Report on Peer Reviews for the Report on Carcinogens

Introduction

Helicobacter pylori

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Office of the Report on Carcinogens
National Institute of Environmental Health Sciences

NTP Board of Scientific Counselors Meeting
9 October 2018
Outline

Report on Carcinogens
• Background
• Process

Helicobacter pylori
• Background
• Report of the peer review
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
Four-Part Process

Process for the Preparation of the RoC

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)
    - NTP Director
  - Finalize concepts and select substances for review

Prepare draft RoC monographs

- Develop protocol as needed
  - Scientific and/or public input as needed
- Develop draft RoC monograph
  - Interagency review of NTP listing recommendation

Peer review and finalize RoC monographs

- Release draft RoC monograph
  - Public comment
    - Expert peer review draft RoC monograph
      - NTP Peer review panel* or letter review
    - Present summary of peer review; prepare revised draft RoC monograph
      - NTP BSC (public meeting)
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    - Finalize RoC monograph

Publish and release RoC

- Submit recommended listing status of new substances
  - NTP Executive Committee
  - Secretary, HHS reviews and approves
  - 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
## Opportunity for Public Comment

### Process for the Preparation of the RoC

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<td>Select substances for evaluation</td>
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<td>2</td>
<td>Prepare draft RoC monographs</td>
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<td>3</td>
<td>Peer review and finalize RoC monographs</td>
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Scientific Input

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**Peer Review**

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Next Steps

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Report to the NTP BSC

Two substances recommended for listing in the RoC

Antimony trioxide
- Flame retardant
- Panel review
- Amy Wang

H. pylori (chronic infection)
- Bacteria
- Letter review
- Ruth Lunn
Outline

Report on Carcinogens
- Background
- Process

*Helicobacter pylori*
- Background
- Report of the peer review
**Background**

*H. pylori is an important public health concern*

- Gram negative, multi-flagellated bacterium
- Colonizes the stomach and causes peptic ulcers
- Genome codes for a number of virulence factors which modify cancer risk
- Spread primarily via person-to-person contact
- Significant number of U.S. residents are infected with *H. pylori*
- Disproportionately affects low and middle income countries and minorities and immigrants in the United States
Selection of H. pylori for review

• Nominated by a private citizen

• Broad consensus that *H. pylori* causes cancer
  – *H. pylori* contributes to 6.2% of all cancers and is responsible for close to 800,000 cancer deaths per year
  – Key issue is how to prevent *H. pylori* caused cancers
  – Congressional mandate is to provide a list of carcinogens
**H. pylori review used a strategy to use resources more efficiently and focus on key issues**

- Cancer hazard assessment captured in substance profile
  - Took advantage of the IARC assessment
- Peer review was conducted by letter rather than panel
- Monograph also provided a summary of the status of research and activities to prevent *H. pylori* related cancers
  - Consistent with NIEHS strategic goals of global public health and environmental justice
  - Consistent with spirit of congressional mandate to provide information on decreasing exposure and risk to public health
Review process

Interagency review
• Comments from 3 agencies
  • NCI, CDC, OSHA

Opportunity for public comment
• No comments received

External peer review
• Letter review
  • 3 reviewers
## Review Process

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### External peer review
- Letter review
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<th>Rolando Herrero, MD, PhD</th>
<th>Traci L. Testerman, PhD</th>
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<tbody>
<tr>
<td>Prevention and Implementation Group</td>
<td>Department of Pathology, Microbiology, and Immunology</td>
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<tr>
<td>Early Detection and Prevention Section</td>
<td>University of South Carolina School of Medicine</td>
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<tr>
<td>International Agency for Research on Cancer</td>
<td>Columbia, SC</td>
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<td>Lyon, France</td>
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<th>Julie Parsonnet, MD</th>
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<tr>
<td>Health Research and Policy, Division of Epidemiology</td>
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<tr>
<td>Stanford University Medical Center</td>
<td>Stanford, CA</td>
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Reviewers largely agreed with NTP preliminary level of evidence conclusions

**Sufficient Evidence**
- Gastric cancer (non-cardia)
  - 3-Fold excess risk
  - Higher risk with virulence subtypes
  - Cofactors important
- Gastric MALT lymphoma
  - Based on intervention studies
  - All 3 reviewers agreed

**Sufficient evidence**
- Gastric adenoma in mice and gerbils
- Gastric lymphoma in mice
- 2 reviewers agreed and 1 agreed in principle
Reviewers concurred with NTP preliminary listing recommendation

Known to be a human carcinogen

Sufficient evidence from studies in humans

Supporting mechanistic and toxicological data

Sufficient evidence from experimental animal studies
Monograph provides a summary of research and expert opinion related to screen and treat programs

Key issues of screen and treat program

**Benefits**
- Reduce peptic ulcers and other diseases
- Reduce gastric cancer
- Cost effective

**Concerns**
- Some health benefits of *H. pylori* infection
- Antibiotic resistance & changes in natural flora
- Reinfection

**Expert consensus statements**

- Recommended caution before implementing wide-scale planned prevention
- Prevention programs should be based on local consideration
  - Gastric cancer risk
  - Antibiotic resistance
  - Cost-benefit
- Randomized clinical trials and prevention programs (mainly in high risk areas) are ongoing
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- Randomized clinical trials and preventions programs (mainly in high risk areas) are ongoing
• Agreed with limiting the assessment to gastric cancers as evidence for other types of cancer is not as developed
  – Monograph appendices provide an overview of the database on pancreatic and colorectal cancers

• Most comments were relatively minor and related to improving the monograph
  – Clarifying information on exposure, treatment, properties, detection and exposure, and prevention studies
  – All these comments were addressed

• A few comments that were not addressed
  – Providing more information on genetics of gastric cancer
  – Make conclusions about recommendation for screening and treatment programs
Acknowledgements

**Project leads**
- Ruth Lunn, DrPH, NIEHS
  - Whitney Arroyave, PhD, ILS

**Contributors**
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- Brandy Beverly, PhD
- Michelle Hooth, PhD
- David Malarkey, PhD
- Scott Masten, PhD
- Suril Mehta, MPH
- Charles Rabkin, MD (NCI)
- Amy Wang, PhD

**Peer review**
- Mary Wolfe, PhD, (oversight)
- Elizabeth Mauull, PhD
- Canden Byrd, BS, ICF
- Kelly Shipkowski, PhD, ICF

NCI = National Cancer Institute
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