

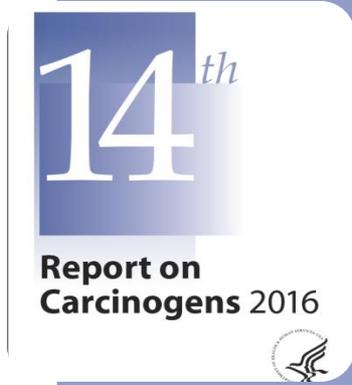
Report on Peer Reviews for the Report on Carcinogens Introduction *Helicobacter pylori*

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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

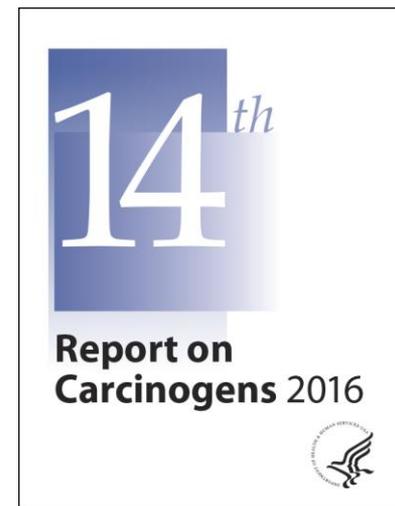


Helicobacter pylori

- 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



Four-Part Process

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

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

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

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

Opportunity for Public Comment

Process for the Preparation of the RoC

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Release draft RoC monograph

↓ **Public comment**

↓ Expert peer review draft RoC monograph

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Scientific Input

Process for the Preparation of the RoC

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Peer Review

Process for the Preparation of the RoC

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Current Step

Process for the Preparation of the RoC

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Peer review and finalize RoC monographs



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Next Steps

Process for the Preparation of the RoC

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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



Outline

14th

Report on
Carcinogens 2016



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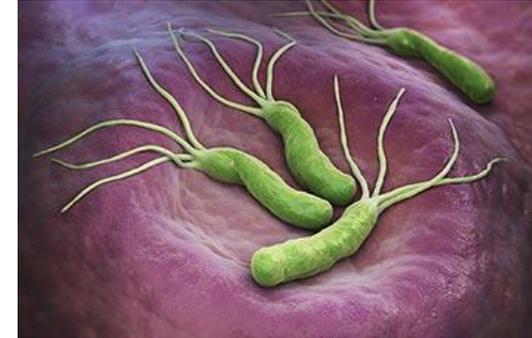
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H. pylori is an important public health concern

- 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

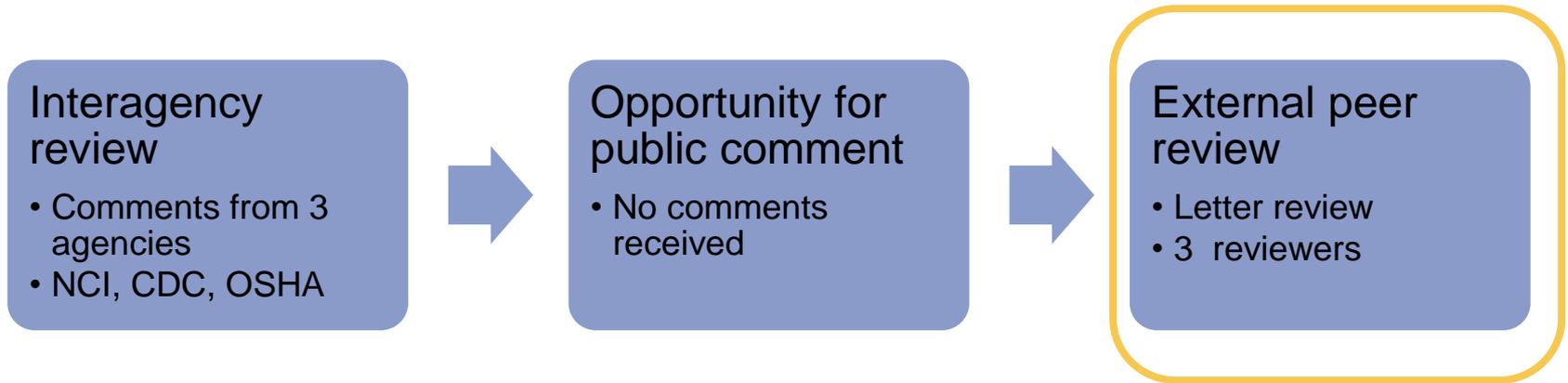


External peer review

- Letter review
- 3 reviewers



Review Process



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



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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

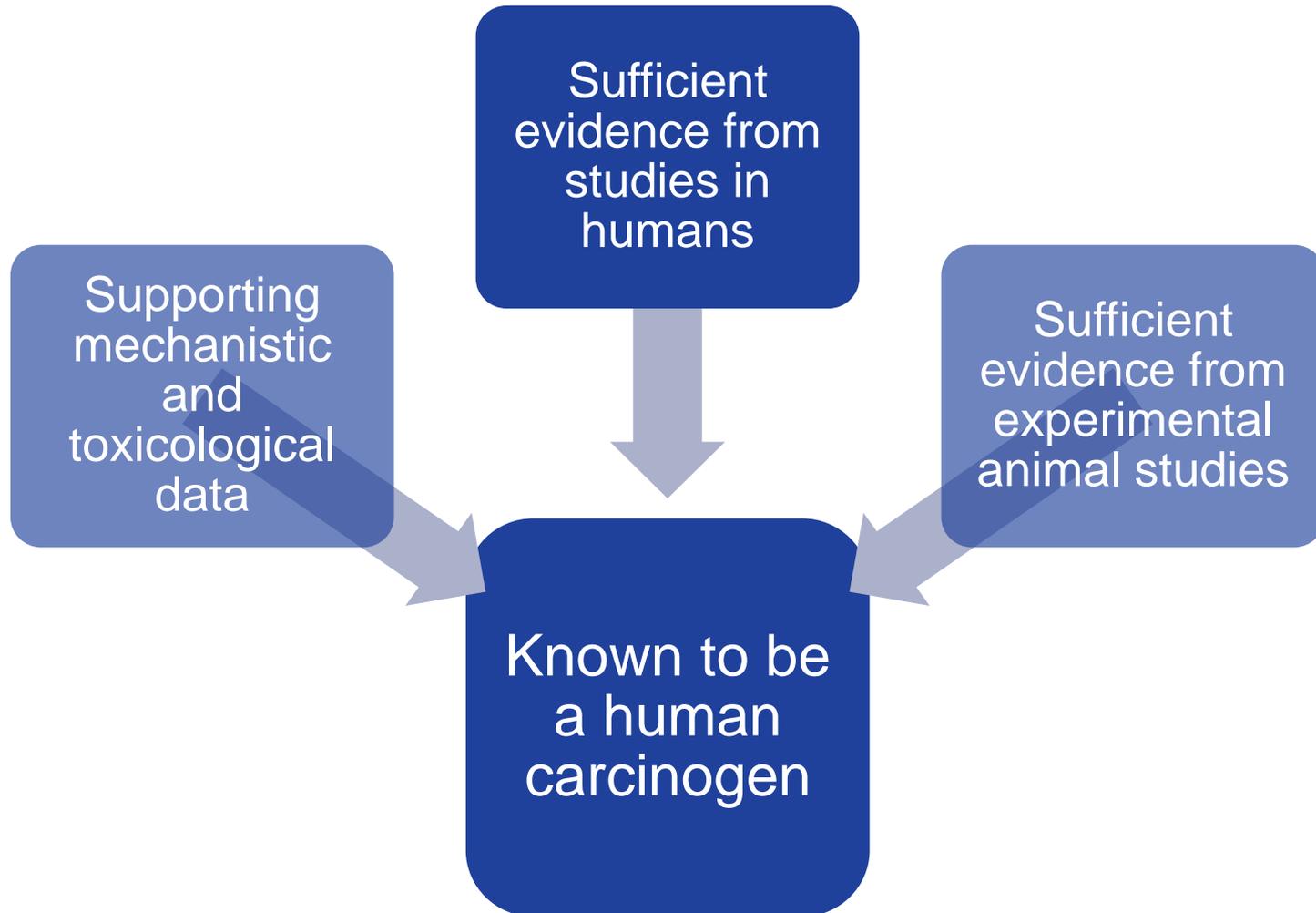


Sufficient evidence

- 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



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 preventions programs (mainly in high risk areas) are ongoing

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- 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

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Contributors

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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 Maull, PhD

Canden Byrd, BS, ICF

Kelly Shipkowski, PhD, ICF

NCI = National Cancer Institute

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