Report on Peer Reviews for the Report on Carcinogens

Introduction

Helicobacter pylori

Ruth M. Lunn, DrPH, MS
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
- Develop draft concepts
- Finalize concepts and select substances for review

Prepare draft RoC monographs

- Develop protocol as needed
- Develop draft RoC monograph
- Interagency review of NTP listing recommendation

Peer review and finalize RoC monographs

- Release draft RoC monograph
- Present summary of peer review; prepare revised draft RoC monograph
- NTP BSC (public meeting)
- NTP Director

Publish and release RoC

- Submit recommended listing status of new substances
- 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

Select substances for evaluation → Prepare draft RoC monographs → Peer review and finalize RoC monographs → Publish and release RoC

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
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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
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- Submit recommended listing status of new substances
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Scientific Input

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Peer Review

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Current Step

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Next Steps

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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
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*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
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

**Interagency review**
- Comments from 3 agencies
  - NCI, CDC, OSHA

**Opportunity for public comment**
- No comments received

**External peer review**
- Letter review
  - 3 reviewers

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**Rolando Herrero, MD, PhD**
Prevention and Implementation Group
Early Detection and Prevention Section
International Agency for Research on Cancer
Lyon, France

**Traci L. Testerman, PhD**
Department of Pathology, Microbiology, and Immunology
University of South Carolina School of Medicine
Columbia, SC

**Julie Parsonnet, MD**
Health Research and Policy, Division of Epidemiology
Stanford University Medical Center
Stanford, CA
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

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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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Reviewer Comments

• 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
- Andy Ewens, PhD, ILS
- Sandy Garner, PhD, ILS
- Lara Handler, MSLS, ILS
- Gloria Jahnke, DVM, NIEHS
- Alton Peters, MS, ILS

### Acknowledgments
- Ella Darden, BS, ILS
- Tracy Saunders, BS, ILS
- Susan Dakin, PhD, [independent contractor (Editor)]

### NIEHS internal reviewers
- John Bucher, PhD (Chair)
- 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

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NCI = National Cancer Institute  
Contract support: ICF and Integrated Laboratory Systems; (ILS)