ETHANOL

Its Use in Gasoline:
Expected Impacts and
Comments of
Expert Reviewers

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Executive Summary

This paper summarizes information about ethanol's health and environmental effects, in the context of ethanol's use as a fuel oxygenate. The conclusions are:

- ethanol is readily degraded in the environment;
- anticipated human exposures to ethanol are very low; and
- voluminous information on metabolism of ethanol by humans, and on the health effects of ingested ethanol, strongly suggests that environmental exposures to ethanol will have no adverse health impact.

Also summarized are some findings of a recent, extensive report by the State of California regarding ethanol's potential impact on air and water quality. Appended to the report is a compilation of comments by various expert bodies regarding the same issues discussed in this paper.

Health effects of inhaled ethanol

The data strongly suggest that exposure of the general public to ethanol vapors coming from ethanol-blended gasoline is very unlikely to have any adverse consequences. The reasons for this are:

- the tiny doses that might be received, which might not be observable in light of naturally-occurring levels of ethanol in blood;
- the body's rapid elimination of ethanol; and
- the relatively large doses of ethanol and high blood levels of ethanol associated with toxic effects in people.

No data in the scientific literature support the hypothesis that chronic exposure to non-irritating levels of ethanol in air could cause significant elevation of blood ethanol levels (unless exposed individuals are exercising at the time), or that a risk of cancer or birth defects would be created.

A review by the Health Effects Institute of the potential health effects of ethanol inhaled from ethanol-blended fuels reached similar conclusions. HEI states, "It is unlikely that these [adverse health] effects would result from the very low exposure levels (by inhalation) in refueling situations, because the preexisting levels of ethanol in the blood from normal metabolic processes would not be significantly affected." A recent survey of the literature regarding the inhalation toxicity of ethanol by the Swedish Institute for Environmental Medicine concluded that "a high blood concentration of ethanol is needed for the development of adverse effects" and "ethanol at low air concentrations should not constitute a risk for the general population."

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Environmental persistence

Ethanol is not persistent in the environment. Virtually any environment supporting bacterial populations is believed capable of biodegrading ethanol. Ethanol in water is expected to undergo rapid biodegradation, as long as it is not present in concentrations directly toxic to microorganisms. The half-life of ethanol in surface water is reported to range from 6.5 to 26 hours. Atmospheric degradation is also predicted to be rapid.

Air pollution

Detailed modeling of atmospheric pollution in southern California suggests that using ethanol will not increase the risk of adverse health effects due to emissions or formation of ethanol, acetaldehyde, or peroxyacetyl nitrate (PAN). In fact, the predicted concentrations of ethanol in air were at least 500-fold less than the identified health-protective concentration of 53 ppm.

Water pollution

California also assessed the potential for ethanol to increase pollution of water wells by gasoline components following underground leaks of ethanol-blended fuel. Screening modeling suggests that ethanol might increase the probability of well pollution during the first five to 10 years after a leak occurs, but that the probability would decrease beyond that period.

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Introduction

The purpose of this short paper is to summarize information about ethanol's health and environmental effects, given ethanol's use as a fuel oxygenate. The conclusions are: (1) ethanol is readily degraded in the environment; (2) anticipated human exposures to ethanol are very low; and (3) voluminous information on metabolism of ethanol by humans, and on the health effects of ingested ethanol, strongly suggests that environmental exposures to ethanol will have no adverse health impact. Also summarized are some findings of a recent, extensive report by the State of California regarding ethanol's potential impact on air and water quality. Appended to this report is a compilation of comments by various expert bodies regarding the same issues discussed in this paper. Those comments largely support the material given here.

Health effects of inhaled ethanol

Ethanol, the active ingredient of alcoholic beverages, has been part of the human diet — and the human environment — for thousands of years. It is produced by fermentation by fungi and other microorganisms, and is found at low levels in the blood and breath of persons who do not drink alcohol. Biological exposures and responses to ethanol are typically evaluated in terms of the blood concentrations, where the units of concentration are milligrams of ethanol per deciliter of blood, or mg/dl. Some blood ethanol concentrations (BEC) and associated effects are shown in Table 1. Endogenous blood levels of ethanol range from non-detectable to 0.02 mg/dl to 0.15 mg/dl (Jones, 1985; Lester, 1962). A typical alcoholic beverage contains 12 g of alcohol, which corresponds to a dose of about 170 mg/kg for a 70-kg adult, and produces a peak blood ethanol concentration on the order of 25 mg/dl. Legal limits on blood alcohol for drivers of vehicles are typically 80-100 mg/dl.

Ethanol is widely ingested in alcoholic beverages, usually with only mild effects. However, at sufficiently high doses, ethanol can cause toxic effects in humans, both short-term (such as inebriation) and long-term (such as cirrhosis of the liver). If ethanol becomes a common fuel additive, there may be opportunities for exposure by inhalation: ethanol vapors might be inhaled at gasoline stations or in automobiles, for example. Thus, concern has been raised about the possible health consequences of using ethanol for this purpose.

The scientific literature contains virtually no reports of injury to humans from inhaled ethanol. The apparent lack of harm may be attributable to rapid metabolism of ethanol and the difficulty in significantly raising blood ethanol concentrations by inhalation exposure, which keep internal doses extremely low except in unusual situations, such as heavy exercise in the presence of concentrated vapors. The occupational standard for ethanol in air is 1000 ppm (1900 mg/m^3) on an eight-hour basis.

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The occupational experience with ethanol in air appears to be favorable: no symptoms at levels below 1000 ppm are reported: at this or higher concentrations, ethanol vapor causes eye and upper respiratory tract irritation, fatigue, headache, and sleepiness (ACGIH, 1991; Clayton and Clayton, 1994). No reports regarding chronic exposure of humans to ethanol vapors have been located.

Laboratory animals, chiefly rats, have been subjected to inhalation exposure in a variety of experiments, most investigating aspects of central nervous system or developmental toxicity. The majority of exposures have been short-term, of less than two weeks, but many of these were continuous. The study of longest duration, 90 days, also used the lowest concentration of ethanol, 86 mg/m^3 (45 ppm); otherwise, experimental designs typically produced atmospheres of thousands of mg/m^3 (or ppm), frequently in order to develop ethanol dependence. Blood ethanol concentrations were often, but not always, determined. The great majority of BEC measurements were above 100 mg/dl. The 90-day study, in which male and female Sprague-Dawley and Long-Evans rats, male and female guinea pigs, male New Zealand rabbits, male squirrel monkeys, and male beagle dogs were exposed, examined only hematologic endpoints and some tissues, but observed no exposure-related changes or clinical signs of toxicity (Coon *et al.*, 1970).

Scientists at the Swedish Institute for Environmental Medicine published a literature review of the inhalation toxicology of ethanol, prompted by the use of alcohols in vehicle fuels (Andersson and Victorin, 1996). They identified three studies in which rodents were exposed to ethanol concentrations of 1,800 mg/m^3 (1,000 ppm) or less (and far more studies with much higher exposures). These lower-dose studies examined bronchoconstriction, sleeping patterns, reinforced behavior, and serum hormones. A two-hour exposure to 190 mg/m^3 ethanol (100 ppm; the lowest exposure examined in any study) caused an increase in the waking stage and a decrease in REM sleep of male rats, but no change in EEG power spectra. Exposure to higher concentrations (1,500 mg/m^3 [790 ppm] or more) did not cause these changes (Ghosh *et al.*, 1991a). Two- or five-hour exposures to 140 ppm ethanol, or 80 minutes of exposure to 100 ppm, had no effect on measures of reinforced behavior (Ghosh *et al.*, 1991b). Cannulated guinea pigs did not develop bronchoconstriction when exposed to up to 11,520 mg/m^3 (6,060 ppm) of ethanol. Male rats exposed to 1,880 mg/m^3 (1,000 ppm) for six hours per day showed decreased serum testosterone after one day, but not after seven days of exposure.

The paucity of direct evidence regarding the possible effects of inhaled ethanol does not mean that the possible consequences are entirely unpredictable. In fact, the data strongly suggest that exposure of the general public to ethanol vapors coming from ethanol-blended gasoline is very unlikely to have any adverse consequences. While there are little, if any, data on the toxicity of ingested ethanol itself in humans, it is generally accepted that the vast literature on the effects of alcoholic beverages is highly relevant. Alcohol abuse is a significant medical and social problem, and is the impetus for most research into ethanol toxicology, both in humans and experimental animals. A consequence of this is that little experimental data address the levels of internal exposure that can be reasonably anticipated to result from using ethanol as an oxygenate. A second motivation for experimental work in ethanol is fetal

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alcohol syndrome (or fetal alcohol effects) which, in theory at least, could be caused by relatively brief maternal exposures to ethanol during pregnancy.

Since ethanol's important toxic effects require that the material first enter the bloodstream, one can evaluate inhalation exposures in terms of the blood alcohol concentrations they would produce. Prediction of BEC following exposure to ethanol vapors must consider several factors: (a) the concentration of ethanol in air, (b) the duration of exposure, (c) breathing rate, (d) absorption of ethanol across the lungs, and (e) the body's elimination rate of ethanol. Two of these factors are more or less constant in every situation. Experiments in humans have shown that from 55% to 60% of inhaled vapors are absorbed into the bloodstream (Kruhoffer, 1983; Lester and Greenberg, 1951). The rate of clearance of ethanol from the blood (V_{max}) is about 15 mg/dl/hr (Pohorecky and Brick, 1987) but may be as high as 23 mg/dl/hr (Holford, 1987); these rates correspond to elimination of 83 mg/kg/hr to 127 mg/kg/hr, or about 6 to 9 g of ethanol per hour for an adult. For comparison's sake, it should be noted that a single alcoholic drink contains about 12 g of ethanol (IARC, 1988).

As long as a person's intake of ethanol does not exceed V_{max}, blood alcohol levels will stay low. In Table 2 are shown the intake rates for ethanol inhaled under a variety of conditions, assuming absorption across the lungs of 55% and a standard body weight of 70 kg. In bold type are intakes above 83 mg/kg/hr, the lower estimate of alcohol clearance: exposure under these conditions could lead to an accumulation of ethanol in the blood and a rising BEC. Under the other conditions given, the body's ability to eliminate ethanol is not exceeded, and BEC levels would remain below toxic levels.

The calculations suggest that exposure to ethanol vapors that are irritating to the eyes and mucous membranes, while uncomfortable, would not cause a significant rise in BEC in persons at rest. As activity increases, ethanol intake increases, but vapor concentrations would need to exceed the occupational limit by a substantial margin in order to cause a rise in BEC. Some experimental work demonstrates that significant uptake of ethanol through the air is unusual, or difficult, as shown in Table 3. Moderate activity in the presence of irritating vapors is required.

Environmental behavior

Recent reviews of the environmental behavior of gasoline oxygenates generally note that ethanol is not likely to accumulate or persist for long in the environment. For example, the Interagency Assessment of Oxygenated Fuels (NSTC, 1997) observes that ethanol is expected to be rapidly degraded in groundwater and is not expected to persist beyond source areas. Virtually any environment supporting bacterial populations is believed capable of biodegrading ethanol (Ulrich, 1999). Ethanol in surface water is also expected to undergo rapid biodegradation, as long as it is not present in concentrations directly toxic to microorganisms (NSTC, 1997; Malcolm Pirnie, Inc., 1998). The half-life of ethanol in surface water is reported to range from 6.5 to 26 hours (Howard *et al*., 1991). Atmospheric degradation is also predicted to be rapid (Malcolm Pirnie, Inc., 1998).

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In part, expectations of ethanol's degradability rely on experiments that use microcosms of groundwater and soil mixtures to demonstrate that ethanol is rapidly degraded both aerobically (100 mg/l in 7 days, Corseuil *et al.*, 1998) and anaerobically (100 mg/l in 3 to 25 days, depending on conditions Corseuil *et al*., 1998; 96 mg/l within 30 days, Suflita and Mormile, 1993; 100 mg/l within 14 days, Yeh and Novak, 1994). In these experiments, ethanol generally delays degradation of benzene, toluene, and xylenes, but not always, and some investigators (Corseuil *et al*., 1998) caution against generalizations about ethanol's effect.

Possible inhalation exposures to ethanol due to use in gasoline

Opportunities for inhalation exposure of the general public to ethanol used as a gasoline oxygenate include vapors inhaled while fueling vehicles and ambient air. The first sort of exposure would be relatively brief, no more than five minutes, perhaps, while the second could last for many hours. These scenarios are considered in more detail below.

Very limited investigations of personal exposures during refueling have so far failed to detect ethanol, where detection limits were 50 ppm or less (HEI, 1996). If refueling involved five-minute exposures at the occupational limit of 1,000 ppm, an adult might receive an ethanol dose of 0.13 g (about 2 mg/kg). Such an exposure might increase BEC by about 0.3 mg/dl, at most. Exposure to such a high level of ethanol is unlikely. The Health Effects Institute evaluated hypothetical exposures of 1 ppm for three minutes and 10 ppm for 15 minutes, and determined that incremental changes in BEC would be insignificant (HEI, 1996).

Data on ambient air concentrations of ethanol are few. The average ambient level in air in the city of Porto Alegre, Brazil, where 17% of vehicles run entirely on ethanol, is 12 ppb (0.023 mg/m^3) (Grosjean *et al*., 1998). The lowest concentration of ethanol tested for toxicity in animals was almost 4,000-times greater than this (86 mg/m^3, 45 ppm). A person might receive half a milligram of ethanol per day from ambient air containing 12 ppb of ethanol, a negligible dose.

Several agencies in the State of California recently completed a large investigation into the possible impacts of using ethanol more extensively as a fuel oxygenate (State of California, 1999). To estimate the effects of oxygenates on air quality, modelers predicted airborne concentrations of various pollutants in the southern California air shed (a particularly polluted region) resulting from five fuel scenarios. Total concentrations of airborne pollutants, that is the contributions from vehicles plus all other sources, were estimated, both maximum one-hour-averages and maximum daily averages. Two ethanol scenarios were assessed, in which the oxygenate is used to give fuel oxygen content of 2 or 3.5%. Predicted concentrations of ethanol in air over any averaging period were at least 500-fold less than the identified health-protective concentration of 53 ppm.

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Atmospheric byproducts of ethanol use

Not only ethanol itself, but byproducts of ethanol's use as an oxygenate are of concern, particularly contributions of acetaldehyde and peroxyacetyl nitrate (PAN) to the atmosphere. The State of California included these chemicals in its air contaminant modeling and inhalation risk assessment. For acetaldehyde, no acute or chronic non-cancer impacts were predicted, and while the increased level of acetaldehyde poses a small additional cancer risk (under standard low-dose potency assumptions), the increase is small compared to the risks posed by other gasoline components, and is offset by reductions in formaldehyde. PAN was predicted to occur at levels that might present a health risk, but these levels did not differ by future-use oxygenate scenario (*i.e.*, MTBE, ethanol at 2 or 3.5%, or otherwise compliant fuel), and were in all cases lower than past PAN exposures during MTBE use.

Effect of ethanol on sub-surface benzene plumes

Although ethanol-blended gasoline contains less benzene (or any gasoline component) per gallon than does non-oxygenated gasoline, there is concern that ethanol might affect the sub-surface behavior of leaked gasoline components, and perhaps worsen sub-surface contamination. Since ethanol biodegradation is likely favored over benzene biodegradation, the presence of ethanol may allow larger amounts of benzene to remain in the ground for dispersal. As there are no observational (*i.e.*, field) data on this subject, the State of California and others have addressed the potential effect of ethanol on sub-surface benzene plume lengths created by leaking underground fuel tanks by conducting mathematical modeling of an idealized physical situation. All three models necessarily make assumptions in order to simplify the complex physical situation and to fill data gaps, but these assumptions, according to California, tend to exaggerate the possible influence of ethanol. California's assessment is that the models are in good agreement, and that ethanol present in ethanol-blended gasoline has a "modest potential" for extending benzene (represented by benzene) plumes by less than 100%.

California extended its analysis to address the question, would elongation of sub-surface benzene plumes in the presence of ethanol cause an increase of contamination of drinking water? The screening analysis compared the likelihood of drinking water contamination by MTBE (MTBE being the dominant oxygenate in California at the present) and the likelihood of contamination by benzene if ethanol replaced MTBE as the oxygenate, with contamination by benzene in the absence of ethanol as the base case. Contamination of drinking water by ethanol itself was not examined because such contamination is expected to be much less significant than contamination by benzene or MTBE. The analysis thus had to consider the distribution of leaking underground fuel tanks (LUFTs) in the state, the distribution of drinking water wells, and benzene and MTBE contamination data. In California, 32% of LUFTs are within about 2,000 feet of a drinking water well, and about 38% of wells are within about 2,000 feet of a LUFT.

The analysis derived plume lengths for each leaking fuel scenario, and then, given the distances from

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LUFTs to nearby wells, calculated how many wells might become contaminated. Because plumes grow (and shrink) over time, numbers of wells affected were also estimated over time, up to 100 years. Because of the many simplifying assumptions used, the analysis could not calculate the true probabilities that wells would be affected; however, relative probabilities could be calculated by comparing the probability under one scenario (*e.g.*, contamination by benzene in the presence of ethanol) to the probability under another (*e.g.*, contamination by benzene in the absence of ethanol).

The likelihood of well contamination by MTBE increased over the entire 100-year period analyzed, due to lack of biodegradation of this compound. In the case of benzene, likelihood of well contamination reaches a maximum five to 10 years after the fuel release, whether or not ethanol is present, but then declines. This pattern is due to eventual attenuation of the source and biodegradation of benzene. In comparing the two benzene scenarios, it was found that ethanol increased the chance of benzene contamination of wells by about 10% overall within the first five years, although for a small fraction of sites, the probability increased by about 20%. However, starting about five years after fuel release, the probability of well contamination by benzene was thereafter *decreased* for almost all sites by the presence of ethanol.

Other health effects issues

Some of ethanol's known or suspected toxic effects have not been, or can not be, quantified in terms of BEC. Fetal alcohol syndrome (FAS), for example, is a constellation of physical and mental deficiencies in children linked to maternal alcohol ingestion. Risk of FAS is a function of alcohol intake during pregnancy: the frequency of this syndrome is twice as great for children of heavy drinkers as for children of moderate or non-drinkers (Schardein, 1993). While it may be prudent to abstain from alcohol during pregnancy, a risk from daily consumption of less than 30 g of alcohol has not been proved (Schardein, 1993). Cancer of certain organs has been observed to occur at elevated rates in some groups of drinkers — the World Health Organization, for example, has linked alcohol consumption to cancers of the oral cavity, pharynx, esophagus, larynx, and liver (IARC, 1988). In almost all of the studies, risks were observed among alcoholics or were seen to increase with consumption.

In addition, if we look to human experience with alcohol consumption for information regarding toxic effects of ethanol, it is fair also to look at the evidence for possible health benefits. Numerous epidemiologic studies have observed that light-to-moderate drinkers of alcohol have lower mortality rates than either alcohol abstainers or heavy drinkers. Reduced mortality is due to decreased rates of fatal coronary heart disease and cardiovascular disease. To be sure, the picture is complicated, varying by sex, age, and disease risk factors, and competing causes of death. We are not suggesting that low-level exposures to ethanol due to its use as an oxygenate is desirable. At the least, however, the apparent beneficial effects of alcohol (or ethanol) for some cohorts should be recognized.

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Conclusion

It is highly unlikely that exposure to airborne ethanol associated with gasoline use could produce toxic effects. The reasons for this are (a) the tiny doses that might be received, which might not be observable in light of endogenous levels of ethanol in blood, (b) the body's rapid elimination of ethanol, and (c) the relatively large doses of ethanol and high blood levels of ethanol associated with toxic effects in people. No data in the scientific literature support the hypothesis that chronic exposure to non-irritating levels of ethanol in air could cause significant elevation of BEC (unless exposed individuals are exercising at the time), or that a risk of cancer or birth defects would be created. A recent survey of the literature regarding the inhalation toxicity of ethanol by the Swedish Institute for Environmental Medicine reached similar conclusions, namely that "a high blood concentration of ethanol is needed for the development of adverse effects" and "ethanol at low air concentrations should not constitute a risk for the general population" (Andersson and Victorin, 1996). Detailed modeling of atmospheric pollution in southern California indicates that using ethanol will not increase the risk of adverse health effects due to exposure to ethanol, acetaldehyde, or PAN. Screening modeling of impacts of sub-surface gasoline contamination on drinking water wells suggests that ethanol might increase the probability of water pollution during the first five to 10 years after a leak occurs, but that the probability would decrease beyond that period.

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Potential health and environmental impacts of ethanol used as a fuel oxygenate: Compilation of comments by expert reviewers[1]

1. Air

a. Toxicity of inhaled ethanol

The rapid metabolism is the reason why very high air concentrations of ethanol combined with a prolonged exposure or a very fast ventilation rate is necessary in order to produce substantial blood concentrations from inhalation. Inhalation of ethanol vapor at the concentration representing the short term Occupational Exposure Limit of Sweden and many other countries (1900 mg/m^3, the 8 h average is 1000 mg/m^3 [sic]) seem to result in a blood concentration of only 2 mg/l. [Sweden[2] pages 14-15]

Inhalation of ethanol vapors at normal concentrations [occupational, one infers] will thus not result in any significant blood concentration. The metabolic elimination of ethanol from the blood will in most cases exceed the uptake. The only exception is when the air concentration is well above the exposure limit combined with a high ventilation rate. [Sweden page 15]

Inhalation of ethanol vapor does not seem to cause any severe acute effects [in humans] at ethanol concentrations below 10,000 mg/m^3. However, headache and cough have been reported after about 30 minutes of inhaling ethanol vapor at concentrations of 2600 and 3400 mg/m^3 respectively. [Sweden page 19]

[effects on respiratory system:] Ethanol vapor does not seem to induce oxidative stress in the lungs of rats and no bronchoconstriction was seen in guinea pigs studied, but acetaldehyde vapor did induce bronchoconstriction. However, human asthmatic subjects did show decreased airway calibre after inhalation of ethanol at concentrations from 3400 to 3800 mg/m^3. [Sweden page 22]

[effects on CNS:] Animal inhalation studies have revealed an effect on CNS at relatively low ethanol concentrations. Disturbances in the REM-phase of sleeping rats and a decrease in self-adjusted reinforcement rate were seen at concentrations between 190 and 746 mg/m^3 (REM-sleep) and between 302 and 748 mg/m^3 (reinforcement). Ethanol also inhibits or potentiates the neurotransmitter-gated ion

[1] Except for outline headings and bracketed text, information is directly quoted from the cited sources. In-text references are omitted.

[2] Andersson, P. and Victorin, K. (1996). *Inhalation of Ethanol: Literature Survey and Risk Assessment*. Karolinska Institute for Environmental Medicine: Stockholm, Sweden.

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channels in the CNS. Alterations of receptors and their affinities, as well as altered gene expression has also been seen in animals after inhalation of ethanol vapors. However, these animals were exposed to very high concentrations (25,000 mg/m^3). [Sweden page 24]

[effects on liver:] Chronic inhalation of high concentrations of ethanol may lead to the elevation of liver triglycerides, fatty infiltration and eventually liver cirrhosis. Rats exposed to high concentrations (22,000 mg/m^3) showed increased lipid peroxidation and rats exposed to 20,000 mg/m^3 showed elevated levels of liver triglycerides. [Sweden page 26]

Some of the most serious effects of alcohol abuse is damage to the fetus and reduced fertility. However, inhalation does not seem to produce such effects. [Sweden page 31]

Experiments where both male and female rats were exposed to ethanol vapor of relatively high and high concentrations (19,000 and 30,240 mg/m^3) before mating and during gestation, did not result in any effects on fertility nor behavioral changes in the pups. [Sweden page 31]

The reported effects on humans after inhaling ethanol vapors have been reversible and mostly of an irritating nature. The decreased airway calibre seen at 3400-3800 mg/m^3 was not of great magnitude and has not been supported by animal experiments. There seems to be an effect on the CNS at low concentrations, but it is difficult to evaluate the biological importance of these studies. The effects seen in animal experiments have mostly been seen at high blood concentrations, obtained only at high air concentrations . . . [Sweden page 36]

b. Incremental exposure to and health risk of inhaled ethanol

i. U.S. EPA[3]

The health effects of ingested ethanol have been extensively investigated. Given that ethanol is formed naturally in the body at low levels, inhalation exposure to ethanol at the low levels that humans are likely to be exposed are generally not expected to result in adverse health effects. [EPA page 16105]

[3] U.S. EPA. (2000). "Methyl tertiary butyl ether (MTBE); Advance notice of intent to initiate rulemaking under the Toxic Substances Control Act to eliminate or limit the use of MTBE as a fuel additive in gasoline." *Federal Register 65(58)*:16093-16109.

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ii. National Science and Technology Council[4]

It is not likely that the health effects associated with ingestion of moderate to large quantities of ethanol would occur from inhalation of ethanol at ambient levels to which most people may be exposed from use of ethanol as a fuel oxygenate. [NSTC page vii]

iii. University of California[5]

Ethanol's detection threshold in air is 49 ppm. . . its recognition threshold in air is approximately 100 ppm. [95 and 190 mg/m^3, respectively; UC page 25]

iv. State of California[6]

The atmospheric lifetime for ethanol is similar to MTBE- about two to three days under polluted conditions and longer during periods of good air quality. [California, page 1-5]

. . . the maximum, estimated outdoor air-quality levels of ethanol and alkylates are at least a factor of 10 below any level of concern identified by OEHHA . . . [California, page 1-5]

Health effects due to ethanol exposure under any of the five fuel scenarios are not expected to occur at modeled ambient levels. There is no evidence that ethanol is carcinogenic via the inhalation route. Exposure to high concentrations of ethanol vapor may result in transient irritation to eyes and the respiratory system under either acute or chronic conditions. However, the acute and chronic noncancer HQs [hazard quotients] generated for ethanol by each of the five fuel scenarios are 0.002 or less,

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[4] National Science and Technology Council. (1997). *Interagency Assessment of Oxygenated Fuels.*

[5] University of California (1998). *Health and Environmental Assessment of MTBE: Report to the Governor and Legislature of the State of California as Sponsored by SB 521.*

[6] State of California. (1999). *Health and Environmental Assessment of the Use of Ethanol as a Fuel Oxygenate.* California State Water Resources Control Board, California Air Resources Control Board, and California EPA Office of Environmental Health Hazard Assessment.

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indicating that modeled concentrations are at least 500-fold below the HPCs. [health-protective concentrations; California, page 5-16]

. . . even if ethanol were regarded as a human carcinogen by the inhalation route, with linear low-dose response, the cancer risks predicted on this basis from ethanol are negligible. [California, page 5-16]

Under these exposure scenarios, the concentrations of irritants (including both air toxics and criteria pollutants) may achieve levels at which the margins of safety for short-term and long-term exposures are reduced. Adverse health effects are not necessarily expected at these levels, but more sensitive individuals may be affected. There were no substantial differences between the different fuel types with regard to the resulting levels of irritant air pollutants. [California, page 1-21]

There were no substantial differences between the different fuel types with regard to the cumulative cancer risks from air pollutants. Principal contributors to this risk are the fuel-related pollutants, benzene and 1,3-butadiene. Other pollutants (including formaldehyde and acetaldehyde, which may be partly related to oxygenate use in fuels, and MTBE) make a smaller contribution. [California, page 1-21]

v. NESCAUM[7]

Anticipated health effects of potential exposures from inhalation of low levels of ethanol and ethanol by products should not be inferred from the high dose studies in humans or animals. [NESCAUM Att. 1 page 25]

Generally reviews of the literature have concluded that ethanol inhalation from RFG has little public health significance. The highest inhalation exposure occurs during refueling, levels of 1 to 49 ppm have been determined. . . 50 ppm appears to be the most severe exposure anticipated with the use of RFG containing ethanol. The corresponding blood ethanol level increase under this exposure scenario would be 1.1 mg/l, given the endogenous levels of 1.5 mg/l reported in unexposed individuals, this would result in a total blood ethanol content of 2.6 mg/l. [NESCAUM Att. 1 page 25]

The lowest demonstrated blood level peak associated with a concurrent adverse health effect is the demonstrated threshold for reproductive injury in a human fetus at a maternal blood ethanol level of 350 mg/l . . . These data would suggest a greater than two orders of magnitude safety factor between the worst case exposure in humans from inhalation of ambient ethanol with RFG use and the lowest threshold for a toxic effect in humans. [NESCAUM Att. 1 page 25]

[7] Northeast States for Coordinated Air Use Management (NESCAUM) (1999). *RFG/MTBE: Findings & Recommendations.* Boston, MA.

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vi. HEI[8]

The blood level that would be expected from a possible exposure scenario can be estimated from the ethanol concentration, the duration of exposure, and the ventilation rate. For a typical refueling exposure scenario of 1 ppm (1.9 mg/m^3) for 3 minutes, and assuming that 60% of inhaled ethanol is taken up by the body, the resulting dose is equal to . . . 0.05 mg.

Assuming an average body weight of 70 kg, the dose per kilogram is . . . 0.7 µg/kg . . . the corresponding incremental blood level would be . . . 1 µg/l. . . For an extreme exposure scenario of 10 ppm for 15 minutes, the estimated incremental blood level is 40 µg/l. The resulting incremental blood levels are below the range of endogenous blood levels (0.3 to 27 mg/l), so ethanol would not significantly increase in blood under either of these exposure scenarios. [HEI page 40]

Because exposure to ethanol from its use in gasoline is not expected to cause an increase in maternal blood ethanol levels above the endogenous level, no increase in exposure to the fetus is expected. [HEI page 42]

[with regard to acute effects:] there is a large difference between the lowest blood levels of ethanol at which neurotoxic effects have been reported in humans (10 mg%) and the predicted blood levels arising from inhalation of gasoline containing ethanol. In exposure scenarios encountered by the general public, it is unlikely that an increase in ethanol blood levels will be measurable. On the basis of one community survey of symptoms conducted in Alaska, it does not appear that ethanol-containing fuel causes an increase in prevalence of symptoms. [HEI page 61]

Existing evidence demonstrates unequivocally that ingestion of ethanol can increase the risks of certain forms of human cancer, depending on the conditions of exposure. Ethanol itself has not proved to be carcinogenic to laboratory animals, but it has been found to enhance the carcinogenicity of other agents under appropriate experimental conditions. The carcinogenic effects of ethanol remain to be elucidated in full . . . the carcinogenic effects of ethanol have been observed only after ingestion of the substance in relatively large quantities. It is doubtful that comparable effects could result from inhaling ethanol at the low concentrations found when using ethanol in fuels. [HEI page 97]

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[8] Health Effects Institute (HEI). (1996). *The Potential Health Effects of Oxygenates Added to Gasoline: A Review of the Current Literature*. Cambridge, MA.

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Ethanol has been shown to be neurotoxic at high levels in both animal and human studies. The most sensitive functional outcome of acute exposure is impaired performance. [HEI, page 105]

It is well documented that embryonic exposure to ethanol by maternal drinking can result in serious developmental effects. The Fetal Alcohol Syndrome, which includes characteristic malformations and functional deficits, results from alcohol abuse during pregnancy, particularly binge drinking. Lower levels of maternal ethanol consumption result in Fetal Alcohol Effects, characterized by functional deficits that result from brain damage. Although a statistically definable threshold is elusive, some investigators have proposed an apparent threshold of about one drink (one-half ounce alcohol) per day, corresponding to a peak blood level of about 350 mg/l. Periodic exposures to ethanol in refueling stations or other exposures to fuel containing ethanol are predicted to produce ethanol levels at least 4 orders of magnitude lower than this proposed threshold and thus should not contribute to developmental effects. [HEI page 105]

vii. Sweden

Several experimental data support that [a high] blood concentration of ethanol is needed for the development of adverse effects. The metabolism of ethanol follows zero-order kinetics, which means that the rate of elimination is independent of the ethanol concentration. The elimination will occur at the same rate as long as the enzyme systems are not saturated. Ethanol will probably only accumulate and give a significant blood concentration when the metabolic systems are saturated, which happens only at high concentrations. Therefore, ethanol at low air concentrations should not constitute a risk for the general population. [Sweden page 36]

c. Incremental exposure to and health risk of inhaled acetaldehyde

i. State of California

The major products of concern for ethanol are acetaldehyde (a toxic-air contaminant) and peroxyacetyl nitrate (PAN, an eye irritant and cause of plant damage). These compounds are offset by reductions in formaldehyde (a toxic-air contaminant) due to the elimination of MTBE. [California, page 1-5]

There are increased ambient concentrations of acetaldehyde from the ethanol-based fuel containing 3.5% oxygen, compared to the other formulations evaluated for the year 2003. This results in an increase of up to two in a million excess lifetime cancer cases in the upper bound estimate. However, in view of the uncertainties both in the emission and exposure predictions, and in the acetaldehyde lifetime cancer risk estimate, this predicted increase in risk may be regarded as of marginal significance when comparing the other consequences of the different fuel formulations. [California, page 5-14]

In the case of acetaldehyde, the extensive metabolism of the compound in vivo (and its occurrence as a

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normal intermediary metabolite) is an additional source of uncertainty with respect to the standard assumption in risk assessment that the dose-response curve is linear down to the low ambient levels of this compound. [California, page 5-14]

The acute (one-hour maximal average) and chronic (maximum annual exposure) noncancer Hazard Quotients (HQs) for acetaldehyde generated by each of the fuel scenarios are will below one. . . Toxicological endpoints considered include eye, skin, and respiratory tract irritation with acute exposure, and inflammation of the respiratory tract and degeneration of the olfactory epithelium with chronic exposure. [California, page 5-14]

ii. NESCAUM

Use of ethanol, as a gasoline supplement will increase the combustion by-product emission rate of acetaldehyde, a probable human carcinogen, in the Northeast by between 50-70%. Ambient levels currently exceed health-protective thresholds [10^{-6} risk levels in air] at a majority of monitoring locations in the northeast. [NESCAUM Att. 1 page 6]

d. Incremental exposure to and health risk of inhaled PAN

The acute noncancer HQs for PAN based on the results of air modeling are above the threshold at which toxic effects may occur . . . The most sensitive acute toxic endpoint is eye irritation. The one-hour maximum predicted average HQ is 5.5 or less under all fuel scenarios. It appears than none of the scenarios for the year 2003 involves an exacerbation of the adverse health impact of PAN compared to the 1997 data. [California, page 5-18]

e. Incremental exposure to and health risk of formaldehyde

There is no apparent difference between year 2003 fuel formulations regarding cancer risk from formaldehyde. [California, page 5-17]

The 2003 fuel scenarios have lower [chronic] HQs [for formaldehyde, compared to 1997], but indicate that the concentrations of formaldehyde are almost two-fold above the REL. There is no apparent difference between fuel formulations for year 2003 of possible chronic health effects of formaldehyde. Toxicological endpoints include eye and respiratory system irritation. . . The acute health effects from formaldehyde, primarily due to eye irritation, are not anticipated to occur at the predicted maximal ambient levels. The upper bound maximum one-hour average concentrations for all five fuel scenarios were two-fold below the acute REL. [California, page 5-17]

2. Surface water and groundwater

a. Persistence

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By comparison [to MTBE], in a December 1999 report to the California Environmental Policy Council the authors report that under aerobic conditions, the reported half-lives of ethanol in surface waters are short. Half-lives span 6.5 to 26 hours for ethanol. Anaerobic biodegradation in oxygen-limited environments is also expected to proceed at rapid rates. Reported half-lives for ethanol biodegradation under anaerobic conditions range from 1 to 4.3 days. [EPA, page 16096]

Ethanol is not expected to persist in groundwater . . . because it biodegrades easily. Thus, ethanol itself does not appear to pose as great a danger to groundwater supplies as MTBE. [EPA, page 16105]

Ethanol is a naturally-occurring intermediate produced during the fermentation of organic matter in anoxic environments and is expected to rapidly biodegrade in essentially all environments with conditions . . . that support microbial activity. Microorganisms capable of metabolizing ethanol are ubiquitously distributed in the environment and relatively rapid rats of ethanol biodegradation have been measured under aerobic and anaerobic conditions. Thus, ethanol is a short-lived compound in surface waters and subsurface aquifers. [Ulrich, page 1]

b. Incremental exposure to and health risk of ingested ethanol

Though pure ethanol is poisonous, it is less toxic than the benzene, toluene, ethyl benzene, and xylenes (BTEX) that are components of gasoline. Ethanol is present in pharmaceuticals, mouthwash products, alcoholic beverages, cleaning products, solvents, dyes, and explosives. Humans frequently ingest fermented beverages that contain about 12% ethanol by volume. [California, page 1-3]

Due to the ubiquitous occurrence of microorganisms capable of ethanolic fermentation, virtually all sugar-containing foodstuffs are liable to contain a low level of ethanol. This is generally at the ppm level, or less than 1% by weight . . . Ethanol is also a minor product of general metabolism in plants and animals, so a certain amount of endogenous exposure occurs even in the absence of external exposure. [California, page 5-A-13]

Taste thresholds [for ethanol] range from approximately 6 ppm to 42 ppm. [UC page 25]

The draft health-protective concentration for oral exposures to drinking water for ethanol is 1,100,000 µg/l . . . [California, page 1-16]

Ingestion of ethanol in relatively large quantities, increases the risks for several forms of human cancer. However, it is highly unlikely that the public will be exposed to large quantities of ethanol from drinking water contamination. [EPA, page 16105]

Predictions of ethanol dispersion and degradation in the environment indicate that ethanol is unlikely to

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occur in drinking water at levels having any toxicological significance. [California, page 5-A-16]

Ethanol and its oxidation products such as acetaldehyde are toxic only at very high levels and are also very rapidly biodegraded, so in general these are not expected to present major long-term [drinking water] contamination problems. [California, page 5-28]

Overall, these findings indicate that ethanol contamination of the water due to use of ethanol in gasoline should present very minimal toxic and carcinogenic risk and no objectionable taste or smell problems for public drinking water. [California, page 5-29]

Screening-level calculations for a scenario that simulates a discrete, seven-day period of watercraft discharges of fuel-borne ethanol to Donner Lake in northern California showed that the peak concentration of ethanol was only 2 µg/l . . . For accidental tank-car releases of ethanol to a river or stream, toxic levels of ethanol could occur in the immediate downstream area of a spill. [California, page 1-16]

c. Incremental exposure to and health risk of ingested acetaldehyde and/or acetic acid

Acetic acid is the intermediate [of ethanol biodegradation] that is most likely to accumulate to a significant extent, but it is commonly used as a food supplement. [Ulrich, page 2]

3. Effect of subsurface ethanol on BTEX plumes

Ethanol's ability to biodegrade does present another potential issue of concern. Laboratory data and hypothetical modeling indicate that based on physical, chemical, and biological properties, ethanol will likely preferentially biodegrade in groundwater compared with other gasoline components. As a result, the levels of BTEX in water may decline more slowly, and BTEX plumes may extend further than they would without ethanol present. However, BTEX does not migrate as quickly as MTBE. Thus, even with the presence of ethanol, BTEX plumes would not be expected to travel as far as MTBE plumes. [page EPA, 16105]

Because ethanol is a metabolic byproduct, many organisms tolerate concentrations that may be encountered during accidental releases into the environment. A variety of indigenous microorganisms within the environment are capable of using ethanol as an energy source and will preferentially utilize ethanol over gasoline hydrocarbons, such as benzene. [California, page 1-3]

Although the dissolved equilibrium concentrations of gasoline components- benzene, toluene, ethylbenzene, and xylenes- increase in the presence of high concentrations of ethanol, the 10% ethanol

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expected to be added to gasoline in California should have only a minor effect on the dissolution of these gasoline components. [California, page 1-22]

. . . EtOH would be expected to degrade much more rapidly than BTEX hydrocarbons, therefore, EtOH is not expected to persist much beyond the source area and the immediate contaminant plume at a gasoline spill site. [NSTC page 2-9]

In general the investigations have demonstrated that the alkyl ether oxygenates (MTBE, TAME, ETBE, DIPE) are difficult to biodegrade. In contrast, BTEX, EtOH and MeOH are readily biodegraded. [NSTC page 2-60]

4. Aquatic toxicity

For accidental tank-car releases of ethanol to a river or stream, toxic levels of ethanol could occur in the immediate downstream area of a spill. [California, page 1-16]

Aside from the acute toxicity for aquatic species that might be affected by a spill and their associated recovery, it is unlikely that there would be any long-term toxic effects, because the ethanol will not persist in water due to its rapid degradation. [California, page 1-6]

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Table 1: Ethanol Dose-Response Data

BEC (mg/dl)	Observation	Reference
0.02-0.15	Endogenous (*i.e.* natural) level	Jones, 1985; Lester, 1962
50	central nervous system stimulant; talkativeness; relaxation	Pohorecky and Brick, 1987
100	legal limit for automobile drivers in many states	
>100	central nervous system depressant; decreased sensory and motor function; decreased mental and cognitive ability	Pohorecky and Brick, 1987
110	no effect on heart function	Pohorecky and Brick, 1987
140	no effect on cerebral blood flow; effects occur above this level	Pohorecky and Brick, 1987
300	stupefaction	Pohorecky and Brick, 1987
400	possible lethal level	Pohorecky and Brick, 1987

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Table 2: Intake Rate of Ethanol Under Various Exposure Conditions

Ventilation rate (l/min)	Intake rate of ethanol (mg/kg/hr) when the concentration in air is (mg/l)				
	1.9 (occupational standard)	5	10 (causes coughing and eye irritation; adaptation occurs)	20	30 (causes continuous lacrimation)
6 (rest)	5	14	28	57	**85**[9]
25 (moderate activity)	22	59	**118**	**236**	**354**
40 (heavy activity)	36	**94**	**189**	**377**	**566**
50 (very heavy activity)	45	**118**	**236**	**471**	**707**

[9] Bold type indicates intake rates that might be larger than the clearance rate for ethanol.

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Table 3: Experimental studies of vapor uptake by humans

Ventilation rate (l/min)	Concentration of ethanol in air (mg/l)	Duration of exposure (hr)	BEC (mg/dl)	Symptoms	Reference
rest (approx. 6)	1.9	3	<0.2	none reported	Campbell and Wilson (1986)
15	15		steady at 7-8	vapors irritating but adaptation occurred; no intoxication	Lester and Greenberg (1951)
22	16	6	47 and rising	vapors irritating but adaptation occurred; no intoxication	Lester and Greenberg (1951)
rest (approx. 6)	maximum of 17 average approx. 9	2.5	<5	vapors irritating but adaptation occurred; no intoxication	Mason and Blackmore (1972)

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