

ASTSWMO State Symposium on Fuel Oxygenates:  
Analysis, Assessment, and Remediation  
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# Fuel Oxygenates: How Do Their Health Effects Compare?



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# Outline

- **Methyl tert butyl ether (MTBE)**
- **Ethanol (EtOH)**
- **Other ethers/alcohols:**
  - **Ethyl tert butyl ether (ETBE)**
  - **Tert amyl methyl ether (TAME)**
  - **Di-isopropyl ether (DIPE)**
  - **Tert butanol (TBA)**
- **Comparisons**
- **Future Directions**

# MTBE

- **More inhalation than ingestion data**
- **Non-cancer RfC for chronic inhalation**
- **Several health reviews/assessments:**  
mixed conclusions on cancer potential and acute inhalation symptom reports
- **TSCA Proposed Rulemaking**
- **EPA IRIS file under review**

# Primary MTBE Effects in Laboratory Animals

| Route      | Duration           |  |
|------------|--------------------|--|
|            | acute - subchronic | chronic  |
| inhalation | neurobehavioral    | kidney / liver;<br>testicular & kidney tumors<br>(male rats);<br>liver tumors (mice) |
| oral       | kidney / liver     | testicular tumors (male rats)<br>lymphoma / leukemia<br>(female rats)                |

# Inhalation Reference Concentration (RfC)

An estimate (with uncertainty spanning about an order of magnitude) of a daily lifetime exposure to the human population (including sensitive subgroups) **likely to be without appreciable risk** of deleterious non-cancerous effects.

# Reference Concentration (RfC) for MTBE

- **Critical Effects (in lab animals):**
  - Increased liver & kidney weights
  - Increased severity of spontaneous kidney lesions
  - Swelling around eyes
  - Prostration
- **Current RfC = 3 mg/m<sup>3</sup>**

# **MTBE/Oxyfuel Health Assessments and Reviews**

- **EPA Office of Research and Development (1993, 1994)**
- **Health Effects Institute (1996)**
- **National Research Council (1996)**
- **OSTP/NSTC Interagency Assessment (1996, 1997)**
- **EPA Office of Water Drinking Water Advisory (1997)**
- **World Health Organization (1998)**
- **International Agency for Research on Cancer (1999)**
- **National Toxicology Program / NIEHS (2000)**
- **Calif. Prop 65 (1998); other state-level evaluations**

# Cancer Issues

- Liver tumors (mice):  
transient proliferation + promoter?
- Kidney tumors (male rats):  
alpha-2u-globulin?
- Testicular tumors (two rat strains):  
historical controls? malignant?
- Lymphoma/leukemia (female rats):  
pathology criteria?

# Toxic Substances Control Act (TSCA) Advance Notice of Proposed Rulemaking (ANPR)

- **Blue Ribbon Panel (1999):** MTBE use should be reduced substantially, if not phased out completely
- **TSCA Sect. 6 ANPR (2000):** may propose to ban or limit use of MTBE in gasoline due to taste/odor costs; alternative is ethanol
- **TSCA Sect. 6 NPR (2002 ?):** cost-benefit analysis

# EPA Integrated Risk Information System (IRIS) File for MTBE

- Update inhalation reference conc. (RfC)
- New oral reference dose (RfD)
- New cancer assessment
- Uses pharmacokinetic (PK) modeling
- External Review Draft, Fall 2002 ?
- External peer review and public comment
- Final on IRIS: 2002-2003 ?

# Ethanol

- More ingestion than inhalation data
- Developmental toxicant: Am. Med. Assoc. has not identified “safe level” for pregnant women
- Class 1 carcinogen (IARC): based on human data for *alcoholic beverage* consumption; no quantitative potency estimate
- EPA IRIS file in preparation
- Calif. Environmental Policy Council Report

# Primary Effects of Ethanol

| Route      | Duration                          |   |
|------------|-----------------------------------|---|
|            | acute - subchronic                | chronic   |
| inhalation | neurobehavioral                   | —   |
| oral       | neurobehavioral;<br>developmental | GI tract, liver, other cancers<br>(alcoholic beverages);<br>developmental;<br>immunological; reproductive |

# California Environmental Policy Council Report (1999)

- “...unlikely that ethanol will contaminate groundwater to any degree approaching a public health concern.”
- “...no substantial differences in the public-health impacts of the different nonMTBE [ethanol or no oxygenate] fuel formulations considered....”
- However:
  - Conclusions for California specifically
  - Need full life-cycle evaluation

# ETBE, TAME, DIPE, TBA

- Qualitative similarities to MTBE:
  - kidneys/liver most sensitive target organs
  - pharmacokinetics (except no PK data for DIPE)
- TBA (NTP drinking water study):
  - male/female rat nephropathy
  - male/female mouse bladder hyperplasia
  - tumors: male rat kidney, mouse thyroid
- No quantitative cancer potency or non-cancer reference values to date
- Clean Air Act Sect. 211(b)-mandated testing of gasoline-oxygenate evaporative emissions to be completed in 2004

# Health Effects Comparison Summary

|             | Key Effects              | PK | EPA RfC                               | EPA RfD        | EPA Cancer Value | Other Assmts |
|-------------|--------------------------|----|---------------------------------------|----------------|------------------|--------------|
| <b>MTBE</b> | Liver, Kidney & Tumors   | ✓  | 3 mg/m <sup>3</sup><br>(under review) | In Preparation |                  | Several      |
| <b>EtOH</b> | Developmental & Cancer * | ✓  | In Preparation                        |                |                  | IARC; Calif. |
| <b>ETBE</b> | Liver & Kidney           | ✓  |                                       |                |                  |              |
| <b>TAME</b> | Liver & Kidney           | ✓  |                                       |                |                  |              |
| <b>DIPE</b> | Liver & Kidney           |    |                                       |                |                  |              |
| <b>TBA</b>  | Kidney & Tumors          | ✓  |                                       |                |                  |              |

\*Based on human data for alcoholic beverage consumption

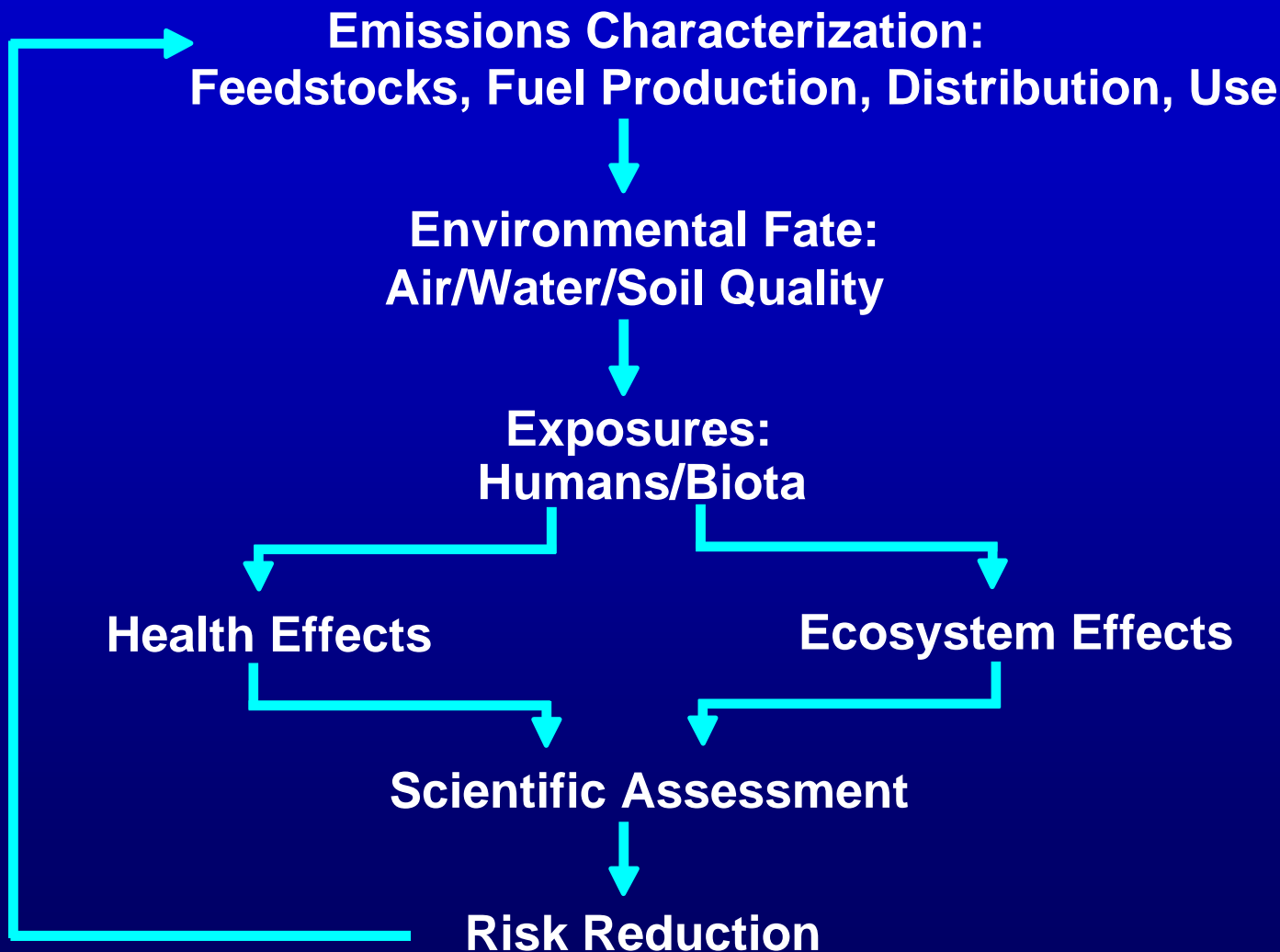
# Odor/Taste Characteristics

- **CAVEATS:**
  - data are limited
  - taste/odor are complex multi-dimensional phenomena
  - oxygenates have not been compared directly
- ETBE, TAME odor/taste thresholds similar to (possibly lower than) MTBE
- Odor threshold for Ethanol possibly orders of magnitude higher than ethers
- Odor threshold for TBA similar to (possibly lower than) Ethanol

# So, Which Oxygenate is Best?

- Health effects inconclusive at present; unable to make quantitative comparisons
- Ethanol odor may be better in water, but what about air around production plants?
- Need multi-media, life-cycle perspective to weigh trade-offs, e.g.:
  - Emissions/releases across entire life cycle
  - Secondary products (changes in fuel formulation; transport & transformation)

# Schematic for Evaluation of Multi-media, Life-cycle Environmental / Health Impacts



# Future Directions

- EPA Screening Life-Cycle Assessment of RFG with: MTBE / Ethanol / No Oxygenate (in preparation)
- Need “*comprehensive evaluation of multi-media, life-cycle environmental impacts*” of different fuels (National Water Research Institute Workshop, 2002)
- Energy Policy Act of 2002 (pending)

# Draft Energy Policy Act of 2002

## Sect. 835 “Public Health and Environmental Impacts of Fuels and Fuel Additives”

- Expansion of 211(b) to include testing for environmental as well as health effects
- Study on the “effects on public health, air quality, and water resources” and on feasibility as MTBE-substitutes of:
  - ETBE
  - TAME
  - DIPE
  - TBA
  - Ethanol
  - Iso-octane
  - Alkylates
  - Other ethers/alcohols?