

Impacts of Fuels and Fuel Additives

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1990 CAAA Section 211(b) requirements:

- Registration of Fuels and Fuel Additives
- Testing of health effects and exposure

API manages a 211(b) Research Group

Health Effects Testing and Exposure Assessment

- Testing per final negotiated and approved program (1998)
- Specific Protocols Developed by Research Group and Approved by EPA

Health Effects Testing and Exposure Assessment - Objectives

Health Effects

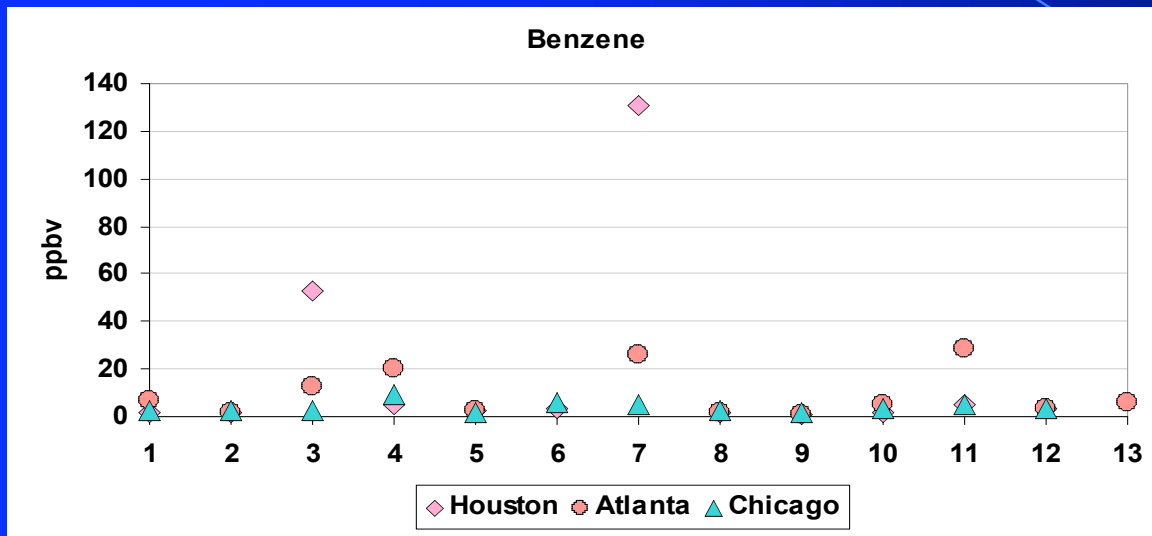
- Assess and compare the toxicity of the evaporative emissions of base gasoline and gasoline containing 6 different oxygenates.
- Develop new pharmacokinetic data on the oxygenates that can be used with existing PK data by the EPA to develop PBPK models.

Health Effects Testing and Exposure Assessment - Objectives

Exposure Assessment

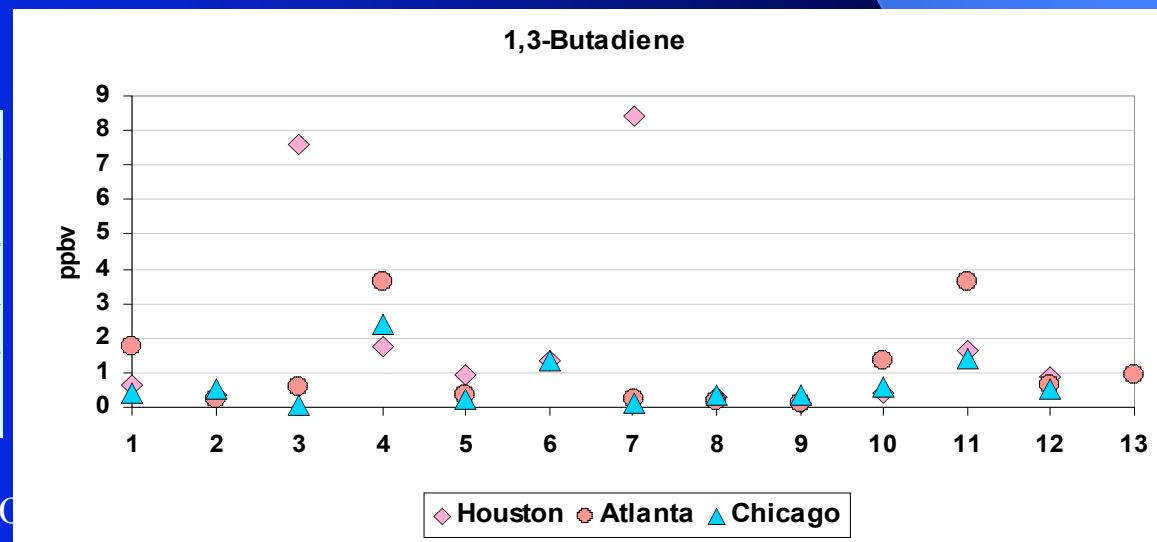
- During both summer and winter, in high-end microenvironments in 3 Cities with different fuel types (Baseline Gasoline, MTBE RFG, EtOH RFG)
 - Measure airborne concentrations of selected automobile emissions
 - Measure several biomarkers in breath samples of exposed subjects

Benzene & 1,3-Butadiene – Preliminary 3 Cities Comparisons



ME	Outdoor
9	Bus Stop
10	Surface Parking
11	Underground Garage
12	Toll Plaza
13	High Emitters

ME	In-cabin	ME	In-cabin/Outdoor
1	Congested Freeway	5	Toll Plaza
2	Urban Canyon	6	Roadway Tunnel
3	Refueling	7	Outdoor Refueling
4	Underground Garage	8	Sidewalk



Timeline and Data Availability

Health Effects

- Toxicity testing - 2000 – 2005
- ADME/PK – 2006 - 2007

Exposure Assessment – 2002 – 2005

Reports submitted to the 211(b) docket

Does not address Alternative Fuels (E85, Methanol, etc)

EPAct 2005 amends CAA Section 211(b) requirements:

- Manufacturers to test health **and environmental** effects
- EPA to study health, air, and water quality effects of various oxygenates and EtOH blendstock by mid-2007

Backup Slides

Health Effects Testing – Materials

Toxicity Studies

- Evaporative vapor condensate (EVC) of baseline gasoline (BG) (i.e., “light ends”)
- EVC of BG containing one of the following oxygenates:
 - 25.5% Methyl Tertiary Butyl Ether (MTBE)
 - 11.6% Ethyl Tertiary Butyl Ether (ETBE)
 - 12.7% Tertiary Amyl Ether(TAME)
 - 12.1% Di-Isopropyl Ether (DIPE)
 - 16.8% Tertiary Butyl Alcohol (TBA)
 - 15.4%% Ethanol (EtOH)

ADME/PK Studies

- DIPE
- TBA
- EtOH

Extensive Health Effects Testing Completed – Specific Toxicity Tests

Baseline Gasoline (BG) and BG with MTBE:

- 90-day subchronic toxicity in rats with additional assessments:
 - Genotoxicity (MN and SCE)
 - Immunotoxicity (PFA)
 - Neurotoxicity (Neuro-behavioral and pathology)
- 2-Generation reproductive toxicity in rats
- Developmental toxicity in rats & mice
- Carcinogenicity in rats

BG with ETBE, TAME, DIPE, TBA, or EtOH:

- 90-day subchronic toxicity in rats with additional assessments:
 - Genotoxicity (MN and SCE)
 - Immunotoxicity (PFA)
 - Neurotoxicity (Neuro-behavioral and pathology)
- 1-Generation reproductive toxicity in rats
- Developmental toxicity in rats
- Carcinogenicity in rats

Study Quality

Methods and Standards

- **Health Effects Testing**
 - US EPA Vehicle Emissions Inhalation Exposure Guideline 79.61, CFR Vol. 59, No. 122, 27 June 1994
 - US EPA OPPTS Health Test Guidelines
 - Good Laboratory Practices
- **Exposure Assessment**
 - US EPA Standard Methods
 - QA Review of Laboratory and Field Studies
 - Specific Protocols Developed by RG and Approved by EPA

Work Product Reviews

- **Health Effects Testing - Reports**
 - 211(b) RG Toxicology/Technical Experts
 - External Expert Peer Review
 - EPA Scientists
- **Exposure Assessment – Protocols and Reports**
 - 211(b) RG Technical Experts
 - External Expert Peer Review
 - EPA Scientists