Written Public Comments Summaries for Draft RoC Monographs for 1-Bromopropane and Cumene

National Institute of Environmental Health Sciences

NTP Peer Review Meeting
March 21-22, 2013

Cumene: Public Comments

- Written public comments: 2 submissions
  - American Chemistry Council
    - Richard A. Becker, PhD, DABT and Jonathan T. Busch
  - Dow Chemical Company
    - James S. Bus, PhD, DABT, ATS

Cumene Public Comments: Scientific Issues

- The draft monograph does not document that a significant number of persons in the United States are exposed.
- Tumor findings in animals may be mediated through modes of action of questionable quantitative and/or qualitative relevance to human cancer outcomes.
  - Male rat specific kidney tumors are mediated through α_{2u}-globulin.
  - Mouse lung tumors are mediated through mouse lung specific metabolism by CYP2F2.
  - Cumene mouse liver tumors are plausibly mediated through a phenobarbital-like liver enzyme induction.
- Cumene and its structural analogues are not genotoxic.
- Studies of structural analogs of cumene are important for understanding cumene's mode of action.
- Postulated genotoxic mode of action for cumene mediated through formation of a genotoxic epoxide metabolite of α-methylstyrene is not highly plausible.

1-Bromopropane (1-BP): Public Comments

- Written public comments: 2 submissions from Albemarle Corporation
  - Carr J. Smith, PhD, DABT
  - Tina D. Craft
- Scientific issues in public comments
  - 1-BP is not a direct acting mutagen.
  - The tumor response observed in NTP mouse and rat inhalation study can be assumed to possess a threshold under which 1-BP exposure would not be expected to be carcinogenic.