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

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

2. Prepare draft RoC monographs
   - Develop protocol as needed
   - Develop draft RoC monograph
   - Interagency review of NTP listing recommendation

3. 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)
     - NTP Director
   - Finalize RoC monograph

4. 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

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

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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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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
**Case Study**

*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

Interagency review
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  • NCI, CDC, OSHA

Opportunity for public comment
• No comments received

External peer review
• Letter review
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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

- Supporting mechanistic and toxicological data
- Sufficient evidence from studies in humans
- 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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**Key issues of screen and treat program**

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**Expert consensus statements**

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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

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NCI = National Cancer Institute
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