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 \( \alpha_{2u} \)-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 \( \alpha \)-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.