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

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Office of the Report on Carcinogens
National Institute of Environmental Health Sciences
July 24, 2017
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

http://ntp.niehs.nih.gov/go/roc
Process for the Preparation of the RoC

1. **Select substances for evaluation**
   - Invite nominations
   - Conduct scoping and problem formulation activities
     - Scientific and/or public input as needed
   - Develop draft concepts
     - Public comment
     - NTP BSC review (public meeting & comment)
   - Finalize concepts and select substances for review

2. **Prepare draft RoC monographs**
   - Develop draft concepts
   - Public comment
   - NTP BSC review
   - NTP Director
   - Interagency review of NTP listing recommendation

3. **Peer review and finalize RoC monographs**
   - Peer review draft RoC monograph
     - NTP Peer review panel* or letter review
   - Present summary of peer review; prepare revised draft RoC monograph
     - NTP BSC mtg.
     - Public mtg.
     - NTP Director
   - Finalize RoC monograph

4. **Approve and release the RoC**
   - Submit substance profiles
   - NTP Executive Committee
   - Approval of listing status by Secretary, HHS
   - Publish and release RoC

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

https://ntp.niehs.nih.gov/go/rocprocess
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.

Important public health concern

Select HAA for Evaluation

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Develop protocol

Informational group: External and government scientists

Develop draft RoC monograph

Technical advisors: External and government scientists

Interagency review of NTP listing recommendation

Methods for preparing the monograph such as approaches for evaluating study quality and integrating data

Discussed approaches to determine if HAAs could be evaluated as a chemical class, or a subclass.
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

https://ntp.niehs.nih.gov/go/790113
# Reach RoC Conclusions

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

<table>
<thead>
<tr>
<th>Congressional mandate</th>
<th>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.</th>
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</table>
| 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)

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- 13 HAAs as a class?
- Subclasses of HAAs?
- Individual HAAs?

Overall cancer hazard evaluation (Section 8)

Animal cancer studies
ADME and TK
Mech.
Read-across

RoC Listing Criteria
Preliminary Listing Recommendations

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Read-across

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.
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
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Acknowledgments

Monograph Preparation

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  Steve Ferguson, DNTP, NIEHS
  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
  Canden Byrd

*Contract Support
Questions?