Styrene and the Report on Carcinogens (RoC)

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Styrene was first listed in the 12th Report on Carcinogens as *Reasonably Anticipated to be a Human Carcinogen*

What is the National Toxicology Program and the Report on Carcinogens?

What does reasonably anticipated to be a human carcinogen mean?

What was the process used and the scientific evidence for the styrene listing?

How are people exposed to styrene?

What is the potential exposure to styrene from polystyrene containers?
National Toxicology Program

Expands the scientific basis for making public health decisions on potential toxicity of environmental agents

• Interagency program
  – Established in 1978
  – Headquartered at NIEHS

• Research
  – Thousands of agents evaluated in comprehensive toxicology studies

• Analysis activities
  – Office of Report on Carcinogens (ORoC)
  – Office of Health Assessment & Translation (OHAT)
  – NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM)

US Department of Health and Human Services (DHHS)

NIH  CDC  FDA

NIEHS  NIOSH  NCTR

http://ntp.niehs.nih.gov
The Report on Carcinogens (RoC) is congressionally mandated

- Public Health Service Act, Section 301(b)(4) (1978, amended 1993)
  - Directs Secretary, Health and Human Services (HHS) to publish a list of carcinogens for people in the United States
  - Defines the language and number of listing categories: “known” or “reasonably anticipated human carcinogens”
  - Does not define the listing criteria or process for listing a substance

- Cancer hazard evaluation; does not address “risk”

- National Toxicology Program (NTP) prepares the RoC for the HHS Secretary using a four-part formal process and established listing criteria

- Each edition of the report is cumulative

http://ntp.niehs.nih.gov/go/roc
Reasonably anticipated to be a human carcinogen means.....

- Causal relationship in humans has not been clearly established
- NTP has established to standards (RoC Listing Criteria) for listing substances
- Examples of other substances listed as reasonably anticipated to be a human carcinogen
  - Acrylamide
  - Di(2-ethylhexyl) Phthalate (used in plastics)
  - Lead and lead compounds
  - Polycyclic aromatic hydrocarbons
Report on Carcinogens

NTP developed criteria for each listing category

**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 using all relevant information
Preparation of the 12th RoC followed an established process
(scientific input, external peer review, public comments)

Nominations and Selection of Candidate Substances
- Invite nominations
- Propose nominations for review
- Solicit public comments on nominations
- Select candidate substances

Scientific Review of Candidate Substances
- Prepare & release draft background document
- Solicit public comments on draft background document
- Expert Panel (public meeting: peer review draft background document & recommend listing status)
- Release final background document
- Solicit public comments on panel’s recommendation
- Interagency Scientific Review Group (closed meeting: recommend listing status)
- NIEHS/NTP Scientific Review Group (closed meeting: recommend listing status)

Peer Review of Draft Substance Profiles
- Prepare & release draft substance profiles
- Solicit public comments on draft substance profiles
- NTP Board of Scientific Counselors (public meeting: peer review draft substance profiles)

Preparation of RoC and Transmittal
- Prepare draft RoC
- Director, NTP
- NTP Executive Committee
- Secretary, HHS (transmit RoC to Congress and public)
- Release NTP response documents (NTP’s response to the expert panel peer review report, the BSC peer review report, and the public comments)

BSC = Board of Scientific Counselors
HHS = Health and Human Services
NIEHS = National Institute of Environmental Health Sciences
NTP = National Toxicology Program
RoC = Report on Carcinogens
Styrene is *reasonably anticipated to be a human carcinogen*

- **Rationale for NTP conclusions (2009)**
  - Studies of styrene-exposed workers show an association between exposure to styrene and lymphohematopoietic cancer and genetic damage in their lymphocytes (*limited evidence*)
  - Styrene causes lung tumors in laboratory mice by two routes of exposure (*sufficient evidence*)
  - Styrene is metabolized to styrene-7,8-oxide, which is listed as a *reasonably anticipated human carcinogen* in the RoC

- **National Academy of Sciences (National Research Council) (2014)**
  - Endorsed listing of styrene in the 12th RoC as reasonably anticipated to be a human carcinogen and agreed with NTP conclusions for each type of evidence (human, animal and mechanistic)
People are potentially exposed to styrene in the workplace, from the environment, indoor air, food and tobacco smoke.

**Workplace**

- High exposure
  - Parts per million (PPM) range
  - Blood levels (µg/L)
  - 8.9 to 83

**General public**

- Low exposure
  - Parts per billion (PPB) range
  - Blood levels (µg/L)
  - 0.13 (95 percentile)

**Occupational exposure to styrene (PPM)**

- Reinforced plastics (after 1980)
- Styrene-butadiene
- Production

**Styrene exposure to general public (PPB)**

- Tobacco smoke*
- Food**
- Indoor air
- Near industry*
- Outdoor air*

1 ppm = 1000 ppb

* lifetime; **most 0.05-119
Low exposure to styrene from food in polystyrene containers

Polystyrene (PS)
- USDA regulations (mg/kg) for PS
  - Fatty food: 10,000
  - Non-fatty food: 5,000

Low migration of styrene monomer
- Food: lipophilicity
- Container: surface to volume ratio
- Conditions: duration, contact, temperature

Low levels (ppb) of styrene in food

Styrene levels (μg/kg) in polystyrene containers
- butter
- cookies
- beverages
- raw meat
- coffee lids, yogurt cups
- Styrofoam cup
- take out containers
• Styrene is listed as *reasonably anticipated to be a human carcinogen* in the Report on Carcinogens
  
  – Cancer studies in workers exposed to high levels of styrene reported an increased risk of cancer
  
  – Lung tumors developed in mice exposed to 20 to 160 ppm (almost lifetime)

• NTP evaluation is a cancer hazard evaluation and does not estimate cancer risks to individuals associated with exposures in their daily lives

• The general public is exposed to low levels of styrene (orders of magnitude lower than workers) from the environment, indoor air, food, and tobacco smoke
  
  – Low levels of styrene in food can occur from the environment, natural sources, mold contamination (e.g. cinnamon), or contact with polystyrene