

Process for Preparing the Draft RoC Monograph on Haloacetic Acids Found as Water Disinfection By-Products



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Haloacetic Acids (HAA) Peer Review Meeting

Outline

Background on Report on Carcinogens (RoC)

Select HAAs for evaluation for the RoC

Draft RoC monograph

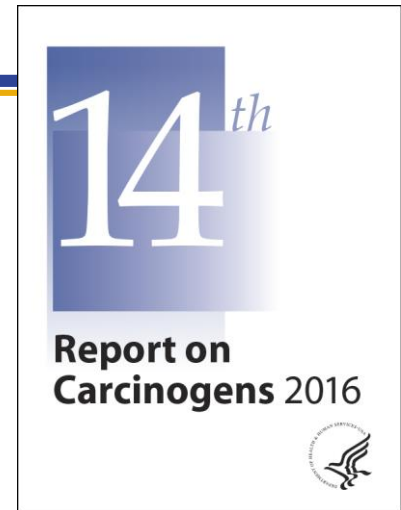
Reach RoC conclusions and RoC listing criteria

Next steps



The Report on Carcinogens (RoC) is congressionally mandated

- Identifies substances that pose a cancer *hazard* to people residing in the United States
 - Two listing categories: known and reasonably anticipated to be a human carcinogen
- Substance profile is written for each listing
 - Listing status, scientific information key to listing and data on properties, uses, production, exposure, and regulations to limit exposure
- Each edition of the report is cumulative
- NTP prepares the RoC for the Secretary of the Department of Health and Human Services using a four-part formal process and established listing criteria





Process for the Preparation of the RoC

Select substances for evaluation



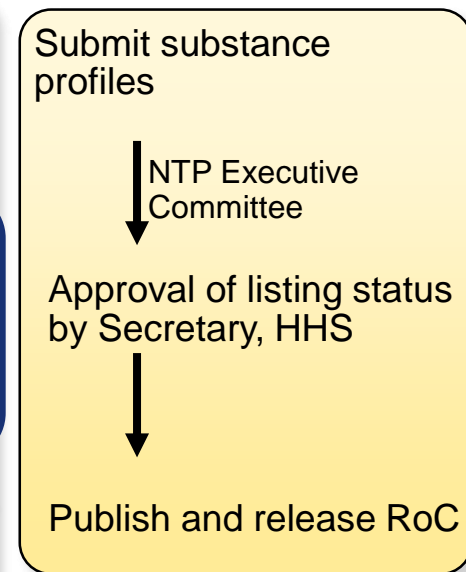
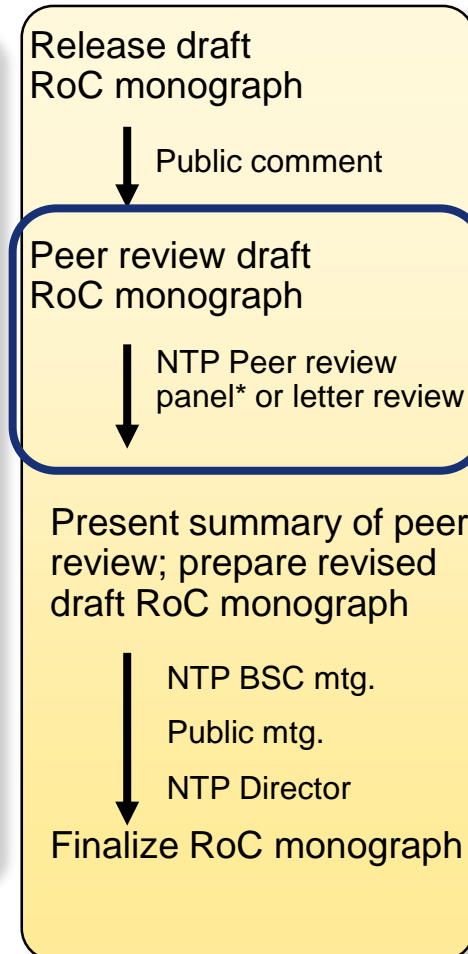
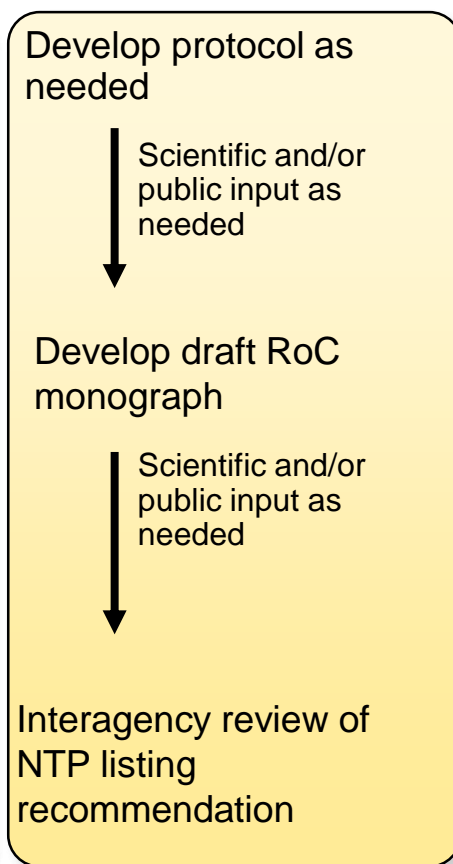
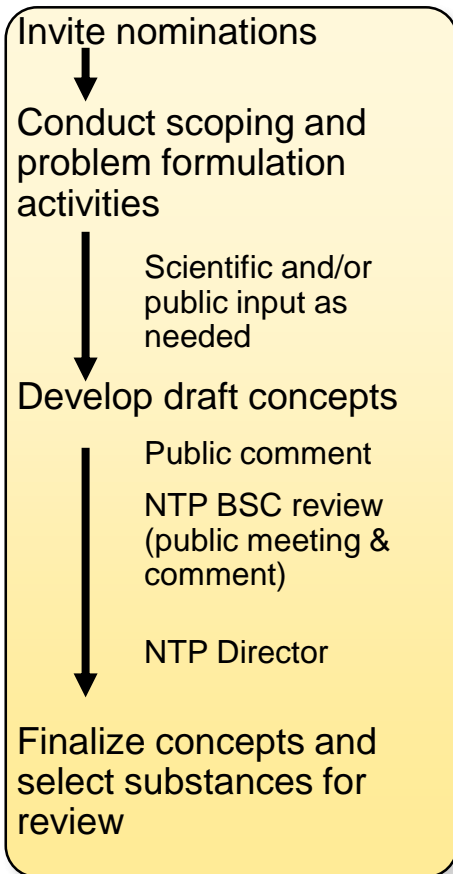
Prepare draft RoC monographs



Peer review and finalize RoC monographs



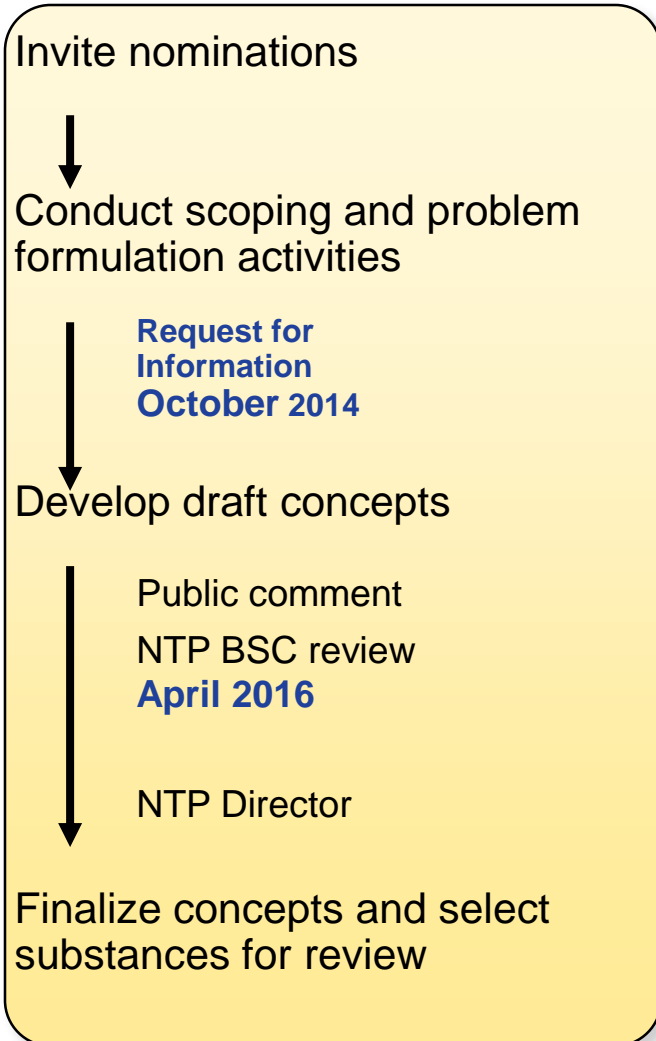
Approve and release the RoC



Key
BSC = Board of Scientific Counselors
HHS = Health and Human Services
NTP = National Toxicology Program
RoC = Report on Carcinogens
* Federally chartered advisory groups



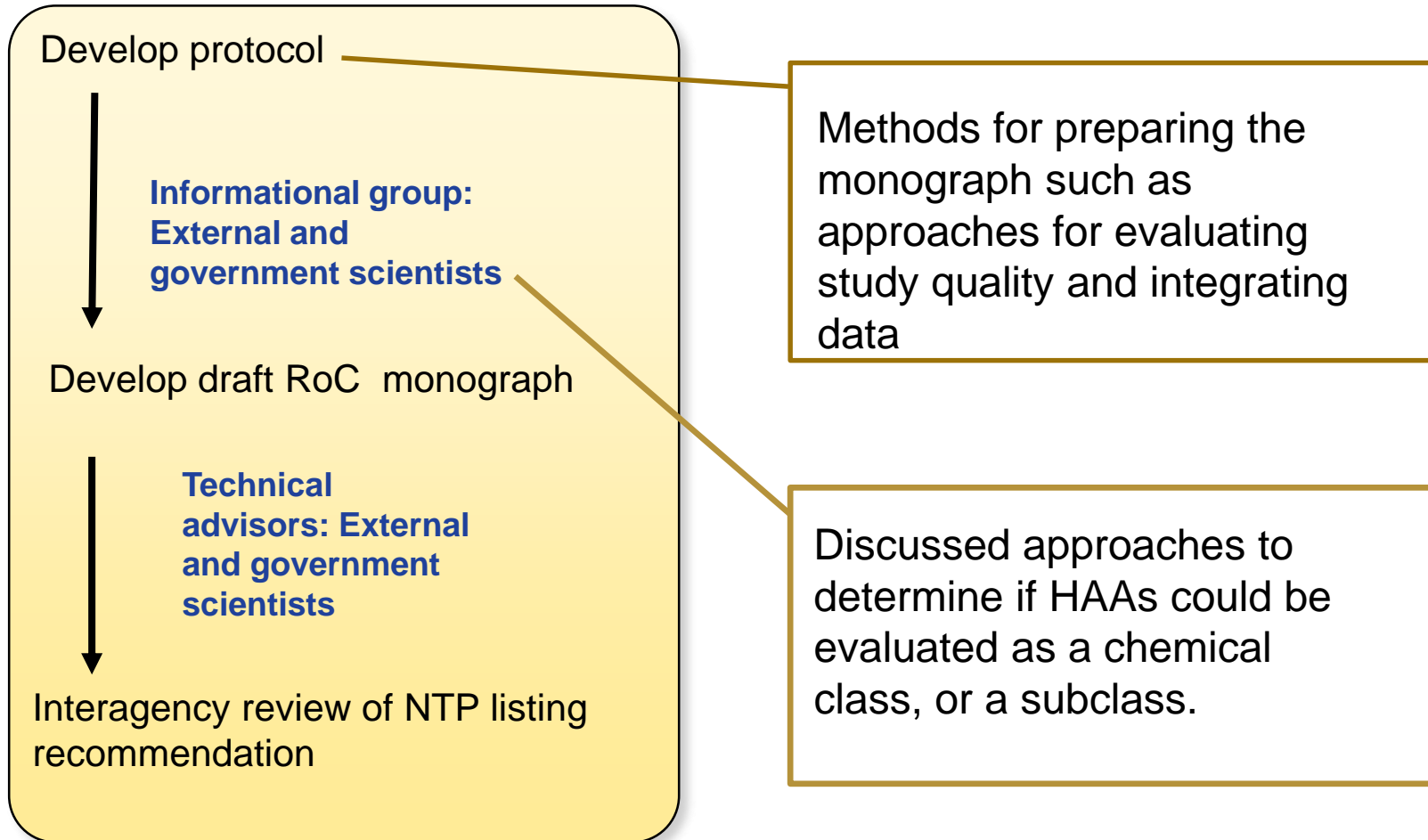
Important public health concern



- Nearly everyone in the United States is potentially exposed to HAAs found as drinking water disinfection by-products (DBPs)
- Some human studies report a potential association with urinary bladder cancer with chlorinated water exposure
- Large database of experimental cancer and mechanistic studies.
- Some DBPs are listed in the RoC but HAAs have not been evaluated
- Regulations are for specific DBPs



Prepare draft RoC monographs





Draft RoC Monograph on HAAs Found as Water DBPs

Objective

- Evaluate relevant scientific information, assess its quality, apply RoC listing criteria to the information, and reach a listing status recommendation
- Evaluate individual (13) HAAs, HAAs as one class, HAAs as several subclass(es)

Contents

- Background and methods
- Monograph sections: Human exposure, carcinogenicity, and other relevant information
- Substance profiles
- Appendices (separate document): Study quality and result tables



Evaluate whether a significant number of U.S. residents are exposed to HAA

Congressional mandate

- Publish a report that lists substances which are *known or reasonably anticipated to be human carcinogens* **and to which a significant number of persons residing in the United States are exposed.**

Evaluate data (Section 2)

- Number of people served by public water supply
- Levels of HAAs in water
- Not a formal exposure assessment

Reviewer instructions

- Use their judgment as to whether the exposure information in the draft monograph supports the NTP conclusion that a significant number of U.S. residents are exposed to HAAs

Type of evidence:
Individual HAAs (Section 1 to 6)

Properties
(Section 1)

- Defines class of 13 HAAs and how members of the class differ

ADME and TK
(Section 3)

- Informs MOAs
- Informs evaluation of HAAs without cancer data

Animal cancer studies
(Section 4)

- Cancer assessments of 6 individual HAAs
- Informs evaluation of HAAs without cancer data

Mechanism
(Section 6)

- Identifies biological effects, patterns (potencies) across events, and potential MOAs

Evidence integration:
Class/subclass assessments
(Section 7)

Endpoint	3 mono HAAs	6 di HAAs	4 tri HAAs
Properties (reactivity)	Electrophilicity, pKa		
TK	Comparative data		
Biological effects	Potencies		
Animal cancer data	Predicted TD ₅₀ and BMDs for carcinogenicity		

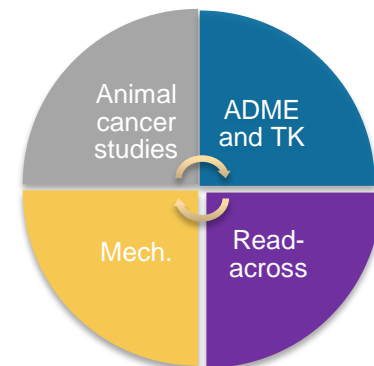
Read-across like approaches

13 HAAs as a class?

Subclasses of HAAs?

Individual HAAs?

Overall cancer hazard evaluation
(Section 8)



RoC Listing Criteria

Preliminary Listing Recommendations



RoC Listing Criteria: Two Categories

Known to be a human carcinogen

- Sufficient evidence of carcinogenicity from studies in humans

Reasonably anticipated to be a human carcinogen

- Limited evidence from studies in humans
OR
- Sufficient evidence from studies in experimental animals
OR
- Belongs to well-defined structurally related class of substances listed in the RoC or demonstrates convincing mechanistic evidence

Conclusions based on scientific judgment considering all relevant information such as chemical structure, metabolism, pharmacokinetics, genetic effects, and mechanisms of action.



Level of evidence from studies in experimental animals

Sufficient evidence

- Increased incidence of malignant and/or a combination of malignant and benign tumors
 - In multiple species or at multiple tissue sites
 - By multiple routes of exposure
 - To an unusual degree with regard to incidence, site, or type of tumor, or age at onset



Process for the Preparation of the RoC

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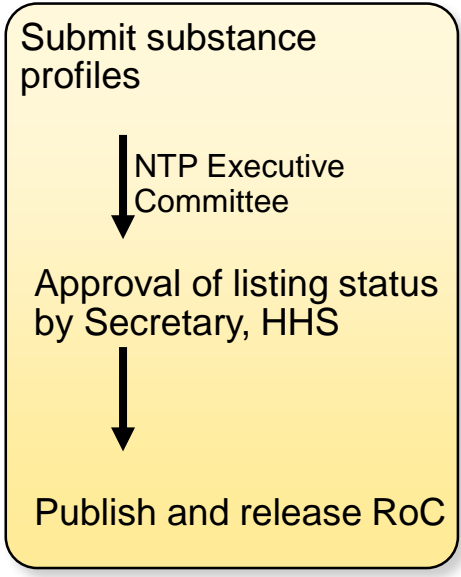
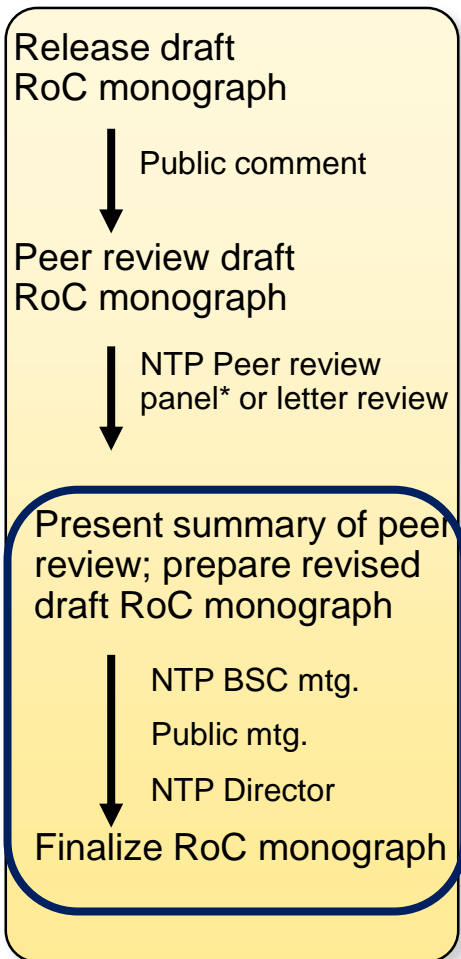
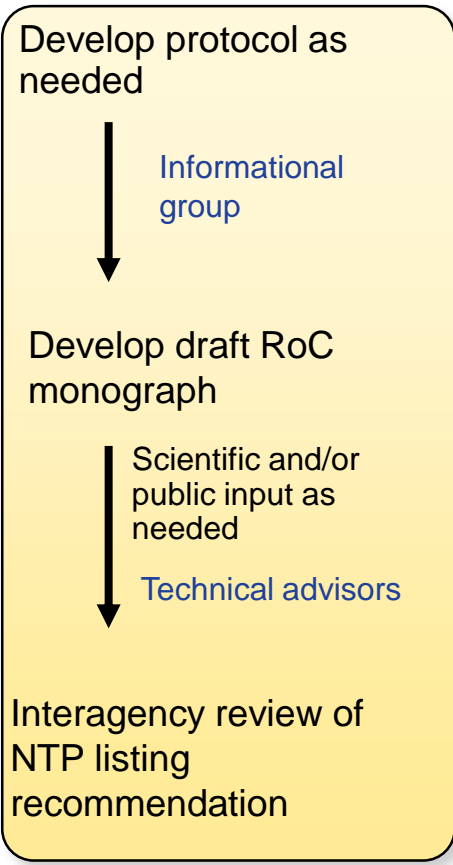
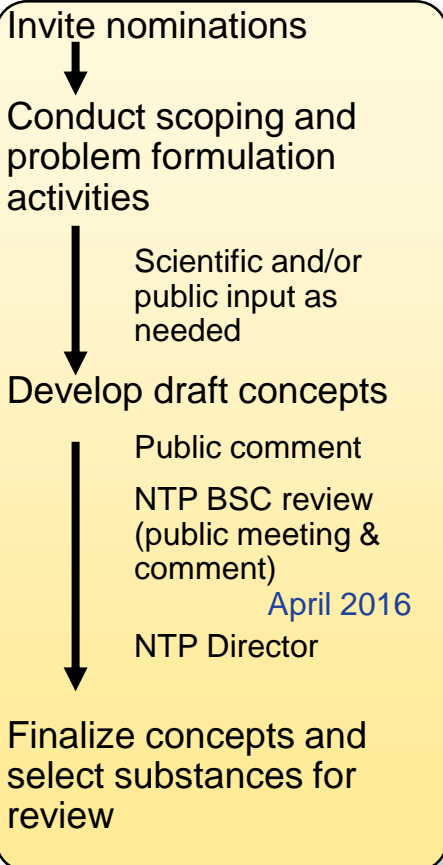
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Acknowledgments

Monograph Preparation

NTP/ORoC

Gloria Jahnke, Co-Project Lead

Ruth Lunn, Director ORoC

Suril Mehta

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Stan Atwood, Co-Project Lead

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Peer Review Meeting

NTP/Office of Policy, Liaison & Review

Mary Wolfe, Director

Robbin Guy

Anna Lee Mosley (Kelly Services, Inc.)*

ICF, Inc.*

Susan Blaine

Camden Byrd

A close-up photograph of a hand holding a clear glass under a chrome faucet. Water is being poured from the faucet into the glass, creating bubbles. The background is a white tiled wall. The word "Questions?" is overlaid in blue text on the left side of the image.

Questions?