8.0 ACETALDEHYDE

8.1 Chemical and Physical Properties

The information below is excerpted from the EPA health assessment draft document (EPA, 1987) and Perry and Chilton, 1973.

Acetaldehyde is a saturated aldehyde with a pungent and suffocating odor, but at more dilute concentrations the odor is fruity and pleasant. It has the chemical formula CH_3CHO. It is a colorless liquid, volatile at room temperature, and both the liquid and the vapors are highly flammable. Acetaldehyde as a liquid is lighter than water, and the vapors are heavier than air. It is soluble in water, alcohol, ether, acetone, and benzene. The chemical and physical properties are listed in Table 8-1.

As the vapor pressure of acetaldehyde is very high and it is soluble in water, the most important environmental behavior will be in air and water. This is due to vaporization from the soil (and other sources) into the air and leaching from soil into the water. Acetaldehyde may remain bound in the soil because of its high reactivity, but it is also readily metabolized by soil microorganisms.

Acetaldehyde is a component of photochemical smog, and as such its movement within the atmosphere corresponds to that of the smog front. The high solubility of acetaldehyde in water increases the likelihood of its being leached into the soil.

In the atmosphere, acetaldehyde would be degraded through photooxidation and oxidation by the hydroxyl radical. The main product of photooxidation in the presence of NO_x is peroxyacetyl nitrate.

Table 8-1. Chemical and Physical Properties of Acetaldehyde.

Properties	Value
Molecular weight	44.06 g/mole
Melting point	-123.5°C (-190.3°F)
Boiling point	20.16°C (68.3°F)
Density at 18°C (64.4°F)	0.783 g/ml
Vapor pressure at 20°C (68°F)	0.97 atm.
Flash point (closed cup)	-38.0°C (-36.4°F)
Solubility in water at 25°C	infinite
Conversion at 25°C (77°F) and 760 mm Hg	1 ppm = 1.8 mg/m^3

8.2 Formation and Control Technology

Acetaldehyde is another aldehyde which is found in vehicle exhaust and is formed as a result of incomplete combustion of the fuel. Acetaldehyde is emitted in the exhaust of both gasoline and diesel-fueled vehicles. It is not a component of evaporative emissions.

Use of a catalyst has been found to be effective for controlling formaldehyde and other aldehyde emissions. Acetaldehyde emissions are presumed to be controlled to roughly the same extent as total hydrocarbon emissions with a catalyst.

8.3 Emissions

8.3.1 Emission Fractions Used in the MOBTOX Emissions Model

Like 1,3-butadiene and formaldehyde, emission fractions for acetaldehyde were developed using vehicle emissions data (Appendix B2). Acetaldehyde emission fractions for different components included in the scenarios are included in Appendix B6. Emission fractions for the various vehicle class/catalyst technology groups were based on the same number of cars and studies as the formaldehyde emission fractions.

To calculate TOG fractions for vehicles running on MTBE blends and 10% ethanol, adjustment factors were applied to the baseline emission fractions for each vehicle class/catalyst combination, in the same manner as was done for 1,3-butadiene and formaldehyde. The average percent change numbers for vehicle class/catalyst combinations by study are contained in Appendix B4. The 15% MTBE and 10% ethanol adjustment factors for LDGVs/LDGTs with various catalyst technologies are summarized in Table 8-2. Note that use of oxygenated fuels increases acetaldehyde emissions for all catalyst technologies, and that acetaldehyde increases more than 200% for all catalyst technologies with 10% ethanol use.

These 15% MTBE and 10% ethanol numbers were estimated using data from the same studies as formaldehyde. Once again, since the average percent change was calculated for 15% MTBE (2.7% weight percent oxygen), and 11.0% MTBE (2.0% oxygen) was assumed for reformulated fuel and California standards components, average percent changes in the formaldehyde TOG fraction from 0 to 15% MTBE were multiplied by 2.0/2.7. For HDGVs with three-way catalysts and with no catalysts, we assumed the same 15% MTBE and 10% ethanol adjustment factors as for LDGVs/LDGTs with the same catalyst technologies.

Table 8-2. 15% MTBE and 10% Ethanol Emission Fraction Adjustment Factors for Acetaldehyde.

Vehicle Class	Catalyst Technology	15% MTBE Adjustment Factor	10% EtOH Adjustment Factor
LDGV/LDGT	3-way	1.0826	2.1369
LDGV/LDGT	3-way + ox	1.0136	2.2453
LDGV/LDGT	oxidation	1.2114	2.9609
LDGV/LDGT	non-cat	1.4377	2.1445

8.3.2 Emission Factors for Baseline and Control Scenarios

The fleet average acetaldehyde emission factors as determined by the MOBTOX emissions model are presented in Table 8-3. When comparing the base control scenarios relative to 1990, the emission factor is reduced by 40% in 1995, by 57% in 2000, and by 62% in 2010. The expansion of reformulated fuel use in 1995 actually has no net impact on the emission factor. In 2000, the expansion of reformulated fuel usage also has no net impact on the emission factor, whereas the expanded California standard scenario increases the emission factor by 1%, relative to 1990. In 2010, there is a decrease from the 2010 base control for the reformulated fuels scenario of 1% and the California standards scenario of 4%.

8.3.3 Nationwide Motor Vehicle Acetaldehyde Emissions

The nationwide acetaldehyde metric tons are presented in Table 8-4. Total metric tons are determined by multiplying the emission factor (g/mile) by the VMT determined for the particular year. The VMT, in billion miles, was determined to be 1793.07 for 1990, 2029.74 for 1995, 2269.25 for 2000, and 2771.30 for 2010. When comparing the base control scenarios relative to 1990, the metric tons are reduced by 32% in 1995, by 46% in 2000, and by 42% in 2010, which is actually an increase when compared to 2000.

8.3.4 Other Sources of Acetaldehyde

The motor vehicle contribution to ambient acetaldehyde levels contains both direct (primary) and secondary acetaldehyde formed from photooxidation of VOC, though the rate of photooxidation is much less than that of formaldehyde. It appears that roughly 39% of acetaldehyde emissions may be attributable to motor vehicles. Section 8.5.2 contains a complete explanation of how this number is determined.

Table 8-3. Annual Emission Factor Projections for Acetaldehyde.

Year-Scenario	Emission Factor g/mile	Percent Reduction from 1990
1990 Base Control	0.0119	–
1995 Base Control	0.0071	40
1995 Expanded Reformulated Fuel Use	0.0071	40
2000 Base Control	0.0051	57
2000 Expanded Reformulated Fuel Use	0.0051	57
2000 Expanded Adoption of California Standards	0.0052	56
2010 Base Control	0.0045	62
2010 Expanded Reformulated Fuel Use	0.0044	63
2010 Expanded Adoption of California Standards	0.0041	66

Table 8-4. Nationwide Metric Tons Projection for Acetaldehyde.

Year-Scenario	Emission Factor g/mile	Metric Tons
1990 Base Control	0.0119	21,338
1995 Base Control	0.0071	14,411
1995 Expanded Reformulated Fuel Use	0.0071	14,411
2000 Base Control	0.0051	11,573
2000 Expanded Reformulated Fuel Use	0.0051	11,573
2000 Expanded Adoption of California Standards	0.0052	11,800
2010 Base Control	0.0045	12,471
2010 Expanded Reformulated Fuel Use	0.0044	12,194
2010 Expanded Adoption of California Standards	0.0041	11,362

Acetaldehyde is ubiquitous in the environment and is naturally released. It is a metabolic intermediate of higher plant respiration and alcohol fermentation. It is also found in many flowers, herbs, and fruits and could be available for release to the ambient air. Acetaldehyde is also produced from aliphatic and aromatic hydrocarbon photooxidation reactions.

Acetaldehyde is formed as a product of incomplete wood combustion in residential fireplaces and woodstoves and is released into the atmosphere by the coffee roasting process. Together these two processes accounted for 78% of the national acetaldehyde emissions (Eimitus et al., 1978). Acetaldehyde is also released through the burning of tobacco (Braven et al., 1967), the combustion of organic fuels, coal refining, and coal waste processing (Versar Inc., 1975), and also as a product of plastics combustion (Boettner et al., 1973).

Manufacturing plants that produce acetaldehyde also emit acetaldehyde, as do manufacturing plants that produce ethanol, phenol, acrylonitrile, and acetone (Eimitus et al., 1978; Mannsville Chemical Products Corp., 1984; Delaney and Hughs, 1979). Chemical processes that involve acetaldehyde as an intermediate also emit acetaldehyde. This includes the production of peracetic acid, pentaerythritol, pyridine, terephthalic acid, 1,3-butylene glycol, and crotonaldehyde.

8.4 Atmospheric Reactivity and Residence Times

The processes involved in transformation and residence times were previously discussed in Section 5.4. For a more detailed explanation of the various parameters involved in these processes please refer to Section 5.4. The information that follows on transformation and residence times has been mainly excerpted from a report produced by Systems Applications International for the EPA (Ligocki and Whitten, 1991).

8.4.1 Gas Phase Chemistry of Acetaldehyde

The atmospheric transformation chemistry of acetaldehyde (CH_3CHO) is similar in many respects to that of formaldehyde. Like formaldehyde, it can be both produced and destroyed by atmospheric chemical transformation. The reaction rate of acetaldehyde with OH is in fact about the same as formaldehyde. However, there are important differences between the two. Acetaldehyde photolyses, but much more slowly than formaldehyde. Whereas formaldehyde produces CO upon reaction or photolysis, acetaldehyde produces organic radicals that ultimately form peroxyacetyl nitrate (PAN) and formaldehyde.

8.4.1.1 Formation

Acetaldehyde is formed from the atmospheric oxidation of many types of organic compounds. Unlike formaldehyde, acetaldehyde is

not produced in the atmospheric oxidations of methane and isoprene, but may be produced in the atmospheric oxidation of other naturally occurring organic compounds such as terpenes. In urban areas, the oxidation of olefins such as propene (C_3H_6), and paraffins such as propane (C_3H_8) and ethanol (C_2H_5OH) produces acetaldehyde.

Paraffins (also termed alkanes and saturated hydrocarbons) are organic compounds containing only single-bonded carbon. Paraffins are generally present in urban atmospheres in high concentrations, but react relatively slowly. The pathways by which paraffins are converted to aldehydes such as formaldehyde and acetaldehyde have been summarized by the National Research Council (NRC, 1981). Briefly, the process is initiated by the reaction of a paraffin (such as propane) with OH. This reaction proceeds forming an organic radical that rapidly reacts with atmospheric O_2 to form an organic peroxy radical (often represented as RO_2). In urban atmospheres, these RO_2 radicals typically react with NO, forming NO_2 and fueling the photochemical ozone production cycle. The organic intermediate formed in these reactions rapidly produces aldehydes. The specific aldehydes formed in a given reaction depend upon the initial chain length of the paraffin and the position along the chain at which the initial OH attack occurred. It can easily be seen that a whole family of aldehydes could be produced in varying yields in the oxidation of a single compound.

Olefins (also termed alkenes and unsaturated hydrocarbons) are species containing one or more double bonds. Both OH and O_3 react rapidly with olefins by addition to these reactive double bonds, again forming radical intermediates that decay through a variety of pathways to form aldehydes. In these cases, the particular aldehyde produced will depend upon the location of the double bond.

8.4.1.2 Gas Phase Reactions

Acetaldehyde reacts more rapidly than formaldehyde with the OH and NO_3 radicals. Acetaldehyde reactions with the HO_2, oxygen atoms, O_3, and Cl radicals are not important to the atmospheric chemistry of acetaldehyde due to low concentrations in the atmosphere and/or low to negligible reaction rates.

Acetaldehyde absorbs ultraviolet (UV) radiation from wavelengths below 290 nanometers (nm) to about 345 nm. Although there are three possible pathways for acetaldehyde photolysis, only one is important at wavelengths >290 nm.

The resulting photolysis rate is less than 10 percent of the formaldehyde photolysis rate. Therefore, photolysis is a relatively minor atmospheric transformation pathway for acetaldehyde.

8.4.1.3 Reaction Products

The oxidation of acetaldehyde by OH, oxygen atoms, and NO_3 radicals form a CH_3CO radical that rapidly reacts with atmospheric O_2 to form the peroxyacetyl radical, $CH_3C(O)OO$. This radical can then react with atmospheric NO and NO_2. The reaction with NO_2

produces peroxyacetyl nitrate (PAN), whereas the reaction with NO ultimately produces formaldehyde. Minor products of the peroxyacetyl radical reactions are peroxyacetic acid and acetic acid. Although acetaldehyde is a PAN precursor, methylglyoxal and other species derived from the oxidation of aromatic compounds are more important PAN precursors in urban atmospheres than acetaldehyde. The photolysis of acetaldehyde produces the CH_3O_2 radical, which reacts with NO to form formaldehyde. Thus, the major acetaldehyde decomposition products are formaldehyde and PAN, both of which are of concern as toxic and/or irritant species. However, in neither case is acetaldehyde a dominant source of these species.

8.4.2 Aqueous Phase Chemistry of Acetaldehyde

Acetaldehyde is slightly soluble, and will be incorporated into clouds and rain, but to a much lesser degree than formaldehyde. The rate of the acetaldehyde-OH reaction is roughly two-thirds of the aqueous formaldehyde reaction rate. The product of the aqueous phase oxidation of acetaldehyde is expected to be acetic acid (Jacob et al., 1989).

Acetaldehyde, like formaldehyde, can participate in sulfur chemistry within clouds. Aqueous acetaldehyde combines with aqueous SO_2 to form the stable adduct 1-hydroxy-1-ethanesulfonate (HES) (Olson and Hoffmann, 1989). However, this species does not appear to be of major importance in cloud chemistry.

8.4.3 Acetaldehyde Residence Times

Residence times for acetaldehyde were calculated by considering gas-phase chemical reactions with OH and NO_3 photolysis, in-cloud chemical reaction with OH, and wet and dry deposition. The results of the residence time calculation for acetaldehyde are presented in Table 8-5. During the daytime, under clear-sky conditions, the residence time of acetaldehyde is determined primarily by its reaction with OH, with photolysis accounting for only 2 to 5 percent of the removal. Calculated residence times under these conditions were on the order of a few hours. The National Research Council (NRC, 1981) did not estimate an atmospheric residence time for acetaldehyde, but stated that it would be comparable to the half-life of formaldehyde (2.6 hours, corresponding to a residence time of 3.8 hours). The residence

TABLE 8-5. Atmospheric residence time calculation for acetaldehyde. All times are in hours unless otherwise noted.

	Los Angeles		St. Louis		Atlanta		New York	
	July	Jan	July	Jan	July	Jan	July	Jan
Clear sky - day	4	20	3	30	3	30	5	60
Clear sky - night	18	700	170	3000	21	300	40	3000
Clear sky - avg	6	50	4	80	4	70	7	160
Cloudy - day	8	50	6	80	6	80	11	140
Cloudy - night	150	1800	300	3000	150	2000	300	3000
Cloudy - avg	14	130	9	190	10	180	17	400
Rainy - day	--[*]	50	6	60	6	70	11	100
Rainy - night	--[*]	400	300	150	130	200	200	200
Rainy - avg	--[*]	110	9	90	10	120	17	140
Monthly Climatological Average	7	70	6	130	6	110	11	200

[*]Not calculated since July rainfall is zero for Los Angeles.

times presented in Table 8-5 are somewhat longer that those calculated for formaldehyde (Ligocki et al., 1991) because of the slower photolysis rate for acetaldehyde.

In contrast to the situation for formaldehyde, neither in-cloud oxidation nor wet deposition is important for acetaldehyde. In-cloud oxidation accounted for only 1 percent or less of the atmospheric removal of acetaldehyde, compared to 10 to 25 percent of the daytime chemical destruction of formaldehyde and 20 to 90 percent of the nighttime chemical destruction of formaldehyde. The presence of clouds would also be expected to decrease the formation rate of acetaldehyde; thus, cloud cover may actually decrease acetaldehyde concentrations despite the predicted increase in residence time.

At night, for Los Angeles, Atlanta, and New York, the reaction of acetaldehyde with NO_3 leads to residence times on the order of tens of hours during the summertime. However, because of the low NO_3 concentration predicted for St. Louis, the loss of acetaldehyde by reaction with NO_3 is only comparable to the loss by reaction with OH, and neither is rapid.

Dry deposition is not an important removal mechanism for acetaldehyde. Residence times due to dry deposition were estimated to range from 20 days under summer, daytime conditions to over a year for the other conditions. For the cases considered here, dry deposition was a minor removal mechanism except under winter, nighttime conditions. Under these conditions, dry deposition is slow, but all other processes are slower.

The differences in acetaldehyde residence time among cities within a season were not as large as the difference between seasons. The calculated summer residence times are short in most cases, whereas the winter residence times are on the order of days. Thus, acetaldehyde must be considered to be persistent in wintertime. Like formaldehyde, however, the effect of this longer winter residence time is difficult to assess for acetaldehyde because of the importance of secondary formation. Rates of formation of acetaldehyde will be roughly an order of magnitude slower in the wintertime. Thus, it is difficult to predict whether ambient concentrations of acetaldehyde will increase or decrease in winter.

The major uncertainty in the residence time calculation for acetaldehyde is the OH radical concentration, which varies from day to day by roughly a factor of two. The uncertainty in the OH rate constant is much smaller than this (about 13 percent). The uncertainties associated with the photolysis rate, NO_3 concentrations, the rate constant, and dry deposition velocity are of minor importance for acetaldehyde because these processes are relatively slow.

8.4.4 Limited Urban Airshed Modeling Results for Acetaldehyde

The Urban Airshed Model (UAM) has been previously discussed in Section 5.4. Please refer to this section for details about the model, its inputs, and modifications. Much of the information below has been excerpted from reports conducted for EPA by Systems Applications International (SAI) (Ligocki et al., 1992, Ligocki and Whitten, 1991).

St. Louis Study

The Carbon Bond Mechanism-IV chemical mechanism in the UAM uses the "lumped structure approach". In this approach individual chemical species are broken up into reactive units based on the type of bonds and functional groups present in the molecule. In this model, the species ALD2 represents acetaldehyde, the aldehyde functional group of higher aldehydes, and olefins containing internal double bonds which react rapidly in the atmosphere to produce aldehydes. These are the primary ALD2 aldehydes.

Secondary ALD2 is produced through the reactions of paraffins (hydrocarbons with single carbon bonds), olefins (hydrocarbons with double carbon bonds), and other species. A large number of aldehydes of varying size can be produced by the oxidation of a single hydrocarbon.

The magnitude of the changes required to model acetaldehyde explicitly, specifically secondary acetaldehyde, placed this beyond the scope of the St. Louis study. Instead, the results of the St. Louis air toxics simulations presented previously (Ligocki et al., 1991) were re-examined in terms of the ALD2 concentrations.

Results are presented as time-series plots of predicted hourly average ALD2 concentrations and include curves from both the reactive and inert simulations. The results from the base-case simulations are shown in Figure D-4 and Figure D-5 in Appendix D for two representative urban grid cells. The grid cell represented in Figure D-4 is located near the area of maximum mobile-source emissions, and thus represents the area with maximum primary ALD2 impact. The grid cell represented in Figure D-5 is located 8 km downwind, and represents an area where secondary ALD2 production is maximized.

In near-source areas of the modeling domain, ALD2 behaved as a primary species, with concentration peaks in the early morning and early evening (Figure D-4). In downwind areas, however, ALD2 behaved as a secondary species, with concentration peaks in the midafternoon (Figure D-5). The simulation also suggested that motor vehicles may be a more important contributor to ambient acetaldehyde levels than they are to formaldehyde levels.

The dominance of primary ALD2 shown in Figure D-4 for the morning commute hours, combined with the 68 percent contribution of motor vehicle of ALD2, suggest that a large fraction of the simulated ALD2 is attributable to motor vehicles. However, a smaller fraction of the secondary ALD2 is attributable to motor vehicles, because the mobile contribution to the major ALD2 precursor emissions is smaller, particularly in the afternoon when the main ALD2 secondary production occurs.

Simulated ALD2 concentrations were three times as high as measured acetaldehyde concentrations. Because simulated formaldehyde concentrations agreed well with measured concentrations, it is likely that this discrepancy for acetaldehyde is due to the inclusion of higher aldehydes in the ALD2 composite species. If this is the case, urban ambient concentrations of higher aldehydes may be comparable to those of formaldehyde and acetaldehyde.

The results from the day-to-day carryover sensitivity simulations, with the exception of the first few hours of the simulation, are comparable to the base-case results. The peak concentrations were not affected by the change in initial concentrations.

Baltimore-Washington and Houston Area Simulations

For the Baltimore-Washington and Houston area simulations, primary and secondary acetaldehyde were modeled explicitly. The modifications made to UAM to model this species explicitly are described in Ligocki et al. (1992).

Simulations for the summer Baltimore-Washington area episode resulted in decreases in ambient acetaldehyde with the use of reformulated gasoline, with little change in primary acetaldehyde and decreased secondary acetaldehyde throughout the domain. Use of California reformulated gasoline resulted in a decrease in secondary acetaldehyde roughly twice as large as in federal reformulated gasoline scenarios. Maximum daily average acetaldehyde for the 1988 base scenario was 6.1 ppb. Motor vehicle-related acetaldehyde accounted for about 36% of total acetaldehyde emissions, based on the 1995 no motor vehicle scenario. Motor vehicle-related acetaldehyde also accounted for about 15% of total simulated ambient acetaldehyde. 90 to 95% of this acetaldehyde was secondary.

Summer Baltimore-Washington area simulations appear to somewhat overpredict the measured data. Since most of the simulated acetaldehyde is secondary, the concentrations are very

sensitive to the product distribution between acetaldehyde and other higher aldehydes in the chemical mechanism.

In the winter 1988 base scenario, the maximum daily average acetaldehyde concentration was 5.2 ppb, slightly lower than in summer. Simulations for the winter Baltimore-Washington area episode resulted in very small decreases in primary and secondary acetaldehyde. Motor vehicle-related acetaldehyde emissions were about the same with reformulated gasoline use. Motor vehicle-related acetaldehyde accounted for about 13% of the maximum simulated concentration, based on the 1995 no motor vehicle scenario.

For the summer 1987 base scenario in Houston, the maximum daily average acetaldehyde concentration was 18.2 ppb. Motor vehicle-related acetaldehyde accounted for about 13% of total acetaldehyde emissions and 18% of the maximum simulated concentration for the 1987 base scenario. Simulations for the summer Houston episode predicted slight decreases in simulated daily average concentration throughout most of the domain with use of reformulated gasoline. Simulated concentrations of acetaldehyde were in good agreement with measured concentrations.

8.5 Exposure Estimation

8.5.1 Annual Average Exposures Using HAPEM-MS

The data presented in Table 8-6 represent the results determined by the HAPEM-MS modeling that was described previously in Section 4.1.1. These numbers have been adjusted to represent the increase in VMT expected in future years.

The HAPEM-MS exposure estimates in Table 8-6 represent the 50th percentiles of the population distributions of exposure, i.e., half the population will be above and half below these values. High end exposures can also be estimated by using the 95th percentile of the distributions. According to the HAPEM-MS sample output for benzene, the 95th percentile is 1.8 times higher than the 50th percentile for urban areas, and 1.2 times high for rural areas. Applying these factors to the exposure estimates in Table 8-6, the 95th percentiles for urban areas range from 0.32 $\mu g/m^3$ for the 2000 expanded reformulated fuel use and the 2010 expansion of the California standards scenarios, to 0.65 $\mu g/m^3$ for the 1990 base control scenario. The 95th percentiles for rural areas range from 0.11 to 0.24 $\mu g/m^3$, respectively.

8.5.2 Comparison of HAPEM-MS Exposures to Ambient Monitoring Data

As stated in section 4.1.2, four national air monitoring programs/databases contain data on air toxics and the data for

Table 8-6.   Annual Average HAPEM-MS Exposure Projections for Acetaldehyde.

Year-Scenario	Urban Exposure µg/m^3	Rural Exposure µg/m^3
1990 Base Control	0.36	0.20
1995 Base Control	0.24	0.13
1995 Expanded Reformulated Fuel Use	0.24	0.13
2000 Base Control	0.19	0.10
2000 Expanded Reformulated Fuel Use	0.18	0.10
2000 Expanded Adoption of California Standards	0.19	0.10
2010 Base Control	0.19	0.10
2010 Expanded Reformulated Fuel Use	0.19	0.10
2010 Expanded Adoption of California Standards	0.18	0.09

acetaldehyde is found in only two. The Aerometric Information
Retrieval System (AIRS), and the Urban Air Toxic Monitoring Program
(UATMP) have data for acetaldehyde. The urban exposure data for
acetaldehyde from the two databases are summarized in Table 8-7.

In the 1990 Urban Air Toxics Monitoring Program (UATMP), 332
measurements of acetaldehyde were taken at 12 sites. These sites
were in the cities listed below.

Baton Rouge, LA	Chicago, IL
Camden, NJ	Houston, TX
Orlando, FL	Pensacola, FL
Port Neches, TX	Sauget, IL
Toledo, OH	Washington, D.C.
Wichita, KS	

The highest average was 4.48 $\mu g/m^3$ (2.49 ppb) at an urban
commercial site in Baton Rouge, Louisiana. Twenty-two samples were
collected at this site. The lowest average was 1.34 $\mu g/m^3$ (0.75
ppb) at a suburban residential site in Houston, Texas. Twenty-
three samples were collected at this site. The overall average of
the averages for each site was 3.10 $\mu g/m^3$ (1.72 ppb). Ozone was
removed from the ambient air collected in this program through the
use of an ozone denuder. The use of an ozone denuder in the
sampling system resulted in higher, but more accurate, reported
acetaldehyde concentrations. Only the 1990 UATMP data will be used
for the comparisons in this study.

HAPEM-MS assumes that the dispersion and atmospheric chemistry
of acetaldehyde is similar to CO. This assumption would appear to
be somewhat valid for acetaldehyde since it is less reactive than
formaldehyde, but acetaldehyde is transformed in the atmosphere to
some extent. To test the reasonableness of the HAPEM-MS modeling
results, the HAPEM-MS results for 1990 are compared to ambient
monitoring results for recent years. Before comparing the HAPEM-MS
results to the ambient data, the ambient monitoring data must be
adjusted to represent the amount that is attributed to motor
vehicles. The data derived from emission inventories and
atmospheric modeling conducted by SAI for St. Louis (Ligocki and
Whitten, 1991) estimate that 39% of the ambient acetaldehyde can be
apportioned to motor vehicles. This number actually represents
acetaldehyde and higher aldehydes.

This estimate is higher than the estimates in the Houston and
Baltimore-Washington Area UAM-Tox simulations (Ligocki et al.,
1992). In these studies, acetaldehyde was modeled explicitly;
thus, the estimates do not represent both acetaldehyde and higher
aldehydes. In Baltimore-Washington, motor vehicle-related
acetaldehyde accounted for about 15% of total simulated ambient
acetaldehyde in summer, while in Houston, motor vehicle-related
acetaldehyde accounted for about 18% of the maximum simulated
concentration.

The estimate of 39% will be used in this study to represent
the nationwide average percentage of ambient acetaldehyde
attributable to motor vehicles, while acknowledging the apparent

area-to-area variations and the possibility that this may
overestimate the motor vehicle contribution to ambient
acetaldehyde, possibly in part because the estimate actually
represents both acetaldehyde and higher aldehydes. The numbers in
the second column of Table 8-7 below are 39% of the ambient levels
and thus represent estimated motor vehicle levels.

The motor vehicle apportionment of the ambient monitoring data
ranges from 0.94 to 1.21 $\mu g/m^3$. When the adjustment factor of
0.622 for the ambient mobile source levels, that was determined in
Section 5.5.2 is applied, this range becomes 0.58 to 0.75 $\mu g/m^3$.
Due to a potential ozone interfernece problem with the ambient data
other than the 1990 UATMP, only the 1990 UATMP adjustment estimate,
0.75 $\mu g/m^3$, will be used for the comparison to HAPEM. When
compared to the HAPEM-MS 1990 base control level of 0.36 $\mu g/m^3$, the
1990 UATMP adjusted ambient monitoring data is observed to be
approximately two times greater then the HAPEM-MS base control
level. The fact that modeled levels are 62% lower than monitored
data is consistent with secondary-formed acetaldehyde. The HAPEM-
MS 1990 base control exposure level of 0.36 $\mu g/m^3$ must be increased
by a factor of 2.09, to 0.75 $\mu g/m^3$ to agree with the ambient data.
All analysis based on the HAPEM-MS ambient mobile source levels
will have this factor applied. Adjusted urban, rural, and
nationwide exposures are found in Table 8-8.

Any acetaldehyde exposures projected by HAPEM-MS itself should
be viewed with caution. The adjusted HAPEM-MS exposure estimates
attempt to account for both primary and secondary acetaldehyde;
however, these estimates are based only on changes in primary
emissions of acetaldehyde. The reactivity of motor vehicle VOC
emissions is likely to change with technology and fuel changes.
Changes in the reactivity of these emissions, which would result in
changes to secondary acetaldehyde levels, cannot be accounted for
by HAPEM-MS.

8.5.3 Short-Term Microenvironment Exposures

The primary emphasis for acetaldehyde exposure will be
exposure in microenvironments that are enclosed, increasing the
exposure to tailpipe emissions. These microenvironments include
in-vehicle and parking garage exposure, though, actual exposure
information is only available for in-vehicle exposure. This
information is taken from the In-Vehicle Air Toxics
Characterization Study in the South Coast Air Basin (Shikiya et
al., 1989), which focused on the driver's exposure to VOC's in the
southern California area. See the information in Section 4.2 for
more details about the methodology, and Section 5.5.3 for a
description of the study.

Table 8-7. Air Monitoring Results for Acetaldehyde.

Program	Years	Ambient Data[a] $\mu g/m^3$	Estimated Mobile Source Contribution[b] $\mu g/m^3$
AIRS	1988	2.93	1.14
	1987	2.41	0.94
UATMP	1989	2.45	0.96
	1990	3.10	1.21

[a]Caution should be taken in comparing these numbers. The methods of averaging the data are not consistent between air monitoring databases. The sampling methodology is also inconsistent.

[b]The ambient data are adjusted to represent the motor vehicle contribution to the ambient concentration, which for acetaldehyde is estimated to be 39%, based on emissions inventory apportionment and modeling.

Table 8-8.   Adjusted Annual Average HAPEM-MS Exposure Projections for Acetaldehyde.

Year-Scenario	Exposure ($\mu g/m^3$)		
	Urban	Rural	Nationwide
1990 Base Control	0.75	0.41	0.67
1995 Base Control	0.49	0.35	0.44
1995 Expanded Reformulated Fuel Use	0.49	0.35	0.44
2000 Base Control	0.38	0.21	0.33
2000 Expanded Reformulated Fuel Use	0.38	0.20	0.33
2000 Expanded Adoption of California Standards	0.39	0.21	0.33
2010 Base Control	0.39	0.21	0.34
2010 Expanded Reformulated Fuel Use	0.38	0.21	0.34
2010 Expanded Adoption of California Standards	0.36	0.19	0.31

The in-vehicle exposure level of acetaldehyde was determined in this study to have a mean of 13.7 µg/m^3 and a maximum measured level of 66.7 µg/m^3. This compares to ambient levels of 2.41 to 3.10 µg/m^3 determined through air monitoring studies and presented in Table 8-7. Since for the majority of the population these are short-term acute exposures to acetaldehyde, the concern would be with non-cancer effects. The primary acute effect of exposure to acetaldehyde vapors is irritation of the eyes, skin, and respiratory tract. At high concentrations, irritation and ciliastatic effects can occur. Clinical effects include erythema, coughing, pulmonary edema, and necrosis. It has been suggested that voluntary inhalation of toxic levels of acetaldehyde would be prevented by its irritant properties, since irritation occurs at levels below 200 ppm (3.6×10^5 µg/m^3). Please see Section 8.8 for more information on non-cancer effects.

A RfC of 9.0 µg/m^3 per day over a lifetime has been developed by EPA. An RfC is an estimate of the continuous exposure to the human population that is likely to be without deleterious effects during a lifetime. The mean and maximum levels, 13.7 µg/m^3 and 66.7 µg/m^3 respectively, observed in Shikiya et al., (1989) are higher than RfC developed by EPA.

Due to more stringent fuel and vehicle regulations, short-term exposure to acetaldehyde in microenvironments is expected to decrease in future years.

8.6 Carcinogenicity of Acetaldehyde and Unit Risk Estimates

8.6.1 Most Recent EPA Assessment

An external review draft document entitled <u>Health Assessment Document for Acetaldehyde</u> (EPA, 1987) has been prepared. Much of the information contained in this section has been taken from this document and the most recent IRIS summary (EPA, 1992).

8.6.1.1 Description of Available Carcinogenicity Data

The majority of information that exists to evaluate the carcinogenicity of acetaldehyde emissions relies on mutagenicity studies and a few animal studies.

<u>Genotoxicity</u>

Acetaldehyde has been shown in studies by several different laboratories to induce sister chromatid exchange (SCE) in cultured mammalian cells, e.g., Chinese hamster cells (Obe and Ristow, 1977; Obe and Beer, 1979; de Raat et al., 1983) and human peripheral lymphocytes (Ristow and Obe, 1979; Jansson, 1982; Böhlke et al., 1983; Norrpa et al., 1985; Obe et al., 1986) in a dose-related manner. A study by He and Lambert (1985) provided evidence that SCE-inducing lesions may be persistent for several cell generations. The induction of SCEs by acetaldehyde has also been detected in the bone marrow cells of whole mammals, namely mice and Chinese hamsters (Obe et al., 1979; Korte and Obe, 1981). In addition to acetaldehyde's ability to induce SCEs, it has been

shown to be a clastogen in mammalian cell cultures (Bird et al., 1982) and plants (Rieger and Michaelis, 1960). Acetaldehyde has produced chromosomal aberrations (micronuclei, breaks, gaps, and exchange-type aberrations) also in a dose-related manner (Bird et al., 1982; Böhlke et al., 1983). In a study by Eker and Sanner (1986), acetaldehyde and formaldehyde were both able to initiate cell transformation, though formaldehyde was 100 times more potent. In *Drosophila*, chromosomal effects (i.e., reciprocal translocations) were not found after acetaldehyde treatment (Woodruff et al., 1985). The clastogenicity of acetaldehyde in whole mammals has not been sufficiently evaluated. In the one study that was available, female rats were intra-amniotically injected on the 13th day of gestation, and the treated embryos had high frequencies of chromosomal gaps and breaks (Barilyak and Kozachuk, 1983).

Although acetaldehyde did not produce chromosomal translocations in *Drosophila*, it was found to induce gene mutations (sex-linked recessive lethals) at the same concentration when administered by injection (Woodruff et al., 1985). Positive results for gene mutations were reported in the nematode, *Caenorhabitis* (Greenwald and Horvitz, 1980), and an equivocal result was obtained for mitochondrial mutations in yeast (Bandas, 1982). *Salmonella* testing in numerous strains has been reported as negative (Commoner, 1976; Laumbach et al., 1976; Pool and Wiesler, 1981; Marnett et al., 1985; Mortelmans et al., 1986). In two studies utilizing *Escherichia coli* to detect a mutagenic effect, one yielded positive results (Veghelyi et al., 1978) and the other study negative results (Hemminki et al., 1980). There were no available data on the ability of acetaldehyde to produce gene mutations in cultured mammalian cells.

Acetaldehyde has not been shown to cause DNA strand breaks in mammalian cells *in vitro* (Sina et al., 1983; Saladino et al., 1985; Lambert et al., 1985). However, if acetaldehyde produces SCEs and chromosomal aberrations by DNA-DNA or DNA-protein cross-linking, it may not necessarily produce DNA strand breaks (Bradley et al., 1979). Acetaldehyde has been shown to produce crosslinks between protein and DNA in the nasal respiratory mucosa of rats (Lam et al., 1986).

In conclusion, there is sufficient evidence that acetaldehyde produces cytogenic damage in cultured mammalian cells. Although there are only three studies in whole animals, they suggest that acetaldehyde produces similar effects *in vivo*. Acetaldehyde produced gene mutations in *Drosophila* but not in *Salmonella*; no studies were found for cultured mammalian cells. Thus, the available evidence indicates that acetaldehyde is mutagenic and may pose a risk for somatic cells. On the other hand, it has been suggested that acetaldehyde may be capable of deactivating free cysteine in bronchial epithelial cells, thereby suppressing the "thiol defense" of the epithelium against the attack of mutagens and carcinogens (Braven et al. 1967; Fenner and Braven, 1968). Current knowledge, however, is inadequate with regard to germ cells (reproductive cells) mutagenicity because the available information is insufficient to support any conclusions about the ability of

acetaldehyde to reach mammalian gonads and produce heritable
genetic damage.

Animal Data

        Acetaldehyde has been tested for carcinogenicity in hamsters
by intratracheal instillation and inhalation and in rats by
subcutaneous injection and inhalation. In the
inhalation/instillation study of hamsters (Feron, 1979), two
testing protocols were used. In part one, male hamsters were
exposed to 0 or 1500 ppm acetaldehyde by inhalation 7 hours/day, 5
days/week, for 52 weeks. These animals were also exposed
intratracheally to benzo[a]pyrene (BaP) for a total concentration
at the end of 52 weeks ranging from 0 to 52 mg. Exposure to
acetaldehyde by inhalation and intratracheal BaP induced
inflammatory changes, hyperplasia and metaplasia of the nasal,
laryngeal, and tracheal epithelium, and tumors of the nose and
larynx. Acetaldehyde enhanced the development of BaP-initiated
tracheobronchial carcinoma yielding twice the incidence of squamous
cell carcinoma compared with the same dose of BaP alone. No
neoplastic effects due to acetaldehyde alone were found.

        In the second part of Feron (1979), male and female hamsters
were intratracheally instilled with 4 or 8 µL acetaldehyde, BaP,
BaP and 4 µL acetaldehyde, diethylnitrosamine (DENA, a tumor
promotor), or DENA and 4 µL acetaldehyde. Acetaldehyde alone
produced no tumors in the larynx, trachea, or bronchi. However,
large numbers of tracheal papillomas and lung adenomas were found
in groups treated with acetaldehyde plus BaP or DENA. There was no
evidence of acetaldehyde enhancing the development of DENA-
initiated respiratory tract tumors.

        In an extension of the above study (Feron et al., 1982), male
and female hamsters were exposed to a high concentration of
acetaldehyde vapor alone or simultaneously with either BaP or DENA.
The animals were exposed 7 hours/day, 5 days/week, for 52 weeks to
a time weighted average concentration of 2028 ppm. Tumors were
slightly increased in the nose and significantly increased in the
larynx of animals exposed to acetaldehyde vapor alone, but no
tracheal tumors were observed. The incidence of carcinomas in the
trachea and bronchi were significantly higher in hamsters exposed
to acetaldehyde and treated with high doses of BaP than in hamsters
treated with the same dose of BaP but exposed to air. There was no
evidence that acetaldehyde exposure increased the incidence or
affected the type of DENA-induced tumors in any part of the
respiratory tract.

        Watanabe and Sugimoto (1956) reported spindle-cell sarcoma in
20% to 25% of the rats tested at the site of repeated acetaldehyde
injection. No conclusion can be drawn from this study because
neither the total doses of acetaldehyde nor the tumor incidence in
controls could be determined from available data.

        The carcinogenicity of acetaldehyde was studied in albino SPF
Wistar rats (Woutersen and Appelman, 1984; Woutersen et al., 1985,

1986). The studies are summarized in Table 8-9. The animals were
exposed by inhalation to atmospheres containing 0, 750, 1500, or
3000 ppm acetaldehyde for 6 hours/day, 5 days/week for 27 months.
The concentration in the highest dose group was gradually reduced
from 3000 to 1000 ppm because of severe growth retardation,
occasional loss of body weight, and early mortality in this group.
Interim sacrifices were carried out at 13, 26, and 52 weeks. One
tumor was observed in the 52 week sacrifice group and none at
earlier times. Exposure to acetaldehyde increases the incidence of
tumors in an exposure-related manner in both male and female rats.
In addition, there were exposure-related increased in the incidence
of multiple respiratory tract tumors. Adenocarcinomas were
increased significantly in both male and female rats at all
exposure levels, whereas squamous cell carcinoma were increased
significantly in male rats at middle and high doses and in the
female rats only at the high dose. The squamous cell carcinomas
incidence showed a clear dose-response relationship. The incidence
of adenocarcinomas was highest in the mid-exposure group (1500 ppm)
in both male and female rats, but this was probably due to the high
mortality and competing squamous cell carcinomas at the highest
exposure level. In the low-exposure group, the adenocarcinoma
incidence was higher in males than in females.

     In a concurrent study, referred to as the "recovery study", 30
animals of each sex were exposed to the same concentrations of
acetaldehyde for 52 weeks followed by a recovery period of 26 weeks
or 52 weeks. Significant increases in nasal tumors were observed
in male and female rats, including adenocarcinomas and squamous
cell carcinomas, in both recovery groups. These findings indicate
that after 52 weeks of exposure to acetaldehyde, proliferative
epithelial lesions of the nose may develop into tumors even without
continued exposure.

Table 8-9. Animal Data Used for EPA's Unit Risk Estimates.

REPORT	ANIMAL	EXPOSURE CONCENTRATION	LENGTH OF EXPOSURE	MAJOR RESULTS
Woutersen and Appelman (1984) also as Wouterson et al., (1986) Woutersen et al. (1985) "lifetime study"	albino SPF Wistar rats male and female	0, 750, 1500, and 3000 ppm (lowered to 1000 ppm) of acetaldehyde	6h/d, 5d/wk, for 27 months	1. Acetaldehyde vapor exposure caused two types of tumors in the nasal tract of rats in an exposure related manner. The four exposure levels gave tumor incidences of 1, 21, 52, and 51% respectively. 2. Degeneration of nasal tissue was observed at all dose levels. 3. Exposure appears not to affect any other organ directly except for lesions of the larynx and, to a minor degree, the trachea. 4. Animals in the high exposure group (3000 ppm) suffered severe growth retardation, respiratory distress, and high early mortality.
Woutersen and Appelman (1984) recovery subgroup of original study	albino SPF Wistar rats male and female	same exposures as used above subjected to a 26 or a 52 week recovery period	same as used above but for 52 weeks	With respect to recovery, during the first 26 weeks the nasal tumor rates and death rates were essentially the same as the lifetime exposure group. From 26-52 weeks both low- and mid-exposure recovery groups had significantly decreased nasal tumor rates. This indicates that nasal lesions may still develop into tumors even after exposure stops, and that the nasal tissue may also be able to repair some damage.

Human Data

The only epidemiological study involving acetaldehyde exposure showed an increased crude incidence rate of total cancer in acetaldehyde production workers as compared to the general population (Bittersohl, 1974). The study was performed on workers from an aldol and aliphatic acetaldehyde factory. The study showed a five times higher cancer rate than that of the general population. An incidence rate of 6000/100,000 population for total cancer was calculated for this study, which contrasts with an incidence rate of 1200/100,000 for the general population of Germany during the same period. Because the incidence rate was not age adjusted, and because this study has several other major methodological limitations (concurrent exposure to cigarette smoke and other chemicals, short duration, small number of subjects, and lack of information on subject selection, age, and sex distribution), the evidence is considered inadequate for the carcinogenicity of acetaldehyde in humans.

8.6.1.2 Weight-of-Evidence Judgement of Data and EPA Classification

The data used for the quantitative estimates for acetaldehyde are limited to the Woutersen and Appelman (1984) and the Woutersen et al., (1985) rat inhalation studies (summarized in Table 8-9) showing an exposure related increase in nasal tumors in Wistar rats and supported by positive results for mutagenicity. This evidence for carcinogenicity of acetaldehyde in animals is considered to be sufficient based on the U.S. EPA cancer assessment guidelines. Neither of the hamster studies (Feron, 1979; Feron et al., 1982) are considered satisfactory based on the fact that one was an intratracheal instillation study and the other was an inhalation study which had very high exposure levels of acetaldehyde and only one exposure group.

The only epidemiological study, Bittersohl (1974), showed an increase in crude incidence rate of total cancer in acetaldehyde production workers as compared with the general population. Because the incidence rate was not age adjusted, and because this study has several other major methodological limitations, the evidence is considered inadequate for the carcinogenicity of acetaldehyde in humans.

On the basis of inadequate evidence for carcinogenicity of acetaldehyde emissions in humans, and relying totally on the sufficient evidence from animals and mutagenicity, acetaldehyde emissions are considered to best fit the weight-of-evidence category B2. This classifies acetaldehyde as a probable human carcinogen.

8.6.1.3 Data Sets Used for Unit Risk Estimates

To actually determine the unit risk of acetaldehyde, only two of the animal studies are selected for risk calculations because they are inhalation studies that involve more than one exposure group. The two rat studies used are Woutersen and Appelman (1984) (also known as Wouterson et al., 1986), and Woutersen et al. (1985). These studies are summarized in Table 8-9.

8.6.1.4 Dose-Response Model Used

The linearized multistage model is used to calculate unit risk estimates using various exposure inputs. All unit risk estimates that currently exist for acetaldehyde are based exclusively on animal data.

8.6.1.5 Unit Risk Estimates

The upper-limit unit risk estimate for acetaldehyde is $2.2 \times 10^{-6} (\mu g/m^3)^{-1}$, derived from the male rat tumor data. Corresponding maximum likelihood estimates (MLE's) were not given.

8.6.2 Other Views and Risk Estimates

This section presents alternate views and/or risk assessments for acetaldehyde.

International Agency for Research on Cancer (IARC)

IARC has classified acetaldehyde as a Group 2B carcinogen. A Group 2B carcinogen is defined as an agent that is *possibly* carcinogenic to humans. This classification is based on inadequate evidence for carcinogenicity in humans and sufficient evidence for carcinogenicity in animals (IARC, 1987).

California Air Resources Board (CARB)

CARB (1992b), like EPA and IARC, has concluded that acetaldehyde is a probable human carcinogen. CARB (1992b) has performed an assessment of the carcinogenic risk of acetaldehyde using the Wouterson et al., (1986) rat nasal carcinoma data (discussed previously in Section 8.6.1) in the linearized time-dependent multistage model. However, their assessment differs from EPA (1987) in the following ways:

(1) The EPA (1987) risk assessment considered all 55 animals in the experimental groups to be at risk, whereas CARB used only the 49-53 animals of each group that were examined for nasal changes.

(2) CARB used only the male rat data from Wouterson et al., (1986) whereas EPA used both the male and the female data. CARB stated that the male rat is more sensitive to

tumor induction by acetaldehyde than the female rat and this is the proper sex to select based on CARB procedures for cancer risk assessment.

(3)   The EPA (1987) risk assessment combined two experiments by Wouterson et al., the lifetime exposure experiment and an experiment in which one year of exposure was followed by one year of recovery. CARB , however, used only the lifetime exposure experiment.

(4)   EPA (1987) used two versions of the linearized multistage model: the standard version and the time-to-tumor version. CARB used only the standard version citing that the information to adequately use the time-to-tumor version was not available in the experimental data and thus should not be used.

(5)   The CARB approach uses three different scaling factors to extrapolate the equivalent dose rate from rats to humans. EPA (1987) did not specifically discuss the issue of scaling to extrapolate from rodents to humans for formaldehyde.

The UCL for unit risk for lifetime exposure calculated by CARB (1992b) using the methods and assumptions described above is 4.8×10^{-6} ppb^{-1} (2.7×10^{-6} $[\mu g/m^3]^{-1}$). CARB also calculated a range of UCL for unit risks. This range is 9.7×10^{-7} ppb^{-1} for female rats without a scaling factor to 2.7×10^{-5} ppb^{-1} for male rats with a contact area correction (1.19×10^{-6} to 3.32×10^{-5} $[\mu g/m^3]^{-1}$).

8.6.3 Recent and Ongoing Research

8.6.3.1 Genotoxicity

Dulout and Furnus (1988) determined that the most notable cytogenetic effect of acetaldehyde in cultured Chinese hamster ovary (CHO) cells was aneuploidy (the chromosome number is not an exact multiple of the haploid number) and not chromosomal breakage. Acetaldehyde added for 24 hours to cultures at concentrations of 0.002%, 0.004%, and 0.006% produced an increased frequency of aneuploidy as compared to controls. The aneuploidy was observed at all doses tested, whereas chromosomal aberrations and sister chromosomal exchanges only occurred at the two highest levels.

The effect of acetaldehyde on the frequency of meiotic micronuclei in groups of four hybrid male mice was assessed 13 days after a single intraperitoneal injection of 0, 125, 250, 375, of 500 mg/kg acetaldehyde in saline solution. No significant increases in the frequency of micronuclei were observed (Lahdetie, 1988). The alkaline dilution technique was used by Garberg, et al. (1988) to determine whether the DNA of mouse lymphoma cells exposed to acetaldehyde contain single-strand breaks. Single -strand breaks were not detected in this cell type or in rat hepatocytes, human lymphocytes, and bronchial epithelial cells studied

previously (Sina et al., 1983, Lambert et al., 1985; Saladino et al., 1985).

8.6.3.2 Metabolism and Pharmacokinetics

The following has been excerpted from EPA (1987). The extensive references have been omitted to facilitate the comprehension of this section. For the complete list of references, please consult Chapter 4 of EPA (1987). Other studies that have been published since the issuance of the 1987 draft document support the 1987 position summarized below.

The principal routes of entry of acetaldehyde into the body are by gastrointestinal and inhalation absorption. Acetaldehyde, whether from exogenous (from outside the body) sources or generated from ethanol metabolism, is known to be very rapidly and extensively metabolized oxidatively in mammalian systems to a normal endogenous (inside the organism) metabolite, acetate, primarily by aldehyde dehydrogenases (specific enzymes) widely distributed in body tissue. Acetate enters the metabolic pool of intermediary metabolism and is used in cellular energy production (end products CO_2 and water) or in synthesis of cell constituents. In contrast to the situation for acetaldehyde generated from ethanol metabolism, there are few studies of the kinetics of acetaldehyde of exogenous origin, i.e., from environmental exposure or experimental dosing. It is known, however, that all mammalian species have a high capacity to rapidly and virtually completely metabolize acetaldehyde by most tissues in the body, including the gastrointestinal mucosa and respiratory mucosa and lungs. Although hepatic (liver) capacity is the highest after oral or inhalation administration, experimental evidence indicates that a substantial first-pass metabolism in the liver or respiratory organs effectively limits acetaldehyde access to the systemic circulation. However, adequate studies have not been conducted to establish dose-metabolism relationships, or dose-blood concentration relationships.

Acetaldehyde readily crosses body compartmental membranes into virtually all body tissues, including the fetus, after administration or endogenous generation. Animal experiments have demonstrated a rapid exponential disappearance from circulating blood, consistent with first-order kinetics, with a short half-time of elimination of less than 15 minutes. Since less than 5 percent escapes unchanged in exhaled breath, and acetaldehyde is not known to be excreted into the urine, the elimination from the body is essentially by metabolism.

Acetaldehyde is a highly reactive compound and at high concentrations episode, for example, at the respiratory mucosa with inhalation exposure, it readily forms adducts nonenzymatically with membranal and intracellular macromolecules. Stable and reversible adduct formation including cross-linking have been demonstrated with proteins, nucleic acids (including DNA), and phospholipids. Moreover, even at physiological levels (10 to 150 μmol/L blood), acetaldehyde has been found to form adducts with cellular macromolecules. From these observations, it has been considered

that acetaldehyde-adduct formation may play a role in the organ and
cellular injury associated with acetaldehyde toxicities, and in the
potential promoter or carcinogenic effect assigned to this
compound. Acetaldehyde also readily reacts nonenzymatically with
cysteine and glutathione (proteins with sulfur groups [thiols]
attached) to form stable and reversible adducts, respectively.
Hence, acetaldehyde may be an effective depleter of these important
cellular nonprotein thiols, which represent a thiol defense against
the attack of toxic aldehydes and other mutagens and carcinogens.

8.7 Carcinogenic Risk for Baseline and Control Scenarios

Table 8-10 summarizes the annual cancer incidences for all the
scenarios. These numbers are presented as decimals due to the fact
that the cancer cases are low enough that rounding the decimal up
or down would significantly affect the total number.   The cancer
cases do decrease slightly from a comparison drawn between base
control scenarios. When compared to the 1990 base control, the
cancer incidence decreases by 32% in 1995, 47% in 2000, and 43% in
2010, which is actually an increase when compared to 2000.   The
reductions are basically due to the tighter tailpipe standards
specified by the Tier 1 standards. In contrast, when compared to
the 1990 base control, the emission factors decrease 24% in 1995,
45% in 2000 and 65% in 2010. The difference observed between the
emission factor and cancer case reductions, and the increases
observed in 2010, is due to the expected increase in population and
VMT, which appear to offset the emission gains achieved through
fuel and vehicle modifications.

From Table 8-10 it can also be observed that the expanded use
of reformulated fuel and the expansion of the California standards
provide no significant decrease in the cancer cases and, in several
scenarios, the cancer cases increase. As mentioned in previous
sections, the exposure estimates are based on changes in direct
emissions of acetaldehyde. Changes in reactivity of the emissions,
which would result in changes to secondary acetaldehyde, are not
accounted for. Since it is probable that secondary acetaldehyde
could be reduced with the use of oxygenates, the cancer risk
estimates given in Table 8-10 should be considered conservative
estimates.

Table 8-10. Annual Cancer Incidence Projections for Acetaldehyde.[a,b]

Year-Scenario	Emission Factor g/mile	Urban Cancer Cases	Rural Cancer Cases	Total Cancer Cases	Percent Reduction from 1990	
					EF	Cancer
1990 Base Control	0.0119	4.5	0.8	5.3	–	–
1995 Base Control	0.0071	3.0	0.6	3.6	40	32
1995 Expanded Reformulated Fuel Use	0.0071	3.0	0.6	3.6	40	32
2000 Base Control	0.0051	2.4	0.4	2.8	57	47
2000 Expanded Reformulated Fuel Use	0.0051	2.4	0.4	2.8	57	47
2000 Expanded Adoption of California Standards	0.0052	2.4	0.4	2.8	56	47
2010 Base Control	0.0045	2.6	0.4	3.0	62	43
2010 Expanded Reformulated Fuel Use	0.0044	2.6	0.4	3.0	63	43
2010 Expanded Adoption of California Standards	0.0041	2.4	0.4	2.8	66	47

[a]Projections have inherent uncertainties in emission estimates, dose response, and exposure.
[b]Cancer incidence estimates are based on upper bound estimates of unit risk, determined from animal studies. Acetaldehyde is classified by EPA as a category B2, probable human carcinogen, based on insufficient evidence in humans and sufficient evidence in animals and in mutagenicity bioassays.

Please note that the cancer unit risk estimate for acetaldehyde is based on animal data and is considered an upper bound estimate for human risk. True human cancer risk may be as low as zero.

8.8 Non-Carcinogenic Effects of Inhalation Exposure to Acetaldehyde

Since the focus of this report is on the carcinogenic potential of the various compounds, the noncancer information will be dealt with in a more cursory fashion. No attempt has been made to synthesize and analyze the data encompassed below. Also, no attempt has been made to accord more importance to one type of noncancer effect over another. The objective is to research all existing data, describe the noncancer effects observed, and refrain from any subjective analysis of the data.

8.8.1 Toxicity

The results of eight acute toxicity studies in mammals, by inhalation in rats (Skog, 1950; Lewis and Tatkin, 1983) and mice (Kane et al., 1980; Barrow, 1982), by the oral route in rats (Windholz et al., 1983; Lewis and Tatkin, 1983; Omel'yanets et al., 1978) and mice (National Research Council, 1977) along with intravenous instillation in guinea pigs (Mohan et al., 1981) and subcutaneous injection in rats and mice (Skog, 1950) all show LD_{50} effects. The acute oral LD_{50} of acetaldehyde ranged from 1232 mg/kg to 5300 mg/kg. The LD_{50} for subcutaneous injection ranged from 560 mg/kg to 640 mg/kg. The acute inhalation LC_{50} was 20,000 ppm in rats exposed to acetaldehyde for 30 minutes. In one study (Lewis and Tatkin, 1983), 4000 ppm for 4 hours killed some exposed rats. The following section will discuss some of these acute toxicity studies in more detail.

Studies with rats and mice showed acetaldehyde to be moderately toxic by the inhalation route, oral, and intravenous routes. Acetaldehyde is a sensory irritant that causes a depressed respiration rate in mice (Kane et al., 1980; Barrow, 1982). This yielded RD_{50}'s (the concentration that produces a 50% decrease in respiratory rate) of 4946 ppm and 2845 ppm, respectively. The current TLV for acetaldehyde is 100 ppm (American Conference of Governmental Industrial Hygienists, 1980), and is between 0.1 and 0.01 times the cited RD_{50} values. In rats, acetaldehyde increased blood pressure and heart rate after exposure by inhalation (Egle, 1972) and intravenous injection (Mohen et al., 1981; Egle et al., 1973).

Three subchronic inhalation studies in rats and one in hamsters have been conducted. Appelman et al. (1982) used the exposure information discussed below in the RfC section. Rats exposed to the highest concentration exhibited severe dyspnea and marked excitation during the first 30 minutes of exposure. Rats at the highest exposure also exhibited decreased body weight, lymphocytes, and liver weights when compared to controls. The neutrophil counts and lung weights were increased. Histopathological alterations of the respiratory system were seen

at all dose levels, with the nose being the most severe. The
study by Appelman et al. (1986) (exposure information is detailed
in RfC section) was also observed for non-cancer effects.
Uninterrupted exposure to 500 ppm did not produce any changes in
condition, behavior, or body weight of the rats; however, rats
exposed to 500 ppm with a peak exposure of 3000 ppm exhibited
irritation, as indicated by eye blinking, excessive running, and
nose twitching. Mean body weights in the latter groups were
significantly lower than in controls. In addition, a reduced
phagocytotic index was significantly decreased at the highest
dose.

   The effect of acetaldehyde on pulmonary mechanics was
studied following exposure of groups of Wistar rats to
acetaldehyde vapors at concentrations of 0 or 243 ppm (0 or 105.3
mg/m^3), 8 hours/day, 5 days/week for 5 weeks. (Hilaro et al.,
1985). A significant increase in respiratory frequency,
functional residual capacity, residual volume, and total lung
capacity was noted. The subchronic inhalation study in hamsters
(Kruysse et al., 1975) is discussed below in the RfC section.

   One subchronic investigation of the effects of acetaldehyde,
on the phospholipid composition of pulmonary surfactant, was
found in the literature (Prasanna et al., 1981). Pulmonary
surfactant is a lipoprotein complex with a high phospholipid
content which prevents alveolar collapse during expiration by
maintaining the stability and physical elasticity of the alveolar
walls, and by reducing the surface tension of the fluid lining
the alveoli. Acetaldehyde injected intraperitoneally to rats at
200 mg/kg significantly reduced the phospholipid concentration of
pulmonary surfactant. In two subchronic intravenous studies, one
in guinea pigs (Mohen et al., 1981), and the other in rats (Egle
et al., 1973), a dosage of 20 mg/kg acetaldehyde or lower caused
an immediate and significant increase in blood pressure.

   In a chronic inhalation study (Feron, 1979), acetaldehyde
vapor at 1500 ppm for 52 weeks produced systemic effects in the
hamster: growth retardation, slight anemia, increased UGOT
(urinary glutamic-oxaloacetic transaminase) activity, increased
urine protein content, increased kidney weights, and
histopathological changes in the nasal mucosa and trachea. In a
separate study (Feron, 1979), intratracheal instillation of
acetaldehyde (2 to 4 percent) to hamsters weekly or biweekly for
up to 52 weeks caused severe hyperplastic and inflammatory
changes in the bronchioalveolar region of the respiratory tract.
In Feron et al. (1982), male and female hamsters exposed to
levels of acetaldehyde vapor decreasing from 2500 ppm to 1650 ppm
over 52 weeks had lower body weights than controls and distinct
histopathological changes in the nose, trachea, and larynx.

   Humans are frequently exposed to acetaldehyde from cigarette
smoke, vehicle exhaust fumes, or other sources. Metabolism of
ethanol would be the major source of acetaldehyde among consumers
of alcoholic beverages.

The primary acute effect of exposure to acetaldehyde vapors is irritation of the eyes, skin, and respiratory tract (Sim and Pattle, 1957). At high concentrations, irritation and ciliastatic effects can occur, which could facilitate the uptake of other contaminants (NRC, 1981). Clinical effects include erythema, coughing, pulmonary edema, and necrosis (Dreisbach, 1980). Respiratory paralysis and death have occurred at extremely high concentrations. It has been suggested that voluntary inhalation of toxic levels of acetaldehyde would be prevented by its irritant properties, since irritation occurs at levels below 200 ppm (Sittig, 1979). It was concluded by the Committee of Aldehydes of the National Research Council (1981) that direct pulmonary sensitization to aldehyde vapors appears to be relatively rare and asthma-like symptoms are rarely caused by the inhalation of aldehydes.

The main route of occupational exposure is by inhalation of acetaldehyde vapor. The allowable federal time weighted average (TWA) is 200 ppm (360 mg/m^3) for eight hours per day, five days per week. The American Conference of Governmental and Industrial Hygienists (1985) recommends a threshold limit value (TLV) of 100 ppm (180 mg/m^3) for eight hours per day, five days per week.

8.8.2 Reference Concentration for Chronic Inhalation Exposure (RfC)

At the present time, the reference dose for chronic oral exposure (RfD) assessment is not available but the reference concentration for chronic inhalation exposure (RfC) has recently been completed (EPA, 1992). An RfC is an estimate of the continuous exposure to the human population that is likely to be without deleterious effects during a lifetime.

Two short term studies conducted by the same research group are the principal studies used. While these studies are short term in duration, together they establish a concentration-response for lesions after only 4 weeks of exposure.

Appelman et al. (1986) conducted two inhalation studies on male Wistar rats exposing them 6 hrs/day, 5 days/week for 4 weeks to 0, 150, and 500 ppm (0, 273, and 910 mg/m^3, respectively. One group was exposed without interruption, a second group was interrupted for 1.5 hours halfway through the exposure, and a third group was interrupted as described with a peak exposure imposed four times in a three hour period (concentration at peak was six times the basic concentration). Degeneration of the olfactory epithelium was observed in rats exposed to 500 ppm. Interruption of the exposure or interruption combined with peak exposure did not visibly influence this adverse effect. No compound-related effects were observed in rats interruptedly or uninterruptedly exposed to 150 ppm during the 4 week exposure period; therefore, the NOAEL is 150 ppm (no-observed-adverse-effect level).

Appelman et al, (1982) exposed Wistar rats for 6 hour.day, 5 days/week for 4 weeks to 0, 400, 1000, 2200, or 5000 ppm

acetaldehyde (0, 728, 1820, 4004, and 9100 mg/m^3). The nasal
cavity was most severely affected and exhibited a concentration-
response relationship. At all levels of acetaldehyde exposure in
this experiment, there was found nasal olfactory degeneration
that increased in severity as the concentration increased. Also
as the concentration increased, the laryngeal and tracheal
epithelium became involved (1000 to 5000 ppm). Based on the
degenerative changes observed in the olfactory epithelium, the
400 ppm level is designated as a LOAEL (lowest-observed-adverse-
effect level).

There are also three additional studies used to support the
inhalation RfC. Woutersen et al. (1986), which was discussed
previously, exposed rats to 0, 750, 1500, and 3000/1000 ppm
acetaldehyde vapor. The only exposure related histopathology
occurred in the respiratory system and showed a concentration-
response relationship. The most severe abnormalities were found
in the nasal cavity. Basal cell hyperplasia of the olfactory
epithelium was seen in the low- and mid-concentration rats. The
decrease in these changes in the olfactory epithelium was
attributed to the incidence of adenocarcinomas at the higher
levels. The lowest exposure concentration, 750 ppm, is clearly a
LOEAL based on the above changes in the olfactory epithelium.

Woutersen and Feron (1987) conducted an inhalation study in
which Wistar rats were exposed to 0, 750, 1500, or 3000/1500 ppm
acetaldehyde (0, 1365, 2730, 5460/2730 mg/m^3, respectively) for 6
hours/day, 5 days/week for 52 weeks with a 26- or 52-week
recovery period. Degeneration of the olfactory epithelium was
similar in rats terminated after 26 weeks of recovery and rats
killed immediately after exposure termination. Histopathological
changes found in the respiratory epithelium were comparable with,
but less severe than, those observed immediately after exposure
termination. After 52 weeks of recovery, the degeneration of the
olfactory epithelium was still visible to a slight degree in
animals from all exposure groups. The data suggest that there is
incomplete recovery of olfactory and respiratory epithelium
changes induced at all exposure concentrations for periods as
long as 52 weeks after exposure termination.

Kruysse et al. (1975) conducted a 90-day inhalation study in
hamsters. The hamsters were exposed to acetaldehyde vapor at
concentrations of 0, 390, 1340, or 4560 ppm (0, 127, 435.3, or
1482 mg/m^3), for 6 hours/day, 5 days/week for 90 days. In this
study, as in the previous studies, the histopathological changes
attributable to exposure were observed only in the respiratory
tract. At the 390 ppm concentration, with one exception, no
adverse effects were observed. The 390 ppm concentration was
identified by the authors as a NOAEL.

The final RfC was calculated using the NOAEL from Appelman
et al. (1986) of 273 mg/m^3, an uncertainty factor (UF) of 1000,
and a modifying factor (MF) of 1. The UF of 1000 was obtained by
assigning an uncertainty factor of 10 to account for sensitive
human populations, another factor of 10 for both uncertainty in

the interspecies extrapolation using dosimetric adjustments and to account for the incompleteness of the data base, and a third factor of 10 to account for subchronic to chronic extrapolation. The MF of 1 is the default and is based upon an assessment of the scientific uncertainties of the toxicological data base not treated with the UF. The final number arrived at for the RfC is 9×10^{-3} mg/m^3 per day over a lifetime.

8.8.3 Reproductive and Developmental Effects

No inhalation studies for reproductive or developmental effects have been performed. In all the *in vivo* studies cited below, acetaldehyde is administered by the oral, intravenous, or intraperitoneal route.

Ali and Persaud (1988) studied the role of acetaldehyde in the pathogenesis of ethanol-induced developmental effects. Sprague-Dawley rats received intraperitoneal injections of a 1% solution of acetaldehyde at a dose of 100 mg/kg/day from days 9 through 12 of gestation. On day 12, the embryos were recovered and examined for
morphological abnormalities and crown-rump and head length. Acetaldehyde produced a significant reduction in head length, but had no significant effect on morphological abnormalities or crown-rump length. The reduction in head length was considered to be important, since it may be a causative factor in the microencephaly and CNS dysfunction found in fetal alcohol syndrome.

Kalmus and Buckenmaier (1989) investigated the effects of acetaldehyde on cultured preimplantation 2-cell stage mouse embryos *in vitro*. Embryos were exposed to 0, 5, 10, 200, or 500 mg acetaldehyde/100 ml culture medium for 60 minutes. Embryo growth was evaluated at a time period corresponding to an embryo age of 105 hours. No effects were observed at 5 and 10 mg/100ml; exposures to 50mg/100ml and higher were lethal. The results indicate that the 2-cell stage embryos are highly resistant to high *in vitro* dosages of acetaldehyde; however, the reason for the apparent resistance is not known.

Zorzano and Herrera (1989) studied the pattern of acetaldehyde appearance in maternal and fetal blood, maternal and fetal liver and placenta after oral ethanol administration or intravenous acetaldehyde administration (10mg/kg) to pregnant Wistar rats. The study demonstrated that acetaldehyde was able to cross the placental barrier at high concentrations; maternal blood concentration had to be greater that 80 μM. The fetal oxidation capacity in liver and placenta was shown to be lower than that of the maternal liver. A threshold above which the removal capacity of acetaldehyde metabolism by the fetoplacental unit would be surpassed was estimated to be 80 μM (maternal blood concentration) in the 21-day pregnant rat and possibly lower at early pregnancy when aldehyde dehydrogenase is absent from fetal liver.

Lahdetie (1988) is the only study available on the *in vivo* effects of acetaldehyde on the male reproductive system. Groups of hybrid male mice were given intraperitoneal injections of saline solution 0, 62.5, 125, or 250 mg acetaldehyde/kg daily for 5 days. No significant effects on sperm were seen for sperm count, sperm morphology, testes weight, or seminal vesicle weight when compared with controls. The authors speculated that, since no significant effects on sperm were seen, although acetaldehyde had been shown to produce mutagenic effects in somatic cells, germ cells were either less sensitive to the genotoxic effects or the acetaldehyde concentrations was too low because of its binding to erythrocytes and limited passage through the blood-testes barrier.

In female, pregnant rats, across several studies (Sreenathan et al., 1982, 1984a,b; Sreenathan and Padmanabhan, 1984; Padmanabhan et al., 1983; Checiu et al, 1984; Barilyak and Kozachuk, 1983; Dreosti et al., 1981), many of the same effects were observed. These include increased fetal resorption, increases in litter malformations, retardation in fetal growth, decreased placental weight, increased placental lesions, decreases in skeletal formation, delayed segmentation and differentiation of the embryo, increased cell fragmentation of the embryo, increased chromosomal abnormalities, and interference in thymidine incorporation into the DNA of the brain and liver.

In female, pregnant mice (Blakley and Scott, 1984a,b; Bannigan and Burke, 1982; Webster et al., 1983; O'Shea and Kaufman, 1979, 1981), there are several studies used to demonstrate reproductive and developmental effects, with most results leading to much uncertainty or doubt as to their advantage to understanding these effects. Several studies found no effects, whereas, some found an increase in fetal resorptions, fetal growth retardation, and increased number of fetuses with malformations. Most of these malformations were neural tube defects.

There are additional data that support the hypothesis that acetaldehyde interferes with placental function. In a series of studies (Henderson et al., 1981, 1982; Asai et al., 1985; Fisher et al., 1981a,b; 1984), the ability of acetaldehyde to interfere with amino acid uptake across the placenta was demonstrated. This demonstrates that this disruption in placental function may create a state of fetal malnutrition that is independent of maternal nutritional status. Such a state may be a factor in intrauterine growth retardation. These studies must be interpreted with some caution. These studies examined the status of term placentas and it remains to be determined what relationship this has to preplacental structures.

There are also several studies (Thompson and Folb, 1982; Higuchi and Matsumoto, 1984; Campbell and Fantel, 1983; Popov et al., 1982; Prescott, 1985) that have examined the direct embryotoxic properties of acetaldehyde utilizing whole embryo cultures (rat and mouse). The majority of these data demonstrate

that acetaldehyde can produce growth retardation and malformations *in vitro*.

The primary support for acetaldehyde-induced reproductive dysfunction is derived from *in vitro* studies examining the influence of acetaldehyde on androgen (male hormone) production. The majority of these studies (Cobb et al., 1978, 1980; Boyden et al., 1981; Badr et al., 1977; Cicero et al., 1980a,b; Santucci et al., 1983; Johnson et al., 1981; Cicero and Bell, 1980) have demonstrated that acetaldehyde significantly depresses HCG-(human chorionic gonadotrophin) stimulated testosterone production; however, the exact mechanism is unknown. This effect has been reported in a number of species, including mice, rats, and dogs.

Only one study has examined the reproductive effects of acetaldehyde aside from endocrine influences. Anderson et al. (1982) assessed the effects of acetaldehyde on sperm capacitation. These authors demonstrated that acetaldehyde did not alter the *in vitro* fertilizing capacity of mouse spermatozoa, though the relevance of this culture system to *in vivo* fertilization is unclear.

In vitro data strongly suggest the possibility of male reproductive toxicity and support the need for such data to be generated in *in vivo* systems.

8.10 References for Chapter 8

Ali, F. and T. Persaud. 1988. Mechanisms of fetal alcohol effects: role of acetaldehyde. Exp. Pathol. 33: 17-21.

American Conference of Governmental Industrial Hygienists. 1980. Documentation of the threshold limit values. Fourth edition: 1980. Cincinnati, OH: American Conference of Governmental Industrial Hygienists; pp. 3-4.

American Conference of Governmental Industrial Hygienists. 1985. TLVs: threshold limit values and biological exposure indices for 1985-86. Cincinnati, OH: American Conference of Governmental Industrial Hygienists; pp. 3-4.

Anderson, R.A. J.M. Reddy, C. Joyce, B.R. Willis, H. Van der Vend, and L.J. Zaneveld. 1982. Inhibition of mouse sperm capacitation by ethanol. Biol. Reprod. 27: 833-840.

Appelman, L.M., R.A. Woutersen, and V.J. Feron. 1982. Inhalation toxicity of acetaldehyde in rats. I. Acute and subacute studies. Toxicology. 23: 293-307.

Appelman, L.M., R.A. Woutersen, V.J. Feron R.N. Hooftman, and W.R.F. Notten. 1986. Effect of variable versus fixed exposure levels on the toxicity of acetaldehyde in rats. J. Appl. Toxicol. 6(5): 331-336.

Asai, M., O. Narita, and S. Kashiwamatu. 1985. Effect of acetaldehyde and/or ethanol on neutral amino acid transport systems in microvillous brush border membrane vesicles prepared from human placenta. Experientia 41: 1566-1568.

Badr, F.M., A. Bartke, S. Dalterio, and W. Bulger. 1977. Suppression of testosterone production by ethyl alcohol. Possible mode of action. Steroids 30: 647-655.

Bandas, E.L. 1982. Study of the role of metabolites and impurities in the mutagenic action of ethanol on yeast mitochondria. Genetika 18: 1056-1061.

Bannigan, J., and P. Burke. 1982. Ethanol teratogenicity in mice: a light microscope study. Teratol. 26: 247-254.

Barilyak, I.R. and S.Y. Kozachuk. 1983. Embryotoxic and mutagenic activity of ethanol after intra-amniotic injection. Tsitologiya i Genetika 17: 57-60.

Barrow, C.S. 1982. Sensory irritation of inhaled aldehydes: structure activity studies. CIIT 2, no. 9.

Bird, R.P., H.H. Draper, and P.K. Basrur. 1982. Effect of malonaldehyde and acetaldehyde on cultured mammalian cells; production of micronuclei and chromosomal aberrations. Mutat. Res. 101: 237-246.

Bittersohl, G. 1974. Epidemiologic investigations on cancer incidence in workers contacted by acetaldol and other aliphatic aldehydes. Arch. Geschwulstforsch. 43: 172-176.

Blakley, P.M. and W.J. Scott. 1984a. Determination of the proximate teratogen of the mouse fetal alcohol syndrome. 1. Teratogenicity of ethanol and acetaldehyde. Tox. Appl. Pharmacol. 72: 355-363.

Blakley, P.M. and W.J. Scott. 1984b. Determination of the proximate teratogen of the mouse fetal alcohol syndrome. 2. Pharmacokinetics of the placental transfer of ethanol and acetaldehyde. Tox. Appl. Pharmacol. 72: 364-371.

Boettner, E.A., G.L. Ball, and B. Weise. 1973. Combustion products from the incineration of plastics. Ann Arbor, MI: University of Michigan, School of Public Health. Available from: NTIS, Springfield, VA; PB-222001/0.

Böhlke, J.U., S. Singh, and H.W. Goedde. 1983. Cytogenetic effects of acetaldehyde in lymphocytes of Germans and Japanese: SCE, clastogenic activity, and cell cycle delay. Hum. Genet. 63: 285-289.

Boyden, T.W., M.A. Silvery, and R.W. Pamenter. 1981. Acetaldehyde acutely impairs canine testicular testosterone secretion. Eur. J. Pharmacol. 70: 571-576.

Bradley, M., I.C. Hsu, and C.C. Harris. 1979. Relationships between sister chromatid exchange and mutagenicity, toxicity, and DNA damage. Nature 282: 318-320.

Braven, J., G.J. Bonker, M.L. Fenner, and B.L. Tonge. 1967. The mechanism of carcinogenesis by tobacco smoke. Some experimental observations and a hypothesis. Br. J. Cancer 21: 623-633.

Campbell, M.A., and A.G. Fantel. 1983. Teratogenicity of acetaldehyde *in vitro*: relevance to fetal alcohol syndrome. Life Sci. 32: 2641-2647.

CARB. 1992a. Preliminary Draft: Proposed identification of acetaldehyde as a toxic air contaminant. Part A Exposure assessment. California Air Resources Board, Stationary Source Division. August, 1992.

CARB. 1992b. Preliminary Draft: Proposed identification of acetaldehyde as a toxic air contaminant. Part B Health assessment. California Air Resources Board, Stationary Source Division. August, 1992.

Checiu, M. S. Sandor, and Z. Garban. 1984. The effect of ethanol on early development in mice and rats. VI. In vitro effect of acetaldehyde upon preimplantation stages in the rat. Morphol. Embryol. (Bucur) (Romania) 30: 175-184.

Cicero, T.J., and R.D. Bell. 1980. Effects of ethanol and acetaldehyde on the biosynthesis of testosterone in the rodent testes. Biochem. Biophys. Res. Commun. 94: 814-819.

Cicero, T.J., R.D. Bell, and T.M. Badger. 1980a. Acetaldehyde directly inhibits the conversion of androstenedione to testosterone in the testes. Adv. Exp. Med. Biol. 132: 211-217.

Cicero, T.J., R.D. Bell, E.R. Meyer, and T.M. Badger. 1980b. Ethanol and acetaldehyde directly inhibit testicular steroidogenesis. J. Pharmacol. Exp. Therap. 213: 228-233.

Cobb, C.F., M.F. Ennis, F. Michael, D.H. Van Thiel, J.S. Gavaler, and R. Lester. 1978. Acetaldehyde and ethanol are direct testicular toxins. Surg. Forum 29: 641-644.

Cobb, C.F., M.F. Ennis, D.H. Van Thiel, J.S. Gavaler, and R. Lester. 1980. Isolated testes perfusion: a method using a cell- and protein-free perfusate useful for the evaluation of potential drug injury. Metabolism 29:71-79.

Commoner, B. 1976. Reliability of bacterial mutagenesis techniques to distinguish carcinogenic chemicals. EPA-600/1-76-022. U.S. Environmental Protection Agency.

Delaney J.L. and T.W. Hughs. 1979. Source assessment: manufacture of acetone and phenol from cumene. Research Triangle Park, NC: U.S. Environmental Protection Agency, Industrial Environmental Research Laboratory: EPA Report No. EPA-600/2-79-019d.

de Raat, W.K., P.B. Davis, and G.L. Bakker. 1983. Induction of sister-chromatid exchanges by alcohol and alcoholic beverages after metabolic activation by rat-liver homogenate. Mutat. Res. 167: 89-105.

Dreisbach, R.H. 1980. Acetaldehyde, metaldehyde, and paraldehyde. In: Handbook of poisoning: prevention, diagnosis, and treatment. Los Angeles, CA: Lange Medical Publications; pp. 177-180.

Dreosti, I.E., F.J. Ballard, G.B. Belling, I.R. Record, S.J. Manuel, and B.S. Hetzel. 1981. The effect of ethanol and acetaldehyde an DNA synthesis in growing cells and on fetal development in the rat. Alcohol: Clin. Exp. Res. 5: 357-362.

Dulout F. and T. Furnus. 1988. Acetaldehyde induced aneuploidy in cultured Chinese hamster cells. Mutagenesis 3: 207-211.

Egle, J.L., Jr. 1972. Effects of inhaled acetaldehyde and propionaldehyde on blood pressure and heart rate. Toxicol, Appl. Pharmacol. 23: 131-135.

Egle, J.L., P.M. Hudgins, and F.M. Lai. 1973. Cardiovascular effects of intravenous acetaldehyde and propionaldehyde in the anesthetized rat. Toxicol. Appl. Pharmacol. 24: 636-644.

Eimutis, E.C., R.P. Quill, and G.M. Rinaldi. 1978. Source assessment: noncriteria pollutant emissions. Research Triangle Park, NC: U.S. Environmental Protection Agency, Industrial Environmental Research Laboratory; EPA Report No. EPA-600/2-78-004t.

Eker, P. and T. Sanner. 1986. Initiation of in vitro cell transformation by formaldehyde and acetaldehyde as measured by attachment-independent survival of cells in aggregates. Eur. J. Cancer Clin. Oncol. 22(6): 671-676.

EPA. 1987. Health assessment document for acetaldehyde. Office of Research and Development, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Research Triangle Park, NC. EPA-600/8-86/015A. (External Review Draft).

EPA. 1992. Integrated Risk Information System (IRIS). Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH.

Fenner, M.L. and J. Braven. 1968. The mechanism of carcinogenesis by tobacco smoke. Further experimental evidence and a prediction from the thiol-defense hypothesis. Br. J. Cancer 22: 474-479.

Feron, V.J. 1979. Effects of exposure to acetaldehyde in Syrian hamsters simultaneously treated with benzo(a)pyrene or diethylnitrosamine. Prog. Exp. Tumor Res. 24: 162-176.

Feron, V.J., A. Kruysse, and R.A. Woutersen. 1982. Respiratory tract tumors in hamsters exposed to acetaldehyde vapour alone or simultaneously to benzo(a)pyrene or diethylnitrosamine. Eur. J. Cancer Clin. Oncol. 18: 13-31.

Fisher, S.E., M. Atkinson, I. Holzman, R. David, and D.H. Van Thiel. 1981a. Effects of ethanol upon placental uptake of amino acids. Prog. Biochem. Pharmacol. 18: 216-223.

Fisher, S.E., M. Atkinson, D.H. Van Thiel, E. Rosenblum, R. David, and I. Holzman. 1981b. Selective fetal malnutrition: effects of ethanol and acetaldehyde upon *in vitro* uptake of alpha amino isobutyric acid by human placenta. Life Sci. 29: 1283-1288.

Fisher, S.E., M. Atkinson, and D.H. Van Thiel. 1984. Selective fetal malnutrition: the effect of nicotine, ethanol, and acetaldehyde upon *in vitro* uptake of a alpha-aminoisobutyric acid by human placenta. Dev. Pharmacol. Ther. 7: 229-238.

Garberg, P., E-L Akerblom, and G. Bolcsfoldi. 1988. Evaluation of a genotoxicity test measuring DNA strand breaks in mouse

lymphoma cells by alkaline unwinding and hydroxyapatite elution. Mutat. Res 203: 155-176.

Greenwald, I.S., and H.R. Horvitz. 1980. unc-93 (e1500): a behavioral mutant of *Caenorhabditis elegans* that defines a gene with a wild-type null phenotype. Genetics 96: 147-164.

He, S.M. and B. Lambert. 1985. Induction and persistence of SCE-inducing damage in human lymphocytes exposed to vinyl acetate and acetaldehyde *in vitro*. Mutat. Res. 158: 201-208.

Hemminki, K., K. Falck, H. Vainio. 1980. Comparison of alkylation rates and mutagenicity of directly acting industrial and laboratory chemicals. Arch. Toxicol. 46: 277-285.

Henderson G.I., D. Turner, R.V. Patwardhan, L. Lumeng, A.M. Hoyumpa, and S. Schenker. 1981. Inhibition of placental valine uptake after acute and chronic maternal ethanol consumption. J. Pharmacol. Exper. Ther. 216: 465-472.

Henderson G.I., R.V. Patwardhan, S. McLeroy, and S. Schenker. 1982. Inhibition of placental amino acid uptake in rats following acute and chronic ethanol exposure. Alcoholism 6: 495-500.

Higuchi, Y., and N. Matsumoto. 1984. Embryotoxicity of ethanol and acetaldehyde: direct effects on mouse embryo *in vitro*. Congen. Anom. (Senten IJO) 24: 9-28.

Hilaro et al. 1985.

IARC. 1987. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans. Supplement 7. Overall Evaluations of Carcinogenicity: An updating of IARC monographs volumes 1 to 42. International Agency for Research on Cancer. World Health Organization, Lyon, France.

Jacob, D. J., E. W. Gottlieb, and M. J. Prather. 1989. Chemistry of a polluted boundary layer. J. Geophys. Res., 94:12975-13002.

Jansson, T. 1982. The frequency of sister chromatid exchanges in human lymphocytes treated with ethanol and acetaldehyde. Hereditas 97: 301-303.

Johnson, D.E., Y.-B. Chiao, J.S. Gavaler, and D.H. Van Thiel. 1981. Inhibition of testosterone synthesis by ethanol and acetaldehyde. Biochem. Pharmacol. 36: 1827-1831.

Kalmus G. and C. Buckenmaier. 1989. Effects of ethanol and acetaldehyde on cultured pre-implantation mouse embryos. Experientia 45: 484-487.

Kane, L.E., R. Dombroske, and Y. Alarie. 1980. Evaluation of sensory irritation from some common industrial solvents. Am. Ind. Hyg. Assoc. J. 41: 451-455.

Korte, A. and G. Obe. 1981. Influence of chronic ethanol uptake and acute acetaldehyde treatment on the chromosomes of bone-marrow cells and peripheral lymphocytes of Chinese hamsters. Mutat. Res. 88: 389-395.

Kruysse, A., V.J. Feron, and H.P. Til. 1975. Repeated exposure to acetaldehyde Vapor. Arch. Environ. Health. 30: 449-452.

Lahdetie, J. 1988. Effects of vinyl acetate and acetaldehyde on sperm morphology and meiotic micronuclei in mice. Mutat. Res. 202: 171-178.

Lam, C.W., M. Casanova, and H. D'A. Heck. 1986. Decreased extractability of DNA from proteins in the rat nasal mucosa after acetaldehyde exposure. Fund. Appl. Toxicol. 6: 541-550.

Lambert, B., Y. Chen, S.M. He, and M. Sten. 1985. DNA cross-links in human leucocytes treated with vinyl acetate and acetaldehyde *in vitro*. Mutat. Res. 146: 301-303.

Laumbach, A.D., S. Lee, J. Wong, U.N. Streips. 1976. Studies on the mutagenicity of vinyl chloride metabolites and related chemicals. Proceedings of the 3rd International Symposium on the Prevention and Detection of Cancer, Vol. 1, pp. 155-169.

Lewis. R.J., and R.L. Tatkin. 1983. Registry of toxic effects of chemical substances. 1981-1982 ed. Cincinnati, OH: U.S. Department of Health and Human Services, National Institute for Occupational Safety and Health; p. 156; DHHS (NIOSH) publ. no. 83-107.

Ligocki, M.P., R.R. Schulhof, R.E. Jackson, M.M. Jimenez, G. Z. Whitten, G.M. Wilson, T.C. Meyers, and J.L. Fieber. 1992. Modeling the effects of reformulated gasolines on ozone and toxics concentrations in the Baltimore and Houston areas. Systems Applications International, San Rafael, California (SYSAPP-92/127).

Ligocki, M.P., G.Z. Whitten, R.R. Schulhof, M.C. Causley, and G.M. Smylie. 1991. Atmospheric transformation of air toxics:

benzene, 1,3-butadiene, and formaldehyde. Systems Applications International, San Rafael, California (SYSAPP-91/106).

Ligocki, M.P. and G.Z. Whitten. 1991. Atmospheric transformation of air toxics: acetaldehyde and polycyclic organic matter. Systems Applications International, San Rafael, California (SYSAPP-91/113).

Mannsville Chemical Products Corporation. 1984. Chemical products synopsis. Acetic acid. Cortland, NY: Mannsville Chemical Products Corporation.

Marnett, L.J., H.K. Hurd, M.C. Hollstein, D.E. Levin, H. Esterbauer, and B.N. Ames. 1985. Naturally occurring carbonyl compounds are mutagenic in *Salmonella* tester strain TA104. Mutat. Res. 148: 381-382.

Mohan, M., U. Rai, L.P. Reddy, C.V. Prasanna, and S. Ramakrishnan. 1981. Cardiovascular effects of acetaldehyde in guinea pigs. Indian J. Physiol. Pharmacol. 25: 246.

Mortelmans, K. S. Haworth, T. Lawlor, W. Speck, B. Tainer, and E. Zeiger. 1986. *Salmonella* mutagenicity tests: II. Results from testing of 270 chemicals. Environ. Mutagen. 8: 1-39.

Norppa, H., F. Tursi, P. Pfäffli, J. Mäki-Paakkanen, and H. Järventaus. 1985. Chromosome damage induced by vinyl acetate through *in vitro* formation of acetaldehyde in human lymphocytes and Chinese hamster ovary cells. Cancer Res. 45: 4816-4821.

National Research Council. 1977. Drinking water and health: part II, chapters 6 and 7. Washington, D.C.: National Academy of Sciences; pp. VI-219-VI-220. Available from: NTIS, Springfield, VA; PB-270423.

National Research Council. 1981. Formaldehyde and other aldehydes. Washington, D.C.: National Academy Press.

Obe, G. and B. Beer. 1979. Mutagenicity of aldehydes. Drug and Alcohol Dependence 4: 91-94.

Obe, G. and H. Ristow. 1977. Acetaldehyde, but no ethanol, induces sister chromatid exchanges in Chinese hamster cells *in vitro*. Mutat. Res. 56: 211-213.

Obe, G., R. Jonas, and S. Schmidt. 1986. Metabolism of ethanol *in vitro* produces a compound which induces sister-chromatid exchanges in human peripheral lymphocytes *in vitro*: acetaldehyde, not ethanol, is mutagenic. Mutat. Res. 174: 47-51.

Obe, G., A.T. Natarajan, M. Meyers, and A. Den Hertog. 1979. Induction of chromosomal aberrations in peripheral lymphocytes of human blood *in vitro*, and of SCEs in bone-marrow cells of mice *in vitro* by ethanol and its metabolite acetaldehyde. Mutat. Res. 68: 291-294.

Olson, T.M. and M.R. Hoffmann, 1989. Hydroxyalkylsulfonate formation: its role as a S(IV) reservoir in atmospheric water droplets. Atmos. Environ., 23: 985-997.

Omel'yantes, N.I., N.V. Mironets, N.V. Martyshchenko, I.A. Gubareva, L.F. Piven, and S.N. Starchenko. 1978. Experimental substantiation of the maximum permissible concentrations of acetone and acetaldehyde in reclaimed potable water. Biol. Aviakosm Med. 1978: 67.

O'Shea, K.S. and M.H. Kaufman. 1979. Teratogenic effects of acetaldehyde: implications for the study of fetal alcohol syndrome. J. Anat. 128: 65-76.

O'Shea, K.S. and M.H. Kaufman. 1981. Effects of acetaldehyde on neuroepithelium of early mouse embryos. J. Anat. 132: 107-118.

Padmanabhan, R., R.N. Sreenathan, and S. Singh. 1983. Studies of the lethal and teratogenic effects of acetaldehyde in the rat. Conge. Anom. (Senten IJO) 23: 13-23.

Perry, R.H. and Chilton, C.H. 1973. Chemical Engineer's Handbook, Fifth Edition. McGraw-Hill Book Company.

Pool, B.L., and M. Wiessler. 1981. Investigations on the mutagenicity of primary and secondary α-acetoxynitrosamines with *Salmonella typhimurium*: activation and deactivation of structurally related compounds by S-9. Carcinogenesis 2: 991-997.

Popov, V.B., B.L. Vaisman, V.P. Puchkov, and T.V. Ignat'eva. 1982. Toxic effects of ethanol and its biotransformation products on post-implantation embryos in culture. Bull. Exp. Biol. Med. (Rus.) 92: 1707-1710.

Prasanna, C.V., S. Ramakrishnan, B. Krishnan, and A. Srinivasa Rao. 1981. Effect of acetaldehyde on lung surfactant. Indian J. Exp. Biol. 19: 580-581.

Prescott, P.K. 1985. The effect of acetaldehyde and 2,3-butanediol on rat embryos developing *in vitro*. Biochem. Pharmacol. 34: 529-532.

Rieger, R., and A. Michaelis. 1960. Chromosomenaberrationen nach Einwirkung von Acetaldehyd auf Primawurzeln von *Vicia faba*. Biol. Zbl. 79: 1-5.

Ristow, H. and G. Obe. 1979. Acetaldehyde induces cross-links in DNA and causes sister-chromatid exchanges in human cells. Mutat. Res. 58: 115-119.

Saladino, A.J., J.C. Willey, J.F. Lechner, R.C. Grafstrom, M. LaVeck, and C.C. Harris 1985. Effects of formaldehyde, acetaldehyde, benzoyl peroxide, and hydrogen peroxide on cultured normal human bronchial epithelial cells. Cancer Res. 45: 2522-2526.

Santucci, L., T.J. Graham, and D.H. Van Thiel. 1983. Inhibition of testosterone production by rat Leydig cells with ethanol and acetaldehyde: prevention of ethanol toxicity with 4-methylpyrazole. Alcoholism 7: 135-139.

Shikiya, D.C., C.S. Liu, M.I. Kahn, J. Juarros, and W. Barcikowski. 1989. In-vehicle air toxics characterization study in the south coast air basin. South Coast Air Quality Management District, El Monte, CA. May, 1989.

Sim, V.M., and R.E. Prattle. 1957. Effect of possible smog irritants on human subjects. JAMA J. Am. Med. Assoc. 165: 1908-1913.

Sina, J.F., C.L. Bean, G.R. Dysart, V.I. Taylor, and M.O. Bradley. 1983. Evaluation of the alkaline elution/rat hepatocyte assay as a predictor of carcinogenic/mutagenic potential. Mutat. Res. 113: 357-391.

Sittig, M. 1979. Haxardous and toxic effects of industrial chemicals. Park Ridge, NJ: Noyes Data Corporation; pp. 1-2.

Skog, E. 1950. A toxicological investigation of lower aliphatic aldehydes. I. toxicity of formaldehyde, acetaldehyde, propionaldehyde butyraldehyde; as well as acrolein and crotonaldehyde. Acta Pharmacol. Toxicol. 6: 299-318.

Sreenathan, R.N. and R. Padmanabhan. 1984. Structural changes of placenta following maternal administration of acetaldehyde in the rat. Z. Mikrosk. Anat. Forsch. (E.Germ.) 98: 597-600.

Sreenathan, R.N., R. Padmanabhan, and S. Singh. 1982. Teratogenic effects of acetaldehyde in the rat. Drug Alcohol Depend. 9: 339-350.

Sreenathan, R.N., S. Singh, and R. Padmanabhan. 1984a. Implications of the placenta in the acetaldehyde-induced intra-uterine growth retardation. Drug Alcohol Depend. 13: 199-204.

Sreenathan, R.N., S. Singh, and R. Padmanabhan. 1984b. Effects of acetaldehyde on skeletogenesis in the rat. Drug Alcohol Depend. 14: 165-174.

Thompson, P.A.C., and P.I. Folb. 1982. An *in vitro* model of alcohol and acetaldehyde teratogenicity. J. Appl. Toxicol. 2: 190-195.

Veghelyi, P.V., M. Osztovics, G. Kardos, L. Leisztner, E. Szaszovszky, S. Igali, and J. Imrei. 1978. The fetal alcohol syndrome: symptoms and pathogenesis. Acta Paediatria Academiae Scientiarum Hungaricae 19: 171-189.

Versar Inc. 1975. Identification of Organic Compounds in Effluents From Industrial Sources.

Watanabe, F. and S. Sugimoto. 1956. Study on the carcinogenicity of aldehyde, 3rd report: four cases of sarcomas of rats appearing in the areas of repeated subcutaneous injections of acetaldehyde. Gann 47: 599-601.

Webster, W.S., D.A. Walsh, S.E. McEwen, and A.H. Lipson. 1983. Some teratogenic properties of ethanol and acetaldehyde in C57BL/6J mice; implications for the study of fetal alcohol syndrome. Teratol. 27: 231-243.

Wilson, A. et al. 1991. Air toxics microenvironment exposure and monitoring study. South Coast Air Quality Management District, El Monte, CA.

Windholz, M., S. Budavari, R.F. Blumetti, and E.S. Otterbein, eds. 1983. Acetaldehyde. In: The Merck Index: an encyclopedia of chemicals, drugs, and biologicals. 10th ed. Rahway, NJ: Merck and Co., Inc.; p. 30.

Woodruff, R.C., J.M. Mason, R. Valencia, and S Zimering. 1985. Chemical mutagenesis testing in *Drosophila*. V. Results of 53 coded compounds tested for the National Toxicology Program. Environ. Mutagen. 7: 677-702.

Woutersen, R.A., and Appelman L.M. 1984. Lifespan inhalation carcinogenicity study of acetaldehyde in rats. III. Recovery after 52 weeks of exposure. Report No. V84.288/190172. CIVO-Institutes TNO, The Netherlands.

Woutersen, R.A. Van Garderen-Hoetmer, A., and Appelman, L.M. 1985. Lifespan (27 months) inflation carcinogenicity study of acetaldehyde in rats. Report No. V85.145/190172. CIVO-Institutes TNO, The Netherlands.

Woutersen, R.A., L.M. Appelman, A. Van Garderen-Hoetmer, and V.J. Feron. 1986. Inhalation toxicity of Acetaldehyde in rats. III. Carcinogenicity study. Toxicology. 41: 213-231.

Woutersen, R.A., and V.J. Feron. 1987. Inhalation toxicity of acetaldehyde in rats. IV. Progression and regression of nasal lesions after discontinuation of exposure. Toxicology. 47: 295-305.

Zorzano, A. and E, Herrera. 1989. Disposition of ethanol and acetaldehyde in late pregnant rats and their fetuses. Pediat. Res. 25: 102-106.

9.0 DIESEL PARTICULATE MATTER

9.1 Chemical and Physical Properties

Diesel exhaust particulate matter consists of a solid core composed mainly of carbon, a soluble organic fraction, sulfates, and trace elements. When comparing the size distribution of diesel particles to gasoline particles the majority of the diesel particles range from 0.1 to 1.0 µm with a peak at around 0.15 µm, while the gasoline particles range from 0.01 to 0.1 µm with the peak at around 0.02 (NRC, 1982). When a particle is less than 1 micron (µm) in diameter it is small enough to be inhaled deeply into the lungs. Although the gasoline particles are smaller, the light-duty diesel engines emit from 30 to 100 times more particles than comparable catalyst-equipped gasoline vehicles (NRC, 1982). At temperatures above 500°C the particles themselves are actually solid chain aggregates of carbon-hydrogen spheres with diameters ranging from 100 to 800 angstroms (Å). These are mainly attributed to the incomplete combustion of fuel hydrocarbons, though some may be due to engine oil or other fuel components. Photomicrographs show that diesel particles have a very light, fluffy structure, with a density of about 0.07 g/m^3 (NRC, 1982).

At temperatures below 500°C, the particles become coated with adsorbed and condensed high molecular weight organic compounds. Typically, about 25 percent of the particle consists of extractable organics, although different vehicles may have extractable fractions of 5-90 percent, depending on operating conditions. These compounds include open-chain hydrocarbons of 14-35 carbon atoms, alkyl-substituted benzenes, and derivatives of the polycyclic aromatic hydrocarbons (PAH), such as ketones, carboxyaldehydes, acid anhydrides, hydroxy compounds, quinones, nitrates, and carboxylic acids (Johnson, 1988). There are also heterocyclic compounds containing sulfur, nitrogen, and oxygen atoms within the aromatic ring. Inorganic compounds also are present and include sulfur dioxide, nitrogen dioxide, and sulfuric acid (NRC, 1982).

To best describe the diesel particle content adequately, the temperature at the time of the sample collection and the means by which that temperature was reached must be specified. Diesel particulate matter is generally defined as any material that is collected, at a temperature of 52°C or less, on a filtering medium after dilution of the raw exhaust gases (NRC, 1982). Water that condenses on the filter is not considered to be diesel particulate matter.

9.2 Formation and Control Technology

The chemical mechanism which accounts for carbon formation by diesel engines is not completely established (EPA, 1990b); the major weight of scientific opinion seems to support some role for intermediate formation of polycyclic aromatic matter (POM) in the process. Carbon is a stable combustion product normally of rich

flames; carbon formation normally takes place over a rather narrow temperature range. A significant fraction of the diesel particulate matter consists of oil-derived hydrocarbons and related solid matter. The formation of the carbon particle is thought to involve polymerization of gaseous intermediates at the surface of the smaller particles. Growth and agglomeration of the carbon particles are probably gas-to-particle processes. The POM's that are produced in the combustion process are adsorbed onto the surface of the carbon particle. Several of these, such as benzo[a]pyrene (B[a]P) and 1-nitropyrene, are known or potential human carcinogens. Recent data have indicated that the particles themselves may have intrinsic toxic and carcinogenic properties.

Studies of diesel particle composition have produced some information about the fate of fuel sulfur (EPA, 1990b). Sulfate has been found to be a significant component of diesel particles. Generally, the sulfate found in particles accounts for only about 2% of the fuel sulfur, the balance being emitted as sulfur dioxide. At present, no means of reducing sulfate formation is available other than reducing the sulfur concentration of diesel fuel.

EPA's Five City Study (EPA, 1989) determined that POM contributed to 27% of the average excess aggregate cancer incidence in the five cities. Of this 27%, diesel particulate matter was the major contributor, accounting for 45% of the total POM.

The control of diesel emissions can take two forms. The first is controlling emissions before they are formed with either engine modifications or aftertreatment systems to the exhaust system. Each of these takes many forms and are in various stages of development (EPA, 1990b).

One way to modify the engine is by refining the combustion process and many different modifications are in use. Many new diesel engines being made today are going from the indirect to the direct injection engine. These direct injection engines are low-emitting and fuel efficient. Also being considered are changes to the combustion chamber design to decrease emissions.

At this time, most diesel engines still rely on mechanical engine control systems. On newer engines, there is now expanded use of computerized electronic control systems that increase the potential flexibility in controlling emissions.

Another technology used to control emissions is the combined technology of turbocharging and intercooling. Most heavy duty diesel engines have them and were required for virtually all engines in 1991. The turbocharger increases the air mass in the cylinder and the intercooler reduces the temperature. This system is successful in reducing both NO_x and diesel particle emissions as well as increasing fuel economy and power output. Also being considered for use on some heavy duty engines is

intake manifold tuning. At this time, it is being used on high-performance cars to enhance the airflow.

Control of the lubricating oil is important to diesel particulate matter reduction since 10 to 50% of the particulates being formed are from engine oil. Oil consumption can be reduced primarily by improved engine manufacturing specifications and engine seals.

A second way to control emissions is to add aftertreatment technologies to the exhaust system. A trap oxidizer is being considered. This is located in the exhaust system to trap the particulate matter and provide some means of cleaning the filter by burning the collected particulate matter. Passive system traps, traps that attain the proper conditions for regeneration during normal operation, require the use of a catalyst in most cases. Some catalysts being considered are platinum, palladium, rhodium, silver, vanadium, and copper. Cerium has also been considered as a fuel additive to be used with the catalyst. There is still development to be done in this area.

Catalytic convertors are another technology being evaluated along with fuel modifications. By reducing the sulfur (now at a maximum of 0.05% by weight) and aromatic hydrocarbon content, emissions of diesel particles and POM can be reduced. Fuel additives are also being tested.

Alternative fuels are being researched for use in diesel engines. The fuels being tested at this time are natural gas, methanol, and liquified petroleum gas.

9.3 Emissions

9.3.1 Diesel Particulate Matter Emission Standards

Diesel particulate matter emission standards for light duty vehicles (LDVs), light duty trucks (LDTs), and HDDEs are summarized in Table 9-1. The LDV and LDT categories include both gasoline and diesel powered vehicles.

9.3.2 Methodology

As mentioned in section 3.2, the urban diesel particulate matter national fleet average emission factors derived by Sienicki (1992a, 1992b) are used for this analysis. The general methodology used by Sienicki to calculate urban diesel particulate matter is summarized in the appendix of MVMA and EMA (1986). All input data

Table 9-1. Diesel Particulate Matter Emission Standards.

Year	LDV[a] (gpm)	LDT1[bc] (gpm)	LDT2[bc] (gpm)	LDT3[bc] (gpm)	LDT4[bc] (gpm)	HDDE Urban bus (g/bhp-hr)	HDDE Other diesels (g/bhp-hr)
1982–1986	0.60	0.60	0.60	0.60	0.60	None	None
1987	0.20	0.26	0.26	0.26	0.26	None	None
1988–1990	0.20	0.26	0.26	0.26	0.26	0.60	0.60
1991	0.20	0.26	0.26	0.26	0.26	0.25	0.25
1992	0.20	0.26	0.26	0.26	0.26	0.25	0.25
1993	0.20	0.26	0.26	0.26	0.26	0.10	0.25
1994	0.08/ 0.10[d]	0.26	0.26	0.10	0.12	0.05	0.10
1995+	0.08/ 0.10[d]	0.08/ 0.10[d]	0.08/ 0.10[d]	0.10	0.12	0.05	0.10

[a]1994 standards are phased in over three years: 40% MY 1994, 80% MY 1995, 100% MY 1996 and after.

[b]1995 standards are phased in over three years: 40% MY 1995, 80% MY 1996, 100% MY 1997 and after.

[c]Light light-duty trucks consist of weight categories LDT1 and LDT2, and are less than or equal to 6000 lbs. gross vehicle weight rating (GVWR). Heavy light-duty trucks consist of weight categories LDT3 and LDT4, and are greater than 6000 lbs GVWR. LDT1 = light light-duty trucks up to 3750 lbs loaded vehicle weight (LVW). LDT2 = light light-duty trucks greater than 3750 lb LVW. LDT3 = heavy light-duty trucks up through 5750 lbs adjusted loaded vehicle weight (ALVW). LDT4 = heavy light-duty trucks greater than 5750 lbs ALVW. LVW = curb weight (nominal vehicle weight) plus 300 lbs. ALVW = numerical average of curb weight and GVWR.

[d]The first number is the 5 year/50,000 mile standard; the second number is the 10 year/100,000 mile standard.

and values calculated in each step of Sienicki's analysis are contained in Appendix G.

Urban diesel particulate matter emissions can simply be considered as the product of urban diesel vehicle miles travelled and the diesel particle emission rate:

$$(1) \quad DP = UVMT_d \times ER$$

where: DP = Urban Diesel Particulate Matter Emissions (g)
            $UVMT_d$ = Urban Diesel Vehicle Miles Travelled (mi)
            ER = Diesel Particulate Matter Emission Rate
(g/mi).

DP is calculated separately for each vehicle class by model year for the 20 most recent model years; these values are then added to obtain overall urban diesel particulate matter for the year of interest. However, to calculate $UVMT_d$ and ER for individual classes in a model year, a series of steps, which will be detailed in the following sections, must first be employed.

An overall national fleet emission factor (EF) in grams per mile can be calculated by dividing the total DP, after applying a freeway road use adjustment (described later), by total UVMT for both gas and diesel vehicles:

$$2) \quad EF = Total\ DP/Total\ UVMT$$

9.3.2.1 Calculation of Urban Diesel Vehicle Miles Travelled

$UVMT_d$ is determined as the product of fleet VMT, diesel mile fraction (DMF), and the diesel urban fraction (DUF):

$$(3) \quad UVMT_d = VMT \times DMF \times DUF.$$

The DMF is the ratio of diesel miles travelled divided by total miles travelled.   It can be calculated using the following equation:

$$(4) \quad DMF = DSF/\{(DSF + (1 - DSF)(VMT_g/VMT_d)\}$$

where: DSF = Diesel Sales Fraction
            VMT_g = gasoline annual vehicle miles travelled
            VMT_d = diesel annual vehicle miles travelled.

DSF is obtained by dividing diesel market shares by 100 (listed for each vehicle class by model year in Appendix G). Sienicki based the diesel market shares he used on industry opinion. The industry opinion he used predicts lower LDDV and LDDT sales than MOBILE4 (EPA, 1988). Sienicki used several sources to obtain his gasoline and diesel annual VMT rates. For all vehicle classes except buses, two sources were used -- the MVMA and EMA analysis (MVMA and EMA, 1986) and MOBILE4 (EPA, 1991a). The annual VMT rates for buses were based on data from the American Public Transport Association (APTA, 1990).

Sienicki calculated fleet VMT by model year in each class (VMT_y) as the product of the VMT fraction for each model year in a given class ($VMTf_y$) and the total VMT for each class (TVMT):

$$(5) \quad VMT_y = VMTf_y \times TVMT$$

$VMTf_y$ is calculated by multiplying vehicle sales per vehicle class for each model year (VEH_y) by annual VMT for gas and diesel vehicles (VMT_y) and the survival rate (SR_y), then dividing the product by the sum of products for all model years:

$$6) \quad VMTf_y = \frac{VEH_y \times VMT_y \times SR_y}{\displaystyle\sum_{y=1}^{20} (VEH_y \times VMT_y \times SR_y)} .$$

Vehicle sales per vehicle class were estimated by first establishing a base 20 year sales fleet from historical data, up to the year 1990. The sales fleet from the MVMA and EMA analysis (MVMA and EMA, 1986) was updated using data mostly from MVMA (1991). For estimation of diesel particulate matter in future years (1995, 2000, 2010), Sienicki had to estimate growth in the size of the sales fleet for each class (and hence, growth in VMT). This was done using fuel usage growth in the transportation sector as a surrogate. Fuel usage predictions were obtained from the Department of Energy (DOE, 1991). Survival rates for all vehicles except buses were obtained from MVMA and EMA (1986). Estimation of survival rates for buses are described in Sienicki and Mago (1991). TVMT is the product of vehicle sales per vehicle class for a 20 year period ending in the target year, annual VMT, and annual SR. Mathematically, it can essentially be expressed as the denominator in Equation 6.

Sienicki's final step in determining UVMT for each class in a given model year was to multiply VMT and DMF by the diesel urban fraction (DUF), the fraction of miles travelled in urban areas by diesel vehicles in a vehicle class. Sienicki used the same DUFs found in UMTRI (1988).

9.3.2.2 Calculation of Diesel Particulate Matter Emission Rate

ERs for all classes prior to 1987 were obtained from MVMA and EMA (1986). HDDE particulate matter emission rates for 1988 through 1991 were based on mean values for each class from federal certification test results. Model years 1992 and 1993 were assumed to be the same as 1991, and for 1994 and later years, emission rates were set at the design target for the 0.10 g/bhp-hr standard at 0.084 g/bhp-hr. LDDV and LDDT rates were set to EPA emission standards (the 10 year/100,000 mile standard for 1994 and later years). Bus emission rates were assumed to be the same as those for vehicles in class VIIIB until 1993, when

they were set to a design target of 0.084 g/bhp-hr. For 1994 and
later, they were assumed to be 0.06 g/bhp-hr.

Conversion factors (CFs) were used to convert heavy duty
emission rates from g/bhp-hr to grams per mile. CFs describe the
average work per mile required for each vehicle class, and can be
calculated as the ratio of fuel density to the product of brake
specific fuel consumption (BSFC) and fuel economy (MPG) (EPA,
1988; MVMA, 1983):

$$6) \quad CF = Fuel\ Density/(BSFC \times MPG)$$

Conversion factors predicted for future years must take into
account any improvements in vehicle efficiency. Although EPA's
MOBILE4 emissions model assumes no improvement in heavy duty
vehicle efficiency after 1986 (EPA, 1988), Sienicki claims that a
number of factors, such as increased market penetration of radial
tires and aerodynamic bodies, higher efficiency radial tires and
electronic emission control will continue to improve vehicle
efficiency. He developed efficiency improvement factors based on
fuel economy improvement and market penetration analysis prepared
by industry market analysts for each vehicle class. CFs for
future years were then calculated using previous years' CFs
divided by one plus the efficiency increase expected:

$$7) \quad CF_{y+1} = CF_y/(1+ \%\ efficiency\ increase/100)$$

EPA recently developed new conversion factors for heavy duty bus
engines (Kitchen and Damico, 1992) to more accurately reflect the
effect that different types of bus operations have on relative
levels of emissions of specific pollutants. These new heavy duty
bus conversion factors are not used in this analysis.

Sienicki also adjusted gram per mile emission rates for the
use of low sulfur fuel in 1991 and later years to obtain final
gram per mile emission rates for the 20 most recent model years
starting with the model year of interest. Sienicki assumed a
0.025 g/bhp-hr reduction in particulate matter resulting from a
0.10 weight percent change in fuel sulfur, based on results from
a recent study which addressed the effects of fuel composition on
diesel exhaust (Ullman, 1989). An earlier study (Ingham and
Warden, 1987) predicted particle reductions from fuel sulfur that
were in the same range, although slightly lower. Sienicki
assumed an average fuel sulfur level of 0.25 weight percent for
1990 and earlier years, reduced to a standard of 0.10 weight
percent in 1991-1993, and a standard of 0.05 weight percent in
1994 and later years (EPA, 1990a).

9.3.2.3 Calculation of Urban Diesel Particulate Matter Emissions

Once UMVT and ER have been calculated, DP for each model
year in a class can then be calculated using Equation 1. The sum
of DPs for the 20 most recent model years in all classes can be
combined to yield a total DP estimate for the year of interest.
After calculating a total DP for each year of interest, Sienicki
then applied a final adjustment to his total DP estimates to

account for freeway road use. While the heavy duty transient
emission test cycle assumes 25% freeway operation, a recent
University of Michigan study (1988) estimated that class VIIIB
vehicles accumulated 73% of their VMT on freeways when in large
urban areas. Sienicki adjusted for this discrepancy using the
following equation:

$$8) \quad DPAdj = DP \times [(1 - FMF) \times (4/3 - 1/3 \times FFR) + FMF \times FFR]$$

where: DPAdj = adjusted diesel particulate mass
                   FMF = freeway mileage factor
                   FFR = freeway factor ratio

FMF values were reported in the recent University of Michigan
study (1988), and FFR is the ratio of freeway and non-freeway
emission rates in grams per mile. A detailed explanation of this
equation, and the derivation of terms in this equation can be
found in Sienicki and Mago (1991).

9.3.2.4 Calculation of the Urban Diesel Particulate Matter
National Fleet Average Emission Factor

     The urban diesel particulate matter national fleet average
EF can be calculated using Equation 2. Total UVMT in Equation 2
is the sum of $UVMT_d$ and gasoline urban vehicle miles travelled
($UVMT_g$):

$$9) \quad Total\ UVMT = UVMT_g + UVMT_d$$

$UVMT_g$ is calculated using the following equation:

$$10) \quad UVMT_g = VMT \times (1 - DMF) \times GUF$$

where: GUF = gasoline urban fraction

Sienicki used the same GUFs found in MVMA and EMA (1986). Urban
diesel particulate matter national fleet average EFs for 1990,
1995, 2000, and 2010 are 0.0573, 0.0305, 0.0160, and 0.009
g/mile, respectively.

     Sienicki's fleet average EFs can be compared to EFs derived
from information in a previous EPA air toxics report (Carey,
1987). Projected 1995 national fleet average EFs assuming low
and high diesel sales can be estimated using vehicle class EFs
and urban VMT fractions from this EPA report. The low diesel
sales scenario in the 1987 EPA report assumed that diesel sales
remained constant at mid-1980's levels, while the high sales
scenario assumed an increase consistent with EPA projections at
that time. The low diesel urban sales EF was 0.0359 g/mi, and
the high diesel urban sales EF was 0.0507 g/mi. The lower EF for
1995 predicted by Sienicki (0.0305 g/mi) is partly due to
development of stricter standards than predicted in 1987, and
also to such factors as even lower light duty diesel vehicle
market shares than in either of the 1987 EPA report scenarios,
Sienicki's low sulfur fuel and freeway road use adjustments, and
the smaller g/bhp-hr to g/mi conversion factors he used.

For this report, Sienicki's fleet average EFs without the freeway road use adjustments will be used for the risk estimates. This is consistent with past EPA practice. However, further investigation of the use of such freeway road use adjustments is warranted. Resulting urban diesel particulate matter national fleet average EFs for 1990, 1995, 2000, and 2010 are summarized in Table 9-2.

Table 9-2. Urban Diesel Particulate Matter National Fleet Average EFs.

Year	EF (g/mi)
1990	0.0669
1995	0.0356
2000	0.0188
2010	0.0105

9.3.3 Nationwide Diesel Particulate Matter Emissions

Sienicki's urban diesel particulate matter fleet average EFs are based on the mix of vehicle classes expected in an urban area. Urban and rural VMT fractions differ, particularly for some of the heavy duty vehicle classes where more rural use occurs. Since these heavy duty subclasses are responsible for the majority of diesel particulate matter emissions, it would not be appropriate to use urban fleet average EFs to calculate nationwide diesel particulate matter emissions. Instead, the EFs by vehicle class calculated by Sienicki (without the freeway road use adjustment) were combined using the nationwide VMT splits from the MOBILE4.1 fuel consumption model (EPA, 1992) to estimate nationwide fleet average EFs. Using this approach, the nationwide fleet average EFs for 1990, 1995, 2000, and 2010 are 0.0910, 0.0523, 0.0291, and 0.0178 g/mi respectively.

These nationwide fleet average EFs were then multiplied by total nationwide fleet VMT obtained from the MOBILE4.1 fuel consumption model to estimate nationwide diesel particulate matter emissions. No recent rural diesel particulate matter fleet average EFs were available; thus, separate rural and urban diesel particulate matter emission levels could not be estimated. Nationwide diesel particulate matter emission estimates are listed in Table 9-3. The 1990 nationwide diesel particulate matter emission estimate of 163,118 metric tons compares with a higher 1990 estimate of 384,000 metric tons for diesel vehicles in a recent EPA report on air pollutant emission estimates (EPA, 1991b).

Table 9-3. Nationwide Diesel Particulate Matter Emissions.

Year	Total Nationwide Fleet VMT (mi)	Nationwide Diesel Particulate Matter (metric tons)
1990	1793.07×10^9	163,118
1995	2029.74×10^9	106,080
2000	2269.25×10^9	66,076
2010	2771.30×10^9	49,441

9.4 Atmospheric Reactivity and Residence Times of Particulate Phase Polycyclic Organic Matter (POM)

POM species can exist in both the gas and particulate phases in the atmosphere. The distribution between the two phases is determined by the vapor pressure of the species, the ambient temperature, and the amount of airborne particulate matter present. Cold temperatures and higher aerosol concentrations lead to greater association of POM with particles. The focus of this section is on particulate phase POM, since most of the POM emitted by motor vehicles is in this form. The information that follows on transformation and residence times has been mainly excerpted from a report produced by Systems Application International for the EPA (Ligocki and Whitten, 1991).

9.4.1 Particulate-Phase Chemistry

The determination of rate constants for POM that are adsorbed to particles is difficult, because these rates are strongly influenced by the characteristics of the surface to which the POM are adsorbed. Thus, the observations reported in the literature regarding the reactivity of adsorbed POM tend to appear contradictory. Early studies and extrapolation from reactivity studies of POM in organic solution suggested that POM compounds react rapidly on surfaces (NAS, 1972). Later work demonstrated that, although POM present on substrates such as silica and alumina photolyze rapidly, POM present on coal fly ash and carbon black were resistant to photochemical degradation (Korfmacher et al., 1980, 1981; Behymer and Hites, 1985). Significant differences in photochemical degradation rates have been reported between two different fly ashes (Dlugi and Güsten, 1983).

Nonetheless, some POM may be capable of being oxidized in the particulate phase. Fox and Olive (1979) reported that 90 percent of anthracene present on atmospheric particulate matter disappeared in four days when exposed to sunlight, whereas only a small fraction of the anthracene which was exposed to ambient air but shielded from light disappeared. The conversion of POM present on diesel particulate matter and exposed to ozone has been reported (Van Vaeck and Van Cauwenberghe, 1984) and appears

to be an important removal pathway for some POM. However, Grosjean and co-workers (1983) found no degradation of benzo[a]pyrene and perylene adsorbed onto a variety of substrates, including diesel soot, over a three hour exposure to 100 ppb ozone. The conversion of POM present in soot and exposed to NO_x has also been reported (Butler and Crossley, 1981). Unfortunately, the species responsible for this observed oxidation was not determined. Even though POM react readily with N_2O_5 in the gaseous phase, the reaction of N_2O_5 with adsorbed POM is significantly lower.

9.4.2 Aqueous Phase Chemistry

POM are slightly soluble in water, and will be incorporated to some degree into clouds and rain. For species which are associated with particles, the water-affinity of the particle surface will determine the degree to which they will be incorporated into clouds and/or rain. Polycyclic ketones and quinones are much more soluble in water than the parent POM and will be incorporated into clouds and rain to a much greater degree.

9.4.3 Reaction Products

Most POM reactions proceed by addition, forming polycyclic aromatic ketones, quinones, epoxides, and nitro compounds.

Much of the focus on POM oxidation products has centered on the nitro-POM, since several of these compounds, such as the dinitropyrenes, are known to be extremely potent mutagens. Although the yields of these species are generally not large, they may still account for a significant fraction of the observed

mutagenicity of ambient POM. In diesel exhaust particulate matter, 3-nitrofluoranthene was the major constituent.

9.4.4 Polycyclic Organic Matter Residence Times

For particulate species, the rate of removal by wet and dry deposition will depend upon the particle size distribution. Large particles are removed rapidly from the atmosphere by sedimentation and impaction. Smaller particles do not contain sufficient mass to sediment or impact, but diffuse much more rapidly than do large particles. As a result, removal rates of atmospheric particles are governed by the competition between these two types of processes, and generally reach a minimum somewhere in the range 0.1 to 1.0 micrometer (μm). This size range is often referred to as the accumulation mode, because particles in this size range tend to persist, and hence accumulate. The National Ambient Air Quality Standard for PM_{10} is based on the particulate matter less than 10 μm in diameter.

Particle size distributions for a few POM have been reported. Evidence suggests that the larger, less volatile POM tend to be present on smaller particles than the smaller, more volatile POM (Pistikopoulos et al., 1990), but that all POM are primarily associated with submicron particles. Van Vaeck and Van Cauwenberghe (1978) measured particle size distributions for a set of POM finding that 90% of the 4-ring POM and 91% of the 5-ring POM are associated with particles ≤1.5 μm in diameter. These data are comprehensive, and were used in calculating the wet and dry deposition of POM.

Residence times are presented for two individual POM species: an intermediate POM (pyrene) and a particulate-phase POM (benzo[a]pyrene). These examples provide comparisons of the importance of chemical transformation to other species versus physical removal, and differences between POM species of varying size. It should be noted, however, that in some cases it is not appropriate to view atmospheric reactions as destruction pathways for toxic species, because the products formed from its destruction may be equally toxic, or even more toxic. Most POM reactions, for instance, proceed by addition, forming polycyclic aromatic ketones, quinones, epoxides, and nitro compounds.

Residence times for POM as a class are also presented. For POM as a class, however, atmospheric residence times are determined by physical processes only. Chemical reactions may transform individual compounds, but available evidence suggests that the products of this transformation are also POM species. Therefore, the residence time of POM as a class may be determined by wet and dry deposition only.

9.4.4.1 Pyrene

	Pyrene has a vapor pressure that falls within the range
where either gas phase or particulate phase processes might
dominate depending upon ambient conditions. Under wintertime
conditions, and/or high particle loading conditions, a majority
of pyrene concentration may be associated with particles.
Therefore, its atmospheric residence time is determined by both
gas-phase and particulate-phase processes.

	Residence times for pyrene were calculated by considering
gas-phase chemical reactions with OH and N_2O_5, particulate phase
chemical reaction with O_3, aqueous phase chemical reactions with
OH and O_3, and wet and dry deposition. The calculated residence
times for pyrene are presented in Table 9-4. Because of the
similarities between the chemical reactivity and physical
properties of pyrene and fluoranthene, the residence times
presented in Table 9.1 also can be considered to apply to
fluoranthene.

	The calculated residence times for fluoranthene and pyrene
range from 0.8 to 1.6 hours under summer, daytime, clear-sky
conditions. These residence times are roughly half as long as
those calculated for naphthalene, a POM present virtually
exclusively in the gas phase. As with naphthalene, gas phase
reaction with OH is the most important atmospheric removal
pathway. However, for fluoranthene and pyrene, particulate-phase
processes including reaction with O_3 and wet and dry deposition
are also significant.

	Under cloudy conditions, in-cloud chemical destruction
accounts for 10 to 30 percent of pyrene removal at night in the
summer. In the daytime and in the winter, in-cloud processes are
less important. Both the OH and O_3 oxidations contribute to the
aqueous reactivity, with the OH pathway more important in the
summertime, and both pathways important in the winter.

	Wet deposition is very rapid for particulate-phase
fluoranthene/pyrene. Particle scavenging leads to residence
times on the order of 2 to 20 hours in the wintertime. Dry
deposition is a major removal mechanism for fluoranthene/pyrene
at night,especially in winter and under cloudy-sky conditions.
Dry deposition of particulate-phase fluoranthene/pyrene is more
efficient than that of gas-phase fluoranthene/pyrene.

	Major uncertainties in the estimate of residence times for
fluoranthene/pyrene include the order-of-magnitude uncertainty in
the particle scavenging rate and the rate of reaction of the
particulate-phase species with ozone. Also significant is the
factor-of-two uncertainty in the OH radical concentration.

TABLE 9-4. Atmospheric residence time calculation for fluoranthene/pyrene. All times are in hours unless otherwise noted.

	Los Angeles		St. Louis		Atlanta		New York	
	July	Jan	July	Jan	July	Jan	July	Jan
Clear sky - day	1.2	9	0.8	18	0.8	14	1.6	30
Clear sky - night	60	80	80	90	70	60	70	130
Clear sky - avg	2	18	1.3	40	1.3	30	2	60
Cloudy - day	3	18	1.8	30	1.8	30	3	50
Cloudy - night	50	110	70	80	50	80	80	130
Cloudy - avg	5	40	3	50	3	50	5	80
Rainy - day	--[*]	2-9[**]	1.5-1.8[**]	1.0-6[**]	1.7	2-9[**]	3	0.9-6[**]
Rainy - night	--[*]	1.2-8[**]	4-18[**]	0.7-5[**]	6-17[**]	1-7[**]	4-20[**]	0.7-5[**]
Rainy - avg	--[*]	1.5-8[**]	2-3[**]	0.8-5[**]	2-3[**]	1-8[**]	3-5[**]	0.7-5[**]
Monthly Climatological Average	2	20	2	30-40[**]	2	18-30[**]	3	20-60[**]

[*]Not calculated since July rainfall is zero for Los Angeles.
[**]Range of values calculated using high and low estimates for particle scavenging.

9.4.4.2 Benzo[a]pyrene (B[a]P)

Benzo[a]pyrene is present in the particulate phase under most conditions. Therefore, its atmospheric residence time is primarily determined by particulate-phase processes. Residence times for benzo[a]pyrene were calculated by considering gas-phase chemical reaction with OH, particulate phase chemical reaction with O_3, aqueous phase chemical reactions with OH and O_3, and wet and dry deposition. The calculated residence times for benzo[a]pyrene are presented in Table 9-5. By comparison to fluoranthene/pyrene, the calculated summertime residence times are longer for benzo[a]pyrene. This is due to the greater association with particles of benzo[a]pyrene. Interestingly, however, the calculated wintertime residence times for benzo[a]pyrene are shorter than fluoranthene/pyrene. In fact the difference in residence time between summer and winter is only a factor of two to three for benzo[a]pyrene.

The reaction of O_3 with particulate-phase benzo[a]pyrene is predicted to be the dominant removal mechanism for benzo[a]pyrene under most conditions. The reaction of gas-phase benzo[a]pyrene with OH is also expected to be significant in the summertime, despite the relatively small fraction of benzo[a]pyrene present in the gas phase.

Unlike the gaseous POM, wet and dry deposition are significant
atmospheric removal mechanisms for benzo[a]pyrene . Wet deposition leads to atmospheric residence times of 0.5 to 3 hours on rainy days and contributes significantly to monthly climatological average residence time. Dry deposition is less important, but still contributes up to 30 percent of the removal.

Major uncertainties in the estimate of residence times for benzo[a]pyrene include the order of magnitude uncertainties in the rate of reaction of the particulate-phase species with ozone, and the particle scavenging rate. The calculated residence times for benzo[a]pyrene are, therefore, significantly more uncertain than those calculated for fluoranthene/pyrene.

9.4.4.3 Other POM Species

Among the particulate-phase POM, the residence times calculated for benzo[a]pyrene are probably valid for other reactive species such as perylene. However, more stable POM, such as the benzofluoranthenes, benzo[e]pyrene, and coronene, may be removed primarily by physical processes, and would have residence times up to ten times longer than that calculated for benzol[a]pyrene.

9.4.4.4 POM as a Class

The summertime residence times for pyrene and B[a]P suggest that POM are transformed relatively rapidly in the summertime. For

TABLE 9-5. Atmospheric residence time calculation for benzo[a]pyrene. All times are in hours unless otherwise noted.

	Los Angeles		St. Louis		Atlanta		New York	
	July	Jan	July	Jan	July	Jan	July	Jan
Clear sky – day	4	13	3	20	4	15	5	30
Clear sky – night	11	30	11	40	11	20	11	90
Clear sky – avg	5	19	5	30	5	17	6	50
Cloudy – day	6	19	6	30	6	18	7	50
Cloudy – night	11	30	11	40	11	20	11	90
Cloudy – avg	7	20	7	40	7	20	8	70
Rainy – day	--[*]	0.5-3[**]	0.5-3[**]	0.5-4[**]	0.5-3[**]	0.5-3[**]	0.5-3[**]	0.5-4[**]
Rainy – night	--[*]	0.5-3[**]	0.5-3[**]	0.5-4[**]	0.5-3[**]	0.5-3[**]	0.5-3[**]	0.5-4[**]
Rainy – avg	--[*]	0.5-3[**]	0.5-3[**]	0.5-4[**]	0.5-3[**]	0.5-3[**]	0.5-3[**]	0.5-4[**]
Monthly Climatological Average	6	10-18[**]	4-6[**]	20-30[**]	5-6[**]	8-17[**]	5-7[**]	16-40[**]

[*]Not calculated since July rainfall is zero for Los Angeles.
[**]Range of values calculated using high and low estimates for particle scavenging.

the case of species such as fluoranthene and pyrene, their
oxidation products will condense onto atmospheric particles. At
that point, they may be relatively stable against further
oxidation, and may persist until removed by wet and dry
deposition.

The atmospheric residence time of a generic non-reactive
particulate-phase POM that is removed only by physical processes
(i.e., wet and dry deposition) is presented in Table 9-6.
Because the algorithms used to calculate the dry deposition
velocities and wet deposition rates did not contain any city-
specific information, the calculated clear-sky and rainy
residence times are the same for all cities. The differences in
the monthly climatological average residence times reflect only
the differences in monthly rainfall among the cities.
Atmospheric residence times range from less than a day to three
days in both summer and winter.

9.4.5 Urban Airshed Modeling of POM

The explicit modeling of POM is difficult to achieve due to
the inherent complexity of POM itself. Major consideration needs
to be given to the relative abundance of the various POM species
in the atmosphere, the availability of emissions data, and
determining an area's specific area, mobile, and point sources.

Since POM basically consists of three distinct species
categories, all three would have to be taken into consideration.
These are the naphthalenes, which are an order of magnitude
higher than the concentrations of any of the other POM (thought
not among the more toxic constituents of POM); the other gas-
phase POM concentrations that are much greater than the
particulate-phase concentrations; and the particulate phase
itself. Each of these species has its own transformation and
reactivity parameters that need to be taken into consideration.

Due to these many considerations and parameters, and the
absence of software to implement these factors, the Urban Airshed
Modeling of POM was not accomplished in the St. Louis study
(Ligocki and Whitten, 1991).

However, POM was treated explicitly in the Baltimore-
Washington and Houston area studies (Ligocki et al., 1992). POM
was assigned to three species categories in the UAM-Tox (as
described above), based upon molecular weight (MW):

       NAPH   MW < 160
       POM1   160 < MW < 220
       POM2   220 < MW

The species NAPH consists largely of naphthalene and substituted
naphthalenes, which account for the bulk of the POM mass. NAPH
reacts rapidly with OH and slowly with N_2O_5. POM1 and POM2 are
represented as nonreactive. Additional information on the
modifications made to UAM to model POM explicitly are described
in the reference cited above.

Simulations for the summer Baltimore-Washington area episode resulted in slight decreases in POM with the use of federal reformulated gasoline. California reformulated gasoline resulted in larger POM decreases than federal reformulated gasoline, because of reductions in the T_{90} distillation point of the fuel. The maximum daily average POM for the 1988 base scenario was 6.8 $\mu g/m^3$. Simulated daily average POM concentrations were much lower in the Washington area (0.5-1.0 $\mu g/m^3$) than in the Baltimore area (1-6.8 $\mu g/m^3$). Motor vehicle-related NAPH accounted for about 15% of total NAPH emissions, motor vehicle-related POM1 accounted for about 43% of total POM1 emissions, and motor vehicle-related POM2 accounted for about 35% of total POM2 emissions. Furthermore, motor vehicle-related POM accounted for about 15% of the total simulated POM concentration, based on the 1995 no motor vehicle scenario.

Since no data were available on measured POM concentrations in the Baltimore-Washington area, simulated concentrations were compared to measured concentrations from other cities. Concentrations of POM in Washington were in line with concentrations in other cities, but concentrations in Baltimore appear to be overpredicted.

In the winter 1988 base scenario, the maximum daily average POM concentration was 4.4 $\mu g/m^3$, lower than in summer. NAPH emissions decreased because they were primarily influenced by evaporative emissions from asphalt paving. Emissions of POM1 and POM2, the larger POM components, increased significantly in winter because of residential wood combustion. Motor vehicle-related POM concentrations with federal reformulated gasoline use decreased more in winter than in summer, ranging from 4 to 8 percent. Motor vehicle-related POM accounted for about 10% of the maximum simulated concentration, based on the 1995 no motor vehicle scenario.

For the summer 1987 base scenario in Houston, the maximum daily average POM concentration was 3.4 $\mu g/m^3$. Motor vehicle-related NAPH accounted for about 17% of total NAPH emissions, motor vehicle-related POM1 accounted for about 24% of total POM1 emissions, and motor vehicle-related POM2 accounted for about 19% of total POM2 emissions. Furthermore, motor vehicle-related POM accounted for about 18% of the maximum simulated concentration, based on the 1995 no motor vehicle scenario. Simulations for the summer Houston episode predicted larger decreases than in the Baltimore-Washington area with the use of reformulated gasoline. Simulated concentrations of POM were in good agreement with concentrations measured in other cities.

TABLE 9-6. Atmospheric residence time calculation for a generic particulate-phase POM which is removed by physical processes only. All times are in hours unless otherwise noted.

	Los Angeles		St. Louis		Atlanta		New York	
	July	Jan	July	Jan	July	Jan	July	Jan
Clear sky – day	60	120	60	120	60	120	60	120
Clear sky – night	90	90	90	90	90	90	90	90
Clear sky – avg	70	100	70	100	70	100	70	100
Rainy – day	--[*]	0.5–4[**]	0.5–4[**]	0.5–4[**]	0.5–4[**]	0.5–4[**]	0.5–4[**]	0.5–4[**]
Rainy – night	--[*]	0.5–4[**]	0.5–4[**]	0.5–4[**]	0.5–4[**]	0.5–4[**]	0.5–4[**]	0.5–4[**]
Rainy – avg	--[*]	0.5–4[**]	0.5–4[**]	0.5–4[**]	0.5–4[**]	0.5–4[**]	0.5–4[**]	0.5–4[**]
Monthly Climatological Average	70	16–60[**]	15–50[**]	30–80[**]	12–40[**]	13–50[**]	15–50[**]	18–60[**]

[*]Not calculated since July rainfall is zero for Los Angeles.
[**]Range of values calculated using high and low estimates for particle scavenging.

9.5 Exposure Estimation

9.5.1 Annual Average Exposures Using HAPEM-MS

To obtain urban and rural annual average exposures, urban diesel particulate matter national fleet average emission factors in Table 9-2 were first multiplied by the urban and rural g/mile to $\mu g/m^3$ conversion factors obtained from HAPEM-MS for 1988 (Johnson et al., 1992):

$$CONV_{urban} = 29.4 \ (\mu g/m^3)/(g/mile)$$
$$CONV_{rural} = 15.9 \ (\mu g/m^3)/(g/mile)$$

This provides an estimate of urban and rural exposure relative to the number of vehicle miles travelled (VMT) in 1988. To obtain exposure estimates for the years of interest, these values were then multiplied by incremental adjustments to allow for the VMT increase in excess of the population increase for the year of interest. The adjustment factors used for 1990, 1995, 2000, and 2010 are 1.031, 1.123, 1.218, and 1.412, respectively. Resulting urban and rural annual average exposures for 1990, 1995, 2000, and 2010 are given in Table 9-7.

9.5.2 Comparison of HAPEM-MS to Ambient Monitoring Data

Using ambient monitoring data (EPA, 1991b, 1991c), the concentration of diesel particulate matter in ambient air samples can be estimated. For 1990, the national average total suspended particle concentration is estimated to be about 48 $\mu g/m^3$ (EPA, 1991c). This can be multiplied by percent contribution of diesel particulate matter to TSP, which is calculated to be 5.12%. This percentage was obtained by dividing an estimate for diesel emissions of 384,000 metric tons (EPA, 1991b) by a TSP estimate of 7.5×10^6 metric tons (EPA, 1991c). The resultant concentration of diesel particulate matter obtained by multiplying 48 $\mu g/m^3$ by 5.12% is 2.46 $\mu g/m^3$. This number was then adjusted for integrated exposure, resulting in integrated exposure estimate of 1.52 $\mu g/m^3$. The HAPEM-MS 1990 urban diesel particulate matter annual average exposure of 2.03 $\mu g/m^3$ is about 134% of this value. The HAPEM-MS 1990 rural diesel particulate matter annual average exposure of 1.10 $\mu g/m^3$ is about 72% of this value.

9.6 Carcinogenicity of Diesel Particulate Matter and Unit Risk Estimates

9.6.1 Most Recent EPA Assessment

A draft health assessment document for diesel emissions has been prepared (EPA, 1990b). Much of the information contained in this section has been taken from this document. An update of this document is expected shortly.

Table 9-7. Diesel Particulate Matter Annual Average Exposures.

Year	Exposure ($\mu g/m^3$)		
	Urban	Rural	Nationwide
1990	2.03	1.10	1.80
1995	1.18	0.64	1.05
2000	0.67	0.36	0.60
2010	0.44	0.24	0.39

9.6.1.1 Description of Available Carcinogenicity Data

To evaluate the carcinogenicity of diesel engine particulate emissions, controlled animal and mutagenicity studies were conducted as well as studies of populations occupationally exposed to diesel exhaust. The following paragraphs contain a brief summary of the EPA evaluation of these studies; the EPA draft document discusses these studies in more detail (EPA, 1990b).

Genotoxicity

Extensive Ames test studies with *Salmonella* have unequivocally demonstrated direct-acting mutagenic activity in both the particle and gaseous fractions of diesel exhaust (Huisingh et al., 1978; Siak et al., 1981; Claxton, 1981, 1983; Claxton and Kohan, 1981; Dukovich et al., 1981; Lewtas, 1983; Brooks et al., 1984; Matsushita et al., 1986). The induction of gene mutations has been reported in several *in vitro* mammalian cell lines after exposure to extracts of diesel particulate matter (Casto et al., 1981; Chescheir et al., 1981; Curren et al., 1981; Liber et al., 1981; Mitchell et al., 1981; Barfnecht et al., 1982; Li and Royer, 1982; Brooks et al., 1984; Morimoto et al., 1986). Dilutions of whole diesel exhaust did not induce sex-linked recessive lethals in *Drosophila* (Schuler and Niemeier, 1981) or specific-locus mutations in male mouse germ (sperm) cells (Russell et al., 1980).

Structural chromosome aberrations and sister chromatid exchanges (SCE) in mammalian cells have been induced by particles and direct diesel exhaust (Guerrero et al., 1981; Mitchell et al., 1981; Lewtas, 1983: Morimoto et al., 1986; Pereira et al., 1982; Tucker et al., 1986). Sister chromatid exchanges, but not chromosomal aberrations, were observed in Chinese hamster cells upon exposure to particle extracts (Brooks et al., 1984). Whole exhaust induced micronuclei, but not SCE or structural aberrations were found in bone marrow of male Chinese hamsters exposed to whole diesel emissions for 6 months. In shorter exposure (7 weeks), neither micronuclei nor structural aberrations were increased in bone marrow of female Swiss mice

(Pereira et al., 1981a). Likewise whole diesel exhaust did not induce dominant lethal or heritable translocations in male mice exposed for 7.5 and 4.5 weeks, respectively (Russell et al., 1980).

Analysis of caudal sperm for sperm head abnormalities was conducted (Pereira et al., 1981b) after exposure to diesel exhaust particles and it was found that the exposed incidence of abnormalities was not above the control levels. Conversely, male Chinese hamsters exposed to diesel particulate matter (Pereira et al., 1981c) exhibited almost a threefold increase in sperm head abnormalities.

Animal Studies

As early as 1955, there was evidence (Kotin et al., 1955) for tumorigenicity and carcinogenicity of acetone extracts of diesel exhaust in skin tumorigenesis tests. Also data suggested a difference in response depending on the engine operating mode. Until the mid 1980's, no chronic studies assessing inhalation of diesel exhaust, the relevant mode for human exposure, had been reported. This is, however, the route of exposure which was used in the most extensive, recent studies. Studies employing rats and an adequate experimental design were nearly all positive in demonstrating diesel exhaust-induced increases in tumorigenicity. The 9.5 percent increase in tumor incidence for female Wistar rats reported by Heinrich et al. (1986a) is supported by the report by Mauderly et al. (1987), which showed a 3.6 percent and 12.8 percent increase in tumor incidence for F344 rats following chronic exposure to diesel exhaust at particle concentrations of 3.5 and 7.0 mg/m^3, respectively. However, only one of the squamous cell tumors reported by Heinrich et al. (1986a) was classified as a carcinoma. In the Mauderly et al. (1987) study, the carcinoma incidence was 0.9, 1.3, 0.5, and 7.5 percent for the control, low, medium, and high exposure groups, respectively.

The inhalation studies by Wong et al. (1986) and Bond et al. (1990) affirm observations of the potential carcinogenicity of diesel exhaust by providing evidence for DNA damage in rats. Similarly, Iwai et al. (1986) demonstrated diesel exhaust-induced tumorigenicity in rats exposed to an exhaust particle concentration of 4.9 mg/m^3, although the sample size was small. This study also reported development of a splenic lymphoma, which represents the only nonpulmonary tumor resulting from inhalation exposure to diesel exhaust. The long-term inhalation study by Ishinishi et al. (1986) showed a greater incidence of carcinomas (6.5 percent) in rats following 30-month exposure to diesel exhaust at 4 mg/m^3, but not at lower (0.4, 1.0, or 2.0 mg/m^3) exposure levels. However, Brightwell et al. (1986) demonstrated a dose-dependent increase in tumor incidence for male and female F344 rats exposed to filtered, but no unfiltered diesel exhaust (five 16 hour periods per week), at concentrations as low as 2.2 mg/m^3 and also at 6.6 mg/m^3. Filtered and unfiltered exhaust are used to discriminate between the gaseous and particle effects. This study indicated that, for unfiltered exhaust, the tumor incidence was higher for female rats (0 percent, 15 percent, or

54 percent at 0.0, 2.2, or 6.6 mg/m^3) than for male rats (1 percent, 4 percent, or 23 percent for 0.0, 2.2, or 6.6 mg/m^3). The filtered exhaust showed no increase in tumors when compared to controls. Thus, these studies demonstrated carcinogenic effects in rats at exposure levels ranging from 2.2 to 7.0 mg/m^3.

The inhalation of whole diesel exhaust by NMRI mice (Heinrich et al., 1986a,b; Stober, 1986), Sencar mice (Pepelko and Peirano, 1983), and in rats (Takaki et al., 1989) also provided evidence of carcinogenicity. In Orthoefer et al. (1981), the exposure of Strain A mice to irradiated diesel exhaust (to simulate sunlight exposure and resulting reactions) did not produce any significant signs of gross toxicity or affect the growth rates of the mice. Exposures ranged from 20 hr/day, 7 days\week, for 7 weeks, diluted 1:13 in one experiment to an 8 week inhalation at 6 mg/m^3 in another. The mice were then held for an additional 26 weeks in clean air after cessation of exposure. Exposures to either irradiated or nonirradiated exhaust did not result in significantly increased lung tumor incidences compared with controls. Due to short exposures selected for these studies they are considered to be screening tests. The short exposure and holding periods prior to sacrifice are based upon the rapid increase in tumor rates in positive tests. The observed increase in mutagenicity of irradiated exhaust observed in chronic bioassys is discussed in Chapter 12, Section 12.4.3.

Both the Heinrich et al. (1986a) and Brightwell et al. (1986) studies provide negative results for tumorigenicity of diesel exhaust in hamsters, a species known for its resistance to tumor induction. Negative results were also presented by several other investigators (Takemoto et al., 1986; Schreck et al., 1982; Barnhart et al., 1981; Karagianes et al., 1981), but these studies tended to employ inadequate exposure durations, low exposure concentrations, or inadequate animal numbers per group. A negative study reported by Kaplan et al. (1982) contained a high incidence of tumors in the control group. Similarly, the studies using monkeys (Lewis et al., 1986) and cats (Pepelko and Peirano, 1986) were of inadequate duration (2 years) for these longer-lived species.

Alternate exposure routes including dermal exposure, skin painting, and subcutaneous injection provided additional evidence for tumorigenic effects of diesel exhaust. Evidence for tumorigenicity was demonstrated by Kotin et al. (1955) for mice to which an acetone extract of diesel exhaust particles was applied dermally. Nesnow et al. (1982) also showed that extracts from some diesel engines were potentially tumorigenic following dermal application to rodents. A significant increase in the incidence of subcutaneous tumors in female C57B1 mice was reported by Kunitake et al. (1988) for subcutaneous administration of light-duty diesel exhaust tar extract at doses of 500 mg/kg. Doses at or below 200 mg/kg, however, were negative. Takemoto et al. (1988) provided additional data for this study and reported an increased tumor incidence in the mice following injection of light-duty engine exhaust extract at doses

of 100 and 500 mg/kg. Negative results were reported by Depass et al. (1982) for skin-painting studies using mice and acetone extracts of diesel exhaust particle suspensions. However, in this study the exhaust particles were collected at temperatures of 100°C, a temperature that would minimize the condensation of vapor-phase organics and, therefore, reduce the availability of potentially carcinogenic compounds that might normally be present on diesel exhaust particles. Intraperitoneal injection studies using Strain A mice were generally negative.

Diesel exhaust is composed of gaseous and particle phases and is known to be a complex mixture containing verified and potential carcinogens. Nevertheless, because of the negative results via inhalation, the fact that most POM is adsorbed onto particles, and because the potentially carcinogenic agents present in the gaseous phase, i.e., benzene, formaldehyde, are not known to induce lung tumors, it is unlikely that this component contributes to the tumorigenic responses. A study by Grimmer et al. (1987) demonstrated that a whole exhaust condensate fraction containing polycyclic aromatic hydrocarbons (PAH) with 4 to 7 rings produced a high tumor incidence when implanted into rat lungs. It was also noted that this fraction represented only 0.8 percent of the total weight of the exhaust condensates, and that some tumorigenicity was also associated with nitroaromatic fractions. The PAH fraction produced a tumor incidence similar to that of a low concentration of benzo[a]pyrene (BaP).

Several of the previously discussed studies indicated that only the whole (unfiltered) diesel exhaust is tumorigenic or carcinogenic and that these properties are eliminated or greatly minimized in filtered diesel exhaust exposure. Inhalation experiments using tumor initiators (Brightwell et al., 1986; Heinrich et al., 1986a; Takemoto et al., 1986) did not provide conclusive results regarding the carcinogenic potential of filtered vs. whole diesel exhaust. Although the tumorigenicity of the gaseous fraction is presently unresolved and most experiments using filtered exhaust were negative, most of these experiments did not provide definitive evidence that a maximum tolerated dose was achieved. The carbon core of the exhaust particle has been determined to have carcinogenic potential. The fact that allegedly inert, insoluble biochemically, "noncarcinogenic" particles such as titanium dioxide (Lee et al., 1986) or instillation of activated carbon (Kawabata et al., 1986) have been shown to induce lung cancer at very high concentrations is of concern in this respect. Studies currently in progress, indicating that carbon black, containing essentially no organics, was as effective as diesel exhaust in lung cancer induction, (see Section 9.6.3.1) supports the approach that the carbon core plays a major role in the pulmonary carcinogenicity of diesel exhaust in rats.

Although uncertainties exist regarding the tumorigenic potential of the gaseous component and the carbon core component of diesel exhaust, it is clear that diesel exhaust is carcinogenic in animals inducing pulmonary tumors. This

contention is supported by positive results in numerous, independent studies in male and females of at least two species and by several routes of administration, including inhalation, intratracheal administration, skin painting, and subcutaneous injection.

Human Data

Certain extracts of diesel exhaust also have been demonstrated to be mutagenic and carcinogenic in humans. Since large working populations are currently exposed to diesel exhaust, and since nonoccupational exposures currently are of concern as well, the possibility that exposure to this complex mixture may be carcinogenic to humans has become an important public health issue.

A major difficulty with the occupational studies considered here was the measurement of the actual diesel exhaust exposure. Most studies compared men in job categories with presumably some exposure to diesel exhaust with either standard populations (presumably no exposure to diesel exhaust) or with men in other job categories from industries with little or no potential for diesel exhaust exposure. A few studies have included measurements of diesel fumes, but there is no standard method for the measurement. No attempt is made to correlate these exposures with the cancers observed in any of these studies, nor is it clear exactly which diesel particulate matter should be measured to assess the occupational exposure to diesel exhaust. The occupations involving potential exposure to diesel exhaust are miners, truck drivers, transportation workers, railroad workers, and heavy equipment operators.

The seven cohort studies reviewed by EPA (1990b) have mainly demonstrated an increase of lung cancer. The three cohort studies of bus company workers by Waller (1981), Rushton et al. (1983), and Edling et al. (1987) failed to demonstrate any statistically significant excess risk of lung cancer, but these studies have certain methodological problems such as small sample sizes, short follow-up periods, lack of information on confounding variables, and lack of analysis by duration of exposure or latency that preclude their use in determining the carcinogenicity of diesel exhaust. Although the Waller (1981) study had a 25-year follow-up period, the cohort was restricted to only employees (ages 45 to 64) currently in service. Employees who left the job earlier, as well as those who were still employed after age 64 and who may have died from cancer, were excluded.

Wong et al. (1985) conducted a mortality study of heavy equipment operators that demonstrated a significant increased risk of liver cancer in the total cohort and in various subcohorts. The same analysis also showed statistically significant deficits in cancers of the large intestine and rectum. Metastasis from the cancers of the large intestine and rectum to the liver probably were misclassified as primary liver cancer which lead to an observed excess risk. This study did

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demonstrate a nonsignificant positive trend for cancer of the lung with length of membership and latency. Individuals without work histories who started work prior to 1967 when records were not kept may have been the ones who were in the same job for the longest period of time. The workers without job histories included those who had the same job before and after 1967 and thus may have worked about 12 to 14 years longer; these workers exhibited significant excess risks of lung cancer and stomach cancer. If this assumption about their jobs is correct, then these site-specific causes may be linked to diesel exhaust exposure. However, this study has quite a few methodological limitations such as the absence of detailed work histories for 30 percent of the cohort and the availability of only partial work histories for the remaining 70 percent; thus, jobs were classified and ranked according to presumed diesel exposure. Information is lacking regarding duration of employment in the job categories (used for surrogate of exposure), and other confounding factors (alcohol consumption, cigarette smoking, etc.).

A two-year mortality analysis of the American Cancer Society's prospective study by Boffetta et al. (1988), after controlling for age and smoking, demonstrated an excess risk of lung cancer in certain occupations with potential exposure to diesel exhaust (railroad workers, heavy equipment operators, truck drivers, and miners). These excesses were statistically significant among miners (RR = 2.67, 95 percent CI = 1.63 to 4.37) and heavy equipment operators (RR = 2.6, 95 percent CI = 1.12 to 6.06). The elevated risks were nonsignificant in railroad workers (RR = 1.59) and truck drivers (RR = 1.24). RR (OR) and CI are defined in Section 6.6.3.4. A dose response was also observed for the truck drivers. With the exception of miners, exposure to diesel exhaust occurred in the three other occupations showing an increase in the risk of lung cancer. This study exhibited two methodological limitations. These include, the lack of representiveness of the study population composed of volunteers only and the questionable reliability of exposure data based on self-administered questionnaires which were not validated. Despite these limitations this study is suggestive of a causal association between exposure to diesel exhaust and excess risk of lung cancer.

There were two mortality studies conducted on railroad workers by Howe et al. (1983) in Canada and Garshick et al. (1988) in the United States. The Canadian study found relative risks of 1.2 and 1.35 among "possibly" and "probably" exposed groups, respectively. The trend test showed a highly significant dose response relationship with exposure to diesel exhaust and the risk of lung cancer. The main limitation of the study was the inability to separate overlapping exposures of coal dust and diesel fumes. Information on jobs was available at retirement only. There was also insufficient detail on the classification of jobs by diesel exhaust exposure. The exposures could have been noncurrent, but since the data are lacking, it is possible that observed excess could be due to the effect of both coal dust and diesel fumes and not due to just one or the other. However,

it should be noted that, so far, coal dust has not been demonstrated to be a pulmonary carcinogen in studies on coal miners. But lack of data on confounders such as asbestos and smoking makes interpretation of this study difficult. The findings of this study are, at best, suggestive of diesel exhaust being a lung carcinogen.

The most definitive evidence for linking diesel exhaust exposure to lung cancer comes from a railroad worker study conducted in the United States (Garshick et al., 1988) which was funded by EPA. Relative risks of 1.57 (95 percent CI = 1.19 to 2.06) and 1.34 (95 percent CI = 1.02 to 1.76) were found for ages 40 to 44 and 45 to 49, respectively, after the exclusion of workers exposed to asbestos. This study also found that risk of lung cancer increased with increasing duration of employment. This large cohort study with lengthy follow up and adequate analysis, including dose response (based on duration of employment as a surrogate) as well as adjustment for other confounding factors such as asbestos and smoking, makes the observed association between increased lung cancer and exposure to diesel exhaust more meaningful.

Among the seven lung cancer case-control studies reviewed in EPA (1990b), the study by Lerchen et al. (1987) was the only one that did not find increased risk of lung cancer, after adjusting for age and smoking, for diesel fume exposure. The major limitation of this study was lack of adequate exposure data derived from the job titles obtained from occupational histories. Next of kin provided the occupational histories for 50 percent of the cases which were not validated. The power of the study was small (analysis done on males only, 333 cases). On the other hand, statistically nonsignificant excess risks were observed for diesel exhaust exposure by Williams et al. (1977) in railroad workers (OR = 1.4) and truck drivers (OR = 1.34), by Hall and Wynder (1984) for workers who were exposed to diesel exhaust versus workers who were not (OR = 1.4 and 1.7 with two different criteria), and by Damber and Larsson (1987) in professional drivers (OR = 1.2). These rates adjusted for age and smoking. Both Williams et al. (1977) and Hall and Wynder (1984) had high nonparticipation rates of 47 percent and 36 percent, respectively. In addition, the self-reported exposures used in the study by Hall and Wynder (1984) were not validated. This study also had low power to detect excess risk of lung cancer for specific occupations.

The study by Benhamou et al. (1988), after adjusting for smoking, found significantly increased risks of lung cancer among French motor vehicle drivers (RR = 1.42) and transport equipment operators (RR = 1.35). The main limitation of the study was the inability to separate the exposures to diesel exhaust from those of gasoline exhausts since both motor vehicle drivers and transport equipment operators probably were exposed to the exhausts of both types of vehicles. Hayes et al. (1989) combined data from three studies (conducted in three different states) to increase the power to detect an association of lung cancer with different occupations that had high potential for exposure to

diesel exhaust. They found that truck drivers employed for more than 10 years had a significantly increased risk of lung cancer (OR = 1.5, 95 percent CI = 1.1 to 1.9). This study also found a significant trend of increasing risk of lung cancer with increasing duration of employment among truck drivers. These relative odds were computed by adjusting for birth cohort, smoking, and state of residence. The main limitation of this study is again the mixed exposures to diesel and gasoline exhausts, since information on type of engine was lacking. Potential bias may have been introduced since the way in which the cause of death was ascertained for the selection of cases varied in the three studies. The methods used in these studies to classify the occupational categories are different, hence probably leading to incompatibility of occupational categories.

In a case-control study by Steenland et al. (1990) involving truck drivers with at least 35 years of experience, the relative odds ratio was 1.89. This study also showed a dose-response trend with the risk of lung cancer increasing with increasing years of exposure when employment after 1959 was considered. The limitations of this study include possible misclassifications of exposure and smoking, lack of levels of diesel exposure, smaller exposed population, and insufficient latency period.

The most convincing comes from the Garshick et al. (1987) case-control study among railroad workers. After adjustment for asbestos and smoking, the relative odds for continuous exposure were 1.39 (95 percent CI = 1.05 to 1.83). Among the younger workers with longer diesel exhaust exposure, the risk of lung cancer increased with the duration of exposure after adjusting for asbestos and smoking. Even after the exclusion of recent diesel exposure (5 years before death), relative odds increased to 1.43 (95 percent CI = 1.06 to 1.94). This study appears to be a well conducted and well analyzed case-control study with reasonably good power. Potential confounders were controlled adequately, and interactions between diesel exhaust and other lung cancer risk factors were tested.

Of the seven bladder cancer case-control studies, four studies found increased risk in occupations with a high potential diesel exhaust exposure. A significantly increased risk of bladder cancer was found in Canadian railroad workers (RR = 9.0, 95 percent CI = 1.2 to 349.5; in Howe et al., 1980) truck drivers (OR = 2.9, Hoar and Hoover et al., 1985) and in Argentinean truck and railroad drivers (RR = 4.32; Iscovich et al., 1987). Significantly increased risks were observed with increasing duration of employment of ≥20 years in truck drivers (OR = 12) and railroad industry workers (OR = 2.21; Steenland and Burnett, 1987). No significant increased risk was found for any diesel-related occupations in studies by Wynder et al. (1985), Iyer et al. (1990), and Steinbeck et al. (1990). All these studies had several limitations including inadequate characterization of diesel exhaust exposure, lack of validation of surrogate measures of exposure, and presence of other confounding factors (urinary retention, concentrated smoke within the truck cab, etc.); most

of them had small sample sizes, and none presented any latency analysis.

In summary, in regard to lung cancer which is the endpoint used for the EPA unit risk, an excess risk of lung cancer was observed in three out of seven cohort studies and six out of seven case-control studies. Of these studies, two cohort and two case-control studies observed a dose-response relationship using duration of employment as a surrogate for dose. However, because of the lack of actual data on exposure to diesel exhaust in these studies and other methodologic limitations such as lack of latency analysis, the evidence of carcinogenicity in humans is considered to be limited for diesel exhaust exposure.

9.6.1.2 Weight-of-Evidence Judgement of Data and EPA Classification

Based upon the inductions of lung tumors in the three F344 rat studies, as well as the other research mentioned above and supported by positive results for mutagenicity, the evidence for carcinogenicity of diesel exhaust in animals is considered to be sufficient based on U.S. EPA cancer assessment guidelines.

Collectively, the epidemiological studies show a positive association between diesel exhaust exposure and lung cancer. However, because of the uncertainties due to limited exposure data and low relative risk ratios in these populations, the evidence for carcinogenicity of diesel engine emissions in humans is considered to be limited. This means that a causal interpretation is credible, but alternative explanations such as chance, bias, or confounding factors cannot be ruled out.

On the basis of limited evidence for carcinogenicity of diesel engine emissions in humans, supported by sufficient evidence in animals and positive mutagenicity data, diesel engine emissions are considered to best fit the weight-of-evidence category B1. Agents

classified into this category are considered to be probable human
carcinogens.

9.6.1.3 Data Sets Used for Unit Risk Estimates

The most critical of the above mentioned animal studies are
those that involve a chronic inhalation exposure of diesel
particulate matter. To actually determine the unit risk of this
particle, only three of the rat inhalation studies are selected
for risk calculations because each study consists of multiple
exposure groups and thus is more appropriate for risk
calculations. The three studies used are Mauderly et al. (1987),
Ishinishi et al. (1986), and Brightwell et al. (1986). These
studies are summarized in Table 9-8.

The EPA also attempted to use two epidemiological studies,
the Garshick et al. studies published in 1987 and 1988 to develop
a unit risk estimate. These are summarized in Table 9-9. Though
a relationship exists between diesel exhaust exposure and the
incidence of lung cancer, both of these studies have strengths
and weaknesses. These studies give a large sample size in a
relatively stable workforce, and also take into account the
confounding factors of smoking and asbestos exposure. The major
weaknesses at this time are the limited qualitative and
quantitative data on the exposure of these individuals and a
short follow-up period. The number of years of exposure to
diesel exhaust was used as a substitute for an actual dose so it
is difficult to accurately assess the amount of diesel exhaust
they were exposed to.

9.6.1.4 Dose-Response Model Used

The linearized multistage model is used to calculate unit
risk estimates using various dose equivalence assumptions. All
unit risk estimates that currently exist for diesel particulate
matter are based exclusively on animal data.

9.6.1.5 Unit Risk Estimates

The approach that has been adopted by EPA in determining the
unit risk from diesel particulate matter is the one that
attributes the carcinogenicity to that of the particle itself
rather than the
organics. The methodology used to develop the most recent EPA
quantitative risk estimate differs from other chronic bioassay
based estimates in several ways. Unlike earlier estimates, the
present one uses a sophisticated dosimetry model to extrapolate
lung burdens of particulate matter from animal exposures to
humans. This model accounts for species differences in
deposition efficiency, respiration rates, normal particle
clearance rates, particle transport to lung associated lymph
nodes, and effect of particle overload upon clearance rates.

TABLE 9-8. Animal Data Used for EPA's Unit Risk Estimates.

REPORT	ANIMAL	PARTICLE EXPOSURE CONCENTRATION AND TIME OF EXPOSURE	ENGINE TYPE AND CYCLE	MAJOR RESULTS
Mauderly, et al. (1987) (Lovelace)	F344/Crl rats, male and female	0.35, 3.5, and 7.0 mg/m^3 7h/d, 5d/week, for 30 mo.	1980 model 5.7L Oldsmobile V8 run at FTP hot start certification cycle	Control and low level exposure shows no statistical increase in lung tumors (0.9% and 1.3% increase in tumors respectively) Medium and high level exposure shows that the lung tumor incidence was statistically higher (3.6% and 12.8% increase in tumors respectively)
Ishinishi, et al. (1986) (JARI)	F344/Jcl rats, male and female	0, 0.1, 0.4, 1.0, or 2.0 mg/m^3 from light duty engine 0, 0.4, 2.0, or 4.0 mg/m^3 from heavy duty engine 16h/d, 6d/week, for 30 mo.	light duty engines were 1.8L-4 cylinder, swirl chamber operated at 1200 rpm heavy duty engines were 11L-6 cylinder, direct injection operated at 1700 rpm	Light duty engine exposure: carcinomas were dose-dependent with the highest incidence in the 1.0 mg/m^3 exposure (4.1% increase), there were no significant changes between groups Heavy duty engine exposure: carcinomas were dose-dependent with the highest incidence in the 4.0 mg/m^3 exposure (6.5% increase), significant changes were found between the 0 and 4.0 mg/m^3 exposure groups
Brightwell, et al.(1986) (Battelle-Geneva)	F344 rats, male and female pretreated 3d prior to exposure with tumor promoter	0.7, 2.2, or 6.6 mg/m^3, filtered and unfiltered 5-16h periods/wk over 2 yrs.	1.5L engine (no manufacturer given) using U.S. 72 (FTP) cycle	No significant increase was found in either group at low or control exposure Medium, unfiltered exposure 4-15% increase, and high, unfiltered exposure 23-54% increase in lung tumors Dose-dependent, promoter had no statistical effect

Table 9-9. Epidemiological Data Used for EPA's Unit Risk Estimates.

STUDY	TYPE AND SUBJECTS	EFFECTIVE START	PARAMETERS OBSERVED	MAJOR RESULTS

Garshick, et al. (1987)	Case-Control study on male railroad workers each cancer death (case) was matched to two randomly selected deceased workers (within 31d of death) with no evidence of cancer (control)	1959 (95% of locomotives were diesel)	Death from lung cancer between March 1, 1981 through February 28, 1982	Relative odds for lung cancer is 1.5 for the highest exposure category (low odds but 95% confidence interval is narrow) and it has been adjusted for smoking and asbestos exposure. This study supports the hypothesis that occupational exposure to diesel exhaust increases lung cancer.
Garshick, et al. (1988)	Cohort study on male railroad workers (a group of individuals having a statistical factor in common in an epidemiological study [i.e. diesel exposure])	same as above	Deaths due to lung cancer from 1959 to 1980	Relative risk for lung cancer is 1.5 (modest risk) and it has been adjusted for smoking and asbestos exposure. This study shows a positive association between occupational diesel exhaust exposure and a modest increase in lung cancer

     A important feature of the dosimetry model is that it accounts for high dose inhibition of particle clearance. If this adjustment is not made, lung burden of particulate matter will be overestimated during extrapolation to low doses with an accompanying overestimation of cancer potency. Since most of the organics desorb from the particle surface even with normal clearance rates, inhibition of particle clearance will affect the concentration of organics only slightly. Cancer potency estimates may

therefore differ depending on whether they are based upon lung burden of particles or organics.

There are two reasons for using a particle based risk assessment. First of all, the concentration of PAH's on the particles is quite small. The quantity present at the exposure levels used in the chronic bioassays is unlikely to be great enough to produce the tumor response seen. B[a]P is present at a concentration of about 1 μg/gm particulate matter. Secondly, insoluble biochemically inert particles such as titanium dioxide (Lee et al., 1986) or activated carbon (Kawabata et al., 1986) can induce lung cancer at very high concentrations. Even more significant were the findings of Mauderly et al. (1991) and Heinrich et al. (1991) (see Section 9.6.3.2) that carbon black, which is very similar to the carbon core of the diesel particle, but contains essentially no adsorbed organics, induced lung cancer at the same concentrations as diesel exhaust. Additional support for the predominance of the particle effects was also contained in the report by Heinrich et al. (1991). In this report, pyrolyzed pitch condensate, which does not have an insoluble particle core, but contains about 1000 fold greater concentration of PAHs than diesel particles, is not that much more potent than diesel exhaust in the induction of lung cancer.

While this method is an improvement over previous ones, an important uncertainty remains. Particles deposited in the alveolar regions are ingested by macrophages, which are then induced to secrete a variety of cytokines, oxidants, and proteolytic enzymes. Some combination of these are thought to act upon adjacent alveolar cells to induce tumor formation. It is uncertain if very low macrophage particle burdens will induce release of these factors, or if there is a threshold for their effects. Use of a linearized multistage model to extrapolate to low doses could result in an overestimate of risk. Data, however, are presently inadequate to prove or disprove this possibility. Thus, EPA still employs the conservative linearized low-dose extrapolation model.

The unit risks based on the long term rat inhalation studies of Mauderly et al., (1987), Ishinishi et al., (1986), and Brightwell et al., (1986) were calculated by EPA using the carbon core only. The availability of preliminary data from studies discussed in Section 9.6.3.2 conducted on animals exposed to carbon black, though not used in the risk calculations, did influence the methodology. A geometric mean of the three unit risks was then

determined to be 1.7×10^{-5} $(\mu g/m^3)^{-1}$. This unit risk was presented at the Air and Waste Management Association meeting in October, 1991 (Pepelko and Ris, 1991d). This unit risk is also presented in the latest EPA diesel draft document (unpublished). It has yet to undergo Science Advisory Board (SAB) review and thus is subject to change. EPA is also in the process of developing a unit risk estimate that attempts to account for both particle and organic effects.

Pepelko and Ris (1991d) also discussed the attempt to develop a unit risk estimate for lung cancer based on human epidemiological data using Garshick et al., (1988). Using data from this study, the EPA carried out more than 50 analyses of the relationship between diesel exhaust exposure and tumor incidence. None of these analyses demonstrated a pattern that was consistent with an association between diesel exhaust exposure and lung cancer. The inability to obtain an adequate dose response was attributed to the limitations regarding exposure estimates for the various job categories, coupled with the small increases in lung cancer mortality. Consequently, it was concluded that the data are inadequate for quantitative risk assessment.

9.6.2 Other Views and Unit Risk Estimates

This section presents alternative views and/or risk assessments for diesel exhaust particulate matter. These alternative risk assessments are summarized in Table 9-10.

Comparative Potency Method

The comparative potency method is a method developed by EPA to predict human cancer risk from mutagenicity and animal bioassay data. The comparative potency method was developed because of a lack of chronic animal bioassays and a need to develop a potency estimate in the early 1980's. It has been applied to the polycyclic organic matter (POM) from selected emission sources, including diesel vehicles (Albert et al., 1983; Lades, 1991). POM is a general term referring to a complex mixture of polycyclic aromatic compounds generally associated with the particles or soot of emissions, and derived from the combustion of fossil fuels, vegetative matter, and synthetic chemicals.

In this comparative potency method, the risk of diesel particulate matter is estimated by comparison of diesel particulate matter bioassay potencies to the bioassay potencies of known human carcinogens (coke oven, roofing tar, cigarette smoke) according to the following equation:

Table 9-10. Comparison of Diesel Exhaust Particulate Matter
Inhalation Unit Risk Estimates.

Source	Method	Cancer Unit Risk Estimate $(\mu g/m^3)^{-1}$ Upper Bound[a]
Albert et al. (1983) Lewtas (1991)	Comparative potency method using extracted organics from one light-duty (LD) diesel engine	3.5×10^{-5}
Albert et al. (1983) Lewtas (1991)	same as above, using an average of three LD engines	2.6×10^{-5}
Harris (1983)	Comparative potency method[b]	2.9×10^{-4}
Cuddihy et al. (1984)	Comparative potency method[b,c]	7.0×10^{-5}
Albert and Chen (1986)	Multistage model, lung cancer in rats[d]	1.2×10^{-5}
Pott and Heinrich (1987)	Straight line extrapolation, lung cancer in rats[e]	$6.0-12.0 \times 10^{-5}$
McClellan et al. (1989)	Logistic regression, lung cancer in rats[f]	8.0×10^{-5}
Smith and Stayner (1990)	Time-to-tumor model, lung cancer in rats[d]	$1.5-3.0 \times 10^{-5}$
Harris (1983)	Epidemiological analysis, London Transport Study (Waller, 1981)	4.1×10^{-3}
McClellan et al. (1989)	Epidemiological analysis, Railroad workers (Garshick et al. 1987)	$0.6-2.0 \times 10^{-3}$

[a]Estimated upper bound of lifetime risk of continuous exposure to 1 $\mu g/m^3$ diesel exhaust particulate matter.
[b]Used data from studies by Albert et al. (1983).
[c]Used data from studies by Harris (1983).
[d]Used data from studies by Mauderly et al. (1987).
[e]Used data from studies by Brightwell et al. (1986), Heinrich et al. (1986a), and Mauderly et al. (1987).
[f]Used data from studies by Brightwell et al. (1986), Ishinishi et al. (1986), Iwai et al. (1986), and Mauderly et al. (1987).

$$unit\ risk\ (diesel) = unit\ risk\ (known\ carc.) \left[\frac{bioassay\ potency\ (diesel)}{bioassay\ potency\ (known\ carc.)} \right]$$

The term in brackets is the ratio of the slopes of the dose responses from the same bioassay, and is referred to as the relative potency. The underlying assumption of the comparative potency method is that the relative potency is constant across different bioassay systems. The equation above was applied using the extract of a light duty Nissan engine in the mouse skin tumor initiation bioassay to estimate the risk of diesel particulate matter. The mouse skin tumor initiation bioassay was chosen because the relative potencies of the known human carcinogens obtained with this bioassay correlated well with the relative potencies obtained with the human data. The mouse skin tumor test was also used because it gave a strong dose-response in the Nissan engine.

Extracts from particle samples from three light-duty diesel vehicles and one heavy-duty diesel engine were used. The unit risk estimates for two other light duty engines and a heavy duty engine were derived by comparing their potencies with that of the Nissan engine using three short-term tests. The average lifetime risk from the three light-duty diesel samples across the three comparative human carcinogens was $2.3\times10^{-4}(\mu g$ organic matter/m$^3)^{-1}$ or $2.6\times10^{-5}(\mu g$ particles/m$^3)^{-1}$. The lifetime cancer risk/μg particles/m^3 ranged from 1.8×10^{-6} for the heavy duty engine, to 3.5×10^{-5} for the most potent light duty diesel engine (Albert et al., 1983; Lewtas, 1991).

The comparative potency method predicted a human lung cancer unit risk very similar to the unit risk estimate for diesel particulate matter that has been recently extrapolated from three rodent inhalation studies. The lifetime unit risk for the rodent studies is the same one cited earlier, $1.7\times10^{-5}(\mu g/m^3)^{-1}$. This compares to $2.6\times10^{-5}(\mu g/m^3)^{-1}$ by the comparative potency method. This demonstrates that these two independent approaches to cancer risk from diesel emissions result in very similar cancer unit risk estimates.

Harris (1983) developed comparative potency estimates for the same four engines used by Albert et al., (1983) but used only two epidemiological based potency estimates, those for coke ovens emissions and for roofing tar. Harris (1983) also used preliminary data for three of the same assays as did Albert et al., (1983). After making adjustments to adjust for lifetime exposure the Harris (1983) overall estimated unit risk value was 2.9×10^{-4} $(\mu g/m^3)^{-1}$ for the three light-duty engines.

Cuddihy et al. (1984) reported a unit risk of about 7.0×10^{-5} $(\mu g/m^3)^{-1}$ using a comparative potency method similar to those reported in the preceding paragraphs. The data base was similar to that used by Albert et al. (1983) and Harris (1983).

The comparative potency method suffers from two major uncertainties. The first being that mutagenicity is not a reliable predictor of carcinogenicity. Secondly, the relative cancer potency of diesel to the other agents used may be much different than relative potency in short-term.

Alternate Risk Estimates Derived From Rat Data

With the availability of chronic cancer bioassays, more recent assessments were based on lung tumor induction in rats. Albert and Chen (1986) reported a risk estimate based upon the chronic rat bioassay conducted by Mauderly et al. (1987). Using a multistage model and assuming equivalent deposition efficiency in humans and rats, they derived an upper bound for a lifetime risk of 1.2×10^{-5} $(\mu g/m^3)^{-1}$. Pott and Heinrich (1987) used a linear extrapolation, including data reported by Brightwell et al. (1986), Heinrich et al. (1986a), and Mauderly et al. (1987). They reported risk estimates of 6.0×10^{-5} to 12.0×10^{-5} $(\mu g/m^3)^{-1}$. Most recently, Smith and Stayner (1990), using a time-to-tumor model based on the data of Mauderly et al. (1987), derived and upper bound of 1.5×10^{-5} to 3.0×10^{-5} $(\mu g/m^3)^{-1}$. In McClellan et al. (1989) a logistic regression was used with the data from Brightwell et al. (1986), Ishinishi et al. (1986), Iwai et al. (1986), and Mauderly et al. (1987) to derived a unit risk estimate of 8.0×10^{-5} $(\mu g/m^3)^{-1}$.

Alternate Risk Estimates Derived From Epidemiological Data

Harris (1983) also assessed the risk of exposure to diesel engine emissions using data from the London Transport Worker Study by Waller (1981). Five groups of employees from the study were used (one high exposure, two intermediate exposure, and two with no exposure. Harris (1983) compared the exposed groups with internal controls. He merged the three exposed groups and compared them with the two groups considered to be unexposed. An adjustment was made for the greatest exposure groups. Using this method, the relative risk of the exposed groups was greater than 1, but was statistically significant for only the highest exposure groups from 1959 to 1960.

Harris (1983) identified a variety of uncertainties in the assessment. Taking the uncertainties into account, he derived a maximum likelihood estimate of 1.0×10^{-3} $(\mu g/m^3)^{-1}$ and a upper bound of 4.1×10^{-3} $(\mu g/m^3)^{-1}$.

McClellan et al. (1989) developed risk estimates based on the Garshick et al. (1987) study in which lung cancer in railroad workers was evaluated. Using a proportional risk model the values
of a lifetime risk of exposure to diesel exhaust ranged from 0.6×10^{-3} to 2.0×10^{-3} $(\mu g/m^3)^{-1}$.

<u>Environ</u>

The Environ report (Environ, 1987), prepared for the Motor Vehicle Manufacturers Association, was in response to the EPA report on air toxics (Carey, 1987). In its report, EPA uses a range of potency estimates, 2.0×10^{-5} to $1.0 \times 10^{-4} (\mu g/m^3)^{-1}$, for estimating the lung cancer risk from diesel exhaust. The range of potencies all involved use of the comparative potency method, described above. This Environ (1987) report as well as Carey (1987) were completed while animal inhalation studies were still in progress, so neither report evaluates more recent data.

Environ, for several reasons, questions the validity of the comparative potency approach. Although there is some evidence that activity in short-term genotoxicity tests may be indicative of carcinogenic potential, Environ cites studies that show the correlation between genotoxicity and carcinogenicity was just 60%. Also, quantitative correlations have not been established for any individual carcinogens let alone a complex mixture such as diesel particles. Environ believes this renders the procedure scientifically unsound.

Environ raises further questions regarding the validity of the procedure by challenging the fact that it is based solely on extracts of diesel particles and ignores substances in the emissions that are not associated with the particle or are not extractable. Environ also states that organics adsorbed onto the particle may not be bioavailable so using extract overestimates the potency.

Environ states that these factors may increase the uncertainty associated with the Carey (1987) risk estimates for diesel emissions. They then offer no new or additional data analysis to support their claims or a unit risk estimate of their own.

<u>International Agency for Research on Cancer (IARC)</u>

IARC (IARC, 1989), does not estimate potencies for carcinogens, but has classified diesel engine exhaust into cancer weight-of-evidence Category 2A. Agents classified into Category 2A are considered to be *probable* human carcinogens. This classification is based on limited evidence for carcinogenicity in humans. This is supported by sufficient evidence for carcinogenicity in animals with whole diesel engine exhaust and in animals with extracts of the diesel engine exhaust particles. IARC considers the evidence for the carcinogenicity in animals of the gas-phase of diesel engine exhaust (with particles removed) to be inadequate. EPA did not develop separate weight-of-evidence evaluations for the gaseous and particle phases of diesel exhaust.

<u>National Institute for Occupational Health and Safety (NIOSH)</u>

In 1986, NIOSH evaluated the health effects of diesel exhaust in <u>Evaluation of the Potential Health Effects of</u>

Occupational Exposure to Diesel Exhaust in Underground Coal Mines. This document describes the short-term effects as well as stating that there is a causal association between exposure to whole diesel exhaust and cancer.

In a later publication, NIOSH (1988), the recent animal studies in rats and mice discussed previously in Section 9.6.1 (Brightwell et al. 1986; Heinrich et al. 1986; Ishinishi et al. 1986; Iwai et al. 1986; Mauderly et al. 1987) are used to confirm an association between the induction of cancer and exposure to whole exhaust. The lung is the primary site identified with carcinogenic or tumorigenic responses following inhalation exposures. Limited epidemiological evidence (Edling et al. 1987; Garshick et al. 1987, 1988) suggests an association between occupational exposure to diesel engine emissions and lung cancer. The consistency of these toxicologic and epidemiologic findings suggests that a potential occupational carcinogenic hazard exists in human exposure to diesel exhaust.

9.6.3 Recent and Ongoing Research

9.6.3.1 Metabolism and Pharmacokinetics

Much of the information in this section is summarized from the more detailed report, the Draft Health Assessment Document for Diesel Emissions (EPA 1990b). To examine this information further please refer to the document mentioned above.

Several studies affirm the bioavailability from inhaled diesel exhaust particles of compounds such as B[a]P and 1-nitropyrene (1-NP) which are known to be carcinogenic or mutagenic. Biotransformation of B[a]P, 1-NP, and some of the dinitropyrenes to reactive intermediates following inhalation of diesel exhaust particles has been verified. Furthermore, several reports have provided data indicating the formation of DNA adducts, considered an underlying mechanism of carcinogenicity, following administration of these compounds. The development of lung tumors in experimental laboratory animals following chronic exposures to particulate diesel exhaust occurs under conditions in which alveolar macrophage-mediated particle clearance from the lung is compromised. Although tumors have also been found to develop with other types of particles (e.g., titanium oxide) when this clearance mechanism is diminished, tumors developing in the lungs of diesel emissions-exposed rats with smaller lung mass or comparatively less volume burden of diesel particles suggest that the carcinogenic response is not exclusively related to an overabundance of the particles in the lungs *per se*. Therefore, the organic components on diesel particles may be importantly involved in the development

of lung tumors. The lung's pulmonary macrophages, which phagocytize deposited diesel particles, probably participate in the gradual *in situ* extraction and metabolism of procarcinogens associated with the diesel particles. Additionally, the normal tumoricidal activities of the pulmonary macrophages may be

compromised upon interaction with excessive numbers of diesel particles, and diesel particle-macrophage interactions could lead to the generation of reactive oxygen species that have been shown to be at least mutagenic. Alternatively, there is evidence that particles with a very large surface area/unit volume, such as diesel particles or carbon black, can stimulate production of harmful products by macrophages at much lower lung burdens, perhaps even at lung burdens insufficient to inhibit clearance. Processes and potential mechanisms discussed herein have largely been derived from animal data, and further research is required to determine how the activities of human pulmonary macrophages in response to particulate diesel exhaust compare with pulmonary macrophages from experimental animals. Most importantly, valid dosimetry for the human condition will require the elucidation of the underlying mechanisms involved in the development of lung tumors following chronic exposure to whole diesel exhaust.

An understanding of the pharmacokinetics associated with pulmonary deposition of diesel exhaust particles and their adsorbed organics is critical in understanding the carcinogenic potential of diesel engine emissions. The pulmonary clearance of diesel exhaust particles is multiphasic and involves several processes including a relatively rapid mucociliary transport and slower macrophage-mediated processes. The observed dose-dependent increase in the particle burden of the lungs is due, in part, to an overloading of alveolar macrophage function. The resulting increase in particle retention has been shown to increase the bioavailability of particle adsorbed mutagenic and carcinogenic components such as B[a]P and 1-NP. Experimental data also indicate alveolar macrophage-mediated metabolism and phagolysosomal solubilization of particle-adsorbed components. Although macromolecular binding of diesel exhaust particle-derived PAH and the formation of DNA adducts following exposure to diesel exhaust have been reported, a quantitative relationship between these and increased carcinogenicity is not available.

In addition to the aforementioned points, one must also consider the fact that other compounds (e.g., gas-phase chemical irritants) may alter respiratory rate and, therefore the actual inhaled dose of potentially toxic components. Moreover, a better knowledge of particle dissolution rate and particle removal rate is necessary for more accurately assessing bioavailability of potentially carcinogenic components of diesel exhaust.

9.6.3.2 Carcinogenicity - Animal Studies

In a recent study by the Fraunhofer Institute (Heinrich et al. 1991) female Wistar rats were exposed to carbon black (CB), tar/pitch condensate (yielding PAH in the form of benzo(a)pyrene [BaP]), and mixtures of these compounds to assess their carcinogenic effect. Exposure time for all groups was 17 hrs/day, 5 days/week, for 10 and 20 month periods. A 17% increase in lung tumors incidences was reported following exposure of rats to carbon black particles for 10 months at a concentration of 6 mg/m^3, then clean air for the remainder of their lifetime. This is very close to the TLV value. The tar/pitch condensates (BaP) at 20 or 50 μg/m^3 gave increases in lung tumors of 4% and 39% at 10 months and 33% and 97% at 20 months, respectively. The mixture (2 or 6 mg/m^3 CB and 50 μg/m^3 BaP) test results were only for the 10 month period, and the increases ranged from 72 to 89%. In the abstract submitted, the authors claim carbon black in this experiment induced almost the same lung tumor rates in rats as diesel soot did in Heinrich et al. (1986a). No inferences were made concerning the greater increases in tumor incidences with pitch plus carbon black than with carbon black alone. This study shows that particles alone, devoid of organics are capable of inducing lung cancer. The study also shows that the effects of particles are enhanced by the presence of BaP. It should be noted, however, BaP concentrations in this study were much greater than those present on diesel particles.

In a study by Pott et al. (1991), also from the Fraunhofer Institute, lung tumors were observed in female Wistar rats intratracheally instilled with various non-fibrous and fibrous dusts. The percent of rats with primary lung tumors ranged from a 60 to 66% increase following exposure to 30 to 60 mg diesel soot (two types) or carbon black. The rats exposed to 45 mg of one type of diesel soot and those exposed to 45 mg of carbon black gave identical rates of 65%. This appears to support the contention that the carbon particle itself is the carcinogen. The abstract does not detail the differences in the two diesel soot types tested, nor does it provide data regarding the amounts of types of particle bound organics.

In a recent and as yet uncompleted Health Effects Institute study by Mauderly et al. (1991) of the Inhalation Toxicology Research Institute (ITRI), there was a direct comparison of carbon black particles and diesel exhaust. The study exposed F344/N rats 16 hours/day, 5 days/week for 24 months to carbon black (2.5 or 6.6 mg/m^3) or diesel exhaust (2.4 or 6.4 mg/m^3). They were sacrificed at 3, 6, 12, 18 and 23 months with remaining rats held for post-exposure observation. The results at this time are interim, but the responses to diesel exhaust and carbon black were qualitatively similar. Diesel exhaust caused a greater response than carbon black in lung weight (increased), lung burden of retained particles, and lung inflammation and cytotoxicity. Diesel exhaust and carbon black caused approximately similar responses in body weight (decreased), lymph node burden of retained particles and mortality. The numbers of

lung tumors observed grossly at necropsy were nearly identical for diesel exhaust and carbon black. Observations to date do not suggest that there is a difference between diesel exhaust and carbon black in lung tumor type, multiplicity or growth in nude mice. Mauderly et al. (1991), in the interim, concludes that the information at this time suggest that soot-associated organic compounds do not play a significant role in the pulmonary carcinogenicity of diesel exhaust in rats.

Dr. Werner Stober of the Fraunhofer Institute of Technology and Aerosol Research, whose research is funded in part by the German automobile manufacturers, states his position in several papers. This position is outlined in Stober (1987, 1989) and more recently by Stober (1991), in which the present epidemiological data, comparative potency method, and animal inhalation studies are evaluated.

A search of the scientific literature for data on the health effects (especially carcinogenic risk) of inhaled diesel emissions was performed. Dr. Stober states that this search provides some very weak and disputed epidemiological evidence suggesting that, at certain occupational exposures, there may have been a health hazard for certain workers. The major confounding factor in all of these investigations is the influence of the cancer statistics of cigarette smoking. He states that it is most likely the residual effects which are attributed to occupational diesel exposure are due to surrogate and incomplete information about the smoking habits of the cohorts. He finds it interesting that the supporters of occupational risk from diesel emissions do not propose a risk to the general populations at the present level of diesel emissions.

Stober (1989) also states that the labeling of diesel exhaust as a potential or probable carcinogen by Germany, the World Health Organization (IARC), and the U.S. EPA were made without any reference to the evaluation of risk. He states that the risk determined by the epidemiological studies should not be used for the general public. The risk for the public at large, at present levels of diesel emissions, is actually non-existent, according to Dr. Stober. He compares the lifetime carcinogenic risk from 1 $\mu g/m^3$ diesel emissions to the risk of being struck by lightning in Germany (a lifetime risk of 2:100,000 or 2.0×10^{-5}).

Stober (1989) does concede that if a genotoxic mechanism can be shown to play a significant role in experimental tumor induction, then a small residual risk may be assumed to have been obscured by the uncertainties of past epidemiological studies. In that case, proper development and implementation of target control strategies is advisable to lower the cancer risk.

Stober (1989) states further that he does not imply that it is unnecessary to regulate diesel exhaust emissions today. The future growth of unregulated diesel-powered vehicles would degrade the present particle levels, and the general public will resent this deterioration. But there is only a very low probability, if any, that this issue involves more than an insignificantly small residual risk of a health effect.

In Dr. Stober's Air and Waste Management Association presentation in October, 1991 (Stober 1991), he mentions several points regarding the limitations of the rat studies. At present, the rat data suggest that a threshold may exist for the exposure to diesel particulate matter and the appearance of tumors. He goes on to further state that the particle overload at the two highest levels where the tumors occurred is also an issue. Using the preliminary data from recent ITRI and Fraunhofer research (see Section 9.6.3 for details), he states that it shows qualitatively similar results or more pronounced responses from carbon black than diesel particulate matter. He proposes a possible epigenetic mechanism of tumor induction (i.e., the tumors have not been caused by a metabolic degradation of organic matter associated with the particles, but by the particle deposits itself).

9.7 Carcinogenic Risk

Urban and rural diesel particulate matter carcinogenic risks, expressed as annual cancer deaths, were calculated following the methodology discussed in Section 4.1, based on the HAPEM-MS exposure estimates from Section 9.5.1 and the EPA unit risk estimate given in Section 9.6.1.5. The resultant urban, rural, and total cancer deaths are given in Table 9-11. These cancer incidences are upper bound estimates and the risk may be less, but is unlikely to be more.

Table 9-11. Diesel Particulate Matter Cancer Deaths.[a,b]

Year	Urban	Rural	Total
1990	92	17	109
1995	56	10	66
2000	33	6	39
2010	23	4	27

[a]Projections have inherent uncertainties in emission estimates, dose-response, and exposure.
[b]Cancer deaths are based on the EPA 1991 draft unit risk, determined using animal data. This unit risk has not been peer reviewed and is subject to change.

9.8 Non-carcinogenic Effects of Inhalation Exposure to Diesel Particulate Matter

Since the focus of this report is on the carcinogenic potential of the various compounds, the noncancer information will be dealt with in a more cursory fashion. No attempt has been made to synthesize and analyze the data encompassed below. Also, no attempt has been made to accord more importance to one type of noncancer effect over another. The objective is to research all existing data, describe the noncancer effects observed, and refrain from any subjective analysis of the data.

Diesel Particulate Matter

The symptoms of acute (short) exposure to high levels (i.e. above ambient) of diesel exhaust have been detailed through the study of occupationally exposed workers. These workers include underground miners, bus garage workers, dock workers, and locomotive repairmen. The symptoms may be manifested as one or more of the following: mucous membrane and eye irritation, headache, light-headedness, nausea, vomiting, heartburn, weakness, numbness and tingling in extremities, chest tightness, and wheezing. The odors associated with diesel exhaust emissions also cause some effects, such as nausea, headache, and loss of appetite.

Even though this appears to be a formidable list of symptoms, the effects of a short-term diesel exhaust exposure are dissipated as soon as the exposure stops or the subject leaves the area. Any of the changes in respiratory symptoms and pulmonary function over the course of a workshift were generally found to be minimal.

The chronic (long-term) exposure to diesel exhaust emissions have also been followed in occupationally exposed workers, but the data are insufficient to make a correlation between the effects and the exposure experienced. Most of the chronic exposure data are derived from the use of animal studies.

Many of the changes observed in rats and other small animals exposed to diesel exhaust affect the cellular and structural make-up of the lung. These effects include: accumulation of particles in the lungs, increased lung weight, tissue inflammation, increased macrophages and leukocytes (white blood cells), macrophage aggregation, hyperplasia (excess cell formation) in the alveolar and bronchiolar epithelium (surface cell layer), and a thickening of alveolar septa (partitions). In some studies, a reduction in the growth of animals is also observed at 2 mg/m^3 for 16h/day, and alterations of pulmonary function parameters were seen at 2 to 6 mg/m^3.

All of these changes appear to be dependent on the concentration of the exhaust particulate matter, the pulmonary deposition of the particle, and the ability of the lung to clear the particulate matter.

Reference Concentration for Chronic Inhalation Exposure (RfC)

The reference concentration for chronic inhalation exposure (RfC) for diesel particulate matter has recently been established (EPA, 1993). This RfC was determined to be 5.0×10^{-3} mg/m^3 per day, over a lifetime. An RfC is an estimate of the continuous exposure to the human population that is likely to be without deleterious effects during a lifetime. As such, it is useful in evaluating non-cancer effects.

The two critical studies used in determining the diesel particulate RfC are chronic rat inhalation studies by Mauderly et al. (1998) and Ishinishi et al. (1988). These two studies observed various non-cancer endpoints and at various time points.

In Mauderly et al. (1988), rats and mice were exposed to target diesel particulate matter concentrations of 0, 0.35, 3.5, or 7.0 mg/m^3 for 7 hours/day, 5 days/week for up to 30 months for the rats or 24 months for the mice. Endpoints examined in this study include carcinogenicity, respiratory tract histopathology and morphometric analysis, particle clearance, lung burden of diesel particulate matter, pulmonary function testing, lung biochemistry, lung lavage biochemistry and cytology, immune function, and lung cell labeling index. Aggregates of particle-laden macrophages were seen after 6 months in rats exposed to 7.0 mg/m^3 target concentrations and, after 1 year of exposure, histological changes were seen including focal areas of epithelial metaplasia. Fibrosis and metaplasia increased with increasing duration of exposure and were observable in the 3.5 and 7.0 mg/m^3 group of rats at 24 months. In the 0.35 mg/m^3 group of rats, there was no inflammation or fibrosis.

A NOAEL of 0.353 mg/m^3, based on inflammatory, histological, and biochemical changes in the lung and impaired particle clearance was established. A LOAEL of 3.47 mg/m^3 based on the chronic rat inhalation study described above was also developed. To establish a human equivalent NOAEL and LOAEL for this study a conversion factor was applied. The human equivalent concentrations (HEC) were estimated from the experimental conditions using the particle retention model of Yu and Yoon (1990) assuming a continuous human exposure and using mass of diesel particle carbon core per unit of surface area in the pulmonary region as the dose expression. Using this conversion factor the NOAEL(HEC) = 0.042 mg/m^3 and the LOAEL = 0.36 mg/m^3.

In Ishinishi et al. (1986, 1988) both light-duty and heavy-duty diesel engines were operated under constant velocity and load conditions. Particle concentrations were 0.11, 0.41, 1.18, and 2.32 mg/m^3 for the light duty engine and 0.46, 0.96, 1.84, and 3.72 mg/m^3 for the heavy duty engines. Fischer 344 rats were exposed for 16 hours/day, 6 days/week, for 30 months. No histopathological changes were observed in the lungs of rats exposed to 0.4 mg/m^3 particulate matter or less. At concentrations above 0.4 mg/m^3 particulate matter, accumulation of particle-laden macrophages was observed. Hyperplastic lesions were reported at a lowest observed adverse effect level (LOAEL)

in chronically exposed rats at 1.18 mg/m^3 for light duty and 0.96 mg/m^3 for the heavy duty series.

A NOAEL of 0.46 mg/m^3, based on histological changes in the rat lung exposed to heavy duty diesel emissions was established. A LOAEL of 0.96 mg/m^3 based on the chronic rat inhalation study described above was also developed from the heavy duty emissions exposure. As described previously, to establish a human equivalent NOAEL and LOAEL for this study a HEC conversion factor must be applied. Using this conversion factor the NOAEL(HEC) = 0.155 mg/m^3 and the LOAEL = 0.30 mg/m^3.

To develop an RfC, the no-observable-adverse-effect level (NOAEL) of 0.46 mg/m^3 from the Ishinishi et al. (1986, 1988) study was converted to continuous lifetime exposure conditions [0.46 mg/m^3 × 16/24 hours/day × 6/7 days/week = 0.26 mg/m^3 NOAEL(ADJ). The NOAEL(ADJ) from the heavy duty emissions was adjusted based on the retention model Yu and Yoon (1990) to achieve a NOAEL(HEC) of 0.155 mg/m^3. The NOAEL(HEC) of 0.155 mg/m^3 had an uncertainty factor of 30 that was then applied to derive the RfC of 5.0×10^{-3} mg/m^3. The factor of 30 reflects a factor of 10 to protect sensitive individuals and 3 to adjust for interspecies extrapolation because dosimetric adjustments based on a particle deposition and retention model were applied (Yu and Yoon, 1990). The confidence in the RfC is high. The research programs performed were well conducted chronic studies with adequate numbers of animals and identified LOAELs and NOAELs at levels which are consistent across studies. The full data base contains 10 chronic studies as well as developmental and reproductive studies, resulting in high confidence.

<u>PM$_{10}$</u>

The following studies cited from the Federal Register (EPA, 1987) are those that were utilized to establish a final National Ambient Air Quality Standard (NAAQS) for PM$_{10}$ (particulate matter less than 10 microns in diameter) with a substantial margin of safety. These non-cancer inhalation human studies apply to PM$_{10}$ in general and are applicable to both diesel and gasoline particles.

To evaluate the short term effects of PM$_{10}$, the studies of Dockery et al. (1982) and Dassen et al. (1986) were useful. The Dockery study observed physiologically small but statistically significant decreases in lung function in a group of children exposed to peak PM$_{10}$ levels of 140-250 µg/m^3. The decrements persisted for 2-3 weeks following the exposures. The study also suggested the possibility of larger responses in a subset of the children, including those with existing respiratory symptoms. The Dassen study recorded similar decrements in children in the Netherlands following exposure to PM$_{10}$ levels estimated at 200-250 µg/m^3, but no observable effects two days after exposure to PM$_{10}$ levels estimated at 125 µg/m^3.

Long term examination of respiratory health in the same community studied by Dockery et al. (1982) suggests that the

children in that community have a higher incidence of respiratory illness and symptoms than children in communities with lower particle levels.

The most important study of long-term effects is an examination of six U.S. cities (Ware et al., 1986). The study indicates the possibility of increased respiratory symptoms and illnesses in children at multi-year levels across a range of 40 to over 58 $\mu g/m^3$ as PM_{10}, but found no evidence of reduced lung function at such concentrations. This study did not find similar gradients in symptoms and illness within some of the cities, which had somewhat smaller localized pollution gradients. The results of a separate series of studies on long and intermediate term (2 to 6 weeks) exposures in a number of U.S. metropolitan areas (Ostro, 1987; Hausman et al., 1984) are more supportive of the possibility of effects within cities (respiratory related activity restrictions in adults) at comparable U.S. exposure levels. The results of these more recent studies are generally consistent with the earlier U.S. studies. In particular, the findings of symptomatic responses in children with no change in lung function (Ware et al., 1986) is consistent with similar findings in adults (Bouhuys et al., 1978) at estimated long-term PM_{10} levels down to 50 $\mu g/m^3$. However, the information available to support the existence of significant adverse effects at annual PM_{10} levels below 50 $\mu g/m^3$, especially when 24 hour levels are maintained below 150 $\mu g/m^3$, is quite limited and uncertain.

To add some perspective to the levels of PM_{10} that are produced by various vehicle types, automobile with diesel engines can emit up to 100 times greater volume of particulate matter per mile than gasoline engine cars burning unleaded gasoline (Lewtas, 1991). When directly comparing the mutagenic emission rates for a number of certification vehicles, it was found that the diesel vehicles emitted 45 to 800 times as much mutagenic activity per mile as the gasoline catalyst-equipped vehicles (Claxton and Kohan, 1981). It should be noted, however, while gasoline engine automobiles produce a much smaller volume of particulate matter, they greatly outnumber diesel vehicles.

Since the establishment of the PM_{10} standard, a number of new epidemiological studies seem to indicate that particulate matter might influence daily mortality rates at concentrations lower than the ranges encountered in the earlier studies. In particular, studies that examined particulate matter pollution in Philadelphia, PA (Schwartz and Dockery, 1992a), Steubenville, OH (Schwartz and Dockery, 1992b), and Detroit, MI (Schwartz, 1991), found that in each case the relative risk of daily mortality increases in a generally linear fashion with increasing concentrations of particulate matter. In some cities, the association was seen between particulate matter and mortality even when particle levels never violate the current standard. All the studies (Schwartz and Dockery, 1992a,b; Schwartz, 1991) emphasize the lack of an apparent threshold, and that particulate matter may be influencing mortality even at levels well below the current standard of 150 $\mu g/m^3$.

Determining the specific causes of death which seen to be exacerbated by particulate matter pollution is more difficult, but the Philadelphia study found significant increases in death from chronic obstructive pulmonary disease and cardiovascular disease, with the large majority of death occurring in individuals aged 65 and older.

In two studies of a Western city, Provo, UT, it was also found that an increase in PM_{10} correlated with specific health indicators (Ransom and Pope, 1991) and school absenteeism (Pope et al., 1991). Particulate matter pollution in Provo, UT has been found to be associated with increased daily elementary school absenteeism, increased hospital admissions for respiratory disease, increased respiratory symptoms, and increased medicine used by asthmatics. The impact of particulate matter on the endpoints mentioned above occurred at levels well below the current 24 hour NAAQS standard of 150 $\mu g/m^3$.

9.9 References for Chapter 9

Albert, R.E., J. Lewtas, S. Nesnow, T.W. Thorslund, and E. Anderson. 1983. Comparative potency method for cancer risk assessment: Application to diesel particulate emissions. Risk Analysis. 3: 101-117.

Albert, R.E., and C. Chen. 1986. U.S. EPA diesel studies on inhalation hazards. In: Ishinishi, N., Koizumi, A., McClellan, R., Stober, W., eds. Carcinogenic and Mutagenic Effects of Diesel Engine Exhaust. Amsterdam: Elsevier, pp. 411-419.

American Public Transport Association. 1990. 1990 Transit Fact Book. September 1990.

Barfnecht, T.R., R.A. Hites, E.L. Cavaliers, and W.G. Thilly. 1982. Human cell mutagenicity of polycyclic aromatic hydrocarbon companies of diesel emissions. In: Lewtas, J., ed. Toxicological Effects of Emissions from Diesel Engines. New York: Elsevier, pp. 277-294.

Barnhart, M.L., S. Chen, S.O. Salley, and H. Puro. 1981. Ultrastructure and morphometry of the alveolar lung of guinea pigs chronically exposed to diesel engine exhaust: Six months experience. J. Appl. Toxicol. 1: 88-103.

Behymer, T.D. and R.A. Hites. 1985. Photolysis of polycyclic aromatic hydrocarbons adsorbed on simulated atmospheric particulates. Environ. Sci. Technol., 19: 1004-1006.

Benhamou S., E. Benhamou, and R. Flamant. 1988. Occupational risk factors of lung cancer in a French case-control study. Br. J. Ind. Med. 45: 231-233.

Boffetta, P. and S.D. Stellman. 1988. Association between diesel exhaust exposure and multiple myeloma an example of confounding. Prev. Med. 17: 236-247.

Bond, J.A., N.F. Johnson, M.B. Snipes, and J.L. Mauderly. 1990. DNA adduct formation in rat alveolar type II cells: cells potentially at risk for inhaled diesel exhaust. Environ. Molec. Mutagen. 16: 64-69.

Bouhuys, A., Beck, G.J., and Schoenberg, J.B. 1978. Do present levels of air pollution outdoors affect respiratory health? Nature 276: 466-471.

Brightwell, J., X. Fouillet, A.L. Cassano-Zoppi, R. Gatz, and F. Duchosal. 1986. Neoplastic and functional changes in rodents after chronic inhalation of engine exhaust emissions. In: Ishinishi, N., Koizumi, A., McClellan, R., Stober, W., eds. Carcinogenic and Mutagenic Effects of Diesel Engine Exhaust. Amsterdam: Elsevier, pp. 471-485.

Brooks, A.L., A.P. Li, J.S. Dutcher, C.R. Clark, S.J. Rothenberg, R. Kiyoura, W.E. Bechtold, R.O. McClellan. 1984. A comparison of genotoxicity of automobile exhaust particles form laboratory and environmental sources. Environ. Mutagen. 6: 651-668.

Butler, J.D. and P. Crossley. 1981. Reactivity of polycyclic aromatic hydrocarbons adsorbed on soot particles. Atmos. Environ., 15: 91-94.

Carey, P.M. 1987. Air toxic emissions from motor vehicles. Ann Arbor, MI: U.S. Environmental Protection Agency, Office of Mobile Sources, EPA Report no. EPA-AA-TSS-PA-86-5.

Casto, B.C., G.G. Hatch, S.L. Huang, J.L. Huisingh, S. Nesnow, and M.D. Waters. 1981. Mutagenic and carcinogenic potency of extracts of diesel and related environmental emissions: *In vitro* mutagenesis and oncogenic transformation. Environ. Int. 5: 403-409.

Chescheir, G.M. III, N.E. Garrett, J.D. Shelburne, J.L. Huisingh, and M.D. Waters. 1981. Mutagenic effects of environmental particulates in the CHO/HGPRT system. In: Waters, M.D. Sandhu, S.S., Huisingh. J.L., Claxton, L.C., Nesnow, S., eds. Application of short-term bioassays in the fractionation and analysis of complex environmental mixtures. New York: Plenum Press, pp. 337-350.

Claxton, L.D. 1981. Mutagenic and carcinogenic potency of diesel and related environmental emissions: Salmonella bioassay. Environ. Int. 5: 389-391.

Claxton, L.D. 1983. Characterization of automotive emissions by bacterial mutagenesis bioassay: A review. Environ. Mutagen. 5: 609-631.

Claxton, L.C. and M. Kohan. 1981. Bacterial mutagenesis and the evaluation of mobile-source emissions. In: Waters, M.D. Sandhu, S.S., Huisingh. J.L., Claxton, L.C., Nesnow, S., eds. Application of short-term bioassays in the fractionation and analysis of complex environmental mixtures. New York: Plenum Press, pp. 299-317.

Cuddihy, R.G., W.C. Griffith, and R.O. McClellan. 1981. Health risks from light-duty diesel vehicles. Environ. Sci. Technol. 18: 14-21a.

Curren, R.D., R.E. Kouri, D.M. Kim, and L.M. Schectman. 1981. Mutagenic and carcinogenic potency of extracts from diesel related environmental emissions: Simultaneous morphological

transformation and mutagenesis in BALB/c 3T3 cell. Environ. Int.
5: 411-415.

Damber, L.A., and L.G. Larsson. 1987. Occupation and male lung
cancer: A case-control study in northern Sweden. Br. J. Ind.
Med. 44:446-453.

Dassen, W., Brunekreff, B., Hoek, G., Hofschreuder, P., Staatsen,
B., deGrout, H., Schouten, E., and Biersteker, K. 1986. Decline
in children's pulmonary function during an air pollution episode.
J. Air. Pollut. Control Assoc. 36: 1223-1227.

Depass L.R., K.C. Chen, and L.G. Peterson. 1982. Dermal
carcinogenesis bioassays of diesel particulates and
dichloromethane extract of diesel particulates in C3H mice. In:
Lewtas, J., ed. Toxicological Effects of Emissions from Diesel
Engines. Amsterdam: Elsevier. pp. 321-327.

Dlugi, R. and H. Güsten. 1983. The catalytic and photocatalytic
activity of coal fly ashes. Atmos. Environ., 17: 1765-1771.

Dockery, D.W., Ware, J.H., Ferris Jr., B.G., Speizer, F.E., Cook,
N.R., and Herman, S.M. 1982. Change in pulmonary function in
children associated with air pollution episodes. J. Air. Pollut.
Contrl. Assoc. 32: 937-942.

Dukovich, M., R.E. Yasbin, S.S. Lestz, T.H. Risby, and R.B.
Zweidinger. 1981. The mutagenic and SOS-inducing potential of
the soluble organic fraction collected form diesel particulate
emissions. Environ. Mutagen. 3: 253-264.

Edling, O., C.G. Anjou, O. Axelson, and H. Kling. 1987.
Mortality among personnel exposed to diesel exhaust. Int. Arch.
Occup. Environ. Health 59: 559-565.

Environ Corporation. 1987. Risk assessment issues in EPA's
technical report "Air Toxics Emissions from Motor Vehicles".
Prepared for the Motor Vehicle Manufacturers Association.

EPA. 1987. Federal Register, 40 CFR Part 50, July 1, 1987,
pages 24634-24669.

EPA. 1989. Analysis of Air Toxics Emissions, Exposures, Cancer
Risks and Controllability in Five Urban Areas: Volume I: Base
Year Analysis and Results. Office of Air Quality Planning and
Standards, Research Triangle Park, NC. July, 1989. EPA Report
No. EPA-450/2-89-012a.

EPA. 1990a. Regulation of Fuels and Fuel Additives: Fuel Quality Regulations for Highway Diesel Fuel Sold in 1993 and Later Calendar Years; Final Rule. Federal Register 55 (162): 34120-34151.

EPA. 1990b. Health assessment document for diesel emissions; workshop review draft. Office of Research and Development, Office of Health and Environmental Assessment, Washington, DC. EPA-600/8-90/057A.

EPA. 1991a. Compilation of Air Pollutant Emission Factors -- Volume II: Mobile Sources. Ann Arbor, Michigan: Office of Mobile Sources. Publication no. AP-42, Supplement A.

EPA. 1991b. National Air Pollutant Emission Estimates 1940-1990. Research Triangle Park, North Carolina: Office of Air Quality Planning and Standards. Publication no. EPA-450/4-91-026.

EPA. 1991c. National Air Quality and Emissions Trends Report, 1990. Research Triangle Park, North Carolina: Office of Air Quality Planning and Standards. Publication no. EPA-450/4-91-023.

EPA. 1991d. Presentation at Air and Waste Management's "Air Toxics from Mobile Sources" conference by Dr. William Pepelko, October 16-18, 1991.

EPA. 1992. MOBILE4.1 Fuel Consumption Model. Ann Arbor, Michigan: Office of Mobile Sources.

EPA. 1993. Integrated Risk Information System. U.S. Environmental Protection Agency. Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH.

Fox, M. A. and S. Olive. 1979. Photooxidation of anthracene on atmospheric particulate matter. Science, 205: 582-583.

Garshick, E., M.B. Schenker, A. Munoz, M. Segal, T.J. Smith, S.R. Woskie, S.K. Hammond, and F.E. Speizer. 1987. A case control study of lung cancer and diesel exhaust exposure in railroad workers. Am. Rev. Respir. Dis. 135: 1242-1248.

Garshick, E., M.B. Schenker, A. Munoz, M. Segal, T.J. Smith, S.R. Woskie, S.K. Hammond, and F.E. Speizer. 1988. A retrospective cohort study of lung cancer and diesel exhaust exposure in railroad workers. Am. Rev. Respir. Dis. 124: 820-825.

Grimmer, G., H. Brune, R. Deutsch-Wenzel, G. Dettbarn, J. Jacob, K.W. Naujack, U. Mohr, and H. Ernst. 1987. Contribution of polycyclic aromatic hydrocarbons and nitro-derivatives to the carcinogenic impact of diesel exhaust condensate evaluated by implantation into the lungs of rats. Cancer Lett. 37: 173-180.

Grosjean, D., K. Fung, and J. Harrison. 1983. Interactions of polycyclic aromatic hydrocarbons with atmospheric pollutants. Environ. Sci. Technol., 17: 673-679.

Guerrero, R.R., D.E. Rounds, and J. Orthoefer. 1981. Sister chromatid exchange analysis of Syrian hamster lung cells treated *in vivo* with diesel exhaust particulates. Environ. Int. 5: 445-454.

Hall, N.E., and E. Wynder. 1984. Diesel exhaust exposure and lung cancer. Environ. Res. 34: 77-86.

Harris, J.E. 1983. Diesel emissions and lung cancer. Risk Analysis. 3: 83-100.

Hausman, J.A., Ostro, B.D., and Wise, D.A. 1984. Air pollution and lost work. Cambridge, MA: National Bureau of Economic Research, NBER Working Paper no. 1263.

Hayes, R.B., T. Thomas, D.T. Silverman, et al. 1989. Lung cancer in motor exhaust occupations. Am. J. Ind. Med. 16: 685-695.

Heinrich, U., H. Muhle, S. Takenaka, H. Ernst, R. Fuhst, U. Mohr, F. Pott, and W. Stober. 1986a. Chronic effects on the respiratory tract of hamsters, mice, and rats after long-term inhalation of high concentrations of filtered and unfiltered diesel engine emissions. J. Appl. Toxicol. 6: 383-395.

Heinrich, U., F. Pott, and S. Rittinghausen. 1986b. Comparison of chronic inhalation effects in rodents after long-term exposure to either coal oven flue gas mixed with pyrolized pitch or diesel engine exhaust. In: Ishinishi, N., Koizumi, A., McClellan, R., Stober, W., eds. Carcinogenic and Mutagenic Effects of Diesel Engine Exhaust. Amsterdam: Elsevier. pp. 441-457.

Heinrich, U., D. Dungworth, F. Pott, A. Schulte, L. Peters, C. Dasenbrock, K. Levsen, W. Koch and O. Creutzenburg. (1991). The carcinogenic effects of carbon black particles and tar/pitch condensation aerosol after inhalation exposure of rats. Seventh International Symposium on Inhaled Particles, Edinburgh, September 16-20, 1991.

Hoar, S., and R. Hoover. 1985. Truck driving and bladder cancer mortality in rural New England. J. Natl. Cancer Int. 74: 771-774.

Howe, G.R., J. D. Burch, and A.B. Miller. 1980. Tobacco use, occupation, coffee, various nutrients, and bladder cancer. J. Natl. Cancer Inst. 64: 701-713.

Howe, G.R., D. Fraser, J. Lindsay, et al. 1983. Cancer mortality (1965-77) in relation to diesel fume and coal exposure in a cohort of retired railway workers. J. Natl. Cancer Inst. 3NCI 70: 1013-1019.

Huisingh, J., R. Bradow, R. Jungers, L. Claxton, R. Zweidinger, S. Tejada, J. Bumgarner, F. Duffeild, M. Waters, V.F. Simmon, C. Hare, C. Rodrigues, and L. Snow. 1978. Application of bioassay to the characterization of diesel particle emissions. In: Waters, M.D. Sandhu, S.S., Huisingh. J.L., Claxton, L.C., Nesnow, S., eds. Application of short-term bioassays in the fractionation and analysis of complex environmental mixtures. New York: Plenum Press, pp. 381-418.

Ingham, M. C., and R. B. Warden. 1987. Cost-effectiveness of diesel fuel modifications for particulate control. SAE Paper 870556.

International Agency for Research on Cancer. 1989. IARC monographs on the evaluation of carcinogenic risks to humans; diesel and gasoline engine exhausts and some nitroarenes, Volume 46.

Iscovich, J., R. Castelleto, J. Esteve, et al. 1987. Tobacco smoking, occupational, exposure, and bladder cancer in Argentina. Int. J. Cancer 40: 734-740.

Ishinishi, N., N. Kuwabara, S. Nagase, T. Suzuki, S. Ishiwata, and T. Kohno. 1986. Long-term inhalation studies on effects of exhaust from heavy and light duty diesel engines on F344 rats. In: Ishinishi, N., Koizumi, A., McClellan, R., Stober, W., eds. Carcinogenicity and mutagenicity of diesel engine exhaust. Amsterdam: Elsevier, pp. 329-348.

Ishinishi, N., N. Kuwabara, Y. Takaki, et al. 1988. Long term inhalation experiments on diesel exhaust. In: Diesel Exhaust and Health Risk. Results of the HERP Studies. Entire text of discussion, Research Committee for HERP Studies. Japan Automobile Research Institute, Inc. Tsukuba, Ibaraki 305, Japan.

Iwai, K., T. Udagawa, M. Yamagishi, and H. Yamada. 1986. Long-term inhalation studies of diesel exhaust on F344 SPF rats. Incidence of lung cancer and lymphoma. In: Ishinishi, N., Koizumi, A., McClellan, R., Stober, W., eds. Carcinogenicity and mutagenicity of diesel engine exhaust. Amsterdam: Elsevier, pp. 349-360.

Iyer et al. 1990. Diesel exhaust exposure and bladder cancer risk. Eur. J. Epidemiol. 6: 49-54.

Johnson, J.H. 1988. Automotive emissions. In: Air pollution, the automobile, and public health. Health Effects Institute, National Academy Press, Washington, D.C.

Johnson, T. R., R. A. Paul, and J. E. Capel. 1992. Draft Report: Application of the Hazardous Air Pollutant Exposure Model (HAPEM) to Mobile Source Pollutants. Durham, North Carolina: International Technology Corporation.

Kaplan, H.L., W.F. Mackenzie, K.J. Springer, R.M. Schreck, and J.J. Vostal. 1982. A subchronic study of the effects of exposure of three species of rodents to diesel exhaust. In: Lewtas, J., ed. Toxicological Effects of Emissions from Diesel Engines. New York: Elsevier Biomedical, pp. 161-220.

Karagianes, R.F., R.F. Palmer, and R.H. Busch. 1981. Effects of inhaled diesel emissions and coal dust in rats. Am. Ind. Hyg. Assoc. J. 42: 382-391.

Kawataba, Y., K. Iwai, T. Udagawa, K. Tukagoshi, and K. Higuchi. 1986. Effects of diesel soot on unscheduled DNA synthesis of tracheal epithelium and lung tumor formation. In: Ishinishi, N., Koizumi, A., McClellan, R., Stober, W., eds. Carcinogenicity and Mutagenicity of Diesel Engine Exhaust. Amsterdam: Elsevier, pp. 213-222.

Kitchen, M. and W. Damico. 1992. Development of Conversion Factors for Heavy Duty Bus Engines g/bhp-hr to g/mile. Ann Arbor, MI: U.S. Environmental Protection Agency, Office of Mobile Sources, EPA Report no. EPA-AA-EVRB-92-01.

Korfmacher, W.A., G. Mamantov, E.L. Wehry, D.F.S. Natusch, and T. Mauney. 1981. Nonphotochemical decomposition of fluorene vapor-adsorbed on coal fly ash. Envirn. Sci. Technol., 15: 1370-1375.

Korfmacher, W.A., D.F.S. Natusch, D.R. Taylor, G. Mamantov, and E.L. Wehry. 1980a. Oxidative transformations of polycyclic aromatic hydrocarbons adsorbed on coal fly ash. Science, 207: 763-765.

Korfmacher, W.A., E.L. Wehry, G. Mamantov, and D.F.S. Natusch. 1980b. Resistance to photochemical decomposition of polycyclic aromatic hydrocarbons vapor-adsorbed on coal fly ash. Environ. Sci. Technol., 14: 1094-1099.

Kotin P., H. Falk, and M. Thomas. 1955. Aromatic hydrocarbons. III. Presence in the particulate phase of diesel engine exhausts and the carcinogenicity of exhaust extracts. Arch. Ind. Health 11: 113-120.

Kunitake, E., A. Imase, K. Shimamura, N. Ishinishi, A. Hisanaga, and A. Tanaka. 1988. Skin application and subcutaneous injection experiments of diesel particulate extracts using ICR mice and nude mice. In: Diesel Exhaust and Health Risks. Research Committee for HERP Studies, Ibaraki, Japan. pp. 217-225.

Lee, K.P., N.W. Henry III, H.J. Trochimowicz, and C.F. Reinhardt. 1986. Pulmonary response to impaired lung clearance in rats

following excessive TiO$_2$ dust deposition. Environ. Res. 41: 144-167.

Lerchen M.L., C.L. Wiggins, and J.M. Samet. 1987. Lung cancer and occupation in New Mexico. J. Natl. Cancer Inst. 79: 639-645.

Lewis, T.R., F.H. Green, W.J. Moorman, J.A. Burg, and D.W. Lynch. 1986. A chronic inhalation toxicity study of diesel engine emissions and coal dust alone and combined. In: Ishinishi, N., Koizumi, A., McClellan, R., Stober, W., eds. Carcinogenicity and mutagenicity of diesel engine exhaust. Amsterdam: Elsevier, pp. 361-380.

Lewtas, J. 1982. Mutagenic activity of diesel emissions. In: Lewtas J. ed. Toxicological Effects of Emissions from Diesel Engines, New York: Elsevier; pp.243-264.

Lewtas, J. 1983. Evaluation of the mutagenicity and carcinogenicity of motor vehicle emissions in short-term bioassays. Environ. Health Perspect. 47: 141-152.

Lewtas, J. 1991. Carcinogenic risks of polycyclic organic matter (POM) from selected emission sources. Health Effects Research Laboratory, Research Triangle Park, NC. Deliverable report no. 3128.

Li, A.P., and R.E. Royer. 1982. Diesel-exhaust-particle extract enhancement of chemical-induced mutagenesis in cultured Chinese hamster ovary cells: possible interaction of diesel exhaust with environmental chemicals. Mutat. Res. 103: 349-355.

Liber, H.L., B.M. Andon, R.A. Hites and W.G. Thilly. 1981. Diesel soot: Mutation measurements in bacterial and human cells. Environ. Int. 5: 281-284.

Ligocki, M. P. and G.Z. Whitten. 1991. Atmospheric transformation of air toxics: acetaldehyde and polycyclic organic matter. Systems Application International, San Rafael, California (SYSAPP-91/113).

Ligocki, M. P., R. R. Schulhof, R. E. Jackson, M. M. Jimenez, G. Z. Whitten, G. M. Wilson, T. C. Meyers, and J. L. Fieber. 1992. Modeling the effects of reformulated gasolines on ozone and toxics concentrations in the Baltimore and Houston areas. Systems Applications International, San Rafael, California (SYSAPP-92/127).

Machiele, P. A. 1988. Heavy-Duty Vehicle Emission Conversion Factors II, 1962-2000. Ann Arbor, Michigan: U.S. Environmental Protection Agency, Office of Mobile Sources. Publication no. EPA-AA-SDSB-89-01.

Matsushita, H., S. Gotto, O. Endo, J. Lee, and A. Kawai. 1986. Mutagenicity of diesel exhaust and related chemicals. In: Ishinishi, N., Koizumi, A., McClellan, R., Stober, W., eds.

Carcinogenicity and mutagenicity of diesel engine exhaust. New York: Elsevier, pp. 103-118.

Mauderly, J.L., R.K. Jones, W.C. Griffith, R.F. Henderson, and R.O. McClellan. 1987. Diesel exhaust is a pulmonary carcinogen in rats exposed chronically by inhalation. Fundam. Appl. Toxicol. 9: 208-221.

Mauderly, J.L., Rr.K. Jones, R.F. Henderson, R.K. Wolff, J.A. Pickrell, R.O. McClellan, and N.A. Gillett. 1988. Relationship of lung structural and functional changes to accumulation of diesel exhaust particles. Ann. Occup. Hyg. 32: 659-669.

Mauderly, J.L., M.B. Snipes, E.B. Barr, W.E. Bechtold, S.A. Belinsky, R.F. Henderson, C.E. Mitchell, K.J. Nikula, and D.G. Thomassen. 1991. Influence of particle-associated organic compounds on carcinogenicity of diesel exhaust. Seventh International Symposium on Inhaled Particles, Edinburgh, September 16-20, 1991.

McClellan, R.O., R.G. Cuddihy, W.C. Griffith, and J.L. Mauderly. 1989. Integrating diverse data sets to assess the risks of airborne pollutants. In: Mohr, U., ed Assessment of Inhalation Hazards. Springer Verlag: New York, pp. 3-22.

Mitchell, A.D., E.L. Evans, M.M. Lotz, E.S. Riccio, K.E. Mortelmans, and V.F. Simmon. 1981. Mutagenic and carcinogenic potency of extracts of diesel and related environmental emissions: *In vitro* mutagenesis and DNA damage. Environ. Int. 5: 393-401.

Morimoto, K., H. Kondo, M. Kitamura, and A. Koizumi. 1986. Genotoxicity of diesel exhaust emissions in *in vitro* short-term assays. In: Ishinishi, N., Koizumi, A., McClellan, R., Stober, W., eds. Carcinogenicity and Mutagenicity of Diesel Engine Exhaust. New York: Elsevier, pp. 85-102.

Motor Vehicle Manufacturers Association. 1991. MVMA Motor Vehicle Facts and Figures '91.

Motor Vehicle Manufacturers Association and Engine Manufacturers Association. 1986. Analysis of the Environmental Protection Agency's Diesel Particulate Study and a Diesel Particulate Emissions Projection. September 22, 1986.

National Academy of Sciences. 1972. Particulate polycyclic organic matter. National Academy of Sciences, National Academy Press, Washington, D.C.

National Research Council. 1982. Impacts of diesel-powered light-duty vehicles: diesel technology. National Academy Press, Washington, D.C.

Nesnow, S., C. Evans, A. Stead, J. Creason, T.J. Slaga, and L.L. Triplett. 1982. Skin carcinogenesis studies of emission extracts. In: Lewtas, J., ed. Toxicological Effects of Emissions from Diesel Engines. Amsterdam: Elsevier, pp. 295-320.

NIOSH. (1988). Carcinogenic effects of exposure to diesel exhaust. Current Intelligence Bulletin 50, August 1988.

Orthoefer J.G., W. Moore, and D. Kraemer. 1981. Carcinogenicity of diesel exhaust as tested in strain A mice. Environ. Int. 5: 461-471.

Ostro, B.D. 1987. Air pollution and morbidity revisited: a specification test. J. Environ. Econ. Manage. 14(1): 87-98.

Pepelko, W.E., and W.B. Peirano. 1983. Health effects of exposure to diesel engine emissions. J. Amer. Coll. Toxicol. 2: 253-306.

Pepelko, W.E. and C.H. Ris. 1991. Update on U.S. Environmental Protection Agency Activities in the Assessment of Mobile Source Air Toxics. Proceedings from the Air and Waste Management Association's specialty conference "Air Toxics Pollutants from Mobile Sources: Emissions and Health Effects." October 16-18, 1991.

Pereira, M.A., T.H. Conner, J. Meyne, and M.S. Legator. 1981a. Metaphase analysis, micronucleus assay and urinary mutagenicity assay of mice exposed to diesel emissions. Environ. Int. 5: 435-438.

Pereira, M.A., P.S. Sabharwal, L. Gordon, and A.J. Wyrobek. 1981b. The effect of diesel exhaust on sperm-shape abnormalities in mice. Environ. Int. 5: 459-460.

Pereira, M.A., L. McMillan, P. Kaur, D.K. Gulati, and P.S. Sabharwal. 1982. Effect if diesel exhaust emissions, particulates, and extract on sister chromatid exchange in transplacentally exposed fetal hamster liver. Environ. Mutagen. 4: 215-220.

Pereira, M.A., P.S. Sabharwal, P. Kaur, C.B. Ross, A. Choi, and T. Dixon. 1981c. *In vitro* detection of mutagenic effects of diesel exhaust by short-term mammalian bioassays. Environ. Int. 5: 439-443.

Pistikpopulos, P., H.M. Worthwm, L. Gomes, S. Masclet-Beyne, E.B. Nguyen, P.A. Masclet, and G. Mouvier. 1990. Mechanisms of formation of particulate polycyclic aromatic hydrocarbons in relation to the particle size distribution; effects on the meso-scale transport. Atmos. Environ., 24A: 2573-2584.

Pope, C.A. III, D.W. Dockery, J.D. Spengler, and M.E. Raizenne. 1991. Respiratory health and PM_{10} Pollution; a daily time series analysis. Am. Rev. Respir. Dis. 144:668-674.

Pott, F., D.L. Dungworth, U. Heinrich, H. Muhle, K. Kamino, P.G. German, M. Roller, and R.M. Rippe. (1991). Lung tumors in rats after intratracheal instillation of dusts. Seventh International Symposium on Inhaled Particles, Edinburgh, September 16-20, 1991.

Pott, F. and U. Heinrich. 1987. Dieselmotorabgas und Lungenk auf die Gefanfrdung des Menschen. In: Umwelthygiene, Vol. 19. Med. Institut. F. Umwelthygiene, Annual Report 1986/87. Dusseldorf, F.R.G., pp. 130-167.

Ransom, M.R. and C.A. Pope III. 1992. Elementary school absences and PM_{10} pollution in Utah valley. Environ. Res. 58:204-219.

Rushton, L., M.R. Alderson, and C.R. Nagarajah. 1983. Epidemiological survey of maintenance workers in London Transport executive bus garages at Chiswick works. Br. J. Ind. Med. 40: 340-345.

Russell, L.B., W.M. Generoso, E.F. Oakberg, W.L. Russell, J.W. Bangham, and K.F. Stelzner. 1980. Tests for heritable effects induced by diesel exhaust in the mouse. ORNL-5685. Martin Marietta Energy Systems, Inc. Oak Ridge Natl. Lab.

Schreck, A.M., S.C. Collins, L. Dooley, A. Fiks, J.L. Graf, and M.M. Preache. 1982. Experimental conditions in GMR chronic inhalation studies of diesel exhaust. J. Appl. Toxicol. 1: 68-76.
Schuler, R.L., and R.W. Niemeier. 1981. A study of diesel emissions on *Drosophila*. Environ. Int. 5: 431-434.

Schwartz, J. 1991. Particulate air pollution and daily mortality in Detroit. Environ. Res. 56:204-213.

Schwartz, J. and D.W. Dockery. 1992a. Increased mortality in Philadelphia associated with daily air pollution concentrations. Am. Rev. Respir. Dis. 145:600-604.

Schwartz, J. and D.W. Dockery. 1992b. Particulate air pollution and daily mortality in Steubenville, Ohio. Am. J. Epidemiol. 135:12-19.

Siak, J.S., T.L. Chan, and P.S. Lees. 1981. Diesel particulate extracts in bacterial test systems. Environ. Int. 5: 243-248.

Sienicki, E. J. and R. S. Mago. 1991. Reevaluation of Diesel Engine Particulate Emission Inventories. Presented at Air and Waste Management Association Conference, October 16-18, 1991, Detroit, Michigan.

Sienicki, E. J. 1992a. Letter from E. J. Seinicki, Navistar International Transportation Corporation, to Phil Lorang, Environmental Protection Agency, January 6, 1992.

Sienicki, E. J. 1992b. Letter from E. J. Seinicki, Navistar International Transportation Corporation, to Phil Lorang, Environmental Protection Agency, April 23, 1992.

Smith, R.A., and L. Stayner. 1990. An exploratory assessment of the risk of lung cancer associated with exposure to diesel exhaust based on a study with rats. Final Report. Division of Standards Development and technology transfer. NIOSH. Cincinnati, OH.

Steenland, K. et al. 1990. Case-control study of lung cancer and truck driving in the Teamster Union. Am. J. Public Health 80: 670-674.

Steenland, K., C. Burnett, and A.M. Osoria. 1987. A case-control study of bladder cancer using city directions as a source of occupational data. Am. J. Epidemiol. 126: 247-257.

Steinbeck et al. 1990. Increased risk of urothelial cancer in Stockholm during 1985-87 after exposure to benzene and exhausts. Int. J. Cancer 45: 1012-1017.

Stober, W. 1986. Experimental induction of tumors in hamsters, mice, and rats after ling-term inhalation of filtered and unfiltered diesel engine exhaust. In: Ishinishi, N., Koizumi, A., McClellan, R., Stober, W., eds. Carcinogenicity and Mutagenicity of Diesel Engine Exhaust. New York: Elsevier, pp. 421-439.

Stober, W. 1987. On the health hazards of particulate diesel engine exhaust emissions. SAE Technical Paper 871988.

Stober, W. 1989. Estimates of health hazards from exposures to diesel exhaust. Air and Waste Management Association Paper 89-34A.2.

Stober, W. 1991. Health Hazards Associated with Public Exposure to Diesel Exhuast-An Experimental Data Update. Proceedings from the Air and Waste Management Association's specialty conference "Air Toxics Pollutants from Mobile Sources: Emissions and Health Effects." October 16-18, 1991.

Takaki Y., S. Kitamura, N. Kuwabara, and Y. Fukuda. 1989. Long-term inhalation studies of exhaust from diesel engine in F344

rats: The quantitative relationship between pulmonary hyperplasia and anthracosis. Exp. Pathol. 37: 56-62. Report of poster presentation.

Takemoto, K., H. Yoshimura, and H. Katayama. 1986. Effects of chronic inhalation studies exposure to diesel exhaust on the development of lung tumors in di-isopropanol-nitrosamine-treated F344 rats and newborn C57BL and ICR mice. In: Ishinishi, N., Koizumi, A., McClellan, R., Stober, W., eds. Carcinogenicity and mutagenicity of diesel engine exhaust. New York: Elsevier, pp. 311-327.

Takemoto, K., H. Katayama, T. Kuwabara,. and M. Hasumi. 1988. Carcinogenicity by subcutaneous administration of diesel particulate extracts in mice. In: Diesel Exhaust and Health Risks. Research Committee for HERP Studies, Ibaraki, Japan. pp. 227-234.

Tucker, J.D., J. Xu, J. Stewart, P.C. Baciu, and T. Ong. 1986. Detection of sister chromatid exchanges induced by volatile genotoxicants. Teratogen. Carcinogen. Mutagen. 6: 15-21.

Ullman, T. L. 1989. Investigation of the Effects of Fuel Composition and Injection and Combustion System Type on Heavy-Duty Diesel Exhaust Emissions. Final Report, CRC Project VE-1. March, 1989.

University of Michigan Transportation Research Institute. 1988. Analysis of Heavy-Duty Truck Use in Urban Areas. Ann Arbor, Michigan: University of Michigan. Publication no. UMTRI-88-31.

U.S. Department of Energy. 1991. National Energy Stategy: Powerful Ideas for America. First Edition 1991/1992. Washington, D. C. February, 1991.

Van Vaeck, L. and K. Van Cauwenberghe. 1978. Cascade impactor measurements of the size distribution of the major classes of organic pollutants in atmospheric particulate matter. Atmos. Environ., 12: 2229-2239.

Van Vaeck, L. and K. Van Cauwenberghe. 1984. Conversion of polycyclic aromatic hydrocarbons on diesel particulate matter upon exposure to ppm levels of ozone. Atmos. Environ., 18: 323-328.

Waller, R.E. 1981. Trends in lung cancer in London in relation to exposure to diesel fumes. Environ. Int. 5: 479-483.

Ware, J.H., Ferris, Jr., B.G., Dockery, D.W., Spengler, J.D., Stram, D.O., and Speizer, F.E. 1986. Effects of ambient sulfur oxides and suspended particles on respiratory health of preadolescent children. Am. Rev. Respir. Dis. 133: 834-842.

Waxweiler, R.J., J.K. Wagoner, and V.E. Archer. 1973. Mortality of potash workers. J. Occup. Med. 15: 486-489.

Williams, R.R., N.L. Stegens, and J.R. Goldsmith. 1977. Associations of cancer site and type with occupation and industry from the Third National Cancer Survey interview. J. Natl. Cancer Inst. 59: 1147-1185.

Wong, D., C.E. Mitchell, R.K. Wolf, J.L. Mauderly, and A.M. Jeffrey. 1986. Identification of DNA damage as a result of exposure of rats to diesel engine exhaust. Carcinogenesis 7: 1595-1597.

Wong, O., R.W. Morgan, L. Kheyts, S.R. Larson, and M.D. Whorton. 1985. Mortality among members of a heavy construction equipment operators' union with potential exposure to diesel exhaust emissions. Br. J. Ind. Med. 42: 435-448.

Wong, P.O., R.E. Gregory, and A.L. Brooks. 1983. *In vitro* evaluation of the tumor-promoting potential of diesel-exhaust-particle extracts. J. Toxicol. Environ. Health 11: 188-197.

Wynder, L.E., G. Dieck, and N.E. Hall. 1985. A case control study of diesel exhaust exposure and bladder cancer. Environ. Res. 34: 475-489.

Yu, C.P. and K.J. Yoon. 1990. Retention modeling of diesel exhaust particles in rats and humans. Research Report No. 40. Health Effects Institute, Cambridge, MA.

10.0 GASOLINE PARTICULATE MATTER

10.1 Chemical and Physical Properties

Gasoline particulate exhaust consists of a solid core composed mainly of carbon, a soluble organic fraction, sulfates, and trace elements. The gasoline particulate matter ranges from 0.01 to 0.1 µm in diameter with the peak at around 0.02 µm while the majority of the diesel particulate matter ranges from 0.1 to 1.0 µm with a peak at around 0.15 µm. When a particle is less than 1 micron (µm) in diameter it is small enough to be inhaled deeply into the lungs.

Light-duty diesel engines emit from 30 to 100 times more particles than comparable catalyst-equipped gasoline vehicles (NRC, 1982). This is offset to some degree by the greater number of catalyst-equipped gasoline vehicles on the road, relative to diesel vehicles.

The remaining chemical and physical properties of gasoline particulate matter are very similar to those of diesel particulate matter. Please consult Section 9.1 concerning diesel particulate matter for further information. No mention of the gasoline exhaust phase will be attempted here since this chapter discusses gasoline particulate matter exclusively. Motor vehicle emissions have been shown to substantially increase the mutagenic activity of bacterial strains following irradiation of the gas phase rather than the particulate phase of mixtures. These findings are discussed further in Section 12.4.3.

10.2 Formation and Control Technology

Gasoline particulate matter is formed as a result of incomplete combustion of gasoline. Lubricating oil and other fuel hydrocarbons may also contribute. It consists of a carbon core with various organic compounds associated with it. The sulfate particles experienced by gasoline engines is mostly from catalyst equipped vehicles utilizing unleaded gasoline (EPA, 1985). At present, there are no controls being implemented for gasoline particulate matter, though new standards that take effect in 1994 will limit particulate matter to 0.08 g/mile for all light-duty engines.

EPA's Five City Study (EPA, 1989) determined that POM contributed to 27% of the average excess aggregate cancer incidence in the five cities. Of this 27%, gasoline particulate matter accounted for 32%.

10.3 Emissions

10.3.1 Emission Factors for Baseline Scenarios

Gasoline particulate matter is emitted at the mg/mile level. Because it is emitted at such low levels, it is difficult to measure accurately. The available emissions data are limited and scattered. Furthermore, all the available data, with the exception of one study, apply to 1986 and prior model year vehicles.

For this study, the available emissions data were summarized (Hammerle, et al., 1992; Lewtas, 1991; Carey, 1987; Lang, et al., 1981; EPA, 1985; Volkswagen, 1991; Smith, 1981; Urban, 1980a, 1980b, 1980c; CARB, 1986). A summary table is provided in Appendix H. Gasoline particulate emissions are given in mg/mile and expressed as total hydrocarbons (THC), as measured by the FID. The gasoline particulate mass emissions data vary considerably, but appear more consistent when expressed as a percentage of THC. In general, gasoline particulate emissions tend to increase as THC emissions increase.

Since this report is meant to provide a prospective look at emissions, the data from Hammerle, et al. (1992), the only study which includes post-1986 model year vehicles, were used solely. Data from the other studies were used as support for the apparent correlation between gasoline particulate matter and THC. Use of the Hammerle, et al. (1992) data offers several advantages. First, data were collected from current 1991 model year Escorts and Explorers equipped with three-way and dual three-way catalysts, respectively. Second, data were collected at various mileage intervals up to 105,000 miles. Data from this study indicate that the mass of gasoline particulate matter is roughly 1.1% of the mass of THC as measured by the FID. This percentage was used as input to MOBTOX and applied to all gasoline vehicle categories.

10.4 Atmospheric Reactivity and Residence Times

The atmospheric reactivity and residence times are very similar to those discussed previously for diesel particulate matter and POM in Section 9.4.

10.4.1   Urban Airshed Modeling of Reformulated Gasoline Impact on Ambient POM

Treatment of POM in the UAM-Tox model is discussed in Section 9.4.5.

Simulations for the summer Baltimore-Washington area episode resulted in slight decreases in POM with the use of federal reformulated gasoline. California reformulated gasoline resulted in larger POM decreases than federal reformulated gasoline, because of reductions in the T_{90} distillation point of the fuel.

In addition, motor vehicle-related POM concentrations with federal reformulated gasoline use decreased more in winter than in summer, ranging from 4 to 8 percent.   Simulations for the summer Houston episode predicted larger decreases than in the Baltimore-Washington area with the use of reformulated gasoline.

10.5 Exposure Estimation

The data presented in Table 10-1 represent the results determined by HAPEM-MS modeling that was described previously in Section 4.1.1. These numbers have been adjusted to represent the increase in VMT expected in future years.

Table 10-1.   Annual Average HAPEM-MS Exposure Projections for Gasoline Particulate Matter.

Year-Scenario	Exposure ($\mu g/m^3$)		
	Urban	Rural	Nationwide
1990 Base Control	0.58	0.31	0.51
1995 Base Control	0.32	0.17	0.29
1995 Expanded Reformulated Fuel Use	0.31	0.17	0.28
2000 Base Control	0.23	0.12	0.20
2000 Expanded Reformulated Fuel Use	0.22	0.12	0.19
2000 Expanded Adoption of California Standards	0.22	0.12	0.19
2010 Base Control	0.19	0.10	0.17
2010 Expanded Reformulated Fuel Use	0.18	0.09	0.16
2010 Expanded Adoption of California Standards	0.17	0.09	0.15

10.6 Carcinogenicity of Gasoline Particulate Matter and Unit Risk
Estimates

10.6.1 Most Recent EPA Assessment

At this time there exists no official EPA document detailing the carcinogenicity evidence relating to gasoline particulate matter. Much of the information in this section will be taken from several sources, some relating to particles in general and others focusing on the organic compounds associated with gasoline particulate matter.

10.6.1.1 Description of Available Carcinogenicity Data

The information on the actual carcinogenicity of gasoline particulate matter is based mainly on *in vitro* and *in vivo* bioassays. This information is based on gasoline particulate matter collected from a 1977 Mustang II-302 with a V8 engine, catalyst and EGR, running on unleaded fuel. Also tested was a 6 cylinder Ford van without a catalyst, running on leaded fuel. The organic material was extracted from the particles and five to seven doses or concentrations were used in the bioassays discussed below (Lewtas, 1991).

There were four *in vitro* bioassays, *Salmonella typhimurium* (Ames test), L5178Y mouse lymphoma, BALB/c 3T3, and Chinese hamster ovary assays, conducted to determine the possibility of gene mutation. The organics from the gasoline particles were found to be mutagenic in the *S. typhimurium*, L5178Y mouse lymphoma, and BALB/c 3T3 assays, with the Chinese hamster ovary assay showing a relatively weak to negative response. In the four *in vitro* bioassays conducted to determine DNA damage (recombination, chromatid exchanges, unscheduled DNA repair, and sister chromatid exchanges) the gasoline particle organics did produce DNA strand breaks and sister chromatid exchanges. There was no evidence to support chromosomal aberrations in any of the related studies.

In the *in vivo* bioassays, the organics extracted from the gasoline particles were able to transform embryonic cells into malignant cells. The most critical of the *in vivo* bioassays, skin tumor initiation in mice, produced both benign and malignant tumors. This assay is critical because of the fact that it is used to determine a unit risk for gasoline particulate matter using the comparative potency method.

10.6.1.2 Weight-of-Evidence Judgement of Data and EPA
        Classification

At the present time, there is only a unit risk based on the comparative potency method (no human data) and an EPA classification does not exist.

10.6.1.3 Data Sets Used for Unit Risk Estimate

The unit risk available for gasoline particulate matter is based on the comparative potency method. This method, as described previously under diesel particulate matter in Section 9.6.2, utilizes epidemiological data from coke oven emissions, roofing tar emissions, and cigarette smoke and develops a correlation with the gasoline particle organics based on the relative potencies in the mouse skin tumor initiation assay. This process then determines the unit risk. See Section 9.6.2 for a more complete description of the comparative potency method.

Although gasoline engine emission particulate matter is similar to diesel exhaust in terms of chemical and most physical properties, the cancer unit risk estimate for gasoline engine exhaust is based on the comparative potency method rather than particles, for a number of reasons. The comparative potency method is believed, at present, to be the most logical approach for estimating cancer risk from gasoline engine exhaust because, first, the EPA's particle based unit risk estimate is not an official estimate and is subject to change. Also, while the composition of gasoline exhaust particulate matter may be similar to that of diesel exhaust, the particles are considerably smaller. Cancer potency may therefore differ from diesel exhaust because of greater particle surface area per unit volume and because of altered deposition patterns. Finally, since no chronic inhalation bioassays have been carried out on gasoline engine emissions, a particle based cancer risk estimate, using the same methodology as for diesel would contain a considerable degree of uncertainty.

10.6.1.4 Dose-Response Model Used

Since the comparative potency method is being used to determine the unit risk, no single dose-response model was used. In this comparative potency estimate, gasoline exhaust particulate matter was compared with coke oven emissions, roofing tar, and cigarette smoke condensate using skin papilloma multiplicity data (papillomas/mouse at 1 mg dosage).

10.6.1.5 Unit Risk Estimate

The lifetime unit risks developed for gasoline particulate matter use the response of the organics associated with the particles in the comparative potency method. For the automobile with a catalyst using unleaded fuel, the unit risks are 1.2×10^{-4} (μg organic matter/m^3)$^{-1}$ and 5.1×10^{-5} (μg particulate matter/m^3)$^{-1}$. For the automobile without a catalyst using leaded fuel, the unit risk is 1.6×10^{-5} (μg particulate matter/m^3)$^{-1}$ (Lewtas, 1991). Maximum likelihood estimates have not been developed.

10.6.2 Other Views and Risk Estimates

International Agency for Research on Cancer (IARC)

IARC (IARC, 1989) has not developed a potency for gasoline engine exhaust but has classified gasoline engine exhaust into cancer weight-of-evidence Group 2B. Agents classified into this category are considered to be *possible* human carcinogens. This classification is based on inadequate evidence for carcinogenicity of gasoline engine exhaust in humans. There is also inadequate evidence in animals with whole gasoline engine exhaust, but sufficient evidence exists for carcinogenicity in animals using condensate/extracts of gasoline engine exhaust.

The condensate/extract of gasoline engine exhaust has been tested by skin painting, subcutaneous injection, intratracheal instillation, or implantation into the lungs in mice, rats, and Syrian hamsters. There were excess skin tumors, lung tumors, and tumors at the injection site in the studies cited.

No consistent increase in lung tumors could be detected following exposure of either animals or humans to whole gasoline engine exhaust.

10.6.3 Recent and Ongoing Research

None are available at this time.

10.7 Pro Forma Carcinogenic Risk

The cancer incidences calculated below are based on uncertain emissions data, exposure estimations, and an unofficial EPA unit risk estimate. The unit risk estimate, as mentioned above, is based on the mutagenicity of the extractable organics from the particles in the comparative potency method using only the emissions from one unleaded gasoline vehicle. Due to these factors, the cancer incidences below should be considered *pro forma*.

Table 10-2 summarizes annual *pro forma* cancer incidences for all the scenarios. For estimating *pro forma* annual cancer incidences, the gasoline unit risk for catalyst vehicles based on particulate matter was used. When comparing *pro forma* cancer incidence for the base control scenarios relative to 1990, there is a 42% reduction in cancer incidence in 1995, a 58% reduction in 2000, and a 63% reduction in 2010. The reduction in emissions are higher, particularly in the out years. The projected increase in both population and vehicle miles traveled (VMT) from 2000 to 2010

Table 10-2. Annual Pro Forma Cancer Incidence Projections for Gasoline Particulate Matter.[a,b]

Year-Scenario	Emission Factor g/mile	Urban Cancer Cases	Rural Cancer Cases	Total Cancer Cases	Percent Reduction from 1990	
					EF	Cancer
1990 Base Control	0.0198	79	14	93	–	–
1995 Base Control	0.0110	46	8	54	44	42
1995 Expanded Reformulated Fuel Use	0.0107	45	8	53	46	43
2000 Base Control	0.0078	33	6	39	61	58
2000 Expanded Reformulated Fuel Use	0.0073	32	6	38	63	59
2000 Expanded Adoption of California Standards	0.0075	32	6	38	62	59
2010 Base Control	0.0062	29	5	34	69	63
2010 Expanded Reformulated Fuel Use	0.0060	27	5	32	70	66
2010 Expanded Adoption of California Standards	0.0056	26	5	31	72	67

[a]Projections have inherent uncertainties in emission estimates, dose-response, and exposure.
[b]Cancer incidence estimates are based on upper bound estimates of an unofficial EPA unit risk. This unit risk was determined from animal studies using the comparative potency method.

appears to offset some of the gains in emissions achieved through fuel and vehicle modifications.

Please note that the *pro forma* cancer unit risk estimates for gasoline particulate matter are derived using the comparative potency method and are considered an upper bound estimate for human risk. True human cancer risk may be as low as zero, but are unlikely to be greater.

10.8 Non-carcinogenic Effects of Inhalation Exposure to Gasoline   Particulate Matter

No studies exist that specifically address gasoline particulate matter. The studies cited previously in Section 9.8 relating to PM_{10} in general are applicable to both diesel and gasoline particulate matter. These studies are from the Federal Register (EPA, 1987) and were those that were utilized to establish a final National Ambient Air Quality Standard (NAAQS) for PM_{10} (particulate matter less than 10 microns in diameter) with a substantial margin of safety. Please refer to Section 9.8 for this information.

References for Chapter 10

California Air Resources Board. 1986. Particulate Exhaust Emissions: Gasoline Powered Vehicles. Emissions Studies Section, El Monte, CA. Project no. 2R8618.

Carey, P. M. 1987. Air Toxics from Motor Vehicles. Ann Arbor, Michigan: U.S. Environmental Protection Agency, Office of Mobile Sources. Publication no. EPA-AA-TSS-PA-86-5.

Environmental Protection Agency. 1985. Size Specific Total Particulate Emission Factors for Mobile Sources. Office of Mobile Sources, Emission Control Technology Division, Ann Arbor, MI. August, 1985. EPA Report No. EPA-460/3-85-005.

Environmental Protection Agency. 1987. Federal Register, 40 CFR Part 50, July 1, 1987, pages 24634-24669.

Environmental Protection Agency. 1989. Analysis of Air Toxics Emissions, Exposures, Cancer Risks and Controllability in Five Urban Areas: Volume I: Base Year Analysis and Results. Office of Air Quality Planning and Standards, Research Triangle Park, NC. July, 1989. EPA Report No. EPA-450/2-89-012a.

Hammerle R. H., T. J. Korniski, J. E. Weir, E. Chladek, C. A. Gierczak, R. E. Chase, and R. G. Hurley. 1992. Effect of Mileage Accumulation on Particulate Emissions from Vehicles Using Gasoline with Methylcyclopentadienyl Manganese Tricarbonyl. SAE Paper 920131.

International Agency for Research on Cancer. 1989. IARC monographs on the evaluation of carcinogenic risks to humans; diesel and gasoline engine exhausts and some nitroarenes, Volume 46.

Lang, J. M., L. Snow, R. Carlson, F. Black, R. Zweidinger, and S. Tejeda. 1981. Characterization of Particulate Emissions from In-Use Gasoline-Fueled Motor Vehicles. SAE Paper 811186.

Lewtas, J. 1991. Carcinogenic risks of polycyclic organic matter (POM) from selected emission sources. Health Effects Research Laboratory, Research Triangle Park, NC. Deliverable report no. 3128.

National Research Council. 1982. Impacts of diesel-powered light-duty vehicles: diesel technology. National Academy Press, Washington, D.C.

Smith, L. R. 1981. Characterization of Exhaust Emissions from High-Mileage Catalyst-Equipped Automobiles. Ann Arbor, Michigan: U.S. Environmental Protection Agency, Office of Mobile Sources. Publication no. EPA-460/3-81-024.

Urban, C. M. 1980a. Regulated and Unregulated Exhaust Emissions from Malfunctioning Non-Catalyst and Oxidation Catalyst Gasoline

Automobiles. Ann Arbor, Michigan: U.S. Environmental Protection Agency, Office of Mobile Sources. Publication no. EPA-460/3-80-003.

Urban, C. M. 1980b. Regulated and Unregulated Exhaust Emissions from Malfunctioning Three-Way Catalyst Gasoline Automobiles. Ann Arbor, Michigan: U.S. Environmental Protection Agency, Office of Mobile Sources. Publication no. EPA-460/3-80-004.

Urban, C. M. 1980c. Regulated and Unregulated Exhaust Emissions from a Malfunctioning Three-Way Catalyst Gasoline Automobile. Ann Arbor, Michigan: U.S. Environmental Protection Agency, Office of Mobile Sources. Publication no. EPA-460/3-80-005.

Volkswagen. 1991. Unregulated Motor Vehicle Exhaust Gas Components. Volkswagen AG, Research and Development, Wolfsburg, Germany.

11.0 GASOLINE VAPORS

11.1 Chemical and Physical Properties

Unleaded gasoline is a refined product of crude oil (petroleum) composed of a complex mixture of hydrocarbons, additives, and blending agents. This mixture of hydrocarbons that distills within the range of 100 to 400°F is comprised of paraffins (alkanes), olefins (alkenes), and aromatics. Compounds containing sulfur, nitrogen, and oxygen are also present in the gasoline refinery streams. Different refinery streams are blended to achieve industry specifications for physical properties, including boiling point range and vapor pressure, and desired seasonal performance standards, such as octane rating, to minimize pre-ignition or knock. Additives and blending agents are added to improve the performance and stability of gasoline. Blending agents, such as tert-butyl alcohol, methyl tert-butyl ether (MTBE), and other alcohols and ethers are used in unleaded gasoline as replacements for organometallic anti-knock agents such as tetraethyl lead. Trace concentrations of various elements including manganese, chromium, zinc, copper, iron, boron, magnesium, lead, and sulfur are also present in most gasolines. For the most part, these metals are native to the crude oil prior to refining.

Gasoline exists in two phases, liquid and vapor, with the hydrocarbon compositions being different. Liquid gasoline consists principally of 66 to 69 percent paraffins (alkanes), 24 to 27 percent aromatics, and 6 to 8 percent olefins (alkenes) (Battelle, 1985). Unleaded gasoline contains higher concentrations of isoparaffins and aromatics than does leaded gasoline. Typical gasoline product lines may contain more than 150 separate compounds. Gasoline vapors consist mainly of short-chained and iso- alkanes and their percent in gasoline vapors, as determined by four separate studies, are detailed in Table 11-1.

Table 11-1. Vapor Composition of Gasoline (Volume %).

	McDermott	Halder	Battelle	Runion	Liquid Phase
Alkanes	84	93	92	92	66-69
Alkenes	6	2	5	8	6-8
Aromatics	3	4	5	1	24-27

SOURCE: McDermott and Killiany, 1978; Halder et al., 1984; Battelle, 1985; Runion, 1975.

11.2 Exposure Estimation

Emissions of gasoline vapors to the atmosphere occur throughout the entire process of fuel handling and marketing. This process begins at the refinery and continues through bulk loading, transport, and unloading operations, then down to the service stations where vehicle refueling occurs. Gasoline vapors are also released from the vehicle itself through evaporative and tailpipe emissions. Vapors released into the atmosphere are subject to the processes of transport, dilution, and dispersion, thus, spreading the vapor over a wide area. Due to the differences in the partial pressure of various hydrocarbons, gasoline vapors emitted in the manner described above, consist of relatively more of the lighter compounds (e.g., alkanes) and less of the heavier ones (e.g., branched alkanes) than liquid fuel.

The major sources of exposure to gasoline vapors are from service station operations and as a result of gasoline leakage from underground storage tanks. The principle exposure pathways are from the ambient air, gasoline migration into the basements of homes, and the ingestion of gasoline contaminated groundwater (NESCAUM, 1989). The populations that receive the greatest exposure in the chain of fuel handling are refinery workers, bulk fuel truck drivers, service station attendants, self-service customers, and residents of neighborhoods close to refineries, bulk storage terminals, and service stations.

NESCAUM (1989) attempted to estimate the occupational and the general population exposure to gasoline vapors based on six separate scenarios. This information is summarized from NESCAUM (1989) in Table 11-2. The exposure information is based upon existing monitoring studies and limited case-study information.

11.3 Carcinogenicity of Gasoline Vapors and Unit Risk Estimates

11.3.1 Most Recent EPA Assessment

The information presented here was obtained from EPA's Evaluation of the Carcinogenicity of Unleaded Gasoline (EPA, 1987a). In the development of this document, the scientific literature has been reviewed through 1985. New issues concerning the carcinogenicity of gasoline vapors will be presented in Section 11.3.3, which summarizes recent and ongoing research not included in the 1987 EPA evaluation.

11.3.1.1 Description of Available Carcinogenicity Data

Genotoxicity

Mutagenesis tests of unleaded gasoline have been carried out in *Salmonella* (Litton Bionetics, 1977), yeast (Litton Bionetics,

Table 11-2. Summary of Ambient Concentrations and Exposure Doses Associated with Exposure to Gasoline and Benzene (NESCAUM, 1989).

Scenario	Ambient Concentrations (mg/m^3)		Estimated Exposure Doses based on alveolar ventilation (mg/kg/day)	
	Mean	Maximum	Mean	Maximum
Scenario 1: Self-service customer at gas station exposed via inhalation.				
Gasoline	369.8	1882.3	9.4×10^{-3}	1.0×10^{-1}
Benzene	2.9	13.4	7.3×10^{-5}	7.2×10^{-4}
Scenario 2: Gas station attendant exposed via inhalation.				
Gasoline	54.6	–	1.8	–
Benzene	0.6	4.1	$21.\times10^{-2}$	1.4×10^{-1}
Scenario 3: Resident living downwind of gas station exposed via inhalation.				
Gasoline	1.5×10^{-2}	7.7×10^{-2}	3.1×10^{-3}	1.6×10^{-2}
Benzene	1.3×10^{-4}	5.1×10^{-4}	2.6×10^{-5}	1.1×10^{-4}
Scenario 4: Resident inhaling vapors from nearby leaking underground storage tank.				
Gasoline	–	–	–	–
Benzene	1.8	9.3	3.6×10^{-1}	1.9
Scenario 5: Resident exposed to gasoline via ingestion of contaminated well water.				
Gasoline	16	276	1.0×10^{-1}	2.9
Benzene	1.6	7.3	1.4×10^{-2}	7.0×10^{-2}
Scenario 6: Resident exposed via inhalation and dermal contact during showering.				
Gasoline	NA	NA	1.7×10^{-1}	3.4×10^{-1}
Benzene	NA	NA	1.4×10^{-2}	2.8×10^{-2}

1977), and mouse lymphoma *in vivo* cytogenetics (Phillips Petroleum, 1984; Litton Bionetics, 1977) to determine mutation frequency. These studies, when taken collectively, indicate no increase in the mutational frequency of unleaded gasoline. A study by Phillips Petroleum (1984) to determine sister chromatid exchanges in Chinese hamster ovary cells was also negative except at the highest dose with metabolic activation.

In a series of *in vivo* studies conducted by Litton Bionetics (1977), rats received acute and subacute intraperitoneal injections of unleaded gasoline. The rate of mutation in the rat bone marrow cells showed aberrations at the intermediate dose levels, but no dose-response was observed, and the subchronic studies showed no increase in chromosomal aberrations. Litton Bionetics (1977) also administered unleaded gasoline orally for 5 days at three concentrations which yielded no significant increases in chromosomal aberrations.

Fregda et al. (1979) evaluated chromosomal aberrations among 65 males occupationally exposed to gasoline and benzene through fuel handling. There was a significant increase in frequency of chromosomal aberrations in all road tanker drivers but it may not have been primarily due to benzene exposure since both those delivering gasoline and milk had the same incidence of chromosome aberrations. Fregda et al. (1982) also investigated the incidence of chromosomal changes in men occupationally exposed to automobile fuels and exhaust gases. The chromosomal analysis showed that smokers exposed to either gasoline or diesel fuel had a higher frequency of sister chromatid exchanges (SCE) than did the non-smokers. However, the authors were unable to determine an association between the work environment and frequency of chromosomal changes.

Taken collectively, the results of these assays have not met the criteria for positive responses for genotoxicity.

Animal Data

A lifetime inhalation bioassay of aerosolized whole unleaded gasoline (zero, 67, 292, and 2056 ppm exposures) in Fischer 344 rats and B6C3F1 mice (International Research and Development Corporation (IRDC), 1982; MacFarland et al., 1984) induced a significant increase in renal carcinomas in the kidney cortex of male rats and a larger, also significant increase in hepatocellular (liver) carcinomas in female mice. Female rats and male mice had no significant treatment related induction of tumors at any organ site. The incidence of renal carcinomas was significantly increased only at the highest dose tested (2056 ppm). However, if renal adenomas, carcinomas, and sarcomas are combined, the increase was significant at both the high and intermediate dose levels. In mice, the increase in the incidence of liver carcinomas alone and adenoma and carcinomas combined was statistically significant only in the highest dose group. Moderate decrements in body weight gain in the high-dose groups indicate that the maximum tolerated dose was reached.

Glomerulonephrosis occurred in nearly all male rats, and mineralization of the pelvis was correlated with dose. However, there was no correlation between animals with tumors and those with mineralization.

MacFarland (1983) conducted a 90-day inhalation exposure study of the toxicity of unleaded gasoline vapor in Sprague-Dawley rats and squirrel monkeys as a prechronic test in preparation for the carcinogenicity study with unleaded gasoline in rats and mice. Rats and monkeys were exposed 6 hours/day, 5 days/week for 13 weeks to totally vaporized unleaded EPA reference gasoline (exposures of 0, 384, and 1552 ppm) and a leaded commercial gasoline (0, 103, 374 ppm). The animals were examined for mortality, body-weight, food consumption, toxic signs, hematological changes, urinary changes, tissue lead levels, pathology, and pulmonary tests (monkeys only). Many changes were observed in the above mentioned areas in both the rats and monkeys. Most changes were decrements in various organ weights, hematological components, and respiratory functions at the highest exposure level for both gasolines.

The initial pathological examinations showed no treatment related effects. Histopathologic reexamination of tissue sections showed subtle but discernible changes in the kidneys of the high exposure, unleaded gasoline group of male rats.

The acute and subchronic renal toxicity of decalin (Alden et al., 1983), a volatile hydrocarbon of the same general type as those contained in gasoline, is confined to male rats and does not occur in female rats or in mice, dogs, or guinea pigs. In a series of 21-day inhalation exposures of male rats to a variety of chemical fractions of gasoline (Halder et al., 1984), renal toxicity was correlated with the paraffin components, specifically, those having C6-C9 carbons with one or more branches, and not with the aromatic compounds in the mixture. In a four week study conducted by Tegeris Laboratories (1985), rats were administered by oral gavage a variety of C8 and C10 branched hydrocarbons. It was determined that two C8 branched compounds produced severe to moderate effects in the induction of kidney toxicity.

The same pattern of renal toxicity as well as positive renal tumor response occurs in response to chronic inhalation of two synthetic fuels (RJ-5 and JP-10) (MacHaughton and Uddin, 1983). Chronic inhalation studies with the jet fuels used by the Air Force and Navy (JP-4 and JP-5) have shown the same nephrotoxic lesions, but information on the carcinoma response is not available.

The Universities Associated for Research and Education in Pathology, Inc. (UAREP, 1983) analyzed the toxicology and carcinogenicity of unleaded gasoline and other hydrocarbons. This group agrees that a renal toxicity pattern is observed with exposure to hydrocarbon mixtures in Fischer 344 and Sprague-Dawley rats, involving protein accumulation in renal tubules, but

it is clearly different than the kidney lesions occurring spontaneously in old rats. The lesions do not occur in females of these strains or in mice or monkeys. Old-rat nephropathy was morphologically different from preneoplastic lesions in the API carcinogenicity study (IRDC, 1982; MacFarland et al., 1984) of unleaded gasoline vapor. However, a possible causal relationship between old-rat nephropathy and toxic lesions from exposure to unleaded gasoline vapor cannot be ruled out.

Human Data

There were fifty-five studies reviewed by the EPA in its evaluation of the carcinogenicity of unleaded gasoline (EPA, 1987a) to determine if there is any epidemiological evidence for an association between gasoline exposure and cancer risk. Only a cursory review of these studies will be included in this chapter; for more detail, consult EPA (1987a). Since unleaded gasoline was only introduced in the mid-1970's, many epidemiological studies are not likely to show an unleaded gasoline effect because of the long latency period generally associated with cancer. Therefore, the EPA review was not limited to unleaded gasoline exposure, but addressed any potential gasoline exposure. None of the studies reviewed provided qualitative as well as quantitative estimates of gasoline exposure (EPA, 1987a).

Seven studies were identified that evaluated the association between employment in the gasoline service industry and cancer risks; the industry here includes gasoline service station owners and attendants, garage workers, gasoline and fuel truck drivers, and these who reported working with gasoline. The study by Stemhagen et al. (1983) provided some evidence of an association between gasoline service station employment and risk of primary liver cancer. The remaining six studies were judged inadequate.

Twenty-five studies were reviewed that evaluated the association between employment in a petroleum refinery (a work environment with potential gasoline exposure) and cancer risk. Judged individually, these studies provided inadequate evidence of an association. However, judged collectively these studies provide suggestive evidence of an association between employment in a petroleum refinery and risk of stomach cancer, respiratory system cancer (i.e., lung, pleura, nasal cavity and sinuses), and cancer of the lymphatic and hematopoietic tissues.

Nineteen case-control studies were reviewed which evaluated employment in the petroleum industry as a cancer risk factor. The study by Howe et al. (1980) provided limited evidence of an association between petroleum industry employment and risk of bladder cancer.

Overall, these epidemiological studies provide limited evidence that employment in the petroleum industry is associated with certain types of cancer. However, the epidemiologic evidence for evaluating gasoline as a potential carcinogen is considered inadequate.

11.3.1.2 Weight-of-Evidence Judgement and EPA Classification

EPA classifies gasoline vapor as a Group B2, probable human carcinogen. This is based on sufficient evidence in animals (IRDC, 1982; MacFarland et al., 1984) that inhalation of wholly vaporized gasoline is carcinogenic. Although employment in the petroleum refineries is possibly associated with cancers of the stomach, respiratory system, and lymphopoietic and hematopoietic tissues, exposure to gasoline cannot be implicated as a causative agent because of confounding exposure to other chemicals and inadequate information on gasoline exposure. Gasoline vapors from vehicle refueling might be less carcinogenic than indicated by animal experiments using wholly aerosolized gasoline, since it is the less volatile components that apparently contribute to the carcinogenic response.

11.3.1.3 Data Sets Used for Unit Risk Estimate

The chronic inhalation study of unleaded gasoline vapor conducted by the International Research and Development Corporation (IRDC, 1982; MacFarland et al., 1984) and sponsored by the American Petroleum Institute (API) is the only study that can be used to derive the carcinogenic potency of aerosolized whole unleaded gasoline. This study is summarized in Section 11.3.1.1.

11.3.1.4 Dose-Response Model Used

The linearized multistage model is used to calculate the unit risk estimate for wholly vaporized gasoline. The unit risk estimate that currently exists for gasoline vapors is based exclusively on animal data.

11.3.1.5 Unit Risk Estimate

In the calculation of unit risk, ppm in air is assumed to be equivalent between animals and humans. The data from the highest dose group have been excluded from the calculation because the model does not fit well if these data are included and the data seem to indicate a toxic effect in the highest dose group. The results of the calculation are presented in Table 11-3 (EPA, 1987a). Both the upper bound estimate and the maximum likelihood estimate are given. The kidney data in rats and the combined hepatocellular adenoma/carcinoma data in mice are similar, spanning a range from $2.1 \times 10^{-3} (ppm)^{-1}$ to $3.5 \times 10^{-3} (ppm)^{-1}$.

Table 11-3.   Estimates of Carcinogenic Potency Due to Exposure to 1 ppm of Leaded Gasoline Vapor (EPA,1987a).

Data Base	Upper Bound Estimate	Maximum Likelihood Estimate
(1) Kidney tumors in male rats	3.5×10^{-3}	2.0×10^{-3}
(2) Hepatocellular carcinoma/adenoma in female mice	2.1×10^{-3}	1.4×10^{-3}
Hepatocellular carcinoma in female mice	1.4×10^{-3}	8.5×10^{-4}
Geometric Mean of (1) and (2)	2.7×10^{-3}	1.7×10^{-3}

11.3.2 Other Views and Unit Risk Estimates

IIT Research Institute

According to the results of subchronic studies sponsored by API, the 0° to 145°F distillate fraction (lighter, more volatile) of unleaded gasoline as well as C4-C5 (short-chain) olefinic (alkene) hydrocarbons, which are the primary components of this fraction, did not cause detectable nephrotoxicity in rats (IIT Research Institute, 1985a,b). It was further shown that the 145° to 280°F fractions contained most of the nephrotoxic activity and that the specific compounds responsible for most of the toxicity were branched-chain olefins (alkene) 6 to 9 carbons in length. Since the 0° to 145° distillate fraction is much more volatile at ambient temperatures than the heavier distillates, the vapor fraction would be expected to contain a much greater percentage of short-chain hydrocarbons. Thus, the composition of whole aerosolized gasoline used in chronic cancer assessments and gasoline vapors at ambient temperatures results in a degree of uncertainty. There are no data to indicate which fraction is responsible for induction of liver tumors in mice.

Cancer Risk Attributable to Benzene Content in Gasoline Vapor

EPA (1987a) estimates the cancer incidence which could be attributed to the benzene content of gasoline vapor. To accomplish this, two assumptions were made; the tumor response to benzene is additive to the response produced by other components of gasoline and a particular air concentration produces the same effect in animals and humans. While benzene in gasoline may be additive with other components in terms of total tumor response, it is unlikely to be additive for the types of tumors detected. Gasoline exposure induced kidney and liver tumors, whereas, benzene is known to induce other tumors such as leukemia. The benzene component was calculated to account for about 20% of the

total response. This small incidence was determined to be undetectable, since 20% of the kidney cancer incidence (16%) at the high dose (MacFarland et al., 1984) is only 0.2×16% = 3%, which is only about one animal out of 45 in that group.

There is no evidence from the benzene or gasoline literature to support or deny the additivity assumption. There is abundant evidence that a carcinogen or noncarcinogen could modify (enhance or inhibit) the carcinogenic action of another compound. Since gasoline vapor contains more than one chemical compound, such interactive effects are possible.

Health Effects Institute 1985 and 1988

The Motor Vehicle Manufacturers Association (MVMA) and the EPA requested that the Health Effects Institute (HEI) undertake a review of the issues concerning potential adverse health effects of exposure to vapors of unleaded gasoline (HEI, 1985). On the basis of the study by MacFarland et al., (1984), HEI concluded that wholly vaporized gasoline is an animal carcinogen and a presumptive human carcinogen. Taken collectively, the epidemiological studies were considered to provide weak evidence, but no proof of an association between exposure to petroleum vapors and an increase in kidney cancer. Thus, the available epidemiological evidence can neither confirm or deny the association between gasoline vapor and possible human carcinogenicity.

HEI considers the development of a realistic quantitative risk assessment too difficult to resolve or decide due to several uncertainties. Uncertainties remain regarding the difference in composition of gasoline vapors to which humans are exposed and the wholly vaporized gasoline used in the animal studies and because of the different patterns of exposure in humans and experimental animals. On the basis of the available animal studies and established guidelines, HEI agreed that the existing data can be used to calculate an upper-bound risk factor for gasoline vapors as EPA has done. HEI cautioned that the health hazard, if any, cannot be established without additional data, and that the actual risk may be anywhere between zero and the upper bound.

In January of 1988, HEI issued an update (HEI, 1988) on the issue of gasoline vapor and human cancer, evaluating the scientific information published between 1985 and 1987. This information will be summarized in the following section on recent and ongoing research. HEI concluded that the research conducted since 1985 has reduced some of the uncertainty surrounding the issues that HEI detailed in 1985. The new research lends additional support to the cautious approach adopted at that time: that the information is not available to draw accurate conclusions concerning the degree of human risk that results from exposure to gasoline vapors.

Northeast States for Coordinated Air Use Management (NESCAUM)

       In its 1989 report (NESCAUM, 1989), NESCAUM concluded that
gasoline and at least one of its major constituents, benzene, are
presumed human carcinogens. Exposure to gasoline and its
components is also associated with other adverse health effects
such as toxicity to the hematopoietic, kidney, liver,
reproductive/developmental, and nervous systems. NESCAUM agrees
that many uncertainties still exist. The major uncertainties
being that the vapor composition in MacFarland et al., (1984)
animal study is different than ambient human exposure and that
the kidney tumors observed in male rats may be the result of a
mechanism specific to the male rat and not female rats of other
species.

       Potential individual lifetime (70 years) cancer risks
associated with exposure to unleaded gasoline and benzene are
presented in Table 11-4. These cancer risks are based on a
cancer potency value of 0.0035 per mg/kg/day for gasoline and
0.026 mg/kg/day for benzene. The exposure doses corresponding to
one in a million cancer risk for gasoline and benzene are
estimated to be 2.8×10^{-4} mg/kg/day and 3.8×10^{-5} mg/kg/day,
respectively. NESCAUM uses a variety of research studies, case
studies (most specific to the northeast states), and computer
models for each of the six scenarios to derive the estimated
lifetime cancer risk. Several uncertainties exist, including the
following: estimates may exclude gasoline components of
potential concern; inaccuracies in the assumptions about the
intensity and duration of exposure; lack of information on
interactive effects among constituents in the complex mixture;
and uncertainties associated with exposure of sensitive
individuals. These and other uncertainties cause NESCAUM to
develop a conservative approach, when possible.

Motor Vehicle Manufacturers Association (MVMA)

       The MVMA petitioned the EPA (MVMA, 1991) to reexamine the
evidence for gasoline vapor carcinogenicity and, in light of new
information, to reclassify the category of gasoline vapors from
Group B2 (probable) to C (possible human carcinogen). MVMA feels
this reclassification is essential so that the need for public
protection from the risk of cancer due to exposure to evaporated
gasoline can be properly assessed and any proposed regulatory
action involving vapor can be appropriately updated. MVMA states
that the animal tumors are of questionable relevance and there is
inadequate epidemiological evidence for predicting the true human
risk. MVMA cites HEI (1985;1988), EPA (1987a), EPA (1991b)
discussed in Section 11.3.3.1, and the SAB concurrence with that
document to support their position. MVMA states that this new

Table 11-4. Potential Cancer Risks Associated with Exposure to Gasoline and Benzene (NESCAUM, 1989).

Exposure Scenario	Mean Lifetime Cancer Risk-Gasoline (risk/person/lifetime)	Mean Lifetime Cancer Risk-Benzene (risk/person/lifetime)
Self-service customer at gas station exposed via inhalation.	3.3×10^{-5}	1.9×10^{-6}
Gas station attendant exposed via inhalation.	6.3×10^{-3}	5.5×10^{-4}
Resident living downwind of gas station exposed to inhalation.	1.1×10^{-5}	6.8×10^{-7}
Resident inhaling vapors from nearby leaking underground storage tank.	--	9.4×10^{-3}
Resident exposed to gasoline via ingestion of contaminated well water.	6.0×10^{-4}	3.6×10^{-4}
Resident exposed via inhalation and dermal contact during showering.	6.0×10^{-4}	3.6×10^{-4}

information indicates that gasoline vapor exposure does not pose significant risks to humans.

<u>EPA Response to MVMA Petition Letter</u>

In response to MVMA's letter (EPA, 1991a) the Agency has not initiated any specific effort to re-examine the weight-of-evidence for gasoline vapors based on the new tumor evaluation criteria (EPA, 1991b). It may seem timely to review the data for gasoline because of the new criteria; however, re-examination would not be limited to evaluating the kidney tumor position. EPA would also consider other newly available data relevant to the overall framework of weight-of-evidence evaluation including epidemiological data, toxicology data on non-cancer endpoints, mechanism of action, information for complex mixtures, and chemical specific information on gasoline components. It is possible that the resulting classification could be lower, higher, or unchanged, based on this comprehensive review.

11.3.3 Recent and Ongoing Research

The information contained below summarizes the information released since EPA (1987a). This document reviewed the literature available through 1985.

11.3.3.1 Alpha$_{2u}$-globulin: Association with Chemically Induced Renal Toxicity and Neoplasia in the Male Rat

EPA's Risk Assessment Forum report, <u>Alpha$_{2u}$-globulin: Association with Chemically Induced Renal Toxicity and Neoplasia in the Male Rat</u> (EPA, 1991b), provides Agency wide guidelines for evaluating renal tubule tumors in the male rat. According to this report, risk assessment approaches generally assume that a chemical producing tumors in laboratory animals is a potential hazard to humans. For most chemicals, including many rodent kidney carcinogens, this assumption remains suitable. The report describes to EPA risk assessors the scientific conditions under which the information on certain renal tubule tumors or nephrotoxicity should not be used to assess human risk. In this situation, the chemical in question induces accumulation of the protein alpha$_{2u}$-globulin in the proximal tubule of the male rat kidney. This initiates a sequence of events, specific to the male rat kidney, that appears to lead to renal tubule tumors. This EPA policy is an important change in EPA's general approach to cancer risk assessment.

The Forum report stresses the need for a full review of a substantial data set to determine when it is reasonable to presume that renal tumors in male rats are linked to a process involving alpha$_{2u}$-globulin accumulation. Only then can the appropriate procedures be selected to estimate human risks under such

circumstances. Complete details of this analysis can be found by referring to the Risk Assessment Forum report (EPA, 1991b).

11.3.3.2 Genotoxicity

Dooley et al. (1987) tested unleaded gasoline, a DMSO (dimethylsulfoxide) extraction of unleaded gasoline, and an evaporative residue of unleaded gasoline for their ability to induce mutation in a modified Ames bioassay performed with and without activation. No increase in reverent colonies were observed for unleaded gasoline or the unleaded gasoline extraction. A reduction in the revertant colonies at the highest doses indicated that the unleaded gasoline extraction was toxic, but not mutagenic. The evaporative residue induced a less than two-fold increase in the mutant colonies, and, therefore, was not considered mutagenic in the assay.

Dooley et al. (1987) also tested unleaded gasoline, extraction of unleaded gasoline, and an evaporative residue for increases in the mutational frequency in the mouse lymphoma cells assay. Dooley et al. (1987) reported that at concentrations of unleaded gasoline yielding 10 percent or greater cell survival, no appreciable increase in mutation frequency with or without activation was observed. There was a greater mutational frequency observed at concentrations yielding less than 10 percent growth, but this was not considered mutagenic. It is suggested by the authors that unleaded gasoline may contain weakly mutagenic components that are masked by the toxicity of the total mixture.

Richardson et al. (1986) reported no significant increases in the mutational frequency or sister chromatid exchange frequency in human lymphoblast tested with unleaded gasoline, 2,2,4-trimethylpentane (branched C5 alkane found in gasoline), and a volatile fraction of unleaded gasoline.

Loury et al. (1986) conducted a series of *in vivo* and *in vitro* assays to assess the ability of unleaded gasoline and 2,2,4-trimethylpentane to induce unscheduled and replicative DNA synthesis in Fischer 344 rats, B6C3F1 mice, and human hepatocytes. Unscheduled DNA synthesis is a measurement of DNA repair, and therefore, an indicator of genotoxic activity. Replicative DNA synthesis is an indirect measure of cell proliferation activity.

In the unscheduled DNA synthesis assays, there are many results. In the assays involving *in vivo*/*in vitro* hepatocytes exposed to unleaded gasoline by gavage, the rat hepatocytes showed no increase, whereas the mouse hepatocytes exhibited a statistically significant increase in activity in male and female mice 12 hours after treatment. In the assays that were exclusively *in vitro*, unleaded gasoline produced statistically significant increases in DNA activity in the male mouse hepatocytes and a dose-dependent increase in activity in the rat hepatocytes. The highest doses which produced unscheduled DNA

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synthesis in rat hepatocytes were toxic to mouse and human cells. Trimethylpentane yielded no positive results.

In the second part of the experiments, both unleaded gasoline and trimethylpentane were tested for their effects on replicative DNA synthesis. *In vitro*/*in vivo* exposure of both rat and mouse hepatocytes to unleaded gasoline produced no statistically significant results. When both were exposed to 2,2,4-trimethylpentane, the replicative DNA synthesis was significantly increased.

Loury et al. (1987) also assessed the ability of unleaded gasoline to induce unscheduled DNA synthesis and replicative DNA synthesis in kidney cells of Fischer 344 rats exposed *in vivo* and *in vitro* by gavage and inhalation. The purpose of the study was to determine whether the induction of kidney tumors by unleaded gasoline is related to genotoxicity or cell proliferative effects. The *in vivo*/*in vitro* assay for unscheduled DNA synthesis produced no detectable unscheduled DNA synthesis by either gavage or inhalation. There was a significant increase in replicative DNA synthesis activity in male kidneys but not female rat kidneys.

Dooley et al. (1987) also performed the dominant lethal assay of sperm cells of CD-1 mice exposed to unleaded gasoline by inhalation. These experiments produced only a non-significant increase in pre- and post-implantation loss of embryos as compared to controls.

11.3.3.3 Metabolism and Pharmacokinetics

Overall, there is not an abundance of information on the action of unleaded gasoline in the human body. What is known is that, once absorbed in to the blood, the gasoline components partition themselves between the plasma and serum. Binding to serum proteins reduces the amount of free compounds available for exchange with air and tissues. Bound and unbound gasoline components are transported through the blood to various tissues.

Tissue clearance is accomplished by the metabolism of the parent hydrocarbons into more polar compounds, which can be excreted more efficiently. Many hydrocarbons are metabolized by enzyme systems in the liver, although metabolism may occur in other organs as well. Metabolic efficiency is dependent on several variables, including the tissue concentration, the affinity of the specific compound for the enzyme system, the enzyme interactions with other gasoline components, the nutritional status of the individual, exposure to other chemicals, the influence of metabolism (e.g., ethanol), and the presence or absence of tissue injury.

Much, but not all, of the pharmacokinetic data that has been accomplished since the publication of EPA (1987a) has been devoted to trying to determine the mechanism involved in the

development of the chemically-induced kidney tumors observed in the male rat. The brief summary that follows is excerpted from a Chemical Industry Institute of Toxicology technical report (CIIT, 1991) which also contains the qualitative and quantitative evidence used to support the position. Other mechanistic information from 1986 and 1987 is summarized in HEI (1988).

Alpha$_{2u}$-globulin is synthesized and secreted at a rapid rate from the liver into the blood of the male, but not female rats. Approximately 50% of the protein filtered by the kidney is resorbed by the proximal tubule cells (PTC) of the kidney. Chemical treatment does not appear to increase the synthesis of alpha$_{2u}$-globulin in the liver or change the amount that is resorbed by the PTC. The most plausible explanation for the accumulation of alpha$_{2u}$-globulin in the kidney cells is that the rate of hydrolysis of alpha$_{2u}$-globulin in the kidney is decreased when the protein is bound to the chemical. This then results in protein droplet accumulation and increased cell proliferation in the PTC. This has been observed in male rats exposed to unleaded gasoline or 2,2,4-trimethylpentane.

Chemical-mediated accumulation of alpha$_{2u}$-globulin is thought to be responsible for killing cells, which in turn stimulates cell division as the kidney attempts to repair itself. With prolonged exposure, repeated cycles of cell death and reparative replication are proposed to be responsible for the observed tumorigenic response.

11.3.3.4 Carcinogenicity - Animal Studies

Studies have been accomplished linking other chemicals to the production of lesions in the male rat kidney. Similar findings have been reported for decalin (Kanerva et al., 1987a), d-limonene (Kanerva et al., 1987b), 1,4-dichlorobenzene (Charbonneau et al., 1988), and 2,2,4-trimethylpentane (Stonard et al., 1986). Some of these compounds also cause a sex-specific increase in renal adenomas and/or carcinomas in rats. The three compounds decalin, d-limonene, and trimethylpentane have been used as model compounds for studying the mechanisms of renal toxicity because of their ability to produce the characteristic lesions.

Two studies were conducted that evaluated the renal toxicity associated with the light hydrocarbons. These hydrocarbons are more characteristic of the major fraction of ambient gasoline vapors. These two inhalation experiments (Halder et al., 1986; Aranyi et al., 1986) used Sprague-Dawley rats exposed to vapor mixtures representative of ambient gasoline vapors. In both studies, there was no evidence of nephrotoxicity in rats of either sex after either 3 or 13 weeks of exposure.

All the rest of the animal research has been conducted to further the understanding of the mechanisms involved in the toxicity and potential carcinogenicity of hydrocarbons in the male rat kidney due to gasoline vapor exposure. The results of

this body of work were summarized in Section 11.3.3.3. Little research has been directed toward furthering a better understanding of the role of hydrocarbons in the induction of female mouse liver tumors observed in MacFarland et al. (1984).

11.3.3.5 Carcinogenicity - Epidemiological Studies

In a literature survey by Harrington (1987), 22 cohort studies and 19 case-control studies of the health experience of workers in the petroleum manufacturing and distribution industry published between 1972 and 1986 were reviewed. The standard mortality ratio for kidney cancer was elevated for exposed workers in two studies, decreased in four studies, and unchanged in three studies. Taken collectively, the epidemiological studies observed do not provide support for and association between exposure to petroleum hydrocarbons and renal cancer.

In a study not reviewed by Harrington (1987), McLaughlin et al. (1985) examined renal cell carcinoma in relation to employment in the petroleum industry. This study was based on data collected in a case-control study of renal carcinoma in the Minneapolis-St. Paul area (McLaughlin et al., 1984). In this analysis of the 1984 study, using only male data, no evidence was produced to support a positive association between kidney cancer and employment in the petroleum industry.

Schwartz (1987) conducted a proportionate mortality ratio analysis of automobile mechanics and gasoline service station workers in New Hampshire. There were significant increases in the association between workplace and the incidence of suicide and leukemia, but no significant increases in other tumors.

11.4 Pro Forma Carcinogenic Risk

The cancer incidences in Table 11-5 below are based on uncertain exposure estimations and an unofficial EPA unit risk estimate. The unit risk estimate, as mentioned above, is based on wholly vaporized gasoline and may not be representative of actual exposure. Furthermore, when considering the other views and the recent and ongoing research summarized in Sections 11.3.2 and 11.3.3, it is reasonable to assume that the gasoline vapor risk estimates are conservative and more highly uncertain than the risk estimates for the other pollutants examined in this report. Due to these factors, the cancer incidences should be considered *pro forma*.

Table 11-5. Summary of Annual Average Baseline Risks (1988 to 2020) of Exposure to Whole Gasoline Vapor (EPA, 1987b).[a,b]

Facility Category	Annual Average Incidence	
	Benzene	Gasoline Vapors
Bulk Terminals	0.1	3.5
Bulk Plants	0.05	1.4
Service Stations		
1) Community Exposure		
a) Stage I	0.1	3
b) Stage II	0.4	10
2) Self-Service	4.4	33
Total Public Incidence	5.1	51
Occupational (Service Stations)	1.7	17
Total Incidence for Gasoline Marketing Source Category	6.8	68

[a]Projections have inherent uncertainties in emission estimates, dose-response, and exposure.
[b]Cancer incidence estimates are based on upper bound estimates of an unofficial EPA unit risk. This unit risk was determined from animal studies based on wholly vaporized gasoline and may not be representative of actual exposure.

Table 11-5 contains the baseline average annual cancer incidence from high exposure to gasoline vapor that was conducted by EPA (1987b) in a draft regulatory impact analysis. The aerosolized whole unleaded gasoline risk values are based on the upper bound estimate of the API sponsored rat studies (IRDC, 1982; MacFarland et al., 1984). The values presented in Table 11-5 are the average annual values for the study period of 1988 to 2020. The cancer cases attributed to benzene have already been accounted for by considering benzene evaporative emissions in Chapter 5.

11.5 Non-carcinogenic Effects of Inhalation Exposure to Gasoline Vapors

Since the focus of this report is on the carcinogenic potential of the various compounds, the noncancer information will be dealt with in a more cursory fashion. No attempt has been made to synthesize and analyze the data encompassed below. Also, no attempt has been made to accord more importance to one type of noncancer effect over another. The objective is to research all existing data, describe the noncancer effects observed, and refrain from any subjective analysis of the data.

Exposure to gasoline vapors through inhalation at low concentrations and/or acute exposure may cause a variety of symptoms including respiratory tract irritation and burning with cough and sore throat, and central nervous system depression with headache, nausea, and mental confusion. Higher concentrations may cause respiratory difficulty, pulmonary edema (accumulation of fluid in the lungs) or bronchial pneumonia with fever. Heart damage and further central nervous system depression may also occur with muscular incoordination, blurred vision, unconsciousness, or convulsions. Even brief exposure to high concentrations may cause unconsciousness, coma, or death from severe central nervous system depression resulting in respiratory failure (MSDS, 1985;1987;1989).

Chronic exposure to gasoline vapors may cause dizziness, weakness, nervousness, limb pain, peripheral numbness, or other abnormalities in sensation. Other effects that may develop include anorexia, weight loss, pallor, fatigue, confusion, or anemia (MSDS, 1985). An important hazard associated with chronic gasoline inhalation (of even low concentrations which are the most common) is exposure to aromatic hydrocarbons, especially benzene. Severe exposure can result in irreversible effects such as encephalopathy (any disease of the brain); aplasticanemia (low oxygen carrying capacity due to bone marrow failure); and leukemia (EPA, 1980).

The threshold limit value (TLV), or the level which is considered to be safe by NIOSH for exposure for an eight hour work day, is set at 300 ppm for gasoline. The short term exposure limit (STEL), or the level considered to be safe for a period of 15 minutes, is set at 500 ppm.

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11.6 References for Chapter 11

Alden, C.L., R.L. Kanerva, G. Ridder, and L.C. Stone. 1983. The
pathogenesis of nephrotoxicity of volatile hydrocarbons in the
male rat. G.P. Hemstreet III, J.J. Thorpe, and M.L. Kane, eds.
Proceedings of the Workshop on the Kidney Effects if
Hydrocarbons, Boston, MA July 18-20. American Petroleum
Institute, pp. 154-170.

Aranyi, C., W.J. O'Shea, C.A. Halder, C.E. Holdsworth, and B.Y.
Cockrell. 1986. Absence of hydrocarbon-induced nephropathy in
rats exposed subchronically to volatile hydrocarbon mixtures
pertinent to gasoline. Toxicology and Industrial Health, 2:85-
98.

Battelle. 1985. Literature evaluation of gasoline vapor
toxicology. Prepared for Health Effects Institute. Richland,
MI: Battelle Pacific Northwest Laboratories.

Charbonneau, M., J. Strasser, E.A. Lock, M.J. Turner, and J.A.
Swenberg. 1988. 1,4-Dichlorobenzene-induced nephrotoxicity:
similarity with unleaded gasoline-induced renal effects. In:
Nephrotoxicity: Extrapolation from *in vitro* to *in vivo* and from
animals to man, P. Bach and E.A. Lock ed.

CIIT. 1991. Protein Nephrotoxicity and Kidney Cancer in Male
Rats: Qualitative and Quantitative Issues and Human Relevance.
Vol. 11, No. 1, January 1991.

Dooley, J.F., M.J. Skinner, T.A. Roy, G.R. Blackbuar, C.A.
Schreiner, and C.R. Mackerer. 1987. Evaluation of the
genotoxicity of API reference unleaded gasoline. In:
Polynuclear aromatic hydrocarbons. Proceedings of the tenth
international symposium. Battelle Press.

EPA. 1980. Facts and issues associated with the need for a
hydrocarbon criteria document. Office of Research and
Development, Environmental Criteria and Assessment Office,
Internal Document, February 1980.

EPA. 1987a. Evaluation of the Carcinogenicity of Unleaded
Gasoline. EPA Report No. 600/6-87/001, April 1987.

EPA. 1987b. Draft Regulatory Impact Analysis: Proposed
Refueling Emission Regulations for Gasoline-Fueled Motor
Vehicles. Volume I: Analysis of Gasoline Marketing Regulatory
Stategies. EPA Report No. 450/3-87-001a, July 1987.

EPA. 1991a. Letter from William Farland of EPA to Thomas Carr
of MVMA, October 28, 1991.

EPA. 1991b. Alpha$_{2u}$-Globulin: Association with Chemically Induced Renal Toxicity and Neoplasia in the Male Rat. Risk Assessment Forum, Washington, D.C. EPA Report No. 625/3-91/019F, September 1991.

Fregda, K., J. Reitalu, and M. Berlin. 1979. Chromosome studies in workers exposed to benzene. In: Genetic Damage in Man Caused by Environmental Agents, Vol. 1, pp. 187-203. Edited by E.K. Berg. New York: Academic Press.

Fregda, K., L. Davring, M. Sunner, B.O. Bengtsson, C.G. Elinder, P. Sigtryggsson, and M. Berlin. 1982. Chromosome changes in workers (smokers and nonsmokers) exposed to automobile fuels and exhaust gases. Scand. J. Environ. Health 8:209-221.

Halder, C.A, T.M. Warne, and N.S. Hatoum. 1984. Renal toxicity of gasoline and related petroleum naphthas in male rats. In: Advances in Modern Environmental Toxicology, Volume VII. Renal Effects of Petroleum Hydrocarbons, p. 73-88. Edited by M.A. Mehlman, C.P. Hemstreet, J.J. Thorpe, and N.K. Weaver. Princeton: Princeton Scientific Publishers, Inc.

Halder, C.A., G.S. Van Gorp, N.S. Hatoum, and T.M. Warne. 1986. Gasoline vapor exposures: Part II. Evaluation of the nephrotoxicity of the major C4/C5 hydrocarbon components. Am. Ind. Hyg. Assoc. J. 47:173-175.

Harrington, J.M. 1987. Health experience of workers in the petroleum manufacturing and distribution industry: a review of the literature. Am. J. Indust. Med. 12:475-497.

HEI. 1985. Gasoline Vapor Exposure and Human Cancer: Evaluation of Existing Scientific Information and Recommendations for Future Research. Cambridge, MA, September 1985.

HEI. 1988. Supplement to: Gasoline Vapor Exposure and Human Cancer: Evaluation of Existing Scientific Information and Recommendations for Future Research. Cambridge, MA, January 1988.

Howe, G.R., J.D. Burch, A.B. Miller, G.M. Cook, J. Esteve, B. Morrison, P. Gordon, L.W. Chambers, G. Fodor, and G.M. Wilson. 1980. Tobacco use, occupation, coffee, various nutrients, and bladder cancer. J. Natl. Cancer Inst. 64:701-713.

IIT Research Institute. 1985a. Thirteen-week inhalation toxicity study of a 0 to 145°F gasoline distillate fraction in rats. Sponsored by the American Petroleum Institute. Chicago, IL: IIT Research Institute.

IIT Research Institute. 1985b. Thirteen-week inhalation toxicity study of C4/C5 hydrocarbon blends in rats. Sponsored by

the American Petroleum Institute. Chicago, IL: IIT Research
Institute.

IRDC. 1982. Motor Fuel Chronic Inhalation Study. Six Volumes.
Mattawan, MI: Sponsored by the American Petroleum Institute.

Kanerva, R.L., M.S. McCracken, C.L. Alden, and L.C. Stone.
1987a. Morphogenesis of decalin-induced renal alterations in the
male rat. Fd. Chem. Toxic. 25:53-61.

Kanerva, R.L., G.M. Ridder, F,R, Lefever, and C.L. Alden. 1987b.
Comparison of short-term renal effects due to oral administration
of decalin or d-limonene in young adult male Fischer 344 rats.
Fd. Chem. Toxicol. 25:345-353.

Litton Bionetics, Inc. 1977. Mutagenicity Evaluation of
Unleaded Gasoline. Final Report. Submitted to the American
Petroleum Institute, Washington, D.C.

Loury, D.J., T. Oliver-Smith, S. Strom, R. Jirtle, G.
Michalopoulos, and B.E. Bitterworth. 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. and App. Pharm. 85:11-23.

Loury, D.J., T. Oliver-Smith, and B.E. Butterworth. 1987.
Assessment of unscheduled and replicative DNA synthesis in rat
kidney cells exposed in vitro or in vivo to unleaded gasoline.
Tox. and App. Pharm. 87:127-140.

MacFarland, H.N. 1983. Xenobiotic-induced kidney lesions:
Hydrocarbon--the PS-6 90-day and 2-year gasoline studies. G.P.
Hemstreet III, J.J. Thorpe, and M.L. Kane eds. Proceedings of
the Workshop on the Kidney Effects of Hydrocarbons, Boston, MA,
July 18-20. American Petroleum Institute, pp. 68-74.

MacFarland, H.N., C.E. Ulrich, C.E. Holdsworth, D.N. Kitchen,
W.H. Walliwell, and S.C. Blum. 1984. A chronic inhalation study
with unleaded gasoline vapor. J. Am. Coll. Toxicol. 3:231-248.

MacHaughton, M.G. and D.E. Uddin. 1983. Toxicology of mixed
distillates and high-energy synthetic fuels. G.P. Hemstreet III,
J.J. Thorpe, and M.L. Kane eds. Proceedings of the Workshop on
the Kidney Effects of Hydrocarbons, Boston, MA, July 18-20.
American Petroleum Institute, pp. 171-185.

McDermott, H.J. and S.E. Killiany. 1978. Quest for gasoline
TLV. Amer. Indus. Hyg. Assoc. J. 39:110-117.

McLaughlin, J.K., J.S. Mandel, W.J. Blot, L.M. Schuman, E.S.
Mehl, and J.F. Fraumeni. 1984. A population-based case-control
study of renal cell carcinoma. JNCT 72:275-284.

McLaughlin, J.K., W.J. Blot, J.S. Mandel, E.S. Mehl, P.A. Stewart, F.S. Venable, and J.F. Fraumeni. 1985. Petroleum-related employment and renal cell cancer. J. Occup. Med. 27:9, 672-674.

MSDS. 1985. Material Safety Data Sheet: Gasoline/Automotive. Occupational Health Services, Inc., September 1985.

MSDS. 1987. Material Safety Data Sheet: Gasoline; Evaporated Exhaust Emissions Test Fuel. Howell Hydrocarbons, Inc., April 1987.

MSDS. 1989. Material Safety Data Sheet: Unleaded Premium Gasoline. Sun Oil Company. June 1989.

MVMA. 1991. Letter to William K. Reilly of EPA from Thomas J. Carr of MVMA. September 1991.

NESCAUM. 1989. Evaluation of the Health Effects From Exposure to Gasoline and Gasoline Vapors. Final Report. August 1989.

Phillips Petroleum Company. 1984. Toxicity study summary for unleaded gasoline. Submitted to the American Petroleum Institute in November 12, 1984.

Richardson, K. A., J.L. Wilmer, D. Smith-Simpson, and T.R. Skopek. 1986. Assessment of the genotoxic potential of unleaded gasoline and 2,2,4-trimethylpentane in human lymphoblasts *in vitro*. Toxicol. and Appl. Pharm. 82:315-322.

Runion, H.E. 1975. Benzene in Gasoline. Am. Ind. Hyg. Assoc. J. 36:338-350.

Schwartz, E. 1987. Proportionate mortality ratio analysis of automobile mechanics and gasoline service station workers in New Hampshire. New Hampshire Department of Health and Human Services, Division of Health Services. Amer. J. Indus. Med. 12:91-99.

Stemhagen, A., J. Slade, R. Altman, and J. Bill. 1983. Occupational risk factors and liver cancer. A retrospective case-control study of primary liver cancer in New Jersey. Am. J. Epidemiol. 177:443-454.

Stonard, M.D., P.G.N. Phillips, J.R. Foster, M.G. Simpson, and E.A. Lock. 1986. Alpha$_{2u}$-globulin: measurement in rat kidney following administration of 2,2,4-trimethylpentane. Toxicol. 41:161-168.

Tegeris Laboratories, Inc. 1985. Four-week oral nephrotoxicity screening study in male F334 rats. Temple Hills, MD. Sponsored by the American Petroleum Institute.

UAREP. 1983. Hydrocarbon toxicity: Acute, subchronic, and chronic effects in relation to unleaded gasoline exposure of rodents, with comments on the significance to human health. Prepared for the American Petroleum Institute.

12.0 EPA'S INTEGRATED AIR CANCER PROJECT

12.1 Background

The Integrated Air Cancer Project (IACP) is an EPA interdisciplinary research program aimed at identifying the major carcinogenic chemicals emitted into the air, the specific sources of these chemicals and the impact on humans of exposure to ambient concentrations of these chemicals. The IACP research strategy was designed to focus on products of incomplete combustion (PICs). PICs include polycyclic organic matter (POM), primarily absorbed to respirable particles. This POM comprises most of the human cancer risk of PICs.

The IACP has primarily taken the approach of measuring the mutagenicity of ambient air samples and apportioning this mutagenicity to sources. The IACP has looked at apportionment in Raleigh, North Carolina; Albuquerque, New Mexico; and Boise, Idaho. In Boise, the IACP has also assessed exposure from airborne carcinogens based on ambient measurements and human time-activity profiles, analyzed the role of atmospheric transformation on mutagenicity, and estimated human cancer risk using the comparative potency method. A field study has also been conducted in Roanoke, Virginia, but to date, little analysis has been done.

The Raleigh and Albuquerque efforts were essentially done to develop methodologies and validate them in the field. The Boise program was a much more extensive effort in a simple airshed with two main pollution sources -- residential wood combustion and motor vehicle emissions. The Roanoke program involves a more complex airshed, with pollution from residential oil combustion, woodsmoke, and motor vehicle emissions. The IACP program will conclude with the analysis of the Roanoke study. Although IACP studies have focused on air toxics from residential wood combustion, distillate oil combustion appliances, and motor vehicle emissions, this summary only includes information relevant to the subject of air toxics from motor vehicle emissions.

12.2 Methodology for Mutagenicity Apportionment

Mutagenicity studies focused on extractable organic material (EOM) obtained from samples. EOM is basically the amount of particulate organic material that can be extracted from ambient air samples collected on filters using methylene chloride. Typically, EOM accounts for about 60% of the fine particles collected at both the residential and mobile source sites (Highsmith et al., 1988). Some detailed characterization of the chemical content of collected samples was done using procedures such as gas chromatography, matrix isolation, and Fourier transform infrared spectrometry. Some mutagenicity studies were also done on semivolatile organic compounds (SVOCs), extracted

from ambient air samples using an absorbent known as XAD-2. In addition, volatile organic compounds (VOCs) were collected in canisters, and in the Boise study, mutagenicity was measured before and after irradiation to determine the effects of atmospheric transformation.

The IACP has primarily used variations on a test known as the *Salmonella* mutagenicity assay to determine the mutagenicity of organic compounds (EPA, 1989). These findings have been validated by animal bioassays and human epidemiological data. The assay involves exposing colonies of the bacterium *Salmonella typhimurium* to single compounds, complex mixtures, or fractions of complex mixtures. This assay, unlike whole animal assays, can be interlaced with analytical chemistry methods to identify the major classes or specific compounds responsible for the mutagenicity. The *Salmonella* mutagenicity assay uses strains of *S. typhimurium* having specific genetic mutations which make them more sensitive to mutagenesis than "normal" *S. typhimurium*. The IACP studies used a strain designated TA98, with the addition of a rat liver homogenate, designated +S9. When exposed to a mutagenic compound or a mutagenic fraction from an air sample, cells from the TA98 strain can undergo another mutation which causes them to revert back to "normal." Thus, mutagenicity of an air sample is measured in terms of the number of revertants per cubic meter (rev/m^3). The potency of EOM collected from that sample can be expressed in terms of revertants per microgram EOM ($rev/\mu g$ EOM).

To determine source apportionment of mutagenicity, the IACP has used what is referred to as the receptor-model approach (EPA, 1989). This approach is most effective where the number of sources are small and well-characterized and involves using an element or compound as a tracer to identify a given source (Lewtas and Cupitt, 1987). For instance, the element lead (Pb) has traditionally been used as a tracer for motor vehicle sources of emissions and is the primary tracer used in this study. However, since it is being phased out as a component of gasoline, other tracers have been suggested. Among these are the organic compounds xylene, methylhexane, methylcyclohexane, methylpentane and trimethylpentane (Zweidinger et al., 1990). Potassium (K) and Carbon-14 (^{14}C) are often used as tracers for residential wood burning.

In summary, the IACP approach involves the following series of steps for EOM:
1) Ambient air samples are collected on filters and the organic material is extracted. Detailed chemical characterization is done using gas chromatography and other techniques.
2) Mutagenicity is determined using the *Salmonella* mutagenicity assay.
3) Mutagenicity is apportioned using the receptor model approach, involving the use of chemical tracers to identify sources.

The procedure for measuring mutagenicity in SVOCs and VOCs varies somewhat, due to the different collecting techniques.

12.3 Apportionment of Mutagenicity from Field Measurement Programs

To date, the IACP has completed two field measurement programs. The first involved sampling in two locations -- Raleigh, North Carolina and Albuquerque, New Mexico, while the second involved sampling in Boise, Idaho.

The first field measurement program, conducted in Winter, 1985, was designed primarily to assess proposed sampling and analytical methods, and to provide a field test of the methods available. The Raleigh sampling effort focused on assessing proposed sampling and analytical methods, while the Albuquerque effort focused on providing a field test of available methods in a simple airshed.

The Boise, Idaho field program was a much more extensive program than the sampling programs in Raleigh or Albuquerque. Boise was selected for an extensive sampling effort because of the predominance of residential wood combustion and motor vehicle emissions as pollution sources in the winter and because of the ready availability of good sampling sites. Because there is little industry in Boise, and because of meteorological conditions that result in retention of local emissions, Boise is a relatively simple airshed to study.

12.3.1 Raleigh, North Carolina

Samples were collected for 12 hour periods beginning at 7:00 A.M. and 7:00 P.M., at two ambient monitoring sites, one in a residential area and one in a rural area. The residential monitoring site was impacted by woodsmoke, while the rural site was chosen to evaluate regional source contributions to the airshed. Source sampling was conducted at three residences with wood stoves, to determine if mutagenicity of organics in the ambient air was higher than the wood stove source samples (Stevens, et al., 1990; Highsmith, et al., 1987). The field study was conducted from January through March 1985.

As previously mentioned, source apportionment of samples collected at ambient monitoring sites was done using the receptor-modeling approach. Receptor-modeling assumes that the ambient concentration of a pollutant can be represented as a sum of terms, with each term representing the contribution of a particular source category (EPA, 1989). These terms are the product of a chemical species tracer (e.g., Pb for motor vehicle emissions) and some coefficient determined by regression analysis of data obtained from ambient sampling. Regression analysis determines how the value of one variable affects another variable. Thus, this analysis could be used to determine what

pollutant concentration could be expected for a given concentration of a specific tracer.

This receptor-modeling approach was used to apportion EOM to sources. It was found that almost all EOM was from woodsmoke or motor vehicles (>99%). This verified that Raleigh was indeed a simple airshed with two major pollution sources. For both monitoring sites combined, approximately 93% of EOM was from woodsmoke and approximately 7% was from motor vehicles (Stevens, et al., 1990).

Mutagenicities and potencies of woodsmoke and motor vehicle emissions from ambient samples were determined using the results of the regression analysis (Stevens, et al., 1990). Results indicated that almost all mutagenic activity for samples could be attributed to wood burning and motor vehicles. Although only about 7% of EOM was from motor vehicles, it accounted for over 20% of the total mutagenicity. This was because the mutagenic potency for motor vehicle emissions was much higher than for woodsmoke (3.7 ± 1.5 rev/µg EOM for motor vehicle emissions, as determined from the Albuquerque work discussed later, versus 0.8 ± 0.1 rev/µg EOM for woodsmoke).

In addition, the mutagenic potency of organics in the ambient air (1.1-1.9 rev/µg EOM) was significantly higher than the mutagenicity of wood stove source samples (0.2-0.6 rev/µg EOM). This difference is likely due to the contribution of motor vehicle emissions to ambient air samples and the effects of atmospheric transformation.

[14]C content was measured in a small number of samples to confirm the results obtained using K as a tracer for woodsmoke (Stevens et al., 1990). The ^{14}C isotope of carbon is found in emissions resulting from wood burning, in a characteristic ratio to the more common isotope, ^{12}C, but is absent from emissions resulting from combustion of fossil fuels. The ^{14}C approach provides a direct estimate of the fraction of carbon in an ambient air sample resulting from woodsmoke. Estimates of source apportionment using this approach corresponded well to estimates obtained using the receptor-modeling approach with K as a tracer for woodsmoke emissions and Pb as a tracer for motor vehicle emissions.

Analysis of source samples from three residences in Raleigh with wood stoves was also done to compare indoor and outdoor samples (EPA, 1989). It was found that, although the distribution of volatile organic compounds (VOCs) was similar both indoors and outdoors, the mass of fine particles was lower indoors than outdoors. In contrast, aldehyde concentrations were higher indoors than outdoors, because aldehyde concentrations were probably affected more by building materials, furnishings, and homeowner activities more than woodsmoke or motor vehicle emissions.

12.3.2 Albuquerque, New Mexico

As with the Raleigh sampling effort, samples were collected for 12 hour periods beginning at 7:00 A.M. and 7:00 P.M. Samples were collected at two ambient monitoring sites, one a residential site impacted by woodsmoke and the other a roadway site. The field study was conducted from December, 1984 to February, 1985.

In Albuquerque, as in Raleigh, most EOM was from woodsmoke and motor vehicles (94%) (Stevens et al., 1990, Lewis et al., 1988). However, in Albuquerque, motor vehicles contributed much more to the total EOM than in Raleigh (17% in Albuquerque versus 7% in Raleigh). Moreover, motor vehicles accounted for about 36% of the total mutagenicity. The measured mutagenic potency for motor vehicle emissions was 3.7 ± 1.5 rev/µg, which was also used in the Raleigh work. The identical motor vehicle potencies result from the same coefficient being used to express the relationship of Pb and motor vehicle emissions in both cities. In Raleigh, motor vehicle emissions made up such a small percentage of the total that the coefficient for that site could not accurately be determined as it was for Albuquerque. The potency of woodsmoke emissions in Albuquerque was 1.3 ± 0.3 rev/µg, comparable to the value of 0.8 ± 0.1 rev/µg for Raleigh. Once again, results using the ^{14}C approach to determine amount of emissions resulting from woodsmoke supported results using K as a tracer.

12.3.3 Boise, Idaho

The sampling effort in Boise took place in two phases (Cupitt and Fitz-Simons, 1988; Highsmith et al., 1988, 1992). The first phase occurred during August and September 1986 when ambient samples were collected for 12 hour periods beginning at 7:00 A.M. and 7:00 P.M. These samples were collected at two sites, one in a residential area impacted by wood combustion emissions and the other a background location not impacted by any local sources. The second phase was conducted during the November 1986 through February 1987 winter heating season, when extensive wood combustion takes place. Ambient samples in this phase were collected for 12 hour periods beginning at 7:00 A.M. and 7:00 P.M. at 7 sites: three primary sites and four auxiliary sites. The primary sites were a woodsmoke site, a roadway site, and a third site in a background location not impacted by any local sources. A residential monitoring program similar to the one in Raleigh was conducted in conjunction with the winter effort.

The first phase of the Boise study was designed to test existing IACP sampling, analysis, and data management procedures, and to train personnel. No source apportionment analyses were done on data collected in this phase.

Data collected from the second phase of the Boise study indicated that over 90% of EOM could be attributed to either woodsmoke or motor vehicles (Lewis et al., 1991). Although about 27% of ambient EOM was estimated to be from motor vehicles, based on tracer studies, it accounted for 56% of total mutagenicity.

The mutagenic potency for motor vehicle emissions was 3.0 ± 1.1 rev/μg and 0.84 ± 0.25 rev/μg for woodsmoke. It should be noted, however, that recent research (Kleindienst et al., 1991) indicates that mutagenicity of the gas phase is influenced by HC/NO_x ratio. In the Kleindienst et al. study, plates of *S. typhimurium* bacteria were exposed to a mixture of VOCs (similar to that which may be found in Boise) under controlled conditions, with a VOC/NO_x ratio of either 20 or 11. On average, observed mutagenic activity at a VOC/NO_x ratio of 11 was 24 rev/h, while at a ratio of 20 it was 58 rev/h. This work also states that the gas phase reaction products are far more mutagenic than the particle phase. As was the case with the Albuquerque analyses, results using the ^{14}C approach to determine the amount of emissions resulting from woodsmoke supported results using K as the tracer.

Across sampling periods, over 60% of the mutagenicity from ambient air samples could typically be attributable to EOM. Most of the remainder could be attributed to SVOCs, with a very small fraction attributable to VOCs (EPA, 1989). The contribution of SVOCs to total mutagenicity was greater indoors than outdoors. However, the significance of the SVOC contribution to mutagenicity is unknown, since the carcinogenicity of SVOCs has not been studied.

12.4 Other IACP Studies

12.4.1 Human Cancer Risk Estimates

The Boise effort, unlike the Raleigh and Albuquerque efforts, involved animal tumorigenicity studies of the collected ambient samples. This study was the first to quantitatively estimate tumor potency and human cancer risk from EOM in an urban airshed (Lewtas et al., 1991, 1992).

Skin tumorigenesis studies were conducted in female mice. An initiator was applied over a 1 to 4 day period to the skin. The initiator was either a woodsmoke dominated sample (89% woodsmoke, 11% motor vehicle emissions) or a motor vehicle emissions dominated sample (64% motor vehicle emissions, 36% woodsmoke) applied in several dose levels on 1, 2, or 4 successive days. A positive control group was given a single dose of benzo(a)pyrene (BaP), a polycyclic aromatic hydrocarbon (PAH) known to cause lung tumors in laboratory animals. A negative control group was given a single dose of acetone (the solvent for the samples and BaP). After application of the initiator and a one week rest period, a skin tumor promotor was applied twice a week for 26 weeks. After 26 weeks the woodsmoke dominated sample was found to have a tumor initiation potency of 0.0954 skin tumors/mouse/mg (maximum likelihood estimate) and the motor vehicle emissions dominated sample was found to have a tumor initiation potency of 0.215 skin tumors/mouse/mg. Tumor initiation potencies for the positive and negative controls were not given in Lewtas et al. (1991).

These tumor initiation potencies were converted into cancer
unit risks using the comparative potency method. The tumor
initiation potencies were compared to potencies of human
carcinogens for which unit risks exist to determine relative
potencies. These relative potencies were then multiplied by the
known unit risks for the human carcinogens to get unit risk
estimates for the woodsmoke and motor vehicle emissions dominated
samples. The other known carcinogens used in the study were
emissions from coke ovens, roofing tar, and cigarettes. The
cancer unit risk estimates obtained using this approach were 0.57
x 10^{-4} lifetime risk/µg EOM/m^3 for woodsmoke dominated samples and
1.28 x 10^{-4} lifetime risk/µg EOM/m^3 for motor vehicle emissions
dominated samples. This compares to combustion source EOM unit
risks of 2.3 x 10^{-4} lifetime risk/µg EOM/m^3 for diesel vehicles
and 1.2 x 10^{-4} lifetime risk/µg EOM/m^3 for a gasoline catalyst-
equipped vehicle (Lewtas, 1991).

12.4.2 Human Exposure

In order to determine human exposure, the IACP measured
indoor and outdoor exposure levels to various carcinogens, and
applied these exposure levels to human activity patterns.

A variety of methods were used to measure levels of organic
compounds. As described previously, extractable organic matter
was collected from ambient air samples on filters using methylene
chloride. VOCs were collected in canisters and identified by gas
chromatography, and aldehydes were collected on 2,4-
dinitrophenylhydrazine silica cartridges and eluted from the
cartridges with acetonitrile. Elements were measured by X-ray
fluorescence of fine fraction dichot filters; inorganic ions,
acids and bases were determined using annular denuders and ion
chromatography (Highsmith et al., 1991).

Human activity patterns were determined by having 43
residents complete daily diaries of their activities, estimating
the fraction of time spent in different microenvironments (Glen
et al., 1991). Exposure in microenvironments was based on
ambient concentration and time spent in the microenvironment.
Total exposure, then, was the sum of exposures in different
microenvironments.

The exposure analysis indicated that while the ambient
concentration of EOM in Boise during winter averaged 15.3 µg/m^3
from woodsmoke and 4.2 µg/m^3 from mobile sources, human exposure
concentrations were 9.5 µg/m^3 from woodsmoke and 2.1 µg/m^3 from
mobile sources. These winter exposures result in annual
estimates of 3.4 µg/m^3 and 1.2 µg/m^3, respectively. Thus, mobile
sources account for about 27% of the annual exposure to
residential wood combustion and mobile sources (Cupitt et al.,
1992).

12.4.3 Atmospheric Transformation

Although wintertime conditions in Boise, Idaho are not considered conducive to photochemical reactions, IACP analyses (Nishioka and Lewtas, 1992) indicate appreciable ambient concentrations of nitrous acid. Nitrous acid is readily oxidized to hydroxyl radicals, which can then initiate atmospheric transformation processes. Also, certain compounds which occur primarily in atmospheric transformation reactions, such as nitro-aromatic and hydroxy-nitro-aromatic species, were found in ambient Boise samples (Nishioka and Lewtas, 1992). Thus, data suggest that atmospheric transformations did occur in Boise, at least on sunny days, even in winter.

Clearly, atmospheric transformation must be considered throughout the year. In fact, smog chamber simulations done as part of the IACP program (Cupitt et al., 1988, Kleindienst et al., 1991) have demonstrated an important role of atmospheric transformation in the formation of mutagens. The Cupitt et al. (1988) smog chamber studies indicate that emissions from wood stoves and motor vehicles can give substantial increases in mutagenic activity of bacterial strains following irradiation. These substantial increases are found primarily in the gas phase rather than the particulate phase of the mixtures. Whereas most mutagenicity is associated with EOM and SVOCs before irradiation, after irradiation in a smog chamber 80-99% of mutagenicity is in the gas phase. The Kleindienst et al. (1991) smog chamber study shows similar results, indicating that surrogate hydrocarbon mixtures representative of urban atmospheres can give substantial increases in mutagenic activity of bacterial strains following irradiation. As previously mentioned, the Kleindienst et al. (1991) study also indicated greater mutagenicity of irradiated VOC mixtures at higher VOC/NO$_x$ ratios.

12.5 Roanoke Field Study

A field study similar in size and duration to the Boise study was conducted in Roanoke, Virginia during the winter of 1988-1989 (EPA, 1989; Highsmith et al., 1991). The objectives and approach of the Roanoke study paralleled those of the Boise study, except that the Roanoke airshed contained emissions from residential distillate oil combustion appliances. Once again, ambient samples were collected for 12 hour periods, beginning at 7:00 A.M. and 7:00 P.M. at three primary and four auxiliary sites. A residential monitoring program was also conducted.

Analyses of samples collected in the Roanoke study are still being performed. Some preliminary analyses indicate that total NMHC at the primary mobile source site in Roanoke was 1.3 to 1.8 times the level measured at the primary residential site. This is similar to results from Boise. Furthermore, total carbonyls at the Roanoke primary mobile source site were 1.4 times higher than those at the primary residential site.

12.6 Implications

EPA's Updated Six-Month Study (EPA, 1990) indicated that roughly 50% of cancer exposure from airborne toxics may be from mobile sources. Results of the IACP study support this conclusion, with mobile sources accounting for 20% of the mutagenicity of EOM from ambient samples in Raleigh, 36% in Albuquerque, and 56% in Boise. In larger cities, where mobile sources would be expected to contribute more of the ambient EOM, this contribution to mutagenicity would be even higher. Furthermore, the mutagenic potency of EOM from mobile sources was roughly three times higher than for woodsmoke, and the lifetime unit risk for mobile sources, based on the comparative potency method, was roughly two and a half times higher than for woodsmoke. Moreover, human exposure estimates from the Boise study indicate that mobile sources account for about 27% of the annual EOM exposure. Finally, atmospheric transformation may greatly exacerbate the risk from mobile sources, since the contributions of VOCs to mutagenicity of ambient samples increases dramatically following irradiation. Thus, efforts to control cancer incidence from airborne toxics must include mobile sources.

12.7 References for Chapter 12

Cupitt, L. and T. Fitz-Simons. 1988. The Integrated Air Cancer Project: Overview and Boise survey results. Published in: Proceedings of the 1988 EPA/APCA International Symposium on Measurement of Toxic and Related Air Pollutants. APCA Publication VIP-10; EPA Report No. 600/9-88-015; pp. 799-803.

Cupitt, L., L. D. Claxton, T. E. Kleindienst, D. F. Smith and P. B. Shepson. 1988. Transformation of Boise sources: The production and distribution of mutagenic compounds in wood smoke and auto exhaust. Published in: Proceedings of the 1988 EPA/APCA International Symposium on Measurement of Toxic and Related Air Pollutants. APCA Publication VIP-10; EPA Report No. 600/9-88-015; pp. 885-889.

Cupitt, L., G. Glenn and J. Lewtas. 1992. Exposure and risk from ambient particle bound pollution in an airshed dominated by residential wood combustion and mobile sources. Risk Analysis (submitted).

Environmental Protection Agency. 1990. Cancer Risk from Outdoor Exposure to Air Toxics. Research Triangle Park, North Carolina: Office of Air Quality Planning and Standards. Publication no. EPA-450/1-90-004a.

Environmental Protection Agency. 1989. Integrated Air Cancer Project: Status Report. Research Triangle Park, North Carolina: Office of Research and Development. February 1989.

Glen, W. G., V. R. Highsmith and L. Cupitt. Development of an exposure model for application to wintertime Boise. Published in: Proceedings of the 1991 AWMA Annual Meeting, paper 91-131.7.

Highsmith, V. R., R. B. Zweidinger, C. W. Lewis, R. K. Stevens, L. D. Claxton and J. Wu. 1992. Characterization of the wintertime Boise, Idaho airshed. Atmospheric Environment (submitted).

Highsmith, V. R., A. J. Hoffman, R. B. Zweidinger, L. T. Cupitt and D. B. Walsh. 1991. The IACP: Overview of the Boise, Idaho, and the Roanoke, Virginia, field studies. Published in: Proceedings of the 1991 AWMA Annual Meeting, paper 91-131.1.

Highsmith, V. R., R. Zweidinger, J. Lewtas, A. Wisbith and R. Hardy. 1988. Published in: Proceedings of the 1988 EPA/APCA International Symposium on Measurement of Toxic and Related Air Pollutants. Impact of residential wood combustion and automotive emissions on the Boise, ID airshed. APCA Publication VIP-10; EPA/600/9-88-015; pp. 841-852.

Highsmith, V. R., R. E. Baumgardner, B. Harris, T. Lumkin, R. Grago, R. Zweidinger and R. Merrill. 1987. The collection of neighborhood air samples impacted by residential wood combustion in Raleigh, NC and Albuquerque, NM. Published in: Proceedings of the 1987 EPA/APCA Symposium on Measurement of Toxic and Related Air Pollutants, May 3-6, 1987. APCA Publication VIP-8; EPA Report No. 600/9-87-010; pp. 562-572.

Kleindienst, T. E., D. F. Smith, E. E. Hudgens, C. D. McIver, E. Perry, L. T. Cupitt, J. J. Bufalini and L. D. Claxton. 1991. The atmospheric transformation of combustion source emissions and the formation of mutagenic products. Published in: Proceedings of the 1991 AWMA Annual Meeting, paper 91-131.5.

Lewis, C. W., R. K. Stevens, R. B. Zweidinger, L. D. Claxton, D. Barraclough and G. A. Klouda. 1991. Source apportionment of mutagenic activity of fine particle organics in Boise, ID. Published in: Proceedings of the 1991 AWMA Annual Meeting, paper 91-131.3.

Lewis, C., R. Baumgardner, R. Stevens, L. Claxton and J. Lewtas. 1988. The contribution of wood smoke and motor vehicle emissions to ambient aerosol mutagenicity. Environ. Sci. Technol., 22:968-971.

Lewtas, J. 1991. Carcinogenic risks of polycyclic organic matter (POM) from selected emission sources: Development of a comparative potency method. U.S. Environmental Protection Agency, Health Effects Research Laboratory, Research Triangle Park, NC. Deliverable Report No. 3128.

Lewtas, J., M. Moore, C. T. Helms, and S. Nesnow. 1992. Comparative tumor-initiating activity of urban aerosol and source emissions from wood smoke and motor vehicles. Carcinogenesis (submitted).

Lewtas, J. R. B. Zweidinger and L. Cupitt. 1991. Mutagenicity, tumorigenicity and estimation of cancer risk from ambient aerosol and source emissions from woodsmoke and motor vehicles. Proceedings of the 1991 AWMA Annual Meeting, paper 91-131.6.

Lewtas, J. and L. Cupitt. 1987. Overview of the Integrated Air Cancer Project. Published in: Proceedings of the 1987 EPA/APCA Symposium on Measurement of Toxic and Related Air Pollutants, May 3-6, 1987. APCA Publication VIP-8; EPA Report No. 600/9-87-010; pp. 555-561.

Nishioka, M. G. and J. Lewtas. 1992. Quantification of nitro- and hydroxylated nitro-aromatic/polycyclic aromatic hydrocarbons in selected ambient air daytime winter samples. Atmospheric Environment (in press).

Stevens, R. K., C. W. Lewis, T. G. Dzubay, L. T. Cupitt and J. Lewtas. 1990. Sources of mutagenic activity in urban fine particles. Toxicol. and Indust. Health 6: 81-94.

Zweidinger, R., R. Stevens, C. Lewis and H. Westburg. 1990. Identification of volatile hydrocarbons as mobile source tracers of fine-particulate organics. Environ. Sci. Technol. 24: 538-542.

13.0 TOXICS ASPECTS OF ALTERNATIVE FUELS

The CAAA of 1990 provide for a centrally fueled clean fuel fleet program, covering fleets of 10 or more vehicles capable of central refueling. Under this program, beginning in 1998, 30 percent of new light duty vehicles and trucks purchased by centrally fueled fleets in certain ozone and CO nonattainment areas will be required to use clean fuels. There will be a separate requirement for heavy duty trucks. Rental vehicles, police vehicles, emergency vehicles, and nonroad vehicles are exempt from this requirement.

Clean fuels are defined simply by exhaust emission performance standards and result in tailpipe emissions substantially lower than those in place for general passenger cars. Vehicles could meet requirements of the program through the use of various alternative fuels and also reformulated gasolines. It is likely, however, that reformulated gasolines will capture most of the market. Initiation of the program may be delayed until 2001 if cars meeting these stringent tailpipe standards when running on clean fuels are not already being produced in California. Beginning with the model year 2001, the 50,000 mile emission certification standards for light duty clean fuel vehicles are 0.075 g/mi NMOG, 3.4 g/mi CO and 0.2 g/mi NO_x. If the program starts in 1998, the purchase requirement for clean fuel light duty vehicles and trucks will be 70 percent of the new vehicles and trucks purchased for the applicable fleet in the year 2000 and later.

The new California motor vehicle standards are intended to encourage the consideration of alternative fuels. Nevertheless, as previously mentioned, it is likely that most vehicles meeting California LEV standards will run on reformulated gasoline. It should be noted, however, that the ZEV portion of the California standards in effect require the development of electric vehicles, since electric vehicles are the only vehicles which could feasibly meet the California requirement for ZEVs at this time. The California standards are discussed in detail in Section 3.1.3.1.

Also, the Comprehensive National Energy Policy Act of 1992 requires non-gasoline alternative fueled vehicles in government and certain other fleets in the petroleum and alternative fuels industry beginning with 30 percent of new fleet purchases in 1996 and phasing up to 90 percent in 1999. The Act also requires alternative fueled vehicles in state fleets starting at 10% in 1996 and phasing up to 75% in the year 2000. In addition, the Department of Energy may extend the program to other fleets if it determines such a program is necessary.

As a result of the centrally fueled clean fuel fleet program, the new California standards, and the Comprehensive National Energy Policy Act of 1992, more alternatively fueled vehicles could possibly be added to the fleet over the next two decades. It is likely that most of these alternatively fueled

vehicles would run on high level methanol/gasoline blends, neat methanol (M100), high level ethanol/gasoline blends, neat ethanol (E100), or compressed natural gas (CNG), with a small number of electric vehicles produced to meet California's ZEV requirement. Thus, the potential cancer reduction benefits resulting from the combustion of these alternative fuels should be addressed. Although engine technology for these fuels is still being developed, potential cancer reduction benefits can be projected with reasonable confidence based on fuel differences. This chapter gives a brief overview of toxics aspects from methanol, ethanol, and CNG fuel use. A brief discussion of liquid propane gas (LPG) as a motor vehicle fuel follows.

13.1 Methanol

A promising alternative fuel for motor vehicles appears to be methanol. Although methanol has about one-half the energy per gallon as gasoline, it is a more energy efficient fuel than gasoline. Methanol is liquid, high octane, and has a reasonable range, which makes it easily adaptable. Because of its lower volatility, methanol use would result in a reduction of collision related vehicle fires (Machiele, 1990). Moreover, combustion of methanol produces a slight increase in engine power. Methanol can be used in a combustion system which operates lean much of the time. In addition, methanol can be produced easily and economically from natural gas and a range of other feedstocks (EPA, 1989). This is done today all over the world. However, non-dedicated engines burning M100 are difficult to start at low temperatures. Also, combustion of M100 does not produce a visible flame, causing a potential safety hazard in those cases where only fuel is burning. Another potential safety hazard is the possibility of fuel tank explosions with methanol. This is not expected to be a frequent occurrence, but when it does occur, the explosion is typically minor and frequently contained by the fuel tank. Also, simple design modifications can drastically reduce this possibility. Moreover, methanol is odorless, colorless and tasteless, which combined with a high toxicity, means steps must be taken to assure it is not ingested (accidentally or otherwise) by humans. Denaturant type additives are needed to prevent ingestion. Because of these concerns, small quantities of gasoline are often added to methanol. One commonly used gasoline/methanol blend is M85, with 15% gasoline and 85% methanol. Nonetheless, preliminary data obtained in tests with both M85 and M100 suggest a much greater potential for reduction in the emission of ozone precursors exists with M100 usage (Gabele, 1990). Thus, it is desirable to solve problems related to usage of M100 fuel.

13.1.1   Health Effects of Toxic Emissions from Methanol Use

The two toxic emissions resulting from methanol use which are of the most concern are methanol itself and formaldehyde. The health effects of formaldehyde were discussed in Chapter 6. The Office of Toxic Substances is revising the formaldehyde

cancer risk assessment, which will assist in estimating impacts of ambient lifetime exposures.

A large percentage of total exhaust and evaporative organic emissions from motor vehicles running on either M100 or methanol blends is methanol itself (Gabele, 1990; California Air Resources Board, 1989, 1991; Auto/Oil, 1992a,b). The health effects of M85 evaporative and combustion emissions will be some combination of those associated with both methanol and gasoline. Because the noncancer health effects of neither emissions from unleaded gasoline nor methanol are adequately understood, more research on M85 is needed.

Also, the release of methanol in the atmosphere can potentially result in the increased formation of dimethyl sulfate under certain conditions. Dimethyl sulfate is a carcinogen, is acutely toxic to the nervous system, and is highly irritating to the eyes, respiratory system, and skin. The compound has been observed in ambient air downwind of power plants, presumably as a product of the reaction of hydrocarbons with sulfur dioxide on particles. Research is needed to determine whether dimethyl sulfate is also formed to any significant degree with methanol as the hydrocarbon and, if so, to assess its potential for increasing human cancer incidence, neurotoxicity, and/or respiratory effects in areas using methanol fuels.

13.1.1.1 Effects of Chronic and Acute Exposures -- Humans

To date, little research has been done dealing with chronic effects of long term low level inhalation exposure. Chronic exposure to low levels (less than 200 ppm) of methanol has not been observed to cause serious adverse health effects in the workplace (ACGIH, 1986). As a consequence it may be that methanol has no toxic effect at the anticipated low levels of exposure from automotive methanol vapor (Kavet and Nauss, 1990; Health Effects Institute, 1987). There are currently reports of possible health effects that require further consideration. These are discussed in more detail below. The Health Effects Institute report (HEI, 1987) summarized the health effects of methanol and concluded that methanol exposure from motor vehicles would not be significant compared to methanol exposure from the diet (e.g., from a number of fruits, vegetables, diet beverages). Additional research to verify this conclusion is currently underway.

Chronic or acute exposure to methanol vapor at low levels, however, can cause symptoms such as eye irritation, headache, dizziness, nausea, and blurred vision. In humans, methanol is absorbed following oral and inhalation exposure (HEI, 1987). Once ingested or inhaled, methanol is slowly eliminated from the body, hence chronic or repeated exposures result in increased concentrations in blood and tissues (Henderson and Haggard, 1943). A primary issue is microenvironmental exposure to methanol, which would increase if methanol were used as an alternative fuel. A recent pilot clinical study sponsored by the

Health Effects Institute (Cook et al., 1991) suggests there may be slight impairment of memory and concentration due to chronic exposure at low levels (192 ppm). These results are preliminary and need to be confirmed by more definitive studies.

Oral ingestion of methanol is toxic in doses as small as 18 ml or more (Machiele, 1990). NIOSH (1976) suggests that the critical effects most associated with relatively high acute methanol exposure are visual disturbances and metabolic acidosis. Acute exposure, via oral and inhalation routes, has frequently caused death or blindness (McNally, 1937; Jacobson et al., 1945). Following ingestion of methanol by 23 men in Korea, six men died, while the others experienced nausea, epigastric pain, vomiting, headache, dizziness, delirium, varying degrees of transitory blindness, acidosis, and acetonuria (Keeney and Mellinkoff, 1951). Similar effects have also been reported after occupational exposure to high levels (4,000 to 13,000 ppm[1] for 12 hours) of methanol vapor (Browning, 1965). Acute occupational exposure to 800 to 1,000 ppm methanol has been associated with frequent headaches and blurred vision (McNally 1937). Henson (1960) noted partial vision loss in one worker exposed to 1,200-8,000 ppm methanol for four years.

Formate, a toxic metabolite of methanol which is associated with acute methanol toxicity in humans, does not appear to accumulate in blood when methanol exposure concentrations are below 200 ppm (Lee et al., 1992). The key to methanol toxicity in folate-deficient (folic acid) animals is a diminished capacity to detoxify formate in the liver. This is due to the fact that a metabolite of folate is necessary in the detoxification pathway of formate. This pathway has been demonstrated in both rats and non-human primates. In these cases, the effect of dietary folate (folic acid) on formate metabolism was the direct link to altered sensitivity to methanol; slowing formate metabolism induced a methanol-sensitive state. The role of formate in toxicity resulting from repeated acute or chronic exposures is currently unclear.

13.1.1.2 Effects of Chronic and Acute Exposures -- Animal Studies

In animals, inhalation exposure to methanol caused alterations and degeneration in the ganglionic cells, retina, and choroid of the eye (Scott et al., 1933). Additionally, rats gavaged daily with methanol for 38-90 days experienced elevated levels of serum alkaline phosphatase (SAP) and serum glutamate pyruvic transaminase (SGPT), decreased brain weights, and statistically insignificant increases in liver weights (EPA, 1986). Increases in the levels of the serum enzymes (SAP and SGPT) indicate the possibility of liver damage.

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[1]Conversion factors for methanol = 1 ppm = 1.31 mg/m^3; 1 mg/m^3 = 0.76 ppm

Inhalation exposure has also been shown to have reproductive effects on male rats. Mature rats were exposed to 260, 2,600, and 13,000 ppm methanol for 8 hours per day for 1 to 6 weeks; decreased circulating free testosterone was noted at the two lower levels (Cameron, et al., 1984). Moreover, another study by Cameron et al. (Cameron et al., 1985) also suggests that exposure to low levels of methanol could alter serum testosterone levels in rats. However, Lee et al., 1991 found that low level methanol exposure may not cause an inhibitory effect on testosterone synthesis. Rats exposed by inhalation to 200 ppm for 6 weeks (8 hr/d, 5d/wk) did not have reduced serum testosterone levels. The testes-to-body ratios of rats exposed to up to 800 ppm methanol for up to 13 weeks (20 hr/d, 7 d/wk) were not different from those of air-exposed rats. Methanol had no adverse effect on testicular morphology at the end of the 13 week exposure period at 800 ppm in either normal rats or folate-reduced methanol-sensitive rats at age 10 months. Even so, a greater incidence of testicular degeneration was noticed in the 18 month old folate-reduced rats exposed to 800 ppm for 13 weeks, suggesting that methanol may have a potential to accelerate the age-related degeneration of the testes.

Recent EPA studies show that inhalation of methanol causes birth defects in rodents. Pregnant mice exposed to 5,000 ppm of methanol, for 7 hours/day on days 6-15 of pregnancy, produced offspring with cleft palates and exencephaly (deformation of the brain where the brain forms outside of the cranium) (Rogers, et al., 1991). These data confirm developmental effects seen in other tests on rats exposed to higher concentrations of methanol (Nelson, et al., 1985).

Two recent EPA studies that are now in press, (Rogers et al., 1992; Andrews et al., 1992) continue to investigate reproductive and developmental toxicity resulting from methanol inhalation. Rogers et al., (1992) exposed pregnant CD-1 mice by inhalation to 1000, 2000, 5000, 7500, 10,000, and 15,000 ppm methanol for 7 hr/day on days 6-15 of gestation. Significant increases in exencephaly and cleft palate were observed at 5000 ppm and above, increased postimplantation mortality at 7500 ppm and above (including an increasing incidence of full-litter resorption), and reduced fetal weight at 10,000 ppm and above. A dose-related increase in skeletal abnormalities were significant at 2000 ppm and above. The No Observed Adverse Effect Level (NOAEL) for developmental toxicity in this study was 1000 ppm. The dose-response data were qualitatively modeled to estimate the added risk of developmental toxicity of inhaled methanol. The lowest maximum likelihood estimate for 5% added risk of developmental toxicity was in the dose range of the NOAEL. The results of this study indicate that inhaled methanol is developmentally toxic in the mouse at exposure levels which were not maternally toxic.

In Andrews et al., rat embryos were explanted and cultured in 0, 2, 4, 8, 12, or 16 mg MeOH/ml rat serum for 24 hours. Embryonic development of the 2 and 4 mg/ml MeOH exposure groups

were not significantly different than that of the control groups. Exposures at the higher concentration resulted in a dose related decrease in the embryos segment number and overall development. The 12 mg/ml exposure resulted in some embryo lethality as well as abnormal formation and differentiation of tissues and organs (dysmorphogenesis), while the 16 mg/ml MeOH exposure level was embryolethal. Methanol was dysmorphogenic *in vitro* to rat embryos at concentrations comparable to serum levels reported to be developmentally toxic after *in vivo* exposure. In the same study, mouse embryos were explanted and cultured in 0, 2, 4, 6, and 8 mg MeOH/ml culture medium. At all exposure levels the crown rump length and developmental score were significantly lower when compared to controls. The high dose group produced 80% lethality. Since the mouse exhibits dysmorphogenesis and embryotoxicity at lower methanol concentrations than the rat, it may be intrinsically more sensitive to methanol exposure. This species difference in sensitivity is consistent with the in vivo exposure results.

Based on these laboratory studies, inhalation of methanol vapors in excess of 1000 ppm can cause birth defects in both rats and mice. Thus, qualitatively, methanol would be called a developmental toxicant using EPA's developmental toxicity guidelines. The implications of these findings for humans, however, must await the results of further pharmacokinetics and health effects research. Pregnant women may be of special concern as a sensitive subpopulation because many have folate deficiency, which may increase susceptibility to birth defects in the developing fetus.

13.1.1.3 Health Based Criteria

An oral reference dose (RfD) of 0.5 mg/kg/day for methanol has been derived by EPA (1992). The value was based on a rat gavage subchronic study by EPA (1986) in which the increases in SAP and SGPT, and decreases in brain weights were evaluated. A no-observed-adverse-effect-level (NOAEL) of 500 mg/kg/day and an uncertainty factor of 1,000 were used to calculate the RfD. An uncertainty factor of 10 was used to account for interspecies extrapolation, 10 for range of sensitivity within the human population to xenobiotics and 10 to account for extrapolation from subchronic to chronic exposure. A reference concentration (RfC) for methanol is unavailable at this time. Methanol has not been evaluated by the EPA for evidence of human carcinogenicity potential.

The ACGIH Threshold Limit Value (TLV-TWA) is 200 ppm (260 mg/m^3) for methanol, with a short-term exposure limit (STEL) of 250 ppm (328 mg/m^3) (ACGIH, 1990). Methanol has a skin designation (ACGIH, 1990). The OSHA Permissible Exposure Limit (PEL) time-weighted average (TWA) and STEL values correspond with ACGIH's TLV-TWA and STEL for methanol, respectively (OSHA, 1989). These values were based on occupational studies in which the NOAEL was 300 ppm (Leaf and Zatman, 1952).

13.1.2   Effects of Methanol Use on Air Toxic Levels

Use of methanol in motor vehicles will result in substantial reductions or elimination of benzene, 1,3-butadiene, acetaldehyde, gasoline refueling vapors, and particulate. However, tailpipe emissions of formaldehyde (i.e. primary formaldehyde) will go up. Conversely, the use of methanol, with its lower hydrocarbon emissions, is likely to result in decreased levels of secondary formaldehyde, which is formed in the ambient air from photochemical oxidation of hydrocarbons. Projected changes in air toxics levels were given in a recent comparison of gasoline and M85 emissions from flexible fuel and variable fuel vehicles (Auto/Oil, 1992a), and toxics reductions for M100 and M85 from optimized FFVs were estimated in EPA's Methanol Special Report (EPA, 1989). Data from these sources are given in Table 13-1.

Table 13-1. Percent Change in Air Toxics Levels for M85 and M100 Relative to Gasoline.

	Auto/Oil Study (1992a)	EPA Methanol Special Report (1989)	
Pollutant/Source	M85	M85	M100
Exhaust Benzene	-84	-77	-97
Evaporative Benzene	–	-67	-100
Running Loss Benzene	–	-69	-100
Refueling Benzene	–	-14	-100
Other Gasoline Refueling Vapors	–	-14	-100
Exhaust 1,3-Butadiene	-93	-64	-99
Exhaust Gasoline POM	–	-72	-99
Primary Formaldehyde	+436	+600	+200
Secondary Formaldehyde	–	-43	-80

In addition, Auto/Oil (1992b) recently released a study comparing toxic emissions from three dedicated methanol vehicles, one running on M85 and two on M100, to toxic emissions from the FFV/VFV fleet in Auto/Oil (1992a). The dedicated methanol vehicle running on M85 was a Chevrolet Lumina designed to target California TLEV emission levels. The formaldehyde emission level for this vehicle was 5.7 g/mi (217% larger than the average formaldehyde emission level from dedicated gasoline vehicles running on baseline fuel). Benzene emissions were 1.0 g/mi (89% lower). The two dedicated methanol vehicles running on M100, a Nissan Sentra and Toyota Corolla, were designed to optimize fuel

economy, not emissions. While the Toyota Corolla's formaldehyde emission level was 7.5 g/mi (317% higher than for dedicated gasoline vehicles running on baseline fuel), the Nissan Sentra's formaldehyde emission level was 27.2 g/mi (well over 1000% higher). This disparity in emission levels is indicative that dedicated methanol vehicles are still in early stages of development, and thus a definitive assessment of toxic emissions typical of such vehicles is premature. In fact, EPA tested the same Nissan Sentra vehicle as Auto/Oil with a resistively heated palladium:cerium catalyst (Hellman and Piotrowski, 1990), and formaldehyde was measured at 0.20 g/mi.

As mentioned previously, combustion of M100 and methanol blends produces more primary formaldehyde emissions than combustion of gasoline. However, most of these formaldehyde exhaust emissions occur during the cold start portion of emissions testing (Gabele, 1990), which is reasonable since formaldehyde is a partial combustion product of methanol. A dedicated methanol vehicle (i.e., one using only methanol) burns methanol more efficiently than a flexible fuel vehicle (which can use various mixtures of gasoline and methanol ranging from 0% to 85%). Thus, it is likely that a dedicated methanol vehicle would have lower primary formaldehyde emissions than an FFV operated on M85. Also, as indicated by Hellman and Piotrowski (1990), it is also likely that dedicated methanol vehicles could have catalysts more effective in removing formaldehyde than catalysts designed for gasoline vehicles, as gasoline catalysts must be designed to reduce a wide variety of HC compounds. Also, placement of the catalyst can be optimized. The durability of the emission control systems in methanol fueled vehicles would also affect formaldehyde levels. Clarification of whether the formaldehyde fraction of methanol vehicle exhaust will increase with catalyst deterioration is needed. If formaldehyde emissions rates are observed to increase beyond acceptable levels, then new more durable catalyst formulations may need to be developed.

Moreover, a study of formaldehyde emissions from one variable gasoline/methanol fueled car, running on gasoline, M25, M50, M85, and neat methanol, indicates that primary formaldehyde emissions increase progressively for methanol blends, but are lower for M100 than M85 (Gabele, 1990). In any case, secondary formaldehyde emissions from combustion of neat methanol should be lower than for gasoline, due to the relative decrease in reactive hydrocarbons emitted (EPA, 1989). In fact, when improvement in methanol engine and emission control technology are considered along with secondary formaldehyde emissions reductions, EPA projects no substantial increase in overall formaldehyde emissions with use of M100 in dedicated vehicles (EPA, 1989).

Any possible increase in cancer incidence due to primary formaldehyde exposure from methanol fuel combustion would be more than offset by the dramatic reduction in 1,3-butadiene exposure, with its much higher unit risk (2.8×10^{-4} for 1,3-butadiene versus 1.3×10^{-5} for formaldehyde), as well as by reductions in benzene, acetaldehyde, refueling vapors, and particulate

exposure. Overall, EPA's Methanol Special Report (EPA, 1989) estimates that neat methanol vehicles can be designed to have only 10% of the air toxics emissions of gasoline vehicles, and FFVs can be designed to have about half. Thus, use of neat methanol and methanol/gasoline blends should result in cancer incidence reductions, although reductions with the M85 vehicles are lower than with M100. Possible noncancer risks posed by exposure to methanol, particularly in microenvironments, is currently under evaluation and no definitive statements can be made at this time.

13.2 Ethanol

Low level ethanol mixtures (10% ethanol and 90% gasoline) are already widely used in the U.S., and account for about 6% of total fuel use nationwide (Section 3.1.3.2). Higher level ethanol mixtures (e.g., 85% ethanol, or E85) and neat ethanol may be used as an alternative fuel source in the future for vehicles specifically designed for them. Ethanol has a higher octane than gasoline; thus, vehicles could be designed for improved fuel efficiency. It also has a lower vapor pressure, which would result in lower evaporative emissions. Moreover, it can be produced from renewable resources, such as corn and other biomass. Its flammability is lower than gasoline, which should result in fewer vehicle fires. However, without subsidies, ethanol cannot presently compete with gasoline in price. Also, cold starting is more difficult than with gasoline.

Like methanol, use of ethanol as a clean fuel would result in substantial reductions in air toxics emissions. Emissions data for higher level ethanol blends and E100 vehicles are sparse though. According to EPA's Ethanol Special Report (EPA, 1990a), substantial reductions in benzene, 1,3-butadiene, refueling vapors and particulate would occur, while formaldehyde would be emitted at levels similar to gasoline vehicles. Acetaldehyde emissions, on the other hand, would increase substantially. Since the acetaldehyde cancer potency (2.2×10^{-6} unit risk) is much lower than the 1,3-butadiene potency (2.8×10^{-4} unit risk), any increase in cancer incidence due to acetaldehyde would be greatly offset by the large decrease in cancer incidence due to 1,3-butadiene exposure. It should be noted, however, that acetaldehyde is an irritant and may have some chronic and acute respiratory effects (Section 8.8). Thus, non-carcinogenic health effects of increased acetaldehyde exposure due to ethanol combustion may be a concern (to a lesser extent, this would be a concern with methanol combustion as well).

Although a large percentage of total emissions from motor vehicles running on either neat ethanol or ethanol blends is ethanol itself (California Air Resources Board, 1989, 1991), ethanol is not considered a toxic pollutant at the low levels likely to be inhaled due to its use as a motor fuel.

13.3 Compressed Natural Gas

Worldwide, compressed natural gas (CNG) has been used extensively as a motor vehicle fuel, and is currently used in the U.S. to power a wide range of vehicles and equipment, including some light duty trucks and some urban buses. Generally, most CNG use has involved retrofitting existing engines to run on either gasoline or CNG. However, the greatest benefits from using CNG can be realized with dedicated vehicles, optimized to make use of the specific combustion properties of CNG.

Based on an energy equivalent price comparison in EPA's Compressed Natural Gas Special Report (EPA, 1990b), CNG can be comparable to gasoline in cost. There are several drawbacks to CNG use, however, including decreased driving range, safety hazards due to carrying a fuel under pressure, and the effect of large, heavy storage tanks on vehicle range, performance, and efficiency. Nevertheless, substantial environmental benefits may be achieved from the use of CNG as an alternative fuel, due to the low reactivity of exhaust emissions from CNG fueled vehicles relative to gasoline.

Since use of CNG as a fuel requires a closed delivery system, evaporative emissions from a dedicated CNG vehicle are assumed to be zero. Also, CNG contains no benzene, so refueling and running losses of this toxic would also be zero. Moreover, exhaust emissions of benzene and 1,3-butadiene are very low (California Air Resources Board, 1989, 1991). Formaldehyde and acetaldehyde exhaust emissions are roughly the same as for gasoline. Thus, the air toxics benefits are greater than those with M100.

Since methane fueled vehicles emit large quantities of methane, the health effects and global climate change of methane emissions should also be considered. Methane is present at low levels in the atmosphere from natural sources (e.g., decaying vegetation). Methane is generally not thought to have adverse health effects at low levels, although high levels can cause asphyxiation. However, methane can contribute significantly to the potential for global climate change. This aspect must be thoroughly evaluated.

13.4 Liquid Propane Gas

Liquid propane gas (LPG) is another possible alternative fuel for motor vehicles. As for CNG, most LPG use has involved retrofitting existing engines to run on either gasoline or CNG. However, the greatest benefits from using LPG would be realized with dedicated vehicles, optimized to make use of the specific combustion properties of the fuel.

LPG would be expected to have very little evaporative emissions. The California Air Resources Board has speciated exhaust emissions from several LPG vehicles (CARB, 1989, 1991).

LPG has very low 1,3-butadiene and benzene emissions, but aldehyde emissions increase substantially, as with alcohol fuels. However, these higher aldehyde emissions would likely be reduced with a catalyst specifically designed for an LPG vehicle.

13.5 References for Chapter 13.0

ACGIH. 1986. Documentation of the threshold limit values. 5th ed. Cincinnati, OH: American Conference of Governmental Industrial Hygienists.

ACGIH. 1990. Threshold limit values and biological exposure indices for 1990-1991. Cincinnati, OH: American Conference of Governmental Industrial Hygienists.

Andrews, J.E., M. Ebron-McCoy, L.L. Mole, T.R. Logsdon, R.J. Kavlock, and J.M. Rogers. 1992. Developmental toxicity of methanol in whole embryo culture: a comparative study with mouse and rat embryos. Teratology, in press.

Auto/Oil Air Quality Improvement Research Program. 1992a. Technical Bulletin No. 7: Emissions and Air Quality Modeling Results from Methanol/Gasoline Blends in Prototype Flexible/Variable Fuel Vehicles.

Auto/Oil Air Quality Improvement Research Program. 1992b. Technical Bulletin No. 10: Emissions of Three Dedicated-Methanol Vehicles.

Browning, E. 1965. Toxicity and metabolism of organic solvents. Elsevier, Amsterdam.

California Air Resources Board. 1989. Definition of a Low-Emission Motor Vehicle in Compliance with the Mandates of Health and Safety Code Section 39037.05 (Assembly Bill 234, Leonard, 1987). El Monte, California: Mobile Source Division.

California Air Resources Board. 1991. Proposed Reactivity Adjustment Factors for Transitional Low-Emission Vehicles: Technical Support Document. El Monte, California: Mobile Source Division. Updated Version, November 13, 1991.

Cameron, A.M., Nilsen, O.G., Haug, E., and Eik-Nes, K.B. 1984. Circulating concentrations of testosterone, luteinizing hormone, and follicle stimulating hormone in male rats after inhalation of methanol. Arch. Toxicol., Suppl., 7:441-443.

Cameron, A. M., K. Zahlsen, E. Haug, O. G. Nilsen, and K. B. Eik-Nes. 1985. Circulating steroids in male rats following inhalation of n-alcohols. Arch. Toxicol., Suppl. 8: 422-424.

Cook, M. R., F. J. Bergman, H. D. Cohen, M. M. Gerkovich, C. Graham, R. K. Harris, and L. G. Siemann. 1991. Effects of Methanol Vapor on Human Neurobehavioral Measures. Health Effects Institute Research Report No. 42.

Davis, M. and L. D. Grant. 1991. Health Effects Issues
Associated with Methanol Fuels. Presented at: AWMA Specialty
Conference -- Toxic Air Pollutants from Mobile Sources: Emissions
and Health Effects, Detroit, Michigan, October, 1991.

Environmental Protection Agency. 1986. Rat Oral Subchronic
Toxicity study with Methanol. Washington, DC: Environmental
Protection Agency, Office of Solid Waste.

Environmental Protection Agency. 1989. Analysis of the Economic
and Environmental Effects of Methanol as an Automotive Fuel. Ann
Arbor, Michigan: Office of Mobile Sources. Special Report,
September, 1989.

Environmental Protection Agency. 1990a. Analysis of the
Economic and Environmental Effects of Ethanol as an Automotive
Fuel. Ann Arbor, Michigan: Office of Mobile Sources. Special
Report, April, 1990.

Environmental Protection Agency. 1990b. Analysis of the
Economic and Environmental Effects of Compressed Natural Gas as a
Vehicle Fuel. Volume I: Passenger Cars and Light Trucks.
Special Report, April, 1990.

Environmental Protection Agency. 1992. Integrated Risk
Information System. U.S. Environmental Protection Agency.
Office of Health and Environmental Assessment, Environmental
Criteria and Assessment Office, Cincinnati, OH.

Gabele, P. A. 1990. Characterization of emissions from a
variable gasoline/methanol fueled car. J. Air Waste Manage.
Assoc. 40: 296-304.

Health Effects Institute. 1987. Automotive Methanol Vapors and
Human Health: An Evaluation of Existing Scientific Information
and Issues for Future Research. Report of HEI Health Research
Committee, May, 1987.

Hellman, K. H., and G. K. Piotrowski. 1990. Recent results from
prototype vehicle and emission control technology evaluation
using methanol fuel. SAE Technical Paper 901112.

Henderson Y. and H.W. Haggard. 1943. Noxious Gases. Reinhold
Publishing Corp., New York. 218.

Henson, E.V. 1960. J. Occup. Med. 2:497.

Jacobson, B.M., H.K. Russell, J.J. Grimm, and E.C. Fox. 1945.
U.S. Naval Med. Bull. 44:1099.

Kavet, R., and K. M. Nauss. 1990. The toxicity of inhaled methanol vapors. Critical Reviews in Toxicology 21: 21-50.

Keeney, A.H. and S.M. Mellinkoff. 1951. Ann. Int. Med. 34: 331.

Leaf, G. and L.J. Zatman. 1952. Brit. J. Ind. Med. 9: 19.

Lee, E.W., T.S. Terzo, J.B. D'Arcy, K.B. Gross, and R.M. Schreck. 1992. Lack of blood formate accumulation in humans following exposure to methanol vapor at the current permissible exposure limit of 200 ppm. Am. Ind. Hyg. Assoc. J. 53:99-104.

Lee, E.W., A.N. Brady, M.J. Brabec, and T. Fabel. 1991. Effects of methanol vapors on testosterone production and testis morphology in rats. Toxicol. Ind. Health 7:261-275.

Machiele, P. 1990. A health and safety assessment of methanol as an alternative fuel. In: Kohl, W. L., ed. Methanol as an Alternative Fuel Choice: An assessment. Washington, D.C.: The Johns Hopkins Foreign Policy Institute.

McNally, W.D. 1937. Toxicology. Industrial Medicine, Chicago, Illinois. p. 615.

Nelson, B.K., Brightwell, S.W., MacKenzie, D.R., Kahn, A., Burg, J.R., Weigel, W.W., and Goad, P.T. 1985. Teratological assessment of methanol and ethanol at high inhalation levels in rats. Fund. Appl. Toxicol. 5: 727-736.

NIOSH. 1976. Criteria for a recommended standard-occupational exposure to methyl alcohol. Washington, DC: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health. DHEW Pub. No. 76-148.

OSHA. 1989. Preamble to OSHA final rule revising workplace air contaminant limits. A BNA special supplement. Washington, DC: U.S. Department of Labor, Occupational Safety and Health Administration. Federal Register 54: 2332-2929.

Rogers, J.M., Chernoff, N., and Mole, M.L. 1991. Developmental toxicity of inhaled methanol in mice. The Toxicologist, Vol. 11, page 344.

Rogers, J.M., M.L. Mole, N. Chernoff, B.D. Barbee, C.I. Turner, T.R. Logsdon, and R.J. Kavlock. 1992. The developmental toxicity of inhaled methanol in the CD-1 mouse, with application of quantitative dose-response modeling for estimation of benchmark doses. Teratology, in press.

Scott, E., M.K. Helz, and C.P. McCord. 1933. Am. J. Clin. Pathol. 3:311.

14.0 NONROAD MOBILE SOURCES

A brief discussion of toxic emissions from nonroad sources was provided in an EPA document, <u>Nonroad Engine and Vehicle Emission Study</u> (NEVES), EPA report number 21A-2001, produced by the Office of Mobile Sources in Ann Arbor, Michigan in November, 1991. For a complete analysis of the emission inventories and methodology used in this study, this document should be consulted. While Section 202(l) of the Act only addresses toxic air pollutants associated with motor vehicles and motor vehicle fuels, EPA included nonroad engines and vehicles in this study for purposes of completeness and to assess the relative impact of onroad and nonroad sources to total mobile source emissions.

The term "nonroad engines" and "nonroad vehicles" cover a diverse collection of equipment ranging from small equipment like lawn mowers and chain saws, to recreational equipment, farm equipment, and construction machinery. EPA considered more than 80 different types of equipment in the NEVES. Locomotive and aircraft are not included in the NEVES because the Clean Air Act amendments provide for them separately.

Nonroad engines are not currently regulated for emissions, and very few nonroad engines currently use emission control technology. However, EPA plans to propose regulations setting standards for certain categories of nonroad equipment. Such regulations may include emission standards for diesel engines at or above 50 horsepower and small gasoline engines. Because of the diversity of nonroad equipment, characterization of the emissions from nonroad engines is a complex task. As a group, nonroad engines represent the last major uncontrolled mobile source category.

Because nonroad sources are among the few remaining uncontrolled sources of pollution, their emissions appear large in comparison to the emissions from sources that are already subject to substantial emission control requirements. For example, the Clean Air Act requires extreme ozone nonattainment areas to employ Reasonable Available Control Technology (RACT) on all stationary sources with VOC or NO_x emissions above 10 tons per year (tpy). Annual operation of only 10 crawler tractors or 24 agricultural tractors will produce 10 tpy of NO_x. Typical annual operation with only 74-142 boats with outboard motors or 730-1630 chain saws will emit 10 tpy of VOC. In contrast, it takes 700 new, current-technology passenger cars driving an average of 13,000 miles each year (a total of more than 9 million miles) to produce 10 tpy of VOC.

Nonroad engines were studied for their contribution to CO and the pollutants that contribute to ozone formation, namely volatile organic compounds (VOC) and oxides of nitrogen (NO_x). However, as mentioned above, the NEVES also briefly addressed

pollutants discussed in this report, including particulate matter (PM), benzene, aldehydes, 1,3-butadiene, and gasoline vapor.

Nonroad sources contribute substantially to summertime VOC and NO_x emissions and winter CO emissions. The median contribution of total nonroad emissions to VOC and NO_x inventories in summer, and CO inventories in winter, ranges from 7.4-12.6% VOC, 14.5-17.3% NO_x, and 5.2-9.4% winter CO, depending on the area. Under the most conservative assumptions, using new engine emission factors and choosing the lowest emission estimates from the combined emission inventories, the minimum contribution by pollutant for all cities studied in the NEVES (19 ozone and 16 CO nonattainment areas) were as follows: 2.9% VOC, 7.6% NO_x, and 2.2% CO.

The individual nonroad categories contributing most heavily to the results vary by pollutant and season. For instance, lawn and garden equipment and recreational marine equipment are major contributors to summertime VOC emissions, accounting for a median ranging from 2.4% to 4.7% and 2.2% to 4.0% of the total VOC inventory, respectively, in tons per summer day, depending on the area. Light commercial equipment and industrial equipment account for a median ranging from 2.0% to 3.7% and 1.1% to 1.5% of the total CO tons per winter day inventory, respectively. By far the largest contributors to nonroad NO_x emissions is construction equipment. Construction equipment accounts for a median of 8.4% to 9.7% of the total NO_x inventory. Agricultural, industrial, airport service, and commercial marine engines are also important contributor of NO_x in some areas. Particulate matter (PM) from nonroad sources is estimated to contribute a median of 1.8% of the total PM inventory. The two equipment categories that are the major contributors are construction equipment and commercial marine engines.

The limited availability of toxic emission data for nonroad sources makes it difficult to quantify precisely the contribution from these sources. Section 5.3.4 indicates that approximately 30% of mobile source benzene emissions, or 25% of total benzene emissions, is attributable to nonroad sources. This is almost identical to the estimate of 25.37% in the NEVES. The NEVES also provides an estimate of 13.05% of total formaldehyde from nonroad sources, and an estimate of 5.55% of total particulate matter from nonroad sources. The NEVES report does not provide an estimate of the 1,3-butadiene contribution from nonroad sources, but Section 7.3.4 indicates that approximately 41% of mobile source 1,3-butadiene emissions, or about 39% of total 1,3-butadiene emissions, is attributable to nonroad sources. Neither this report nor the NEVES provides an estimate of the nonroad contribution to total acetaldehyde emissions.

15.0 INITIAL COST CONSIDERATIONS

15.1 Costs of Various Regulatory Programs

EPA has not done an independent evaluation of cost considerations associated with controlling toxic emissions from motor vehicles. Instead this study summarizes available cost information for various regulatory programs which may result in reductions of motor vehicle-related air toxics. Cost information will be addressed more fully in any subsequent regulatory activity.

The cost information in this section was taken from various regulatory impact analyses and related documents. The following regulatory programs were examined: Tier 1 standards, California standards, reformulated gasoline program, Inspection/Maintenance programs, winter oxygenated fuels CO program, diesel particulate standards, and the diesel fuel sulfur regulation. Cost information estimates for all the gasoline related programs are summarized in Table 15-1. Where available, costs are expressed per ton of VOC reduction. It should be noted that cost-effectiveness varies if all the cost is assigned to VOC, spread out over the sum of VOC and NO_x, assigned to NO_x, etc. The costs for the diesel related standards are not included in Table 15-1 since they are associated with reduction of diesel particulate rather than VOC emissions.

15.1.1 Tier 1 Standards

The estimate for the dollar cost/ton of volatile organic compounds (VOC) reduction as it relates to the Tier 1 Standards ranges from $3700 to $6018/ton. For the lower end of the range, the estimated year 2005 reductions in VOC for light-duty vehicles and trucks is 160,000 tons, at a cost of $590 million, or a cost-per-ton of about $3700 (EPA, 1991b; Pechan and Associates, 1990). This figure does not incorporate discounting of either the national cost or national emissions reduction. The 2005 model represents full implementation of the NMHC phase-in and reasonable turnover of older vehicles.

For the upper end of the range, EPA calculated a cost per ton of $6018 by adjusting the lower estimate to incorporate a 10 percent discount rate (EPA, 1991a,b). The discount factor is determined by $1/(1 + r)^{(t-0.5)}$, where r equals the appropriate discount rate (in this case 10% or 0.10) and t equals the age of the vehicle in years. The use of (t-0.5) as the exponent of the denominator has the effect of assigning the benefits for a given year at the mid-year point, rather than at the end. This process assumes a survival rate at 20 years of age of 33%, with all costs being discounted by 10% to adjust the benefits received in each year of the vehicle's life to 1991 dollars.

Table 15-1. Cost/Effectiveness of Various Regulatory Programs.

Program	Cost	References
Tier 1 Standards	$3700 or $6018/ton VOC	Regulatory Impact Analysis: Tier 1 Light-Duty Tailpipe Standards and Useful Life Requirements, January, 1991
Reformulated Gasoline Program	$1500 to $3700/ton VOC	Memo from Christine M. Brunner to John Chamberlin: Cost-Effectiveness of Phase I Reformulated Gasoline, March 1993
I/M Programs	$461 and $4518/ton VOC accounting for CO and NO_x (approximately 33 to 41% of the VOC reduction is attributable to exhaust emissions)	I/M Costs, Benefits, and Impacts Analysis (draft), February 1992
Winter Oxygenated Fuels Program	$685 to $880 million per year	Assessment of the Long-Run Costs of the Oxygenated Fuel Provisions, Sobotka and Co., Inc. for EPA, June 26, 1991

15.1.2 California Standards

EPA has not done a cost-effectiveness analysis of the California LEV Program and has not presented information on the cost per ton of VOC or toxics reductions. A range of cost estimates has been submitted to EPA as part of California's request for a waiver of federal preemption, pursuant to Section 209(b) of the Clean Air Act, for the California low-emission vehicle standards and vehicle test procedures. Many of these estimates are associated with the cost of electrically heated catalyst systems, which may be used to meet LEV standards. At the low end of the range of cost estimates, the California Air Resources Board estimated an added cost, in 1990 dollars, of $70 for gasoline-powered TLEVs, and $170 for gasoline-powered LEVs and ULEVs (Albu et al., 1992). However, a consulting firm estimates that electrically heated catalyst systems will add, on average, a $1010 incremental retail price increase in 1991 dollars to the cost of a vehicle (Automotive Consulting Group, 1991). In contrast, an electrically heated catalyst manufacturer has estimated the cost of a system would range from $200 to $330, depending on engine size, in the first years of production (W. R. Grace and Co., 1992). In addition, CARB claims that improved fuel controls and conventional catalysts will be sufficient for most vehicles to achieve the LEV standards, without the need for electrically heated catalysts (CARB, 1992).

15.1.3 Reformulated Gasoline Program

EPA's cost-effectiveness estimates for a Phase I reformulated gasoline is $1,500 to $3,700/ton VOC (EPA, 1993). This range includes the effects of RVP class and type of I/M program. Since it was evaluated as a VOC control strategy, only the cost of summertime RVP and oxygenate use is included in this estimate because they alone contribute to VOC reductions. The costs associated with toxics reductions, namely, the cost of benzene control and wintertime oxygenate use, were not included.

15.1.4 Inspection/Maintenance (I/M) Programs

The cost of an I/M program is determined by summing the estimated inspection fee costs, the estimated repair costs, and the negative cost of estimated fuel economy benefits (gallons of fuel saved × dollars per gallon). The emission benefits of an I/M program are determined by subtracting the estimated emissions with the program from the emissions with no I/M program (EPA, 1992a). By using the Cost Effectiveness Model (CEM) and Mobile 4.1, a variety of runs are conducted to interpolate the final ton per year value.

Since the I/M program yields CO benefits as well as VOC benefits, and some areas need reductions in both, the determined costs have been split among pollutants. High-option I/M can also obtain significant NO_x benefits, so the cost is also split to account for this. The actual estimated costs for I/M programs, based on the cost of VOC reduction per ton accounting for NO_x and

CO benefits, can range from $461 to $4518. These costs represent both ends of the I/M spectrum, the biennial high option and the basic I/M program, respectively.

15.1.5 Winter Oxygenated Fuels Program

Most of the information below is contained in a document prepared by Sobotka and Company, Inc. for EPA (Sobotka and Company, 1991).

The Clean Air Act Amendments of 1990 require, starting in 1992, that gasoline sold during the winter in CO nonattainment areas must contain at least 2.7 percent oxygen by weight. The time period during which gasoline must contain oxygenates depends on local conditions but must be at least four months (a shorter time period is possible). The period runs from November through February for most of the cities affected by the regulation. However, the period may last year-long for the New York metropolitan area.

The long-run social costs of the oxygenate program probably would be in the range of about $685 to $880 million per year, depending on the extent of spillover and on the price of crude oil, or about 4.2 to 4.9 cents per gallon of oxygenated fuel. This includes the cost of the ethanol subsidy ($140 million), the cost of the mileage loss associated with oxygenated gasoline ($160 million), the cost of a summer oxygenate program for the New York Consolidated Metropolitan Statistical Area (CMSA) ($20 to $40 million), the cost of transporting to the Gulf Coast Alaskan crude oil that is displaced from the West Coast ($90 million), and other costs incurred by refiners to produce oxygenated gasoline ($270 to $450 million).

Costs for the program on the West Coast are projected to be about double those for the rest of the country on a per gallon basis, mainly because the percentage of West Coast gasoline that would be oxygenated is high, about 90 percent. This limits the ability of refiners to offset the cost of MTBE and ethanol by shifting high value blendstocks to conventional gasoline.

Prices of oxygenated gasoline at the pump are likely to increase by about 4.2 to 5 cents per gallon on the West Coast and by about 2.4 to 3.4 cents per gallon elsewhere. The effects of oxygenates on mileage effectively would increase gasoline costs to the consumer by about another cent a gallon. Cost estimates expressed as cost per ton VOC or CO reduced were not estimated for this program.

15.1.6 Diesel Particulate Standards

Various particulate standards for heavy-duty diesel engines are in place for the 1988 through 1990 model years, the 1991 through 1993 model years, and for 1994 and later model years. Cost estimates are presented in Table 15-2 for 1988-90, 1991-93, and 1994-96 for the heavy-duty diesel particulate standards (EPA, 1985). All figures are in 1984 dollars, and a 10 percent discount rate is assumed. The ranges given for the three year aggregate costs are due to the range of projected fuel economy penalties.

15.1.7 Diesel Fuel Sulfur Regulation

The diesel fuel sulfur regulation was developed to reduce the amount of diesel particulate matter emitted by heavy-duty diesel engines. The costs are expressed as cost per ton of particulate matter reduced and were estimated using a calendar-year approach discounted over a 33-year period (1994-2025). Cost effectiveness of sulfur control, in dollars per ton of particulate reduced, are shown in Table 15-3 for three engine wear benefit scenarios, as well as results assuming no engine wear benefits exist (EPA, 1990b). This rule was finalized on May 7, 1992 (EPA, 1992b).

The cost effectiveness of sulfur control was developed by taking into account the wear credit. The wear credit is the result of lower engine wear with low sulfur fuel. The potential effects of reduced engine wear could result in lower engine oil cost and less frequent oil change intervals, or longer engine and vehicle life, or longer engine life with fewer total rebuilds (EPA, 1990a).
Benefits were estimated for three different scenarios. The maximum wear credits scenario includes both an extension in engine and vehicle life. This credit is three to six times the refining cost for sulfur controls. The minimum wear credits result from an increase in oil change intervals and a slight decrease in oil cost per quart (lower total additive content due to low sulfur fuel). This credit is applicable to 1991 and later vehicles. In 2025, this credit is between 31 percent and 74 percent of the refinery costs. In all cases, the credits for medium and heavy-duty diesel vehicles together are at least 65 percent of the total credit.

15.2 Qualitative Discussion of Toxics Benefits

The reduction in vehicle emissions basically take two forms, exhaust and evaporative, and the regulatory programs discussed above address either one or both of these emissions. The four pollutants addressed most often are benzene, 1,3-butadiene, formaldehyde, and acetaldehyde. As discussed in the previous chapters, all are produced in the combustion process and emitted to the environment via the tailpipe. This is also true for diesel particulate matter. Only benzene contributes to the ambient level through evaporative emissions due to its presence in gasoline.

Table 15-2.   Cost Associated With Achieving the Heavy-Duty Diesel Particulate Standards.

Time Period	Standard To Be Achieved	Three Year Aggregate Cost
1988-1990	0.60 g/BHP-hr	$44 million (discounted to 1988)
1991-1993	0.25 g/BHP-hr	$746 to $868 million (discounted to 1991)
1994-1996	0.10 g/BHP-hr	$338 to $394 million (discounted to 1994)

Table 15-3.   33-Year Urban Cost-Effectiveness Analysis of Sulfur Control.

Wear Credit Scenario	Cost-Effectiveness ($/ton)
Maximum Wear Credit	-$68,148 to -$19,253
Minimum Wear Credit	-$3906 to $4304
No Wear Credit included	$2826 to $6773

Thus, those regulatory programs that are most effective in reducing exhaust emissions will be the most successful in reducing the greatest number and mass of air toxics. This is generally true assuming that you are using gasoline, but the emissions do change as the fuels are modified. With many of the new fuels there will be an immediate effect on many toxic emissions (some reduced, some increased) since these programs affect all vehicles simultaneously. The exhaust emission standards will only affect vehicles from a particular model year onward and total effects will not be seen until there is a complete fleet turnover.

15.2.1 Tier 1 Standards

The Tier 1 standards were developed to reduce exhaust emissions and will be phased in beginning with the 1994 model year. This regulation will reduce exhaust VOC and thus should reduce benzene, 1,3-butadiene, formaldehyde, and acetaldehyde proportionally. These standards should also reduce the atmospheric transformation of hydrocarbons into secondary aldehydes due to the reduction of VOCs. There is no measure included in this regulation to control evaporative emissions.

15.2.2 California Standards

The California standards, as they relate to LEVs and ULEVs using gasoline, should also reduce exhaust emissions as discussed above. They should also affect atmospheric aldehyde formation and not influence evaporative emissions. This program adopts these increasingly stringent vehicle certification standards beginning in 1994.

15.2.3 Reformulated Gasoline Program

During Phase 1 of the program, which runs from January 1, 1995 through 1999, federal reformulated fuel must contain at least 2.0% oxygen, and must not result in a NO_x increase. This program is mandated in the nine worst ozone areas, with other areas able to opt in to the program. During the high ozone season, reduction of both ozone forming VOCs and air toxics must be at least 15%, relative to emission levels of the 1990 model year vehicles with baseline gasoline. The approach for achieving the Phase 1 reductions is to reduce the RVP, add an oxygenated component, and limit the benzene and aromatics content of the gasoline. This results in both exhaust and evaporative emissions reductions.

During Phase 2 of the program, which begins in 2000, VOC and NO_x reductions must be at least 25%, or 20% if the 25% reduction is judged to be unfeasible. A complex model is being developed by EPA to predict VOC and toxics benefits as a function of a number of fuel parameters. At this point in time, it is difficult to predict the future composition of Phase 2 gasoline; however, since air toxics reductions are implicitly required, both Phase 1 and 2 reformulated gasolines should clearly result in air toxics benefits.

15.2.4 Inspection/Maintenance (I/M) Programs

In addition to tighter standards on new vehicles and their fuels, the Clean Air Act Amendments of 1990 required the implementation of I/M programs in areas that have been determined to be in non-attainment for ozone or carbon monoxide. Depending on the severity of the problem, moderate non-attainment areas (or marginal areas with an I/M program) will have to implement a basic I/M program. Enhanced I/M programs will be implemented in serious, severe, and extreme non-attainment areas.

The basic I/M program includes an annual, centralized idle test and a visual inspection for the catalyst and fuel inlet restrictor. For the basic program, EPA estimates that there will be an 11% reduction in total VOCs for light-duty gas vehicles (LDGV) when compared to a non-I/M scenario. Basic I/M assumes only exhaust control; thus, the 11% decrease in VOCs is totally attributable to exhaust VOC. Exhaust VOC is approximately 33% of the total VOCs emitted by the vehicle.

The biennial high-option includes an IM240 exhaust test and purge testing of the evaporative control system of 1986 and later vehicles. The high-option I/M program then addresses both exhaust and evaporative emissions and results in a 34% reduction in total VOCs for LDGV when compared to a non-I/M scenario. The increase in the VOC reduction for LDGV is mainly accounted for by the enhanced testing of the evaporative control system (44% of VOC reduction) when compared to a non-I/M scenario. The reduction in exhaust emissions improves slightly, increasing by about 9% over the basic I/M program. The exhaust VOC would account for approximately 41% of the total VOC for LDGV due to the increased control of evaporative emissions. Air toxics would decrease in proportion to the exhaust VOC reductions and benzene would be reduced further due to the tighter evaporative controls.

15.2.5 Winter Oxygenated Gasoline Program

The winter oxygenated gasoline program should have very similar benefits to that of the Phase 1 reformulated gasoline program due to the similarity of the fuels. This program is scheduled to go into effect in November 1992.

15.2.6 Diesel Particulate Standards and Fuel Sulfur Regulation

The overall effects of the diesel particulate standards and the diesel fuel sulfur regulation have been combined to determine the benefits of controlling diesel emissions. The analysis of these effects is based on the cancer risks determined in Section 9.7 and represent a composite of light and heavy duty diesel engines.

It was determined that 106 cancer cases would be due to diesel particulate exposure in 1990. This number decreases by 40% in 1995, 57% in 2000, and 72% in 2010.

15.3 References for Section 15

Albu, Steve, Liwen Kao, and Tom Cackette. 1992. The
Effectiveness of the California Low-Emission Vehicle Program.
Prepared for the Air and Waste Management Association. AWMA
Paper 92-168.01.

Automotive Consulting Group. 1991. The Electrically Heated
Catalyst: A "Systems" Cost Analysis. Automotive Consulting
Group, Ann Arbor, MI, September 10, 1991.

CARB. 1990. Proposed Regulations for Low-Emission Vehicles and
Clean Fuels, Technical Support Document. August 13, 1990.

CARB. 1992. Supplemental Submittal of the California Air
Resources Board to EPA Docket No. A-91-71. Submittal IV-G-49,
August 19, 1992.

EPA. 1985. Federal Register, 40 CFR Parts 86 and 600, March 15,
1985, pages 10606-10708.

EPA. 1990a. Regulatory Impact Analysis: Control of Sulfur and
Aromatics Contents of On-Highway Diesel Fuel. Office of Air and
Radiation, Office of Mobile Sources, Ann Arbor, MI. June, 1990.

EPA. 1990b. Federal Register, Vol. 55, 40 CFR Parts 80 and 86,
August 21, 1990, pages 34120-34151.

EPA. 1991a. Analysis of NMHC Cost-Effectiveness. Memo from
James McCargar to Bob Maxwell. January 31, 1991.

EPA. 1991b. Regulatory Impact Analysis: Tier 1 Light-Duty
Tailpipe Standards and Useful Life Requirements. Office of Air
and Radiation, Office of Mobile Sources, Ann Arbor, MI. January,
1991.

EPA. 1992a. I/M Costs, Benefits, and Impacts, Draft. Office of
Air and Radiation, Office of Mobile Sources, Ann Arbor, MI.
February, 1992.

EPA. 1992b. Federal Register, Vol. 57, No. 89, 40 CFR Parts 80
and 86, May 7, 1992, pages 19535-19537.

EPA. 1993. Cost-Effectiveness of Phase I Reformulated Gasoline.
Memo from Christine M. Brunner to John Chamberlin. March 18,
1993.

Pechan and Associates, Inc. 1990. Ozone Nonattainment Analysis
A Comparison of Bills. January 26, 1990.

Sobotka and Company, Inc. 1991. Assessment of the Long-Run
Costs of the Oxygenated Fuel Provisions, Draft. June 26, 1991.

W. R. Grace and Co. 1992. Letter from Alan D. Fiers, Vice President and Director of Government Relations to Charles Freed, EPA. November 30, 1992. Submittal IV-G-73 to EPA Docket No. A-91-71.

16.0 MOTOR VEHICLE TOXICS IN TITLE III AND METALLIC POLLUTANTS

The list of 189 compounds in Title III of the Clean Air Act Amendments of 1990 were reviewed to identify those compounds that are either known or, based on their structure, have the potential to be emitted from motor vehicles. The metals chosen are all potential fuel additives. The various health-based criteria that have been developed for these compounds are presented in Table 16-1. This information has been largely excerpted from the contractor report, <u>Motor Vehicle Air Toxics Health Information</u>, Clement International Corporation, September, 1991 and updated where appropriate. A section devoted to dioxins is included, since EPA has received public comments specifically related to dioxins from motor vehicles. In addition, a section on methyl tertiary butyl ether (MTBE) is included due to recent public health issues associated with gasoline containing 15% MTBE. Finally, a brief section on n-nitrosodimethylamine (NDMA) is included, since it has been measured in vehicle interior emissions and in diesel crankcase emissions. NDMA is classified by EPA as a probable human carcinogen and is present in the Title III list.

16.1 Dioxins

Over 75 different chlorinated dioxin isomers have been identified. One of the 22 isomers with four chlorinated atoms is 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD). This dioxin compound and other PCDDs have high molecular weights and in the atmosphere are expected to preferentially adsorb to airborne particulate matter, particularly the more chlorinated species. Removal mechanisms include dry and wet deposition and photodegradation. Photodegradation appears to be the most significant natural degradation mechanism for PCDDs. 2,3,7,8-TCDD is the dioxin compound of most interest since it is thought to be the most toxic of the chlorinated dioxins and is most often associated with exposure and potential health risks to humans based on available data.

There has been recent interest expressed to the EPA Office of Mobile Sources (see specific comments by Konheim and Ketcham and Zephyr Consulting in Appendix I) that gasoline and diesel powered vehicles may be responsible for more dioxin emissions than the combined emissions from waste incineration sources. Several European studies, Rappe, et al., (1988), Ballschmitter, et al., (1986), and Marklund, et al., (1987) appear to indicate that much of the background ambient dioxin levels are attributable to the use of leaded gasoline and the use of halogenated additives. Marklund, et al., (1987) could not find PCDDs or PCDFs in exhaust samples using unleaded gasoline fueled vehicles equipped with catalytic converters. A Norwegian tunnel study (Larssen et al., 1990) appears to implicate diesel engines as a major source of dioxin.

Several commentors reiterated these points with particular emphasis on dioxin emissions from diesels.

In the U.S., a preliminary study by the California Air Resources Board (CARB, 1987), described an exploratory dioxin sampling program that was conducted on exhaust from seven vehicles. The major limitations CARB cites in the study itself are the small sample size, the use of low resolution (rather than high resolution) mass spectrometry, and the presence of interferences from other organic compounds in the samples which prohibit the use of the data for estimating emissions. CARB states that this report was not intended to support general conclusions about dioxins in motor vehicle exhaust. CARB also has stated that, due to the report's preliminary nature, it should not be cited or quoted (CARB, 1992). More definitive dioxin measurements from motor vehicles would be helpful to better quantify emissions and reduce the uncertainties.

CARB also commissioned a study to assess the ambient concentrations of polychlorinated dibenzodioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs) in the South Coast Air Basin (Hunt et al., 1990). The objective of this research effort was to determine baseline ambient concentrations of PCDDs/PCDFs, particularly in areas of high population density. In general, the conclusions state that the evidence is strongly suggestive that combustion sources are the major contributing factor to atmospheric burdens of PCDDs/PCDFs; however, confirmation of the vehicular contribution cannot be provided by examination of the data currently available from these samples.

It was further found that the majority of the atmospheric burdens of PCDDs/PCDFs in the South Coast Air Basin are represented by non 2,3,7,8-substituted species, which are not of toxicological significance as defined by the California Department of Health Services. TCDDs, and in particular 2,3,7,8-TCDD, are virtually non-existent in the South Coast Air Basin. 2,3,7,8-TCDD was confirmed in only two samples, both of which were collected during the Spring 1989 session. These levels were measured as 8.6 fg/m^3 at West Long Beach (monitor near a petroleum refinery) and 34 fg/m^3 at the Cal Trans site (monitor near a highway intersection). The measurement fg/m^3 is 1×10^{-15} (one quadrillionth) gram per cubic meter. Photochemical degradation of this isomer may account in part for its virtual absence in the atmosphere in Southern California. It was also stated that the average PCDDs/PCDFs concentrations for all sessions (excluding the high measurements from the December 1987 campaign) represent values typically found in other U.S. urban and suburban locations.

It should also be noted that the EPA's Office of Research and Development is presently carrying out a scientific reassessment of dioxins and related compounds. A workshop draft report is presently undergoing agency and public review. Also, EPA OMS plans a reevaluation of mobile source data.

16.2 MTBE

The Clean Air Act, as amended in 1990, requires the use of oxygenated gasoline in the winter months in 39 areas of the country that exceed national health standards for carbon monoxide (CO). In these areas, gasoline was changed by adding oxygenates such as ethanol or methyl tertiary butyl ether (known as MTBE), and reducing certain other organic compounds.

Recently, a public health issue has arisen as a result of public complaints in three cities using oxyfuels with approximately 15% MTBE. Although the program in other cities has run relatively smoothly, citizens in Fairbanks and Anchorage, Alaska, and Missoula, Montana have complained of health symptoms (headaches, coughs, eye irritation, nausea, and dizziness) which they believe are associated with exposures to gasoline blended with MTBE. While current data suggest these acute symptoms are generally mild and of short duration, EPA is currently conducting a cooperative research program to determine whether there is, in fact, an increase in such symptoms associated with exposures to MTBE-blended gasoline. This research is being supported and/or conducted by EPA, the State of Alaska, the Centers for Disease Control and Prevention of the Department of Health and Human Services, and industry. In the interim, EPA recently completed a paper which discusses the public health issues associated with MTBE-oxygenated gasolines (EPA, 1993). This paper will be revised this summer based on the findings of ongoing research.

16.3 N-Nitrosodimethylamine

N-Nitrosodimethylamine (NDMA) is classified by EPA as a B2, probable human carcinogen. This classification is based on the induction of tumors at multiple sites in both rodents and nonrodent mammals exposed by various routes. The unit risk estimate from inhalation exposure is 1.4×10^{-2} per $\mu g/m^3$. No RfD or RfC is available (EPA, 1992).

Nitrosamines have been measured at low levels in vehicle interior emissions and in diesel crankcase emissions. In Smith and Baines (1982), fifty-eight vehicle interiors were sampled for nitrosamines, including NDMA. Of the fifty-eight vehicles sampled in the program, forty-nine contained NDMA at concentrations ranging from 0.024 to 0.388 $\mu g/m^3$. Total nitrosamine levels ranged from 0.01 to 0.63 $\mu g/m^3$. The study estimated that the daily intake of nitrosamines from vehicle interiors for a commuter in a vehicle 3 hours/day is less than that from a can of beer or from a strip of bacon.

An artifact-free method for the analysis of nitrosamines in diesel engine crankcase emissions was developed (Goff et al., 1980a). Nitrosamine emissions from diesel engine crankcases were measured from three heavy-duty engines and one light-duty engine (Goff et al., 1980b). NDMA was present in all engine tests. The maximum concentration was 28 $\mu g/m^3$. The study

concludes that nitrosamine levels in both heavy-duty and light-duty diesel crankcase emissions result from nitrosation of amine-type compounds in the lubricating oil vapors by oxides of nitrogen in the crankcase emissions.

No work has been done since these studies.

Table 16-1. Health-Based Criteria for CAAA Title III Motor Vehicle Air Toxics and Metals.

Chemical Name	Reference Concentration (RfC)(mg/m^3)	Reference Dose (RfD) (mg/kg/day)	OSHA Final Rule Limits	ACGIH Threshold Limit Values	
			STEL (ppm) [mg/m^3]	TLV-TWA (ppm) [mg/m^3]	STEL (ppm) [mg/m^3]
Acetonitrile	Under review	6×10^{-3}	60 [105]	40 – S[1] [67]	60 [101]
Acrylic Acid	3×10^{-4}	8×10^{-2}	NA[2]	10 – S [30]	NA
Acrolein	2×10^{-5}	NA	0.3 [0.8]	0.1 [0.23]	0.3 [0.69]
Carbon Disulfide	NA	0.1	12 [36]	10 – S [31]	NA
Catechol	NA	NA	NA	5 [23]	NA
Chlorine	NA	NA	1 [3]	0.5 [1.5]	1 [3]
Cresols	NA	5×10^{-2}	NA	5 – S [22]	NA
Carbonyl Sulfide	NA	NA	NA	NA	NA
Dimethyl Sulfate	NA	NA	NA	0.1 – S [0.5]	NA

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[1]"S," or "skin designation," refers to the prevention of employee skin absorption through use of gloves, coverall, goggles, or other appropriate personal protective equipment, engineering controls or work practices.

[2]Not Available

| Chemical Name | Reference Concentration (RfC)(mg/m^3) | Reference Dose (RfD) (mg/kg/day) | OSHA Final Rule Limits | ACGIH Threshold Limit Values | |
			STEL (ppm) [mg/m^3]	TLV-TWA (ppm) [mg/m^3]	STEL (ppm) [mg/m^3]
1,4-Dioxane	NA	NA	NA	25 – S [90]	NA
Diethyl Sulfate	NA	NA	NA	NA	NA
Dibenzofurans	NA	NA	NA	NA	NA
Ethylene Dibromide	NA	NA	NA	NA	NA
Ethyl Benzene	1	0.1	125 [545]	100 [435]	125 [545]
Ethylene Dichloride	NA	NA	2 [8]	10 [40]	NA
Hexane	2×10^{-1}	NA	NA	50 [180]	NA
Hexane Isomers	NA	NA	1,000 [3,600]	500 [1,800]	1,000 [3,600]
Lead	NA	NA	NA	[0.15]^3	NA
Methanol	NA	0.5	250 [328]	200 – S [260]	250 [328]
Methyl Ethyl Ketone	1	5×10^{-2}	300 [885]	200 [590]	300 [885]
Methyl t-Butyl Ether	5×10^{-1} ^{4}	NA	NA	NA	NA

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^{3}For inorganic dusts and fumes

^{4}The RfC for MTBE is in a state of flux and is likely to change.

Chemical Name	Reference Concentration (RfC)(mg/m^3)	Reference Dose (RfD) (mg/kg/day)	OSHA Final Rule Limits STEL (ppm) [mg/m^3]	ACGIH Threshold Limit Values TLV-TWA (ppm) [mg/m^3]	STEL (ppm) [mg/m^3]
Naphthalene	NA	Withdrawn	15 [79]	10 [52]	15 [79]
Phenol	NA[5]	0.6	NA	5 – S [19]	NA
PAHs	NA	NA	NA	NA	NA
Propionaldehyde	NA[6]	NA	NA	NA	NA
Styrene	1	0.2	100 [426]	50 – S [213]	100 [426]
Toluene	4×10^{-1}	0.2	150 [565]	100 [377]	150 [565]
2,2,4-Trimethylpentane	NA	NA	NA	NA	NA
Xylenes	Under review	2	150 [651]	100 [434]	150 [651]
Copper	NA	1.3 mg/l[7]	NA	0.38[8] [1]	NA
Copper fumes	NA	NA	NA	0.08 [0.2]	NA

[5]Health effects data have been reviewed by EPA and determined to be inadequate for derivation of an RfC.

[6]EPA has determined that the database is insufficient to develop an RfC for propionaldehyde.

[7]No oral RfD exists for copper. This drinking water standard was derived by EPA for chronic and subchronic exposure.

[8]Copper dusts and mists.

| Chemical Name | Reference Concentration (RfC)(mg/m^3) | Reference Dose (RfD) (mg/kg/day) | OSHA Final Rule Limits | ACGIH Threshold Limit Values | |
			STEL (ppm) [mg/m^3]	TLV-TWA (ppm) [mg/m^3]	STEL (ppm) [mg/m^3]
Iron	NA	NA	NA	0.77[9] [5]	NA
Cerium	NA	NA	NA	NA	NA
Manganese	4×10^{-4}	1×10^{-1}	NA	2.23[10] [5]	NA
Manganese fumes	NA	NA	1.34 [3]	0.45 [1]	1.34 [3]
Selenium	NA	5×10^{-3}	NA	0.06 [0.2]	NA
Platinum	NA	NA	NA	0.13[11] [1]	NA
Platinum soluble salts	NA	NA	NA	0.0003 [0.002]	NA

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[9]Iron oxides.

[10]Manganese dust and compounds.

[11]Platinum metals.

16.2 References for Chapter 16

Ballschmitter, K. et al. 1986. Automobile exhausts versus municipal waste incineration as sources of the polychlorinated dibenzodioxins (PCDD) and furans (PCDF) found in the environment. Chemosphere 15:901.

CARB. 1987. Evaluation Test for PCDD and PCDF Emissions from Motor Vehicles. Draft Report No. C-87-029, October, 1987.

CARB. 1992. Letter from William V. Loscutoff, Chief, CARB Monitoring and Laboratory Division to David Cleverly, U.S. EPA. November 25, 1992.

EPA. 1993. MTBE-Oxygenated Gasoline and Public Health Issues. Office of Research and Development. February, 1993.

EPA. 1992. Integrated Risk Information System (IRIS). Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH.

Goff, E.U., J.R. Coombs, D.H. Fine, and T.M. Baines. 1980a. Determination of n-nitrosamines from diesel engine crankcase emissions. Anal. Chem. 52:1833-1836.

Goff, E.U., J.R. Coombs, D.H. Fine, and T.M. Baines. 1980b. Nitrosamine Emissions from Diesel Engine Crankcases. SAE Technical Paper 801374.

Hunt, G., B. Maisel, and M. Hoyt. 1990. Ambient Concentrations of PCDDs/PCDFs in the South Coast Air Basin. Final Report prepared for the California Air Resources Board Document No. 1200-005-700. January 1990.

Larssen, S., E.M. Brevik, and M. Oehme. 1990. Emission factors of PCDD and PCDF for road vehicles obtained by a tunnel experiment. Dioxin 90, Vol. I.:453-456.

Marklund, S., C. Rappe, M. Tyskling, and K.E. Egebäck. 1987. Identification of polychlorinated dibenzofurans and dioxins in exhausts from cars run on leaded gasoline. Chemosphere, 16:29-36.

Rappe, C. et al. 1988. Identification and quantification of PCDDs and PCDFs in urban air. Chemosphere, 17:1.

Smith L.R. and T.M. Baines. 1982. Nitrosamines in Vehicle Interiors. SAE Technical Paper 820785.