

Styrene and the Report on Carcinogens (RoC)

Ruth M. Lunn, DrPH, Director Office of the RoC
Division of the National Toxicology Program
National Institute of Environmental Health Sciences

Maui County Council
May 9, 2017



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**

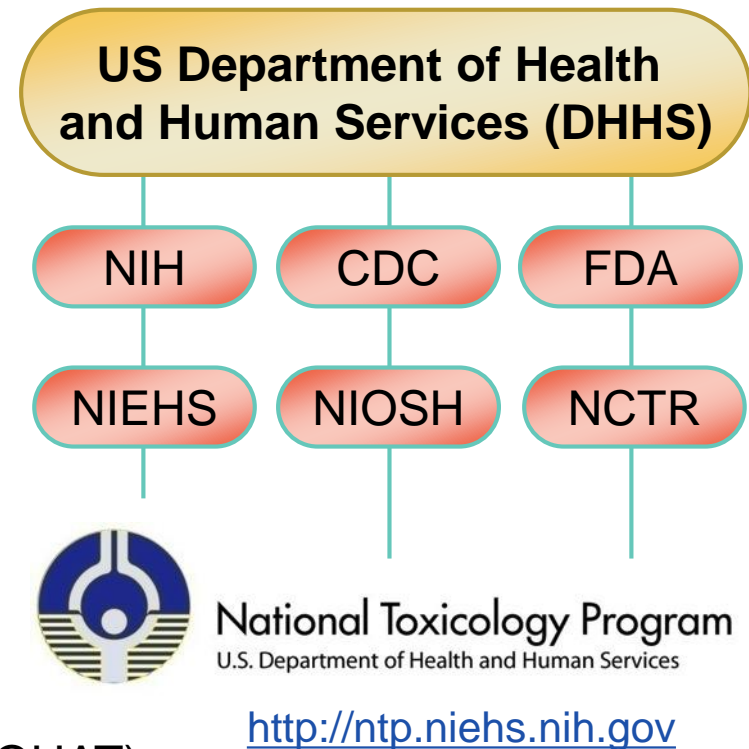
- Established in 1978
- Headquartered at NIEHS

- **Research**

- Thousands of agents evaluated in comprehensive toxicology studies

- **Analysis activities**

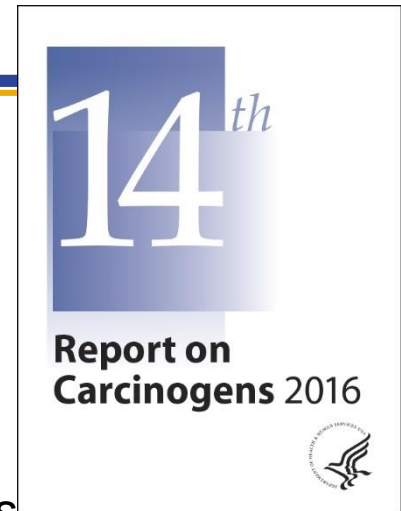
- Office of Report on Carcinogens (ORoC)
- Office of Health Assessment & Translation (OHAT)
- NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM)





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





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



NTP developed criteria for each listing category

Known to be a human carcinogen

- Sufficient evidence of carcinogenicity from studies in humans

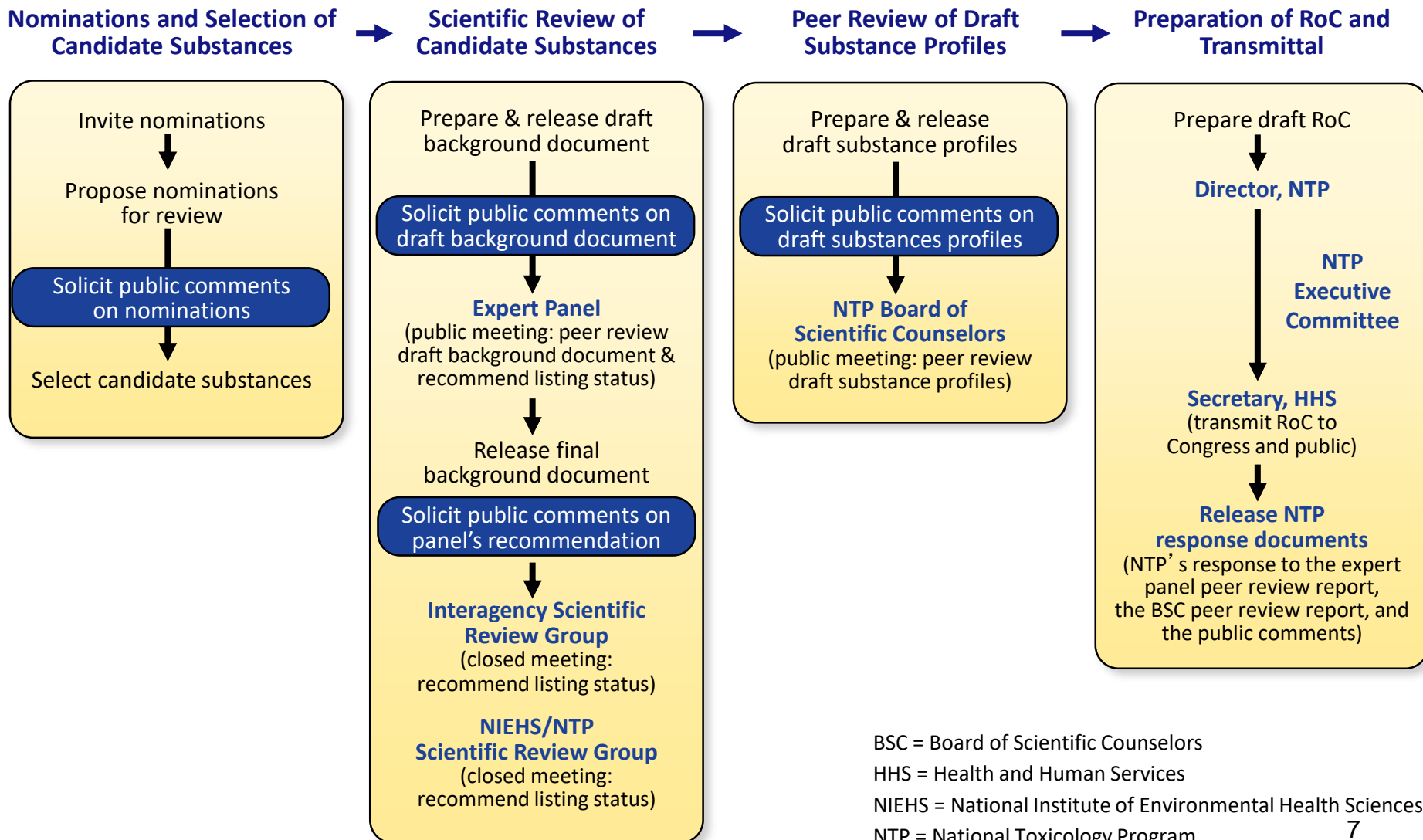
Reasonably anticipated to be a human carcinogen

- 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)



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

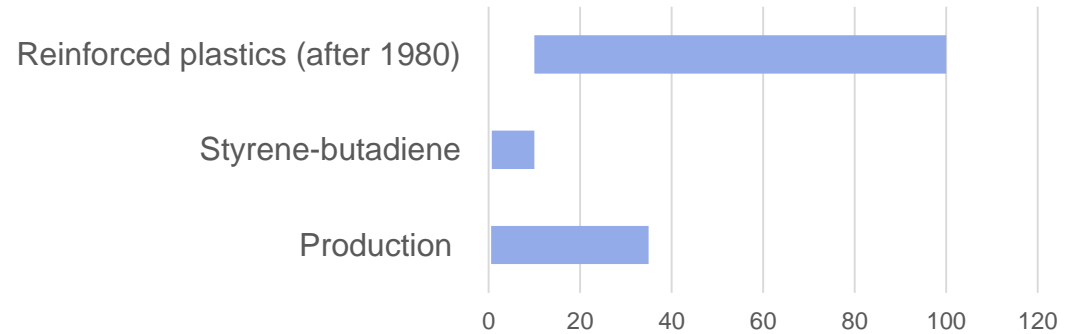
Blood levels
($\mu\text{g/L}$)
8.9 to 83

General public

Low exposure
Parts per billion
(PPB) range

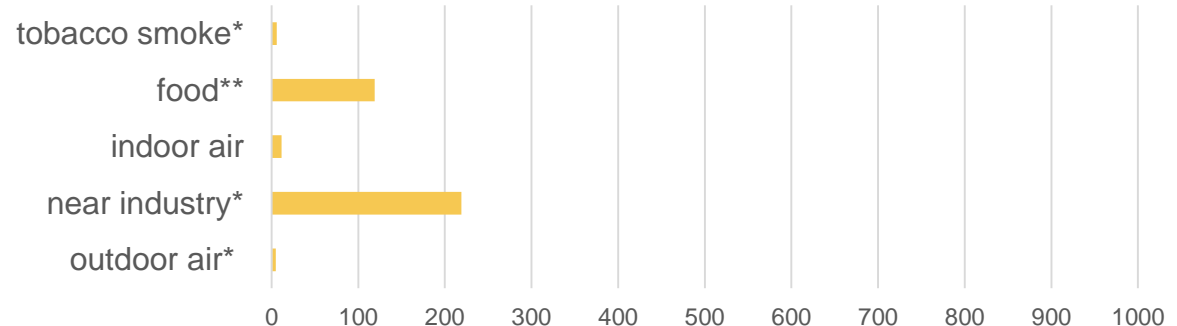
Blood levels
($\mu\text{g/L}$)
0.13 (95
percentile)

Occupational exposure to styrene (PPM)



1 ppm = 1000 ppb

Styrene exposure to general public (PPB)



* lifetime; **most 0.05-119

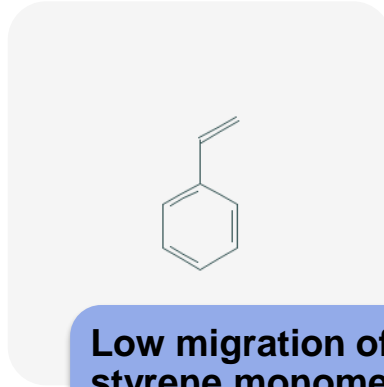


Low exposure to styrene from food in polystyrene containers



Polystyrene (PS)

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



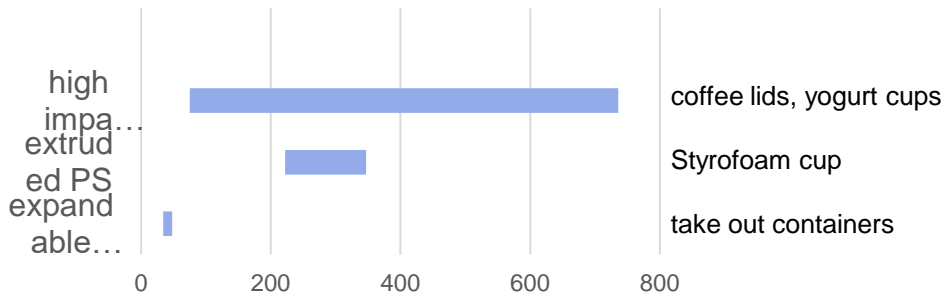
Low migration of styrene monomer

- Food: lipophilicity
- Container: surface to volume ratio
- Conditions: duration, contact, temperature

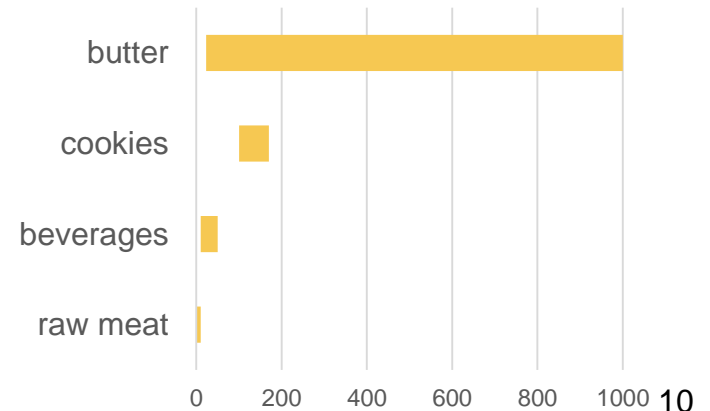


Low levels (ppb) of styrene in food

Styrene levels (mg/kg) in polystyrene containers



Styrene levels ($\mu\text{g}/\text{kg}$) food packaged with PS





Summary

- 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