

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



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National Institute of Environmental Health Sciences  
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# Haloacetic Acids (HAA) Peer Review Meeting

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## Outline

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Background on Report on Carcinogens (RoC)

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Select HAAs for evaluation for the RoC

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Draft RoC monograph

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Reach RoC conclusions and RoC listing criteria

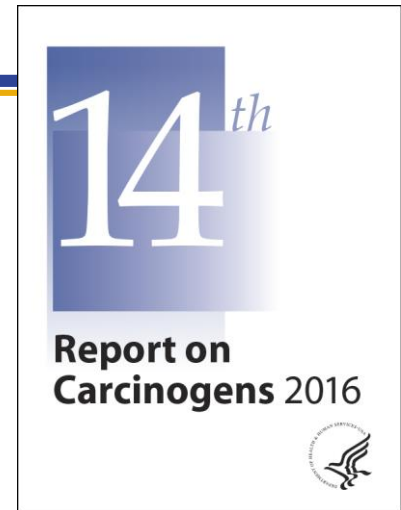
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Next steps



## 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



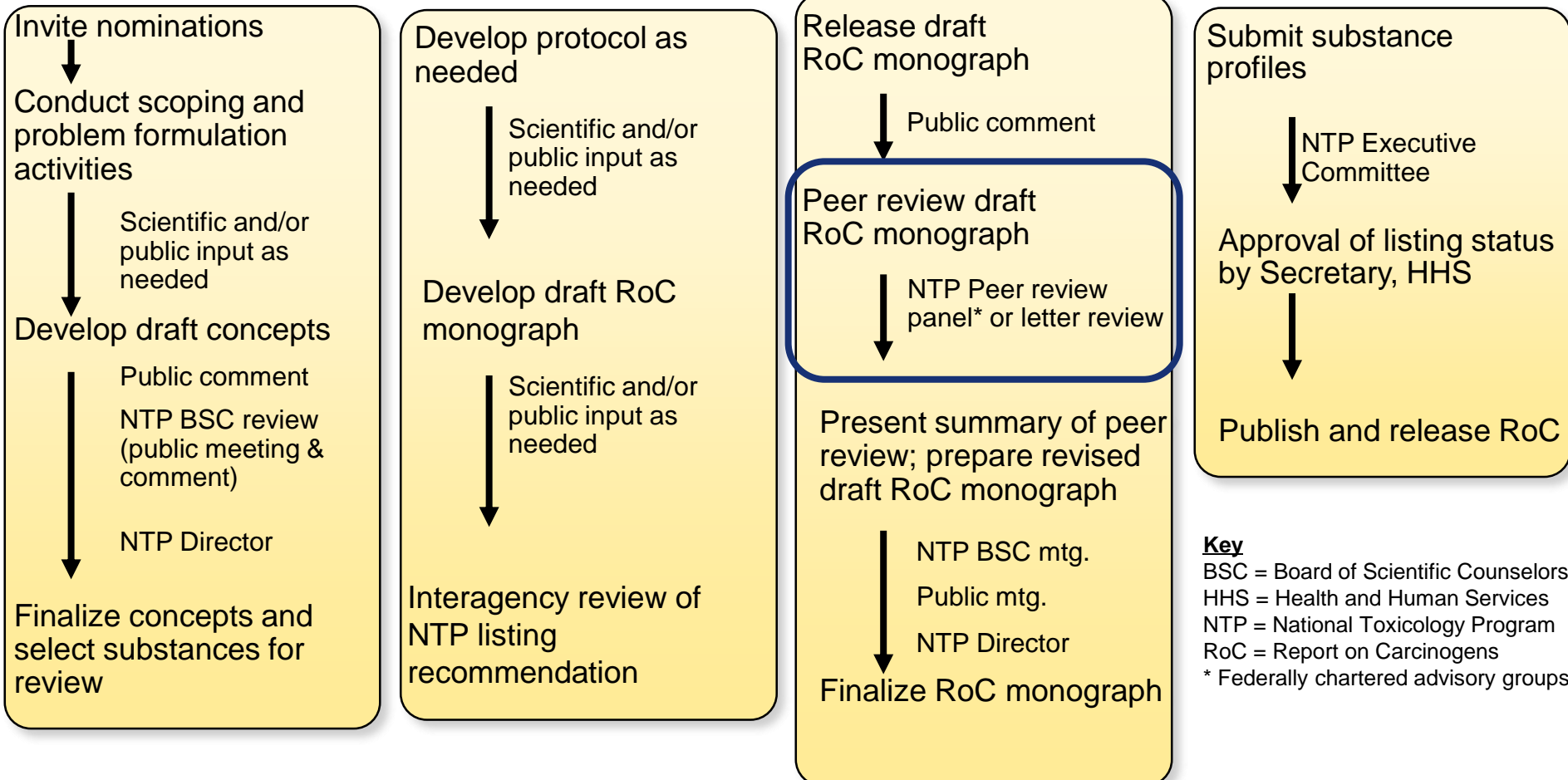
### Prepare draft RoC monographs



### 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



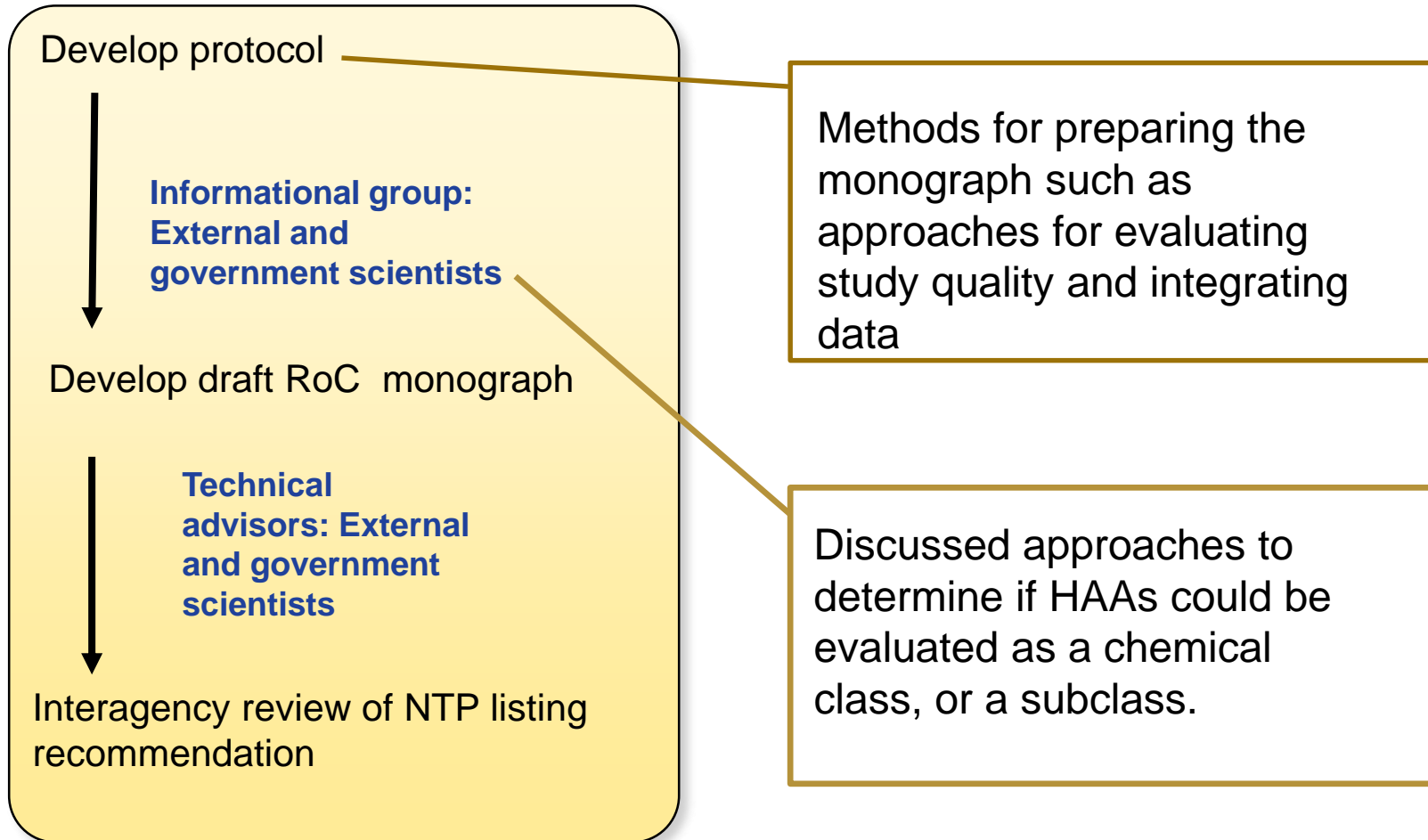
## Important public health concern



- 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

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## 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 <sub>50</sub> and BMDs for carcinogenicity |           |            |

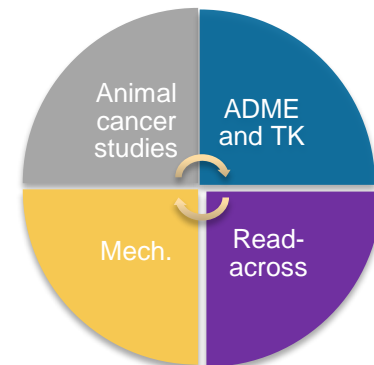
Read-across like approaches

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

### Select substances for evaluation



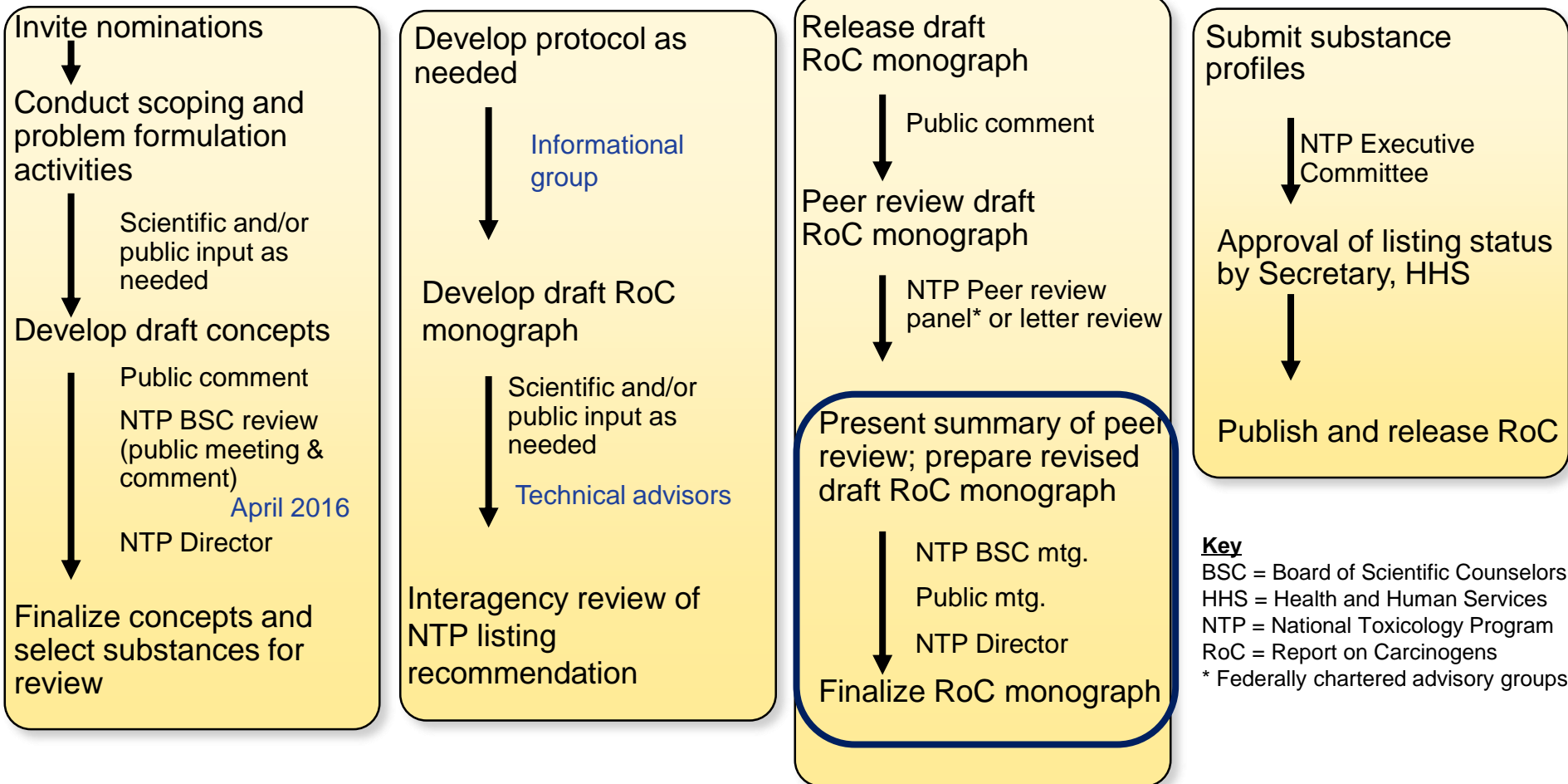
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# Acknowledgments

## Monograph Preparation

### **NTP/ORoC**

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Ruth Lunn, Director OROc

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Andy Shapiro, DNTP, NIEHS

## 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?**