consulting
S. Katharine Hammond, PhD, CIH	University of California, Berkeley
Lawrence H. Lash, PhD	Wayne State University
Marie-Elise Parent, PhD	Université du Québec
David B. Richardson, PhD, MSPH	University of North Carolina, Chapel Hill
Paolo Vineis, MD, MPH, FFPH	Imperial College London



Charge

To comment on the draft cancer evaluation component, specifically, whether it is technically correct and clearly stated, whether the NTP has objectively presented and assessed the scientific evidence, and whether the scientific evidence is adequate for applying the listing criteria

To comment on the draft substance profile, specifically, whether the scientific justification presented in the substance profile supports the NTP's preliminary policy decision on the RoC listing status of TCE

Actions (votes)

Whether the scientific evidence supports the NTP's conclusion on the level of evidence for carcinogenicity from cancer studies in human of TCE

Whether the scientific evidence supports the NTP's preliminary listing decision for TCE in the RoC



The Panel agreed with draft NTP conclusions

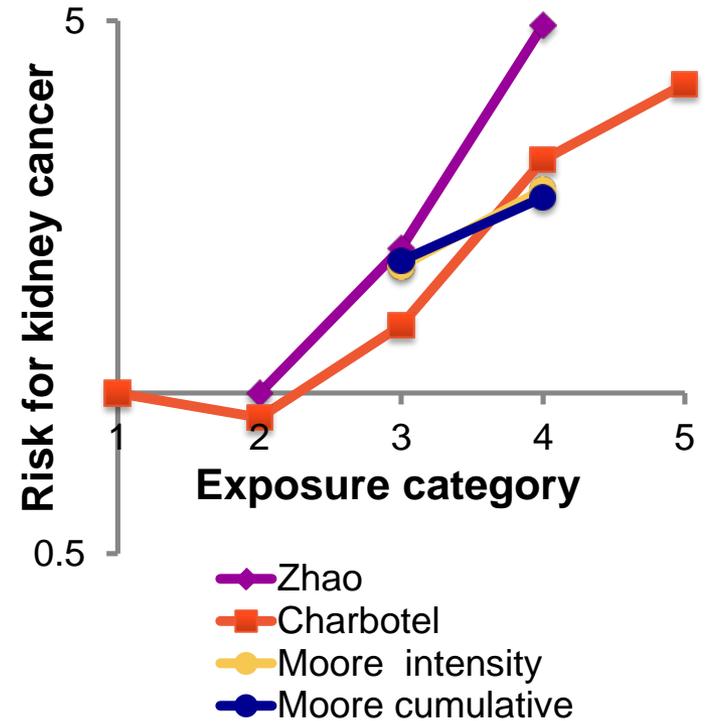
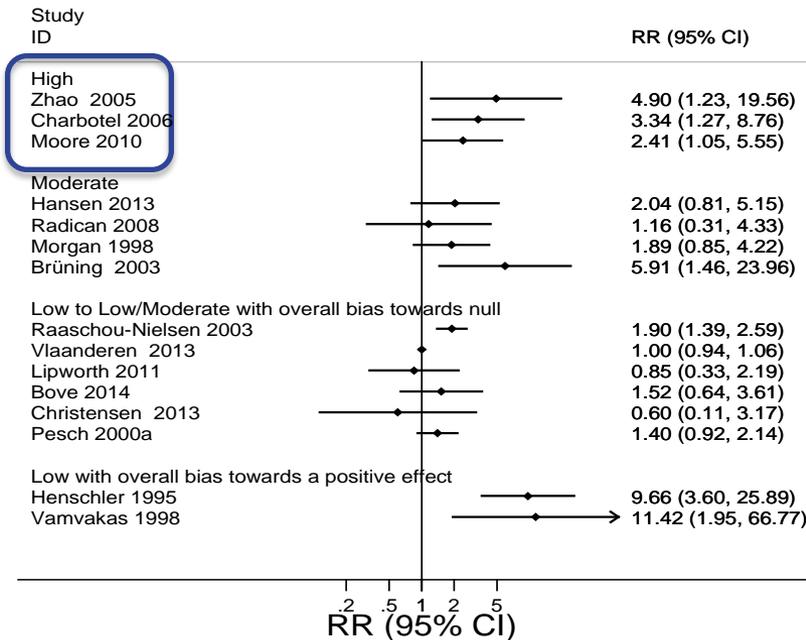
	NTP draft recommendation	Panel
Kidney cancer	Sufficient evidence of carcinogenicity from studies in humans	Agreed
non-Hodgkin lymphoma	Limited evidence for a causal association from studies in humans	Agreed
Liver cancer	Data are inadequate to evaluate the relationship between liver cancer and exposure to trichloroethylene	Agreed
Listing recommendation	<i>Known to be a human carcinogen</i>	Agreed



TCE is *known to be a human carcinogen*

Sufficient evidence for kidney cancer

TCE & Kidney Cancer High Exposure By Study Quality



- Consistent findings across studies (different designs, settings, populations)
- Evidence of increasing risk with increasing level or duration of exposure
- Meta-analyses showing statistically significant increased risk across studies
- Adequately rule out bias and confounding



Monograph revised based on Panel comments

Peer-review report

- Recommendations on NTP draft conclusions
- Scientific and technical peer-review comments

NTP response to the peer-review report

- Responses to comments
- Rationale for accepting/not accepting peer review recommendations

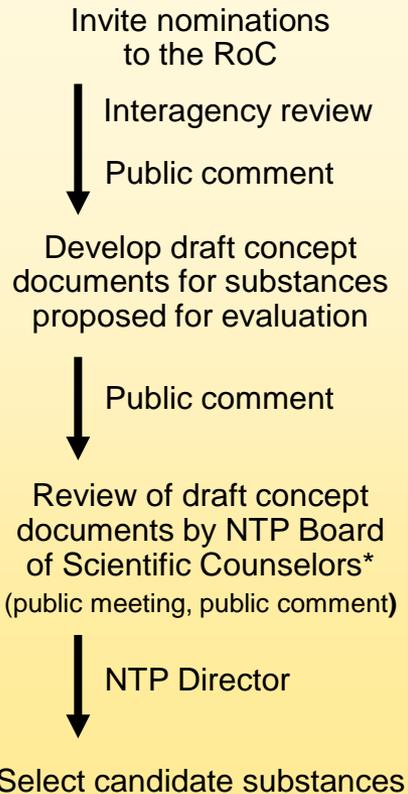
Revised draft monograph

- Revised based on NTP review of peer-review comments

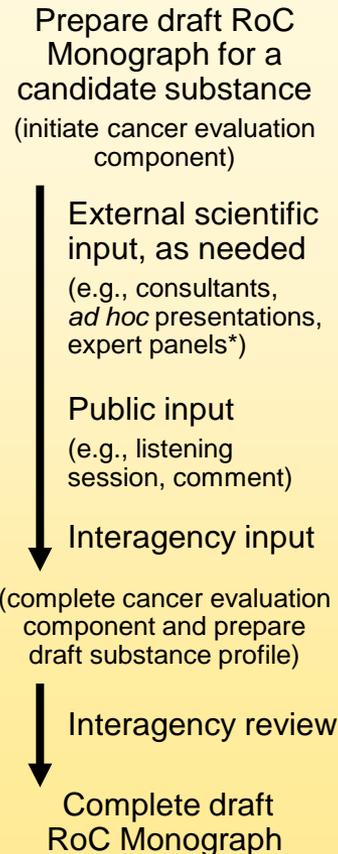


Process for preparation of the RoC

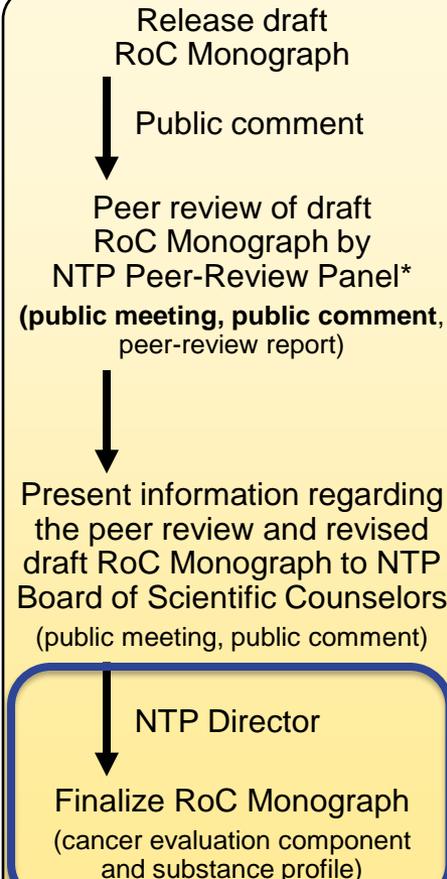
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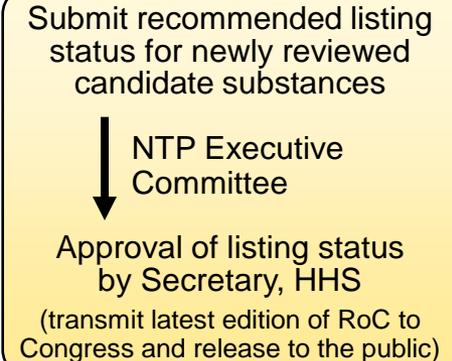
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Acknowledgements

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Peer-Review Panel

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Assessments

Questions