

Report to Congress on Public Health, Air Quality, and Water Resource Impacts of Fuel Additive Substitutes for MTBE



EPA

United States
Environmental Protection
Agency

Report to Congress on Public Health, Air Quality, and Water Resource Impacts of Fuel Additive Substitutes for MTBE

Office of Research and Development
Office of Transportation and Air Quality
U.S. Environmental Protection Agency

Report to Congress on Public Health, Air Quality, and Water Resource Impacts of Fuel Additive Substitutes for MTBE

Table of Contents

Executive Summary

- I.** Introduction
- II.** Potential Public Health Effects of MTBE, Its Substitutes and Related Emissions Products
- III.** Commercial Feasibility of Ethanol and Other Additives
- IV.** Potential Air Quality Effects
- V.** Potential Water Quality Effects
- VI.** Potential Approach for Further Analyses: Comprehensive Environmental Assessment of Fuel Additive Substitute Options
- VII.** Catalog of Scientific Activities Related to MTBE and Its Substitutes and Information Gaps

Appendix A: Summary of the Impacts of Gasoline Regulation on Fuel Composition

Appendix B: Phase Partitioning of Compounds from Gasoline

Executive Summary

In the Energy Policy Act of 2005 (EPAAct), Congress directed the Administrator of the Environmental Protection Agency to conduct a study on the effects on public health, air quality and water resources of the increased use of replacements for the fuel additive methyl tertiary butyl ether (MTBE), as well as the feasibility of such replacements. Specifically, Congress directed attention to ethyl tertiary butyl ether (ETBE), tertiary amyl methyl ether (TAME), diisopropyl ether (DIPE), tertiary butanol (TBA), other ethers and heavy alcohols, ethanol, isooctane, and alkylates. EPAAct also required other actions that significantly altered the commercial fuels market and the feasibility for broad commercial use of many of the potential replacement additives, including removal of the oxygenate standard in the federal reformulated gasoline program and establishment of the national renewable fuels standard program. These actions ultimately affected the priority focus of this report toward ethanol, which currently dominates the gasoline market as a replacement for the use of MTBE. This report summarizes scientific information regarding the health effects, air quality impacts, and water quality impacts of ethanol and the other additives but does not attempt to weigh their relative risks and benefits. The focus of the report is limited to the feasibility and impacts of MTBE replacements once the additive has been blended with gasoline and distributed to service stations.

Consistent with Congressional intent, the report is not meant to address the larger issues surrounding the increased use of alternative or renewable fuels. However, due to legislative mandates for renewable fuels and the primacy of ethanol in the marketplace, particular attention is given to the potential impacts of its use as a fuel additive.

Health Effects

This report highlights the adverse health effects that have been linked to MTBE and its alternatives. All of these compounds have the potential to cause adverse health effects, depending on the nature and degree of exposure. In general, humans can be exposed to fuel additives by way of evaporative or exhaust emissions (leading to potential inhalation exposure) or by spills or leaking tanks (leading to potential dermal and ingestion exposure). However, characterization of exposure levels was beyond the scope of this report. For this reason and because MTBE and several other fuel additive compounds are currently undergoing health effects assessment under EPA's Integrated Risk Information Service (IRIS) program, this report does not attempt to estimate quantitative risks or hazards of these chemicals. Section 1505 specifies that health effects include effects on "children, pregnant women, minority or low-income communities, and other sensitive populations." Where possible, such information is included in this report, but for many fuel additive compounds detailed information for sensitive human populations is lacking, although extrapolations from animal data in IRIS assessments may take sensitive populations into account.

In addition to the potential direct effects of the fuel additives themselves, use of these fuel additives can affect (either positively or negatively) environmental levels of other pollutants such as particulates, ozone, benzene, formaldehyde, and acetaldehyde. This report presents brief summaries of the adverse health effects associated with such secondary pollutants as well.

EPA is currently involved in numerous scientific activities related to fuels and fuel additives. A health effects testing program for gasoline and mixtures of gasoline with six respective oxygenates (MTBE, ethanol, ETBE, DIPE, TAME and TBA), required pursuant to Section 211(b) of the Clean Air Act, is currently being conducted by a consortium of fuel and fuel additive manufacturers. This testing program is administered by the American Petroleum Institute with oversight by EPA. EPA will use the results of this testing program to help make better informed risk assessment and risk management decisions regarding the future use of fuel oxygenate compounds.

Air Quality

For criteria air pollutants and their precursors, increased use of ethanol at 10% volume (E10) can lead to: an increase in VOC emissions due to increased fuel evaporation and permeation (even though exhaust VOC emissions decrease slightly); a decrease in CO emissions, and an increase in NOx emissions (primarily from nonroad engines). Further, the decrease in the aromatic content of E10 fuel is likely to lead to a decrease in secondary PM formation. Ambient ozone and PM levels are of particular concern for achieving and maintaining attainment with National Ambient Air Quality Standards (NAAQS). For air toxics, present analyses suggest that the increase in E10 usage will decrease emissions of benzene, 1,3-butadiene, and possibly formaldehyde and increase emissions of others such as acetaldehyde. Other air toxics have not been examined in this report. Potential public health impacts resulting from the increase in acetaldehyde depend upon exposure levels, which are not known at this time, and a fuller understanding of acetaldehyde toxicity, which is currently being reviewed under the IRIS program. Given that both formaldehyde and acetaldehyde are also formed through atmospheric reactions, a more complete analysis of potential exposures to these pollutants would require an assessment of those atmospheric reactions and is beyond the scope of this report.

Further analyses of emission and evaporative impacts due to increased ethanol usage and resulting impacts on air quality are being conducted to accompany the second renewable fuels standard (RFS2) required by EISA. These standards mandate the use of 36 billion gallons of ethanol by 2022 and are anticipated to be proposed early in 2009. EPA is also currently conducting tests on the effect of ethanol blends on exhaust and evaporative emissions from newer model vehicles and nonroad engines.

Water Quality

The potential for exposure to fuel components and/or additives can occur when underground fuel storage tanks leak fuel into ground water that is used for drinking water supplies or when spills occur that contaminate surface drinking water supplies. MTBE was banned or phased out in several states due to its appearance in drinking water supplies and exceedance of odor/taste thresholds. Unlike MTBE, which itself is a contaminant in water supplies, ethanol biodegrades quickly and is not necessarily the pollutant of greatest concern. Instead, its high biodegradability can cause the plume of BTEX (benzene, toluene, ethylbenzene and xylenes) compounds in fuel to extend farther (by as much as 70%) and persist longer in ground water, thereby increasing potential exposures to these compounds.

EPA is beginning to assess the impacts of ethanol on storage tanks and associated infrastructure. First, material incompatibility of existing underground storage tanks systems with ethanol-fuel blends can result in equipment failure and releases to ground water. Second, storage of denatured ethanol in aboveground storage tanks and steel piping can lead to stress corrosion cracking. Further, ethanol-blended fuels may have an impact on the existing leak detection systems that are designed for petroleum hydrocarbons. Although some of these issues are beyond the scope of this report, these data gaps need to be addressed to prevent impacts to ground water resources.

EPA is presently exploring the possibility of collaborative field studies with states to examine the fate and transport of ethanol releases from underground storage tanks and their potential impact on water supply wells. This work will assess the influence of water supply pumping rates on the movement of the contaminated plume and allow for the development of a tool for remediation site managers and water utilities that allows for integration of contaminant source modeling and water supply pumping rates to determine the rate and extent of remediation needed to protect existing and future water supplies.

An additional potential hazard from spills from fuels containing ethanol is currently being evaluated. Laboratory and field studies have found biodegradation of ethanol can produce concentrations of methane in excess of the water solubility of methane (i.e., more methane was produced than could be dissolved by the available water). This methane could bubble out of the ground water and enter the soil gas (gases that occur in the small spaces between particles of soil) at potentially explosive concentrations, although it is not possible to quantify the risk at this time. EPA is developing modeling software for the assessment of fuels of varying composition on ground water, with simulation of methane production being one component of this work.

Further Analyses

In order to truly weigh the benefits and trade-offs between various fuels and fuel additives, a comprehensive multimedia analysis of the environmental impacts is needed. Due to the extensive qualitative and/or quantitative analyses this would require, which are beyond the scope and timeframe of this report, we suggest other potential methods for obtaining this information. Section 204 of EISA 2007 requires that EPA produce a report every three years on the multimedia impacts of increased renewable fuel production and use, which will enhance our understanding of the impacts of ethanol and other renewable fuels and fuel additives. In this regard, Comprehensive Environmental Assessment (CEA) can be used to compare the advantages and disadvantages of various fuels and fuel additives. CEA combines the risk assessment paradigm with a product life cycle framework to evaluate multimedia environmental impacts, including both ecological and human health effects, and uses collective expert judgment methods to deal with limitations in empirical data, thus providing a qualitative comparison between options. Although not necessarily quantitative in nature, this methodology can nevertheless inform decision makers as to future policy direction.

I. INTRODUCTION

This Report to Congress was prepared in response to Section 1505 of the 2005 Energy Policy Act (EPAAct), which directs the Administrator to:

(i) conduct a study on the effects on public health (including the effects on children, pregnant women, minority or low-income communities, and other sensitive populations), air quality, and water resources of increased use of, and the feasibility of using as substitutes for methyl tertiary butyl ether in gasoline—

(I) ethyl tertiary butyl ether;

(II) tertiary amyl methyl ether;

(III) di-isopropyl ether;

(IV) tertiary butyl alcohol;

(V) other ethers and heavy alcohols, as determined by then Administrator;

(VI) ethanol;

(VII) iso-octane; and

(VIII) alkylates....

Methyl tertiary butyl ether (MTBE) serves as an impetus as well as a point of reference for this report. MTBE is an ether-based gasoline additive that has been used in the U.S. since the late 1970s. It improves octane, provides other positive blending properties and also contains oxygen, which has been shown to reduce certain harmful emissions from vehicles. MTBE use expanded greatly in the mid-1990s as a result of the Clean Air Act Amendments mandate that clean burning reformulated gasoline (RFG) be used in cities with the worst air pollution. (See Appendix A for more details on how the RFG requirement affected fuel composition.) RFG accounts for about 30% of the total US gasoline pool.

Under the 1990 amendments, every gallon of RFG was required to contain a minimum of 2 weight percent oxygen. While there are a number of oxygenates that could be used to satisfy the requirement, a significant portion of the RFG pool contained MTBE. At the height of its use, MTBE was used in about 60 percent of the RFG gasoline pool. Ethanol, another oxygenate, was used in the remaining RFG gasoline pool. With passage of the Energy Policy Act of 2005 (EPAAct), Congress removed the statutory oxygenate requirement from the RFG program. EPA made corresponding changes to its regulations in the spring of 2006. Since that time, MTBE has basically been removed from use in the U.S. gasoline market.

While MTBE helps to reduce some emissions from vehicles, its chemical properties cause it to persist in ground water if it is spilled or leaked into the environment. As a result of numerous fuel leaks, primarily from underground gasoline storage tanks, MTBE contaminated drinking water supplies in several areas of the country. The threat it posed to water resources was found to be unacceptable and led to a call to ban or limit its use (Blue Ribbon Panel, 1999) at both state and national levels and, ultimately, Congressional removal in EPAAct 2005 of the statutory oxygenate requirement for RFG.

This report takes a first step in examining some of the possible public health, air quality, and water resource impacts related to other gasoline fuel replacement additives. It is important to emphasize that this document does not present a set of final conclusions. Although work investigating MTBE and other fuel additives has been underway at EPA and in other organizations over the past several years, a comprehensive evaluation of the comparative advantages and disadvantages of substitutes for MTBE remains to be undertaken. Therefore, definitive judgments regarding the relative risks and/or benefits of various fuel additives cannot be offered at present. Nevertheless, a substantial body of information, including work carried out by EPA, will be summarized here, along with a suggested approach for conducting a comprehensive environmental assessment of fuel additive substitute options.

In looking at the air and water quality effects associated with the use of MTBE and its substitutes, this report is focused strictly on direct effects from usage as an additive (i.e., vehicle emissions and associated air quality impacts and leaks from underground storage tanks), not the effects associated with additive production (e.g., air quality impacts from refineries and water quality impacts from increased corn production) or other upstream effects

This document is organized in seven chapters comprising (I) Introduction, (II) Potential Public Health Effects of MTBE, Its Substitutes and Related Emissions Products, (III) Commercial Feasibility of Ethanol and Other Additives, (IV) Potential Air Quality Effects, (V) Potential Water Quality Effects, (VI) Potential Approach for Further Analyses: Comprehensive Environmental Assessment of Fuel Additive Substitute Options, and (VII) Catalog of Scientific Activities Related to MTBE and Its Substitutes and Information Gaps.

Chapter II, Potential Public Health Effects, first summarizes available information on the health effects of MTBE as a point of reference for other fuel additives and blending components. In addition to a section on MTBE, Chapter II includes sections on ethanol, ethyl tertiary butyl ether (ETBE), tertiary amyl methyl ether (TAME), di-isopropyl ether (DIPE), tertiary butanol (also referred to as tertiary butyl alcohol) (TBA), and alkylates/iso-octane, as well as some mention of other alcohols and ethers for which information is quite limited. Moreover, Chapter II provides brief summaries on the health effects of various emission products associated with gasoline and the primary additives listed here. These products include aldehydes, peroxyacetyl nitrate (PAN), particulate matter, ozone, and other substances that could be produced through chemical transformation processes in air or water.

Chapter III, Commercial Feasibility of Ethanol and Other Additives, discusses current indications on which additives and blending components are thought most likely to be present in the U.S. marketplace. In particular, with the removal of the oxygen requirement and passage of the Renewable Fuels Standard, ethanol currently dominates the market as a major component of the gasoline pool. We provide information on where it is currently made, and the current prevalence of use across the U.S. Chapter III also discusses other additives such as ETBE, TAME, DIPE, and TBA. Since these historically constitute a small portion of the gasoline additive market and given their historical use as well as currently passed renewable fuel volume requirements in the Energy Security and Independence Act of 2007 (EISA), it does not currently appear that these substances will attain commercially significant volumes. As the renewable

fuels market continues to expand and second generation biofuels develop, additional analysis of the fuels and additive market will be necessary.

Chapter IV, Potential Air Quality Effects, summarizes results of analyses on emissions and associated air quality effects related to fuel additives and blending components identified in Chapter II. Information is provided on projected changes in air pollutant emissions as a result of increased use of ethanol and the results of an analysis that project the effect of such emissions on air quality.

Chapter V, Potential Water Quality Effects, covers subsurface water effects identified with various fuel additives and blending components. This section focuses on potential ground water impacts as a result of spills from leaking underground storage tanks. The potential impact of spills into surface water during shipment of fuel grade ethanol (typically E95) is beyond the scope of this report, which focuses on impacts once ethanol has been blended and stored in underground storage tanks at service stations. A qualitative discussion of surface water impacts from spills of ethanol may be included in the Notice of Proposed Rulemaking for the upcoming Renewable Fuels Standard that is required by EISA.

Chapter VI, Potential Approach for Further Analyses: Comprehensive Environmental Assessment of Fuel Additive Substitute Options, describes an approach for evaluating environmental trade-offs among fuel additive substitute options in a systematic manner that incorporates a product life cycle framework with the risk assessment paradigm and uses expert judgment methods to take advantage of the collective insights of an array of technical experts and stakeholders.

Chapter VII, Catalog of Scientific Activities Related to MTBE and Its Substitutes and Information Gaps, lists recent and current projects that EPA and other organizations have been carrying out and highlights some of the more salient questions about fuel additives and blendstocks that remain to be addressed if more definitive judgments are to be reached about the comparative risks and benefits of specific fuel additives and blendstocks.

References

- Blue Ribbon Panel. (1999) Achieving clean air and clean water: the report of the Blue Ribbon Panel on oxygenates in gasoline. Washington, DC: U.S. Environmental Protection Agency, Office of Transportation and Air Quality; report no. EPA420-R-99-021. Available: <http://www.epa.gov/OMS/consumer/fuels/oxypanel/blueribb.htm> [2000, December 5].
- U. S. Environmental Protection Agency. (2007) Regulation of fuels and fuel additives: renewable fuel standard program. Final rule. F. R. 72 (May 1): 23899-24014.

II. POTENTIAL PUBLIC HEALTH EFFECTS OF MTBE, ITS SUBSTITUTES AND RELATED EMISSION PRODUCTS

This chapter highlights information on the health effects of MTBE as a point of reference for other fuel additives. In addition, this chapter includes sections on ethanol, ethyl tertiary butyl ether (ETBE), tertiary amyl methyl ether (TAME), di-isopropyl ether (DIPE), tertiary butanol (TBA), and alkylates/iso-octane, as well as BTEX compounds present in gasoline. Furthermore, this chapter provides brief summaries on the health effects of several secondary pollutants associated with the primary additives listed here. These secondary pollutants include ozone, particulate matter, formaldehyde, acetaldehyde, and peroxyacetyl nitrate (PAN). Where possible, health effects information has been taken from existing EPA documents, including the Integrated Risk Information System (IRIS) files for MTBE, iso-octane (2,2,4-trimethylpentane), benzene, toluene, ethylbenzene, xylenes, formaldehyde, and acetaldehyde, as well as *Air Quality Criteria Documents* for ozone and particulate matter. Information on the status of ongoing IRIS assessments is available at <http://cfpub.epa.gov/ncea/iristrac/index.cfm>. The Regulatory Impact Analysis for the Mobile Source Air Toxics rulemaking also presents brief summaries of these pollutants as well as other mobile source pollutants that may be affected to a lesser degree by the replacement of MTBE from vehicle fuels (U.S. EPA, 2007a).

Note that this chapter does not provide an exhaustive review of the literature but focuses on assessments by governmental and other agencies that have undergone peer review and public comment. Readers should look to existing EPA assessments (such as those supporting the IRIS database and Integrated Science Assessments for criteria air pollutants) for more extensive reviews of the scientific literature. Moreover, not all of the health effects noted in this chapter are necessarily associated with exposure levels commonly seen (or anticipated) under environmental conditions. Because this report does not attempt to estimate ambient concentrations or exposures, the reader should not assume that all the effects described here are actually occurring in the U.S. population; however, some effects may be. Such an evaluation is beyond the scope of this report. The Regulatory Impact Analysis for the Mobile Source Air Toxics rulemaking contains a summary of this type of information (U.S. EPA, 2007b).

A program of inhalation toxicity studies of several oxygenate-gasoline mixtures was established under the Fuel/Fuel Additive (F/FA) Rule (CFR, 1994) under the authority of Section 211(b) of the Clean Air Act. The fuels under investigation are baseline gasoline, i.e., gasoline without added oxygenates, MTBE-gasoline, ETBE-gasoline, TAME-gasoline, DIPE-gasoline, ethanol-gasoline, and TBA-gasoline. A summary of the requirements and results of these studies to date may be found in Chapter VII.

Figure II-1 shows the chemical structure for several chemicals that are or could be of relevance as additives or gasoline blending components. The chemicals containing oxygen are ethers or alcohols and have been or could be used as oxygenates in gasoline. The one chemical shown in Figure II-1 that is not an oxygenate is iso-octane, which is an example of an alkylate, and is an important blending component of gasoline. Alkylates, along with other compounds such as aromatics and other high-octane hydrocarbon components including other branched chained paraffins, may be added to gasoline to offset changes in fuel volume that accompany changes in the percentage volume of different oxygenates. To illustrate, if the percentage

volume of MTBE in gasoline is reduced from 11% to 0%, the loss of volume can be made up by adding more iso-octane. Thus, iso-octane or other alkylate usage may be coupled with changes in oxygenate usage.

FIGURE II-1. Chemical structure of several chemicals of interest as oxygenates or blendstock components

<p>a. Methyl <i>tertiary</i> Butyl ether (MTBE)</p> $\begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_3-\text{O}-\text{C}-\text{CH}_3 \\ \\ \text{CH}_3 \end{array}$	<p>b. Ethanol</p> $\text{CH}_3-\text{CH}_2-\text{OH}$
<p>c. Ethyl <i>tertiary</i> Butyl ether (ETBE)</p> $\begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_3-\text{CH}_2-\text{O}-\text{C}-\text{CH}_3 \\ \\ \text{CH}_3 \end{array}$	<p>d. <i>tertiary</i> Amyl methyl ether (TAME)</p> $\begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_3-\text{CH}_2-\text{C}-\text{CH}_3 \\ \\ \text{CH}_3 \end{array}$
<p>e. Diisopropyl ether (DIPE)</p> $\begin{array}{c} \text{CH}_3 \qquad \qquad \text{CH}_3 \\ \diagdown \quad \diagup \quad \diagdown \quad \diagup \\ \text{CH}-\text{O}-\text{CH} \\ \diagup \quad \diagdown \quad \diagup \quad \diagdown \\ \text{CH}_3 \qquad \qquad \text{CH}_3 \end{array}$	<p>f. <i>tertiary</i> Butyl alcohol (TBA)</p> $\begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_3-\text{C}-\text{CH}_3 \\ \\ \text{OH} \end{array}$
<p>g. Iso-octane or 2,2,4-Trimethylpentane</p> $\begin{array}{c} \text{CH}_3 \qquad \qquad \text{CH}_3 \\ \qquad \qquad \diagup \quad \diagdown \\ \text{CH}_3-\text{C}-\text{CH}_2-\text{CH} \\ \qquad \qquad \diagdown \quad \diagup \\ \text{CH}_3 \qquad \qquad \text{CH}_3 \end{array}$	<p>h. Propanol</p> $\text{CH}_3-\text{CH}_2-\text{CH}_2-\text{OH}$
<p>i. Butanol</p> $\text{CH}_3-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{OH}$	<p>j. <i>tertiary</i> Amyl alcohol (TAA)</p> $\begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_3-\text{CH}_2-\text{C}-\text{OH} \\ \\ \text{CH}_3 \end{array}$
<p>k. <i>tertiary</i> Amyl ethyl ether (TAAE)</p> $\begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_2 \\ \\ \text{O} \\ \\ \text{CH}_3-\text{CH}_2-\text{C}-\text{CH}_3 \\ \\ \text{CH}_3 \end{array}$	

A. MTBE

In general, the health effects database for MTBE is more complete than for most other fuel additives, but it has limitations, particularly the lack of epidemiological studies of the long-term effects of MTBE in humans. Also, the majority of animal studies have focused on the inhalation route of exposure, although extrapolation from inhalation to oral exposure may be feasible for at least some endpoints by using pharmacokinetic modeling. Route-to-route extrapolation is being evaluated as part of the current update of the IRIS file for MTBE.

When MTBE use significantly expanded in the United States with the initiation of the 1992 winter oxygenated fuels program and the 1995 reformulated gasoline program, public health attention was primarily focused on symptom reports (e.g., eye and nose irritation, headache) associated with acute exposures such as those that occur during refueling or while near exhaust emissions (U.S. EPA, 1993a, 1994). In response to these concerns, several assessments were undertaken by EPA and other organizations (e.g., U.S. EPA, 1993a, 1994; Interagency Oxygenated Fuels Assessment Steering Committee, 1996, 1997; Health Effects Institute, 1996; National Research Council, 1996; Blue Ribbon Panel, 1999). In essence, these assessments, which generally were conducted by panels of independent experts, concluded that no imminent public health threat was posed by inhalation of MTBE, but the possibility of effects in sensitive individuals or from longer term exposure could not be ruled out based on the available evidence. Subsequent efforts to identify and evaluate self-described MTBE-sensitive individuals (e.g., Fiedler et al., 2000; Hong et al., 2001) have provided some support for the possibility of biological differences among the general population in sensitivity to MTBE, but results are equivocal.

During the mid- to late-1990s attention was drawn to the contamination of water resources by MTBE in gasoline leaking from underground storage tanks (U.S. EPA, 1998a). EPA's Drinking Water Advisory on MTBE (U.S. EPA 1997) analyzed the cancer and non-cancer data that was available on MBTE at the time, but the primary outcome of this action was to provide a consumer advisory level for MTBE based on taste and odor. Studies under controlled conditions indicated that some individuals can detect the taste of MTBE in water at concentrations as low as around 2 µg/L (e.g., Dale et al., 1997, as cited in EPA, 1997), although group mean average detection levels are of course higher. Based on data from several studies, the 1997 EPA Advisory recommended that levels of contamination should not be higher than 20 to 40 µg/L to protect consumer acceptance of the water resource and indicated that such levels would also provide a large "margin of exposure (safety)" from toxic effects¹.

¹ The EPA Advisory used a risk characterization method called "Margin of Exposure (or safety)" which is different from traditional slope factors and reference doses (RfDs) as estimates of response to defined exposures. The "margin" is how far the environmental exposure of interest is from the lower end of the exposures at which animals or humans have shown some toxicity effect. The use of the margin of exposure approach is helpful in the following ways: (1) It allows for comparison of exposures associated with carcinogenic potential to those associated with non-cancer health effects; (2) It provides the risk manager with a quick check to decide if the margin of exposure (safety) appears to be adequate even when mathematical extrapolation of data from high to low dose cannot be done; and (3) It gives a better understanding of the degree of risk associated with extrapolation of exposure data from animal studies to humans. For example, given the limited number of animals that usually can be used in experiments, they, at best, would detect a one in ten response (1×10^{-1}). A common procedure for carcinogens is to mathematically extrapolate from the exposure levels of animal tests to estimate risk at lower, environmental exposure levels. If the

Since then, the State of California established a secondary maximum contaminant level (MCL) of 5 µg/L (to address taste and odor concerns) in 1999 and a primary MCL of 13 µg/L (for protection of health) in 2000 (CDHS, 2006). Note that the California health-based MCL is higher (less stringent) than the secondary MCL. While EPA has not developed a Reference Dose for MTBE, in 1996 the Agency for Toxic Substances and Disease Registry (ATSDR) developed ingestion Maximal Risk Levels for MTBE (0.4 mg/kg/day for acute exposures, 0.3 mg/kg/day for intermediate-duration exposures).

EPA has an ongoing effort to update the IRIS file for MTBE, but given that the IRIS assessment is not yet complete, the present summary draws from past assessments and reviews. As noted above, most of the toxicology studies of MTBE have been conducted via inhalation. The existing inhalation reference concentration (RfC)² for MTBE was last updated in 1993 and was based on a chronic (24-month) inhalation study in rats (Chun et al., 1992) that showed increased liver and kidney weights along with increased severity of spontaneous lesions of the kidney in females, increased prostration in females, and swelling around the eyes in both males and females (U.S. EPA, 1993b). These effects were seen at MTBE exposure levels of ~10,900 mg/m³ and higher, with a no-observed-adverse-effect level (NOAEL) of ~1450 mg/m³. An uncertainty factor of 100 (comprising a factor of 10 for sensitive subpopulations, a factor of 3 for extrapolation across species, and a factor of 3 for deficiencies in data reporting), along with adjustment of the NOAEL to a human equivalent concentration, was applied to yield an RfC of 3 mg/m³.

Cancer risks of MTBE have been examined in various reports (e.g., U.S. EPA 1994, 1997; Interagency Oxygenated Fuels Assessment Steering Committee, 1997; National Research Council, 1996; WHO, 1998; California EPA, 1999; IARC, 1999; U.S. DHHS, 2000a). In some cases these assessments have characterized MTBE as a potential human carcinogen (e.g., U.S. EPA, 1994, 1997; Interagency Oxygenated Fuels Assessment Steering Committee, 1997), whereas other assessments concluded that the currently available data did not allow that conclusion (e.g., NRC, 1996; WHO, 1998; IARC, 1999; U.S. DHHS, 2000a). The database for MTBE cancer effects consists of two chronic inhalation studies, one in rats and one in mice (both reported in Bird et al., 1997), and a chronic oral (gavage) study in rats (Belpoggi et al., 1995, 1998). The inhalation studies reported tumors in the kidneys and testes of male rats and in the liver of female mice, while the oral study reported lymphomas and leukemias in female rats and testicular tumors in male rats. The oral study was conducted using olive oil as the medium for administration of MTBE; no study to date has investigated the chronic effects of MTBE in drinking water.

One of the issues that has complicated evaluations of MTBE cancer risks for humans is the relevance of kidney tumors found in male rats. Some evidence implicates alpha-2u-globulin, a protein found only in male rats, as a significant factor in the formation of kidney tumors in

extrapolation is done as a straight line, a risk estimate of 1×10^{-6} generally corresponds to a margin of exposure of 100,000. If the true, but unknown, relationship is downward sloping, not a straight line, the risk at a 100,000 margin of exposure would be less than 1×10^{-6} and might be zero.

² The inhalation reference concentration (RfC) is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily inhalation exposure of the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime.

male rats exposed to MTBE (e.g., Prescott-Matthews et al., 1997). If male rat kidney tumors were to result from exposure to a chemical such as MTBE solely because of the mechanistic role of alpha-2u-globulin, such tumors would not be considered predictive of cancer in humans and would not contribute to the qualitative weight of evidence regarding the human carcinogenicity potential of the chemical (U.S. EPA, 1991a). EPA's position on this issue will be examined in conjunction with the updating of the IRIS file on MTBE. Questions also remain about other (e.g., testicular, hepatic) tumor effects in laboratory rodent studies that have been the subject of post-hoc analysis and differing conclusions (e.g., Goodman et al., 2007; Kissling et al., 2007). These and other issues will be addressed in the updated IRIS file for MTBE.

Attempts to analyze the quantitative carcinogenic potency of MTBE have been limited, perhaps reflecting the mixed qualitative picture. However, the few analyses reported to date do not suggest that MTBE is a potent carcinogen (U.S. EPA, 1994; Interagency Oxygenated Fuels Assessment Steering Committee, 1997).

B. Ethanol

The chemical structure of ethanol (Figure II.1.b) comprises an alcohol group (hydroxyl) attached to an ethyl group, making the molecule small and weakly polar (Wallgren, 1967). It blends well with gasoline, although it is freely miscible with water and insoluble in fats and oils, and it can pass freely through biological membranes because of its small size (Riveros-Rosas, 1997; Wallgren, 1967). Odor and taste thresholds for ethanol in water are >100,000 and ~50,000 µg/L, respectively (Fazzalari, 1978; Amoores and Hautala, 1983), which implies that ethanol is less readily detected than many other chemicals, notably ethers such as MTBE, ETBE, and TAME.

There are a wide variety of health effects that have been linked to ethanol exposures, which are summarized below. Note that in general, these data are derived from ingestion exposures and that route-to-route extrapolations of these findings generally are either not possible at present or have not been undertaken.

1. Noncancer Effects

The health risks of drinking alcohol have been extensively studied and evaluated (WHO, 2004; U.S. DHHS, 2000b, 2005; IARC, 1988). (Note that although alcoholic beverages may predominantly consist of ethanol and water, other constituents may also be present, and thus alcoholic beverages and ethanol are not necessarily equivalent chemically or toxicologically. This point is primarily relevant to epidemiological studies; animal toxicity studies typically administer ethanol in water to avoid potential confounding by other substances in alcoholic beverages.) High levels of alcoholic beverage consumption have been shown to result in, among other things, immune system effects, reproductive dysfunction, cardiovascular disease (e.g., hypertension and possibly stroke), and liver and pancreas toxicity. However, as is the case with many high-level exposure studies, the relevance of such effects to lower level exposures likely associated with ethanol-gasoline mixture use is unclear.

Unfortunately, the toxicological effects of low-level ethanol exposure, especially by the inhalation route, have not been well studied. As part of EPA's ongoing IRIS assessment, pharmacokinetic models are being evaluated as a means of extrapolating across routes and exposure levels to better characterize the health hazards and dose-response relationships for low-level ethanol exposure by both the oral and inhalation routes. In some people, genetic factors influencing the metabolism of ethanol can lead to differences in internal levels of ethanol and may render some subpopulations more susceptible to risks from the effects of ethanol.

The neurological consequences of prenatal ethanol exposure on the developing fetus (both animal and human) are one of the most prominent hazards of ethanol and have been examined in numerous reviews (Goodlett et al., 2005; Riley and McGee, 2005; Zhang et al., 2005; Riley et al., 2004; Gunzerath et al., 2004; WHO, 2004; Chen et al., 2003; U.S. DHHS, 2000b; Driscoll et al., 1990). Neurobehavioral problems encountered in children prenatally exposed to alcohol include hyperactivity and attention deficits, impaired motor coordination, a lack of regulation of social behavior or poor psychosocial functioning, and deficits in cognition, mathematical ability, verbal fluency, and spatial memory. Facial abnormalities, growth retardation, and spontaneous abortion may occur at higher levels of alcohol exposure; however, less obvious but potentially serious effects on the developing brain have been reported across a continuum of exposure levels with no clear threshold yet determined (Sampson et al., 2000).

Neurodevelopmental effects of ethanol have been investigated in relation to oral ethanol exposure in a large number of laboratory animal and epidemiology studies, with results in animal models corresponding closely with the effects observed in humans. Neuroanatomical studies in laboratory animals indicate that prenatal exposure to ethanol may lead to microencephaly (small brain relative to body size), neuronal loss, fewer dendritic spines, modification of neural circuitry, disrupted mitochondrial membranes, and changes in cell adhesion molecules (Chen et al., 2003). Ethanol exposure during the brain growth spurt (the early postnatal period in rats) decreased the weight of the forebrain, brainstem, and cerebellum. Neuronal cell loss was observed in the Purkinje cells of the cerebellum, cells of the olfactory bulb, and the pyramidal cells in the CA1 region of the hippocampus. The structural integrity of dendrites and the number of dendritic spines were altered in neurons located in the substantia nigra (a brain region involved in movement), cortex, and hippocampus (involved in spatial learning and memory) (Berman and Hannigan, 2000).

In human studies, primary evidence of neurodevelopmental toxicity stemming from prenatal exposure includes neuroanatomical data from autopsy and neuroimaging studies demonstrating changes in brain structure and data from epidemiological studies documenting neuropsychological and behavioral effects in children over time. Those studies have suggested that the corpus callosum, cerebellum, and basal ganglia are areas of the developing brain most susceptible to prenatal alcohol exposure (Riley and McGee, 2005; U.S. DHHS, 2000b). Prenatal exposure to alcohol in humans has also been associated with a wide range of neuropsychological deficits and behavioral changes including impairments in cognitive function (e.g., decreased IQ), learning, memory, attention, language development, reaction time, visual-spatial abilities, executive functioning, fine and gross motor skills, and social functioning (Coles et al., 1992, 1991, 1987a, b, 1985; Sood et al., 2001; Jacobson et al., 1998, 1994, 1993a, b; Sampson et al., 2000; Streissguth et al., 1989, 1986a, b). In addition to neuroanatomical parallels,

neurobehavioral outcomes observed in laboratory animals are similar to the cognitive and behavioral outcomes observed in humans (Driscoll et al., 1990, Slawecki et al., 2004, Berman and Hannigan, 2000).

The above information pertains to the qualitative effects of ethanol on health but does not provide a dose-response perspective. Most epidemiology studies report alcohol intake as drinks per day or per week. However, studies vary in their definitions of low, moderate, and high intake. Laboratory animal studies generally express the oral intake of ethanol in units of grams per kilogram body weight per day (g/kg bw-day) accompanied by an estimate of the blood ethanol concentration (BEC). The BEC is generally presented in units of milligrams of ethanol per deciliter (100 milliliters) of blood (mg/dL). The BEC can be a more reliable measure of exposure than the amount of alcohol consumed, due to the large degree of variability in ethanol metabolism and tolerance. However, epidemiological studies typically do not measure intake or BEC in such a precise manner, and thus dose-response information may be uncertain. Note that ethanol is also produced endogenously in the human body as a metabolic by-product of intestinal flora, and is therefore always present in human blood at a low background concentration.

Longitudinal prospective studies on prenatal alcohol exposure and developmental toxicity were performed in five areas of the United States (Atlanta, Cleveland, Detroit, Pittsburgh, and Seattle). Study populations were followed for extended time periods ranging from 5 to 14 years and were evaluated for measures of growth and physical development, cognitive ability, academic achievement, attention, learning, memory, and adaptive behavior. These studies have generally shown that maternal age (Jacobson et al., 1998) and trimester of pregnancy (Streissguth et al., 1989, 1986a,b, Coles et al., 1992, 1991, 1987a,b, 1985) are important considerations, with early pregnancy exposure of greatest concern. Sampson et al. (2000) characterized the dose-response relationship for the Seattle cohort and reported that their analysis suggests a linear dose-response for some of the alcohol-associated neurobehavioral effects, that is, without any clear threshold down to the lowest nonzero levels of exposure. However, they also noted that there was considerable variability in low-dose exposure data and that the slope of the regression line appeared to be heavily influenced by higher-level exposures.

Only three prenatal inhalation exposure animal studies are known to have used multiple air concentrations for ethanol (Nelson et al., 1985a,b, 1988). Exposure levels were relatively high at 10,000, 16,000, and 20,000 ppm (7 hours/day throughout gestation) and resulted in peak BECs of 3, 50, and 180 mg/dL, respectively. Although several reproductive and developmental endpoints were examined (e.g., fertility, number of pups per litter, fetal body weight, incidence of soft tissue or skeletal anomalies, tests of neuromotor coordination, activity level, and learning ability in offspring), no clear treatment-related effects were seen. However, significant biochemical changes were found in offspring of rats (paternal as well as maternal) that had been exposed at air concentrations of 10,000 and 16,000 ppm (Nelson et al., 1988).

2. Cancer

Epidemiological data supporting the role of alcohol consumption in cancer development in humans have been extensively reviewed (e.g., Boffetta and Hashibe, 2006; Gunzerath et al., 2004; WHO, 2004; Poschl and Seitz, 2004; IARC, 1988) and support a clear association between

low-to-moderate consumption of alcohol (2 drinks/day) and increased risk of cancers of the oral cavity and pharynx, larynx, esophagus, and female breast. Several other studies suggest that low to moderate consumption may also be associated with an increased risk of liver and colorectal cancers (Boffetta and Hashibe, 2006; Corrao et al., 2004; Cho et al., 2004), although the data supporting these findings are not as strong (as reviewed in Gunzerath et al., 2004; WHO, 2004).

Although an increase in risk of breast cancer associated with alcohol consumption is modest, the increase has been demonstrated in a number of large, well-conducted prospective cohort studies (e.g., Horn-Ross et al., 2002; Willett et al., 1987) as well as large case-control studies (e.g., Longnecker et al., 1995).

Despite epidemiologic evidence relating breast cancer with alcohol consumption, animal studies on the carcinogenic effect of ethanol have largely been inconclusive. However, most animal studies suffer from a variety of limitations, most importantly the failure to use controls on equivalent caloric intake diets. Of the few studies conducted using isocalorically fed controls, Hackney et al. (1992) reported no effect of ethanol on mammary tumorigenesis, but this study had a number of other methodological limitations. In a well-conducted chronic bioassay, Holmberg and Ekström (1995) reported a significant increase in pituitary tumors in high-dose females as well as a significant increase in benign tumors of the mammary glands in low-dose females. Several animal studies using initiation-promotion or co-carcinogenicity protocols report an increased incidence or multiplicity of mammary tumors with ethanol administration, but also without a clear dose-response relationship (Singletary and Gapstur, 2001). However, Hilakivi-Clarke et al. (2004) reported a dose-related increase in mammary tumors in rats exposed to ethanol in utero and treated with an initiator within a few weeks of maturation. Finally, a study by Soffritti et al. (2002) provides indications that early life exposure could be associated with increased risk of oral cancers compared with exposure during adulthood. Rats treated with 10% ethanol in drinking water beginning in utero and continuing into adulthood had a significantly increased incidence of tumors of the oral cavity, tongue, and lips, among other carcinogenic effects relative to a similarly treated group of animals treated from age 39 weeks.

Genotoxicity data for ethanol have been reviewed in Phillips and Jenkinson (2001) and IARC (1988). Ethanol was not mutagenic in bacterial or mammalian cell systems, but mixed findings were reported in other test systems (*S. cerevisiae*, *A. nidulans*, and *D. melanogaster*). Acetaldehyde, a metabolite of ethanol, has been observed to produce DNA adducts, point mutations, SCE, and chromosome aberrations; and to interfere with DNA repair (reviewed in Brooks and Theruvathu, 2005; Poschl and Seitz, 2004; Homann, 2001; Phillips and Jenkinson, 2001).

Finally, genetic factors may predispose some persons to greater susceptibility to cancer from alcohol exposure. Polymorphisms have been reported to modify the risk of alcohol-induced cancers, including both breast and oral cancers (Dumitrescu and Shields, 2005; Peters et al., 2005).

C. ETBE

Ethyl tertiary butyl ether (ETBE) has not been investigated to the extent that MTBE has, but the limited information available on ETBE suggests that it is comparable to MTBE in various respects. The chemical structures of ETBE (Figure II.1.c) and MTBE (Figure II.1.a) are similar except for ETBE having an ethoxy group (-O-CH₂-CH₃) instead of the methoxy group (-O-CH₃) in MTBE.

Like MTBE, the odor of ETBE can be detected at relatively low concentrations, with thresholds of <1 ppm for ETBE odor and taste in both air and water (Vetrano, 1993). Limited studies of odor thresholds suggest that ETBE may be detected at even lower concentrations than MTBE (Vetrano, 1993) and that a 15% blend of ETBE in gasoline lowers the odor threshold well below that for gasoline alone (TRC Env. Corp., 1993). At relatively high air concentrations (50 ppm), volunteer subjects reported throat and airway irritation for ETBE but not MTBE (Nihlén et al., 1998a,b).

ETBE is currently under assessment as part of EPA's IRIS program. Although final conclusions cannot be stated at this time regarding the qualitative or quantitative health hazard potential of ETBE, some information on the health effects of ETBE can be summarized here based on the available literature.

Although no chronic inhalation studies of ETBE have been conducted, inhalation studies have been carried out with mice and rats for shorter periods of time. In a 4-week study by White et al. (1995), the only treatment-associated responses in rats exposed to concentrations of 0 – 4000 ppm ETBE in air were increased liver weight at 2000 and 4000 ppm in females and increased liver, kidney, and adrenal weight at 4000 ppm in males. Similar results were found by Medinsky et al. (1999), who exposed rats and mice for 13 weeks to ETBE by inhalation and found increased liver weight (with associated centrilobular hypertrophy) at 5000 ppm in female rats, at 1750 and 5000 ppm in male rats, and at 1750 and 5000 ppm in male and female mice, albeit in the absence of hepatic lesions, elevated serum enzymes characteristic of hepatotoxicity, or other evidence of irregular pathology. Likewise, an increase in adrenal weight was seen in both male and female rats at 5000 ppm but was not supported by histopathological findings.

In the same study, Medinsky et al. (1999) observed increased kidney weight at 1750 and 5000 ppm in male rats and at 5000 ppm in female rats; no change in kidney weight occurred in mice. Female rats showed increased kidney weight unaccompanied by significant histopathology and a small but unsustained increase in cell proliferation. Male rats showed increased kidney weight associated with the presence of regenerative foci, hyaline droplet accumulation, and alpha-2u-globulin immunoreactivity. This, along with other findings, raises the question that was discussed in relation to MTBE, namely the role of alpha-2u-globulin in accounting for nephropathy in male rats. This issue is undergoing evaluation by EPA in connection with the IRIS assessment of ETBE.

In their 13-week inhalation study, Medinsky et al. (1999) also observed testicular effects, namely a slight increase in the percentage of seminiferous tubules with degenerated spermatocytes, at ETBE concentrations of 1750 and 5000 ppm. Neurotoxicological studies have

found transient ataxia (staggering or unsteady gait) at air concentrations of 4000 to 5000 ppm ETBE but no indications of long-term neurotoxicity (Dorman et al., 1997; White et al., 1995).

Few studies have examined the toxicity of ETBE by ingestion. Maltoni et al. (1999) focused on the carcinogenicity of chronic oral-route exposure to ETBE administered in olive oil at 0, 250, and 1000 mg/kg body weight. The authors reported increased incidence of malignant uterine tumors in the low-dose group and increased incidence of pathologies of oncological interest of the mouth in high-dose male rats. Uncertainties in the Maltoni et al. (1999) study including the low-dose only effect of the uterine tumors and the combined inclusion of precancers and tumors in the pathologies in the mouth contribute to uncertainty in the evaluation of the results. Berger and Horner (2003) reported no effects on fertilizability of oocytes in female rats exposed to ETBE or 2M2P (a metabolite of ETBE) in drinking water for 2 weeks.

Unpublished studies of ETBE administered to rats via the oral route at doses of 250, 500, or 1000 mg/kg-day in corn oil evaluated reproductive, developmental, and other effects over two generations (CIT, 2003, 2004a,b). At the two highest doses, significant decreases in body weight gain in pregnant dams and some parental males were recorded but the effects were not observed consistently in other rats exposed over a longer time period or in the subsequent generation. Increased kidney weights and liver weights were observed in male and female rats, with more pronounced effects in males, but the findings are difficult to interpret due to limited histological evaluation. No effects were reported for fertility, gonadal function, reproductive performance, parturition, lactation in the parental generations, and development of the offspring to weaning or sexual maturity. The lack of testicular effects in particular contrasts with male reproductive effects in the 13-week inhalation study of Medinsky et al. (1999) noted above. A transient increase in salivation was also noted.

D. TAME

In terms of chemical structure (Figure II.1.d), tertiary amyl methyl ether (TAME) and MTBE (Figure II.1.a) are both ethers with a basic structure of an oxygen atom bonded to two carbon atoms. TAME contains a methyl group on one side of the ether oxygen atom and a tertiary amyl group on the other. The taste of TAME in water has been described as “highly objectionable” by a panel of volunteer testers (Vetrano, 1993). Odor threshold studies suggest that, as with ETBE and MTBE, mixing TAME with gasoline results in a much lower (by about half) threshold compared to gasoline alone (TRC Environmental Corp., 1993). Also, compared with odor thresholds for MTBE and ETBE, TAME appears to be intermediate.

TAME is currently under assessment as part of EPA’s IRIS program; therefore, final conclusions cannot be stated regarding its qualitative or quantitative health hazard potential. Information on the health effects of TAME is limited, particularly for ingestion exposure. In a subchronic oral study, rats were dosed with TAME for 7 days/week for 29 days (Daughtrey and Bird, 1995). Treatment-related effects occurred at 1000 mg/kg-day with the deaths of 2 out of 10 animals and a decreased body weight gain in female rats. Absolute and relative adrenal weights increased in females, and relative kidney weight increased in males at 500 and 1000 mg/kg-day. A preliminary report by Belpoggi et al. (2002) evaluated the carcinogenic effects of chronic oral

dosing rats 4 days/week for 78 weeks. The authors noted a statistically significant increase in the number of total lymphomas and leukemias in TAME-treated females at 1000 mg/kg-day.

Inhalation studies of TAME include a subchronic study by White et al. (1995), who investigated neurotoxicologic and other effects in rats inhaling TAME for 6 h/day, 5 days/week for 4 weeks. The authors reported transient clinical signs (e.g., sedation, coma, ataxia) and other indications of neurotoxicity (e.g., reduced tail pinch response, righting reflex, body temperature) at 2000 ppm; however, none of the effects remained by 18 h after the last exposure. Other transient effects noted at 2000 ppm included increased serum cholesterol in males and an increased relative liver weight in both sexes unaccompanied by clear treatment-related histopathological changes in the liver or in other tissues.

The American Petroleum Institute (API) funded a study conducted by Huntingdon Life Sciences (1997) to evaluate effects of subchronic TAME inhalation exposures in rats and mice. Rats inhaled concentrations of TAME ranging from 0 to 3500 ppm for 6 h/day, 5 days/week for 13-14 weeks. Clinical signs of neurotoxicity and hematological and clinical chemistry changes occurred at 1500 ppm. Transient signs of neurotoxicity (lethargy and prostration) occurred during and immediately after daily exposure for the first 4 weeks. Increased platelet counts and serum protein (total protein, albumin, and globulin) levels persisted to the end of the 13- to 14-week exposure period. Transient increases in liver and adrenal weights occurred at exposure levels as low as 250 ppm but were not accompanied by histopathologic changes or increased liver enzyme levels. Pathological changes related to alpha-2u-globulin accumulation in the kidney were noted at and above 250-ppm exposures in male rats (see discussion regarding alpha-2u-globulin in Section A on MTBE). In another portion of the study, mice inhaled concentrations of TAME on the same regimen as the rats. High mortality rates (~56% male, ~30% female) occurred within three exposures at the 3500-ppm level. At 1500 ppm, clinical signs of acute neurotoxicity such as lethargy and prostration occurred during and immediately after daily exposure periods for the first 3 weeks. An effect on the liver (increased serum alanine transaminase) occurred at 2500 ppm.

Reproductive and developmental effects of TAME in rodents were also investigated under API sponsorship (Tyl et al., 2003; Welsch et al., 2003). Adult systemic toxicity was evident at 1500 and 3000 ppm in rats, along with offspring toxicity at the same levels. However, the only effects on reproductive function were at 3000 ppm in male rats (Tyl et al., 2003). Developmental effects were more pronounced in mice than in rats and included increased incidences of cleft palate at 1500 and 3500 ppm, along with increased late fetal deaths, reduced fetal body weights, and enlarged lateral ventricles of the cerebrum at 3500 ppm (Welsch et al., 2003).

E. DIPE

The chemical structure of di-isopropyl ether (DIPE) is shown in Figure II.1.e. DIPE contains a secondary propyl group on each side of the oxygen atom. Odor and taste thresholds for DIPE have not been investigated. Little toxicity information has been collected for DIPE, and no chronic exposure studies have been conducted. DIPE is currently under assessment as

part of EPA's IRIS program; therefore, final conclusions cannot be stated regarding its qualitative or quantitative health hazard potential.

The primary study of DIPE toxicity was a subchronic inhalation study conducted for Mobil and published in reports by Dalbey and Feuston (1996) and Rodriguez and Dalbey (1997). Rats inhaled DIPE at concentrations ranging from 0 to 7100 ppm for 6 h/day, 5 days/week for 14 weeks (Dalbey and Feuston, 1996). At 3300 ppm, liver and kidney weights were slightly increased, but no discernable morphological changes in liver and kidney were noted. Increased liver weight with liver cell hypertrophy and increased kidney weight with increased incidences of hyaline droplets in the proximal tubules occurred at 7100 ppm in males. This study also evaluated developmental toxicity and found a concentration-related increase in the incidence of rudimentary 14th ribs in the fetuses, although this effect was not supported by any other evidence of teratogenicity. Dams showed a treatment-related, slightly decreased body weight gain and decreased food intake at 6700 ppm.

Neurotoxic effects of DIPE were also evaluated (Rodriguez and Dalbey, 1997). At 450 ppm, males showed a decreased reflexive response to touch after two weeks of exposure, but this response was not seen in other groups at any time point. A biphasic response was seen for general activity levels in female rats, with decreased activity at week 4 and increased activity at week 8. No treatment-related morphological changes were detected in the central or peripheral nervous system structures examined.

Brooks et al. (1988) reported no positive responses in evaluations of DIPE in bacterial mutation assays, a yeast mitotic gene conversion assay, and mammalian cell cultures for structural chromosome damage.

F. TBA

Tertiary butyl alcohol (TBA) is a four-carbon alcohol with a methyl group and an alcohol group (hydroxyl) attached to the second carbon of its three-carbon skeleton (Fig. II.1.f), making it miscible in water. In addition to being a fuel oxygenate additive and constituent of various consumer products, TBA is a metabolite and a degradation by-product of MTBE. Odor detection thresholds for TBA have been reported at roughly half the levels for ethanol (Amoore and Hautala, 1983). TBA is currently under assessment as part of EPA's IRIS program; therefore, final conclusions cannot be stated regarding its qualitative or quantitative health hazard potential.

Most of the information on the health effects of TBA comes from animal studies. Oral and inhalation toxicity studies in rodents were conducted by the National Toxicology Program (1995, 1997), including a chronic drinking water bioassay (Cirvello et al., 1995). Among the more significant effects of long-term exposure to TBA in drinking water were kidney tumors in male rats and thyroid tumors in female mice, along with dose-related nephropathy in male and female rats and chronic inflammation and hyperplasia of the urinary bladder in male and female mice (Cirvello et al., 1995). Subchronic TBA exposure also yielded signs of male rat nephropathy and urinary tract inflammation and lesions in rats and mice of both sexes (Lindamood et al., 1992). The issue of alpha-2u-globulin in male rat kidney effects arises here as well (see discussion in Section A on MTBE).

A few reproduction and/or developmental studies of TBA have been performed. In a study with mice gavaged at a high dose (>1500 mg/kg-day) on gestational days 6-18, Faulkner et al. (1989) found treatment-related increases in resorptions and reductions in fetal viability. In another oral exposure study (Huntingdon Life Sciences, 2004), reductions in litter size, pup survival, and neonatal body weight were seen in the offspring treated at 1000 mg/kg-day. Of two inhalation studies of TBA developmental toxicity in rats (Nelson et al., 1989, 1991), one showed reduced fetal body weight at 2000 ppm, albeit accompanied by some evidence of maternal toxicity.

The pharmacokinetics of TBA have been extensively investigated, both as a parent compound and as a metabolite of both MTBE and ETBE (e.g., Borghoff et al., 1996; Nihlén et al., 1998a; Amberg et al., 2000; Prah et al., 2004; Blancato et al., 2007). In the latter regard, it has not been determined to what extent, if any, the observed effects of MTBE and ETBE are mediated by the metabolite they share. Unlike ethanol, TBA is not primarily metabolized by alcohol dehydrogenase and is metabolized more slowly than ethanol (Thurman et al., 1980) or the ether oxygenates (Prah et al., 1994; Nihlen et al., 1998a).

Some animal studies have suggested that TBA is more potent than ethanol in terms of neurobehavioral effects such as psychomotor performance and learned behavior (Daniel and Evans, 1982; Witkin and Leander, 1982; Dudek and Phillips, 1983; Witkin, 1984)

G. Alkylates/iso-octane

Alkylates are a class of organic chemicals, of which iso-octane is a leading example. The chemical structure of the most prominent isomer of iso-octane (2,2,4-trimethylpentane) contains no oxygen (Figure X.g), unlike the oxygenates in this discussion. Instead, this alkane comprises a five-carbon chain (pentane) with three methyl groups attached, two to the second carbon and one to the fourth carbon. Iso-octane is pertinent to this document because it (along with similar branched-chain paraffins) could be used in increased amounts in some formulations of gasoline using alcohols in place of ethers. As such it would help increase the volume of gasoline but would not itself add oxygen to the fuel.

A *Toxicological Review of 2,2,4-Trimethylpentane* (a synonym for iso-octane) was recently posted on the EPA IRIS database (<http://www.epa.gov/IRIS/toxreviews/0614-tr.pdf>). The Review indicates that insufficient information is available to allow quantification of carcinogenic or non-carcinogenic risks for iso-octane. The following qualitative information is summarized from the *Toxicological Review of 2,2,4-Trimethylpentane* (U.S. EPA, 2007c).

Epidemiological or poisoning case studies of iso-octane in humans are not available, but animal studies (mice, rats, guinea pigs) indicate that high levels (>8300 ppm) of iso-octane can be lethal. Limited data in rats suggest that the chemical is readily absorbed via ingestion and distributed to the kidneys, fat, and liver, with higher concentrations detected in the kidneys of males compared with females (Kloss et al., 1986). Absorption via the respiratory tract appears to be around 7-12% of the inhaled concentration (Dahl, 1989).

Although no subchronic or chronic oral animal studies are available, a number of acute and short-term oral studies point to altered renal function, an increase in alpha-2u-globulin protein and hyaline droplet accumulation in the proximal tubules, necrosis of the tubule epithelium, increased cell turnover, and foci of regenerative epithelium in male rats (Blumbach et al., 2000; Saito et al., 1992; Borghoff et al., 1992; Burnett et al., 1989; Lock et al., 1987a,b; Short et al., 1986; Stonard et al., 1986; API, 1983). However, no increases in alpha-2u-globulin protein and hyaline droplet accumulation and no necrosis of the tubule epithelium were noted to occur in female rats (Blumbach et al., 2000; Lock et al., 1987a,b) or in mice, guinea pigs, dogs, or monkeys (Alden, 1986). In the only known subchronic study of iso-octane via the inhalation route (Short et al., 1989) rats were exposed for 3-50 weeks to 50 ppm iso-octane. As with oral studies, alpha-2u-globulin protein levels increased and hyaline droplets accumulated in males but not females. Based on criteria described by U.S. EPA (1991a), it appears that the renal effects of iso-octane are associated with alpha-2u-globulin accumulation and therefore are not relevant to humans (U.S. EPA, 2007c). Note that this determination is made on a case-by-case basis and is therefore specific to iso-octane; other chemicals (e.g., MTBE, ETBE, TBA) must be independently evaluated regarding the role of alpha-2u-globulin.

One acute study also reported effects on the liver in a small number of male rats given iso-octane by gavage for 2-3 days (Fowlie et al., 1987). Liver weights were significantly increased, with centrilobular necrosis and hydrophobic degeneration of hepatocytes. No studies are available on the reproductive or developmental effects of iso-octane. Limited genotoxicity data are negative (Richardson et al., 1986; McLaren et al., 1994; Loury et al., 1986).

H. Associated chemicals and pollutants

This section summarizes health effects information for chemicals and pollutants that are either constituents of fuels or are produced as a result of combustion and/or evaporation. BTEX compounds (benzene, toluene, ethylbenzene and the xylenes) are components of fuels and enter the atmosphere as evaporative emissions. The BTEX compounds can also contaminate ground water from spills or when leaking occurs from underground fuel storage tanks, and their concentrations are affected by presence of fuel additives (see Chapter V for more detail). Ozone, particulate matter, acetaldehyde, peroxyacetyl nitrate (PAN), and formaldehyde are created in the atmosphere as secondary products of fuel combustion or evaporation; particulate matter, formaldehyde and acetaldehyde are also directly emitted as combustion products. Concentrations are dependent on the fuel additive mixture (see Chapter IV for more detail).

1. Ozone

Tropospheric or ground-level ozone (O₃) has been the subject of a great deal of scientific study and evaluation. The following information is taken from *Air Quality Criteria for Ozone and Photochemical Oxidants* (U.S. EPA, 2006), which provides a scientific basis for the National Ambient Air Quality Standards for O₃.

When found in the earth's troposphere (as opposed to the stratosphere, where it is beneficial in shielding the Earth from harmful solar ultraviolet radiation), ozone generally originates from photochemical reactions that involve the interaction of sunlight with precursor

compounds, especially nitrogen oxides (NO_x), carbon monoxide (CO), and volatile organic compounds (VOCs) such as hydrocarbons emitted by various sources, including evaporative and combustion emissions from motor vehicle fuels. Tropospheric O₃ is the primary constituent of smog and can have adverse effects on humans, nonhuman animal species, and vegetation.

Inhalation of O₃ can trigger a variety of health problems including chest pain, coughing, throat irritation, and congestion. It can worsen bronchitis, emphysema, and asthma and can also reduce lung function, inflame the linings of the lungs, and increase susceptibility to respiratory infection. Repeated exposure to O₃ may permanently scar lung tissue. In some people, these effects can lead to increased medication use (among asthmatics), more frequent doctor visits, school absences, and increased emergency room visits and hospital admissions. Moreover, breathing ozone may contribute to premature death in people with heart and lung disease.

Ozone can also have harmful effects on plants and ecosystems. When sufficient O₃ enters the leaves of a plant, it can interfere with the ability of sensitive plants to produce and store food, making them more susceptible to certain diseases, insects, other pollutants, competition and harsh weather. Further, O₃ can visibly damage the leaves of trees and other plants, harming the appearance of urban vegetation, national parks, and recreation areas. Ultimately, the effects of O₃ may lead to reduced forest growth and crop yields.

Primary and secondary National Ambient Air Quality Standard (NAAQS) for ozone were revised in 2008 to 0.075 parts per million (ppm) averaged over 8 hours for protection of both public health and welfare effects, most notable those on vegetation.

2. Particulate Matter

The health effects of particulate matter (PM) have been intensively investigated and have been characterized in depth in *Air Quality Criteria for Particulate Matter* (U.S. EPA, 2004a), which provides a scientific basis for the PM National Ambient Air Quality Standards. Particles in the ambient air come from a variety of sources and have a broad range of sizes, composition, and other characteristics. Particles smaller than 2.5 μm in aerodynamic diameter (PM_{2.5}) include both directly emitted particles and particles that are products of chemical reactions of gases in the atmosphere. Examples of directly emitted particles (both PM_{2.5}, or "fine" particles, and larger, or "coarse," particles with aerodynamic diameter of 2.5 - 10 μm) include those from combustion sources such as vehicle tailpipe emissions, agricultural open burning, coal and oil fired power plants and industries, as well as dust particles from roads and fields. Particles formed in the atmosphere are referred to as "secondary" particles, and the majority of these particles in many areas of the country are formed from gases from fuel combustion in automobiles, trucks, and power plants such as sulfur dioxide (SO₂) and nitrogen oxides (NO_x) released by anthropogenic and natural sources. In addition, aromatic compounds in fuels, such as toluene and even benzene, have been shown to play an important role in secondary PM formation. Other hydrocarbon components can also form secondary organic aerosol in substantial amounts. These include long-chained alkanes as well as biogenic isoprene, monoterpenes, and sesquiterpenes. These biogenic compounds can, especially in summer conditions, form tremendous quantities of secondary organic aerosol.

Particle pollution, especially fine particles, contains microscopic solids or liquid droplets that are so small that they can get deep into the lungs and cause serious health problems. Numerous scientific studies have linked particle pollution exposure to a variety of health problems, including increased respiratory symptoms, such as irritation of the airways, coughing, or difficulty breathing; decreased lung function; aggravated asthma; development of chronic bronchitis; irregular heartbeat; nonfatal heart attacks; and premature death in people with heart or lung disease. People with heart or lung diseases, children and older adults are the most likely to be affected by particle pollution exposure. However, even healthy persons may experience temporary symptoms from exposure to elevated levels of particle pollution. The PM Air Quality Criteria Document also notes that the PM components of gasoline and diesel engine exhaust represent one class of hypothesized likely important contributors to the observed ambient PM-related increases in lung cancer incidence and mortality. Environmental effects of particulate matter can be far-reaching. Fine particles (PM_{2.5}) are the major cause of reduced visibility (haze) in parts of the United States, including many national parks and wilderness areas. Particles can also be carried over long distances by wind and then settle on ground or water. The effects of this settling include acidification of lakes and streams, alteration of the nutrient balance in coastal waters and large river basins, depletion of nutrients in soil, damage to sensitive forests and farm crops, and reduction of the diversity of ecosystems. In addition, particle pollution can stain and damage stone and other materials, including culturally important objects such as statues and monuments.

The current National Ambient Air Quality Standards (NAAQS) for particulate matter, as revised in 2006, are expressed for different averaging times and for different size fractions as follows: PM₁₀, 150 $\mu\text{g}/\text{m}^3$ over 24 hours; PM_{2.5}, 15.0 $\mu\text{g}/\text{m}^3$ annually and 35 $\mu\text{g}/\text{m}^3$ over 24 hours.

3. Acetaldehyde

While acetaldehyde is an emission product from combustion engines running on ethanol-free fuels, it is emitted in increased amounts in the exhaust of vehicles burning gasoline/ethanol blends. Acetaldehyde is also produced in substantial amounts in the atmosphere resulting from photochemical reactions of ethanol and other hydrocarbons. Moreover, some atmospheric acetaldehyde undergoes further photochemical reactions in the atmosphere to yield PAN (see below). In addition, this compound is an important metabolite of ethanol in the body.

In humans, acute exposure to acetaldehyde vapor can cause eye irritation at a concentration of 50 ppm for 15 minutes or as low as 25 ppm in sensitive individuals (Verschueren, 1983). Dermal exposures in humans may result in contact dermatitis, erythema, or burns, and in rabbits acute exposure has also been reported to cause mild skin and severe eye irritation (ACGIH, 1991).

An inhalation reference concentration (RfC) of 0.009 mg/m^3 was derived for acetaldehyde in 1991 (U.S. EPA, 1991b). The RfC was based primarily on degeneration of olfactory epithelium in rats that had been exposed to acetaldehyde for 4 weeks (Appleman et al., 1982, 1986), consistent with effects seen at exposures lasting up to 52 weeks (Woutersen et al., 1986; Woutersen and Feron, 1987). No information on reproductive or developmental effects

was found at the time of the 1991 review. Some asthmatics have been shown to be a sensitive subpopulation to decrements in forced expiratory volume and increased bronchoconstriction upon acetaldehyde inhalation (Myou et al., 1993).

Acetaldehyde has been classified by EPA as a probable human carcinogen based on animal studies (U.S. EPA, 1991b). Nasal epithelial cancers occurred in rats exposed by inhalation for up to 28 months (U.S. EPA, 1991b), and hamsters exposed for 52 weeks had significant increases in laryngeal tumors (IARC, 1985).

Note that acetaldehyde is currently under assessment as part of EPA's IRIS program; therefore, conclusions are being revised regarding its qualitative or quantitative health hazard potential.

4. PAN

Peroxyacetyl nitrate (PAN) is a photochemical oxidant associated with ground-level ozone and smog. Information on the health effects of PAN is limited, but it appears to be less toxic than ozone at comparable acute exposure levels (U.S. EPA, 2006 [Ozone Criteria Document]). At environmental levels it can cause eye irritation, and at concentrations approximately 100- to 1,000-fold higher than levels typically found in ambient air, it can cause changes in lung morphology, behavioral modifications, weight loss, and susceptibility to pulmonary infections. Cytogenetic studies indicate that PAN is not a potent mutagen, clastogen, or DNA-damaging agent in mammalian cells in vivo or in vitro at concentrations several orders of magnitude higher than those generally encountered in ambient air in most cities. Some studies suggest that PAN may be a weak bacterial mutagen at concentrations much higher than exist in present urban atmospheres.

5. Formaldehyde

Formaldehyde is the most prevalent aldehyde in engine exhaust. In addition, while it is not a constituent of gasoline and thus is not a component of evaporative emissions, it is also formed photochemically in the atmosphere from precursor hydrocarbons present in motor vehicle exhaust. The primary route of human exposure is by inhalation.

Since 1987, EPA has classified formaldehyde as a probable human carcinogen based on evidence in humans and in rats, mice, hamsters, and monkeys (U.S. EPA, 1987). EPA's IRIS database provides an upper bound cancer unit risk estimate of 1.3×10^{-5} per $\mu\text{g}/\text{m}^3$ (U.S. EPA, 1991d). In other words, there is an estimated risk of as many as thirteen excess leukemia cases in one million people exposed to $1 \mu\text{g}/\text{m}^3$ of formaldehyde over a lifetime.

In the past 15 years there has been substantial research on the inhalation dosimetry for formaldehyde in rodents and primates by the CIIT Centers for Health Research (formerly the Chemical Industry Institute of Toxicology), with a focus on use of rodent data for refinement of the quantitative cancer dose-response assessment (Conolly et al., 2003, 2004; CIIT, 1999). CIIT's risk assessment of formaldehyde incorporated mechanistic and dosimetric information on formaldehyde. The risk assessment analyzed carcinogenic risk from inhaled formaldehyde using

approaches that were consistent with the 1999 draft EPA guidelines for carcinogenic risk assessment. In 2001, Environment Canada relied on this cancer dose-response assessment in their assessment of formaldehyde (Health Canada, 2001). In 2004, EPA also relied on this assessment during the development of the plywood and composite wood products national emissions standards for hazardous air pollutants (NESHAPs) (U.S. EPA, 2004b). In these rules, EPA concluded that the CIIT work represented the best available application of the available mechanistic and dosimetric science on the dose-response for portal of entry cancers due to formaldehyde exposures. The value that EPA used for these assessments was $5.5 \times 10^{-9}/\mu\text{g}^3$.

In 2004 the International Agency for Research on Cancer concluded that formaldehyde is carcinogenic to humans (Group 1 classification), on the basis of sufficient evidence in humans and sufficient evidence in experimental animals—a higher classification than previous IARC evaluations. In addition, the National Institute of Environmental Health Sciences recently nominated formaldehyde for reconsideration as a known human carcinogen under the National Toxicology Program. Since 1981 it has been listed as a “reasonably anticipated human carcinogen.” More recently the German Federal Institute for Risk Assessment classified formaldehyde as a known human carcinogen (BfR, 2006).

EPA is currently reviewing the health literature on formaldehyde, including several recently published epidemiological studies. For instance, research conducted by the National Cancer Institute (NCI) found an increased risk of nasopharyngeal cancer and lymphohematopoietic malignancies such as leukemia among workers exposed to formaldehyde (Hauptmann et al, 2003, 2004). NCI is currently performing an update of these studies. A recent National Institute of Occupational Safety and Health (NIOSH) study of garment workers also found increased risk of death due to leukemia among workers exposed to formaldehyde (Pinkerton, 2004). Extended follow-up of a cohort of British chemical workers did not find evidence of an increase in nasopharyngeal or lymphohematopoietic cancers, but a continuing statistically significant excess in lung cancers was reported (Coggon et al., 2003). EPA is reviewing the recent work cited above from the NCI and NIOSH, as well as the analysis by the CIIT Centers for Health Research and other studies (e.g., Subramaniam et al., 2007), as part of a reassessment of the human hazard and dose-response associated with formaldehyde.

Formaldehyde exposure also causes a range of noncancer health effects, including irritation of the eyes, nose and throat. Decreased pulmonary function has been observed in humans. Effects from repeated exposure in humans include respiratory tract irritation, chronic bronchitis and nasal epithelial lesions (ATSDR, 1999b). Animal studies suggest that formaldehyde may also cause airway inflammation – including eosinophil infiltration into the airways (Coon et al., 1970; Fujimaki et al., 2004; Jung et al., 2007). There are several studies suggesting that formaldehyde (up to about 3 ppm) may induce mild, reversible changes in human pulmonary function (Green et al., 1987; Sauder et al., 1986; Horvath et al., 1988). Other studies indicate that formaldehyde exposure may increase the risk of asthma – particularly in the young (Franklin et al., 2000; Garret et al., 1999; Rumchev et al., 2002). However, EPA has not developed an RfC for formaldehyde to date.

6. Benzene

Benzene is an aromatic hydrocarbon that is a major constituent of gasoline, along with toluene, ethylbenzene, and xylenes, collectively referred to as BTEX. As such, it is emitted into the air both as exhaust and evaporative emissions. Besides being emitted in the exhaust as an uncombusted gasoline component, benzene is also emitted in the exhaust as a combustion product of other aromatic compounds. Also, it is emitted in evaporative emissions from the fuel system. It can be emitted as evaporative emissions while the vehicle is running or even after it is shut off. It is also emitted as refueling emissions and as fuel spillage. Inhalation is the most common route of human exposure to benzene in the occupational and non-occupational setting; however, leakage of gasoline from underground storage tanks into ground water has also posed a source of exposure. Benzene has well-documented carcinogenic and other adverse health effects in humans and laboratory animals.

The EPA's IRIS database lists benzene as a known human carcinogen (causing leukemia) by all routes of exposure, based on convincing evidence in humans and supporting evidence from animal studies (U.S. EPA, 2000). Epidemiologic studies and case studies provide clear evidence of a causal association between exposure to benzene and acute nonlymphocytic leukemia and also suggest evidence for chronic nonlymphocytic leukemia and chronic lymphocytic leukemia. Other neoplastic conditions that are associated with an increased risk in humans are hematologic neoplasms, blood disorders such as preleukemia and aplastic anemia, Hodgkin's lymphoma, and myelodysplastic syndrome (MDS). These human data are supported by animal studies. The experimental animal data add to the argument that exposure to benzene increases the risk of cancer in multiple species at multiple organ sites (hematopoietic, oral and nasal, liver, forestomach, preputial gland, lung, ovary, and mammary gland). It is likely that these responses are due to interactions of the metabolites of benzene with DNA (Ross, 1996; Latriano et al., 1986). Recent evidence supports the viewpoint that there are likely multiple mechanistic pathways leading to cancer and, in particular, to leukemogenesis from exposure to benzene (Smith, 1996). Exposure to benzene and/or its metabolites has also been linked with chromosomal changes in humans and animals and increased proliferation of mouse bone marrow cells (U.S. EPA, 1998b; Irons et al., 1992)

The excess risk of developing leukemia from inhalation exposure to benzene has been estimated at 2.2×10^{-6} to 7.8×10^{-6} per $\mu\text{g}/\text{m}^3$. In other words, there is an estimated risk of about two to eight excess leukemia cases in one million people exposed to $1 \mu\text{g}/\text{m}^3$ of benzene over a lifetime³. Based on the cancer assessment for benzene by inhalation, a cross-route extrapolation yielded an oral unit risk estimate range of 4.4×10^{-7} to $1.6 \times 10^{-6}/\mu\text{g}/\text{L}$ (U.S. EPA, 2000). These estimates pertain to ingestion of drinking water but do not account for total exposure that could include dermal uptake during bathing and inhalation of volatilized benzene from drinking water. Data that were considered by EPA in its carcinogenic update suggested that the dose-response relationship at doses below those examined in the studies reviewed in EPA's most recent

³This range of unit risks reflects the maximum likelihood estimates (MLEs) calculated from different exposure assumptions and dose-response models that are linear at low doses. At present, the true cancer risk from exposure to benzene cannot be ascertained, even though dose-response data are used in the quantitative cancer risk analysis, because of uncertainties in the low-dose exposure scenarios and lack of clear understanding of the mode of action. A range of estimates of risk is recommended, each having equal scientific plausibility. There are confidence intervals associated with the MLE range that reflect random variation of the observed data. For the upper end of the MLE range, the 5th and 95th percentile values are about a factor of 5 lower and higher than the best fit value.

benzene assessment may be supralinear⁴. This relationship could support the inference that cancer risks are as high, or higher than the estimates provided in the existing EPA assessment. However, since the mode of action for benzene carcinogenicity is unknown, the current cancer unit risk estimate assumes linearity of the low-dose response.

In addition to carcinogenic effects, a number of adverse noncancer health effects, particularly blood disorders and immunotoxicity, have been associated with long-term occupational exposure to benzene (U.S. EPA, 2003a). People with long-term occupational exposure to benzene have experienced harmful effects on the blood-forming tissues, especially in the bone marrow. These effects can disrupt normal blood production and suppress the production of important blood components, such as red and white blood cells and blood platelets, leading to anemia (a reduction in the number of red blood cells), leukopenia (a reduction in the number of white blood cells), or thrombocytopenia (a reduction in the number of blood platelets, thus reducing the ability of blood to clot). Chronic inhalation exposure to benzene in humans and animals results in pancytopenia,⁵ a condition characterized by decreased numbers of circulating erythrocytes (red blood cells), leukocytes (white blood cells), and thrombocytes (blood platelets). Individuals that develop pancytopenia and have continued exposure to benzene may develop aplastic anemia, whereas others exhibit both pancytopenia and bone marrow hyperplasia (excessive cell formation), a condition that may indicate a preleukemic state. The most sensitive noncancer effect observed in humans, based on current data, is the depression of the absolute lymphocyte count in blood.

Childhood may be a stage of life where individuals are at increased risk from benzene exposure. Limited data suggest an increased risk to children whose parents were occupationally exposed to benzene (Shu et al., 1988; McKinney et al., 1991), supported by animal studies indicating that benzene exposures resulted in damage to the hematopoietic (blood cell formation) system during development (Keller and Snyder, 1986, 1988; Corti and Snyder, 1996).

The EPA inhalation reference concentration (RfC) for benzene is 30 $\mu\text{g}/\text{m}^3$ (U.S. EPA, 2003a). A total uncertainty factor of 300 (10 for intraspecies variability, 3 for interspecies

⁴ Recent data on benzene adducts in humans, published after the most recent IRIS assessment, suggest that the enzymes involved in benzene metabolism start to saturate at exposure levels as low as 1 ppm (Rappaport et al., 2002; 2005; Lin et al., 2007). These data highlight the importance of ambient exposure levels and their contribution to benzene-related adducts. Because there is a transition from linear to saturable metabolism below 1 ppm, the assumption of low-dose linearity extrapolated from much higher exposures could lead to substantial underestimation of leukemia risks. This is consistent with recent epidemiological data which also suggest a supralinear exposure-response relationship and which "[extend] evidence for hematopoietic cancer risks to levels substantially lower than had previously been established (Hayes et al., 1997; 2001; Lan et al., 2004). These data are from the largest cohort study done to date with individual worker exposure estimates. However, these data have not yet been formally evaluated by EPA as part of the IRIS review process, and it is not clear how they might influence low-dose risk estimates. A better understanding of the biological mechanism of benzene-induced leukemia is needed.

⁵ Pancytopenia is the reduction in the number of all three major types of blood cells (erythrocytes, or red blood cells, thrombocytes, or platelets, and leukocytes, or white blood cells). In adults, all three major types of blood cells are produced in the bone marrow of the skeletal system. The bone marrow contains immature cells, known as multipotent myeloid stem cells, that later differentiate into the various mature blood cells. Pancytopenia results from a reduction in the ability of the red bone marrow to produce adequate numbers of these mature blood cells.

extrapolation, 3 for database deficiencies, 3 for subchronic-to-chronic extrapolation) was used in deriving the RfC, with an overall confidence rating of medium. The RfC is based on suppressed absolute lymphocyte counts seen in humans under occupational exposure conditions (Rothman et al., 1996). The oral reference dose (RfD) for benzene was derived through route-to-route extrapolation of the results of benchmark dose (BMD) modeling of the absolute lymphocyte count data from the occupational epidemiologic study by Rothman et al. (1996), in which workers were exposed to benzene by inhalation. Based on these and other analyses, an RfD of 4.0×10^{-3} mg/kg/day was derived, with a total uncertainty factor of 300 and overall confidence rating of medium (U.S. EPA, 2003a). In addition, the Agency for Toxic Substances and Disease Registry Minimal Risk Level for acute exposure to benzene is $160 \mu\text{g}/\text{m}^3$ for 1-14 days exposure.

Since development of this RfC, there have appeared reports in the medical literature of benzene's hematotoxic effects in humans that provide data suggesting a wide range of hematological endpoints that are triggered at occupational exposures of less than 5 ppm (about $16 \text{ mg}/\text{m}^3$) (Qu et al., 2002) and at air levels of 1 ppm (about $3 \text{ mg}/\text{m}^3$) (Lan et al., 2004) or less among genetically susceptible populations. These studies had large sample sizes and extensive individual exposure monitoring. One recent study found benzene metabolites in mouse liver and bone marrow at environmental doses, indicating that even concentrations in urban air may elicit a biochemical response in rodents that indicates toxicity (Turteltaub and Mani, 2003). EPA has not evaluated these recent studies as part of the IRIS review process to determine what role they might play in any future revisions to the RfC.

7. Toluene

Toluene is found in evaporative as well as exhaust emissions from motor vehicles, and can be a significant contributor to secondary PM. Other aromatic compounds contribute to secondary organic PM as well (such as benzene), but the extent of their contribution has not been quantified. As a major constituent of gasoline, toluene (in BTEX) may be found in ground water due to leaking fuel storage tanks. Thus, exposure to toluene may occur by inhalation, ingestion, and dermal contact.

The health effects of toluene were recently described in a Toxicological Review by EPA (2005). The central nervous system (CNS) is the primary target for toluene toxicity in both humans and animals for acute and chronic exposures. CNS dysfunction (which is often reversible) and narcosis have been frequently observed in humans acutely exposed to low or moderate levels of toluene by inhalation; symptoms include fatigue, sleepiness, headaches, and nausea. Central nervous system depression has been reported to occur in chronic abusers exposed to high levels of toluene. Symptoms include ataxia, tremors, cerebral atrophy, nystagmus (involuntary eye movements), and impaired speech, hearing, and vision. Chronic inhalation exposure of humans to toluene also causes irritation of the upper respiratory tract, eye irritation, dizziness, headaches, and difficulty with sleep.

Human studies have also reported developmental effects, such as CNS dysfunction, attention deficits, and minor craniofacial and limb anomalies, in the children of women who abused toluene during pregnancy. A substantial database examining the effects of toluene in subchronic and chronic occupationally exposed humans exists. The weight of evidence from

these studies indicates neurological effects (i.e., impaired color vision, impaired hearing, decreased performance in neurobehavioral analysis, changes in motor and sensory nerve conduction velocity, headache, dizziness) as the most sensitive endpoints. The data from these human studies were found to be sufficient for EPA to develop an RfC of 5 mg/m³ for toluene exposure. The total uncertainty factor for the RfC is 10 (interspecies extrapolation) and the overall confidence in this RfC is high.

Data on the effects of toluene in humans following oral exposure are limited to case reports of accidental oral ingestions. A subchronic study of oral exposure to toluene in rodents (rats and mice) showed significant ($p < 0.05$) increases in absolute and relative weights of both the liver and kidney in male rats at doses greater than or equal to 446 mg/kg-day (NTP, 1990). Based on this study, EPA derived an RfD of 80 µg /kg-day for toluene oral exposure. The total uncertainty factor for the RfD is 3000 (10 for interspecies extrapolation, 10 for intraspecies variation, 10 for subchronic-to-chronic extrapolation and 3 for database insufficiencies and contradictions in immunotoxicity data) and the overall confidence in the RfD is medium.

Under the 2005 Guidelines for Carcinogen Risk Assessment, there is inadequate information to assess the carcinogenic potential of toluene (U.S. EPA, 2005). Toluene was not found to be carcinogenic in inhalation cancer bioassays of rats and mice exposed for life, but increased incidences of mammary cancer and leukemia were reported in a lifetime rat oral bioassay. Toluene has generally not been found to be genotoxic in short-term testing.

8. Ethylbenzene

Ethylbenzene is one of the BTEX compounds that are the major constituents of gasoline. It is found in both exhaust and evaporative emissions from gasoline-powered vehicles and may also be found in ground water due to leaking fuel storage tanks. Thus, exposure to ethylbenzene may occur by inhalation, ingestion, and dermal contact.

Limited information is available on the carcinogenic effects of ethylbenzene in humans and animals. Under the 1987 Cancer Guidelines, EPA (1991c) classified ethylbenzene as a Group D carcinogen, meaning it is not classifiable as a human carcinogen. This classification was the result of the lack of animal bioassays or human data to evaluate its carcinogenic potential at that time. In 1999, the National Toxicology Program (NTP) published the results of a 2-year chronic bioassay that concluded that there was clear evidence of ethylbenzene carcinogenicity in male rats (renal and testicular), and some evidence in female rats and both sexes of mice (NTP, 1999). These results, in the context of the full health science literature for ethylbenzene, are being reviewed by EPA in its ongoing review of the IRIS file for ethylbenzene.

Chronic exposure to ethylbenzene by inhalation in humans may result in effects on the hematological system, kidney and liver, and endocrine system (California EPA, 2007). No information is available on the developmental or reproductive effects of ethylbenzene in humans, although animal studies have reported developmental effects via inhalation. The data from these studies were found to be sufficient for EPA to develop an RfC of 1 mg/m³ for ethylbenzene exposure by inhalation (U.S. EPA, 1991c). The total uncertainty factor used was 300 (10 for intraspecies variation, 3 for interspecies extrapolation, 10 database insufficiencies), and

confidence in the RfC is considered low because no chronic studies or multi-generational developmental studies were available at the time. An animal study has reported effects on the blood, liver, and kidneys from oral exposure to ethylbenzene (Wolf et al., 1956). The data from this study were found to be sufficient for EPA to develop an RfD for oral ethylbenzene exposure of 100 µg/kg-day (U.S. EPA, 1991c). The total uncertainty factor was 1000 (10 for intraspecies variability, 10 for interspecies extrapolation, 10 for subchronic-to-chronic extrapolation), and confidence in this RfD is considered low because rats (single species) of only one sex were tested, no chronic studies were then available, and no other supporting oral toxicity data were found. Since the 1991 review, the NTP (1999) completed a chronic animal bioassay, as noted above; the relevance of the results from this study in reviewing the RfC will be evaluated in EPA's ongoing IRIS assessment. In addition, more recent studies characterizing the toxicity of ethylbenzene by the oral route are being considered in the ongoing review of the IRIS assessment (e.g., Mallerat et al., 2007).

With respect to short-term inhalation exposures, ATSDR has derived a 10 ppm Minimal Risk Level for exposure to ethylbenzene for 14 days or less, based on effects of the auditory system in animals. (ATSDR, 1999a; Cappaert et al., 1999, 2000, 2001).

9. Xylenes

Mixed xylenes are blended into gasoline as part of the BTEX compounds. Xylenes are emitted in the exhaust and evaporative emissions of gasoline-powered engines and may also be found in ground water due to leaking fuel storage tanks. Thus, exposure to xylenes may occur by inhalation, ingestion, and dermal contact. Xylenes, along with other aromatics, may be contributors to secondary organic PM as toluene and even benzene have been shown to be.

The health effects of xylenes were described in a Toxicological Review (U.S. EPA, 2003b). Chronic inhalation exposure in humans to mixed xylenes results primarily in central nervous system effects, such as headache, nausea, fatigue and also included eye and nose irritation and sore throat. Animal studies have reported developmental effects, such as an increased incidence of skeletal variations in fetuses, and fetal resorptions via inhalation. EPA (2003b) developed an RfC of 100 µg/m³ for xylenes based on impaired motor coordination in rats. The total uncertainty factor is 300 (10 for interspecies extrapolation, 10 for intraspecies variability, 10 for database deficiencies), and the confidence rating assigned to the RfC for xylenes is medium. Data from animal oral exposure studies showing decreased body weight and increased mortality were found to be sufficient for EPA (2003b) to develop an RfD of 200 µg/kg-day for oral xylene exposure. The RfD included a total uncertainty factor of 1000 and was assigned an overall confidence rating of medium.

Acute inhalation exposure to mixed xylenes in humans results in irritation of the nose and throat, gastrointestinal effects such as nausea, vomiting, and gastric irritation, mild transient eye irritation, and neurological effects (U.S. EPA, 2003b).

Inadequate information is available on the carcinogenic effects of mixed xylenes in humans, and animal studies have been inconclusive. Thus, data are inadequate for an assessment of the carcinogenic potential of xylenes (U.S. EPA, 2003b).

References

- Agency for Toxic Substances and Disease Registry (ATSDR). (1999a) Toxicological Profile for Ethylbenzene. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. Available at <http://www.atsdr.cdc.gov/toxprofiles/tp110.html>
- Agency for Toxic Substances and Disease Registry (ATSDR). (1999b) Toxicological Profile for Formaldehyde. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. Available at <http://www.atsdr.cdc.gov/toxprofiles/tp111.html>.
- Alden, C. L. (1986) A review of unique male rat hydrocarbon nephropathy. *Toxicol. Pathol.* 14: 109-111.
- Amberg, A.; Rosner, E.; Dekant, W. (2000) Biotransformation and kinetics of excretion of ethyl *tert*-butyl ether in rats and humans. *Toxicol. Sci.* 53: 194-201.
- American Conference of Governmental Industrial Hygienists (ACGIH). (1991) Acetaldehyde. In: Documentation of the threshold limit values and biological exposure indices. 6th ed. Cincinnati, OH: American Conference of Governmental Industrial Hygienists, Inc.; pp. 1-6.
- American Petroleum Institute. (1983) Four-week oral nephrotoxicity screening study in male F-344 rats: phases I and II with cover letter dated 121383 & EPA acknowledgement dated 031984. Washington, DC. EPA/OTS document # FYI-AX-1283-0280; TSCATS/031327. Available from: NTIS, Springfield, VA; OTS0000280-0.
- Amoore, J. E.; Hautala, E. (1983) Odor as an aid to chemical safety: odor thresholds compared with threshold limit values and volatilities for 214 industrial chemicals in air and water dilution. *J. Appl. Toxicol.* 3: 272-290.
- Appelman, L. M.; Woutersen, R. A.; Feron, V. J. (1982) Inhalation toxicity of acetaldehyde in rats. I. Acute and subacute studies. *Toxicology* 23: 293-307.
- Appelman, L. M.; Woutersen, R. A.; Feron, V. J.; Hoofman, R. N.; Notten, W. R. F. (1986) Effect of variable versus fixed exposure levels on the toxicity of acetaldehyde in rats. *J. Appl. Toxicol.* 6: 331-336.
- Belpoggi, F.; Soffritti, M.; Maltoni, C. (1995) Methyl-tertiary-butyl ether (MTBE) – a gasoline additive – causes testicular and lymphohaematopoietic cancers in rats. *Toxicol. Ind. Health* 11: 119-149.
- Belpoggi, F.; Soffritti, M.; Maltoni, C. (1998) Pathological characterization of testicular tumours and lymphomas-leukaemias, and of their precursors observed in Sprague-Dawley rats exposed to methyl-tertiary-butyl-ether (MTBE). *Eur. J. Oncol.* 3: 201-206.

- Belpoggi, F.; Soffritti, M.; Minardi, F.; Bua, L.; Cattin, E.; Maltoni, C. (2002) Results of long-term carcinogenicity bioassays on *tert*-amyl-methyl-ether (TAME) and di-isopropyl-ether (DIPE) in rats. In: Mehlman, M. A.; Bingham, E.; Landrigan, P. J.; Soffritti, M.; Belpoggi, F.; Melnick, R. L., eds. Carcinogenesis bioassays and protecting public health: commemorating the lifework of Cesare Maltoni and colleagues. Ann. N. Y. Acad. Sci. 982: 70-86.
- Berger, T.; Horner, C. M. (2003) In vivo exposure of female rats to toxicants may affect oocyte quality. Reprod. Toxicol. 17: 273-281.
- Berman, R. F.; Hannigan, J. H. (2000) Effects of prenatal alcohol exposure on the hippocampus: spatial behavior, electrophysiology, and neuroanatomy. Hippocampus 10: 94-100.
- Bird, M. G.; Burleigh-Flayer, H. D.; Chun, J. S.; Douglas, J. F.; Kneiss, J. J.; Andrews, L. S. (1997) Oncogenicity studies of inhaled methyl tertiary-butyl ether (MTBE) in CD-1 mice and F-344 rats. J. Appl. Toxicol. 17(suppl. 1): S45-S55.
- Blancato, J. N.; Evans, M. V.; Power, F. W.; Caldwell, J. C. (2007) Development and use of PBPK modeling and the impact of metabolism on variability in dose metrics for the risk assessment of methyl tertiary butyl ether (MTBE). J. Environ. Protect. Sci. 1: 29-51.
- Blumbach, K.; Pähler, A.; Deger, H. M.; Dekant, W. (2000) Biotransformation and male rat-specific renal toxicity of diethyl ethyl- and dimethyl methylphosphonate. Toxicol. Sci. 53: 24-32.
- Blue Ribbon Panel on Oxygenates in Gasoline (1999) Achieving Clean Air and Clean Water: Report of the Blue Ribbon Panel on Oxygenates in Gasoline. EPA420-R-99-021. Available at <http://www.epa.gov/otaq/consumer/fuels/oxypanel/blueribb.htm>.
- Boffetta, P.; Hashibe, M. (2006) Alcohol and cancer. Lancet Oncol. 7: 149-156.
- Borghoff, S. J.; Youtsey, N. L.; Swenberg, J. A. (1992) A comparison of European high test gasoline and PS-6 unleaded gasoline in their abilities to induce alpha-2u-globulin nephropathy and renal cell proliferation. Toxicol. Lett. 63: 21-33.
- Borghoff, S. J.; Murphy, J. E.; Medinsky, M. A. (1996) Development of a physiologically based pharmacokinetic model for methyl *tertiary*-butyl ether and *tertiary*-butanol in male Fischer-344 rats. Fundam. Appl. Toxicol. 30: 264-275.
- Brooks, T.; Meyer, A.; Hutson, D. (1988) The genetic toxicology of some hydrocarbon and oxygenated solvents. Mutagenesis 3: 227-232.
- Brooks, P. J.; Theruvathu, J. A. (2005) DNA adducts from acetaldehyde: implications for alcohol-related carcinogenesis. Alcohol 35: 187-193.

- Bundesinstitut für Risikobewertung (BfR). (2006) Toxicological Assessment of Formaldehyde. Opinion of BfR No. 023/2006 of 30 March 2006.
www.bfr.bund.de/cm/290/toxicological_assessment_of_formaldehyde.pdf
- Burnett, V. L.; Short, B. G.; Swenberg, J. A. (1989) Localization of alpha 2u-globulin within protein droplets of male rat kidney: immunohistochemistry using perfusion-fixed, GMA-embedded tissue sections. *J. Histochem. Cytochem.* 37: 813-818.
- California Department of Health Services (CDHS). (2006) MTBE: drinking water regulations and monitoring results. Sacramento, CA: Division of Drinking Water and Environmental Management. Available: <http://www.dhs.ca.gov/ps/ddwem/chemicals/MTBE/default.htm> [5 September, 2007].
- California Environmental Protection Agency. (1999) Public health goal for methyl tertiary butyl ether (MTBE) in drinking water. Sacramento, CA: Office of Environmental Health Hazard Assessment. Available: www.oehha.ca.gov/water/phg/allphgs.html [5 July, 2000].
- California Environmental Protection Agency. (2007) Long-term health effects of exposure to ethylbenzene. Sacramento, CA: Office of Environmental Health Hazard Assessment. Available: http://oehha.ca.gov/air/hot_spots/pdf/Ethylbenzene_FINAL110607.pdf [17 July, 2008].
- Cappaert, N. L. M.; Klis, S. F. L.; Muijsers, H., et al. (1999) The ototoxic effects of ethyl benzene in rats. *Hear. Res.* 137: 91-102.
- Cappaert, N. L. M.; Klis S. F. L.; Baretta A. B., et al. (2000) Ethyl benzene-induced ototoxicity in rats: A dose-dependent mid-frequency hearing loss. *J. Assoc. Res. Otolaryngol* 1(4): 292-299.
- Cappaert, N. L. M.; Klis, S. F. L.; Muijsers, H., et al. (2001) Simultaneous exposure to ethyl benzene and noise: Synergistic effects on outer hair cells. *Hear. Res.* 162(1-2): 67-79.
- Chen, W.-J. A.; Maier, S. E.; Parnell, S. E.; West, J. R. (2003) Alcohol and the developing brain: neuroanatomical studies. *Alcohol Res. Health* 27: 174-180.
- Cho, E.; Smith-Warner, S. A.; Ritz, J.; Van Den Brandt, P. A.; Colditz, G. A.; Folsom, A. R.; Freudenheim, J. L.; Giovannucci, E.; Goldbohm, R. A.; Graham, S.; Holmberg, L.; Kim, D.-H.; Malila, N.; Miller, A. B.; Pietinen, P.; Rohan, T. E.; Sellers, T. A.; Speizer, F. E.; Willett, W. C.; Wolk, A.; Hunter, D. J. (2004) Alcohol intake and colorectal cancer: a pooled analysis of 8 cohort studies. *Ann. Intern. Med.* 140: 603-613.
- Chun, J. S.; Burleigh-Flayer, H. D.; Kintigh, W. J. (1992) Methyl tertiary butyl ether: vapor inhalation oncogenicity study in Fischer 344 rats. Export, PA: Union Carbide, Bushy Run Research Center; BRRC report 91N0013B.

- Cirvello, J. D.; Radovsky, A.; Heath, J. E.; Farnell, D. R.; Lindamood, C., III. (1995) Toxicity and carcinogenicity of *t*-butyl alcohol in rats and mice following chronic exposure in drinking water. *Toxicol. Ind. Health* 11: 151-165.
- Chemical Industry Institute of Toxicology (CIIT). (1999) Formaldehyde: Hazard characterization and dose-response assessment for carcinogenicity by the route of inhalation. CIIT, September 28, 1999. Research Triangle Park, NC.
- CIT Safety & Health Research Laboratories. (2003) Ethyl tertiary butyl ether (ETBE), CAS No. 637-92-3: Reproductive/developmental toxicity dose-range finding/probe study by the oral route (gavage) route in two strains of rat. CIT under contract for TOTAL France S. A., Evreux, France.
- CIT Safety & Health Research Laboratories. (2004a) Ethyl tertiary butyl ether (ETBE): prenatal developmental toxicity study by the oral route (gavage) in rats. Paris, France: TOTAL France S.A.; CIT/study no. 24860 RSR.
- CIT Safety & Health Research Laboratories. (2004b) Ethyl tertiary butyl ether (ETBE): two-generation study (reproduction and fertility effects) by oral route (gavage) in rats. Volumes 1 - 5. Paris, France: TOTAL France S.A.; CIT/study no. 24859 RSR.
- Code of Federal Regulations. (1994) Registration of fuels and fuel additives. C. F. R. 40: part 79.
- Coggon, D., Harris, E. C.; Poole, J.; Palmer, K. T. (2003) Extended follow-up of a cohort of British chemical workers exposed to formaldehyde. *J. National Cancer Inst.* 95: 1608-1615.
- Coles, C. D.; Smith, I.; Fernhoff, P. M.; Falek, A. (1985) Neonatal neurobehavioral characteristics as correlates of maternal alcohol use during gestation. *Alcohol.: Clin. Exp. Res.* 9: 454-460.
- Coles, C. D.; Smith, I. E.; Falek, A. (1987a) Prenatal alcohol exposure and infant behavior: immediate effects and implications for later development. *Adv. Alcohol Subst. Abuse* 6: 87-104.
- Coles, C. D.; Smith, I. E.; Lancaster, J. S.; Falek, A. (1987b) Persistence over the first month of neurobehavioral differences in infants exposed to alcohol prenatally. *Infant Behav. Dev.* 10: 23-37.
- Coles, C. D.; Brown, R. T.; Smith, I. E.; Platzman, K. A.; Erickson, S.; Falek, A. (1991) Effects of prenatal alcohol exposure at school age. I. Physical and cognitive development. *Neurotoxicol. Teratol.* 13: 357-367.
- Coles, C. D.; Platzman, K. A.; Smith, I.; James, M. E.; Falek, A. (1992) Effects of cocaine and alcohol use in pregnancy on neonatal growth and neurobehavioral status. *Neurotoxicol. Teratol.* 14: 23-33.

- Conolly, R. B.; Kimbell, J. S.; Janszen, D.; Schlosser, P. M.; Kalisak, D.; Preston, J.; Miller, F. J. (2003) Biologically motivated computational modeling of formaldehyde carcinogenicity in the F344 rat. *Toxicol. Sci.* 75: 432-447.
- Conolly, R. B.; Kimbell, J. S.; Janszen, D.; Schlosser, P. M.; Kalisak, D.; Preston, J.; Miller, F. J. (2004) Human respiratory tract cancer risks of inhaled formaldehyde: Dose-response predictions derived from biologically-motivated computational modeling of a combined rodent and human dataset. *Toxicol. Sci.* 82: 279-296.
- Coon R. A.; Jones, R. A.; Jenkins, L. J., Jr.; Siegel, J. (1970) Animal inhalation studies on ammonia, ethylene glycol, formaldehyde, dimethylamine, and ethanol. *Toxicol. Appl. Pharmacol.* 16:646-655.
- Corrao, G.; Bagnardi, V.; Zambon, A.; La Vecchia, C. (2004) A meta-analysis of alcohol consumption and the risk of 15 diseases. *Prev. Med.* 38: 613-619.
- Corti, M.; Snyder, C. A. (1996) Influences of gender, development, pregnancy and ethanol consumption on the hematotoxicity of inhaled 10 ppm benzene. *Arch. Toxicol.* 70: 209-217.
- Dahl, A. R. (1989) The cyanide-metabolizing enzyme rhodanese in rat nasal respiratory and olfactory mucosa. *Toxicol. Lett.* 45: 199-205.
- Dalbey, W.; Feuston, M. (1996) Subchronic and developmental toxicity studies of vaporized diisopropyl ether in rats. *J. Toxicol. Environ. Health* 49: 29-43.
- Daniel, M. A.; Evans, M. A. (1982) Quantitative comparison of maternal ethanol and maternal tertiary butanol diet on postnatal development. *J. Pharmacol. Exp. Ther.* 222: 294-300
- Daughtrey, W. C.; Bird, M. G. (1995) Genotoxicity and twenty-eight-day subchronic toxicity studies on tertiary amyl methyl ether. *J. Appl. Toxicol.* 15: 313-319.
- Dorman, D. C.; Struve, M. F.; Wong, B. A.; Morgan, K. T.; Janszen, D. B.; Gross, E. B.; Bond, J. A. (1997) Neurotoxicological evaluation of ethyl tertiary-butyl ether following subchronic (90-day) inhalation in the Fischer 344 rat. *J. Appl. Toxicol.* 17: 235-242.
- Driscoll, C. D.; Streissguth, A. P.; Riley, E. P. (1990) Prenatal alcohol exposure comparability of effects in humans and animal models. *Neurotoxicol. Teratol.* 12: 231-238.
- Dudek, B. C.; Phillips, T. J. (1983) Locomotor stimulant and intoxicant properties of methanol, ethanol, tertiary butanol and pentobarbital in Long-Sleep and Short-Sleep mice. *Subst Alcohol Actions Misuse.* 4: 31-6.
- Dumitrescu, R. G.; Shields, P. G. (2005) The etiology of alcohol-induced breast cancer. *Alcohol* 35: 213-225.

- Faulkner, T. P.; Wiechart, J. D.; Hartman, D. M.; Hussain, A. S. (1989) The effects of prenatal tertiary butanol administration in CBA/J and C57BL/6J mice. *Life Sci.* 45: 1989-1995.
- Fazzalari, F. A., ed. (1978) Compilation of odor and taste threshold values data. Philadelphia, PA: American Society for Testing and Materials; ASTM data series DS 48A.
- Fiedler, N.; Kelly-McNeil, K.; Mohr, S.; Lehrer, P.; Opiekun, R. E.; Lee, C.-W.; Wainman, T.; Hamer, R.; Weisel, C.; Edelberg, R.; Liroy, P. J. (2000) Controlled human exposure to methyl tertiary butyl ether in gasoline: symptoms, psychophysiologic and neurobehavioral responses of self-reported sensitive persons. *Environ. Health Perspect.* 108: 753-763.
- Fowlie, A. J.; Grasso, P.; Bridges, J. W. (1987) Renal and hepatic lesions induced by 2,2,4-trimethylpentane. *J. Appl. Toxicol.* 7: 335-341.
- Franklin, P.; Dingle, P.; Stick, S. (2000) Raised exhaled nitric oxide in healthy children is associated with domestic formaldehyde levels. *Am. J. Respir. Crit. Care Med.* 161: 1757-1759.
- Fujimaki, H.; Kurokawa, Y.; Kunugita, N.; Kikuchi, M.; Sato, F.; Arashidani, K. (2004) Differential immunogenic and neurogenic inflammatory responses in an allergic mouse model exposed to low levels of formaldehyde. *Toxicol.* 197:1-13.
- Garrett M. H.; Hooper, M. A.; Hooper, B. M.; Rayment, P. R.; Abramson, M. J. (1999) Increased risk of allergy in children due to formaldehyde exposure in homes. *Allergy* 54: 330-337.
- Goodlett, C. R.; Horn, K. H.; Zhou, F. C. (2005) Alcohol teratogenesis: mechanisms of damage and strategies for intervention. *Exp. Biol. Med.* 230: 394-406.
- Goodman, J. E.; Gaylor, D.; Beyer, L. A.; Rhomberg, L. R.; Beck, B. D. (2007) Effects of MTBE on Leydig cell tumors in Sprague-Dawley rats: range of possible poly-3 results. *Regul. Toxicol. Pharmacol.*: in press.
- Green D. J.; Sauder, L. R.; Kulle, T.J. (1987) Acute responses to 3 ppm formaldehyde in exercising healthy nonsmoker and asthmatics. *Am. Rev. Respir. Dis.* 135(6): 1261-1266.
- Gunzerath, L.; Faden, V.; Zakhari, S.; Warren, K. (2004) National institute on alcohol abuse and alcoholism report on moderate drinking. *Alcsm Clin. Exp. Res.* 28: 829-847.
- Hackney, J. F.; Engelman, R. W.; Good, R. A. (1992) Ethanol calories do not enhance breast cancer in isocalorically fed C3H/Ou mice. *Nutr. Cancer* 18: 245-253.
- Hauptmann, M.; Lubin, J. H.; Stewart, P. A.; Hayes, R. B.; Blair, A. (2003) Mortality from lymphohematopoietic malignancies among workers in formaldehyde industries. *J. Natl. Cancer I.* 95: 1615-1623.

- Hauptmann, M.; Lubin, J. H.; Stewart, P. A.; Hayes, R. B.; Blair, A. (2004) Mortality from solid cancers among workers in formaldehyde industries. *Am. J. Epidemiol.* 159: 1117-1130.
- Hayes, R. B.; Yin, S.; Dosemeci, M.; Li, G.; Wacholder, S.; Travis, L. B.; Li, C.; Rothman, N.; Hoover, R. N.; Linet, M. S. (1997) Benzene and the dose-related incidence of hematologic neoplasms in China. *J. Nat. Cancer Inst.* 89: 1065-1071.
- Hayes, R. B.; Songnian, Y.; Dosemeci, M.; Linet, M. (2001) Benzene and lymphohematopoietic malignancies in humans. *Am J. Indust. Med.* 40: 117-126.
- Health Canada (2001) Priority Substances List Assessment Report. Formaldehyde. Environment Canada, Health Canada, February 2001. The document may be accessed at http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/psl2-lsp2/formaldehyde/index_e.html
- Health Effects Institute. (1996) The potential health effects of oxygenates added to gasoline: a review of the current literature, a special report of the Institute's Oxygenates Evaluation Committee. Cambridge, MA: Health Effects Institute, Oxygenates Evaluation Committee.
- Hilakivi-Clarke, L.; Cabanes, A.; De Assis, S.; Wang, M.; Khan, G.; Shoemaker, W. J.; Stevens, R. G. (2004) In utero alcohol exposure increases mammary tumorigenesis in rats. *Br. J. Cancer* 90: 2225-2231.
- Holmberg, B.; Ekström, T. (1995) The effects of long-term oral administration of ethanol on Sprague-Dawley rats – a condensed report. *Toxicology* 96: 133-145.
- Homann, N. (2001) Alcohol and cancer: the role of acetaldehyde. In: Agarwal, D. P.; Seitz, H. K., eds. *Alcohol in health and disease* [papers from the international Titisee symposium on health effects of alcohol intake; December 1999; Titisee, Germany]. New York, NY: Marcel Dekker Inc.; pp. 473-492.
- Hong, J.-Y.; Wang, Y.-Y.; Mohr, S. N.; Bondoc, F. Y.; Deng, C. (2001) Human cytochrome P450 isozymes in metabolism and health effects of gasoline ethers. In: *Metabolism of ether oxygenates*. Cambridge, MA: Health Effects Institute; research report no. 102; pp. 7-27.
- Horn-Ross, P. L.; Hoggatt, K. J.; West, D. W.; Krone, M. R.; Stewart, S. L.; Anton, H.; Bernstein, C. L.; Deapen, D.; Peel, D.; Pinder, R.; Reynolds, P.; Ross, R. k.; Wright, W.; Ziogas, A. (2002) Recent diet and breast cancer risk: the California Teachers study (USA). *Cancer Causes Control* 13: 407-415.
- Horvath, E. P; Anderson H.; Pierce W. E. (1988) Effects of formaldehyde on the mucous membranes and lungs: A study of an industrial population. *JAMA* 259: 701-707.

- Huntingdon Life Sciences. (1997) A 13-week inhalation toxicity/neurotoxicity study of tert-amyl methyl ether (TAME) in the rat and mouse via whole-body exposures with a 4-week recovery period (volumes I - VI) [final report]. Washington, DC: American Petroleum Institute, Health and Environmental Sciences Department; study no. 95-6101.
- Huntingdon Life Sciences. (2004) TBA: reproduction/development toxicity screening in rats with cover letter dated Feb. 27, 2004. Final report. Washington DC. Study no. 03-4254 submitted by Lyondell Chemical Company. Available from: NTIS, Springfield, VA; 89040000106.
- Interagency Oxygenated Fuels Assessment Steering Committee. (1996) Interagency assessment of potential health risks associated with oxygenated gasoline. Washington, DC: National Science and Technology Council and Office of Science and Technology Policy.
- Interagency Oxygenated Fuels Assessment Steering Committee. (1997) Interagency assessment of oxygenated fuels. Washington, DC: National Science and Technology Council, Committee on Environment and Natural Resources and Office of Science and Technology Policy.
- International Agency for Research on Cancer (IARC). (1985) Acetaldehyde. In: Allyl compounds, aldehydes, epoxides and peroxides. Lyon, France: International Agency for Research on Cancer; pp. 101-132. (IARC monographs on the evaluation of carcinogenic risks to humans: v. 36).
- International Agency for Research on Cancer (IARC). (1988) Alcohol drinking. Lyon, France: International Agency for Research on Cancer. (IARC monographs on the evaluation of carcinogenic risks to humans, v. 44).
- International Agency for Research on Cancer (IARC). (1999) Methyl tert-butyl ether. In: Some chemicals that cause tumours of the kidney or urinary bladder tumours in rodents, and some other substances. Lyon, France: International Agency for Research on Cancer; pp. 339-383. (IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans: v. 73).
- Irons, R. D.; Stillman, W. S.; Colagiovanni, D. B.; Henry, V. A. (1992) Synergistic action of the benzene metabolite hydroquinone on myelopoietic stimulating activity of granulocyte/macrophage colony-stimulating factor in vitro. *Proc. Natl. Acad. Sci.* 89: 3691-3695.
- Jacobson, J. L.; Jacobson, S. W.; Sokol, R. J.; Martier, S. S.; Ager, J. W. (1993a) Prenatal alcohol exposure and infant information processing ability. *Child Develop* 64: 1706-1721.

- Jacobson, J. L.; Jacobson, S. W.; Sokol, R. J.; Martier, S. S.; Ager, J. W.; Kaplan-Estrin M.G. (1993b) Teratogenic effects of alcohol on infant development. *Alcsm Clin. Exp. Res.* 7(1): 174-183.
- Jacobson, J. L.; Jacobson, S. W.; Sokol, R. J. (1994) Effects of prenatal exposure to alcohol, smoking, and illicit drugs on postpartum somatic growth. *Alcsm Clin. Exp. Res.* 18(2): 317-323.
- Jacobson, J. L.; Jacobson, S. W.; Sokol, R. J.; Ager, J. W., Jr. (1998) Relation of maternal age and pattern of pregnancy drinking to functionally significant cognitive deficit in infancy. *Alcsm Clin. Exp. Res.* 22: 345-351.
- Jung, W-W.; Kim, E-M.; Lee, E-H.; Yun, H-J.; Ju, H-R.; Jeong, M-J.; Hwang, K-W.; Sul, D.; Kang, H-S. (2007) Formaldehyde exposure induces airway inflammation by increasing eosinophil infiltrations through the regulation of reactive oxygen species production. *Environ. Toxicol. Pharmacol.* 24: 174-182.
- Keller, K. A.; Snyder, C. A. (1986) Mice exposed in utero to low concentrations of benzene exhibit enduring changes in their colony forming hematopoietic cells. *Toxicology* 42: 171-181.
- Keller, K. A.; Snyder, C. A. (1988) Mice exposed in utero to 20 ppm benzene exhibit altered numbers of recognizable hematopoietic cells up to seven weeks after exposure. *Fundam. Appl. Toxicol.* 10: 224-232.
- Kissling, G. E.; Portier, C. J.; Huff, J. (2007) MtBE and cancer in animals: statistical issues with poly-3 survival adjustments for lifetime studies. *Regul. Toxicol. Pharmacol.*: in press.
- Kloss, M. W.; Swenberg, J.; Bus, J. S. (1986) Sex-dependent differences in disposition of w[14C-5]-2,2,4-trimethylpentane in Fischer 344 rats with cover sheet. Washington DC. EPA document no. 86-870001586; TSCATS/400212. Available from: NTIS, Springfield, VA; OTS0516167.
- Lan, Q., Zhang, L., Li, G., Vermeulen, R., Weinberg, R. S.; Dosemeci, M.; Rappaport, S. M.; Shen, M.; Alter, B. P.; Wu, Y.; Kopp, W.; Waidyanatha, S.; Rabkin, C.; Guo, W.; Chanock, S.; Hayes, R. B.; Linet, M.; Kim, S.; Yin, S.; Rothman, N.; Smith, M. T. (2004). Hematotoxicity in workers exposed to low levels of benzene. *Science* 306: 1774-1776.
- Latriano, L; Goldstein, B. D.; Witz, G. (1986) Formation of muconaldehyde, an open ring metabolite of benzene, in mouse liver microsomes: an additional pathway of toxic metabolites. *Proc. Natl. Acad. Sci. USA* 83: 8356-8360.
- Lin, Y-S., Vermeulen, R., Tsai, C. H., Suramya, W., Lan, Q., Rothman, N., Smith, M. T., Zhang, L., Shen, M., Songnian, Y., Kim, S., Rappaport, S. M. (2007) Albumin adducts of electrophilic benzene metabolites in benzene-exposed and control workers. *Environ.*

Health Perspec. 115: 28-34.

- Lindamood, C., III; Farnell, D. R.; Giles, H. D.; Prejean, J. D.; Collins, J. J.; Takahashi, K.; Maronpot, R. R. (1992) Subchronic toxicity studies of *t*-butyl alcohol in rats and mice. *Fundam. Appl. Toxicol.* 19: 91-100.
- Lock, E. A.; Charbonneau, M.; Strasser, J.; Swenberg, J. A.; Bus, J. S. (1987a) 2,2,4-trimethylpentane-induced nephrotoxicity: II. the reversible binding of a TMP metabolite to a renal protein fraction containing "alpha"_{2u}-globulin. *Toxicol. Appl. Pharmacol.* 91: 182-192.
- Lock, E. A.; Stonard, M. D.; Elcombe, C. R. (1987b) The induction of ω and β -oxidation of fatty acids and effect on α_{2u} globulin content in the liver and kidney of rats administered 2,2,4-trimethylpentane. *Xenobiotica* 17: 513-522.
- Longnecker, M. P.; Newcomb, P. A.; Mittendorf, R.; Greenberg, E. R.; Clapp, R. W.; Bogdan, G. F.; Baron, J.; MacMahon, B.; Willett, W. C. (1995) Risk of breast cancer in relation to lifetime alcohol consumption. *J. Natl. Cancer Inst.* 87: 923-929.
- Loury, D. J.; Smith-Oliver, T.; Strom, S.; Jirtle, R.; Michalopoulos, G.; Butterworth, B. E. (1986) Assessment of unscheduled and replicative DNA synthesis in hepatocytes treated *in vivo* and *in vitro* with unleaded gasoline or 2,2,4-trimethylpentane. *Toxicol. Appl. Pharmacol.* 85: 11-23.
- Maltoni, C.; Belpoggi, F.; Soffritti, M.; Minardi, F. (1999) Comprehensive long-term experimental project of carcinogenicity bioassays on gasoline oxygenated additives: plan and first report of results from the study on ethyl-tertiary-butyl ether (ETBE). *Eur. J. Oncol.* 4: 493-508.
- McKinney, P. A.; Alexandria, F. E.; Cartwright, R. A.; et al. (1991) Parental occupations of children with leukaemia in West Cumbria, North Humberside, and Gateshead. *Br. Med. J.* 302: 681-687.
- McLaren, J.; Boulikas, T.; Vamvakas, S. (1994) Induction of poly(ADP-ribosyl)ation in the kidney after *in vivo* application of renal carcinogens. *Toxicology* 88: 101-112.
- Medinsky, M. A.; Wolf, D. C.; Cattley, R. C.; Wong, B.; Janszen, D. B.; Farris, G. M.; Wright, G. A.; Bond, J. A. (1999) Effects of a thirteen-week inhalation exposure to ethyl tertiary butyl ether on Fischer-344 rats and CD-1 mice. *Toxicol. Sci.* 51: 108-118.
- Mellert, W.; Deckhardt, K.; Kaufmann, W.; van Ravenzwaay, B. (2007) Ethylbenzene: 4- and 13-week rat oral toxicity. *Arch. Toxicol.* 81: 361-370.
- Myou, S.; Fujimura, M.; Nishi K.; Ohka, T.; and Matsuda, T. (1993) Aerosolized acetaldehyde induces histamine-mediated bronchoconstriction in asthmatics. *Am. Rev. Respir. Dis.* 148(4 Pt 1): 940-943.

- National Research Council; Committee on Toxicological and Performance Aspects of Oxygenated and Reformulated Motor Vehicle Fuels. (1996) Toxicological and performance aspects of oxygenated motor vehicle fuels. Washington, DC: National Academy Press. Available: <http://www.nap.edu/books/0309055458/html/> [3 October, 2001].
- National Toxicology Program (NTP). (1990) Toxicology and carcinogenesis studies of toluene (CAS No. 108-88-3) in F344/N rats and B5C3F1 mice (inhalation studies). Research Triangle Park, NC: U.S. Department of Health and Human Services; NTP Technical Report no. TR-371. Available from: National Institute of Environmental Health Sciences, Research Triangle Park, NC.
- National Toxicology Program. (1995) Toxicology and carcinogenesis studies of t-butyl alcohol (CAS no. 75-65-0) in F344/N rats and B6C3F1 mice. (Drinking water studies). Research Triangle Park, NC: U.S. Department of Health and Human Services, National Institutes of Health. (National Toxicology Program technical report series no. TR-436). Available: http://ntp.niehs.nih.gov/ntp/htdocs/LT_rpts/tr436.pdf [17 August, 2007].
- National Toxicology Program. (1997) NTP technical report on toxicity studies of t-butyl alcohol (CAS no. 75-65-0) administered by inhalation to F344/N rats and B6C3F1 mice. Research Triangle Park, NC: U.S. Department of Health and Human Services, National Institutes of Health. Report no. NTP-TOXICITY-SER-53; NIH/PUB-97-3942. Available: http://ntp.niehs.nih.gov/ntp/htdocs/ST_rpts/tox053.pdf [24 August, 2007] and from: NTIS, Springfield, VA; PB98-108905.
- National Toxicology Program. (1999) Toxicology and carcinogenesis studies of ethylbenzene (CAS No.100-41-4) in F344/N rats and B6C3F1 mice (inhalation studies). Research Triangle Park, NC: U.S. Department of Health and Human Services, National Institutes of Health. National Toxicology Program Technical Report No. 466.
- Nelson, B. K.; Brightwell, W. S.; MacKenzie, D. R.; Khan, A.; Burg, J. R.; Weigel, W. W.; Goad, P. T. (1985a) Teratological assessment of methanol and ethanol at high inhalation levels in rats. *Fundam. Appl. Toxicol.* 5: 727-736.
- Nelson, B. K.; Brightwell, W. S.; Burg, J. R. (1985b) Comparison of behavioral teratogenic effects of ethanol and n-propanol administered by inhalation to rats. *Neurobehav. Toxicol. Teratol.* 7: 779-783.
- Nelson, B. K.; Brightwell, W. S.; Mackenzie-Taylor, D. R.; Burg, J. R.; Massari, V. J. (1988) Neurochemical, but not behavioral, deviations in the offspring of rats following prenatal or paternal inhalation exposure to ethanol. *Neurotoxicol. Teratol.* 10: 55-22.
- Nelson, B. K.; Brightwell, W. S.; Khan, A.; Burg, J. R.; Goad, P. T. (1989) Lack of selective developmental toxicity of three butanol isomers administered by inhalation to rats. *Fundam. Appl. Toxicol.* 12: 469-479.

- Nelson, B. K.; Conover, D. L.; Brightwell, W. S.; Shaw, P. B.; Werren, D.; Edwards, R. M.; Lary, J. M. (1991) Marked increase in the teratogenicity of the combined administration of the industrial solvent 2-methoxyethanol and radiofrequency radiation in rats. *Teratology* 43: 621-634.
- Nihlén, A.; Löf, A.; Johanson, G. (1998a) Experimental exposure to methyl *tertiary*-butyl ether: I. Toxicokinetics in humans. *Toxicol. Appl. Pharmacol.* 148: 274-280.
- Nihlén, A.; Wålander, R.; Löf, A.; Johanson, G. (1998b) Experimental exposure to methyl *tertiary*-butyl ether: II. Acute effects in humans. *Toxicol. Appl. Pharmacol.* 148: 281-287.
- Peters, E. S.; McClean, M. D.; Liu, M.; Eisen, E.A.; Mueller, N; Kelsey, K. T. (2005) The ADH1C polymorphism modifies the risk of squamous cell carcinoma of the head and neck associated with alcohol and tobacco use. *Cancer Epidemiol. Biomarkers Prev.* 14(2): 476-482.
- Phillips, B. J.; Jenkinson, P. (2001) Is ethanol genotoxic? A review of the published data. *Mutagenesis* 16: 91-101.
- Pinkerton, L. E. (2004) Mortality among a cohort of garment workers exposed to formaldehyde: an update. *Occup. Environ. Med.* 61: 193-200.
- Poschl, G.; Seitz, H. K. (2004) Alcohol and cancer. *Alcohol* 39: 155-165.
- Prah, J. D.; Goldstein, G. M.; Devlin, R.; Otto, D.; Ashley, D.; House, D.; Cohen, K. L.; Gerrity, T. (1994) Sensory, symptomatic, inflammatory, and ocular responses to and the metabolism of methyl tertiary butyl ether in a controlled human exposure experiment. *Inhalation Toxicol.* 6: 521-538.
- Prah, J.; Ashley, D.; Blount, B.; Case, M.; Leavens, T.; Pleil, J.; Cardinali, F. (2004) Dermal, oral, and inhalation pharmacokinetics of methyl tertiary butyl ether (MTBE) in human volunteers. *Toxicol. Sci.* 77: 195-205.
- Prescott-Mathews, J. S.; Wolf, D. C.; Wong, B. A.; Borghoff, S. J. (1997) Methyl *tert*-butyl ether causes α 2u-globulin nephropathy and enhanced renal cell proliferation in male Fischer-344 rats. *Toxicol. Appl. Pharmacol.* 143: 301-314.
- Qu, Q., R. Shore, G. Li, X. Jin, L.C. Chen, B. Cohen, et al. (2002). Hematological changes among Chinese workers with a broad range of benzene exposures. *Am. J. Industr. Med.* 42: 275-285.
- Rappaport, S. M.; Waidyanatha, S.; Qu, Q.; Shore, R.; Jin, X.; Cohen, B.; Chen, L.; Melikian, A.; Li, G.; Yin, S.; Yan, H.; Xu, B.; Mu, R.; Li, Y.; Zhang, X.; and Li, K. (2002) Albumin adducts of benzene oxide and 1,4-benzoquinone as measures of human benzene

- metabolism. *Cancer Research*. 62: 1330-1337.
- Rappaport, S. M.; Waidyanatha, S.; Qu, Q.; Yeowell-O'Connell, K.; Rothman, N.; Smith M. T.; Zhang, L.; Qu, Q.; Shore, R.; Li, G.; Yin, S. (2005) Protein adducts as biomarkers of human enzyme metabolism. *Chem. Biol. Interact.* 153-154: 103-109.
- Richardson, K. A.; Wilmer, J. L.; Smith-Simpson, D.; Skopek, T. R. (1986) Assessment of the genotoxic potential of unleaded gasoline and 2,2,4-trimethylpentane in human lymphoblasts *in vitro*. *Toxicol. Appl. Pharmacol.* 82: 316-322.
- Riley, E. P.; McGee, C. L.; Sowell, E. R. (2004) Teratogenic effects of alcohol: a decade of brain imaging. *Am. J. Med. Genet. Part C: Semin. Med. Genet.* 127: 35-41.
- Riley, E. P.; McGee, C. L. (2005) Fetal alcohol spectrum disorders: an overview with emphasis on changes in brain and behavior. *Exp. Biol. Med.* 230: 357-365.
- Riveros-Rosas, H.; Julian-Sanchez, A.; Pina, E. (1997) Enzymology of ethanol and acetaldehyde metabolism in mammals. *Arch. Med. Res.* 28: 453-471.
- Rodriguez, S. C.; Dalbey, W. E. (1997) Subchronic neurotoxicity of vaporized diisopropyl ether in rats. *Int. J. Toxicol.* 16: 599-610.
- Ross, D. (1996) Metabolic basis of benzene toxicity. *Eur. J. Haematol.* 57: (suppl): 111-118.
- Rothman, N.; Li, G. L.; Dosemeci, M.; et al. (1996) Hematotoxicity among Chinese workers heavily exposed to benzene. *Am. J. Ind. Med.* 29: 236-246.
- Rumchev, K. B.; Spickett, J. T.; Bulsara, M. K.; Phillips, M. R.; Stick, S. M. (2002) Domestic exposure to formaldehyde significantly increases the risk of asthma in young children. *Eur. Respir. J.* 20: 403-408.
- Saito, K.; Kaneko, H.; Isobe, N.; Nakatsuka, I.; Yoshitake, A.; Yamada, H. (1992) Differences in α_{2u} -globulins increased in male rat kidneys following treatment with several α_{2u} -globulin accumulating agents: cysteine protease(s) play(s) an important role in production of kidney-type- α_{2u} -globulin. *Toxicology* 76: 177-186.
- Sampson, P. D.; Streissguth, A. P.; Bookstein, F. L.; Barr, H. M. (2000) On categorizations in analyses of alcohol teratogenesis. *Environ. Health Perspect.* 108(suppl. 3): 421-428.
- Sauder, L. R.; Chatham, M. D.; Green, D. J. (1986) Acute pulmonary response to formaldehyde exposure in healthy nonsmokers. *J. Occup. Med.* 28:420-424.
- Short, B. G.; Burnett, V. L.; Swenberg, J. A. (1986) Histopathology and cell proliferation induced by 2,2,4-trimethylpentane in the male rat kidney. *Toxicol. Pathol.* 14: 194-203.

- Short, B. G.; Burnett, V. L.; Swenberg, J. A. (1989) Elevated proliferation of proximal tubule cells and localization of accumulated α_{2u} -globulin in F344 rats during chronic exposure to unleaded gasoline or 2,2,4-trimethylpentane. *Toxicol. Appl. Pharmacol.* 101: 414-431.
- Shu, X. O.; Gao, Y. T.; Brinton, L. A.; Zheng, W.; Brinton, L. A.; Linet, M. S.; Fraumeni, J. F. Jr. (1988) A population based case-control study of childhood leukemia in Shanghai. *Cancer* 62: 635-644.
- Singletary, K. W.; Gapstur, S. M. (2001) Alcohol and breast cancer: review of epidemiologic and experimental evidence and potential mechanisms. *J. Am. Med. Assoc.* 286: 2143-2151.
- Slawecki, C. J.; Thorsell, A.; Ehlers, C. L. (2004) Long-term neurobehavioral effects of alcohol or nicotine exposure in adolescent animal models. *Ann. N. Y. Acad. Sci.* 1021: 448-452.
- Smith, M. T. (1996) The mechanism of benzene-induced leukemia: a hypothesis and speculations on the causes of leukemia. *Environ. Health Perspec.* 104: 1219-1225.
- Soffritti, M.; Belpoggi, F.; Cevolani, D.; Guarino, M.; Padovani, M.; Maltoni, C. (2002) Results of long-term experimental studies on the carcinogenicity of methyl alcohol and ethyl alcohol in rats. *Ann. N. Y. Acad. Sci.* 982: 46-69.
- Sood, B; Delaney-Black, V; Covington, C; Nordstrom-Klee, B; Ager, J; Templin, T; Janisse, J; Martier, S; Sokol, RJ. (2001) Prenatal alcohol exposure and childhood behavior at age 6 to 7 years: I. Dose-response effect. *Pediatrics* 108(2):1-9.
- Stonard, M. D.; Phillips, P. G. N.; Foster, J. R.; Simpson, M. G.; Lock, E. A. (1986) α_{2u} -Globulin: measurement in rat kidney following administration of 2,2,4-trimethylpentane. *Toxicology* 41: 161-168.
- Streissguth, A. P.; Barr, H. M.; Sampson, P. D.; Parrish-Johnson, J. C.; Kirchner, G. L.; Martin, D. C. (1986a) Attention, distraction and reaction time at age 7 years and prenatal alcohol exposure. *Neurobehav. Toxicol. Teratol.* 8: 717-725.
- Streissguth, A. P.; Sampson, P. D.; Barr, H. M.; Clarren, S. K.; Martin, D. C. (1986b) Studying alcohol teratogenesis from the perspective of the fetal alcohol syndrome: methodological and statistical issues. *Ann. N. Y. Acad. Sci.* 477: 63-86.
- Streissguth, A. P.; Martin, D. C.; Barr, H. (1989) Neurobehavioral dose-response effects of prenatal alcohol exposure in humans from infancy to adulthood. *Ann. N. Y. Acad. Sci.* 562: 145-158.
- Subramaniam, R. P.; Crump, K. S.; Van Landingham, C.; White, P.; Chen, C.; Schlosser, P. M. (2007) Uncertainties in the CIIT model for formaldehyde – Induced carcinogenicity in the rat: A limited sensitivity analysis–I. *Risk Analysis* 27: 1237-1254.

- Thurman, R. G.; Winn, K.; Urquhart, B. (1980) Rat brain cyclic AMP levels and withdrawal behavior following treatment with t-butanol. In: Begleiter, H., ed. Biological effects of alcohol: proceedings of the international symposium on biological research in alcoholism; June, 1978; Zurich, Switzerland. New York, NY: Plenum Press; pp. 271-281. [Advances in experimental medicine and biology: v. 126].
- TRC Environmental Corporation. (1993) Odor threshold studies performed with gasoline and gasoline combined with MTBE, ETBE and TAME. Washington, DC: American Petroleum Institute; API publication no. 4592.
- Turteltaub, K. W.; Mani, C. (2003) Benzene metabolism in rodents at doses relevant to human exposure from urban air. Health Effects Inst. Research Report No.113.
- Tyl, R. W.; Myers, C. B.; Marr, M. C.; Fail, P. A.; Seely, J. C.; Elswick, B.; James, A.; Welsch, F. (2003) Two-generation reproductive toxicity study of inhaled tertiary amyl methyl ether (TAME) vapor in CD rats. J. Appl. Toxicol. 23: 397-410.
- U.S. Department of Health and Human Services (DHHS). (2000a) 9th report on carcinogens, 2000. Washington, DC: Public Health Service, National Toxicology Program. Available: <http://ehis.niehs.nih.gov/roc/toc9.html> [30 August, 2000].
- U.S. Department of Health and Human Services. (2000b) 10th special report to the U.S. Congress on alcohol and health. Washington, DC: National Institute on Alcohol Abuse and Alcoholism. Available: <http://pubs.niaaa.nih.gov/publications/10report/intro.pdf> [23 August, 2007].
- U.S. Department of Health and Human Services. (2005) 11th report on carcinogens. Washington, DC: Public Health Service, National Toxicology Program. Available: <http://ntp.niehs.nih.gov/index.cfm?objectid=32BA9724-F1F6-975E-7FCE50709CB4C932> [4 September, 2007].
- U.S. Environmental Protection Agency (1987) Assessment of health risks to garment workers and certain home residents from exposure to formaldehyde. Office of Pesticides and Toxic Substances. Found in various EPA library collections through <http://www.epa.gov/natlibra/ols.htm> by its OCLC catalog no.16989049.
- U.S. Environmental Protection Agency. (1991a) Alpha 2u-globulin: association with chemically induced renal toxicity and neoplasia in the male rat. Washington, DC: Risk Assessment Forum; EPA report no. EPA/625/3-91/019F. Available from: NTIS, Springfield, VA; PB92-143668/AS.
- U.S. Environmental Protection Agency. (1991b) Acetaldehyde (CASRN 75-07-0). Washington, DC: Office of Research and Development, Integrated Risk Information System (IRIS). Available: <http://www.epa.gov/iris/subst/0290.htm> [4 September, 2007].

- U.S. Environmental Protection Agency. (1991c) Ethylbenzene (CASRN 100-41-4). Washington, DC: Office of Research and Development, Integrated Risk Information System (IRIS). Available: <http://www.epa.gov/ncea/iris/subst/0051.htm> [17 July, 2008].
- U.S. Environmental Protection Agency. (1991d) Formaldehyde (CASRN 50-00-0). Washington, DC: Office of Research and Development, Integrated Risk Information System (IRIS). Available: <http://www.epa.gov/ncea/iris/subst/0419.htm> [18 July, 2008].
- U.S. Environmental Protection Agency. (1993a) Assessment of potential health risks of gasoline oxygenated with methyl tertiary butyl ether (MTBE). Washington, DC: Office of Research and Development; November; report no. EPA/600/R-93/206.
- U.S. Environmental Protection Agency. (1993b) Methyl tert-butyl ether (MTBE) (CASRN 1634-04-4). Washington, DC: Office of Research and Development, Integrated Risk Information System (IRIS). Available: <http://www.epa.gov/iris/subst/0545.htm> [4 September, 2007].
- U.S. Environmental Protection Agency. (1994) Health risk perspectives on fuel oxygenates. Washington, DC: Office of Research and Development; report no. EPA 600/R-94/217.
- U.S. Environmental Protection Agency. (1997) Drinking water advisory: consumer acceptability advice and health effects analysis on methyl tertiary-butyl ether (MTBE). Washington, DC: Office of Water; report no. EPA-822-F-97-008.
- U.S. Environmental Protection Agency. (1998a) Oxygenates in water: critical information and research needs. Washington, DC: Office of Research and Development; report no. EPA/600/R-98/048.
- U.S. Environmental Protection Agency (1998b) Carcinogenic effects of benzene: an update. Washington, DC: National Center for Environmental Assessment; report no. EPA/600/P-97/001F.
- U.S. Environmental Protection Agency. (2000) Benzene (CASRN 71-43-2). Washington, DC: Office of Research and Development, Integrated Risk Information System (IRIS). Available: <http://www.epa.gov/ncea/iris/subst/0276.htm> [18 July, 2008].
- U.S. Environmental Protection Agency. (2003a) Toxicological review of benzene (noncancer effects) (CAS no. 71-43-2). Washington, DC: Integrated Risk Information System (IRIS); report no. EPA/635/R-02/001F. Available: <http://www.epa.gov/ncea/iris/toxreviews/0276-tr.pdf> [17 July, 2008].
- U.S. Environmental Protection Agency. (2003b) Toxicological review of xylenes (CAS no. 1330-20-7). Washington, DC: Integrated Risk Information System (IRIS); report no. EPA 635/R-03/001. Available: <http://www.epa.gov/ncea/iris/toxreviews/0270-tr.pdf> [17 July, 2008].

- U.S. Environmental Protection Agency. (2004a) Air quality criteria for particulate matter. Research Triangle Park, NC: National Center for Environmental Assessment; report no. EPA/600/P-99/002aF-bF. 2v. Available: <http://cfpub.epa.gov/ncea/> [9 November, 2004].
- U.S. Environmental Protection Agency (2004b) National Emission Standards for Hazardous Air Pollutants for Plywood and Composite Wood Products Manufacture: Final Rule. (69 FR 45943, 7/30/04)
- U.S. Environmental Protection Agency. (2005) Toxicological review of toluene (CAS no. 108-88-3). Washington, DC: Integrated Risk Information System (IRIS); report no. EPA/635/R-05/004. Available: <http://www.epa.gov/ncea/iris/toxreviews/0118-tr.pdf> [17 July, 2008].
- U.S. Environmental Protection Agency. (2006) Air quality criteria for ozone and related photochemical oxidants. Research Triangle Park, NC: National Center for Environmental Assessment; report no. EPA/600/R-05/004aF-cF. 3v. Available: <http://cfpub.epa.gov/ncea/> [24 March, 2006].
- U.S. Environmental Protection Agency. (2007a) Regulatory Impact Analysis: Control of Hazardous Air Pollutants from Mobile Sources. Chapter 1: Mobile Source Air Toxics Health Information. Washington, DC: EPA 420-R-07-002. Available: <http://www.epa.gov/otaq/regs/toxics/fr-ria-sections.htm> [February, 2007].
- U.S. Environmental Protection Agency. (2007b) Regulatory Impact Analysis: Control of Hazardous Air Pollutants from Mobile Sources. Chapter 3: Chapter 3: Air Quality and Resulting Health and Welfare Effects of Air Pollution from Mobile Sources. Washington, DC: EPA 420-R-07-002. Available: <http://www.epa.gov/otaq/regs/toxics/fr-ria-sections.htm> [February, 2007].
- U.S. Environmental Protection Agency. (2007c) Toxicological review of 2,2,4-trimethylpentane (CAS no. 540-84-1). Washington, DC: Integrated Risk Information System (IRIS); report no. EPA/635/R-07/003. Available: <http://www.epa.gov/IRIS/toxreviews/0614-tr.pdf> [30 August, 2007].
- Verschueren, K. (1983) Handbook of environmental data on organic chemicals. 2nd ed. New York, NY: Van Nostrand Reinhold Company.
- Vetrano, K. (1993) Odor and taste threshold studies performed with tertiary-amyl methyl ether (TAME). Washington, DC: American Petroleum Institute; API publication no. 4591.
- Wallgren, H. (1967) On the mechanism of the central depressant action of ethanol. *Acta Neurol. Scand.* 43(suppl. 31): 134.
- Welsch, F.; Elswick, B.; James, R. A.; Marr, M. C.; Myers, C. B.; Tyl, R. W. (2003) Developmental toxicity evaluation of inhaled tertiary amyl methyl ether in mice and rats. *J. Appl. Toxicol.* 23: 387-395.

- White, R. D.; Daughtrey, W. C.; Wells, M. S. (1995) Health effects of inhaled tertiary amyl methyl ether and ethyl tertiary butyl ether. *Toxicol. Lett.* 82/83: 719-724.
- Willett, W. C.; Stampfer, M. J.; Golditz, G. A.; Rosner, B. A.; Hennekens, C. H.; Speizer, F. E. (1987) Moderate alcohol consumption and the risk of breast cancer. *N. Engl. J. Med.* 316: 1174-1180.
- Witkin, J. M. (1984) Effects of some volatile sedative-hypnotics on punished behavior. *Psychopharmacology (Berl)*. 84: 16-9.
- Witkin, J. M.; Leander J. D. (1982) Effects of orally-administered ethanol and tertiary-butanol on fixed-ratio responding of rats. *Subst Alcohol Actions Misuse*. 3: 275-9.
- World Health Organization (WHO). (1998) Methyl *tertiary*-butyl ether. Geneva, Switzerland; World Health Organization. (Environmental health criteria 206).
- World Health Organization (WHO). (2004) Global status report on alcohol 2004. Geneva, Switzerland: Department of Mental Health and Substance Abuse. Available: http://www.who.int/substance_abuse/publications/global_status_report_2004_overview.pdf [23 August, 2007].
- Wolf, M. A.; Rowe V. K.; McCollister D. D.; Hollingsworth R. L.; Oyen F. (1956) Toxicological studies of certain alkylated benzenes and benzene. *Arch. Ind. Health*. 14: 387-398.
- Woutersen, R. A.; Appelman, L. M.; Van Garderen-Hoetmer, A.; Feron, V. J. (1986) Inhalation toxicity of acetaldehyde in rats. III. Carcinogenicity study. *Toxicology* 41: 213-231.
- Woutersen, R. A.; Feron, V. J. (1987) Inhalation toxicity of acetaldehyde in rats. IV. Progression and regression of nasal lesions after discontinuation of exposure. *Toxicology* 47: 295-305.
- Zhang, X.; Sliwowska, J. H.; Weinberg, J. (2005) Prenatal alcohol exposure and fetal programming: effects on neuroendocrine and immune function. *Exp. Biol. Med.* 230: 376-388.

III. COMMERCIAL FEASIBILITY OF ETHANOL AND OTHER ADDITIVES

This chapter focuses primarily on ethanol, a renewable fuel blending component that is currently the predominant product blended into gasoline in the U.S. marketplace and is expected to continue to be for the foreseeable future. Several factors have led to the rapid expansion of ethanol use. With passage of the Energy Policy Act of 2005 (EPAct), two important provisions affecting ethanol use occurred. First, EPAct removed the oxygen requirement in the federal reformulated gasoline (RFG) program. This allowed refiners and blenders to produce RFG with or without an oxygenate. In areas where MTBE was still being blended into RFG, refiners shifted away from the use of MTBE and began blending ethanol into RFG. Additionally, passage of the Renewable Fuels Standard in EPAct 2005 required increased volumes of renewable fuel be used in the transportation sector beginning in 2006, requiring a minimum of 4 billion gallons per year and increasing to 7.5 billion gallons per year in 2012. This, along with positive economics for the use and blending of ethanol, saw the market exceed the mandated volumes. Looking forward, with passage of the Energy Independence and Security Act of 2007 which established new market requirements for renewable fuels, ethanol use will continue to see a rapid rise in use in the gasoline or alternative (E85) fuel pool.

Also in this chapter, information is provided on where ethanol is currently produced in the U.S. Finally, other additives such as ETBE, TAME, DIPE, and TBA are discussed. These currently constitute a very small portion of the additive market and given their historical use and other policy and market realities, it does not appear that these products will attain commercially significant volumes.

A. Ethanol

1. Where Ethanol is Produced

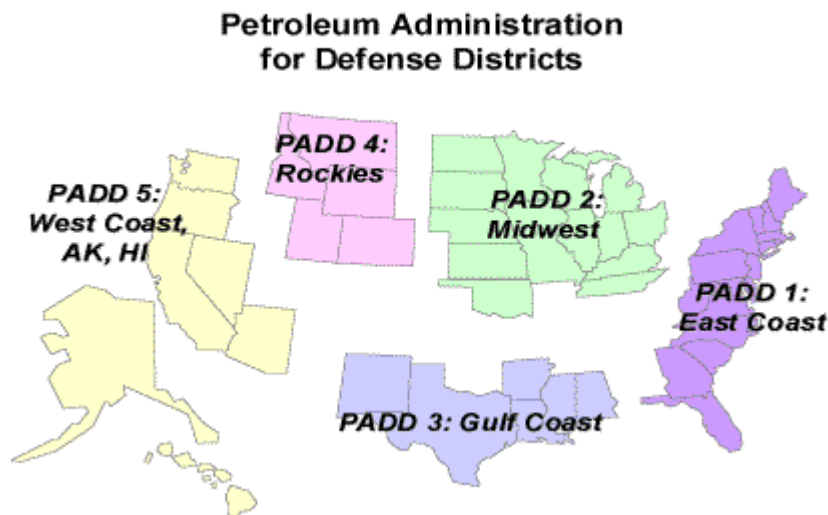
As of September 1, 2007, there were 133 fuel ethanol plants operating in the United States with a combined production capacity of approximately 7 billion gallons per year.⁶ These numbers have increased and will do so in the coming years to support attaining the EISA mandated renewable fuel volumes. Most ethanol currently produced in the US at commercial levels comes from grain or starch-based feedstocks that can easily be broken down via traditional fermentation processes. The majority of domestic ethanol is currently produced in the Midwest within PADD (Petroleum Administration for Defense District) 2 – where most of the corn feedstock is grown. In 2007, of the 133 ethanol production facilities, 119 were located in PADD 2. As a region, PADD 2 accounted for almost 96 percent (or about 6.7 billion gallons) of the total production capacity in 2007, as shown in Table III.A-1. Figure III.A-1 shows the locations of each of the five PADDs.

⁶ The September 1, 2007 ethanol production capacity baseline was generated based on a variety of data sources including: Renewable Fuels Association (RFA), Ethanol Biorefinery Locations (updated August 22, 2007); Ethanol Producer Magazine (EPM), Current plant list (last modified on August 13, 2007) and ethanol producer websites. The baseline includes does not include ethanol plants whose primary business is industrial or food-grade ethanol production. Where applicable, current ethanol plant production levels have been used to represent plant capacity, as nameplate capacities are often underestimated. The baseline does not include idled plants located in Bartow, FL; Hamburg, IA; or Plover, WI nor does it include plants that may be located in the Virgin Islands or U.S. territories.

Table III.A-1. 2007 U.S. Ethanol Production Capacity by PADD

PADD	Capacity MGY	% of Capacity	No. of Plants	% of Plants
PADD 1	0.4	0.0%	1	0.8%
PADD 2	6,679	95.6%	119	89.5%
PADD 3	30	0.4%	1	0.8%
PADD 4	108	1.5%	6	4.5%
PADD 5	170	2.4%	6	4.5%
Total	6,987	100.0%	133	100.0%

Figure III.A-1. PADD Boundary and Regions



Leading the Midwest in ethanol production are Iowa, Nebraska and Illinois followed by South Dakota and Minnesota whose production levels are nearly equal. Together, as of September 2007, these five states were home to 84 ethanol plants with a combined production capacity of 5.2 billion gallons per year (contributing to 74 percent of the total domestic product). Although the majority of ethanol production comes from the Midwest, there are a growing number of plants located outside the traditional corn belt. In addition to the 15 states comprising PADD 2, (all of which have operational ethanol plants besides Ohio⁷), in 2007, ethanol production facilities in the contiguous states were located in Arizona, California, Colorado, Georgia, Idaho, New Mexico, Oregon and Wyoming. Some of these facilities ship in feedstocks (primarily corn) from the Midwest, others rely on locally grown/produced feedstocks, while others rely on a combination of both.

⁷ Ohio does not currently have any operational ethanol plants; however, six plants are under construction.

The U.S. ethanol industry is currently comprised of a mixture of company-owned and locally-owned farmer cooperatives (co-ops). More than two-thirds (93) of ethanol plants are owned by corporations, and, on average, these plants are larger in size than farmer-owned co-ops. Accordingly, company-owned plants account for more than three-quarters of the total 7007 U.S. ethanol production capacity. Furthermore, 30 percent of the total domestic product came from 27 plants owned by just two different companies – Archer Daniels Midland and POET Biorefining (formerly Broin).

. A summary of ethanol production alphabetically by state is found in Table III.A-2.

Table III.A-2. Summary of Ethanol Production by State, 2007

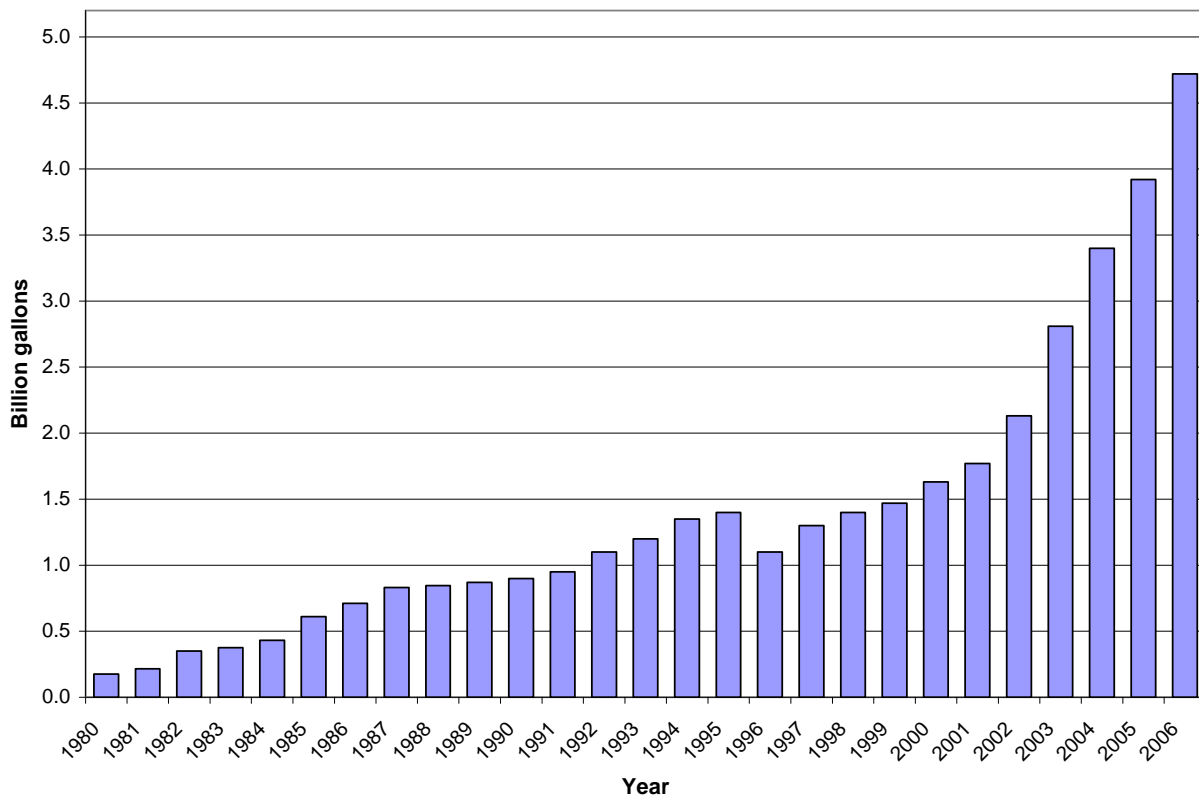
State	Capacity MMgy	% of Capacity	No. of Plants	% of Plants
Arizona	50	0.7%	1	0.8%
California	80	1.1%	4	3.0%
Colorado	96	1.4%	4	3.0%
Georgia	0.4	0.0%	1	0.8%
Iowa	2,031	29.1%	29	21.8%
Idaho	3	0.0%	1	0.8%
Illinois	887	12.7%	8	6.0%
Indiana	300	4.3%	4	3.0%
Kansas	289	4.1%	9	6.8%
Kentucky	38	0.5%	2	1.5%
Michigan	214	3.1%	4	3.0%
Minnesota	634	9.1%	16	12.0%
Missouri	160	2.3%	4	3.0%
North Dakota	136	1.9%	4	3.0%
Nebraska	997	14.3%	18	13.5%
New Mexico	30	0.4%	1	0.8%
Oklahoma	2	0.0%	1	0.8%
Oregon	40	0.6%	1	0.8%
South Dakota	636	9.1%	13	9.8%
Tennessee	67	1.0%	1	0.8%
Wisconsin	289	4.1%	6	4.5%
Wyoming	9	0.1%	1	0.8%
Total	6,987	100.0%	133	100.0%

In addition to the domestic ethanol production described above, the U.S. also receives a small amount of ethanol from other countries.

2. Projected Growth in Ethanol Production

Over the past 25 years, domestic ethanol production has steadily increased due to environmental regulation, federal and state tax incentives, and market demand. More recently, ethanol production has soared due to the phase-out of MTBE, an increasing number of state ethanol mandates, and elevated crude oil prices. As shown in Figure III.A-2, over the past five years, domestic ethanol production has almost tripled from 1.8 billion gallons in 2001 to 4.7 billion gallons in 2006.

Figure III.A-2. Historical Growth in U.S. Ethanol Production (Thru 2006)



Sources: RFA Ethanol Industry Outlook 2007 (1980-2003); EIA September 2007 Monthly Energy Review total ethanol usage less EIA reported ethanol imports (2004-2006)

In addition, according to industry sources, 2007 domestic ethanol production reached approximately 6.5 billion gallons. Not only was production at an all time high, industry growth between 2006 and 2007 (~1.7 billion gallons) was also record-setting. By all indications, growth in ethanol production is expected to continue.

As mentioned earlier, as of September of 2007, there was ~7 billion gallons of ethanol plant capacity online. Even if no new plants/capacity were added, ethanol production would grow from 2007 to 2008 (provided plants continue to operate at or above nameplate capacity). As of September 1, 2007, there were 10 expansion and 67 new construction projects underway

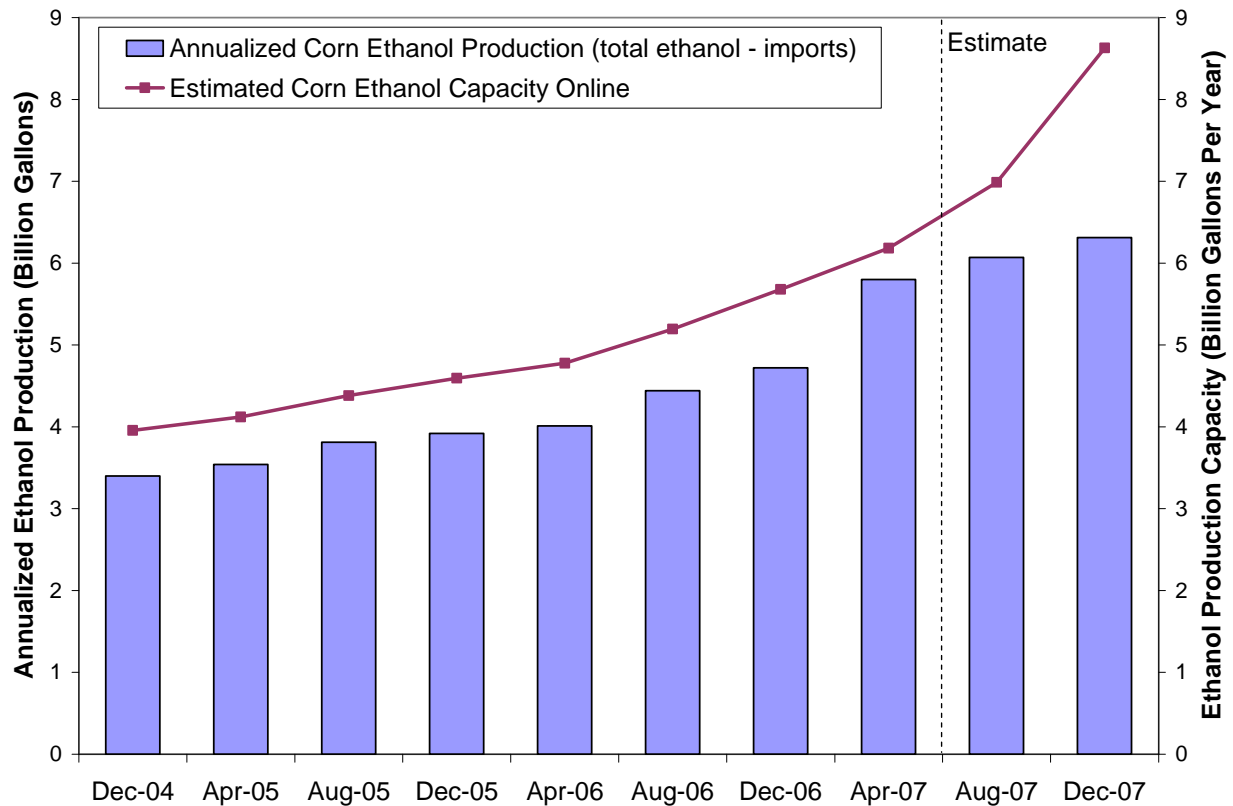
with a combined production capacity of an additional 5.9 billion gallons.⁸ These projects are at various phases of construction from conducting land stabilization/foundation work, to constructing tanks and installing associated structural, mechanical, and electrical components, to completing start-up activities. Once these construction projects are complete, there will be 200 ethanol plants operating in the U.S. with a combined production capacity of nearly 13 billion gallons per year, as shown in Table III.A-3. The growth from 2004 to that projected for “online capacity” is shown in Figure III.A-2.

Table III.A-3. Summary of Under Construction Projects (2007)

PADD	Online		Expansions		New Construction		Total	
	Capacity MGY	No. of Plants	Capacity MGY	No. of Plants	Capacity MGY	No. of Plants	Capacity MGY	No. of Plants
PADD 1	0.4	1	0	0	264	3	264	4
PADD 2	6,679	119	286	9	4,686	54	11,651	173
PADD 3	30	1	0	0	385	5	415	6
PADD 4	108	6	2	1	120	3	230	9
PADD 5	170	6	0	0	168	2	338	8
Total	6,987	133	288	10	5,623	67	12,898	200

⁸ Based on Renewable Fuels Association (RFA), Ethanol Biorefinery Locations (updated August 22, 2007); Ethanol Producer Magazine (EPM), Under Construction plant list (last modified on August 13, 2007), ethanol producer websites, and follow-up correspondence with ethanol producers.

Figure III.A-2. Annualized Ethanol Production with Online Capacities from 2004 to 2007 (projected)



While theoretically it only takes 12 to 18 months to build an ethanol plant, the rate at which these facilities actually come online will likely be slowed as a result of many factors, one of them being that the majority of plants are being built by a few design/build companies (e.g., ICM, Fagen, Delta-T). The schedules of these firms are limiting and require coordination. In addition, construction rates are often slowed by environmental permitting, material/labor constraints, and other unforeseen circumstances. Ultimately, the future growth of the corn ethanol industry will be, to some extent, limited by feedstock pricing.

According to USDA, enough corn will be available in the U.S. to support 20 billion gallons of ethanol production in 2017.⁹ With each new plant that is built, however, corn pricing will affect the costs of ethanol production. Higher corn pricing translates to higher operating costs, possibly lower profit margins, and higher risk for ethanol producers. Under such circumstances, the industry may respond by slowing investments and/or delaying construction plans until corn prices fall or until the market responds with more demand for ethanol (e.g., increase in mandated volumes, more Flexible Fuel Vehicles (FFVs) and more E85 refueling stations) and a viable means for distributing the additional ethanol—a trend that has already begun.

⁹ USDA, An Analysis of the Effects of an Expansion in Biofuel Demand on U.S. Agriculture, May 2007

B. Other Additives

Other alcohols and ethers (e.g. ETBE, TAME, and T-butanol or TBA) have been less widely used and less widely studied than MTBE and ethanol. To the extent that they have been studied, they appear to have similar, but not identical, chemical and hydrogeologic characteristics. Reporting forms that EPA requires gasoline producers to submit (RFG and anti-dumping forms) contain information on ETBE, TAME and TBA usage as well as MTBE and ethanol. Based on survey data completed for 2005, MTBE and ethanol represented 55 and 41% of oxygenate fuel additive use, respectively, while ETBE, TAME and TBA were at 0.29, 3.3 and 0.1%, respectively. Since that time, we know that MTBE use has decreased dramatically, while ethanol use has increased dramatically. Survey data for 2007 are being processed. We also know that usage of the other additives has remained at approximately the same levels. Based on the history of the use of the other additives, it is not expected that they will have any appreciable change in their levels of commercial use as gasoline additives for the foreseeable future. (See Appendix A for more information on historical use of MTBE, ethanol and the other fuel additives.)

U.S. refiners currently value ethanol for several reasons including its octane value and other positive blending properties, particularly as a replacement or substitute for MTBE. Favorable economics for ethanol blending also contribute to an increase in use over the past several years. Production and use of another high value blending component, alkylate, has also increased in the U.S., and trends also appear to be on the rise elsewhere. Alkylates are typically high-octane branched chain hydrocarbons produced at refineries, typically in alkylation units. Alkylates are one hydrocarbon refinery stream. Aromatics make up another common hydrocarbon stream at refineries and consist of benzene and benzene-like structures. Like alkylates, they are high in octane quality, a positive quality for gasoline production. Unlike alkylate content, EPA has traditionally collected data on and controlled aromatic content, since emissions tests have shown that aromatics have been found to contribute to criteria pollutants and to toxic emissions like benzene. Although little specific work has been done on alkylates, alkylate streams in past testing have not been shown to play a primary role in the production of the most toxic materials nor contribute to vehicle emissions in the way aromatics do.

There may also be products developed in the future which could play an increased role in the commercial gasoline market. These products will need to be identified and evaluated if a commercial market develops for new products.

IV. POTENTIAL AIR QUALITY EFFECTS

The bulk of the impact of ethanol use on emissions and air quality is expected to be associated with emissions from spark-ignited vehicles and equipment using low level ethanol-gasoline blends. We expect the use of high level ethanol-gasoline blends, like E85, to see an increase in use and consumption over the next decade, however in the near- and mid-term, this volume will be relatively small in comparison to that of gasoline ethanol blends, and the focus of this Report is on the use of ethanol as a fuel additive, not as a fuel. This section therefore focuses on emissions and air quality effects from the use of low level ethanol blends.

A. Emissions Associated with Ethanol

In April of 2007, EPA promulgated the final Renewable Fuels Standard (RFS1) rule which requires specific volumes of ethanol to be in gasoline by year, with 7.5 billion gallons per year required for 2012. This rule mandated an overall increase of 3.2 billion gallons of ethanol. We projected emission changes and air quality effects associated with the increased use of ethanol in the Regulatory Impact Analysis (RIA) conducted for the RFS1 rule (U.S. EPA, 2007b). EPA is now tasked with writing a new version of the RFS rule under the recently passed Energy Information and Security Act (EISA) of 2007. The new version, referred to as RFS2, mandates the use of 36 billion gallons of ethanol by 2022. Any new analyses of emissions and air quality that we conduct for the RFS2 rule will be made publicly available as part of that rulemaking.

For the current Report to Congress, we have relied on the RIA conducted for the RFS1 rule (U.S. EPA, 2007b). In that analysis, we considered three cases for the future use of ethanol-blend gasoline: a Reference Case, a Renewable Fuels Standard (RFS1) Case, and an Energy Information Administration (EIA) Case. Using the MOBILE model, we evaluated emissions for each of these cases, assuming that exhaust emissions from Tier 1 and later vehicles do not respond to changes in ethanol content of the gasoline.¹⁰ We recognize that these analyses are not strictly relevant to the use of ethanol as a oxygenate fuel additive, and as such will significantly overstate the impacts of its use.

The main difference between the Reference, RFS1 and EIA Cases is the assumption about how much ethanol will be used and where it will go. The Reference Case represents our estimate of fuel quality by county in 2004 when approximately 3.5 billion gallons of ethanol were consumed nationwide. The RFS1 case assumes 6.7 billion gallons of ethanol consumption in 2012, in accordance with the requirements of the RFS1 (Renewable Fuel Standard) mandate. The EIA case assumes 9.6 billion gallons of ethanol is used nationwide in 2012, based on projections made in the Energy Information Agency's 2006 Annual Energy Outlook. For each Case, fuel quality was predicted for each county in the U.S. in 2012. This 2012 fuel matrix was then used for all inventory and air quality assessments.

¹⁰ The Tier 1 standards are emission standards applicable to federal light duty vehicles and trucks that were phased in beginning in 1994 and were phased out beginning in 2004. An implementation schedule for these standards is available at <http://epa.gov/otaq/cert/veh-cert/b00001e.pdf>. The Tier 0 standards were the emission standards applicable prior to the Tier 1 standards. These are light duty vehicle standards required by the 1977 Clean Air Act amendments and first implemented in 1981.

Table IV.A-1 shows ethanol impacts on VOC inventories for each of the three cases of renewable fuel use in years 2012, 2015, and 2020. In any given year, the data suggest that total VOC emissions will increase as ethanol use increases. The largest increase is seen in the EIA case, where the increase is about 1% of the Reference Case inventory.

Our analysis indicates that this increase is a result of VOC non-exhaust emissions, such as those from evaporation or permeation. While VOC exhaust emissions decrease, they do not decrease enough to counteract the increase from non-exhaust emissions.

**Table IV.A-1. National VOC Emissions from Gasoline Vehicles and Equipment:
Reference Case Inventory and Change in Inventory for Control Cases (Tons/Year)**

Primary Case	Tons/Year		
Total	2012	2015	2020
Reference	5,882,000	5,569,000	5,356,000
RFS1 Case (Change)	18,000	25,000	34,000
EIA Case (Change)	43,000	49,000	58,000
On-Road	2012	2015	2020
Reference	3,417,000	3,269,000	3,244,000
RFS1 Case (Change)	10,000	16,000	23,000
EIA Case (Change)	32,000	36,000	42,000
Non-Road	2012	2015	2020
Reference	2,465,000	2,300,000	2,112,000
RFS1 Case (Change)	8,000	9,000	11,000
EIA Case (Change)	11,000	13,000	16,000

Table IV.A-2 shows ethanol impacts on CO inventories for each of the three cases of renewable fuel use in years 2012, 2015, and 2020. In any given year, data suggest that total CO emissions will decrease as ethanol use increases. The largest reduction is seen in the EIA case; this decrease is still less than 3% of the Reference inventory.

**Table IV.A-2. National CO Emissions from Gasoline Vehicles and Equipment:
Reference Case Inventory and Change in Inventory for Control Cases (Tons/Year)**

Primary Case	Tons/Year		
Total	2012	2015	2020
Reference	55,022,000	53,702,000	53,949,000
RFS1 Case (Change)	-483,000	-473,000	-460,000
EIA Case (Change)	-1,366,000	-1,329,000	-1,286,000
On-Road	2012	2015	2020
Reference	37,656,000	36,171,000	35,723,000
RFS1 Case (Change)	-45,000	-39,000	-19,000
EIA Case (Change)	-359,000	-321,000	-252,000
Non-Road	2012	2015	2020
Reference	17,366,000	17,531,000	18,226,000
RFS1 Case (Change)	-438,000	-434,000	-441,000
EIA Case (Change)	-1,007,000	-1,008,000	-1,034,000

Table IV.A-3 shows ethanol impacts on NO_x inventories for each of the three cases of renewable fuel use in years 2012, 2015, and 2020. In any given year, the data suggest that total NO_x emissions will increase as ethanol use increases. The largest increase is seen in the EIA case, which is around 2% of the Reference inventory.

Our analysis also indicates that nonroad NO_x emissions increase much more than onroad emissions. While onroad inventories increase less than one percent in control cases, nonroad inventories increase up to 11% in the EIA case.

**Table IV.A-3. National NO_x Emissions from Gasoline Vehicles and Equipment:
Reference Case Inventory and Change in Inventory for Control Cases (Tons/Year)**

Primary Case	Tons/Year		
Total	2012	2015	2020
Reference	2,487,000	2,059,000	1,695,000
RFS1 Case (Change)	23,000	18,000	17,000
EIA Case (Change)	40,000	33,000	32,000
On-Road	2012	2015	2020
Reference	2,240,000	1,797,000	1,407,000
RFS1 Case (Change)	9,000	3,000	0
EIA Case (Change)	13,000	4,000	0
Non-Road	2012	2015	2020
Reference	247,000	262,000	288,000
RFS1 Case (Change)	14,000	15,000	17,000
EIA Case (Change)	27,000	29,000	32,000

Table IV.A-4 shows ethanol impacts on air toxic emissions for each of the three cases of renewable fuel use in 2012. We emphasize that the toxics inventories are based on very limited data, especially when it comes to emissions from nonroad equipment.

For all air toxics shown, the most extreme changes occur in the EIA case. The data suggest that, in 2012, total benzene emissions will decrease by about 4%. Total 1,3-butadiene emissions decrease by less than 2% while total formaldehyde emissions decrease by up to 1.5%. On the other hand acetaldehyde emissions increase by as much as 36%.

Generally, the emissions trends in 2015 and 2020 parallel those of 2012 shown in the table below (U.S. EPA, 2007b). Benzene maintains a drop of up to about 6% with increased ethanol use. Formaldehyde remains fairly flat, ranging from a 0.5% increase to a 1.2% decrease. Acetaldehyde maintains an increase of as much as 37%. Finally, 1,3-butadiene remains fairly flat, ranging from no change to a 0.5% increase.

Table IV.A-4. National Toxic Emissions from Gasoline Vehicles and Equipment in 2012: Reference Case Inventory and Change in Inventory for Control (Tons/Year)

Primary Case	Benzene	1,3-Butadiene	Formaldehyde	Acetaldehyde
Total				
Reference	178,000	18,900	40,400	19,900
RFS1 Case (Change)	-3,200	-200	-600	3,400
EIA Case (Change)	-7,200	-300	-200	7,100
Onroad				
Reference	124,100	12,000	29,900	15,500
RFS1 Case (Change)	-2,300	-200	-600	2,400
EIA Case (Change)	-5,400	-200	-300	5,400
Nonroad				
Reference	53,900	6,900	10,500	4,400
RFS1 Case (Change)	-900	0	0	1,000
EIA Case (Change)	-1,800	-100	100	1,700

1. Local and Regional CO, VOC and NOx Emissions (Summer 2015)

We also estimated the percentage change in VOC, NOx, and CO emissions from gasoline fueled motor vehicles and equipment in those areas of the country where we expect the most significant changes in ethanol use. Specifically, we focused on areas where the market share of ethanol blends was projected to change by 50 percent or more and also focused on summertime emissions, because these are most relevant to ozone formation. We modeled 2015 because the ozone Response Surface Model (RSM) used for air quality modeling is based upon a 2015 emissions inventory, though we would expect similar results in 2012. Finally, we developed separately estimates for: 1) RFG areas, including the state of California and the portions of Arizona where their CBG fuel programs apply, 2) low Reid Vapor Pressure (RVP) areas (i.e., RVP standards less than 9.0 RVP), and 3) areas with a 9.0 RVP standard. This set of groupings helps to highlight the emissions impact of increased ethanol use in those areas where emission control is most important.

Table IV.A-5 presents our primary analysis estimates of the percentage change in VOC, NOx, and CO emission inventories for these three types of areas when compared to the 2015 reference case.

Table IV.A-5. Change in July 2015 Emissions from Gasoline Vehicles and Equipment in Counties Where Ethanol Use Changed Significantly – Primary Analysis

Ethanol Use	RFS1 Case	EIA Case
RFG Areas		
Ethanol Use	Down	Up
VOC	0.8%	2.3%
NOx	-3.4%	1.6%
CO	6.1%	-2.6%
Low RVP Areas		
Ethanol Use	Up	Up
VOC	4.2%	4.6%
NOx	6.2%	5.7%
CO	-12%	-13%
Other Areas (9.0 RVP)		
Ethanol Use	Up	Up
VOC	3.6%	4.6%
NOx	7.3%	7.0%
CO	-6.4%	-6.0%

As expected, increased ethanol use tends to increase NOx emissions. The increase in NOx emissions in “Low RVP Areas” and “Other Areas” is greater than in “RFG Areas”, since the gasoline in the RFG Areas included in this analysis all contained MTBE. Also, increased ethanol use tends to increase VOC emissions, indicating that the increase in non-exhaust VOC emissions exceeds the reduction in exhaust VOC emissions. This effect is muted with RFG due to the absence of an RVP waiver for ethanol blends.

Table IV.A-6 presents the percentage change in VOC, NOx, and CO emission inventories under our sensitivity analysis (i.e., when we apply the emission effects of the EPA Predictive Models to all motor vehicles).

Table IV.A-6. Change in July 2015 Emissions from Gasoline Vehicles and Equipment in Counties Where Ethanol Use Changed Significantly – Sensitivity Analysis

Ethanol Use	RFS1 Case	EIA Case
RFG Areas		
Ethanol Use	Down	Up
VOC	-1.0%	1.0%
NOx	-0.9%	5.6%
CO	7.3%	-3.0%
Low RVP Areas		
Ethanol Use	Up	Up
VOC	3.4%	3.7%
NOx	10.4%	10.8%
CO	-15.0%	-16.4%
Other Areas (9.0 RVP)		
Ethanol Use	Up	Up
VOC	3.0%	3.9%
NOx	10.8%	11.0%
CO	-9.0%	-8.9%

Directionally, the changes in VOC and NOx emissions in the various areas are consistent with those from our primary analysis. The main difference is that the increases in VOC emissions are smaller, due to more vehicles experiencing a reduction in exhaust VOC emissions, and the increases in NOx emissions are larger.

B. Potential air quality impacts

1. Ozone Impacts

We performed ozone air quality modeling simulations for the eastern United States using the ozone Response Surface Model (RSM) to estimate the effects of the projected changes in emissions from gasoline vehicles and equipment associated with the RFS1 rule. Details on how the modeling was conducted are contained in Chapter 5 of the RIA (U.S. EPA, 2007b).

The ozone RSM used for assessing the air quality impacts of expanded ethanol use in fuel was developed broadly to look at various control strategies with respect to attaining the 8-hour ozone NAAQS. The experimental design for the ozone RSM covered three key areas: type of precursor emission (NOx or VOC), emission source type (i.e., onroad vehicles, nonroad vehicles, area sources, electrical generating utility (EGU) sources, and non-utility point sources), and location in or out of a 2015 model-projected residual ozone nonattainment area. This resulted in a set of 14 emissions factors.

The impact of the RFS1 rule's increased ethanol use on the 8-hour ozone design values in 2015 is presented in Table IV.B-1. The changes presented in Table IV.B-1 are for those counties with 2001 modeled design values.¹¹

¹¹ 2001 design values were calculated as an average of the 1999-2001, 2000-2002 and 2001-2003 design values at each monitoring site. Please see the Air Quality Modeling Technical Support Document for the final Clean Air Interstate Rule for additional information.

**Table IV.B-1. Impact of Increased Ethanol Use (RFS1 Rule)
on 8-hour Ozone Design Values in 2015 (ppb)**

	RFS1 Case	EIA Case
Primary Analysis		
Minimum Change	-0.015	0.000
Maximum Change	0.329	0.337
Average Change Across 37 States	0.057	0.079
Population-Weighted Change Across 37 States	0.052	0.056
Average Change Where Ethanol Use Changed Significantly (greater than 50%) States	0.153	0.181
Population-Weighted Change in States Where Ethanol Use Changed Significantly	0.154	0.183
Sensitivity Analysis		
Minimum Change	-0.115	0.000
Maximum Change	0.624	0.549
Average Change Across 37 States	0.111	0.142
Population-Weighted Change Across 37 States	0.092	0.096
Average Change Where Ethanol Use Changed Significantly States	0.300	0.325
Population-Weighted Change Where Ethanol Use Changed Significantly States	0.272	0.315

As can be seen, ozone levels generally increase with increased ethanol use. This is likely due to the projected increases in both VOC and NO_x emissions. Some areas do see a small decrease in ozone levels. In our primary analysis, where exhaust emissions from Tier 1 and later onroad vehicles are assumed to be unaffected by ethanol use, the population-weighted increase in ambient ozone levels is 0.052-0.056 ppb. Since the 8-hour ambient ozone standard is 0.08 ppm (85 ppb), this increase represents about 0.06 percent of the standard, a very small percentage¹². While small, this figure includes essentially zero changes in ozone in areas where ethanol use did not change. When we focus just on those areas where the market share of ethanol blends changed by 50 percent or more, the population-weighted increase in ambient ozone levels rises to 0.154-0.183 ppb. This increase represents about 0.2 percent of the standard.

In our sensitivity analysis, where exhaust emissions from Tier 1 and later onroad vehicles are assumed to respond to ethanol like Tier 0 vehicles, the population-weighted increase in ambient ozone levels across the entire 37 state area is slightly less than twice as high, or 0.092-0.096 ppb. This increase represents about 0.11 percent of the standard. When we focus just on those areas where the market share of ethanol blends changed by 50 percent or more, the

¹² Appendix I of 40 CFR Part 50.

population-weighted increase in ambient ozone levels rises to 0.272-0.315 ppb. This increase represents about 0.35 percent of the standard.

It is important to note that the results of this ozone response surface metamodeling exercise is meant for screening-level purposes only and does not represent the results that would be obtained from full-scale photochemical ozone modeling. In addition, there are several important caveats concerning our estimated ozone impacts using the ozone RSM. The ozone RSM does not account for changes in CO emissions. As shown in Section IV.A, ethanol use should reduce CO emissions, directionally reducing ambient ozone levels in areas where ozone formation is VOC-limited. Accounting for the reduction in CO emissions in NO_x-limited areas, however, may have little impact on the ozone impact of ethanol use.

The ozone RSM does not account for changes in VOC reactivity. With additional ethanol use, the ethanol content of VOC should increase. Ethanol is less reactive than the average VOC. Therefore, this change should also reduce ambient ozone levels in a way not addressed by the ozone RSM. Again, like the impact of reduced CO emissions, this effect applies to those areas where ozone formation is VOC-limited. Another limitation is the RSM's inability to simulate the spatial distribution of emission impacts associated with the proposed standard. Instead, we are forced to make simplifying assumptions about the geographic uniformity of RFS1 emissions impacts, explained above. The caveats and limitations associated with the RSM highlight the fact that it should only be used as a screening-level tool to characterize broad trends associated with changes in different source categories of ozone precursors.

Keeping these limitations in mind, the expanded use of ethanol will impact the national emissions inventory of precursors to ozone, such as VOCs and NO_x. Exposure to ozone has been linked to a variety of respiratory effects including premature mortality, hospital admissions and illnesses resulting in school absences. Ozone can also adversely affect the agricultural and forestry sectors by decreasing yields of crops and forests.

Overall, we estimate that the measurable changes in VOC and NO_x that result from the RFS1 rule's 3.2 billion gallon increase in ethanol use, will, on average, result in small increases in ambient ozone formation. As we discussed above, the ozone modeling results indicate a net increase in the average population weighted ozone design value metric measured within the modeled domain (37 Eastern states and the District of Columbia). EISA of 2007 mandates the use of 36 billion gallons of ethanol by 2022; the air quality impacts of this new mandate will be addressed by the RFS2 rule.

2. Particulate Matter

a. Potential Impact of Changes in Direct PM Emissions

The amount of data evaluating the impact of ethanol and MTBE blending on direct emissions of PM from gasoline-fueled vehicles is extremely limited. In the past, most studies did not test PM emissions from vehicles fueled with unleaded gasoline because the level of PM emissions from properly operating vehicles is usually very low, less than 0.1 g/mi.

Two studies indicate that the addition of ethanol might reduce direct PM emissions from gasoline vehicles (Ragazzi and Nelson, 1999; Mulawa, 2007). However, both studies were performed under wintertime conditions, one at high altitude, and one of the studies only consisted of three vehicles. The available data indicate that ethanol blending might reduce exhaust PM emissions under very cold weather conditions (i.e., 0 F or less), particularly at high altitude. There is no indication of PM emission reductions at higher temperatures or under conditions in which the engine is warmed up sufficiently. Thus, the data are certainly too limited to support a quantitative estimate of the effect of ethanol on direct PM emissions.

b. Potential Impact of Changes in Secondary PM Formation

In addition to being emitted directly from a combustion source, fine particles can be formed through a series of chemical reactions in the atmosphere when SO₂, NO_x, and VOC oxidize or otherwise react to form a wide variety of secondary PM. For example, SO₂ oxidizes to SO₃ and sulfuric acid and NO_x oxidizes to NO₃ and nitric acid which, in turn, react with ammonia in the atmosphere to form ammonium sulfate and ammonium nitrate. Particles generated through this gas-to-particle conversion are referred to as secondary aerosols and represent a significant portion of ambient fine particulate matter. Studies have shown that as much as 70% of the total organic carbon in urban particulate matter can be attributed to secondary organic aerosol (SOA) formation although the amount can also be less (Grosjean, 1992). Secondary PM tends to form more in the summer with higher temperatures and more intense sunlight.

Source-receptor modeling studies conducted in the Los Angeles area in 1993 by Schauer et al. (2002) indicated that as much as 67% of the fine particulate matter collected could not be attributed to primary sources. The authors concluded that much of this unidentifiable organic matter is SOA formed in the atmosphere. This is consistent with previous studies conducted by Turpin and Huntzicker (1991) who concluded that 70% of the total organic carbon in urban PM measurements made in southern California can be attributed to SOA.

Gas phase VOCs are oxidized by OH, NO₂, peroxyacetylnitrate (PAN), and ozone in the atmosphere, but their propensity to condense in the particle phase is a function of two factors: volatility and reactivity. To accumulate as an aerosol, a reaction product must first be formed in the gas phase at a concentration equal to its saturation

concentration. This requirement will not be met if the relevant gas-phase reactions of the VOC are too slow or if the vapor pressure of the reaction product is higher than the initial concentration of its VOC precursor (Pun and Seigneur, 2006). Limited data for reaction rate constants determined both experimentally and estimated by structural relationships are available in the published literature. However, the atmospheric chemistry behind SOA reaction rates and the estimated aerosol yield is highly complex and carries with it a great deal of uncertainty. Research in this area is ongoing and thus the capacity to quantitatively model SOA formation is not yet a straightforward process.

In general, all reactive VOC are oxidized by OH or other compounds. Additionally, alkenes, cycloalkenes, and other olefinic compounds can react with ozone and NO₂ to form secondary aerosols. In fact, ozone is responsible for nearly all the SOA formation from olefins, while OH plays little or no role at all (Grosjean and Seinfeld, 1989; Izumi and Fukuyama, 1990). Many VOC, however, will never form SOA under atmospheric conditions regardless of their reactivity. This is because the reaction products of these compounds have vapor pressures that are too high to form aerosols at atmospheric temperatures and pressures. These include all alkanes and alkenes with up to 6 carbon atoms and many low-molecular weight carbonyls, chlorinated compounds, and oxygenated solvents (Grosjean, 1992).

The VOC that have the greatest propensity to form SOA include aromatic hydrocarbons (such as toluene but even including benzene (Martin-Reviejo and Wirtz, 2005)), higher molecular weight olefins and cyclic olefins, and higher molecular weight paraffins. Kleindienst et al. (1999, 2007) suggest that a high fraction of SOA is due to aromatic hydrocarbon precursors. Furthermore, “aromatic products having a single alkyl group on the aromatic ring were found to represent a ‘high-yield’ family (e.g., toluene, ethylbenzene); compounds having multiple methyl groups (e.g., m-xylene, 1,2,4-trimethylbenzene) were found to represent a ‘low-yield’ family” (Kleindienst et al., 1999, 2007). All of the above mentioned VOC precursors are important either because there are large amounts of these particular VOC emitted per day, or because a large fraction of the VOC reacts, or a combination of the two. Based on VOC emissions inventory data collected in the Los Angeles area, the most important aerosol precursors (in the LA area using 1982 VOC emissions inventories) are listed in Table IV.B-4 below.

**Table IV.B-4. Predicted In Situ SOA Formation
During a Smog Episode in Los Angeles**

VOC Functional Group	Kg emitted daily*	Secondary PM Produced (kg)*	% yield
<u>Aromatics</u>	223985	3061	1.37
<u>Olefins</u>			
Alkenes	31163	608	1.95
Cyclic Olefins	3220	144	4.47
Terpenes	6000	626	10.43
<u>Paraffins</u>			
Alkanes	140493	368	0.26
Cycloalkanes	37996	96	0.25

*Source: Grosjean, 1992

These predictions are a function of input data collected in the Los Angeles area, and assume ambient levels of [ozone] = 100 ppb, [OH] = 1.0×10^6 molecules/cm³, and [NO₃] = 0 with 6 hours of reaction time. Aromatics are the largest functional group in terms of the absolute quantities of VOC emitted daily, and thus they eventually form the most SOA. Likewise, many high molecular weight paraffins (alkanes) form SOA on a significant scale simply because their emissions are high. However, the relative fraction of paraffins that react is less than that of aromatics in smog chamber experiments simulating SOA formation in the atmosphere. For olefins, the alkenes exhibit a combination of both relatively high emissions, and a high fraction of VOC reacted to form SOA. Cyclic olefins, in contrast, are emitted in relatively low levels, but a high fraction of these VOC react and the end result is a proportionally higher SOA yield than with the alkenes. Lastly, there are several “miscellaneous” compounds and terpenes that are emitted on a relatively small scale (in southern California), but that produce a substantial amount of SOA.

Researchers at EPA recently completed a field study in the Raleigh/Durham area of North Carolina that investigated the contribution of various sources to ambient PM 2.5 concentrations (Lewandowski et al., 2007; Kleindienst et al., 2007). In the study they identified toluene as an SOA precursor. They estimate that mobile sources contribute nearly 90% of the total toluene emissions in that region based on a chemical mass balance approach. At the same time, however, SOA attributable to non-fuel-related VOC (i.e., biogenic emissions) was found to be an even larger contributor to SOA (i.e., toluene was not likely the dominant source of SOA in this area). This study is currently undergoing peer review and will be published shortly. Qualitatively, however, this information is still quite useful since the study identifies a contributing source of SOA that is attributable almost entirely to mobile sources.

VOC reaction rates increase with increasing ambient temperature and sunlight intensity, so the level of SOA formed is much higher in summer than in winter. Even in the more temperate coastal climates of southern California, studies have found the summertime concentration of SOA calculated through Chemical Mass Balance models to be anywhere from 2-5 times higher in summer than winter. In a study conducted at both

urban and rural locations in the southeastern United States, the concentration of SOA in the summer and early fall was roughly 2-3 times that of colder months (Zheng et al., 2002).

Due to its high octane, the addition of ethanol will reduce aromatics in gasoline, which will in turn reduce the aromatics emitted in the exhaust. Fully quantifying the emission reduction is not possible at this time due to a lack of speciated exhaust data for newer vehicles (e.g., Tier 2 vehicles first introduced in the 2004 model year) running on ethanol blends. These data are now being obtained (see Section VII.B). In addition, increased NO_x emissions, resulting from the increased use of ethanol, could increase the formation of nitrate PM.

In contrast, gasoline-fueled vehicles and equipment comprise a significant fraction of all national gaseous aromatic VOC emissions¹³. The lower aromatics levels in gasoline with gasoline/aromatic blends will result in less aromatic emissions in both exhaust and evaporative emissions. We are presently doing testing and modeling to calculate the magnitude of these reductions.

The research to facilitate this incorporation is currently underway. EPA ORD scientists are currently carrying out a wide variety of laboratory studies to refine the SOA chemistry mechanisms for use in the next version of the CMAQ model. This information should be available in time for the comprehensive study of the Act's fuel requirements which is due in 2009.¹⁴

¹³ Based on internal analyses of emissions inventories.

¹⁴ Subject to funding.

References

- Grosjean, D., Seinfeld, J. H. (1989) Parameterization of the formation potential of secondary organic aerosols, *Atmos. Environ.* 23, 1733-1747.
- Grosjean, D. (1992) In situ organic aerosol formation during a smog episode: estimated production and chemical functionality. *Atmos. Environ.* 26A: 953-963.
- Izumi, K., Fukuyama, T. (1990) Photochemical aerosol formation from aromatic hydrocarbons in the presence of NO_x. *Atmos. Environ.* 24A, 1433-1441.
- Kleindienst, T.E.; Smith, D.F.; Li, W.; Edney, E.O.; Driscoll, D.J.; Speer, R.E.; Weathers, W.S. (1999) Secondary organic aerosol formation from the oxidation of aromatic hydrocarbons in the presence of dry submicron ammonium sulfate aerosol. *Atmos. Environ.* 33(22): 3669-3681.
- Kleindienst, T. E.; Jaoui, M.; Lewandowski, M.; Offenberg, J. H.; Lewis, C. W.; Bhavsar, P.; Edney, E. O. (2007) Estimates of the contributions of biogenic and anthropogenic hydrocarbons to secondary organic aerosol at a southeastern U.S. location. *Atmos. Environ.*
- Lewandowski, M.; Jaoui M.; Kleindienst T. E.; Offenberg, J. H.; Edney, E. O. (2007) Composition of PM_{2.5} during the summer of 2003 in Research Triangle Park, North Carolina. *Atmos. Environ.* 41(19): 4073-4083.
- Martin-Reviago, M.; Wirtz, K. (2005) Is benzene a precursor for secondary organic aerosol? *Environ. Sci. Technol.* 39: 1045-1054.
- Mulawa, P. A. (1997) Effect of ambient temperature and E-10 on primary exhaust particulate matter emissions from light-duty vehicles. *Environ. Sci. Technol.* 31: 1302-1307.
- Pun, B. K.; Seigneur, C. (2006) Investigative modeling of new pathways for secondary organic aerosol formation. Final Report. CRC Project A-59. Coordinating Research Council.
- Ragazzi, R.; Nelson, K. (1999) The impact of a 10% ethanol blended fuel on the exhaust emissions of Tier 0 and Tier 1 light duty gasoline vehicles at 35F. Colorado Department of Public Health and Environment. March 26, 1999. For additional information or copies, contact Gerald L. Gallagher or Margie M. Perkins.
- Schauer, J. J.; Fraser, M. P.; Cass, G. R.; Simoneit, B. R. T. (2002) Source reconciliation of atmospheric gas-phase and particle-phase pollutants during a severe photochemical smog episode." *Environ. Sci. Technol.* 36: 3806-3814.

- Turpin, B. J., Huntzicker, J. J., Larsen, S. M., and Cass, G. R. (1991) Secondary formation of organic aerosol in the Los Angeles Basin: a descriptive analysis of organic and elemental carbon concentration, *Environ. Sci. Technol.* 25: 1788-1793.
- Turpin, B. J.; Huntzicker, J. J. (1991) Secondary formation of organic aerosol in the Los Angeles basin. A descriptive analysis of organic and elemental carbon concentrations. *Atmos. Environ.* 25(22): 207-215.
- Zheng, M.; Cass, G. R.; Schauer, J. J.; Edgerton, E. S. (2002) Source apportionment of PM_{2.5} in the Southeast United States using solvent-extractable organic compounds as tracers. *Environ. Sci. Technol.* 36: 2361–2371.
- U. S. Environmental Protection Agency. (2007a) “National Emissions Inventory (NEI) Air Pollutant Emissions Trends Data, 1970 - 2006 Average annual emissions.”
- U.S. Environmental Protection Agency. (2007b) Regulatory Impact Analysis: Renewable Fuel Standard Program. EPA 420-R-07-004. April. Available from: <http://www.epa.gov/otaq/renewablefuels/420r07004.pdf>

V. POTENTIAL WATER QUALITY EFFECTS

This chapter focuses on the potential effects of fuel and fuel additives on contamination of ground waters which serve as supplies for drinking water. There are three mechanisms by which fuel additives can contaminate ground water: (1) the additive can itself be a contaminant, (2) the additive can interfere with natural biodegradation of hydrocarbons such as benzene, toluene, ethylbenzene and xylenes (BTEX) in ground water allowing the plumes formed by these petroleum components to extend farther than they otherwise would, and (3) the additive can encourage growth of anaerobic bacteria that produce other toxic or undesirable substances such as hazardous biodegradation products, sulfide, soluble forms of iron, manganese, arsenic, methane (at explosive concentrations), or volatile fatty acids such as butyrate.

The probability of affecting ground water supply wells is related to the length of the plume generated from the source of the contamination in ground water and the rate of water supply withdrawal. Replacing MTBE with an alternative that is either more hazardous than MTBE, has hazardous by-products or causes a significant increase in the length of plumes of benzene and other BTEX compounds can be detrimental to the overall quality of ground water and public health. Ethanol, when blended with gasoline, has the potential to make the plume of benzene and other BTEX compounds persist longer and travel farther than they would in the absence of ethanol.

Potential water quality and quantity impacts due to renewable fuel feedstock production are beyond the scope of this report but will be included in a future report to Congress as directed by Section 204 of the Energy Independence and Security Act of 2007.

A. Factors Influencing Plume Length and Ground Water Contamination

The length of plumes associated with MTBE and its replacements and the possibility that they will adversely affect ground water used as drinking water is related to (1) the hazard associated with the fuel additive and by-products and any resulting concentration-based standard used to define the plume boundary, (2) the tendency of the fuel additive to partition out of spilled gasoline, dissolve into ground water and establish high concentrations in the area of the spill, and (3) the rate and extent of biodegradation of the fuel additive in ground water.

The hazard associated with the individual fuel additives and by-products is evaluated in Chapter II, and studies relating initial concentrations of fuel additive contaminants to plume length will be discussed in the following two sections.

The second factor, the tendency of fuel additives to partition out of gasoline, depends on a number of factors, including: gasoline composition, equilibrium phase partitioning, mass transfer limitations and geologic heterogeneity. As the concentration of an additive in gasoline increases, the concentration in ground water will increase. Equilibrium phase partitioning describes the tendency of the additive to either remain

behind in gasoline or to dissolve in ground water. Additives that are chemically similar to petroleum, such as the alkylates, tend to remain in the gasoline. Additives that are chemically more similar to water, such as the alcohols, tend to dissolve in water. Mass transfer limitations refer to conditions that slow the rate that the additive can dissolve in ground water. Geological heterogeneity refers to variations in the composition of the aquifer that affects the flow of ground water. The flow of ground water carries an additive away from the spill of gasoline to form a plume of contamination in the aquifer. Ground water flows faster through sands and gravels than it does through silts and clays. These processes and interactions are described in more detail in Appendix B.

Compared to the natural components of petroleum in gasoline, MTBE has a higher solubility in water. Benzene is one of the most soluble natural components of gasoline; its solubility in water is 1.8 g/L. In contrast, the solubility of MTBE is near 50 g/L. The solubility of ETBE, TAME, and DIPE in water are 12, 11, and 7 g/L respectively, and they produce concentrations in ground water contaminated by spilled gasoline that are only slightly less than those produced by MTBE. The alcohols (ethanol and TBA) produce concentrations in ground water that are even higher than those produced by MTBE (see Table 3-1 in Wilson, 2003). Based on their higher solubility in water compared to MTBE, the concentrations of 1-propanol, 2-propanol, and 1-butanol, should also be higher than MTBE (Montgomery, 2000). In contrast, the branched chain alkanes (alkylates) have little solubility in water (Montgomery, 2000). The expected concentrations of alkylates is one thousand fold lower than the observed concentrations of MTBE.

The third factor, the biodegradation of the fuel additive, can occur via a variety of mechanisms. Organic compounds are metabolized through a series of oxidation/reduction reactions, where one compound loses electrons and is oxidized, and the other compound receives electrons and is reduced. If the organic compound is entirely oxidized to carbon dioxide, the process is termed respiration. Oxygen, nitrate, sulfate, and iron (Fe(III)) minerals, can serve as the terminal electron acceptors during respiration. When molecular oxygen is reduced to water, the process is called aerobic respiration; when sulfate is reduced to sulfide, the process is termed sulfate reduction; when nitrate is reduced to ammonia or molecular nitrogen, the process is called nitrate reduction or denitrification, and when insoluble Fe(III) minerals are reduced to form soluble Fe(II) salts, the process is termed iron reduction. Organic compounds can also serve as both electron donors and electron acceptors, and reactions where the electron donor and electron acceptor are both organic compounds are called fermentations. Information on the potential for biodegradation of ethanol and other alcohols, MTBE and other ethers, and the BTEX compounds is discussed in detail later in the section and is summarized in Table V.B-3.

Bacteria that carry out aerobic respiration are widely distributed in soil and sediment and have a great metabolic diversity. However, oxygen has limited solubility in water and is usually unavailable in contaminated aquifer sediments, and ambient concentrations of nitrate are usually low in these sediments; as a result, the most

important electron acceptors in contaminated ground water are sulfate and Fe(III) minerals in the aquifer sediment (Wiedemeier et al., 1999; U.S. EPA, 2007).

The biodegradability for each additive and its affect on plume composition and length will be discussed in the following two sections.

B. The Potential Effect of Fuel Additives on Plume Length and Ground Water Contamination

A spill of gasoline may contaminate ground water with natural petroleum hydrocarbons, including benzene and the BTEX compounds, as well as fuel additives such as MTBE, TBA, ETBE, DIPE, heavy alcohols, iso-octane and alkylates, and ethanol. Near the spill, the plume of contaminated ground water will contain all the contaminants found in the particular fuel spilled. As the plume moves away from the spill, individual contaminants will attenuate due to sorption, biodegradation and dilution and dispersion. The concentration of individual ground water contaminants will drop below the MCL, the action level, or other regulatory goal at various distances from the spill, depending on the initial concentration in the source, and the particular rate of attenuation of the individual contaminants. One contaminant will move the greatest distance before it reaches an acceptable concentration, and this contaminant will define the overall size of the plume of contamination from a particular spill of gasoline. The presence of one contaminant, such as ethanol, can influence the size of the plume of other contaminants, such as benzene. This section compares the sizes of plumes formed by benzene, fuel additives such as MTBE, TBA, or ethanol, and the interaction between fuel additives and the size of benzene plumes.

1. MTBE, TBA, ETBE, DIPE, iso-octane and alkylates

The U.S. Geological Survey recently summarized data collected under the National Water Quality Assessment Program on the concentrations of selected volatile organic compounds in untreated ground water (Zogorski et al., 2006). Two of the important contaminants that might be derived from spills of gasoline from underground storage tanks are benzene and MTBE. Benzene and MTBE were found to have a similar distribution in the number of occurrences at unacceptable concentrations. In shallow ground water in urban areas, benzene was detected 9 times in 847 samples at a concentration above its Maximum Contaminant Level (MCL) of 5 µg/L. The median concentration of occurrences of benzene above the standard was 80 µg/L, which is 16 fold above its MCL. In contrast, MTBE was detected 12 times in 847 samples at concentration above 20 µg/L (the lower limit for the U.S. EPA Drinking Water Advisory for MTBE). The median concentration of occurrences of MTBE above the standard was 120 µg/L, which is 6 fold above its lower Drinking Water Advisory. Therefore, as measured by the National Water Quality Assessment Program, the extent of benzene and MTBE contamination in shallow ground water in urban areas is very similar. It should be noted that the MCL for benzene and the Drinking Water Advisory level for MTBE address very different concerns. Benzene is a known human carcinogen, and the MCL is health protective of this endpoint. The Drinking Water Advisory level for MTBE, on the

other hand, is based on odor and taste thresholds. More health effects information on benzene and MTBE can be found in Chapter II.

The published data on the length of plumes of benzene and MTBE produced from leaking underground storage tanks are also consistent with one another. Table V.B-1 compares published data on the lengths of benzene and MTBE plumes in Texas and California. In each of the studies, the plumes were associated with the entire population of gasoline spills in the relevant geographic area that was subject to monitoring by the regulatory authority that collected the data. As a consequence, the population in each study included old and new spills, spills of conventional gasoline, spills of gasoline with MTBE and other ethers added to enhance octane, spills of RFG gasoline, and spills of E10. On average, the MTBE plumes are longer, but not many fold longer, than the plumes of benzene from the same spills of gasoline. Data are also available on the length of plumes of TBA in Greater Los Angeles. This compound is used to manufacture MTBE, has been used in gasoline as an alternative to MTBE, and is produced by natural biodegradation of MTBE in ground water. On average, the length of the TBA plumes is on the same scale as the length of benzene and MTBE plumes. In greater Los Angeles, the average lengths of plumes of ETBE, DIPE and TAME are also on the same scale as the length of benzene and MTBE plumes (Shih et al., 2004). There have been no observational studies of iso-octane or other alkylates.

Table V.B-1. Comparison of plume lengths of volatile organic contaminants in ground water originating from gasoline spills from underground storage tanks.

	MTBE	Benzene	TBA
Mean Plume Length In Texas (to 10 µg/L) (feet) ^a	174	144	--
Mean Plume Length In California (feet) ^b	170	113	--
Geometric mean of measured Plume Length in Greater Los Angeles (feet) ^c	272	167	207
Median estimated plume length in 90 plumes in Greater Los Angeles (feet) ^d	242	148	--

^aMace and Choi, 1998

^bHappel et al., 1998

^cShih et al., 2004

^dTong and Rong, 2002

As discussed previously, the extent of a contaminant plume depends upon the rates of release of mass from the source, transport in the aquifer, and biodegradation. The effect of each transport parameter on the extent and concentration of contaminant plumes can be shown through a sensitivity analysis. Maier and Grathwohl (2006) developed a relationship for plume length from empirical results generated from one- and

two-dimensional model runs. The models were developed for dissolved contamination with reaction between the contaminant and an electron acceptor.¹⁵

For the conditions represented in an example provided by Maier and Grathwohl, assumed source concentrations of MTBE and ethanol and for stoichiometric constants are shown in Table V.B-2. The results show that in every case the result of lowering source concentration is to reduce the plume length. The reduction in plume length, however, is not proportional to the reduction in source concentration. For example, for the stoichiometric conversion of MTBE to TBA a change in source concentration from 1000 mg/L to 100 mg/L resulted in a reduction in plume length from 1560 m to 490 m. In other words, reduction of the source concentration by a factor of 10 resulted in reduction of plume length by a factor of 3.2.

Table V.B-2. Results from Maier and Grathwohl (2006) plume length analysis for an aquifer of 4.5 m contaminated thickness, vertical dispersivity of 0.032, and electron acceptor concentration of 8 mg/L. The concentration and plume length ratios are relative to the first result for each reaction.

Reaction	Electron Acceptor	Source Concentration (mg/L)	β	Plume Length (m)	Concentration Ratio	Plume Length Ratio
MTBE to TBA	Oxygen	1000	0.54	1560	1	1
		100		490	10	3.2
Ethanol to CO ₂	Oxygen	2500	2.08	4840	1	1
		1400		3620	1.8	1.3
		250		1530	10	3.2
		25		484	100	10
Ethanol to CO ₂	Sulfate	2500	3.13	5940	1	1
		250		1880	10	3.2

Although Maier and Grathwohl's results are instructive, the analysis does not include the effect of dissolution from a non-aqueous phase liquid or fuel. The Hydrocarbon Spill Screening Model (HSSM), developed by the EPA (U.S. EPA, 1994, 1995) includes flow of the fuel as a separate phase and dissolution of its components into flowing ground water. In a modeling exercise done by the EPA (U.S. EPA, 2005b), the composition of the released gasoline was varied to represent three scenarios: a state with an MTBE-ban (New York) where MTBE was present at 0.28% volume, which is below

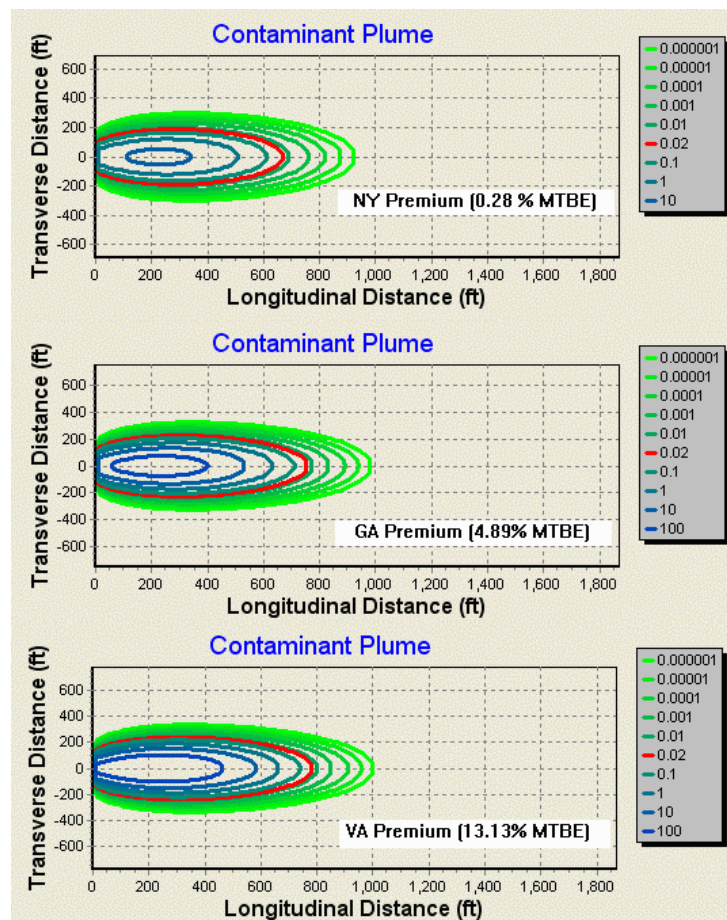
¹⁵ The resulting relationship has the form

$$L = a \frac{M^2}{\alpha_t} \left(\frac{C_s \beta}{C_{ea}} \right)^b$$

where L is the plume length, *a* and *b* are empirical constants determined by Maier and Grathwohl (2006) to be approximately 0.3 and 0.5, respectively, M is the thickness of the contaminant plume, α_t is the vertical transverse dispersivity, *C_s* is the source concentration, *C_{ea}* is a representative electron acceptor concentration and β is the stoichiometric constant representing the use of the electron acceptor for degradation of the source material.

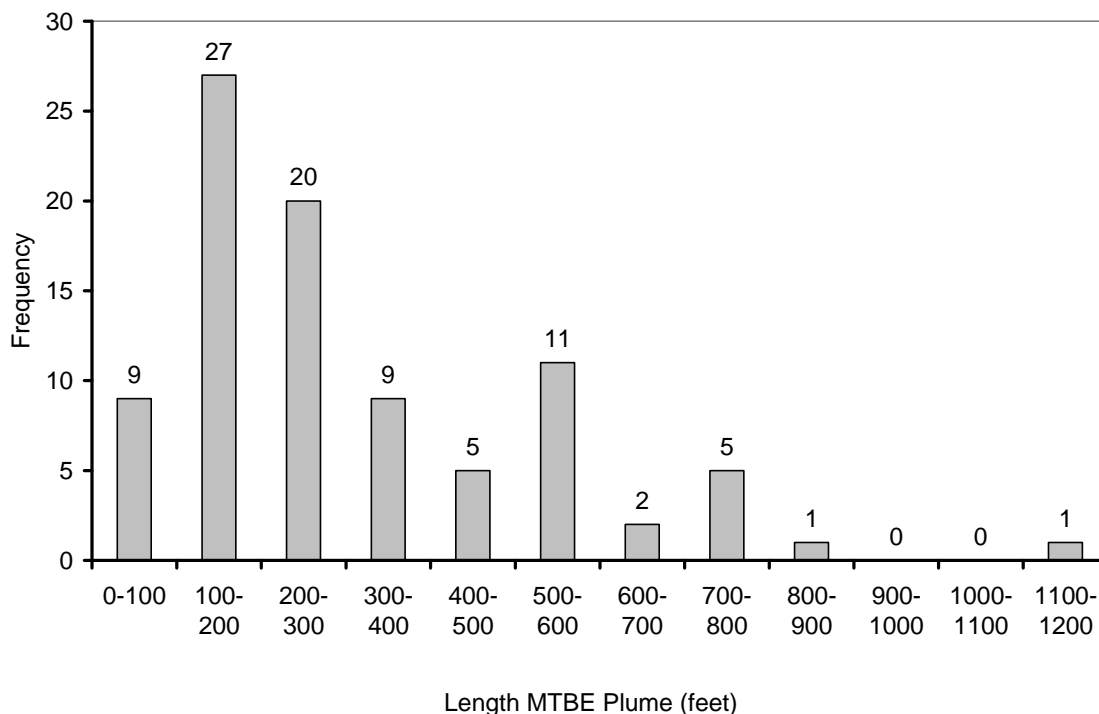
the maximum allowable MTBE content of 0.5% volume; a state where oxygenated gasoline was not required (Georgia) and MTBE's presence in gasoline at 4.89% volume was likely for use as an octane enhancer, and a state where reformulated gasoline was required (parts of Virginia) with a concentration of MTBE at 13.13% volume (U.S. EPA, 2005b). The results of these simulations show that the MTBE concentrations in the aquifer are proportional to the MTBE content in the gasoline (see Figure V.B-1). However, the extent of contamination, defined by the plume boundaries where the concentration of MTBE is 0.02 mg/L or higher, does not appear to be particularly sensitive to source strength. The maximum extent of the plumes increased from about 675 feet to 780 feet as the MTBE content increased from 0.28% volume to 13.13% volume.

Figure V.B-1. HSSM simulation results for three gasoline scenarios. At top, New York premium containing 0.28% volume MTBE; at center, Georgia premium containing 4.89% volume MTBE, and at bottom, Virginia premium containing 13.13% volume MTBE. The concentrations are given in units of mg/L, and the 0.02 mg/L contour is highlighted as it corresponds to the lower limit of the EPA drinking water advisory for MTBE.



Tong and Rong (2002) conducted a statistical analysis of 90 plumes in Greater Los Angeles that had adequate monitoring to establish the behavior and distribution of the plume. They calibrated the analytical model of Domenico (1987) to best fit the monitoring data. The distribution of MTBE plume lengths was strongly asymmetric (Figure V.B-2). Most plumes were short, but a few plumes were much longer than the average. They found that the length of the MTBE plumes did not correlate strongly with the velocity of ground water flow (correlation coefficient of 0.17) or with the maximum concentration at the source (correlation coefficient of 0.31). Instead, the strongest correlation was with the calibrated first order rate constant for biodegradation (correlation coefficient of -0.65). The correlation is negative because the shortest plumes were associated with the highest rates of biodegradation.

Figure V.B-2. Distribution of the lengths of MTBE plumes in ground water in 90 plumes in Greater Los Angeles (Tong and Rong, 2002).



Extrapolating from the analysis of Tong and Rong (2002) for MTBE, the length of a plume of an alternative fuel additive in ground water will be largely controlled by the rate of natural biodegradation of the fuel additive. Table V.B-3 provides a qualitative summary of the potential for biodegradation of MTBE and of the substitutes for MTBE identified by Congress for evaluation. Because ground water contaminated with gasoline is generally devoid of oxygen, the evaluation is limited to the potential for natural anaerobic biodegradation.

As summarized in Table V.B-3, there is no evidence from the literature that the other ether oxygenates (ETBE, TAME, or DIPE) are any more degradable than MTBE.

Anaerobic biodegradation of MTBE produces TBA as the first degradation product (Wilson et al., 2005b; Somsamak et al., 2005; Mackay et al., 2007). As far as is known, the organisms that degrade MTBE do not further metabolize the TBA that they produce (Wilson et al., 2005a; Somsamak et al., 2005). TBA is degraded by other organisms, including sulfate reducing bacteria, iron-reducing bacteria, or bacteria that ferment the TBA to methane (Finneran and Lovley, 2001; U.S. EPA, 2007). For MTBE to be entirely degraded, the TBA produced must be entirely degraded. With respect to iso-octane and the other alkylates¹⁶, there are no reports in the literature for anaerobic biodegradation of branched chain alkanes (alkylates) in the molecular weight range of gasoline components.

Organisms that are capable of anaerobic MTBE biodegradation are not universally distributed in contaminated ground water. Many plumes fail to acclimate to anaerobic biodegradation, and many plumes that do acclimate are heterogeneous, with rapid and extensive degradation in some portions of the plume and limited degradation in others (U.S. EPA, 2005a). Anaerobic biodegradation of TBA in ground water follows the same pattern (U.S. EPA, 2007).

There are a few publications available in the literature that allow for a quantitative comparison of the rates of anaerobic biodegradation of benzene, MTBE and the alternative fuel additives in ground water. Table V.B-4 summarizes what data are available from the literature for biodegradation of benzene, MTBE, and TBA in ground water, and compares the average of the rates of anaerobic biodegradation in the literature to the average rate of biodegradation estimated by EPA for a large population of plumes in Greater Los Angeles.

Shih et al. (2004) provided data on the distribution of plumes of benzene, MTBE, and TBA in Greater Los Angeles. Data were reported on the average length of 95 benzene plumes, 96 MTBE plumes and 86 TBA plumes, and the maximum concentration of organic compounds in the source area of 716 benzene plumes, 718 MTBE plumes and 530 TBA plumes. Using this information, combined with hydrological information from a subset of the plumes observed in the same area by Tong and Rong (2002), we extracted an estimate of the average rate of biodegradation at these release sites.

Tong and Rong (2002) estimated that the mean ground water velocity for 90 of the sites in Greater Los Angeles was 55 feet per year. This estimate is similar in magnitude to the median velocity of 100 feet per year extracted by McNab et al. (2000) from a population of chlorinated solvent plumes, most of which were in the Western United States.

¹⁶ Iso-octane is a component of alkylates.

Table V.B-3, Part 1 of 3. Potential for natural anaerobic biodegradation of additives, the impact of additives on potential for natural anaerobic biodegradation of BTEX, and secondary pollutants associated with additive.

Additive or Category of Additive	Potential for Natural Anaerobic Biodegradation of Additives	Potential for Impact on Natural Anaerobic Biodegradation of BTEX	Secondary Pollutants Associated with Degradation of Additive
Methyl tertiary butyl ether (MTBE)	Degradation rapid and extensive at some sites but only after microbial acclimation. Does <i>not</i> degrade ^{a,b,c,d,e} Does degrade ^{f,g,h,i,j,k,l,m,n}	Yes, metabolism produces TBA and probably acetate. Metabolism of TBA and acetate may consume sulfate, and ferric iron that otherwise could be used to degrade benzene.	TBA ^o
Ethyl tertiary butyl ether (ETBE)	Does <i>not</i> degrade ^{a,f,i} Does degrade ^k	None demonstrated.	TBA ^k
Tertiary amyl methyl ether (TAME)	Degradation rapid and extensive at some sites but only after microbial acclimation. Does <i>not</i> degrade ^{a,f} Does degrade ^{i,j}	Yes, metabolism produces TAA and acetate. Metabolism of acetate may consume sulfate and ferric iron that otherwise could be used to degrade benzene.	Tertiary amyl alcohol (TAA) ^{i,j}
Di-isopropyl Ether (DIPE)	No report of anaerobic biodegradation in the literature. Does <i>not</i> degrade ^a	No known potential	None demonstrated
Tertiary butyl alcohol (TBA)	Degradation rapid and extensive at some sites but only after microbial acclimation. Does <i>not</i> degrade ^{a,h,i,j} Does degrade ^{g,k,n,p,q,r,s}	Yes, metabolism may consume sulfate and ferric iron that otherwise could be used to degrade benzene	Acetone ^t , sulfide, ferrous iron

Table V.B-3, Part 2 of 3. Potential for natural anaerobic biodegradation of additives, the impact of additives on potential for natural anaerobic biodegradation of BTEX, and secondary pollutants associated with additive.

Additive or Category of Additive		Potential for Natural Anaerobic Biodegradation of Additives	Potential for Impact on Natural Anaerobic Biodegradation of BTEX	Secondary Pollutants Associated with Degradation of Additive
Other ethers and heavy alcohols as determined by Administrator				
<i>Other Ethers Alcohols</i>	Tertiary amyl alcohol (TAA)	No known potential Does <i>not</i> degrade ^{a,f}	No known potential	None demonstrated
<i>Other Ethers Alcohols</i>	1-propanol	Degradation rapid and extensive at almost all sites after microbial acclimation. Does degrade ^{u,v}	Metabolism can be expected to consume sulfate and ferric iron that otherwise could be used to degrade benzene	Methane, sulfide, ferrous iron
<i>Other Ethers Alcohols</i>	2-propanol (isopropyl alcohol)	Degradation rapid and extensive at almost all sites after microbial acclimation. Does degrade ^{a,f,u,v}	Metabolism can be expected to consume sulfate and ferric iron that otherwise could be used to degrade benzene	Methane, sulfide, ferrous iron
<i>Other Ethers Alcohols</i>	1-butanol	Degradation rapid and extensive at almost all sites after microbial acclimation. Does degrade ^{u,v}	Metabolism can be expected to consume sulfate and ferric iron that otherwise could be used to degrade benzene	Methane, sulfide, ferrous iron
<i>Other Ethers Alcohols</i>	Methanol	Degradation rapid and extensive at almost all sites after microbial acclimation. Does degrade ^{a,f,r,s,v,w,x}	Yes ^{w,x} , metabolism may consume sulfate and ferric iron that otherwise could be used to degrade benzene	Methane, sulfide, ferrous iron

Table V.B-3, Part 3 of 3. Potential for natural anaerobic biodegradation of additives, the impact of additives on potential for natural anaerobic biodegradation of BTEX, and secondary pollutants associated with additive.

Additive or Category of Additive	Potential for Natural Anaerobic Biodegradation of Additives	Potential for Impact on Natural Anaerobic Biodegradation of BTEX	Secondary Pollutants Associated with Degradation of Additive
Ethanol	Degradation rapid and extensive at almost all sites after microbial acclimation. Does degrade ^{a,b,k,y,z,aa,bb}	Yes ^b and by inference ^{w,x} . Metabolism may consume sulfate and ferric iron that otherwise could be used to degrade benzene ^d	Methane ^{b,cc,dd} , Acetate, propionate, butyrate ^{cc,ee} , sulfide, ferrous iron
Iso-octane (an alkylate) 2,2,4-trimethylpentane Also other alkylates 2,3-dimethylpentane, 2,4-dimethylpentane	Unclear. Degradation of unbranched alkanes rapid and extensive after microbial acclimation ^{ff,gg,hh} . However, branched chain alkanes (alkylates) expected in the range of gasoline are not shown to degrade ^{ff} .	None demonstrated	None demonstrated

^aSuflita and Mormile, 1993

^bDa Silva and Alvarez, 2002

^cRuiz-Aguilar et al., 2002

^dLandmeyer et al., 1998

^eAmerson and Johnson, 2002

^fMormile et al., 1994

^gUS EPA, 2005a

^hWilson et al., 2005a

ⁱSomsamak et al., 2001

^jSomsamak et al., 2005

^kYeh and Novak, 1994

^lKuder et al., 2005

^mKolhatkar et al., 2002

ⁿFinneran and Lovley, 2001

^oWilson et al., 2005b

^pUS EPA, 2007

^qFinneran and Lovley, 2003

^rNovak et al., 1985

^sHickman and Novak, 1989

^tWilson, 2003

^uHovious et al., 1973

^vChou et al., 1978

^wBarker et al., 1990

^xBarker et al., 1992

^yAlvarez and Hunt, 1999

^zMravik et al., 2003

^{aa}Zhang et al., 2006

^{bb}McDowell et al., 2003

^{cc}Mackay et al., 2006

^{dd}Buscheck et al., 2001

^{ee}Powers et al., 2001

^{ff}Rueter et al., 2002

^{gg}Caldwell et al., 1998

^{hh}Widdel and Rabus, 2001

To estimate an average rate of biodegradation from the data reported by Shih et al. (2004), the reported mean plume length was first divided by the average ground water velocity of 55 feet per year. This provided an estimate of the average travel time in ground water from the source to the down gradient margin of the plume. The length of the plume was the distance to the point where the concentrations dropped below California's concentration based goals (5 µg/L for MTBE and benzene and 10 µg/L for TBA). Degradation was assumed to follow a pseudo first order rate law; in other words,

concentrations declined over time following a half life, much like radioactive decay.¹⁷ These rates are reported in Table V.B-4.

Tong and Rong (2002) also reported the average rate of biodegradation necessary to calibrate the analytical equations of Domenico (1987) to the field data from the 90 plumes selected from the larger data set reported in Shih et al. (2004). Their average rate of biodegradation is also presented in Table V.B-4. For MTBE there was good agreement between Tong and Rong's mean and median of the rate constants calibrated to the 90 individual plumes, and our calculated estimates made for the entire set of plumes (described above). There was also good agreement between the average of the rates of biodegradation available in the literature and our estimated rates of biodegradation for the population of plumes in Greater Los Angeles. For benzene, there was also good agreement between the average rate of benzene biodegradation published in the literature for anaerobic biodegradation of benzene at field scale, and our estimated rate of attenuation in the Greater Los Angeles plumes.

The close agreement does not prove that the rates of biodegradation of MTBE and benzene are correct, but they do suggest that the rates published in the literature are plausible. They also suggest that biodegradation is a primary control on the length of benzene and MTBE plumes at field scale. In the absence of a field biodegradation rate constant of at least 1 per year (for substances with a first-order degradation rate), the plumes formed by substitute additives may be longer than those of MTBE and benzene.

For TBA, the agreement between the calculated literature values for biodegradation and our estimated average rate of biodegradation in the Greater Los Angeles plumes are not as close, with the literature rates about an order of magnitude higher. This may be due to the fact that the rates reported in U.S. EPA (2007) are dominated by laboratory studies, and rates extracted from laboratory studies are often faster than rates in the field (Suarez and Rifai, 1999), particularly for degradation limited by the supply of a critical requisite for microbial metabolism of TBA, such as sulfate. The published rates of TBA biodegradation are probably less representative of the achieved rates of TBA biodegradation in contaminated aquifers.

2. Ethanol

Just as with MTBE and the substitutes discussed in the previous section, the impact of ethanol will depend on the concentration of ethanol that is attained in ground water in contact with the spill of gasoline and the extent of the plume of ethanol. The extent of the plume will in turn be controlled by the rate of biodegradation of ethanol.

Anaerobic MTBE biodegradation is dependent upon the presence of a particular variety of acetogenic anaerobic bacteria. In contrast, methanol, ethanol, and the heavy

¹⁷ The half life is equivalent to 0.693 divided by the first order rate constant. The first order rate constant was estimated as follows:

$$\text{rate of decay} = -\text{natural logarithm} \left(\frac{\text{Goal}}{\text{Highest Concentration}} \right) / \text{residence time}$$

alcohols other than TBA (1-propanol, 2-propanol, and 1-butanol) are readily biodegraded by anaerobic bacteria that are common and widely distributed, including sulfate-reducing bacteria and organisms that ferment the alcohols to fatty acids (Eichler and Schink, 1984) and ultimately to methane (Chou et al., 1978). See Powers et al. (2001) for a review of anaerobic ethanol biodegradation.

Biodegradation of benzene in ground water is supported by aerobic respiration, nitrate reduction, sulfate reduction and iron reduction (Suarez and Rifai, 1999; Wiedemeier et al., 1999). Many of the substitutes for MTBE are metabolized more readily than benzene; this is particularly true for the alcohols. If the metabolism of the compounds that substitute for MTBE consumes the available supplies of the electron acceptors, then the rate and extent of biodegradation of benzene should be restricted, and the plumes of benzene should be longer than they would have been in the absence of the substitute (Corseuil et al., 1998; Alvarez and Hunt, 1999; Powers et al., 2001, Da Silva and Alvarez, 2002; Ruiz-Aguilar et al., 2002).

Ulrich (1999) used parameters from the literature to model the effect of 10,000 mg/L of ethanol on the migration of 10 mg/L of benzene in an aquifer. In a simulation of conditions relevant to the Borden Aquifer in Ontario, Canada, the presence of ethanol would make the benzene plume longer by a factor of 1.8. McNab et al. (1999) developed a screening model for a release of E10 gasoline. Compared to gasoline without ethanol, the benzene plume was longer by a factor of 1.2 at the 10 µg/L boundary and by a factor of 2.0 at the 1 µg/L boundary. Following up on McNab et al. (1999), McNab (2001) used a finite-difference-based reactive transport model to evaluate the role of depletion of electron acceptors on the behavior of ethanol and benzene. He modeled the release of E10 and conventional gasoline, both containing 1.5% benzene, into an aquifer with 9 mg/L dissolved oxygen, 10 mg/L nitrate and 20 mg/L sulfate. The benzene plume simulated with E10 was longer than the plume simulated for gasoline without ethanol by a factor of 2.5.

Deeb et al. (2002) showed in laboratory cultures that ethanol inhibited the aerobic biodegradation of benzene. They constructed a two-dimensional mathematical model comparing the aerobic and anaerobic rates of biodegradation of benzene in the presence and in the absence of ethanol. Their simulations indicated that the presence of ethanol could make the benzene plumes increase in length by a factor 1.16 to 1.34. Molson et al. (2002) simulated the effect of the consumption of oxygen by ethanol from an E10 spill on the length of the benzene plume. Under some circumstances, the simulated benzene plume was longer than the plume simulated in the absence of ethanol by a factor of 1.5.

Table V.B-4. Comparison of first order rates of anaerobic biodegradation of TBA, MTBE, and benzene and the zero order rate of biodegradation of ethanol, and the consequences for time of travel along a contaminated flow path in ground water.

	MTBE	Benzene	TBA	Methanol	Ethanol
Summary data from literature on the rate of biodegradation under anaerobic conditions					
Mean	1.0 per year ^a	1.1 per year ^b	9.2 per year ^c		17 mg/L per day ^{d,e} (Table V.B-6)
Median	0.41 per year ^a		7.3 per year ^c		13 mg/L per day ^{d,e} (Table V.B-6)
Number of rates	10 ^a	45 ^b	14 ^c		10 ^{d,e} (Table V.B-6)
	Greater Los Angeles ^f			Ontario, Canada ^g	Northwestern USA ^h
Mean plume length	272 feet	167 feet	207 feet	220 feet	260 feet
Geometric mean of highest concentration at a site	900 µg/L	700 µg/L	1730 µg/L	7,000 mg/L	16,000 mg/L
Plume boundary definition	5 µg/L	5 µg/L	10 µg/L	1 mg/L (Detection Limit)	50 mg/L (Detection Limit)
Estimated travel time along flow path in plume	4.9 years	3.0 years	3.8 years	1.3 years	0.8 years
Estimated rate constant for overall attenuation	1.1 per year	1.6 per year	1.4 per year	15 mg/L per day	55 mg/L per day
Summary data on rate of biodegradation in 90 plumes in Greater Los Angeles Area ⁱ					
Mean	1.6 per year				
Median	1.3 per year				
Number of rates	90				

^aU.S. EPA, 2005a

^bSuarez and Rifai, 1999

^cU.S. EPA, 2007

^dSuflita and Mormile, 1993

^eSomsamak et al., 2001

^fShih et al., 2004

^gBarker et al., 1990

^hBuscheck et al., 2001

ⁱTong and Rong, 2002

The dominant fuel additives detected by Shih et al. (2004) in ground water in Greater Los Angeles were MTBE and TBA. Consistent with the estimations in Table V.B-4 on rates of biodegradation of MTBE and TBA, Shih et al. (2004) recognized that biodegradation of MTBE and TBA should be expected to consume electron acceptors

such as sulfate and Fe(III) in ground water and have an effect on the length of the benzene plume. In an attempt to evaluate the possible effect of readily degradable compounds on the length of benzene plumes, Shih et al. (2004) compared the lengths of benzene plumes that also contained fuel oxygenates to the lengths of plumes that did not contain fuel oxygenates. The median length of plumes without oxygenates was 130 feet, while the median length of plumes with oxygenates was 186 feet. Shih et al. (2004) recognized and acknowledged that the plumes without oxygenates might be shorter because these plumes would be older and further along in their lifecycle and should therefore have fewer plumes that were growing and more plumes that were stabilized and shrinking. Nevertheless, their observation can put a useful upper boundary on the expected increase in size of benzene plumes due to the influence of a biodegradable fuel oxygenate at something on the order of 40% longer.

This observation for TBA and the ether oxygenates can be extrapolated to ethanol by comparing the amount of sulfate required for complete metabolism of MTBE or its substitutes in gasoline. Table V.B-5 compares the amount of sulfate that would be required for complete metabolism of various fuel oxygenates in gasoline. In general, the requirement for sulfate to metabolize the higher alcohols is less than that for MTBE, and the requirement for ethanol at 2% oxygen (i.e., 5.8% volume) is even less. The requirement for sulfate to metabolize the ethanol in gasoline at 10% volume is approximately two-thirds the requirements for metabolism of MTBE at 2% oxygen (i.e., 11% volume).

Table V.B-5. Comparison of the amount of electron acceptor required to metabolize MTBE present in gasoline as a fuel oxygenate to the amount required for TBA and the other butanols, propanols and ethanol.

Fuel Additive	Mass Fraction	Sulfate Requirement (mass sulfate per mass oxygenate)	Sulfate Requirement (kilogram per liter gasoline)
MTBE at 2% oxygen in gasoline (11% volume)	0.11	4.08	0.33
TBA and other butanols at 2% oxygen in gasoline	0.093	3.90	0.27
Propanols at 2% oxygen in gasoline	0.075	3.59	0.20
Ethanol at 2% oxygen in gasoline (5.8% volume)	0.058	3.13	0.13
Ethanol at 10% volume in gasoline	0.10	3.13	0.23

On average, the requirement for soluble electron acceptors will be slightly less for gasoline with 10% ethanol than for gasoline with 11% MTBE. However, the requirement for soluble electron acceptors for MTBE and ethanol is likely to be satisfied in different

ways. Much of the ethanol will stay in the unsaturated zone or the capillary fringe (the interface between the unsaturated zone and the ground water aquifer) and never enter ground water. On the other hand, if the release is large and sudden, the initial concentration of ethanol in ground water can be very high. In general, the plume formed from the initial release of ethanol will be more concentrated and may travel further in the aquifer but will last for a short period. MTBE is not as soluble as ethanol and therefore tends to stay with the residual gasoline. Continued dissolution of MTBE from the residual gasoline will sustain concentrations of MTBE in ground water in contact with the residual gasoline. The plume of MTBE and the requirement for electron acceptors to metabolize MTBE will not extend as far into the aquifer, but the effect on the plume of benzene will last much longer.

Ruiz-Aguilar et al. (2003) collected statistics on the length of benzene plumes from 29 sites in Kansas that were contaminated with gasoline that contained ethanol (most likely E10) and 217 sites in Iowa that were contaminated with gasoline without ethanol. The median benzene plume length for sites with ethanol use was 263 feet and for sites without ethanol use was 156 feet. The presence of ethanol in the gasoline mixture may have increased the length of the benzene plume by approximately 70%.

This postulated effect has now been documented at field scale (Mackay et al., 2006). A plume with known concentrations of benzene, toluene and o-xylene (BToX) was created by pumping ground water, amending the ground water with 1 to 3 mg/L of each of the organic compounds, and injecting the ground water back into the source area of an old plume emanating from a spill of gasoline at Vandenberg Air Force Base, California. A second plume was created adjacent to the first that had the same concentrations of BToX, as well as approximately 50 mg/L ethanol. In the side by side comparison, the pseudo first order rate of biodegradation of benzene was twenty-fold slower, and the benzene plume extended up to ten times further in the presence of ethanol.

There is relatively little direct information available on the concentration of ethanol, methanol, 1-propanol, 2-propanol, or 1-butanol in ground water in contact with gasoline spills. Most states do not routinely monitor for these constituents, and when they are monitored, concentrations are usually below the analytical detection limit. The limited information that is available is either from releases of fuel grade ethanol (typically E95) from tank farms, or from controlled-release experiments at pilot scale or field scale where ethanol or methanol is intentionally introduced at a predetermined concentration.

There are two controlled release experiments where gasoline with ethanol was inserted below the water table into aquifer sediment. These experiments were designed to simulate a spill of gasoline below the water table from an underground storage tank. Brazilian gasoline with 24% ethanol was injected at a site in Florianopolis, Brazil (Corseuil et al., 2000), and gasoline with 10% ethanol was injected into an aquifer in Ontario, Canada (Mocanu et al., 2006). The maximum recorded concentration of ethanol in ground water down gradient of each of these releases was approximately 2,500 and

1,400 mg/L respectively. These concentrations are approximately one thousand-fold higher than the highest concentrations of benzene, MTBE or TBA typically seen in ground water at gasoline spill sites (compare Table V.B-4). The high concentrations of ethanol are caused by the fact that ethanol is miscible in water, and almost all the ethanol originally in the gasoline dissolves in the ground water. In contrast, benzene and MTBE have much lower solubility in water relative to ethanol, and therefore most of the benzene and MTBE remains in the gasoline.

Because the concentrations of ethanol that would be expected from a spill of E10 gasoline are so much higher than concentrations of benzene and MTBE, the rate of biodegradation of ethanol tends to follow a different pattern. Benzene and MTBE decay following a pseudo first order rate law (decay described by a half-life), where the rate of decay depends on the concentration at that particular time. In contrast, the concentration of ethanol declines at a steady rate that is independent of the concentration at any time. When the rate of decay is steady and independent of the concentration of the compound, it is termed a zero order rate. As a consequence, the rate of decay of ethanol should not show the tailing effect associated with a first order rate constant. Table V.B-6 summarizes rate constants extracted from seven reports of field scale releases of ethanol and ethanol in fuel (all at varying concentrations).

With one exception, the ethanol decay rates fell into a range between 61 mg/L per day and 1.4 mg/L per day. The exceptionally high rate of 500 mg/L per day was observed at a site where the ethanol was continuously introduced as a solution in ground water released from an injection well (Mackay et al. 2006). All the other rates were extracted from sites where the ethanol was released as a slug. As bacteria degrade ethanol, they increase in number. It is likely that the continued source of ethanol allowed the accumulation of higher and higher densities of ethanol-degrading bacteria in the aquifer just down gradient of the injection well. This effect has also been noted in the laboratory. The rate of ethanol degradation in a laboratory column study with a continuous supply of ethanol reached 13,000 mg/L per day (Da Silva and Alvarez, 2002).

Table V.B-6 compares the average decay rate of the six field studies where ethanol was released as a slug, plus rates extracted from laboratory studies (Corseuil et al., 1998; Suflita and Mormile, 1993). The mean and median rates derived from these studies were 17 and 13 mg/L per day, respectively. As mentioned earlier, the maximum concentrations attained from spills of gasoline containing ethanol were approximately 2,500 and 1,400 mg/L. The rates above can degrade these ethanol concentrations in 3 to 6 months.

As pointed out by Mocanu et al. (2006), the maximum concentration of ethanol in ground water (1,400 mg/L) obtained in their experiment, which injected gasoline plus 10% ethanol directly into an aquifer, is likely higher that would be attained in a real spill of gasoline containing ethanol. If gasoline with 10% ethanol is released above or near the water table, the ethanol tends to leave the gasoline and accumulate in the capillary fringe just above the ground water in the aquifer (McDowell and Powers, 2003; Cápiro et al.,

2007). Dakhel et al. (2003) showed that ethanol from a gasoline release into the unsaturated zone was readily biodegraded.

Table V.B-4 also compares a large plume of ethanol from a release of fuel grade ethanol from a tank farm at a gasoline distribution terminal (Buscheck et al., 2001; McDowell et al., 2003). Although the concentration of ethanol was about ten-fold higher than would be expected from a gasoline spill from a leaking underground storage tank, the maximum plume length was only 260 feet, which is roughly comparable to the average length of benzene, MTBE and TBA plumes in Greater Los Angeles (Shih et al., 2004). This is the longest ethanol plume documented in the literature (see Table V.B-6). Table V.B-4 also presents data from a long plume of methanol created in a sand aquifer at the Canadian Forces Base Borden in Ontario, Canada (Barker et al., 1990). This is a low-nutrient, oligotrophic aquifer, where we should expect less biodegradation. The field scale rate of biodegradation of methanol was comparable to the mean of the rates of biodegradation of ethanol (see Table V.B-6). Again, the length of the plume was comparable to the average length of benzene, MTBE and TBA plumes in Southern California. In general, the impact of plumes of alcohol in ground water will not be from the alcohol as a contaminant but from the effect on the alcohol on the behavior of benzene plumes. Ethanol can also affect MTBE plumes by promoting natural biodegradation of MTBE to TBA (Mackay et al., 2007).

As discussed above, most of the available data concerning the impact of ethanol on benzene plumes are either from spills of technical grade ethanol at storage facilities, releases of ethanol in pilot scale experiments, or projections of computer models. In contrast, the survey data summarized in Ruiz-Aguilar et al. (2003) were collected from spills of gasoline from actual underground storage tanks at automobile service stations. Therefore, EPA believes that the observations of Ruiz-Aguilar et al. (2003) are the best available description of the current impact of ethanol in gasoline on the size of benzene plumes in ground water. The ethanol in an average release of gasoline with 10% ethanol can be expected to increase the length of the benzene plume by approximately 70%. However, it is likely that the distribution of plume lengths will be strongly skewed. Particularly large plumes of benzene can be expected when there is a large area of the aquifer that is contaminated with liquid phase gasoline [area with floating product more than 200 feet wide], when the background concentration of sulfate in the ground water is low [less than 20 mg/L], when the rate of ethanol biodegradation is low [less than 1 mg/L per day], and when the flow velocity of the ground water is high [more than 1 foot per day].

C. Secondary Pollutants Associated with Releases of Gasoline with Additives

The first biotransformation product of many of the ether fuel oxygenates (MTBE, ETBE, TAME, DIPE) is a compound that is often as problematic (Table V.B-3). TBA accumulates from the initial anaerobic biodegradation of MTBE (Wilson et al., 2005b); or ETBE (Yeh and Novack, 1994). Tertiary amyl alcohol (TAA) accumulates during biodegradation of TAME (Somsamak et al., 2001, 2005). Under these conditions, initial

biodegradation of the ether oxygenate does not restore the environmental quality of the ground water.

Because the alcohols are readily degradable and they can enter ground water at high concentrations, their metabolism can provide significant concentrations of a variety of metabolic end products. If sulfate is available in the ground water, or biologically available Fe(III) minerals are present in the aquifer solids, then hydrogen sulfide and ferrous iron can be produced. Fermentation reactions of the alcohols can also produce methane and fatty acids. These same materials are produced from the normal anaerobic metabolism of the BTEX compounds in gasoline (Wiedemeier et al. 1999). However, adding alcohols at concentrations in the hundreds to thousands of mg/L increases the production of these materials many fold.

There are other potential hazards than those associated with chemical toxicity; some spills of gasoline with ethanol may produce methane concentrations in the soil that pose a risk for explosion (Da Silva and Alvarez, 2002; Powers et al., 2001). Ethanol fed to a laboratory column at a concentration of 1,000 mg/L was degraded to produce concentrations of methane that were in excess of the water solubility of methane (i.e., more methane was produced than could be dissolved by the available water) (Da Silva and Alvarez, 2002). At field scale, the methane could bubble out of the ground water and enter the soil gas (gases that occur in the small spaces between particles of soil) at explosive concentrations. At the controlled release study at Vandenberg AFB, California, a release of 500 mg/L ethanol was biologically degraded to produce concentrations of methane in excess of the water solubility of methane (Mackay et al., 2006). At the spill of fuel grade ethanol at the Northwest Terminal Site, the concentration of methane in many wells exceeded the water solubility of methane, and the concentration of methane in the soil gas above the plume exceeded the upper explosive limit (Buscheck et al., 2001).

Methane is not routinely monitored in ground water at gasoline spill sites or in the soil gas above the spills, and there is not enough information currently available to quantitatively evaluate the risk from explosions associated with methane produced from alcohols in gasoline. This is an area where more research is needed as the use of ethanol expands (see Chapter VII).

Table V.B-6. Comparison of rates of anaerobic biodegradation of ethanol in ground water and the consequences for time of travel along a contaminated flow path in ground water.

Nature of Release	Ethanol dissolved in water ^a	Ethanol dissolved in water ^b	Ethanol dissolved in water ^c	72,000 L Denatured Ethanol ^{d,e}	100 L Brazilian Gasoline 24% Ethanol ^f	50 L Gasoline with 10% Ethanol, followed by 2200 L water ^g	50 L of Ethanol Denatured with 5% Gasoline, followed by 2200 L water ^g
Site	Florida	Platte Valley, Nebraska	Vandenberg AFB, California	Pacific Northwest Terminal Tigard, Oregon	Florianopolis, Brazil	Borden Field Site, Ontario, Canada	Borden Field Site, Ontario, Canada
Initial concentration	10,000 mg/L after pumping	190 mg/L	~500 mg/L	16,000 mg/L	2503 mg/L after 16 months	1390 mg/L	15700 mg/L
Travel distance, final concentration	entire plume	20 feet to 4.4 mg/L	1.5 feet to 1 mg/L	260 feet to <50 mg/L	28 feet to non-detect	51 feet to 560 mg/L	51 feet to 5030 mg/L
Estimated travel time along flow path	3.5 years	13 days	1 day	0.8 years	3 years	1.6 years	1.6 years
Estimated rate of removal	9 mg/L per day**	14 mg/L per day* 61 mg/L per day**	500 mg/L per day*	55 mg/L per day*	2.3 mg/L per day* 2.9 mg/L per day **	1.4 mg/L per day*	18 mg/L per day*

* rate calculated by dividing reduction in concentration by residence time in ground water along the path in the aquifer

** rate estimated by multiplying published pseudo first order rate constant by the initial concentration

^aMravik et al., 2003

^bZhang et al., 2006

^cMackay et al., 2006

^dMcDowell et al., 2003

^eBuschek et al., 2001

^fCorseuil et al., 2000

^gMocanu et al., 2006

References:

- Alvarez, P. J. J.; Hunt, C. S. (1999) Volume 4: Potential ground and surface water impacts. Chapter 3: The effect of ethanol on BTEX biodegradation and natural attenuation. UCRL-AR-135949.
- Amerson, I.; Johnson, R. L. (2002) A natural gradient tracer test to evaluate natural attenuation of MTBE under anaerobic conditions. *Ground Water Monit. Rem.* 23: 54-91.
- Barker, J. F.; Hubbard, C. E.; Lemon, L. A. (1990) The influence of methanol and MTBE on the fate and persistence of monoaromatic hydrocarbons in ground water. In: *Proceedings of the petroleum hydrocarbons and organic chemical in ground water: prevention, detection, and restoration*. National Water Well Association: Dublin, Ohio. pp. 113-127.
- Barker, J. F.; Hubbard, C. E.; Lemon, L. A.; Vooro, K. A. (1992) The influence of methanol in gasoline fuels on the formation of dissolved plumes, and the fate and natural remediation of methanol and BTEX dissolved in groundwater. In: Calabrese, E. J.; Kostecki, P.T., eds. *Hydrocarbon contaminated soils and groundwater*. New York, NY. Lewis Publishers. 103–113.
- Buscheck, T. E.; O'Reilly, K.; Koschal, G.; O'Regan, G. (2001) Ethanol in groundwater at a Pacific Northwest terminal. In: *Ground water: prevention, detection, and remediation: proceedings of the petroleum hydrocarbons and organic chemicals conference*; November, 2001, Houston, TX; National Ground Water Association. pp. 55-66.
- Caldwell, M. E.; Garrett, R. M.; Prince, R. C.; Suflita, J. M. (1998) Anaerobic biodegradation of long-chain n-alkanes under sulfate-reducing conditions. *Environ. Sci. Technol.* 32: 2191-2195.
- Cápiro, N.; Stafford, B. P.; Rixey, W. G.; Bedient, P. B.; Alvarez, P. J. J. (2007) Fuel-grade ethanol transport and impacts to groundwater in a pilot-scale aquifer tank. *Water Res.* 41: 656-664.
- Chou, W. L.; Speece, R. E.; Siddiqi, R. H. (1978) Acclimation and degradation of petrochemical wastewater components by methane fermentation. *Biotechnol. Bioeng. Symp.* 8: 391-414.
- Corseuil, H. X.; Hunt, C. S.; Dos Santos, R. C. F.; Alvarez, P. J. J. (1998) The influence of the gasoline oxygenate ethanol on aerobic and anaerobic BTX biodegradation. *Water Res.* 32: 2065-2072.
- Corseuil, H. X.; Fernandes, M.; do Rosário, M.; Seabra, P. N. (2000) Results of a natural attenuation field experiment for an ethanol-blended gasoline spill. In: *Proceedings*

- of conference on petroleum hydrocarbons and organic chemicals in ground water: prevention, detection, and remediation; Anaheim, CA. pp. 24-31.
- Corseuil, H. X.; Schneider, M. R.; do Rosário, M. (2005) Weathering of ethanol-blended gasoline in aquifers – a field experiment. In: Lyon, W. G.; Hong, J.; Reddy, R. K., eds. Proceedings from the first international conference on environmental science technology; January, 2005; New Orleans, LA; pp. 26-31.
- Deeb, R. A.; Sharp, J. O.; Stocking, A; McDonald, S.; West, K. A.; Laugier, M; Alvarez, P. J. J.; Kavanaugh, M. C.;Alvarez-Cohen, L. (2002) Impact of ethanol on benzene plume lengths: microbial and modeling studies. J. Environ. Eng. 128: 868–875.
- Da Silva, M. L. B.; Alvarez, P. J. J. (2002) Effects of ethanol versus MTBE on benzene, toluene, ethylbenzene, and xylene natural attenuation in aquifer columns. J. Environ. Eng. 128: 862-867.
- Dakhel, N.; Pasteris, G.; Werner, D.; Höhener, P. (2003) Small-volume releases of gasoline in the Vadose zone: Impact of the additives MTBE and ethanol on groundwater quality. Environ. Sci. Technol. 37: 2127-2133.
- Domenico, P. A. (1987) An analytical model for multidimensional transport of decaying contaminant species. J. Hydrol. 91: 49-58.
- Eichler, B.; Schink, B. (1984) Oxidation of primary aliphatic alcohols by *Acetobacterium carbinolicum* sp. nov., a homoacetogenic anaerobe. Arch. Microbiol. 140: 147-152.
- Finneran, K. T.; Lovley, D. R. (2001) Anaerobic degradation of methyl tert-butyl ether (MTBE) and tert-butyl alcohol (TBA). Environ. Sci. Technol. 35: 1785 -1790.
- Finneran, K. T.; Lovley D. R. (2003) Anaerobic in situ bioremediation. In: E.E. Moyer; Kostecki, P.T., MTBE remediation handbook. Amherst Scientific Publishers: Amherst, MA; 265-277.
- Happel, A. M.; Beckenbach, E. H.; Halden, R. U. (1998) An evaluation of MTBE impacts to California groundwater resources. Report submitted to the California State Water Resources Control Board: Underground Storage Tank Program; the U.S. Department of Energy: Office of Fossil Fuels; and the Western States Petroleum Association. Lawrence Livermore National Laboratory: University of California. Livermore, CA. UCRL-AR-130897.
- Hickman, G. T.; Novak, J. T. (1989) Relationship between subsurface biodegradation rates and microbial density. Environ. Sci. Technol. 23: 525-532.

- Hovious, J. C.; Conway, R. A.; Ganze, C. W. (1973) Anaerobic lagoon pretreatment of petrochemical wastes. *J. Water Pollut. Con. F.* 45: 71-84.
- Kolhatkar, R.; Kuder, T.; Philp, P.; Allen, J.; Wilson, J. T. (2002) Use of compound-specific stable carbon isotope analyses to demonstrate anaerobic biodegradation of MTBE in groundwater at gasoline release site. *Environ. Sci. Technol.* 26: 5139-5146.
- Kuder, T.; Wilson, J. T.; Kaiser, P.; Kolhatkar, R.; Philp P.; Allen, J. (2005) Enrichment of stable carbon and hydrogen isotopes during anaerobic biodegradation of MTBE - microcosm and field evidence. *Environ. Sci. Technol.* 39: 213-220.
- Landmeyer, J. E.; Chapelle, F. H.; Bradley, P. M.; Pankow, J. F.; Church, C. D.; Tratnek, P. G. (1998) Fate of MTBE relative to benzene in a gasoline-contaminated aquifer (1993-98). *Ground Water Monit. Rem.* 18: 93-102.
- Mace, R. E.; Choi, W.-J. (1998) The size and behavior of MTBE plumes in Texas. In: Stanley, A., ed., *Petroleum hydrocarbons and organic chemicals in ground water: proceedings of the prevention, detection, and remediation conference*. November, 1998; Houston, TX. National Ground Water Association and American Petroleum Institute, p. 1-11.
- Mackay, D. M.; de Sieyes, N. R.; Einarson, M. D.; Feris, K. P.; Pappas, A. A.; Wood, I. A.; Jacobson, L.; Justice, L. G.; Noske, M. N.; Scow, K. M.; Wilson, J. T. (2006) Impact of ethanol on the natural attenuation of benzene, toluene, and o-xylene in a normally sulfate-reducing aquifer. *Environ. Sci. Technol.* 40: 6123 -6130.
- Mackay, D.; de Sieyes, N.; Einarson, M.; Feris, K.; Pappas, A.; Wood, I.; Jacobson, L.; Justice, L.; Noske, M.; Wilson, J.; Adair, C.; Scow, K. (2007) Impact of ethanol on the natural attenuation of MTBE in a normally sulfate-reducing aquifer. *Environ. Sci. Technol.* 41: 2015 – 2021.
- Maier, U.; Grathwohl, P. (2006) Numerical experiments and field results on the size of steady state plumes. *J. Contam. Hydrol.* 85: 33-52.
- McDowell, C. J.; Powers, S. E. (2003) Mechanisms affecting the infiltration and distribution of ethanol-blended gasoline in the Vadose zone. *Environ. Sci. Technol.* 37: 1803 -1810.
- McDowell, C. J.; Buscheck, T.; Powers, S. E. (2003) Behavior of gasoline pools following a denatured ethanol spill. *Ground Water Monit. Rem.* 41: 746-757.
- McNab, W.; Heermann, S. E.; Dooher, B. (1999) Chapter 4: Screening model evaluation of the effects of ethanol on benzene plume lengths. Cannon, G., ed. In: *Health and environmental assessment of the use of ethanol as a fuel oxygenate, Volume 4: Potential ground and surface water impacts*. Report no. UCRL-AR-135949.

- McNab Jr., W. W.; Rice, D. W.; Tuckfield, C. (2000) Evaluating chlorinated hydrocarbon plume behavior using historical case population analyses. *Biochem. J.*, 4: 311-335.
- McNab, W. (2001) Chapter 5: A finite-difference-based reactive transport model assessment of the effects of ethanol biotransformation on the lengths of benzene plumes from leaking underground fuel tanks. Rice, D. W.; Depue, R. T., eds. In: Report to the California State Water Resources Board, Environmental assessment of the use of ethanol as a fuel oxygenate: Subsurface fate and transport of gasoline containing ethanol. Report no. UCRL-AR-145380.
- Mocanu, M.; Zoby, J. L.; Barker, J.; Molson, J. (2006) The fate of oxygenates and BTEX from gasolines containing MTBE, TBA, and ethanol: Is ethanol more persistent than MTBE? Keynote Presentation: NGWA Petroleum Hydrocarbons and Organic Chemicals in Ground Water: Prevention, Assessment, and Remediation Conference. November, 2006. Houston, TX.
- Molson, J. W.; Barker, J. F.; Frind, E. O.; M. Schirmer, M. (2002) Modeling the impact of ethanol on the persistence of benzene in gasoline-contaminated groundwater. *Water Resour. Res.* 38:(1) 4-12.
- Montgomery, J. H. (2000) Groundwater chemicals desk reference: Third edition. CRC Lewis Publishers: Boca Raton.
- Mormile, M. R.; Liu S.; Suflita, J. M. (1994) Anaerobic biodegradation of gasoline oxygenates: Extrapolation of information to multiple sites and redox conditions. *Environ. Sci. Technol.*, 28, 1727-1732.
- Mravik, S. C.; Sewell, G. W.; Sillan, R. K., Wood, A. L. (2003) Field evaluation of the solvent extraction residual treatment (SERB) technology. *Environ. Sci. Technol.* 37: 5040-5049.
- Novak, J. T.; Goldsmith, C. D.; Benoit, R. E.; O'Brien, J. H. (1985) Biodegradation of methanol and tertiary butyl alcohol in subsurface systems. *Water Sci. Technol.* 17: 71-85.
- Powers, S. E.; Hunt, C. S.; Heermann, S. E.; Corseuil, H. X.; Rice, D.; Alvarez, P. J. J. (2001) The transport and fate of ethanol and BTEX in groundwater contaminated by gasohol. *Crit. Rev. Environ. Sci. Technol.* 31: 79-123.
- Rueter, P.; Rabus, R.; Wilkest, H.; Aeckersberg, F.; Rainey, F. A.; Jannasch, H. W.; Widdel, F. (2002) Anaerobic oxidation of hydrocarbons in crude oil by new types of sulphate-reducing bacteria. *Nature* 372: 455-458.
- Ruiz-Aguilar, G. M. L.; Fernandez-Sanchez, J. M.; Kane, S. R.; Kim, D.; Alvarez P. J. J.; (2002) Effect of ethanol and methy-tert-butyl ether on monoaromatic hydrocarbon

- biodegradation: response variability for different aquifer materials under various electron-accepting conditions. *Environ. Toxicol. Chem.* 21: 2631–2639.
- Ruiz-Aguilar, G. M. L.; O'Reilly, K.; Alvarez, P. J. J. (2003) Forum: A comparison of benzene and toluene plume lengths for sites contaminated with regular vs. ethanol-amended gasoline. *Ground Water Monit. Rem.* 23: 48-53.
- Shih, T.; Rong, Y.; Harmon, T.; Suffet, M. (2004) Evaluation of the impact of fuel hydrocarbons and oxygenates on groundwater resources. *Environ. Sci. Technol.* 38: 42-48.
- Somsamak, P.; Cowan, R. M.; Häggblom, M. M. (2001) Anaerobic biotransformation of fuel oxygenates under sulfate-reducing conditions. *FEMS Microbiol. Ecol.* 37: 259-264.
- Somsamak, P.; Richnow, H. H.; Häggblom, M. M. (2005) Carbon isotopic fractionation during anaerobic biotransformation of methyl *tert*-butyl ether and *tert*-amyl methyl ether. *Environ. Sci. Technol.* 39: 103-109.
- Suarez, M. P.; Rifai, H. S. (1999) Biodegradation rates for fuel hydrocarbons and chlorinated solvents in groundwater. *Biorem. J.* 3: 337-362.
- Suflita, J. M.; Mormile, M. R. (1993) Anaerobic biodegradation of known and potential gasoline oxygenates in the terrestrial subsurface. *Environ. Sci. Technol.* 27: 976-978.
- Tong, W.; Rong, Y. (2002) Estimation of methyl *tert*-butyl ether plume length using the Domenico analytical model. *Environ. Forensics.* 3: 81-87.
- Ulrich, G. (1999) The fate and transport of ethanol-blended gasoline in the environment: A literature review and transport modeling. Governor's ethanol coalition. at <http://www.ethanol-gec.org/fatereport.doc>. [April 18, 2008]
- U.S. Environmental Protection Agency. (1994) The hydrocarbon spill screening model (HSSM) Volume 1: User's guide. Washington, DC; Office of Research and Development; report no. EPA/600/R-94/039a.
- U.S. Environmental Protection Agency. (1995) The hydrocarbon spill screening model (HSSM) Volume 2: Theoretical background and source codes. Washington, DC; Office of Research and Development; report no. EPA/600/R-94/039b.
- U.S. Environmental Protection Agency. (2005a) Monitored natural attenuation of MTBE as a risk management option at leaking underground storage tank sites. Cincinnati, OH: Office of Research and Development; report no. EPA/600/R-04/179.

- U.S. Environmental Protection Agency. (2005b) Predicted ground water, soil and soil gas impacts from U.S. gasolines, 2004: First analysis of the autumnal data. Athens, GA: Office of Research and Development; report no. EPA/600/R-05/032.
- U.S. Environmental Protection Agency. (2006) Regulatory Announcement, Removal of Reformulated Gasoline Oxygen Content Requirement, Office of Transportation and Air Quality, Washington, DC, EPA 420-F-06-035.
- U.S. Environmental Protection Agency. (2007) Natural attenuation of tertiary butyl alcohol (TBA) in ground water at gasoline spill sites. Cincinnati, OH: Office of Research and Development; report no. EPA/600/R-07/100.
- United States Code, Title 42 The Public Health and Welfare, Chapter 85 Air Pollution Prevention and Control, Subchapter II Emission Standards for Moving Sources, Part A Motor Vehicle Emission and Fuel Standards, Section 7545 Regulation of Fuels, 1/19/2004.
- United States Federal Register, 2000, Approval and Promulgation of Air Quality Implementation Plans: New York; Approval of Carbon Monoxide State Implementation Plan Revision; Removal of the Oxygenated Gasoline Program, April 19, 66 (76), 20909.
- United States Federal Register. (1999) Approval and promulgation of air quality implementation plans: New York; Approval of carbon monoxide state implementation plan; Removal of the oxygenated gasoline program. October 8, 64(195) 54851.
- Widdel, F.; Rabus, R. (2001) Anaerobic biodegradation of saturated and aromatic hydrocarbons. *Curr. Opin. Biotechnol.* 12: 259-276.
- Wiedemeier, T. H.; Rifai, H. S.; Newell, C. J.; Wilson, J. T. (1999) Natural attenuation of fuels and chlorinated solvents in the subsurface. John Wiley & Sons, Inc.: New York. 617 pages.
- Wilson, J. T. (2003) Fate and transport of MTBE and other gasoline components. In: Moyer, E.; Kostecki, P., eds. *MTBE remediation handbook*; Amherst Scientific Publishers; pp. 19-61.
- Wilson, J. T.; Adair, C.; Kaiser, P. M.; Kolhatkar, R. (2005a) Anaerobic biodegradation of MTBE at a gasoline spill site. *Ground Water Monit. Rem.* 25(3): 103-115.
- Wilson, J. T.; Kolhatkar, R.; Kuder, T.; Philp, P.; Daugherty S. J. (2005b) Stable isotope analysis of MTBE to evaluate the source of TBA in ground water. *Ground Water Monit. Rem.* 25(4): 108-116.

- Yeh, C. K.; Novak, J. T. (1994) Anaerobic biodegradation of gasoline oxygenates in soils. *Water Environ. Res.* 66: 744-752.
- Zhang, Y.; Khan, I. A.; Chen, X.-H.; Spalding, R. F. (2006) Transport and degradation of ethanol in groundwater. *J. Contam. Hydrol.* 82: 183-194.
- Zogorski, J. S.; Carter, J. M.; Ivahnenko, T.; Lapham, W. W.; Moran, M. J.; Rowe, B. L.; Squillance, P. J.; Toccalino, P. L. (2006) The quality of the nation's waters-volatile organic compounds in the nation's ground water and drinking-water supply wells: U.S. Geological Survey Circular 1292: 101.

VI. POTENTIAL APPROACH FOR FURTHER ANALYSES: COMPREHENSIVE ENVIRONMENTAL ASSESSMENT OF FUEL ADDITIVE SUBSTITUTE OPTIONS

Any choice among fuel options is accompanied by inherent trade-offs. The experience with the environmental trade-offs of MTBE over the past two decades amply illustrates why fuel additive substitute options require careful evaluation in a systematic, holistic manner. This report presents information on the potential health, water and air pollution effects of fuel additive usage, but it does not constitute a full, comparative evaluation of the environmental and health implications of the fuel additives in question, nor does it examine in depth the secondary and indirect impacts potentially associated with different fuel additive substitute options. To evaluate the multimedia environmental benefits and risks of fuels and fuel additives in a scientifically rigorous manner would require a more extensive effort. For example, EPA anticipates that future reports required under Section 204 of 2007's Energy Independence and Security Act will go much further in investigating the full environmental impacts in the context of the production and use of renewable fuels. One approach for such an analysis is comprehensive environmental assessment (CEA), which grew out of the MTBE experience (Davis and Thomas, 2006).

The CEA approach to examining the comparative advantages and disadvantages of various fuel additives and formulations would help avert substituting a different problem or set of problems for those associated with MTBE. The present chapter discusses this CEA approach as a paradigm for future analyses of these issues.

In essence, CEA combines the risk assessment paradigm with a product life cycle framework and uses collective expert judgment methods to deal with limitations in empirical data. Some general features of CEA are illustrated in Figure VI-1. Typical stages of a product life cycle are listed in the first column, including feedstock production, manufacturing processes, distribution, storage, use, and disposal of the product and/or waste by-products. At any of these stages, pollutants (whether the primary chemicals or waste by-products) may be released into one or more environmental media or pathways, namely air, water, soil, and the food web (second column). Transport and transformation processes may then come into play, translocating materials from the immediate area of release and possibly transforming the original pollutants into secondary pollutants (third column). Exposure can occur when humans or other organisms (biota) come into contact with these primary and secondary contaminants in the environment (fourth column). Ultimately, the effects on human health and ecosystems associated with exposures in the aggregate (across routes) and cumulative (across pollutants) need to be considered as part of a CEA (fifth column).

Note that CEA should not be equated with life cycle analysis or life cycle impact assessment. Although CEA can incorporate and build upon such analyses, it involves a greater range of expertise and is more qualitative in nature than typical life cycle assessments. Therefore, while CEA can inform decisions, it does not necessarily provide a definitive quantitative assessment of all impacts associated with different policy options. However, as illustrated by statements more than 15 years ago from the

Alternative Fuels Research Strategy (U.S. EPA, 1992), a precursor to the CEA approach, it is possible to identify potential problems in a qualitative sense even before quantitative assessment is feasible. For example, the *Strategy* noted:

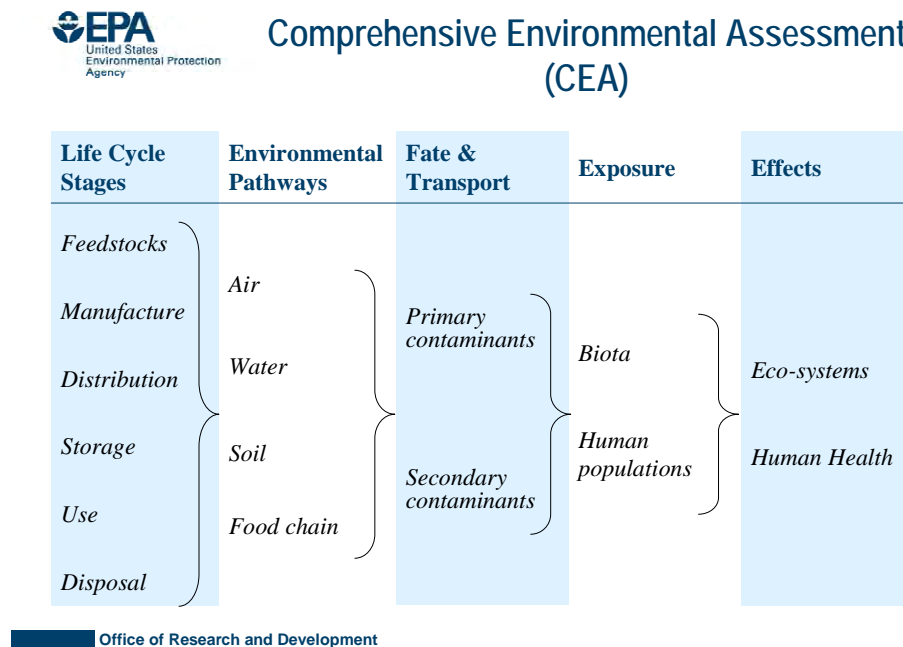
“Compared to gasoline, the ethers MTBE and ETBE have relatively large aqueous solubilities and would likely leach more rapidly through soil and ground water. Also, limited data suggest that ethers may be persistent in subsurface environments.”

and

“Very little is known about emissions and releases from MTBE and ETBE storage and distribution, making this area an appropriate target for research. Effects on existing equipment and controls...need to be evaluated.”

Even though these statements were not conclusive and offered no quantitative estimation of risks, they turned out to be prescient forewarnings of problems that ultimately contributed to the de-selection of MTBE as a fuel additive. In a sense, they offer a proof of the CEA concept and its applicability to a contemporary comparative assessment of fuel additive substitute options.

Figure VI-1. Schematic representation of Comprehensive Environmental Assessment (Source: adapted from Davis and Thomas, 2006)



CEA provides a means to examine both environmental and public health impacts potentially associated with different fuel formulation options. A more extensive discussion of the CEA approach is presented in a paper by Davis and Thomas (2006). That discussion focuses on a comparison of oxygenate options for reformulated gasoline,

namely MTBE, ethanol, and a no oxygenate formulation; however, the CEA approach is easily extended to other fuel formulations. Table VI-1 highlights some examples of issues to be considered in a CEA of fuel additive substitute options. Beginning with feedstocks, for example, one might consider impacts associated with each of the three choices. In North America, methanol is primarily produced from methane, which is an important greenhouse gas, and can be produced from coal. Is an increase, decrease, or no change in methane emissions likely to occur if the amount of MTBE derived from methanol is reduced? In the case of ethanol, the primary feedstock in North America is currently corn, the production of which typically involves the application of fertilizers and pesticides and subsequent run-off with precipitation. The herbicide atrazine, for example, is one of the most prevalent water pollutants in the United States (U.S. EPA, 2006: http://www.epa.gov/safewater/contaminants/dw_contamfs/atrazine.html), which raises the question of whether increased production of ethanol from corn would result in greater use of atrazine and, hence, more or more severe contamination of water resources. Issues about increased nitrous oxide from additional fertilizer utilization have also been raised (Crutzen et al., 2008). Comparable issues surround increased production of iso-octane, which could imply a greater potential for transport of hydrofluoric acid. With transport (e.g., by tank cars) and transfers (e.g., loading and unloading) of hazardous materials comes some risk of ecological, health and safety impacts associated with releases.

In addition to the examples highlighted in Table VI-1, Chapter VII of this report also identifies questions that merit examination as part of a CEA of fuel issues.

A key feature of CEA is the use of the collective intelligence of an array of technical experts and stakeholders in addressing questions for which information is lacking. In this respect, diversity of perspectives is critical for reaching sound collective judgments. Such diversity typically requires consideration of a spectrum of expertise and viewpoints encompassing several scientific and technical disciplines as well as stakeholder groups. Although subjective conjecture cannot substitute for empirical data, the tapping of collective wisdom to deal with scientific uncertainties is a critical component of the CEA approach. Moreover, the assembled group needs to interact in a structured manner (Shatkin and Qian, 2004). Simply having a group engage in free-form discussion is unlikely to achieve a coherent or useful outcome, but structured discussion affords greater potential for deriving sound collective judgments.

Table VI-1. Illustrative issues to be considered in a CEA of fuel additive/ blending options for reformulated gasoline.

		Reformulated Gasoline with:		
		MTBE	Ethanol	No Oxygenate
Source Characterization	Feedstocks	Methanol: methane	Corn: pesticides, fertilizers	Iso-octane: hydrofluoric acid
	Production	VOCs	Air toxics, odors	?
	Distribution	Small/chronic releases	Large/acute releases	?
	Storage		Materials compatibility, product containment	
	Use (evaporative & combustion emissions)	Air toxics, NO, CO, ozone, etc.	Acetaldehyde, PAN, alkylates, etc.	Alkylates, toluene, etc.
Environmental Quality	Air	Formaldehyde, tert butyl formate	Acetaldehyde, ozone	VOCs, secondary organic aerosols
	Subsurface	MTBE, tert butanol	Increased BTEX, reduced water supplies	
	Surface Water	MTBE	Oxygen depletion, increased nitrates, increased dead zones	
Exposure	Human	Acute/chronic; personal and population exposures; cumulative and aggregate; single chemical and mixtures		
	Biota	Acute/chronic, terrestrial/aquatic		
Human Health Effects	Acute	Neurobehavioral, respiratory, organoleptic (sensory), etc.		
	Chronic	Cancer potency, inhalation reference concentration (RfC), oral reference dose (RfD)		
Ecosystem Effects	Terrestrial	Organism, population, community, ecosystem		
	Aquatic (marine & freshwater)			
Global Climate	CO ₂ methane N ₂ O CO NO ₂ VOCs	Increase? decrease? no net change?		

The outcome of a CEA of fuel additives would be, at a minimum, a cataloging of potential environmental and health risks and benefits associated with each option. For aspects of the problem that are data-rich, a more quantitative approach may be taken. Although it is possible that a given additive might have a clear preponderance of advantages or disadvantages, such that little question would exist about its suitability or lack thereof, more often a mix of pros and cons would need to be weighed against a different set of characteristics for an alternative choice. Thus, the CEA outcome may not point to a single option, but it will nevertheless provide decision-makers more complete information to help understand the potential implications of policy options. Most importantly, to the extent that potential problems can be anticipated through the CEA process, it should enable risk managers to take mitigative actions to reduce the occurrence of adverse outcomes. For example, targeted environmental monitoring might be indicated for detecting contaminant releases as soon as possible.

The CEA approach is iterative. As information and experience accumulate with the use of a chosen fuel additive substitute option, it is imperative to reexamine judgments that were based on earlier, less complete data. In this respect, CEA is consistent with the idea of adaptive management, which refers to a continuing evaluation of the implications of a policy decision and adjustment of such decisions as may be warranted (Linkov et al., 2006; Shatkin and Barry, 2006). Adaptive management strategies have typically been applied to major natural resource interventions or conservation actions taken in the face of significant scientific uncertainties. However, the concept seems equally applicable to fuel formulation options and other complex technological issues (Davis, 2007). The key point is that periodic reevaluations and appropriate adjustments need to accompany policy decisions on fuel options.

References

- Crutzen, P. J.; Mosier, A. R.; Smith, K. A.; Winiwarter, W. (2008) N₂O release from agro-biofuel production negates global warming reduction by replacing fossil fuels. *Atmos. Chem. Phys.* 8: 389-395.
- Davis, J. M.; Thomas, V. M. (2006) Systematic approach to evaluating trade-offs among fuel options: the lessons of MTBE. *Ann. N.Y. Acad. Sci.* 1076: 498-515.
- Davis, J. M. (2007) How to assess the risks of nanotechnology: learning from past experience. *J. Nanosci. Nanotechnol.* 7: 402-409.
- Linkov, I.; Satterstrom, F. K.; Kiker, G. A.; Bridges, T. S.; Benjamin, S. L.; Belluck, D. A. (2006) From optimization to adaptation: shifting paradigms in environmental management and their application to remedial decisions. *Integr. Environ. Assess. Manage.* 2: 92-98.
- Shatkin, J. A.; Qian, S. (2004) Classification schemes for priority setting and decision making: a selected review of expert judgment, rule-based, and prototype methods. In: Linkov, I.; Ramadan, A. B., eds. *Comparative risk assessment and environmental decision making: proceedings of the NATO advanced research workshop; October, 2002; Rome (Anzio), Italy*. Dordrecht, The Netherlands: Kluwer; pp. 213-243. (NATO science series IV, earth and environmental sciences: v. 136).
- Shatkin, J. A.; Barry, B. E. (2006) Approaching risk assessment of nanoscale materials. In: *Nanotech 2006: technical proceedings of the 2006 NSTI nanotechnology conference and trade show, volume 1*. Cambridge, MA: Nano Science and Technology Institute (NSTI); pp. 553-556.
- U.S. Environmental Protection Agency. (1992) Alternative fuels research strategy [external review draft]. Washington, DC: Office of Research and Development; report no. EPA/600/AP-92/002. Available: <http://www.epa.gov/ncea/pdfs/mtbe/altfuel.pdf> [28 January, 2008].
- U.S. Environmental Protection Agency. (2006) Consumer factsheet on: ATRAZINE. Washington, DC: Office of Ground Water and Drinking Water. Available: http://www.epa.gov/safewater/contaminants/dw_contamfs/atrazine.html [29 January, 2008].

VII. CATALOG OF ONGOING SCIENTIFIC ACTIVITIES RELATED TO MTBE AND ITS SUBSTITUTES AND INFORMATION GAPS

A. Health Effects Research

1. Ongoing Scientific Activities

a. Alternative Tier 2 Health Effects Testing Program for Gasoline-Oxygenate Blends

A number of studies were done by the American Petroleum Institute (API) in the 1980s that set the stage for current gasoline-oxygenate blends health effects testing. These studies were conducted on rats and mice with vaporized unleaded gasoline (MacFarland et al., 1984; Halder et al., 1984; HEI, 1988). EPA also prepared a major report on the health effects of unleaded gasoline during the same time period (U.S. EPA, 1987). These studies informed the development of the Alternative Tier 2 health effects testing program.

In the mid-1990's, EPA initiated a program to evaluate the potential toxicity of exposure to gasoline vapors alone and containing several potential oxygenate fuel additives including MTBE, ETBE, ethanol (EtOH), TAME, DIPE and TBA. This program was authorized under the Alternative Tier 2 provision of the fuel and fuel additives health effects testing requirements as described in sections 211(b)(2) and 211(e) of the Clean Air Act. The American Petroleum Institute (API) was notified of EPA's intention to develop this testing program on August 20, 1997. Subsequent Federal Register notices provided opportunities for public comments on the proposal, and a letter dated November 2, 1998, from Margo Oge, Director of EPA's Office of Transportation and Air Quality to Carol Henry of API formally established the requirements of the testing program. The API administered a consortium of fuel and fuel additive manufacturers, referred to as the Section 211(b) Research Group, to share compliance burdens and costs of fulfilling the testing requirements.

The 211(b) health effects testing program required that health effects toxicity testing be conducted in laboratory animals exposed to the evaporative emissions of baseline gasoline alone and gasoline plus each of the specified fuel oxygenates added in proportions reflecting their anticipated typical usage. The program focused on evaporative rather than combustive emissions because it was thought that the toxicity from the carbon monoxide concentrations present in gasoline exhaust would likely present a practical limit to the hydrocarbon concentrations achievable in exhaust. Therefore, a testing program based on exposure to exhaust from combustion gasoline plus fuel oxygenates would not yield meaningful data on the relative toxicity of hydrocarbon combustion products arising from presence of the different fuel oxygenates in gasoline. The intention of the testing program, then, was to evaluate and compare the relative toxicity of evaporative emissions of gasoline alone and gasoline with the specified fuel additives present. A separate program of studies was required to evaluate

personal exposure levels of combustion emissions in cities using gasoline with or without oxygenate additives, viz. MTBE and ethanol.

An array of health effects testing was specified in the 211(b) program that was based on specific research needs identified in reports of several expert panels, including the National Science and Technology Council in 1996/1997, the National Research Council in 1996, and the Health Effects Institute Oxygenates Evaluation Committee in 1997. In addition, several data gaps were identified in risk assessments and other analyses performed by EPA (1993, 1994, 1996, 1998). Consistent with these various expert analyses, the testing program sought to gain information on acute health effects, carcinogenicity neurotoxicity, reproductive/developmental effects, pharmacokinetics and potential exposures via air and drinking water. The toxicity testing portion of the program specified more extensive testing for baseline gasoline and MTBE-gasoline than the other oxygenate-gasoline mixtures. Testing required for MTBE included the standard Tier 2 regimen of subchronic toxicity, carcinogenicity, mutagenicity, teratogenicity and neurotoxicity, and also an Alternative Tier 2 requirement of additional neurotoxicity testing, a two-generation reproductive study, developmental toxicity testing in two species, a two-year carcinogenicity study and screening for immunological effects. The Alternative Tier 2 testing required for oxyfuels other than MTBE-gasoline included the standard Tier 2 tests plus additional screening for immunological and histopathological effects. In addition, studies of the pharmacokinetic behavior, consisting of uptake, distribution metabolism and elimination, were required for the neat oxygenates: ethanol, ETBE, TAME, DIPE and TBA. For all the fuel oxygenates, EPA would determine if additional Tier 3 testing would be required after evaluating the results of Tier 2.

The testing rule was designed to incorporate scientific peer review and evaluation of the study protocols and reports (except for protocols where previously reviewed standard guidelines were employed). In addition, quality assurance programs were required to be in accordance with federal guidelines for Good Laboratory Practices and Vehicle Emissions Inhalation Exposures. The scientific peer review required assessment of draft protocols and reports by an independent panel of qualified experts prior to submitting the reports to EPA. EPA then would review the draft reports, the comments of the panel members, and API's response and revisions made in reply to the peer review comments. If EPA's assessment indicated that the response to the peer reviewer was insufficient, or if additional issues of scientific or technical quality were identified, then those comments would be returned to API, who had an opportunity to address them in a revised report. Once the issues were resolved, EPA would determine whether the studies were conducted in a manner sufficient to satisfy the testing requirements. Accepting that the study reports satisfy the testing requirements, however, would not imply necessarily that EPA concurred with the interpretation of the study results or the conclusions stated by the authors.

As of June 2008, some of the study reports required under the Alternative Tier 2 health effects testing program have been received in final form by EPA, while others are in the process of peer review or revision. A summary of the current status of the individual study reports is provided in Table VII.A-1.

Under Section 8e of the Toxic Substances Control Act (TSCA), companies that observe significant new toxicological outcomes are required to report those findings to EPA. There have been several TSCA 8e reports filed to EPA as a result of the 211(b) Alternative Tier 2 testing program. A summary of those reports is provided in Table VII.A-2.

EPA will make an independent evaluation of the results of the studies conducted under the 211(b) program after all of the final reports are received from the Alternative Tier 2 testing of the substances evaluated. EPA will conduct these evaluations as a component of a comprehensive assessment of all the data available for each of the substances involved including, where available, data from other sources and the peer-reviewed scientific literature. In addition, EPA will determine whether substantial data gaps remain regarding potential human health effects that necessitate additional testing. In combination with data on anticipated usage of the fuel oxygenates and estimated levels of human exposures, the toxicity data from the 211(b) testing program, when available, should improve the ability to make informed risk assessment and risk management decisions regarding the use of fuel oxygenate compounds.

Table VII.A-1. Status of reports from health effects portion of the Section 211(b) Alternative Tier 2 testing program

Test Material	Subchronic#	Developmental Rat	Developmental Mouse	Reproductive	Carcinogenicity	ADME/PK*
Baseline gasoline	Final Report Received	Final Report Received	2nd Draft Reviewed	2nd Draft Reviewed	1st Draft Reviewed	
Gasoline + MTBE	Final Report Received	2nd Draft Reviewed	2nd Draft Reviewed	1st Draft Reviewed	1st Draft Reviewed	
Gasoline + EtOH	2nd Draft Reviewed	2nd Draft Reviewed		2nd Draft Reviewed		Sufficient PK data submitted. No additional testing.
Gasoline + TAME	1st Draft Reviewed	2nd Draft Reviewed		2nd Draft Reviewed		Sufficient PK data submitted. No additional testing.
Gasoline + ETBE	1st Draft Reviewed	2nd Draft Reviewed		1st Draft Reviewed		Reviewed final study protocols
Gasoline + DIPE	No Report Received	No Report Received		1st Draft Reviewed		Reviewed pilot study protocols
Gasoline + TBA	No Report Received	1st Draft Reviewed		1st Draft Reviewed		Reviewing draft pilot study report

Includes genotoxicity, neurotoxicity and immunotoxicity outcomes

* Absorption, Distribution, Metabolism and Excretion (ADME) or PK testing is done on “neat” oxygenates only (not mixture)

Table VII.A-2. TSCA 8e reports filed to EPA as a result of the 211(b) Alternative Tier 2 testing program

Substance	Test	Findings
Baseline Gasoline Vapors	Genotoxicity	Statistically significant increases in sister chromatid exchange in peripheral blood lymphocytes cultured from rats exposed for 4 weeks to vapor concentrations of 10,000 or 20,000 mg/m ³ .
	Developmental toxicity	Statistically significant reductions of body weight and body weight gain of pregnant mice during gestational exposure to 20,000 mg/m ³ . Statistically significant reductions in weight of gravid uterus and litter size, and an increase in fetal resorption ratio at 20,000 mg/m ³ .
Gasoline + EtOH	Immunotoxicity	Statistically significant reduction in the number of antibody forming cells in spleens of rats exposed to vapor concentrations of 20,000 mg/m ³ for 4 weeks.
	Neurotoxicity	Statistically significant increases in the concentration of glial fibrillary acidic protein (GFAP) in dissected brain regions of male rats exposed for 13 weeks. Increases over control were observed at all dose levels in the cerebellum, but were not dose related in other brain regions, and were not observed in females.
Gasoline + MTBE	Developmental toxicity	Incidents of fetal malformations in one of 25 litters of mice exposed to low dose (2,000 mg/m ³) and one of 25 litters exposed to mid dose (10,000 mg/m ³), but not observed in control or high dose (20,000 mg/m ³).
	Developmental toxicity	Follow-up to the previous study reports no fetal malformations following exposure to 0, 10,000 or 20,000 mg/m ³ , but one incident of a similar malformation in 33 litters of mice exposed to 30,000 mg/m ³ .
Gasoline + ETBE	Immunotoxicity	Statistically significant reduction in the number of antibody forming cells in spleens of rats exposed to vapor concentrations of 10,000 or 20,000 mg/m ³ for 4 weeks.
Gasoline + TAME	Reproductive Toxicity	Statistically significant decrease in pup weight gain on postnatal days (PND) 7-14 in litters of rats exposed to 10,000 and 20,000 mg/m ³ during development. Significant reduction in male pup weight at PND-21 at 2,000 mg/m ³ , but not at higher concentrations.
Gasoline + DIPE	Immunotoxicity	Statistically significant reduction in the number of antibody forming cells in spleens of rats exposed to vapor concentrations of 20,000 mg/m ³ for 4 weeks.

b. National Health and Environmental Effects Research Laboratory

Within EPA's Office of Research and Development, the National Health and Environmental Effects Research Laboratory (NHEERL) conducts an intramural research program on the health effects of exposure to air pollution, including those effects caused by fuels and fuel additives. The major focus of the NHEERL air research program is to evaluate the health effects of particulate matter in support of establishing National Ambient Air Quality Standards. A component of this work focuses on gasoline and diesel engine emissions, which are major sources of particulate matter in urban air. In addition, a portion of this research program focuses on near roadway environments, for which fuel emissions are a major contributor. Finally, a portion of the research program is evaluating specific fuel components, and is currently assessing pharmacokinetic and neurotoxic properties of acute inhalation exposure to iso-octane (2,2,4-trimethylpentane). The first results of the research regarding iso-octane were presented at the annual meeting of the Society of Toxicology in Seattle, Washington, March 16-20, 2008.

c. IRIS Assessments

The IRIS files for a number of the additives or compounds covered in this report are either under revision or being developed at this time. A summary of the available health effects information for these chemicals is provided in Chapter II of this report. The status of these ongoing assessments can be accessed at <http://cfpub.epa.gov/ncea/iristrac/index.cfm>.

2. Information Gaps

Although scientific uncertainties and questions accompany even the most well studied chemicals, clearly some fuel additives have larger information gaps than others. In particular, more toxicity and pharmacokinetic data are much needed for DIPE and iso-octane. Information gaps also exist for the health effects of TAME, ETBE, and TBA, albeit not to the degree they exist for DIPE and iso-octane. However, these compounds are not presently projected to be used as much as those in renewable fuels, which are mandated by the Energy Independence and Security Act of 2007.

B. Emissions and Air Quality Research

1. Ongoing Activities

EPA's Office of Transportation and Air Quality has initiated a Light Duty Vehicle Fuels Effects Testing Program for exhaust emissions along with a separate program for evaporative emissions. These programs are in response to Section 1506 of the 2005 Energy Policy Act (EPA Act) which contained a provision requiring the EPA to produce an updated fuel effects model representing the 2007 light duty gasoline fleet. Such a model, which will include factors to determine the emissions impacts of ethanol use, will be used

to support future fuel programs and numerous other regulatory activities in the coming years, such as:

- MOVES or Motor Vehicle Emission Simulator model (SIP, inventory and air quality analyses)
- EPAAct and EISA studies (anti-backsliding, fuel harmonization, others)
- Future regulatory programs, legislative and policy discussions

The EPAAct Program is designed to establish the effects of RVP, T50, T90, aromatic content and ethanol content on exhaust emissions from Tier 2 vehicles. Its scope includes exhaust emissions testing of 19 vehicles on 29 fuels over the California Unified Cycle (LA92). Regulated emissions will be measured along with CO₂, NO₂, VOCs (volatile organic compounds), alcohols, carbonyl compounds, N₂O (nitrous oxide), NH₃ (ammonia) and HCN (hydrogen cyanide). Limited testing of high emitter/mileage vehicles will be done. Detailed speciation of over 100 individual VOC compounds, including those for the carbonaceous portion of PM and SVOC (semi-volatile organic compounds), is also being done and will be used for speciation profiles for ozone (and PM) modeling with CMAQ.

The following levels of investigated fuel parameters have been included in the fuel matrix with the 29 fuels:

- RVP: 7, 9, and 10 psi
- T50: 150, 160, 190, 220 and 240°F
- T90: 300, 325, and 340°F
- Aromatic content: 15, 23, 25, 30, and 40%
- Ethanol content: 0, 10, 15 and 20%

Among these 29 fuels are three fuels designed to represent typical gasoline with no ethanol and ethanol blends of 10% (and also 15%).

The test program consists of three phases:

1. Phase 1: 19 Tier 2 vehicles and 3 high emitter/mileage vehicles tested at 75°F on three US “average” E0, E10 and E15 fuels
2. Phase 2: 19 Tier 2 vehicles and 3 high emitter/mileage vehicles tested at 50°F on three US “average” E0, E10 and E15 fuels
3. Phase 3: 19 Tier 2 vehicles, including 4 FFVs (flexible-fueled vehicles), tested on 26 fuels, including an E85 blend.

The EPAAct Program is a collaboration between the EPA and DOE and is being conducted at the Southwest Research Institute in 2008 – 2009.

The above testing is for exhaust emissions. Evaporative emissions testing is also being done largely through the Coordinating Research Council for newer vehicles over

the next several years to address similar issues related to the effect of fuels on VOC emissions, including some information on detailed VOC speciation.

A more limited test program is being done on 12 nonroad engines with 18 fuels representing a variety of gasoline/alcohol blends.

2. Information Gaps

Although these test programs are very comprehensive, there are still some data gaps, including the following:

- **Emission impacts on older vehicles.** Older vehicles (i.e., pre-Tier 2 vehicles) are not being tested in this program. While such vehicles have been tested in prior programs (such as the cooperative Auto/Oil program done in the early 1990s), the earlier testing did not, of course, specifically address current fuels (i.e., Tier 2 low sulfur, RFG) with ethanol.
- **Emissions under cold temperature.** Emission testing is being done at 75 and 50°F. This program will not have results for colder temperatures, such as 20°F, where we know emissions are different.
- **Emissions under extreme driving conditions.** The exhaust testing is being done using the California Unified Cycle (LA 92), which is similar to the Federal Test Procedure (FTP) used in vehicle certification to determine compliance with EPA emission standards. There are other driving conditions, such as extremely high load (pulling a trailer up a hill) or constant low speed driving, that are not included here.
- **Long term emission impacts.** The long term emission impacts of using these blends for, say, 100,000-150,000 miles are not being determined.

C. Water Quality Research

1. Ongoing Activities

Within EPA's Office of Research and Development, the National Risk Management Research Laboratory (NRMRL) and National Exposure Research Laboratory (NERL) have examined the fate and transport of fuel and fuel additives in laboratory and field studies (Mackay, 2006; USEPA, 2005). NRMRL and NERL have also developed conceptual and predictive models to understand the behavior of these plumes in the environment (see the OnSite tool for modeling subsurface petroleum hydrocarbon content <http://www.epa.gov/athens/onsite> and the Center for Subsurface Modeling Support <http://www.epa.gov/ada/csmos.html>). This work has included conducting research on the composition, fate and transport, and active and passive treatment of fuel spills from leaking underground storage tank (LUST) sites. Specific to ethanol, EPA has conducted laboratory and field studies (including at Vandenberg Air

Force Base [Mackay, 2006]). These studies assessed the fate and transport of ethanol in the environment and its impact on the behavior of the conventional constituents in gasoline, such as benzene, toluene and xylene.

2. Information Gaps

In the area of impacts of fuels leaking from storage tanks and associated infrastructure, research is needed in the following areas:

- Ethanol may contribute to the deterioration and corrosion of materials used in the storage of fuels, including tanks, pipes, fittings, and seals. These failures could lead to releases of fuel to ground water. EPA is undertaking an assessment of available data in the public and private sectors to determine the vulnerabilities in the system as a function of the fuel type, e.g. E20, E85. This evaluation will highlight the key areas where further research is needed to reduce these vulnerabilities.
- Further data is needed to determine the impact of ethanol on the performance of leak detection systems for gas stations. There are two aspects to this problem. First, ethanol may affect the integrity of these leak detection systems that have been designed for petroleum hydrocarbons. Performance of these systems needs to be ascertained to ensure their integrity with various fuel blends. Second, as ethanol can extend BTEX plume lengths, the sensitivity of these systems needs to be assessed to minimize ground water impacts.
- A tool is needed for remediation site managers and water utilities that allows them to integrate the contaminant source modeling and the water supply pumping rates to determine the rate and extent of remediation needed to protect existing and future water supplies. EPA is presently exploring the possibility of collaborative field studies with states to examine the fate and transport of ethanol releases from underground storage tanks and their potential impact on water supply wells. This work will assess the influence of water supply pumping rates on the movement of the contaminated plume.
- As documented in the literature, some spills of ethanol may produce methane concentrations at levels that potentially pose an explosion risk. A laboratory column fed with 1,000 mg/L ethanol produced methane concentrations in excess of the solubility of methane (Da Silva and Alvarez, 2002). At the controlled release study at Vandenberg AFB, California, a release of 500 mg/L ethanol was biologically degraded to produce concentrations of methane in excess of the water solubility of methane (Mackay et al., 2006). Once the solubility is exceeded, there is the potential for gas-phase methane to occur at explosive concentrations. At a spill of fuel grade ethanol at the Northwest Terminal Site, the concentration of methane in many wells exceeded the water solubility of methane, and the concentration of methane in the soil gas above the plume exceeded the explosive limit (Buscheck et al., 2001). As part of EPA's research field study assessing the

impact of ethanol on hydrocarbons in fuel, the formation of methane was examined. EPA is developing of modeling software for the assessment of fuels of varying composition on ground water, with simulation of methane production being one component of this work.

In the area of impacts of increased biofuel feedstock production on water quality, which is beyond the scope of this report, more research is needed in the following areas:

- The large-scale production of ethanol from corn may have significant water quality impacts. From a recent NAS report on the water implications of biofuels, expansion of corn production on marginal lands or soils that do not adequately retain nutrients can result in increased loading of nutrients as well as sediment in waterways. This may further accentuate the hypoxia in the Gulf.
- An analysis is needed, at the local and regional scales, to better identify the available water supplies in areas impacted by corn production. Corn is being grown and ethanol produced in areas already managing water shortages. This analysis will be important for the U.S. in managing our existing and future water supply challenges.

References

- Buscheck, T. E.; O'Reilly, K.; Koschal, G.; O'Regan, G. (2001) Ethanol in groundwater at a Pacific Northwest terminal. In: Ground water: prevention, detection, and remediation: proceedings of the petroleum hydrocarbons and organic chemicals conference; November, 2001, Houston, TX; National Ground Water Association. pp. 55-66.
- Da Silva, M. L. B.; Alvarez, P. J. J. (2002) Effects of ethanol versus MTBE on benzene, toluene, ethylbenzene, and xylene natural attenuation in aquifer columns. *J. Environ. Eng.* 128: 862-867.
- Halder, C. A.; Warne, T. M.; Hatoum, N. S. (1984) Renal toxicity of gasoline and related petroleum naphthas in male rats. In: Mehlman, M. A.; Hemstreet, G. P.III; Thorpe, J. J.; Weaver, N. K., eds. *Advances in modern environmental toxicology. Volume VII: Renal effects of petroleum hydrocarbons.* Princeton, N.J.: Princeton Scientific Publishers, 73-88.
- MacFarland, H. N.; Ulrich, C. E.; Holdsworth, C. E.; Kitchen, D. N.; Halliwell, W. H.; Blum, S. C. (1984) A chronic inhalation study with unleaded gasoline vapor. *Int. J. Toxicol.* 3: 231-248.
- Mackay, D. M.; de Sieyes, N. R.; Einarson, M. D.; Feris, K. P.; Pappas, A. A.; Wood, I. A.; Jacobson, L.; Justice, L. G.; Noske, M. N.; Scow, K. M.; Wilson, J. T. (2006) Impact of ethanol on the natural attenuation of benzene, toluene, and o-xylene in a normally sulfate-reducing aquifer. *Environ. Sci . Technol.* 40: 6123-6130.
- U.S. Environmental Protection Agency (1987) Evaluation of the carcinogenicity of unleaded gasoline. Washington, DC: Office of Research and Development; report no. EPA/600/6-87/001.
- U.S. Environmental Protection Agency (2005) Predicted ground water, soil and soil gas impacts from U.S. gasolines, 2004: First analysis of the autumnal data. Athens, GA: Office of Research and Development; report no. EPA/600/R-05/032.

APPENDIX A. SUMMARY OF THE IMPACTS OF GASOLINE REGULATION ON FUEL COMPOSITION

The Clean Air Act Amendments of 1990 called on EPA to regulate gasoline composition throughout the United States. These amendments created the reformulated and winter oxygenated gasoline programs and contained “anti-dumping” provisions that specified requirements for conventional gasoline. Effectively, all areas of the United States were covered by one or more of these programs. This appendix reviews aspects of these regulations and resulting changes in gasoline composition. Characteristics and trends in reformulated gasoline (RFG) composition can be found in the Fuel Trends Report: Gasoline 1995 – 2005, released by the EPA on January 2, 2008 (U.S. EPA, 2008a). Aggregated gasoline parameter data from the RFG property survey data may be found at the “Gasoline Properties Data” link at <http://www.epa.gov/otaq/rfg.htm> (U.S. EPA, 2008b). Information from the Fuel Trends Report and RFG property survey data were not included in this report due to time constraints.

A. Gasoline formulations

1. Reformulated Gasoline

Among other requirements of the Clean Air Act, reformulated gasoline (RFG) used in certain parts of the country (Figure A-1) was nominally¹⁸ required to contain at least 2% oxygen by weight until 2006. This requirement was removed effective May, 2006 (71 FR26691, May 8, 2006) for most of the federal program areas in the U.S. and earlier in California (April 24, 2006 in California, see U.S. EPA, 2006). Because different chemicals could be used to meet the RFG oxygen requirement, the concentrations used of specific oxygenates were variable (see Table A-1). In addition the benzene content of RFG could not exceed a nominal level of 1% by volume. When the oxygenate mandate was in force, for example, because of the ability to choose a per gallon or average basis for meeting the requirements, compliant RFG could contain between 8.4% and 11.7% MTBE, or as much as 1.3 % benzene.

2. Conventional Gasoline

Conventional gasoline (CG) is gasoline that does not meet the requirements of RFG. The benzene content of conventional gasoline is determined from either a default producer/importer baseline or a baseline based on 1990 production levels¹⁹. Since the baselines are associated with the producer/importer and not specific locations, the benzene levels in conventional gasoline at any given location might change, due to supply considerations.

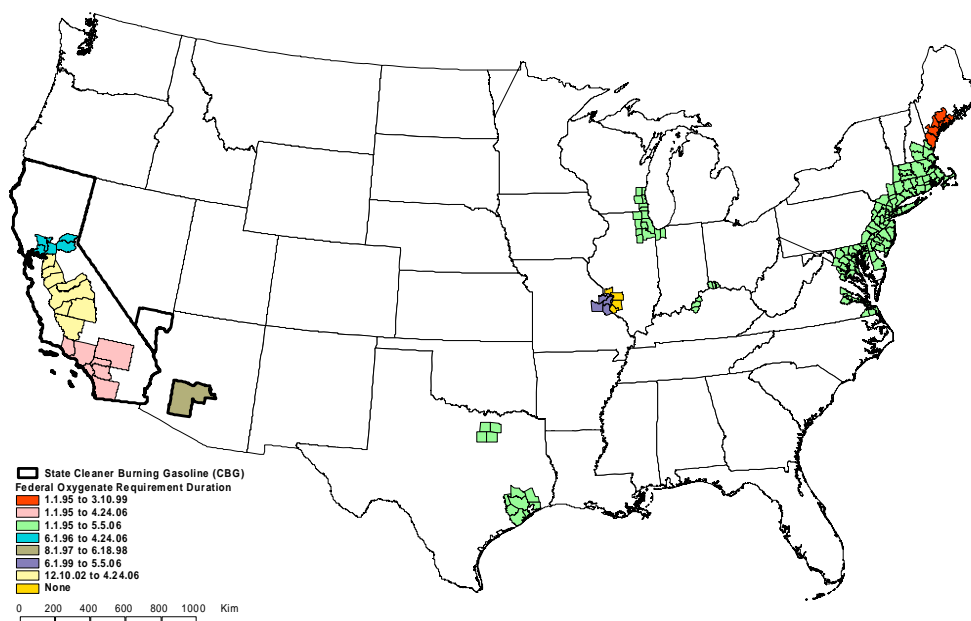
¹⁸ The word nominal is used because the standards could be met either on a per gallon basis or averaged basis.

¹⁹ Note that this refers to gasoline produced before promulgation of the 2007 Mobile Source Air Toxics rule. The impacts of this regulation are not discussed in this report.

Table A-1. Oxygen and approximate amounts of oxygenates to meet requirements of reformulated and winter oxygenate gasoline.

	Required Oxygenate Concentration				
	RFG			Winter Oxygenate	
	Per-gallon Basis	Averaged Basis			
		Standard	Minimum		
Weight percent of oxygen	2.0 %	2.1%	1.5%	2.7%	3.1%
Common Oxygenates and Required Content to Meet Oxygen Requirements (Volume Percent Basis)					
Methyl tertiary butyl ether (MTBE)	11.1%	11.7%	8.4%	15.0%	17.3%
Ethyl tertiary butyl ether (ETBE)	13.0%	13.6%	9.7%	17.5%	20.1%
Tertiary amyl methyl ether (TAME)	12.4%	13.0%	9.3%	16.8%	19.2%
Di-isopropyl ether (DIPE)	13.2%	13.8%	9.9%	17.8%	20.4%
Ethanol	5.5%	5.7%	4.1%	5.1%	5.9%
Approx. Vol % = 100* (required weight fraction oxygen) / (weight oxygen per molecule of oxygenate) x (gasoline density) / (oxygenate density) Gasoline density assumed equal to 0.75 g/ml					

Figure A-1. Locations in the United States where Federal reformulated gasoline has been required. The effective date ranges for use of oxygenated additives are given in the legend.



Conventional gasolines were not required by federal rule to contain oxygenated additives, but these products could be used to boost a gasoline's octane rating and many oxygenates

had been approved by EPA as additives to gasoline. Also, although still considered conventional gasoline, some states may have renewable fuel standards in place for gasoline with specific requirements for blending ethanol (oxygenate) into their state's gasoline pool. Further, samples of premium (i.e., higher octane rated), conventional gasoline often show higher levels of oxygenates than do samples of regular (lower octane rated) gasoline from the same location (U.S. EPA, 2005).

3. Oxygenated gasoline

The 1990 Amendments also required states to mandate at least 2.7% oxygen by weight in gasoline sold in areas of non-attainment of the National Ambient Air Quality Standards (NAAQS) for carbon monoxide (CO) (Figure A-2). This requirement was imposed by statute for at least four months of the year when the ambient CO concentrations were the highest. EPA could reduce this period if a state could demonstrate that there would be no exceedances of the carbon monoxide NAAQS.

The program began during the late fall of 1992 in 36 areas with one more added in 1993. Table A-2 lists the twelve areas that remained in the program until the winter of 2005/2006, along with their required oxygen content and effective months.

B. State MTBE Bans

Because of concerns over ground water contamination due to leaks of MTBE-gasoline, some states began passing bans of MTBE (Figure A-3). One city (Chicago) and one county (Washoe County, Nevada) also banned MTBE. A few states banned other ethers and oxygenates (Arizona, California, Minnesota, New Hampshire, Rhode Island, and Vermont). In the majority of cases, the bans allowed for a relatively low level (0.05 to 1.0 volume %) of MTBE to remain in gasoline (Weaver et al., 2007) and were implemented between the years 2000 and 2007. One ban has yet to become effective (New Jersey).

Figure A-2. Locations of past (triangles) and present (circles) winter oxygenate programs.

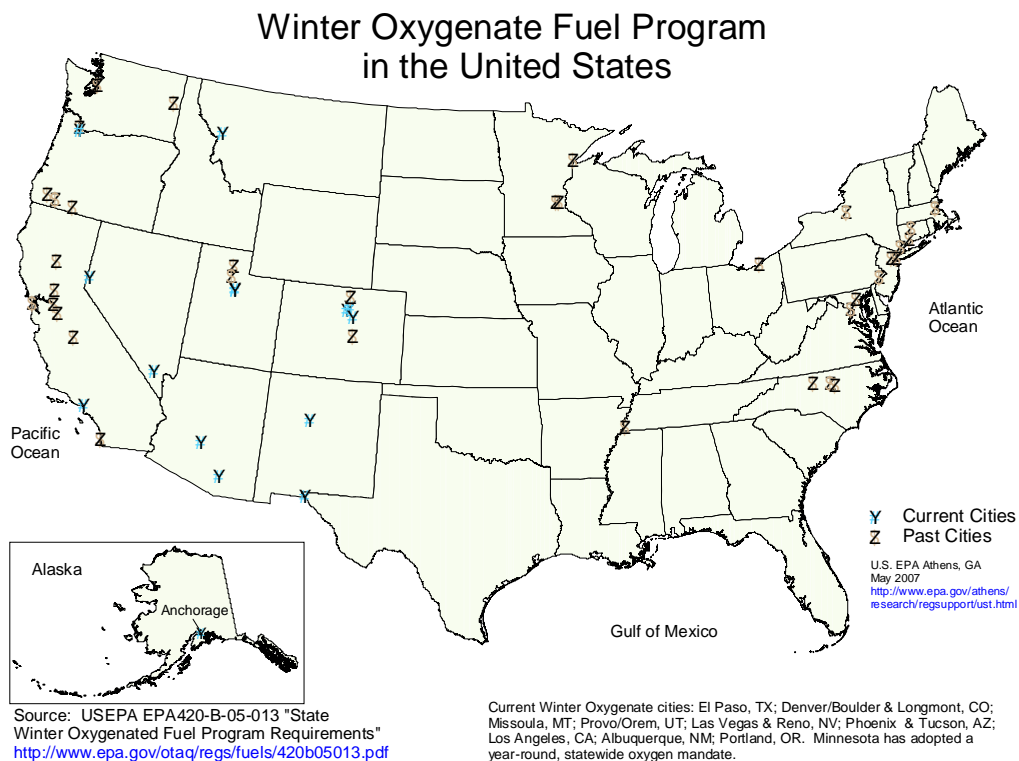
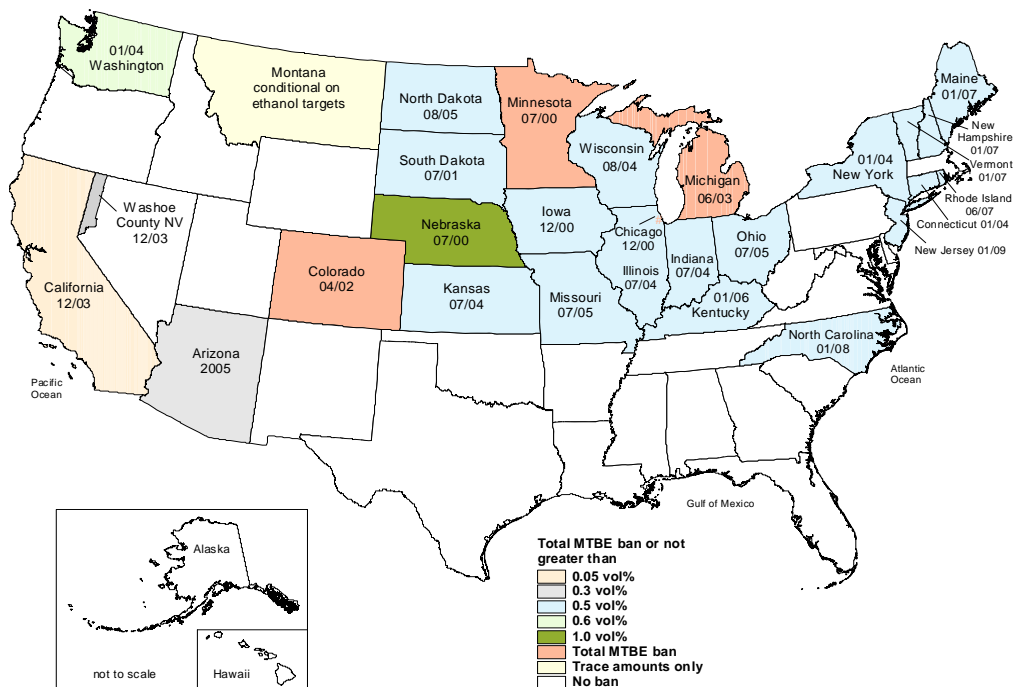


Table A-2. Cities implementing the winter oxygenate program through the winter of 2007-2008 (U.S EPA, 2008c).

Control Period	Area (Consolidated Metropolitan Statistical Area)
10/1 to 1/31	Reno, NV
10/1 to 3/31	El Paso, TX Las Vegas, NV Reno, NV Tucson , AZ
11/1 to 2/29	Albuquerque, NM Missoula, MT Los Angeles, CA
11/2 to 3/31	Phoenix, AZ

Figure A-3. States, cities and counties with MTBE bans and maximum permissible MTBE levels with effective dates from 2000 to 2009.



C. Effect of regulation on gasoline composition

The effects of these regulations can be seen in historical gasoline composition data. The National Institute for Petroleum and Energy Research (NIPER) collected data on gasoline composition beginning in the 1930's. The industry-lead successor (Northrup-Grumman) continues to collect data from roughly 1,000 gasoline samples taken twice a year. Data have been collected in 174 areas around the country, although the number of locations with continuous participation is lower (about 35). The samples are analyzed with industry-standard methods (e.g., Dickson, 2007), but the selection criteria used to determine which locations to include are not disclosed. The data provide the most extensive publicly-available, historical record of both conventional and reformulated gasoline composition throughout the entire United States. These data address issues such as variability of the vendor's local fuel source and changing fuel composition requirements over time. The number of samples per city included, however, is limited in some cases, and the data might under-reflect the true variability. In contrast, a review of composited data from the entire country shows large scale trends in fuel usage. See U.S. EPA (2008) for a comprehensive study of nationwide trends in gasoline composition covering the period from 1995 to 2005. The following section extends this material by examining data for specific cities for a similar time period.

1. Reformulated Gasoline

The MTBE content in premium New York City gasoline is shown in Figure A-4. New York City entered the oxygenated gasoline program in 1993 and continued until 2000. The figure shows that the MTBE content of premium gasoline increased in the winter months, consistent with regulatory requirements. In the summer months, between 1993 and 1995, the MTBE content dropped to levels that are consistent with MTBE use as an octane enhancer. In 1995, the RFG program started and the MTBE content remained near the required level to attain 2.0% oxygen by weight, year round, although some of the required oxygen was supplied by TAME. In 2004, MTBE was banned in New York, and the MTBE level dropped below the state's maximum allowable level of 0.05 vol %. Ethanol replaced the ethers as the oxygenate after this time. In 2006, the oxygenate requirement of RFG was removed. However, ethanol continued to be used in the NY RFG market, likely for a number of reasons, including compliance with the RFG specifications for criteria and toxic pollutants, its value as an octane component, and the positive economics of blending ethanol into gasoline.

Benzene content in New York City gasoline is shown in Figure A-5. Prior to the beginning of the RFG program in 1995, the benzene content ranged above 4% in some samples, and the average was sometimes above 1%. After 1995, the average benzene level remained below 1%. Some individual samples show benzene content above 1%, but these samples may comply with the regulation on an averaged basis, as permitted by the statute.

Since limits on the benzene content of reformulated gasoline were set by regulation, there is little observable difference in the benzene content of reformulated gasoline made with MTBE and reformulated gasoline made with ethanol. EPA RFG survey data for 2002, 2004, and 2006 show that the average MTBE content of RFG had decreased, the average ethanol content had increased, and the average benzene content remained nearly the same over this time period (Table A-3).

Data from five RFG-using cities (Boston, Los Angeles, New York City, San Francisco and Washington, DC) are compared in Figures A-6 and A-7. All contents are plotted as the average value for premium reformulated gasoline from the Northrup-Grumman data set (Dickson, 2007). Regular reformulated gasoline is, for the most part, similar because of the RFG regulations. The benzene content of this gasoline (Figure A-6) varied prior to the implementation of the reformulated gasoline program and, on average, was as high as 2.5% volume. After the beginning of the RFG program in 1995, the benzene content dropped below 1% volume in all cities, with few exceptions. Figure A-7 shows the average MTBE, TAME and ethanol content for the five cities. In each case, the MTBE content in the gasoline increased so that by 1995 the MTBE content in these cities was close to the mandated weight percent level. In two cases, New York and Washington D.C., the large fluctuations in MTBE content are due to wintertime requirements for oxygenated gasoline that began in 1992. Of the other oxygenates (ETBE, TAME, DIPE, TBA and methanol) only TAME had widespread and sustained use in these cities. Its period of usage corresponds to the beginning of the RFG program through the passage of the MTBE bans, when its usage also declined. This decline occurred despite the lack of explicit TAME or other ether bans in most states.

Figure A-4. Historical MTBE usage in New York City. Data points show the average level of MTBE and TAME, which supplied most of the oxygen for this location. The New York State MTBE ban had the effect of eliminating both ethers in 2004, which were then replaced by ethanol. The required oxygen level is given by the thin line and reflects requirements for oxygenated and reformulated gasoline.

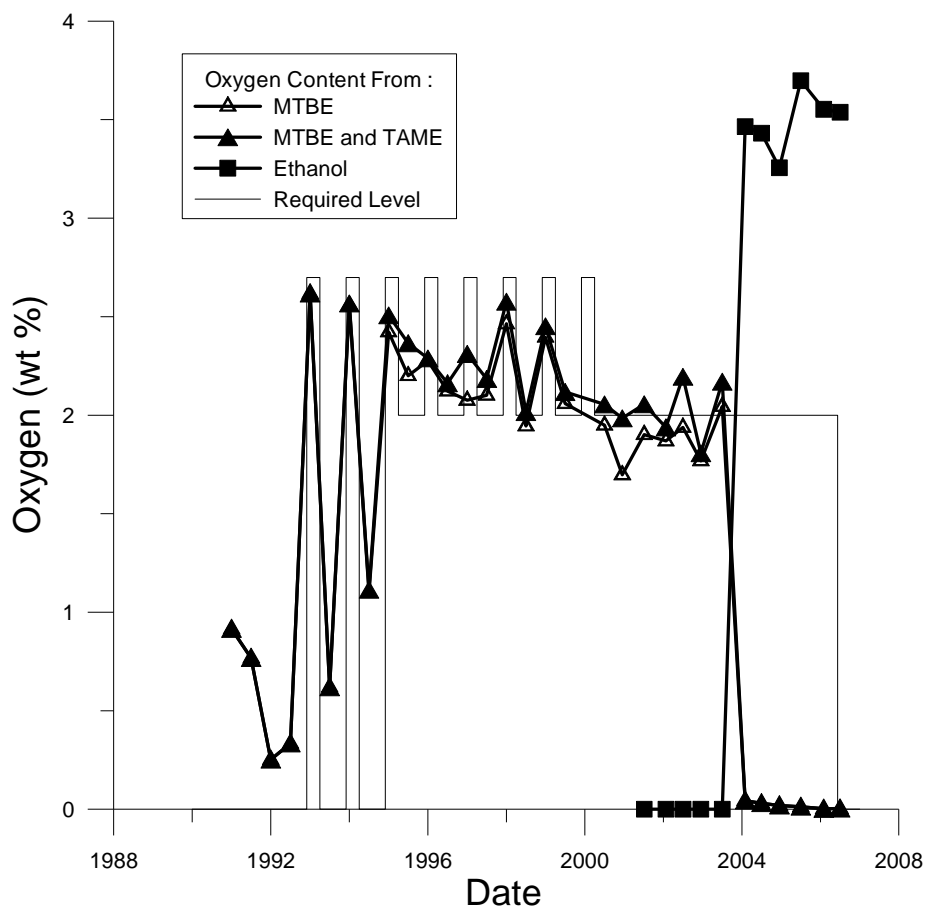


Figure A-5. Benzene concentration in premium, New York City, gasoline. The average benzene concentration was required to be below 1% by volume after adoption of the reformulated gasoline program in 1995.

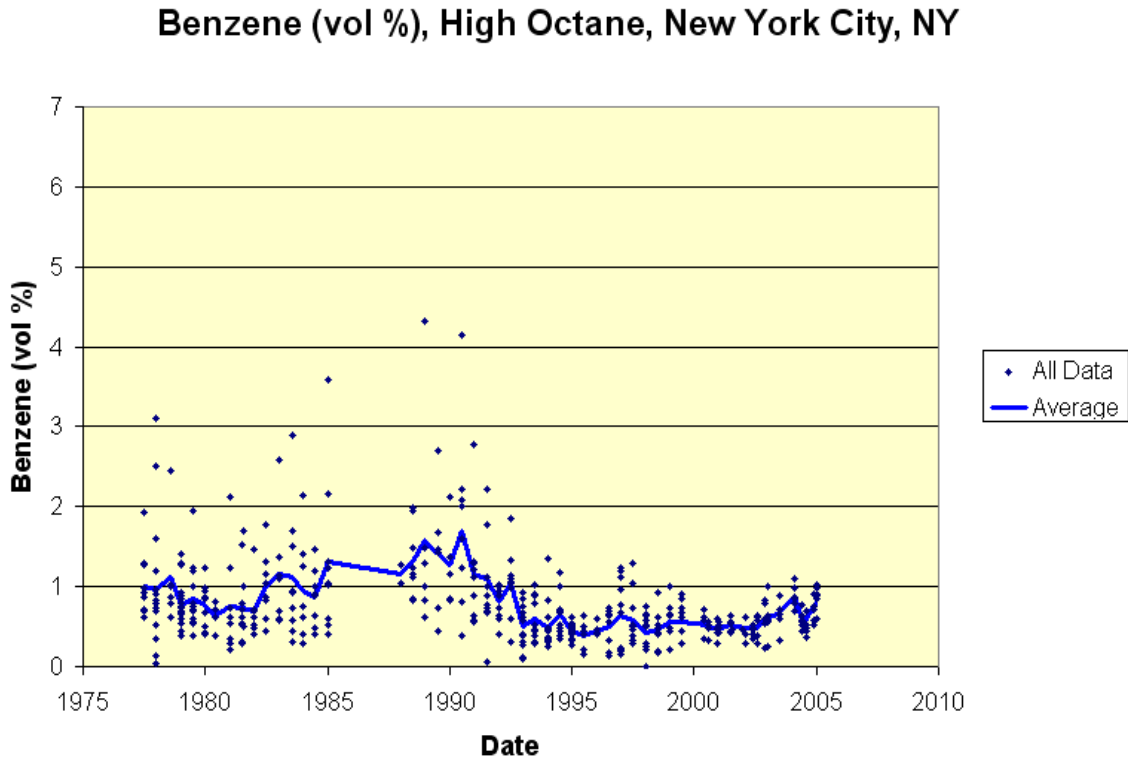


Table A-3. Average MTBE, ethanol, and benzene contents (% vol.) for reformulated gasoline in the United States taken from EPA reformulated gasoline survey data.

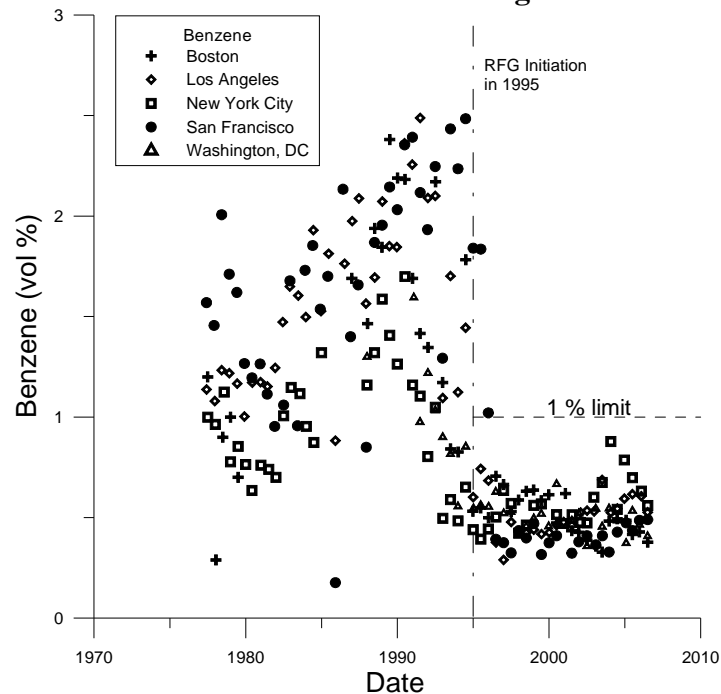
Constituent	Average Content 2002	Average Content 2004	Average Content 2006
MTBE	7.93	5.78	0.008
Ethanol	2.20	4.39	9.20
Benzene	0.61	0.65	0.69

TAME was the second most prevalent ether in these cities and is shown in the second column of Figure A-7. Varying amounts of TAME were used in these cities, the most in Boston and the least in Los Angeles. In Boston, for example, an increase in TAME use prior to the year 2000 corresponds to a decrease in MTBE content. Similar corresponding peaks and valleys can be seen for New York, Washington D.C. and San Francisco. MTBE usage declined either due to the state bans (effective in 2003 in California and 2004 in New York), or due to the removal of the oxygenate mandate in 2006 in states with no MTBE ban (Massachusetts and the District of Columbia for Figure A-7).

Ethanol was used throughout the sampling period at fluctuating levels. Although never used as consistently as MTBE, its usage appears to have decreased during the period of intensive MTBE usage. This pattern is visible for Boston, San Francisco and Los Angeles. Ethanol began to be used again when the New York and California MTBE bans became effective and later when the oxygenate mandate for RFG was removed.

Although TBA had limited independent usage as an oxygenate, it is a known by-product of MTBE manufacture. Typically the TBA content of RFG has been 1% or less of the MTBE content (Figure A-8) for this reason.

Figure A-6. Benzene content in five cities using reformulated gasoline.



**Figure A-7. MBTE, TAME and ethanol content
in five reformulated-gasoline using cities.**

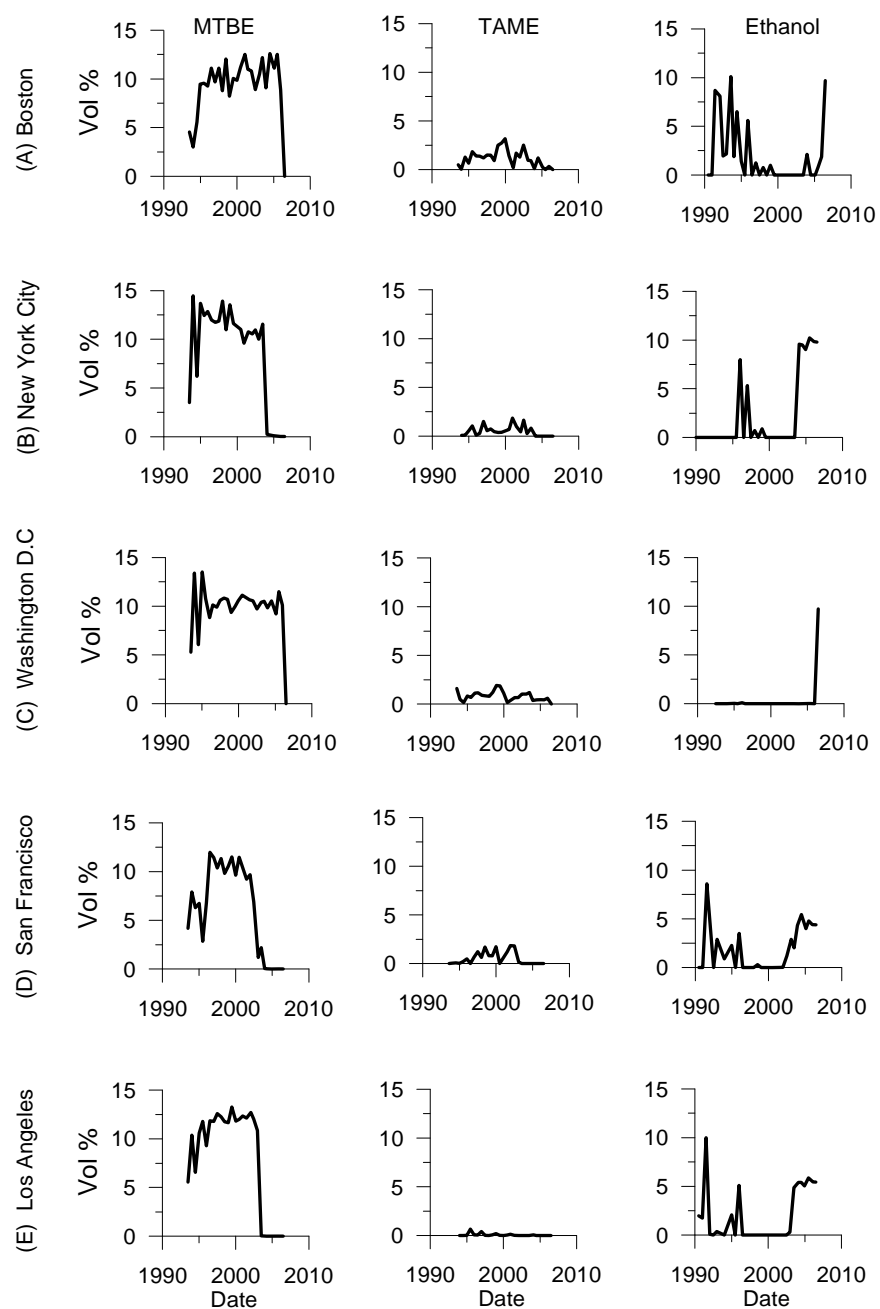
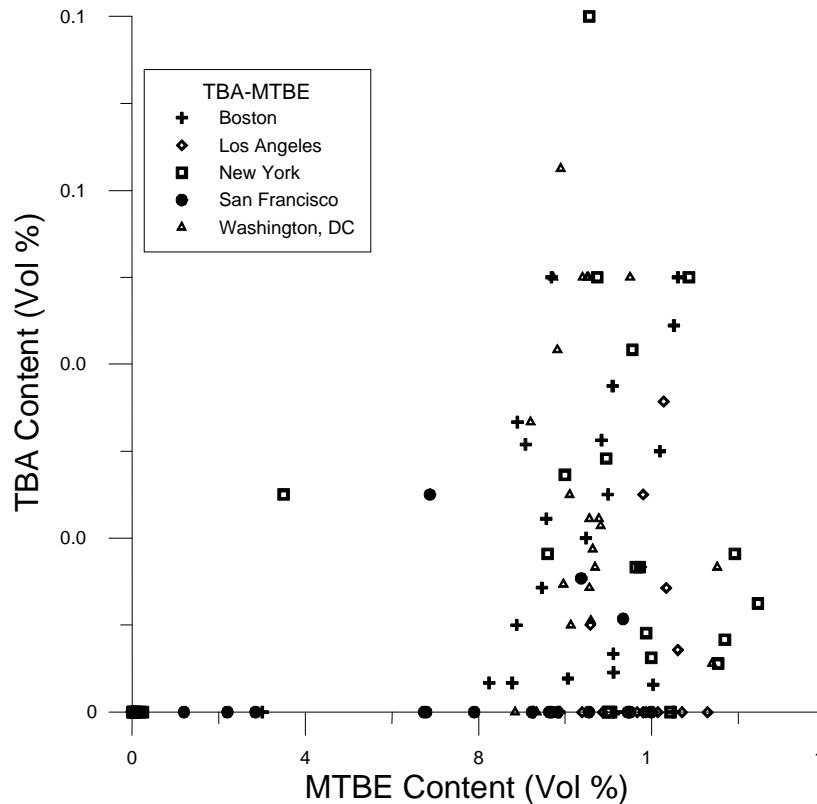


Figure A-8. Scatter plot of TBA content versus MTBE content in five cities using reformulated gasoline.



2. Conventional Gasoline

Average benzene, MTBE and ethanol levels in regular and premium conventional gasoline from six cities are shown in Figure A-9. Average benzene contents above 1% were not uncommon, although the values for Cincinnati, Las Vegas, Kansas City and Miami have tended to stay below 1% since the early 1990s. Average benzene contents for Spokane tended to stay above 1% over the same time period, although these appear to be reduced below the levels for the early 1990s (when these cities were first included in the sampling). The higher benzene levels in Memphis (above 2% volume) may be due to characteristics of the local refinery that produces gasoline in this area or its crude oil sources. In several of these cities (Cincinnati, Kansas City, Miami and Spokane), the benzene content in regular gasoline tended to be slightly higher than in the premium. In these cities, the premium gasoline usually contained significantly more MTBE than the regular gasoline.

For the most part, MTBE was used in premium conventional gasoline at higher levels than in regular conventional gasoline. The majority of the average MTBE contents have been 4% or less, which contrasts with the higher levels used in RFG. In 2004, Kansas and Washington banned MTBE, followed by Ohio in 2005. The MTBE levels in these cities dropped at these times. Memphis is an example where the average MTBE level remained below 4% during the period when other states were banning MTBE.

Miami, however, experienced an increase in MTBE content. By 2006, however, the MTBE was eliminated in both of these cities.

The other ethers (ETBE, TAME and DIPE) were used only occasionally in these cities (Table A-4). ETBE was only seen at low concentrations (less than 0.4% volume) and was used infrequently. TAME had a maximum concentration of 5.9% volume in premium Memphis conventional gasoline and a maximum of 5.4% volume in premium Miami gasoline. Usage in other cities was at concentrations of 1% or lower. TAME was seen frequently in Miami premium conventional gasoline and less so in Miami regular, Memphis premium and Cincinnati premium conventional gasoline. Usage in other cities was infrequent. DIPE was seen most frequently in Memphis premium gasoline, but at a maximum concentration of 0.6%. Other usage of DIPE was less frequent and at lower concentrations.

The average ethanol content in premium conventional gasoline showed variability in the six cities (Figure A-9). Miami had no ethanol usage after the late 1980s, a feature that is probably related to the relatively high levels of MTBE found in Miami gasoline. Memphis ethanol usage became negligible after some usage in the late 1980s. Kansas City had consistent usage at about 2% or less. Las Vegas and Spokane had seasonally varying usage due to their participation in the winter oxygenate gasoline program. These levels were similar for premium and regular in Las Vegas, but ethanol was used only in premium gasoline in Spokane. Cincinnati had a variable amount of ethanol throughout the time period where data were collected. Methanol and TBA were used infrequently and at low levels in regular and premium gasoline in the six cities studied (Table A-5).

Figure A-9. Benzene, MTBE and ethanol content in six cities using conventional gasoline. The gray solid lines indicate premium gasoline, and the dashed lines indicate regular gasoline.

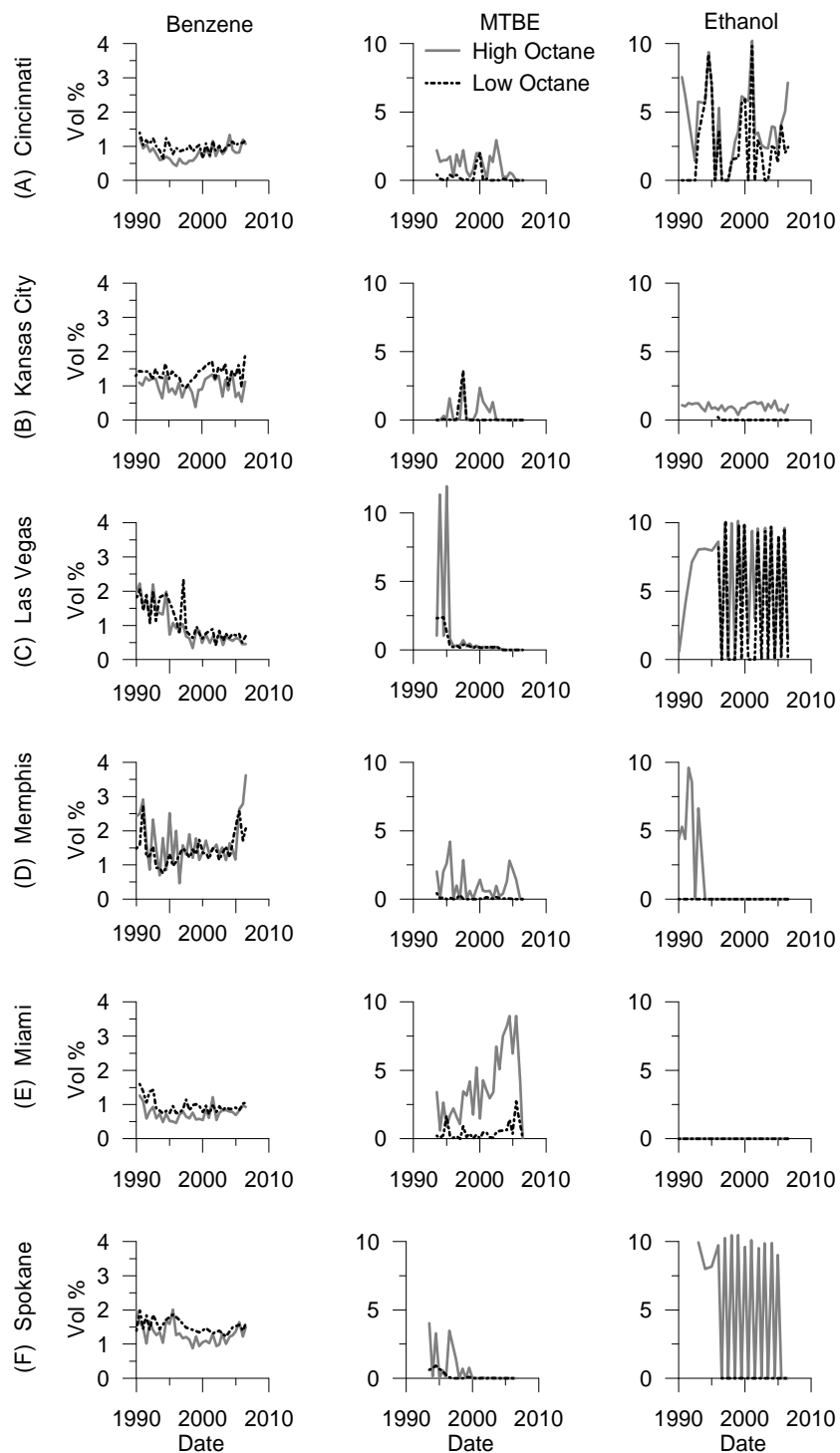


Table A-4. Summary of maximum reported ether (ETBE, TAME, DIPE) concentration, date, and number of non-zero measurements above 0.1% volume per number of times measurements were made for each of the six cities using conventional gasoline.

City	Regular			Premium		
	Max Conc. (%vol)	Date	Number	Max Conc. (%vol)	Date	Number
ETBE						
Cincinnati	0.1	Summer, 1995		0.4	Winter, 96/97	2/23
Kansas City	--	--	0/21	--	--	0/20
Las Vegas	0.1	Winter, 95/96	1/17	--	--	0/20
Memphis	0.2	Summer, 1994	1/24	0.1	Summer, 1994	1/24
Miami	0.2	Summer, 1995	2/24	0.4	Winter, 96/97	2/24
Spokane	--	--	0/10	--	--	0/20
TAME						
Cincinnati	0.2	Winter, 96/97	4/27	0.8	Summer, 1994	11/26
Kansas City	0.6	Summer, 1997	3/21	2.3	Summer, 1997	6/22
Las Vegas	--	--	0/19	0.3	Winter, 94/95	2/23
Memphis	0.3	Summer, 2004	2/24	5.9	Summer, 1994	10/26
Miami	3.3	Winter, 04/05	16/25	5.4	Summer, 2004	25/27
Spokane	0.1	Summer, 1996	1/13	1.2	Summer, 1996	2/22
DIPE						
Cincinnati	0.3	Winter 93/94	4/22	0.3	Winter 94/95	2/22
Kansas City	0.2	Winter 94/95 Summer 1995	3/21	0.2	Winter, 94/95 Summer 1995	3/20
Las Vegas	0.2	Summer, 1995	2/17	0.1	Winter, 94/95 Summer 1995	2/20
Memphis	0.3	Winter, 93/94	8/23	0.6	Summer, 1996 Winter, 99/00 Winter, 00/01 Winter 02/03	11/23
Miami	0.2	Summer, 1994 Winter, 94/95 Summer, 1995	4/23	0.4	Winter 94/95	3/23
Spokane	0.2	Summer, 1995	1/10	0.1	Summer, 1995	1/20

Table A-5. Summary of maximum reported alcohol (methanol, TBA) concentration, date, and number of non-zero measurements above 0.1% volume per number of times measurements were made for each of the six cities using conventional gasoline.

City	Regular			Premium		
	Max Conc. (%vol)	Date	Number	Max Conc. (%vol)	Date	Number
<i>Methanol</i>						
Cincinnati	0.2	Winter 95/96	1/38	(a)		
Kansas City	0.1	Winter 85/86 Summer 1986 Winter 86/87	3/23	0.1	Winter 87/88	1/20
Las Vegas	--	--	0/20	0.1	Winter 94/95 Winter 98/99	2/23
Memphis	--	--	0/36	0.1	Winter 85/86 Summer 1986 Winter 86/87 Winter 90/91 Summer 1991 Summer 91/92	6/40
Miami	0.3	Winter 96/97	3/35	0.1	Winter 85/86 Summer 1996 Summer 1998 Summer 1999 Winter 01/02 Summer 2004	6/37
Spokane	--	--	0/18	0.1	Winter 95/96	2/29
<i>TBA</i>						
Cincinnati	0.3	Winter 96/97	2/38	0.3	Winter 96/97	10/37
Kansas City	1.3	Summer 1985 Winter 85/86	4/23	0.1	Winter 86/87	1/20
Las Vegas	0.2	Winter 90/91	2/20	0.2	Winter 90/91 Winter 91/92	2/24
Memphis	--	--	0/36	0.2	Winter 87/88	7/40
Miami	0.5	Winter 96/97	1/35	0.5	Winter 95/96	11/37
Spokane	--	--	0/18	0.1	Winter 1987	1/27

(a) data not available for Cincinnati premium

References

- Dickson, C.L. (2007) Motor Gasolines, Summer 2006, Northrop Grumman, Bartlesville, Oklahoma, NGMS-246 PPS 2007/1.
- U.S. Environmental Protection Agency (2005) Predicted ground water, soil and soil gas impacts from U.S. gasolines, 2004: First analysis of the autumnal data. Athens, GA: Office of Research and Development; report no. EPA/600/R-05/032.
- U. S. Environmental Protection Agency (2006) Regulatory Announcement, Removal of reformulated gasoline oxygen content requirement. Washington, DC: Office of Transportation and Air Quality. EPA420-F-06-035.
- U. S. Environmental Protection Agency (2008a) RFG Property Survey Data, “Gasoline Properties Data” link at <http://www.epa.gov/otaq/rfg.htm> [9 June, 2008].
- U. S. Environmental Protection Agency (2008b) Fuel Trends Report: Gasoline 1995-2005. Washington, DC: Office of Transportation and Air Quality; report no. EPA420-R-08-002.
- U. S. Environmental Protection Agency (2008c) State Winter Oxygenated Fuel Program Requirements for Attainment or Maintenance of CO NAAQS. Washington, DC: Office of Transportation and Air Quality. EPA 420-B-08-006.
- Weaver, J. W.; Exum, L. E.; Prieto, L. M. (2008) Historical impacts of federal regulation on gasoline composition 1990 – 2007. Accepted for publication in Environ. Forensics.

APPENDIX B. PHASE PARTITIONING OF COMPOUNDS FROM GASOLINE

The dissolution of specific compounds from gasoline depends on at least four factors: gasoline composition, equilibrium phase partitioning, mass transfer limitations and geologic heterogeneity. Gasoline composition is described in more detail in Appendix A.

A. Equilibrium Partitioning

At equilibrium, partitioning of aromatics such as benzene, toluene and xylene has been found to follow Raoult's law which states that the effective solubility, C , is equal to the mole fraction of the chemical in gasoline, X , multiplied by the pure phase solubility of the compound, S . For constituent, i ,

$$C_i = X_i S_i \quad 1$$

From this relationship a partition coefficient, K_i^o can be calculated from

$$K_i^o = \frac{C_i^o}{C_i^w} = \frac{C_i^o}{X_i^o S_i^w} \approx \frac{\rho^o}{MW^o} \frac{1}{S_i^w} \quad 2$$

where ρ^o is the density of the gasoline and MW^o is the average molecular weight of the gasoline. Thus the partition coefficient for chemical (i) is inversely proportional to its solubility. The approximation that replaces the oil phase concentration and mole fraction with the density and average molecular weight requires that the gasoline behaves as an ideal mixture. Cline et al. (1991) showed from the partitioning of 31 gasoline samples that partitioning generally followed Raoult's law; specifically, their calculated partition coefficients varied by less than 30% from the experimentally determined partition coefficients.

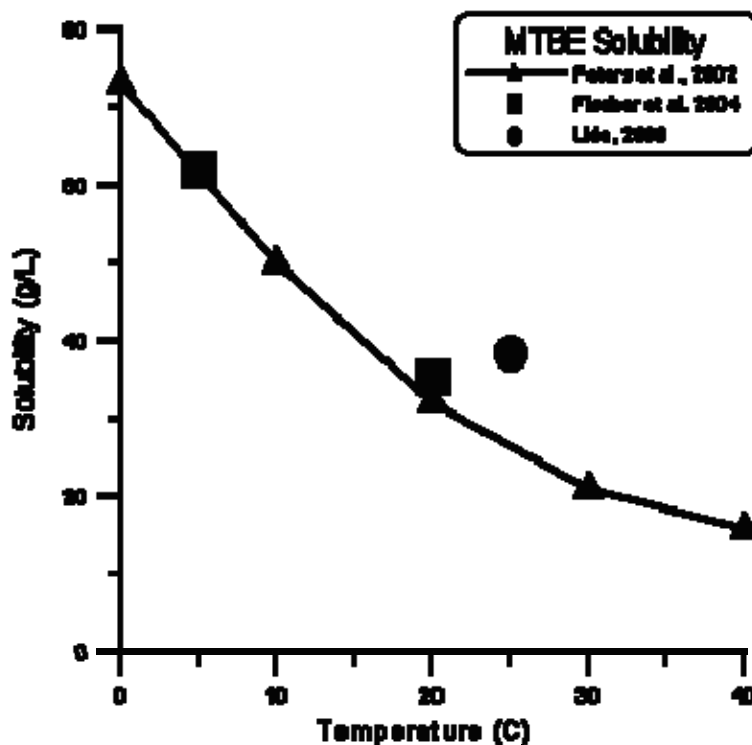
Although a value of about 48,000 mg/L is often cited for the solubility of MTBE, literature data on solubility contain inconsistencies. Data from Peters et al. (2002), Fischer et al. (2004), and Lide (2000) are roughly consistent with each other (Figure B-1). These indicate solubility of MTBE decreases as temperature increases. However, there can also be variability in reported solubility at any given temperature. Some indication of the possible variability in reported MTBE concentrations are given on the figure. Montgomery (2000) cites literature which reports 2,2,4-trimethylpentane (i.e., iso-octane) solubility ranging from 0.56 mg/L to 2.46 mg/L at 25°C. Compounding this single-temperature variability is the variability in average temperature of shallow ground water in the U.S., which ranges from 5°C to 25°C. Thus the reported data give a general indication of solubility, rather than precisely established values.

Table B-1 shows the effective solubility for benzene, ether oxygenates and iso-octane based on various assumptions of the mole fraction of each compound in gasoline. The effective solubilities are ranked in the table from highest effective solubility to lowest.

Although MTBE has virtually been eliminated as an option for blenders, historical considerations indicate that winter oxygenated gasoline with MTBE had the highest effective solubility and iso-octane, with the lowest measured mass fraction in the study, by the U.S.EPA (2005) had the lowest. The maximum MTBE concentrations are consistent with field data presented by Tong and Rong (2002) who reported a maximum MTBE concentration of 1560 mg/L from their study of 90 sites in the Los Angeles area.

The prospects for wide spread ground water contamination generated from iso-octane in gasoline at these levels (up to 19%) is very low because of these very low effective solubility. Alkylation produces high-octane gasoline components called “alkylates,” by reacting isobutane with olefins (alkenes). One example of an alkylate is iso-octane which is also called 2,2,4-trimethylpentane (Owen and Coley, 1995. Similar behavior is expected with other components of alkylate.

Figure B-1. MTBE solubility data
from Peters et al. (2002), Fischer et al. (2004) and Lide (2000).



Heermann and Powers (1998) measured ethanol/water partition coefficients between a one-, two-, three- and eight-component artificial gasoline and water mixture. Their results show similar partitioning behavior between the three- and eight-component mixtures implying that these results better represent an actual gasoline, than the few component mixtures. The measured partition coefficients decreased with increasing ethanol concentration in the water phase. Their results for these mixtures can be represented by

$$f_{\text{ethanol}}^w \approx 150 f_{\text{ethanol}}^o \quad f_{\text{ethanol}}^w < 0.2$$

3

where the concentrations are expressed on a volume fraction basis, and the fraction of ethanol in water, f_{ethanol}^w , is less than 0.2. Thus ethanol is partitioned preferentially into the aqueous phase and the fraction in the water phase is roughly 150 times the fraction in the gasoline phase.

Table B-1. Solubility estimated from the SPARC calculator²⁰ and effective solubility for benzene, ether oxygenates and isooctane. The results are ranked from highest effective solubility to lowest, illustrating the combined impact of solubility and the content of each chemical in gasoline.

Chemical	Condition	Solubility ^a (mg/L)	Molecular Weight (g/mol)	Volume fraction	Approximate Mole fraction (k)	Effective Solubility (mg/L)
MTBE	Winter Oxygenate (wo)	13700	88.15	0.1490	0.1277	1750.
MTBE	RFG	13700	88.15	0.1100	0.0943	1292.
TAME	wo	3860	102.18	0.1720	0.1778	686.5
DIPE	wo	3030	102.18	0.1720	0.1681	509.3
TAME	RFG	3860	102.18	0.1275	0.1318	508.9
ETBE	wo	2350	102.18	0.1720	0.1709	401.7
MTBE	Avg CG 93 octane	13700	88.15	0.0333 ^b	0.0285	391.1
DIPE	RFG	3030	102.18	0.1275	0.1246	377.6
ETBE	RFG	2350	102.18	0.1275	0.1267	297.8
Benzene	Max	1600	78.11	0.0500	0.03446	71.4
MTBE	Avg CG 87 octane	13700	88.15	0.0052 ^c	0.0045	61.1
MTBE	Min	13700	88.15	0.0050	0.0043	58.7
Benzene	Avg CG 87 octane	1600	78.11	0.0145 ^d	0.0130	20.8
Benzene	RFG	1600	78.11	0.0100	0.0089	14.3
TAME	RFG 93 octane	3860	102.18	0.0034 ^e	0.0035	13.4
Benzene	Avg CG 93 octane	1600	78.11	0.0082 ^f	0.0073	9.48
TAME	RFG 87octane	3860	102.18	0.0024 ^g	0.0025	8.92
Iso-octane	Max	0.3	114.23	0.1969 ^h	0.2039	0.062
Iso-octane	Avg	0.3	114.23	0.0562 ⁱ	0.0582	0.018
Iso-octane	Min	0.3	114.23	0.0019 ^j	0.0020	0.0006

^a For background see Hilal et al., 2004

^b Average MTBE content in conventional Georgia 93 Octane Gasoline (U.S. EPA, 2005)

^c Average MTBE content in conventional Georgia 87 Octane Gasoline (U.S. EPA, 2005)

^d Average benzene content in conventional Georgia 87 Octane Gasoline (U.S. EPA, 2005)

^e Average TAME content in reformulated Virginia 93 Octane Gasoline (U.S. EPA, 2005)

^f Average benzene content in conventional Georgia 93 Octane Gasoline (U.S. EPA, 2005)

^g Average TAME content in reformulated Virginia 87 Octane Gasoline (U.S. EPA, 2005)

^h Maximum Isooctane content for reformulated and conventional gasoline (U.S. EPA, 2005)

ⁱ Maximum Iso-octane content for reformulated and conventional gasoline (U.S. EPA, 2005)

^j Maximum Iso-octane content for reformulated and conventional gasoline (U.S. EPA, 2005)

^k Assumed 105 g/mol average molecular weight of gasoline.

1. Co-solvency and Partitioning

²⁰Estimates made from the SPARC Performs Automated Reasoning in Chemistry calculator, see <http://ibmlc2.chem.uga.edu/sparc/>

The presence of a water-miscible component of gasoline, such as ethanol or methanol, has the potential to increase the solubility of other, less soluble compounds in gasoline like benzene. For methanol-gasoline blends with MTBE contents up to 15%, Poulson et al. (1992) reported no increases in benzene, toluene, ethylbenzene, xylenes (collectively, BTEX) concentrations. They also found that when methanol was present in gasoline at 10% or less, there was no appreciable effect on BTEX solubility, if the gasoline to water ratio was 1 to 10.

At higher methanol content, benzene solubility increased dramatically. For 85% methanol, two effects are significant. First, there is less benzene in the gasoline (as would be true for E85 also) but the co-solvency effect was found to produce higher initial benzene concentrations in water when the gasoline to water ratio was higher (1 to 1 versus 10 to 1). As the source is depleted of benzene, then the concentrations dropped to values slightly below those of gasoline containing no methanol, due to the lower benzene content in the methanol-containing gasoline.

Heermann and Powers (1998) developed a model to estimate the effect of ethanol on the gasoline/water partition coefficient of BTEX. The model was comprised of a linear relationship for low ethanol volume fractions and a log-linear model for higher concentrations. For ethanol volume contents from 0% to 25%, variation in measured BTEX partition coefficients was best represented by a linear model (where the partition coefficients varied by as much as 49%). At around 25% ethanol volume content, a log-linear model represents the data better. Above this point the partition coefficients varied by orders-of-magnitude, indicating a strong co-solvency effect, similar to that observed by Poulson et al. (1992) for methanol.

B. Mass-Transfer Limitations

Seagren et al. (1999) report on a study where the flow of water past a pool of non-aqueous phase liquid (NAPL) was evaluated for the establishment of equilibrium between concentrations in the aqueous and non-aqueous phases. Vertical dispersion was the main mechanism that was presumed to move a contaminant from the NAPL pool to the aquifer. These authors concluded that for most of the conditions studied, the local equilibrium model performed as well as or better than a non-equilibrium partitioning model. The effects were quantified through usage of the modified Sherwood number multiplied by the Stanton number²¹. Local equilibrium is appropriate when the product of these two quantities is greater than 400. They note, however, that there are uncertainties in model parameters, particularly, k_1 and D_z for field sites. Conditions where local equilibrium may not be achieved include sites with high seepage velocity and dispersion coefficient, and/or low pool length and small mass transfer coefficient. Arey and Gschwend (2005) presented an analysis of the effects of varying gasoline composition on drinking water well impacts. From their analysis they conclude that partitioning from a NAPL pool into flowing ground water achieves equilibrium for

²¹The modified Sherwood number is represented by $Sh^* = L_x k_1 / D_z$, and the Stanton number by $St = k_1 / v_x$, where L_x is the length of the pool, k_1 is the mass transfer coefficient, D_z is the vertical diffusion coefficient and v_x is the seepage velocity.

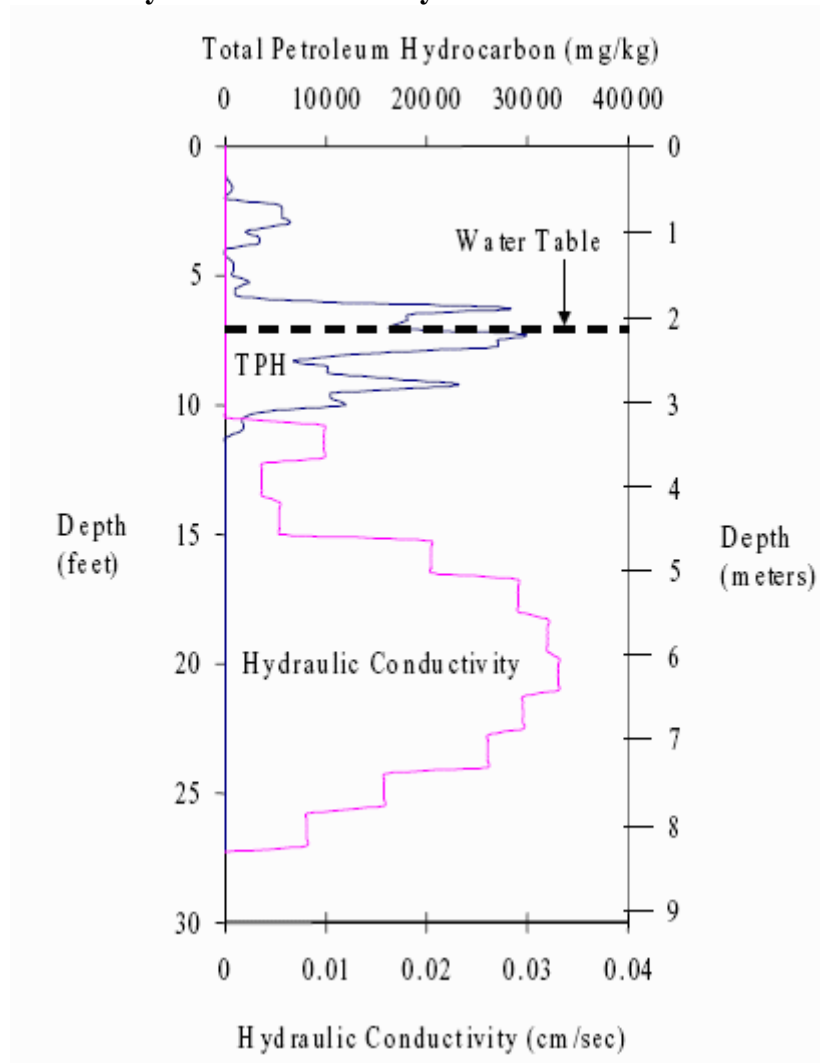
typical conditions (defined in this study as pool length of 10 m, ground water velocity of 0.4 m/d, vertical dispersivity of 0.002 m, and mass transfer coefficient of 1 m/d).

C. Geologic Heterogeneity

Although the maximum observed MTBE concentration reported by Tong and Rong (2002) in their study of 90 Los Angeles LUST sites corresponds closely to the predicted effective solubility of MTBE, the majority of their sites have lower maximum concentrations. These differences could be due to well placement and well screen effects (U.S. EPA, 2004), lower maximum MTBE concentrations in Los Angeles gasoline depending on the release date, or reduced flushing of the gasoline due to geologic heterogeneity. Wilson et al. (2001) presents field results from a North Carolina site with detailed vertical profiling of the total petroleum hydrocarbons (TPH or fuel) distribution along with the distribution of hydraulic conductivity (Figure B-2). The significance of these results is that the TPH is co-located with the lowest hydraulic conductivity values. Ground water flow through this zone will be very low as well. Transport of MTBE or other contaminants away from this zone will be limited by the diffusion rate from the low conductivity zone to the highly conductive aquifer below. In this case, limited diffusion and high velocities below the contaminated zone may result in mass transfer limited partitioning from the TPH to the underlying ground water as indicated by the Seagren et al. (1999) local equilibrium analysis described above.

Since the fining upward geologic sequence is typical of alluvial depositional systems, there may be numerous LUST sites where these phenomena limit observed concentration. Although detailed characterization, as was done by Wilson et al. (2001) of the Tong and Rong (2002) sites is not available, the distribution of TPH within impermeable zones and mass transfer limitations may explain their results.

Figure B-2. Distribution of total petroleum hydrocarbons (TPH or fuel) and hydraulic conductivity at a North Carolina site.



References

- Arey, J. S.; Gschwend, P. M. (2005) A physical-chemical screening model for anticipating widespread contamination of community water supply wells by gasoline constituents. *J. Contam. Hydrol.* 76: 109-138.
- Cline, P. V.; Delfino J. J.; Rao, P. S. C. (1991) Partitioning of aromatic constituents into water from gasoline and other complex solvent mixtures. *Environ. Sci. Technol.* 25: 914-920.
- Fischer, A.; Muller, M.; Klasmeier, J. (2004) Determination of Henry's law constant for methyl tert-butyl ether (MTBE) at groundwater temperatures. *Chemosphere.* 54: 689-694.
- Heermann, S. E.; Powers, S. E. (1998) Modeling the partitioning of BTEX in water-reformulated gasoline systems containing ethanol. *J. Contam. Hydrol.* 34: 315-341.
- Hilal, S.H.; Carreira, L. A.; Karickhoff, S. W. (2004) Prediction of the solubility, activity coefficient and liquid/liquid partition coefficient of organic compounds. *QSAR Comb. Sci.* 709.
- Lide, D.R. (2000) *CRC Handbook of chemistry and physics*. 81st ed. CRC Press. pp. 8-95.
- Montgomery, J. H. (2000) *Groundwater chemicals desk reference: Third edition*. CRC Lewis Publishers: Boca Raton.
- Owen, K.; Coley, T. (1995) *Automotive fuels reference book*. 2nd ed. Society of Automotive Engineers. Warrendale, PA. 963pp.
- Peters, U.; Nierlich, F.; Sakuth, M.; Laugier, M. (2002) Methyl tert-butyl ether, physical and chemical properties. *Ullmanns Encyclopedia of Industrial Chemistry*; Release 2003. 6th ed. VCH Verlag GmbH & Co., KGaA, Wiley, DOI, 10.1002/14356007.a16_543.
- Poulson, M.; Lemon, L.; Barker, J. F. (1992) Dissolution of monoaromatic hydrocarbons into groundwater from gasoline-oxygenate mixtures. *Environ. Sci. Technol.* 26: 2483-2489.
- Seagren, E. A.; Rittman, B. E.; Valocchi, A. J. (1999) A critical evaluation of the local-equilibrium assumption in modeling of NAPL-pool dissolution. *J. Contam. Hydrol.* 39: 109-135.
- Tong, W.; Rong, Y. (2002) Estimation of methyl tert-butyl ether plume length using the Domenico analytical model. *Environ. Forensics.* 3: 81-87.

U.S. Environmental Protection Agency (2004) On-line tools for assessing petroleum releases. Washington, DC: Office of Research and Development; report no. EPA 600/R-04/101.

U.S. Environmental Protection Agency (2005) Predicted ground water, soil and soil gas impacts from U.S. gasolines, 2004: First analysis of the autumnal data. Athens, GA: Office of Research and Development; report no. EPA/600/R-05/032.