Office of Environmental Health Hazard Assessment
Reproductive and Cancer Hazard Assessment Section

Summary of Scientific Meeting Held June, 2000 on Approaches to Assessing Health Impacts of Gasoline-Related Exposures in California

Introduction

California's experience with MTBE has highlighted the need to evaluate human and environmental health risks from exposure to fuel components currently in use and proposed for future use. As part of this effort, the Office of Environmental Health Hazard Assessment (OEHHA) of the California Environmental Protection Agency (Cal/EPA) has begun research in the area of health risk assessment of gasoline-related exposures (exhaust, evaporative emissions, and atmospheric transformation products) in California. In 1999, OEHHA prepared a report comparing the potential health risks associated with gasoline containing ethanol versus other gasoline formulations. OEHHA's work was part of a larger assessment of ethanol ordered by Governor Gray Davis and involving the California Air Resources Board (ARB) and the State Water Resources Control Board (SWRCB). OEHHA is currently conducting a follow up assessment of potential cancer risks and chronic respiratory effects from exposures to the gasoline formulation now in use in California (*i.e.*, California Phase 2 Reformulated Gasoline). OEHHA is also carrying out a cross-sectional study of the respiratory health of children attending schools located near busy motorways.

The field of gasoline health effects and assessment is rapidly changing, with significant new studies currently underway. To bring together experts in the field and obtain state-of-the-art information, OEHHA planned a scientific meeting that was held June 26-27 2000 at the Elihu Harris State Office Building in Oakland, California. Sara Hoover of OEHHA was the meeting organizer, with assistance from Elinor Fanning. Other OEHHA staff who participated in the meeting planning included Martha Sandy, Lauren Zeise, and George Alexeeff. OEHHA contracted with U.C. Berkeley to provide logistical support for the meeting. The list of invited experts who attended the meeting follows:

- Janet Arey, University of California Riverside
- Bart Croes, California Air Resources Board
- Roger Atkinson, University of California Riverside
- Aaron Cohen, Health Effects Institute
- Scott Fruin, California Air Resources Board
- Eric Fujita, Desert Research Institute
- Robert Harley, University of California Berkeley
- Steve Hui, California Air Resources Board
- Doug Lawson, National Renewable Energy Laboratory
- Joellen Lewtas, U.S. Environmental Protection Agency
- Irva Hertz-Picciotto, University of North Carolina
- Kent Pinkerton, University of California Davis

- Peggy Reynolds, California Department of Health Services
- Hanspeter Witschi, University of California Davis

The experts were asked to address a number of general issues including:

- Scope of preliminary risk assessment, particularly chemicals of concern
- Methods for estimating exposure to primary and secondary pollutants
- Toxicology of the individual components and the complex mixture
- Available epidemiological evidence related to gasoline exposures
- Risk assessment methodology

The meeting was organized into two sessions. Session 1 addressed exposure-related issues, including gasoline engine emissions, atmospheric chemistry, personal exposure, and exposure assessment in general. Session 2 focused on issues related to health impacts of gasoline, including toxicology, epidemiology, and risk assessment methods. Specific discussion questions were formulated for each of the two Sessions. The presentations from each Session are summarized below, along with the discussion questions and expert panels' responses for each Session.

Session 1: Exposure Assessment – Gasoline Engine Emissions, Atmospheric Chemistry and Personal Exposures

Ambient Apportionment of Toxic Air Contaminants from Gasoline-Powered On-Road Vehicles

Eric Fujita, Desert Research Institute (DRI)

The focus of Dr. Fujita's talk was source apportionment studies for both particulate matter (PM) and volatile organic compounds (VOCs) that have been conducted by DRI and other groups. He first discussed emission inventories and other related studies that give an indication of the relative contribution of diesel versus gasoline sources to overall emissions, including trends in these emissions over time and other factors that can influence emissions.

Trends in the PM emissions of mobile sources can be observed over the years of 1970 to 1995, using data from the study of National Air Pollutant Emission Trends by the U.S. Environmental Protection Agency (U.S. EPA). In 1970, PM emissions from on-road gasoline vehicles were more than double that for on-road diesel vehicles. By 1980, the PM emissions from on-road gasoline vehicles were virtually identical to those from on-road diesel vehicles. This trend continued, and by 1990, the PM emissions from on-road diesel vehicles were approximately double those from on-road gasoline vehicles and this is still true today.

In terms of non-road emissions, the contributions from gasoline and diesel were approximately equal in 1970 while diesel is the predominant source today.

The trend in emissions data can be related to the results from dynanometer studies conducted at DRI. The dynanometer studies similarly demonstrate the significant decrease in particulate emission rates from heavy-duty diesel vehicles from the early 70's to the late 90's.

Results from tunnel studies carried out by DRI, which are useful for examining relative changes in emissions, show a similar trend. In the early 70's to early 80's, particulate emission rates were around 1 g/mile for diesel vehicles based on studies in the Tuscarora and Allegheny tunnels. For gasoline vehicles, the particulate emission rates ranged between approximately 15 mg/mile to 40 mg/mile during that same time period. In the early to late 90's, particulate emission rates dropped significantly to around 200-400 mg/mile for diesel vehicles according to measurements in the Tuscarora and Fort McHenry tunnels. Based on a study in the Tuscarora tunnel, gasoline vehicle particulate emission rates did not change significantly during the last 20 years, remaining at around 12 mg/mile. This measurement was for hot stabilized emissions from relatively well-maintained vehicles passing through an interstate tunnel.

Cadle and coworkers examined the influence of cold start and harder acceleration on particulate emissions as compared to hot stabilized conditions. Emissions were much greater under conditions of cold start and harder acceleration. Particulate emissions were also much higher from high emitters.

Data from the Northern Front Range Air Quality Study on speciated $PM_{2.5}$ emissions from light-duty gasoline vehicles were presented. As expected, particulate emissions were greater under cold start conditions and from high emitters as compared to hot stabilized emissions. Elemental carbon was a higher fraction of cold start emissions compared to hot stabilized emissions. For high emitters, the fraction of organic carbon was much higher than for well-maintained vehicles.

A source apportionment analysis for particulate emissions in ambient air was compared to the emission inventory for the Denver area. The comparison illustrated the discrepancies between the ambient apportionment and the apportionment based on the emission inventory. Particulate emissions attributable to smoking gasoline vehicles and cold start gasoline vehicle exhaust were significantly lower according to the emission inventory compared to the ambient air analysis. This was true even though smoking vehicles were considered as part of the Denver inventory. The Denver method of selecting high emitters was based on visual inspection, however, which is not an adequate identification method. The particles produced by gasoline vehicles are generally not visible. For diesel on-road and off-road vehicles, the inventory predicted a much greater relative contribution to particulate emissions than did the ambient air analysis.

A source apportionment for $PM_{2.5}$, total carbon, organic carbon (OC) and elemental carbon (EC) was conducted in Welby, Colorado as part of the Northern Front Range Study. Total carbon was predominantly accounted for by gasoline exhaust (cold starts; smokers and high emitters; hot stabilized) and diesel exhaust; the apportionment did not distinguish between on and off-road sources. Smokers and high emitters were the

primary source of OC, followed by cold start exhaust. More than half of the EC was from diesel exhaust, with 32% attributable to cold start gasoline exhaust. Gasoline exhaust (cold start; smokers and high emitters; hot stabilized) accounted for 29% of $PM_{2.5}$, while diesel exhaust was responsible for 10%.

The Northern Front Range Study also analyzed between 80 and 90 specific particulate phase PAHs. More particulate phase PAHs were produced by low, medium and high emitters under hot stabilized conditions compared to cold start conditions. In terms of mg/mile, the total particulate PAH emission rates for gasoline vehicles, including low emitters, are equivalent to or greater than the rates for heavy-duty diesel vehicles. For high emitting gasoline vehicles, the rates are as much as three to four times greater than those for well-tuned vehicles. The same results were found for gas-phase PAH emissions rates.

The phase distribution of organic compounds shifted depending on whether the OC was measured at the emission source (*e.g.*, in dynamometer studies) or after the emissions have been in the atmosphere (*e.g.*, in tunnels or ambient air). More than 50% of the OC was found in the most volatile fraction in dynamometer studies, while 30% was found in that fraction in the ambient air in Denver. Results for tunnel studies were intermediate, showing approximately 40% of the OC in the most volatile fraction.

Fred Rogers of DRI conducted a study on particle size distribution, using samples collected at the tunnel inlet and outlet as well as a background air sample. The mean particle size at the tunnel outlet, reflecting what was being emitted, was about 20 nm. The particle sizes measured in background air were quite a bit larger, with a mean approaching 100 nm, which is in the size range of particles that accumulate. The air sample collected at the tunnel inlet was a mixture of the background air with what is being emitted.

Gertler and coworkers looked at emission rates of volatile organic compounds in two tunnels. The Fort McHenry Tunnel reflected diesel emissions and the Sepulveda Tunnel reflected gasoline vehicle emissions. The emission rates (mg/mile) of 1,3-butadiene were two to three times greater for gasoline vehicles than for diesel. Gasoline vehicles showed greater emission rates of benzene and toluene. Emission rates for ethylbenzene and xylenes were comparable between gasoline and diesel vehicles. Diesel vehicles have higher emission rates for styrene and the trimethylbenzenes and significantly higher emission rates for heavier hydrocarbons such as n-decane and n-undecane.

A typical ambient apportionment from the South Coast Air Basin in 1995 shows that light duty exhaust sources account for about two to three times more of the nonmethane hydrocarbons (NMHC) as compared to diesel exhaust sources. Depending on time of day and location, light duty exhaust sources contributed about 38-50% of the NMHC, with diesel contributing between 12-16%.

The hydrocarbon speciation profile for downtown Los Angeles (LA) and other parts of the basin are very similar. If the contribution from mobile source-related hydrocarbons is

subtracted from the ambient air profile, ethane and propane remain with very little else. This indicates that most of the hydrocarbons in ambient air in the LA basin are related to mobile sources.

In summary, mass emission rates of particulate matter from heavy-duty diesel vehicles have decreased significantly over a 25-year period. Light-duty gasoline and heavy-duty diesel vehicles emit significant numbers of ultrafine particles and these particles are preserved in the atmosphere for a while. Light-duty gasoline vehicles emit particulate matter containing higher fractions of particulate PAHs. Light-duty gasoline vehicles are significant sources of gas phase PAHs. Cold starts, high accelerations, and high emitters account for most of the light-duty gasoline vehicle particulate matter emissions. Based on results from the Northern Front Range Study, it appears that light-duty gasoline vehicle particulate matter emissions are significantly underestimated in current inventories. Light-duty gasoline vehicles are the major source of 1,3-butadiene and BTEX. Heavy-duty diesel vehicles emit relatively higher styrene and trimethylbenzenes.

In terms of research needs, the toxic effects of PM from both gasoline and diesel vehicles need to be investigated further. Most of the health studies in the past have been focused on diesel rather than gasoline PM. The fate of the ultrafine particles over time needs to be characterized. More information is needed on the spatial and temporal variation of PM emissions from on-road vehicles. We also need more information on the chemical composition of PM emissions from non-road diesel and gasoline vehicles. Future versions of the U.S. EPA particle mobile source emissions model should explicitly account for cold start, high acceleration and high emitters. The work on source contribution of diesel and gasoline vehicles to fine PM and particulate organic matter needs to be repeated in other locales. There also should be continued evaluation of mobile source models for VOCs and also PM.

Question period for Fujita

1. Do we know how the particle size distribution has changed over the past 10 –15 years? Has there been a shift if we looked at g/mile in terms of the proportion that is ultrafine, for example?

Fujita: I've heard that the newer diesel engines produce more ultrafine, but I suspect that both gasoline and diesel vehicles have always produced ultrafine particles. From the tunnel study it was apparent that most of the particles were ultrafine (mean diameter of 20 nm), converting to accumulation mode particles by coagulation or condensation as they reside in the atmosphere.

2. In looking at the relative proportions of emissions for diesel and gasoline, how has that been affected by the major fuel changes that have occurred after 1995?

Fujita: In terms of VOCs, there are less benzene and aromatics. Whatever changes in the fuel will be reflected in the emissions, because roughly half of what is emitted is unburned fuel.

3. So the gasoline emissions today of benzene will be about one third lower than what you showed on the chart.

Fujita: Yes.

4. Looks like from your results that a major thing that was being missed by source testing of vehicles was the condensable organic compounds. Do you have any recommendations for test methods to better capture those?

Fujita: Yes. The method that is used by Barbara Zielinska is one, which involves a puff XAD after a cartridge behind a filter. This is an attempt to capture all of the material, not only the particle but also the semivolatiles that pass through the front filter. This is essential for source apportionment, because it's very difficult to do the apportionment if your source sample has a different composition from the ambient sample. If you base the composition on the filter samples you will see a very different composition between the ambient and emission measurements. But if you collect all of the material, then you can relate the two and do the source apportionment correctly. You then have to assume where the phase transition occurs, and that that will change with ambient conditions. For source apportionment it will give you the correct relative apportionment, if you assume that the phase distribution will be the same.

5. You had a very interesting result about the importance of cold starts as a source of light duty particle emissions, which was from a study in Colorado in the wintertime. Do you have any information on how the importance of cold starts changes from winter to summer and whether when temperatures are higher you expect the engine to warm up faster?

Fujita: You expect to see differences. There was some data from summer, which is in the report.

VOCs in Gasoline and in On-Road Vehicle Emissions

Robert Harley, University of California, Berkeley.

The focus of Dr. Harley's talk was on a multi-year field study that is being carried out in the Bay Area to look at trends in vehicle emissions over time, particularly during this period with extensive fuel reformulation occurring in California. The changes in the fuel formulations were made with the intent of reducing vehicle emissions, including toxic air pollutants and criteria air pollutants.

There are a number of major fuel properties that have changed over the past five years, with particularly significant changes occurring in 1996. Between 1995 and 1996, there was a major drop in aromatics, including benzene, olefins and sulfur. Branched alkanes, such as trimethylpentane, also increased significantly from 1995 to 1996 to compensate for the loss of the high-octane aromatic content. RVP, the Reid vapor pressure, is a

measure of the tendency of gasoline to evaporate. By reducing RVP, vapor emissions from refueling and parked vehicles are reduced. Changes in the RVP over time have been more subtle. Other distillation properties of gasoline have been modified, with the median boiling temperature shifting lower. The amount of heavy molecular weight material in gasoline has been reduced, with the lightest material also being reduced. The weight percent oxygen has risen dramatically, with the fuel in the Bay Area using almost entirely MTBE for this purpose. Small amounts of ethanol and TAME have also been added.

An important question is how these fuel changes affect vehicle emissions. The approach taken in this project was to measure on-road vehicle emissions, using the Caldecott Tunnel in the Bay Area as the field study site. The Caldecott Tunnel is one km long, which allows a high buildup of pollutants to occur. There are three bores of the tunnel and diesel trucks are not allowed in the middle bore. Measurements taken in the middle bore are largely unaffected by diesel emissions. The vehicles entering the tunnel heading east are subject to an uphill grade and are fully warmed up. The field study was carried out for 10 days each summer between 1994 and 1997, with a focus on rush hour from 4:00 to 6:00 pm.

In the tunnel, unburned fuel is a major component of the emissions, so the changes in the tunnel mirror the changes in the fuel. The reduction in aromatics and increase in MTBE that occurred in the fuel are also evident in vehicle exhaust. Acetylene, ethylene and propene, which are products of incomplete combustion, are present in exhaust. Other important products of incomplete combustion, formaldehyde and isobutene, both increased after reformulation. In terms of head space vapors, MTBE is a significant contributor to the mass of vapors. The C4 and C5 alkanes are enriched in the vapors relative to fuel, due to their higher vapor pressures relative to other fuel components. By reducing these lighter olefins, which are reactive, the reactivity or ozone-forming potential of evaporative emissions has been reduced.

The top ten VOCs present in the vehicle exhaust by mass are:

- Isopentane (9.9%)
- Toluene (8.5%)
- Ethene (6.2%)
- MTBE (5.5%)
- m/p-Xylene (5.0%)
- Propene (3.7%)
- Isobutene (3.3%)
- Benzene (3.3%)
- 2-Methylpentane (3.2%)
- Acetylene (2.9%)

These ten species account for approximately 50% of the total nonmethane organic compound (NMOC) mass.

The clearest effect of reformulating gasoline has been on benzene emissions. There was a general downward trend attributable to improved emission control technology and retirement of older vehicles, but the steep downward gradient was due to reformulation of fuel.

Other VOC health hazards include the following products of incomplete combustion:

- Formaldehyde (~2%)
- 1,3-Butadiene (~0.6%)
- Acetaldehyde (~0.3%)
- Acrolein (propenal, ~0.1%)
- Crotonaldehyde (butenal, ~0.1%)

Refiners will phase out MTBE by the end of 2002 and will therefore be looking for other ways to boost or maintain the octane rating of the fuel. They are constrained in what they can use by the restrictions on the level of aromatics that are allowed. So other high octane compounds will be used instead, including ethanol and alkylate (highly branched alkanes such as 2,2,4-trimethylpentane, also called isooctane). In isooctane the atoms are in a very compact arrangement, giving the compound a lower surface area and higher vapor pressure than other C_8 alkanes. With increased isooctane in fuel, more will be in vapor that people breathe. Increased emissions of propene and isobutene in vehicle exhaust would also be expected.

One important issue in terms of the use of isooctane and other compounds in this class is the refinery process that is required to make these compounds. Sulfuric acid and hydrofluoric acid (HF), very strong acids, are used as the catalysts in this refinery production process. Acute health effects from a release of HF could be very dire. If the use of highly branched alkanes increases significantly, the risk associated with this refinery process would also increase.

Emissions from heavy duty diesel vehicles were also measured. Diesel vehicles emit about five times as much NOx as gasoline vehicles do. Under the conditions in the Caldecott tunnel, diesel engines produce 15-40 times more particles than the light duty vehicles, using various measures of particles including number, mass and black carbon. The bore with diesel vehicles could also be visually detected, with clouds of black smoke coming from that bore. Smoke was not visually detected from the light-duty bore. The emissions from the diesel vehicles appear to be greater in this study of a tunnel with an uphill grade as compared to a study of a flat tunnel (Tuscarora). Diesel was found to be an important source of light end particle phase PAHs. For some of the heavier PAHs gasoline was the dominant source. Particle phase PAHs from light duty vehicles were predominantly found in the ultrafine size range.

Question period for Harley

1. Do you have emissions data on ethylbenzene and naphthalene, two compounds found recently to be of note in terms of carcinogenicity.

Harley: Ethylbenzene accounts for about one percent of total VOC mass in our tunnel measurements of light duty vehicle emissions. We haven't measured it in diesel engine emissions. We measured naphthalene in Bay Area fuel samples, and found naphthalene levels were higher in gasoline than in diesel fuel. We haven't measured vehicle emissions of this compound in the tunnel, but I expect that gasoline engines would be the dominant source because there is more naphthalene in the fuel, a higher fraction of fuel that escapes combustion in gasoline engines, and more gasoline than diesel fuel used statewide.

2. Can you estimate relative contribution from the gasoline versus the diesel fuel in terms of PM for the tunnel?

Harley: For this tunnel, diesel engines clearly dominate by a factor of 10 to 20. In bore one where diesel vehicles were five percent of the traffic, they contributed 85 to 90 percent of the fine particle mass.

3. How did you account for light duty diesel vehicles?

Harley: We did a license plate survey to get information about the age of the vehicles and whether they were gasoline or diesel. The fraction of light duty diesel was about 1.5% of the total light duty fleet, so we neglected that contribution to emissions in the middle bore.

NREL's Comparative Study of Gasoline and Diesel Exhaust

Doug Lawson, National Renewable Energy Laboratory (NREL)

Changes in fuel properties can have unexpected results. For example, a decrease in the fuel's Reid vapor pressure (RVP), which is beneficial for reducing evaporative emissions, resulted in an increase in the photochemical reactivity of the fuel in Colorado.

There are still questions about PM from gasoline vehicles, and this is an important research need. Based on a visual survey, Lawson estimated that about 2.5% of the fleet is emitting particles. A simple verification of this is that soot is found inside the tailpipes of gasoline vehicles. In terms of the size of particles, the ultrafines and nanoparticles have always been there, but the equipment required to measure them is just now becoming available.

A key issue in source attribution is ensuring that the source profiles are good. One of the key differences in the Northern Front Range study as compared to other studies was the significant effort put into recruiting in-use vehicles for emissions measurement, which will result in a much more accurate source profile.

One surprising result from the Northern Front Range study was that under cold start conditions, there was about as much elemental carbon as organic carbon from gasoline vehicles based on dynamometer testing. Under hot stabilized conditions, about one quarter to one third of the carbon is considered "elemental", which is an operational definition. For smoking light duty vehicles, most of the carbon is organic. There are different types of high emitters. One type emits a puff of smoke on acceleration or cold start. There is not much known about those or the frequency of them on the road. Others are high emitters throughout operation, and those emit mostly organic carbon. The study also found that gasoline vehicles have quite a bit more vapor phase PAHs as compared to the diesel vehicles.

NREL is coordinating a comparative toxicity study of gasoline and diesel exhaust. The groups working on the study include Southwestern Research Institute, Desert Research Institute, University of Dayton Research Institute, Lovelace Respiratory Research Institute, National Institute for Occupational Safety and Health, and Oak Ridge National Laboratory. The objectives of the comparative toxicity study are:

- To collect on-road (in the Fort McHenry Baltimore Tunnel) and dynamometer samples (using ARB's new unified driving cycle, a more aggressive cycle) of gasoline and diesel exhaust, including both PM and semi-volatile organic compounds (SVOCs) to capture the total sample.

- To test vehicles representative of the fleet and not just new vehicles;

- To conduct detailed chemical analysis on the exhaust samples as well as samples of composite fuel and lube oil; and

- To carry out a variety of toxicity testing on the samples, including:

    - *In vitro* testing using the A549 human lung epithelial cell line
    - *In vivo* testing of rats exposed via intratracheal instillation
    - Genotoxicity testing using the standard Ames assay

Some results from the Fort McHenry tunnel samples are available. The light duty bore had a small number of heavy-duty diesel vehicles, 0.3% and 0.5% of the vehicles in the two sampling runs, which could confound the results. The two sampling runs showed 30% and 42% of the vehicles in the heavy duty bore were diesel vehicles. The heavy-duty bore had much higher concentrations of PM/SVOC (172.5 $\mu g/m^3$, 301.0 $\mu g/m^3$) versus the light-duty bore (26.8 $\mu g/m^3$, 41.5 $\mu g/m^3$). The ambient levels for the two runs were 24.5 $\mu g/m^3$ and 16 $\mu g/m^3$. These are hot transient conditions rather than cold start conditions. Cold start conditions are where most of the emissions from the light duty vehicles are observed.

Dynamometer testing of several types of vehicles have been completed and are summarized below.

Description	# of Unified Driving Cycles Required to Generate 4-g Sample	Average PM Rate (mg/mi)	Approx. PM Sample Mass (g)
Gasoline average PM emitter	36	13.6	5.4
Black gasoline smoker	5	85.9	4.8
White gasoline smoker	1	1004	11.1
Diesel high PM emitter	6	419	4.5
Gasoline average PM emitter at 30°F	24	42.9	12.4
Gasoline ULEV[1] (99 Honda Accord)	NA	2.8	0.04
Gasoline NLEV[2] (99 Ford Windstar)	NA	4.3	0.04

1. Ultralow emissions vehicle
2. National low emissions vehicle

Preliminary results from the comparative study indicate that the semivolatile fraction as well as the filter fraction exhibit significant toxicity. No details are available as yet. This is the first time that a head to head comparison of the toxicity of gasoline versus diesel exhaust has been conducted, and also the first time that the SVOCs have been studied.

Question period for Lawson:

1. We are interested in how the sulfur fraction turns into sulfates when you do particulate testing. How is that accounted for?

Lawson: It's typically measured by chromatography and you are looking at an aqueous soluble component. We have learned that lube oil appears to be a fairly important source of sulfur, which is non-sulfate sulfur. As engines age, there tends to be more of a non-sulfate sulfur fraction. There is not much sulfate in the mass, it's a very small component. For overall PM emission, sulfate is not significant.

2. What effect does altitude have on emissions? Some of the studies have been done in California versus Colorado.

Lawson: For PM emissions under cold start conditions it may be important. For high emitters it's probably not important at all. The Denver study is going to be repeated in Los Angeles and the results compared.

3. Did your definition of SVOC include the oxygenated compounds?

Lawson: That would depend on what phase they are in. Another important thing to note is that we tend to focus on PAHs too much; they may only be a small fraction of PM, perhaps only three or four percent. There is a lot unidentified in PM.

Atmospheric Transformation of VOCs

Roger Atkinson, University of California, Riverside

Atkinson began by saying that the bottom line of this talk is that what you breathe may not be what is emitted unless you are right behind the tailpipe.

The organics emitted from gasoline vehicles are largely alkanes, with the non-methane alkanes accounting for about 50% of the VOCs in urban areas. The alkenes emitted from gasoline vehicles are primarily the fairly small ones up through maybe C6 and account for about 10% of the VOCs in urban areas. Aromatic hydrocarbons emitted from gasoline vehicles, including benzene, toluene, xylenes, ethylbenzene and trimethylbenzenes, account for about 20% of the VOCs in urban areas. The oxygenates, carbonyls and MTBE, account for about 10% of VOCs in urban areas.

Organics in the atmosphere partition between the gas and particle phases, with the partitioning dependent on particle loading. This talk focused on chemicals in the gaseous phase.

Gas phase organic compounds can be removed from the atmosphere by physical processes, such as dry and wet deposition.

Chemical transformation processes include:

- Photolysis: Chemical must absorb radiation of wavelengths greater than about 290 nm, which are the wavelengths that make it through the stratosphere into the troposphere. Having absorbed the radiation, the chemical must undergo chemical change. Photolysis in the troposphere is expected to be important for carbonyl compounds and organic nitrates, as two prime examples.
- Reaction with ozone: Ozone is transported down from the stratosphere and is destroyed by dry deposition. Ozone is also produced photochemically in certain urban areas and is destroyed photochemically typically over oceanic areas. Even in remote, “clean”, locations, ozone levels are typically at 10 to 40 ppb.
- Reaction with hydroxyl radicals: A major source of hydroxyl radicals is from the photolysis of ozone. Hydroxyl radicals can also be produced from the photolysis of nitrous acid and from formaldehyde photolysis. Hydroxyl radicals are essentially the garbage disposal system for organic compounds. Essentially all organic compounds except chlorofluorocarbons and certain halons, react with

hydroxyl radicals. Hydroxyl radicals exhibit a diurnal pattern, peaking around solar noon and essentially zero at night.

- Reaction with nitrate radicals: The nitrate radical is a nighttime species, formed from the reaction of NO_2 with ozone. Nitrate is in equilibrium with NO_2 and N_2O_5. The concentrations of nitrate are low in the daytime because nitrate photolyzes rapidly, with a lifetime of only five seconds. Nitrate concentrations are extremely variable. Reactions with NO_3 are important for the alkenes and especially for the more branched olefins.
- Reaction with chlorine atoms: Reaction with chlorine atoms is postulated to occur, especially in areas close to the ocean.

Lifetimes for hydrocarbons in the atmosphere can be calculated based on concentrations of OH, NO_3 and ozone and the rate constants for the reactions of the hydrocarbons with those species. The lifetimes will vary inversely with the assumed concentrations of the OH, NO_3 and ozone. Alkane lifetimes range from 1 to 10 days. Some of the higher alkenes have lifetimes of hours or less. Aromatic lifetimes range from several days for benzene down to a few hours for the more highly substituted aromatics. Formaldehyde photolyzes rapidly, with an overall lifetime of about three to four hours. Acetaldehyde also photolyzes, but its photolysis lifetime is about five days making the dominant loss via reaction with OH radical. Ethanol and MTBE are both fairly long lived, with lifetimes of three to four days with respect to reaction with OH radical. So everything emitted from vehicles reacts away.

The remainder of the talk pointed out the expected reaction products of hydrocarbons emitted from vehicles. Toxicological data are likely not available for these reaction products, which include:

- Organic nitrates, including 1,2- and 1,4-hydroxynitrates, carbonylnitrates and hydroperoxynitrates
- Hydroxycarbonyls (primarily 1,4-hydroxycarbonyls) and dihydroxycarbonyls
- Unsaturated 1,4-dicarbonyls and di-unsaturated 1,6-dicarbonyls
- Unsaturated epoxy 1,6-dicarbonyls
- Hydroperoxides and substituted (nitrooxy-, hydroxy-, carbonyl-) hydroperoxides
- All of the above react to form additional products

Question Period for Atkinson

1. Are all of these compounds mostly emitted from gasoline?

Atkinson: No. Diesel will also emit these compounds. You need detailed emission profiles from both types of vehicles.

2. What is the effect of temperature and atmospheric elevation on these reactions?

Atkinson: For the temperatures typically seen in an urban area, the reactions would not change by more than a factor of two. You would get more photochemistry potentially in

Denver but you probably would not notice a difference in the concentrations of OH and NO_3.

3. Can you give a net benefit to adding an oxygenate to fuel?

Atkinson: No is the bottom line. The reactivity of the emissions do not seem to change whether it's ethanol, or MTBE as the oxygenate, or whether they are in there at all.

4. When you have an air pollution episode, do you see increased levels of the hydroxyl and nitric chemicals?

Atkinson: One wouldn't expect them to change from day to day to any significant extent. There are not really any data, however. Based on data from Claremont in 1993, there was not much of a change from day to day.

5. Based on data from Zielinska from 1995-1996 to look at the ambient effects of reformulated gasoline, she did measure higher formaldehyde in 1996 relative to 1995. Isobutene is one of the degradation products of MTBE. Would it be a reasonable hypothesis to say that that could be the major source of the increased formaldehyde?

Atkinson: Isobutene would certainly lead to some formaldehyde, but nearly all organics when reacted in the atmosphere lead to formaldehyde. In the LA basin, something like 80% of the formaldehyde is secondarily formed from atmospheric reaction. I would not have thought that isobutene would be a major source. It may well depend on atmospheric conditions.

Atmospheric Transformations of PAHs and Formation of Ambient Mutagens

Janet Arey, University of California, Riverside

Sources of PAHs in the atmosphere include unburned fuel, lube oil and pyrosynthesis from lower molecular weight aromatics. Naphthalene is present in fuel. According to Marr and coworkers, naphthalene can be present in gasoline up to 2600 mg/L and in diesel up to 1600 mg/L. The levels of methylnaphthalenes, dimethylnaphthalenes, trimethylnaphthalenes and methylfluoranthenes are all lower in reformulated and low aromatic gasoline as compared to pre-1993 fuel. The levels of fluoranthene and pyrene have increased slightly.

Atmospheric transformation of PAHs depends on whether they are in the gas phase or particle associated. Traditionally the particle-associated PAHs have been more of a concern because the particles can be inhaled into the lung and the larger PAHs tend to be more toxic.

Benzo(a)pyrene (5 rings) is found in the particle phase. Three and four ring PAHs are in the gas phase, but after atmospheric reaction can transition to the particle phase. For

example, pyrene in the gas phase can react to form nitropyrene, which will be mainly particle associated.

Data from a study at seven sites in California in the 80's showed that the gas phase PAHs tend to be the most abundant. At all the sites naphthalene was present at the highest concentrations, by at least an order of magnitude up to three orders of magnitude.

For gas phase PAHs, the possible processes for atmospheric loss are:

- Photolysis: Generally not important for gas phase PAHs, but may be important for particle phase PAHs.
- Reaction with the hydroxyl radical: Definitely an important process for PAHs, with the shortest lifetimes (on the order of several hours to half a day, based on a global average OH concentration).
- Reaction with the nitrate radical: Although this reaction is slow (lifetimes of months to years), it may be important in terms of the type of reaction products produced.
- Reaction with ozone: Generally not very important, except for a few specific PAHs like acenaphthylene and acephenanthrylene. Otherwise, reaction times are long, on the order of one to several months or more, with those times about a factor of four shorter in a polluted area.

An analysis of an ambient air particulate sample compared to a diesel particulate sample illustrates the gas phase reactions of PAHs. Compounds detected in ambient air, such as 2-nitrofluoranthene and 2-nitropyrene, are different than those found in the diesel sample and are likely a result of radical-initiated reactions.

The lower molecular weight PAHs are most abundant, and the reaction products of naphthalene, for example, have been studied. The lifetime of naphthalene is only about seven hours. The products from reaction of naphthalene with OH include:

- 2-Formylbenzaldehyde
- Phthalic anhydride
- 1,4-Naphthoquinone
- 2-Formylcinnamaldehyde (major product, yield ~35%)
- 1-Naphthol
- 2-Naphthol
- 1-Nitronaphthalene
- 2-Nitronaphthalene
- 1-Hydroxy-2-nitronaphthalene
- 2-Hydroxy-1-nitronaphthalene

Reaction with NO_3 produces some of the same products:

- 1,4-Naphthoquinone
- 2-Naphthol
- 1-Nitronaphthalene (yield of ~24%)
- 2-Nitronaphthalene (yield of ~11%)
- 1-Hydroxy-2-nitronaphthalene
- 2-Hydroxy-1-nitronaphthalene

The yield of nitronaphthalenes is much higher in this latter reaction (~35% total) as compared to reaction with OH (~1% for each nitronaphthalene). Although the reaction with NO_3 is much slower, this chemistry will still occur in the atmosphere, particularly in urban areas.

To reiterate, reaction of PAHs with OH and NO_3 will form nitro-PAHs with approximate yields as follows:

PAH	Nitro-PAH Yield	
	OH	NO_3
Naphthalene	~1-2%	35%
1-Methylnaphthalene	~0.4%	27%
2-Methylnaphthalene	~0.2%	39%
Fluoranthene	3%	24%
Pyrene	0.5%	-

Products of these gas-phase reactions can become particle-associated. For example, fluoranthene in the gas phase will react to form 2-nitrofluoranthene, which is particle associated.

Nitro-PAHs in ambient particles can result from direct emissions (1-nitropyrene) as well as atmospheric reactions of gas-phase PAHs. By comparing chromatograms of the products of simulated atmospheric reactions carried out in chambers to chromatograms of ambient air samples, the chemistry that is occurring in ambient air can be elucidated. Direct emissions, products of the OH reaction and products of the NO_3 reaction are all sources of nitro-PAHs observed in ambient air samples under various conditions. The primary source of nitro-PAHs is thought to be atmospheric transformation of PAH, including both OH-radical and NO_3-radical initiated reactions.

Ambient air samples, vapor and particulate phases, were fractionated and tested for genotoxicity, including bacterial mutagenicity and genotoxicity in human cell lines. To obtain further information on which compounds might be responsible for the observed genotoxicity, PAHs were reacted in chambers and the reaction products were fractionated and tested. Based on these studies, PAH reaction products of interest toxicologically include:

- Dialdehydes (including formylcinnamaldehyde)
- Hydroxynitro-PAHs
- Methylnitronaphthalenes
- 3-Nitrobenzanthrone
- Nitro-PAHs
- Nitro-PAH lactones

3-Nitrobenzanthrone, found in diesel samples and ambient air, was the most potent genotoxicant.

Question Period for Arey

1. Are the dialdehydes precursors to dicarboxylic acids?

Atkinson: Transformations of dialdehydes would be a minor pathway for dicarboxylic acid formation.

2. Do we know the source of the dicarboxylic acids in PM?

Arey: No. That is a very important question and a lot of effort is going into answering it right now.

3. What are the possible phase changes related to reactions of PAHs?

Arey: When PAHs react in the atmosphere, something more polar is generally going to be produced, which decreases the vapor pressure. So if the PAH is just barely in the gas phase, such as a 4-ring PAH, then the products of the reactions are likely to be particle associated.

4. An earlier study of yours indicated that lactones could be responsible for as much as 20% of the PAH mutagenicity. What is the status of that result?

Arey: The assay that was used was particularly sensitive to lactones. The results therefore will depend in part on the type of assay used. Lactones do account for 20% of the mutagenicity in the Kado micro suspension modification assay. But trying to rank them is too simplistic. It is important to understand mechanistically what is happening.

Lewtas: Lactones are not as mutagenic in other assays, but some form DNA adducts so are potentially important.

Morning Discussion Period

1. What is the time frame for particles changing from nano particles to particles of larger size? What is it that we are actually breathing, the nano particles or something larger?

Ambient measurements indicate that most particles are in the accumulation mode, so the transition must occur relatively rapidly over a period of a day. Data from the National Renewable Energy Laboratory (NREL) indicates that there are rapid changes in particle size with just fractions of a second. The particle size you observe is very sensitive to where you are sampling and what the sampling conditions are. The greatest concern for nano particles would be immediately next to a source, such as freeways or high traffic areas. Traveling along the roadway with the windows and vents open, for example, would be a scenario in which you would be breathing a lot of nano particles.

2. There seemed to be conflicting information from Fujita and Harley regarding the relative concentrations of PAHs in gasoline engine exhaust versus diesel engine exhaust. What are some possible explanations for this?

Fujita: Part of the issue is that test conditions are not identical. In particular, in the Northern Front Range Study, the test cycle includes the cold start mode, and the study also included higher emitters. Both of those conditions will result in higher PM and PAHs. As shown by the ambient apportionment work, the hot stabilized contribution to total PM is small relative to the contribution from cold starts and high emitters.

Harley: There is not a clear definitive answer on whether gasoline or diesel engines are the dominant source and there is not a single answer that applies to all PAH. For some of the high molecular weight PAH, gasoline appears to be the dominant source. Naphthalene levels are higher in gasoline than in diesel. The differences also may depend on how the data are reported. If a lot of diesel traffic is outside of cities, then the potential for exposure to diesel would be lower than for gasoline.

3. How much do we know about emissions from natural gas vehicles, which are proposed as an alternative to diesel for public transportation?

NREL may soon be doing a study on natural gas particulate size distributions, emissions, composition and toxicity.

4. Is there a research effort regarding measurement of the very low end of the PM size fraction?

One question is how low is low? At NREL the current study is using state of the art measurement equipment. However, there are major problems even getting the material, making sure that what is being sampled is actually being emitted from the vehicles. So while there is equipment in this study to look at ultrafine PM, the results will be highly dependent on the sampling conditions.

Session 1 (continued): Afternoon

Pollutant Concentrations Inside Vehicles and Along California Roadways

Peggy Jenkins, California Air Resources Board (absent)
Scott Fruin, California Air Resources Board (replacement)
Steve Hui, California Air Resources Board (replacement)

This study focused on personal exposure measurement of different pollutants. In order to evaluate people's exposure to these pollutants, the time that receptors spend in different locations must be looked at. Exposure is equal to concentration times time, integrated over 24 hours.

The objective of this particular study was to measure the gaseous and particulate pollutants inside the vehicle, where people are being exposed. The study also provided comparisons to a point immediately outside the vehicle, along the roadway, and also at the closest ambient air station. Certain factors were examined that could influence the in-vehicle concentrations including:

- Vehicle type driven;
- Type of vehicle followed;
- Traffic congestion level;
- Ventilation setting;
- Roadway type;
- Carpool lane; and
- Time of day.

There were a total of 29 trips, most of which were in Los Angeles with some in Sacramento, beginning in September of 1997. The total sampling period was two hours. This period was selected based on activity pattern data which indicated that most people spend approximately one to two hours on the road.

The organic chemicals measured were:

- Acetonitrile
- Benzene
- 1,3-Butadiene
- Dichloromethane
- Ethylbenzene
- Ethyl-t-butyl ether (ETBE)
- Formaldehyde
- Isobutene
- Methyl-t-butyl ether (MTBE)
- Toluene
- Trichlorofluoromethane
- m,p-Xylene
- o-Xylene

The inorganic chemicals measured were:

- Black carbon (real time)
- Carbon monoxide (real time)
- PM 2.5 mass
- PM 10 mass
- Fine particle count (real time)
- Particle-associated metals
    - Cadmium
    - Chromium
    - Lead
    - Manganese
    - Nickel
    - Sulfur
    - Others

The results of this study were compared to work done in 1987. The changes in fleet composition and the reformulations in fuel have had a significant impact on the in-vehicle concentrations, decreasing them as expected and mirroring the changes seen in ambient air concentrations. One interesting finding is that formaldehyde, which is primarily a secondary pollutant, showed no change over this time period.

In terms of spatial effects, the in-vehicle concentrations were very high compared to the roadside or ambient measurements, with a very sharp gradient. It appears that this gradient is sharper for the arterial road as opposed to the freeway, most likely because the source is narrower and the source strength is smaller. With a very strong source, such as an LA freeway, the concentrations are likely to be high well beyond the freeway. The in-vehicle concentrations themselves were comparable for arterial versus freeway. Because the vehicles immediately in front of a vehicle dominate the in-vehicle

concentrations, for rush hour or congested conditions, there was not a clear difference between freeway and arterial. Based on results in LA versus Sacramento, congested traffic conditions produced similar in-vehicle results regardless of location. In terms of roadside conditions, however, there were significant differences.

The real-time black carbon and fine particle count data provided clear markers for diesel events, such as driving behind a smoky bus. The concentration of black carbon and the fine particle count showed significant increases when following a diesel source. The carbon monoxide peaks were more difficult to attribute to specific sources, however.

In summary, some of the significant findings of the study were:

- VOC concentrations inside the vehicle are typically several times higher than roadside concentrations
- Roadside VOC concentrations are often several times higher than ambient concentrations
- Rush hour in-vehicle VOC concentrations are similar on freeways and arterial roadways in both LA and Sacramento
- Roadside VOC concentrations are much higher for freeways and for LA
- Highly elevated in-vehicle fine particle counts and black carbon concentrations occur when trailing diesel vehicles (up to 14 times roadside)
- Driving in carpool lanes reduces exposure

Data from the 1980s on activities of Californians relevant to gasoline exposure indicated that:

- Enclosed transit accounted for 7% of day for ages 12 and over, and 4% for ages 0-11
- 23% of Californians visited gas stations, parking garages or auto repair shops
- 14% of Californians pumped gas
- Mowing a lawn results in three times the normal breathing rate, making it a potentially important source of exposure, particularly given the highly polluting nature of two-stroke engines

The other important potential source of exposure is whether or not the house has an attached garage, because that can significantly impact indoor residential air quality.

Question period for Hui and Fruin

1. How well would carbon monoxide alone predict exposure to other pollutants?

Fruin: That analysis has not been done at this point.

Hui: In general, the level of CO in the vehicle was low.

2. You emphasized that following a diesel vehicle resulted in a peak in the fine particulate matter, but the same thing appeared to occur when you followed a smoking gasoline powered car.

Fruin: It was rare that any passenger vehicle noticeably impacted the black carbon or the particle count. In the one case that it did appear to have an influence, there may have been other contributing factors, such as being stopped at a stoplight.

3. Are you saying that you did not encounter smoking gasoline vehicles or you could not target them?

Fruin: It's both. Diesel vehicles were primarily targeted, with smoking gasoline vehicles being secondary. There was only a single occurrence in which a smoking gasoline vehicle appeared to have a large effect, and in that case it was not entirely clear if that was the only factor.

Biomarkers of Exposure to Gasoline Particle Emissions

Joellen Lewtas, U.S. Environmental Protection Agency

The focus of the talk was on personal exposure to fine particle PAHs and attempts to identify useful biomarkers for gasoline exposure, which would also be useful as source tracers for outdoor fine particles because gasoline sources are generally not significant indoors. Part of this work involved looking at data on urinary PAH metabolites and PAH source profiles for purposes of source apportionment.

PAH source profiles were presented for indoor and outdoor air and included combustion sources with different fuels (coal, petroleum, diesel, gasoline, wood, and tobacco). The focus of the work was on particle phase PAHs.

Samples from a tunnel in Prague, a gasoline van, two diesel cars, coal sources and wood stoves were discussed. An obvious finding was that concentrations of benzo(g,h,i)perylene were relatively high in both the tunnel sample and the gasoline van. The ratio of benzo(g,h,i)perylene to benzo(a)pyrene was over 1.5 for the vehicle tunnel sample and gasoline van sample, with the remaining sources showing ratios of generally less than 0.5.

In reviewing older literature, benzo(ghi)perylene has previously been suggested as a marker for traffic. The talk by Rob Harley this morning indicated that diesel is not a source for benzo(ghi)perylene, making it a promising marker for gasoline.

Personal exposure data was examined. The highest ratio of benzo(ghi)perylene to benzo(a)pyrene was observed in Tokyo.

Urinary metabolite data was examined. There are not any benzo(ghi)perylene metabolite standards available currently but are now in the process of being developed.

The major conclusions of the talk were:

- Benzo(ghi)perylene appears to be a useful tracer for gasoline emissions;
- Most PAHs are highly correlated with each other, making it difficult to find a unique tracer. Some type of factor analysis may be necessary;
- Urinary metabolites are likely the most promising biomarker for purposes of source apportionment. Metabolites are correlated well with exposure to the parent PAH. DNA adduct methods are not well developed or specific enough, and are also costly.
- Methylated PAHs may be even more useful in separating sources

Question period for Lewtas

1. How do the half-lives of the different urinary products range?

Lewtas: There is a good study in humans on the half-life of benzo(a)pyrene. There are some animal data on the half-life of other PAHs and nitro-PAHs. Generally speaking, the longest half-lives are on the order of hours.

2. What about confounding from diet? Is there something that would probably not show up in the diet but that could still be used as a tracer?

Lewtas: I intend to go through all the dietary literature to examine that question. If the source for the PAHs in food were gasoline, then you would expect to see benzo(ghi)perylene. Usually you can address this issue via questionnaire data on what people eat.

Session 1 Panel Questions and Discussion

1. Referring to the preliminary list of chemicals, do you have suggestions of others that should be considered because of potential for significant exposure? [See also question 1 under Session 2.]

Chemical Suggested for Addition	Proposed by	Comments
2,2,4-Trimethylpentane	Harley, UC Berkeley	Expected to increase significantly in gasoline to compensate for loss of high octane as a result of decreased aromatic content. Trimethylpentanes are known to exhibit toxicity, but the database is not complete.
Crotonaldehyde	Harley, UC Berkeley	Crotonaldehyde is present in fuel at a level of approximately 0.1% and has known toxicity
Oxidation products of aromatic hydrocarbons – phenol and cresols	Harley, UC Berkeley	Atkinson responded that those chemicals are probably mostly directly emitted from other sources
$PM_{2.5}$	Croes, ARB	The preliminary list had specified only PM_{10} because $PM_{2.5}$ is not regulated in California as yet.
Hexavalent chromium	Croes, ARB	Hexavalent chromium is ubiquitous in the environment and gasoline powered vehicles may be an important source. This would be related more to the vehicle operation than the fuel itself.
Components of lube oil – zinc dipentasulfate	Lawson, NREL	Should also look carefully at lube oil as source of chlorine and therefore dioxins

Atmospheric transformation products of VOCs and PAHs (unsaturated dicarbonyls; e.g., the 1,6-disaturated dialdehyde from benzene)	Atkinson and Arey, UC Riverside	A number of atmospheric transformation products formed from VOCs and PAHs are likely to be important from a toxicological perspective. Benzene is not highly reactive but dicarbonyls can be formed from other more reactive aromatics
Carbon black	Craft, Monterey Bay Unified Air Pollution Control District; seconded by Lawson, NREL	Carbon black is a component of particulate, present in gasoline emissions
Transition metals	Pinkerton	While iron or other metals may be a reflection of the aging of the engine rather than gasoline per se, metals are still important to consider.

2. Are gasoline-powered engines a potentially important source of dioxins/furans?

The panel suggested several studies to review, including a report by Allen Burger on a tunnel study in the Fort McHenry tunnel in Baltimore, reports from Sweden and a paper by Bruce Harris of U.S. EPA. The Burger study found that dioxin emission rates were below detect in the gasoline bore of the tunnel and were also low in the diesel bore. The Harris study reported low concentrations of dioxin from diesel trucks.

3. What is the state of knowledge of the chemical composition and size distribution of gasoline PM?

Considerable work has been done in this area, though there is always more to do. We know fairly well what the distributions of PAHs are in both gasoline and diesel but PAHs make up only a small fraction of the total organic component. Information on the other chemical constituents of organic carbon is lacking. Cass *et al.* have made a lot of effort to characterize the other components, but there still remains a large fraction that is unresolved. Another area that needs work is the size-resolved chemical composition for gasoline and diesel. The size distribution, however, is fairly well known. Based on tunnel studies, the average particle size is approximately 20 nm on a number count basis. On a mass basis, the average is more like 0.1 micron. Size distribution is NOT a static property of the aerosol; the dynamics of coagulation are rapid, and studies are taking a snapshot of something that is evolving rather than something that is a fixed property of the particle emissions. Sampling conditions can affect the results significantly. Notable

changes in size distributions have been recorded in a very short time frame. Studying ultrafine particles is particularly challenging.

In terms of quantifying exposure, there is no good method to assess particle exposure. U.S. EPA has used carbon monoxide (CO) as a surrogate for various gaseous toxic species, but nothing similar for particle phase. The use of ambient data to infer exposure to particles needs more work.

4. Which PAHs and nitro-PAHs associated with gasoline engine emissions are the most important in terms of potential exposure?

In terms of PAHs, naphthalene would be at the top of the list, because it is abundant and also is likely to produce atmospheric transformation products that are interesting toxicologically. NitroPAHs would be the electrophilic titration products of the PAHs in the gasoline.

The panel members were not aware of any comprehensive study that has fully characterized PAHs found in gasoline. There are many PAHs in both gasoline and diesel, and there is no general rule about which PAHs will be higher in gasoline versus diesel. This would have to be examined on a compound-by-compound basis. For naphthalene and pyrene, generally diesel is comparable to or higher than gasoline. But for heavier end PAHs, there are several where gasoline is the dominant source. Heavy PAH should not be showing up in gasoline, considering that they are not in the right boiling range. However, there are other process units besides distillation in the refinery, specifically the process unit that makes aromatics. As the catalyst for that unit ages, PAH and coke form on the catalyst and end up being dumped into the product stream and blended into gasoline.

Data from the Northern Front Range Study showed that even moderately clean vehicles emitted a lot more or comparable or higher emission rates of both gas phase and particle phase PAHs than diesel vehicles. Some of the smoking cars and high emitters had three to four times more than diesel on a fuel basis, not on a gram per mile basis.

In terms of future work, researchers should look at as many of the PAHs and nitroPAHs as is financially practical, both because of the carcinogenic potential of these compounds and also the potential for using some of them as tracers. This research should be conducted for both emissions and ambient air. The next important question is how to do the exposure assessment. The compounds that actually reach the human receptor have been transformed, with a shift to more polar compounds. Research is needed on what could be monitored as a surrogate for that shift in polarity. This is a difficult problem, however, the bulk of the biological activity is in that more polar fraction based on *in vitro* studies.

5. How should we evaluate exposure to particulate emissions, including exposure to the chemicals that are associated with the particulate emissions?

ARB evaluated exposure to diesel particulate by using PM10 as a surrogate. Data on the individual compounds in the particulate phase are generally not available and it would probably be hard to monitor for those compounds. The model that was used for diesel has nine microenvironments and uses activity location patterns to determine the time people will spend in those microenvironments.

One problem with trying to get concentrations of particulates in different microenvironments is that there is not much known about building penetration rates and removal rates. If in the absence of data you assume that what you see inside is essentially what you see in ambient air, then there is no improvement on the assumption that people are exposed to ambient air all the time. Also, in making this assumption, gradient effects, such as what might occur if the building is close to traffic or there's a parking lot nearby, are ignored. This is an area that has not been studied enough and should be focused on, because a key addition to people's exposure occurs when they are within the localized influence of gasoline-powered vehicles. There is also a definite need to focus on the in-vehicle environment, because the concentrations are going to be several times to maybe an order of magnitude higher than in ambient air.

There are three studies that are going on at Harvard University, New York University and University of Washington. They are looking at susceptible subpopulations, children or the elderly over 65, exposed to $PM_{2.5}$. Looking at $PM_{2.5}$ instead of PM_{10} helps remove a lot of confounding from other sources of particles and improves the relationship between indoor and outdoor measurements. These studies are also attempting to look at speciation and using various chemicals such as sulfate as tracers for outdoor air. Other tracers are being investigated for the Northwest, since there is not as much sulfate there. The studies are also doing personal exposure monitoring using monitors that can give data on mass, metals, OC and EC. The individual compounds will also be extracted and analyzed. The studies are not doing much with gas phase compounds, except for an attempt to look at semivolatiles.

ARB and U.S. EPA are co-funding a personal exposure study for $PM_{2.5}$, which will look at cardiopulmonary disease, $PM_{2.5}$ mass and speciation.

The highest CO in the state is in South Central LA. Since it's probably coming from mobile sources you could design some PM studies to look at primary PM emissions from gasoline-powered vehicles. Though it won't be a one-to-one correlation between high CO emitters and high PM emitters, CO is a good surrogate for what shape the fleet is in. You could design a fine particle study there to get composition and that would give you an idea of exposure. To find the highest gasoline emissions, go where the highest CO is.

6. What ambient monitoring data are available in California for gas-phase and semi-volatile PAHs and nitro-PAHs? In the absence of empirical data, can the ambient concentrations of nitro-PAHs be predicted?

A study in California is available from about 10 years ago that reported on data from seven sites. There was also some work more recently in Riverside which showed that PAHs appeared to be down from 10 years ago, though the meteorology may not have exactly matched so the two studies may not be directly comparable. The nitro-PAHs did not appear to be down as much, and there's really not enough data to indicate a trend. However, these results are consistent with data that others have shown here at this meeting. The decrease was about an order of magnitude. In general, the nitro-PAHs are a couple of orders of magnitude lower than the PAHs. This translates to, for example, the nitronaphthalenes being roughly equivalent in concentration to pyrene, while the naphthalene would be a factor of about 100 to 1000 higher than the nitronaphthalenes. There is also some data from 1997 at a few sites for nitronaphthalene, methylnitronaphthalenes, and 3-nitrobiphenyl, and at seven sites for naphthalene and methylnaphthalene.

Regarding prediction of nitro-PAH concentrations, it is not possible at this time to do that because there are still some mechanistic questions to be answered, which will be examined over the next few years.

7. What is the latest research on the proportion of total PM emissions (PM_{10}, $PM_{2.5}$, ultrafine) that is attributable to gasoline-powered engines vs. total mobile sources? How do we account for secondary PM formation in apportioning total PM? What methods could be used to come up with a reasonable source apportionment for primary and secondary PM associated with gasoline-powered engines?

The Denver Northern Front Range Study looked at 200 vehicles; most studies have looked at much fewer vehicles. There is a study planned to examine the question of gasoline versus diesel engines that is set to begin in early 2001 in the South Coast Air Basin. As part of the study, all past data on particle phase emissions will be reviewed for study design and potential inconsistencies, including selection of chemical analysis methods, whether high emitters were included, and what test cycles were used.

One high emitting car can be equivalent to 500 cleaner cars. Thus, it is critical to know the fleet composition. The Denver study suggested that there wasn't much secondary carbon being formed at all, which needs to be looked at again. It is important to do a good job at apportioning the primary emissions, which will go a long way to improving the understanding of the secondary PM. There is just not much knowledge about the secondary organics and how important they are in the ambient conditions.

In looking at ambient aerosols in California, carbon particles are about 95% of the mass that is directly emitted. Nitrate is also significant in ambient aerosols, and shows up as a big chunk of the mass of fine particles. The nitrate is secondary, it is not directly emitted from sources but is the result of atmospheric processing of NO_x emissions, both from

gasoline and diesel engines. There is still some controversy over emission inventories and the relative contributions to NO_x, but for on-road vehicles about half the NO_x is coming from gasoline engines, with more NO_x coming from off-road diesel sources like railroad locomotives and construction equipment. Diesel engines are a very important source of NO_x, making diesel engines indirectly an important contributor to fine particles through this gas to particle conversion and formation of nitrate, which is an important contributor to PM fine particle mass in California. EC, the black sooty part of carbon, is all from primary emissions. The OC is potentially a mix of both primary and secondary material; a lot of people have been citing Southern California studies about this issue. There was a series of papers from 1987 that looked at ratios of OC to EC, that reported up to 80 percent of the OC may be secondary. However that data was from one day, a Saturday, in an urban area. The diesel truck has a different temporal pattern than the gasoline vehicles in urban areas. On that day, the EC went way down, which made the secondary OC just appear to be high when in fact it was the denominator that went down. Thus, quite a bit of what has been cited is misleading, and, in fact, there have been overestimates of how much of the OC is secondary. One panel member suggested that OC is primarily emitted directly from sources.

EC is often referred to as a tracer for diesel, but it actually comes from a lot of different sources. Substantial amounts also come from gasoline-powered vehicles. Black carbon from gasoline engines can be detected by doing the black finger test in the tailpipe. The other issue is that EC and OC are just operational definitions, as opposed to a clear chemical distinction.

8. What guidance can you provide regarding how to handle gas/particle phase partitioning as it affects using PAH emission source testing data (speciation data) from gasoline exhaust in source apportionment analysis?

In doing emissions testing, both the gas and particle phases should be collected. Experimental conditions such as temperature must be tracked, because what is gas phase under one condition may be particle phase under another condition. The fraction in the particle phase will go up with particle loading and go up with a decrease in temperature. Researchers must be very careful of taking data under a particular set of conditions and trying to use that to represent ambient conditions.

It might be possible to get an understanding of partitioning but it is not clear what this would mean or how relevant it would be to any particular situation. The phase distribution would change quite a bit from when the particle is directly emitted to ambient air. So even if it is possible to get the partitioning "right" for a particular sampling situation, it won't be universally applicable. Thus, sampling under as many conditions as possible is necessary.

Even if partitioning cannot be determined definitively, if both gas and particle phases are collected then at least the total amounts of the different chemical components can be determined. Gas versus particle phase can be reported separately as well, but cautiously.

Modeling can then be used to infer what the phase distribution might be for a particular temperature or other conditions.

9. What suggestions does the panel have for source apportioning secondary gaseous pollutants, such as ozone, and gaseous pollutants that are both primary and secondary (*e.g.*, acrolein, aldehydes)?

The chemicals emitted from gasoline-fueled vehicles are the same as those emitted from diesel and other combustion sources. Thus there is no easy direct way to do the source apportionment, meaning you have to fall back on modeling. Routine methodology is available to source apportion ozone. Given an emissions profile and mass emissions, one can use the maximum incremental reactivity (MIR) scheme to determine the amount of ozone that is formed. This is done routinely and has been used in regulations in California for a decade. Some chemicals may not be included explicitly in a chemical mechanism, making it impossible to model air concentrations. Also for a lot of chemicals referred to in Atkinson's talk, there is no quantitative data, because of a lack of analytical techniques. In some cases there are analytical techniques available for the laboratory but they have not been used in ambient air studies. Thus, it really comes down to modeling. One may have to use a more detailed chemical mechanism than what is presently used in an urban airshed model but that should give you reasonable ideas about the amounts of specific chemicals.

Chemical modeling with urban airshed models can be used to address the question of how much aldehyde is primary versus secondary for example. But a key uncertainty in that is the requirement for an accurate emission inventory, so there are very large uncertainties in the results.

In '87 there was a tunnel study that showed that hydrocarbon emissions were underestimated by factors of three to seven compared with the then EMFAC model. That underestimation dwarfed all other uncertainties. We don't know how accurate EMFAC2000 is. For formaldehyde, it's true that 80% can be secondary, but the highest human doses are likely to be a result of primary emissions.

A group in Australia did a study with two-dimensional gas chromatography and found that a number of organic compounds were hidden in the noise, in the baseline of a normal gas chromatograph. They found that the ambient load of VOCs would be something like 60% or more higher than what one would normally find. The organics were in the C_6 to C_{14} range and they concluded the compounds were aromatic largely. If this is correct it challenges the emissions inventory and/or the modeling. If the models are fitting the data as is, then the models are either insensitive to organics or wrong, or both or none of the above.

There are also indoor sources of pollutants. Transformation processes will change when pollutant is transferred from outdoor to indoor air.

There are also uninventoried sources of pollution, such as organic decay. As part of a study in Austin Texas, samples were taken from a dumpster and very high levels of acetaldehyde and methyl ethyl ketone were found.

10. Which microenvironments are the most important to consider when assessing gasoline-related health endpoints? What factors influence exposure to gasoline-related compounds in particular microenvironments? Which components are of greatest potential concern in particular microenvironments?

People spend a large amount of time in their own homes, making that environment of highest importance. Of particular interest are people who have attached garages. Emissions from the hot and cold soak engines as well as stored gasoline can make indoor levels much higher, at least for the compounds typically found in gasoline vapor. Also important are work and school, but very little data are available on those environments. Still those two microenvironments are the next in line of importance, because of the amount of time spent there and because the ambient air would be the dominant source of the compounds there. The third most important would be in-vehicle, particularly for long commuting times. The fourth most important would be activities that bring the receptor in close proximity to gasoline vapors, such as working on a car or mowing the lawn. There are data on straight emissions from these alternative type gasoline engines and personal exposure data. However, much of the personal exposure studies are integrated samples making it very hard to segregate out the contributors to exposure. One way to look more closely at this issue is to try to characterize the various microenvironments and then combine them to see how well the results match with integrated samples.

There is more evidence now from European studies in particular that nearness to a roadway is a major factor in exposure. Certain practices can also increase exposure. In cold climates, for example, people start their cars and let them run, which produces problems with CO and other gasoline emissions.

A study in Seattle was discussed. VOC concentrations measured at a service station were compared with the general ambient air. The concentrations behind the service station building were a factor of five higher than the general ambient air. Another microenvironment related to gasoline would be underground garages.

In terms of atmospheric transformation products, there will be reactions occurring indoors. The concentration of ozone indoors is about 50% of ozone outdoors, so alkenes will continue to react. OH radicals can be generated from ozone alkene reactions, allowing additional reactions to occur.

Colome and Wilson did a study of what people are exposed to in refueling their own vehicles. As part of the VOC TEAM study (Wallace) there was some analysis done of how important the garage is in terms of exposure to certain compounds.

Session 2: Assessing Health Impacts – Toxicology, Epidemiology, and Risk Assessment Methods

Ozone, NOx and Cancer

Hanspeter Witschi, University of California, Davis

Studies in the 80's and as early as the 50's suggested that ozone could produce lung cancer. Later papers suggested that ozone or NO_x might modify tumor development in animals exposed to other carcinogens. Out of this, the National Toxicology Program (NTP) and the Health Effects Institute collaborated on a major bioassay of ozone. Ozone had no effect in rats. The results were equivocal in male mice and some evidence in female mice. Witschi designed a further bioassay of ozone in female A/J mice using the same protocol as was applied for environmental tobacco smoke (ETS). This protocol had produced an increased lung tumor multiplicity in the A/J mice exposed to ETS, demonstrating the sensitivity of this animal model. Female mice were exposed to the same concentrations of ozone used by NTP. Some of the animals were exposed for the full nine months, some were exposed for five months with a four-month recovery period, and some were exposed to ozone for five months only. There appeared to be an increasing trend in lung tumor multiplicity for animals exposed for five months only, but this was not statistically significant. Mice exposed at the lowest dose for five months with the recovery period had an increased lung tumor multiplicity, but the two highest doses did not show significant increases. Mice exposed for the full nine months did not show statistically significant increases in lung tumor multiplicity.

As an interesting demonstration of the complexity of mixture exposure, mice exposed to ETS for nine months had less of an increased lung tumor multiplicity than mice exposed to ETS for five months and allowed to recover for four months. This result has been repeated. It's possible that cytotoxicity in the nine-month exposure group is affecting the tumor development.

Witschi indicated that there is some evidence that ozone may slow down the growth of lung tumors and that there is no evidence for tumor promotion by ozone.

Witschi highlighted the recommendations of the Presidential Commission on Risk Assessment related to complex mixtures. First, complex mixtures should be tested rather than the individual compounds, and second, in risk assessment of complex mixtures additivity of effects should be considered when agents have different mechanisms of toxicity or different targets. Mixtures are generally not worse than the sum of the individual components. Antagonisms are not generally considered, but may be important based on the results presented for ETS.

Witschi indicated that he does not believe that ozone is a carcinogen.

Question Period for Witschi

1. What are the data on the genotoxicity of ozone and ETS?

Witschi: We have never found any evidence of *in vivo* genotoxicity.

2. The data seem to indicate that ozone could be a weak carcinogen and the doses tested were not much different than the current regulatory standard.

Witschi: The protocol for the cancer testing was selected by NTP.

3. Is there any direct evidence that cigarette smoke is tumoricidal?

Witschi: I have a preliminary communication from a friend who has repeated these results. Also, I have exposed the mice to the carcinogens urethane and methylcholanthrene with ETS. With ETS, they have fewer tumors; when the smoke is taken away, they catch up.

4. Can you explain why an earlier study found tumor increases in A/J mice and you did not?

Witschi: Our study used the NTP protocol. The study by Hassett had problems. In one study he found more tumors and in another he did not. In addition, he used urethane pre-treatment.

5. Have the experiments that have been performed so far addressed the possibility of an early in life sensitivity to ozone?

The experiments have not been done for ozone.

The Effects of Complex Mixtures on the Lungs

Kent Pinkerton, University of California, Davis

ETS was used as an example of a complex mixture. ETS has more than 3,800 constituents in the gas, vapor and particulate phases. The components include metals and organics, including polyaromatics. ETS is known to contain carcinogens and free radicals.

The experimental set up allowed precise exposure to ETS. The total suspended particulate was used as one measure of exposure. Carbon monoxide and nicotine were also used.

There was a clear dose response for CYP 1A1 activity in rats, beginning at 0.3 mg/m^3 and continuing at higher levels of particulate matter. The study was also carried out in monkeys. Infant Rhesus monkeys were exposed to the same concentrations of sidestream

smoke as the rats. The monkeys had a 15-fold increase in the induction of the 1A1 isoform, whereas in the rats the highest induction was about three-fold. So for identical exposures, there are different responses from different species.

Lung resistance was also studied. Animals that were exposed to ETS for the first three weeks of life showed persistent increases in airway hyperactivity compared to controls at age eight weeks.

The next question was to ask why there was this persistent airway activity. A specific type of epithelial cell, called a neuroendocrine cell, was examined. These cells are rare cells that release peptides and increase airway narrowing. A massive increase in neuroendocrine cells was observed in animals exposed to ETS compared to controls. Another finding was that five weeks of exposure to ETS resulted in a significant alteration of C-fibers, which are important sensory fibers thought to be involved in regulating airway tone. So exposure to complex mixtures can result in all sorts of changes, particularly in the lung that is undergoing tremendous development in children.

Another study looked at the effects of exposure to ETS on response to other types of pollutants, in particular ozone. Animals were exposed to a high level of particulate (30 mg/m^3) for six hours per day over three days, followed by a single day of exposure to 0.5 ppm ozone. There were four groups total in the study: animals exposed to filtered air, to ETS alone, to ozone alone, and to ETS followed by ozone. The transitional region from the conducting airways to the gas exchange region was examined for evidence of cell proliferation. In animals exposed to ozone, or to ETS plus ozone, there was a marked increase in active DNA synthesis, based on the observation of increase BrdU labelling. The increase was greater for the animals exposed to ETS followed by ozone.

Other parameters were also examined. ETS exposure followed by exposure to ozone resulted in a significant increase in the amount of protein in the bronchoalveolar lavage fluid relative to controls and also relative to ozone exposure alone. This is suggestive of cell injury. The level of IL-6 released by alveolar macrophages was also studied, both spontaneous release and LPS (lipid polysaccharide) stimulated release. Animals exposed to ozone have reduced levels of IL-6; animals pre-exposed to ETS had even lower levels.

The final study discussed involved exposures to a mixture of soot and iron. Adult animals exposed to the soot/iron mixture showed a significant increase (25%) in glutathione-S-transferase (GST) in the lavage fluid relative to controls. In neonatal animals, the increase in GST was 300% above controls. GST is an enzyme that will become elevated if the lungs undergo oxidative stress. Animals exposed to the soot/iron combination also showed a significant decrease in ability to handle oxidant stress, which was even more marked in the lung tissue. In neonatal animals, the effect is magnified by five-fold relative to adults. The exposure to soot/iron also resulted in significant elevations in two of the cytochrome P450 isoforms (1A1 and 2E1), which was unexpected.

The parallels between ETS and gasoline emissions are numerous:

- Both are ubiquitous
- Both are present at low concentrations
- Both have potential for high, intermittent exposure
- ETS has long-term chronic effects, which are likely to be associated with gasoline emissions as well
- ETS is a carcinogen, and gasoline emissions have carcinogenic components

Complex mixtures, such as ETS can lead to many things including bioactivation and airway hyperactivity. Pre-exposure to a complex mixture such as ETS can potentiate the effects of other pollutants such as ozone. Particles with metals may be very important in producing oxidative stress and bioactivation of compounds within the lungs.

Question Period for Pinkerton

1. Have you looked at the effects of early exposure to primates who were born prematurely?

Pinkerton: The studies that we have done so far that have resulted in airway hyperactivity in young animals required the exposure to begin prior to the birth of the infant. Maternal exposure followed by post-natal exposure seem to be the critical windows of exposure to induce an asthmatic-like condition. With only in utero exposure, or only post-natal exposure, we do not see the development of an asthmatic like condition.

2. It is possible to deliver some animals prematurely and keep them on a ventilator. Have you done studies with that type of animal?

Pinkerton: No we have not done those. We have found that maternal exposure to environmental pollutants does not necessarily lead to premature births of the animals, and therefore the animals, we assume, are fully developed at birth. We have not looked at the premature lung and how it may be affected by direct exposure to inhaled pollutants.

3. Is the concentration of total suspended particulate (TSP) (1 mg/m^3) that you used like a smoky bar, or was that a lot higher than what you might see under normal circumstances?

That would be on the high side for ETS. One tenth of a milligram per cubic meter is very realistic. Someone who is actually smoking, however, can generate a cloud around himself or herself of about 2 mg/m^3, which is higher than what we used in our experiment. Thus, if a mother is smoking, a child may experience exposures very similar to the experimental exposures.

4. Have you done experiments at levels closer to environmental levels?

At lower levels, we still see effects, but the trend was not statistically significant.

5. Are there any plans to do studies on fuel combustion mixtures to try to identify changes to the lungs?

I am not aware of anyone doing studies like that. It would be interesting to do, since naphthalene is an important component of gasoline, and there are a number of studies that suggest that it is an important toxicant to the lungs.

Epidemiologic Studies of Air Pollution and Cancer: Distinguishing the Effect of Gasoline Emissions

Aaron Cohen, Health Effects Institute

Cohen focused on reviewing the body of evidence concerning the effects of air pollution in general on lung cancer, an additional body of evidence focused on mobile source air pollution and lung cancer, and then a small body of evidence concerning the effects of gasoline combustion products specifically.

The biggest challenge in studying air pollution and lung cancer is that everyone is exposed, making it very difficult to create a meaningful contrast that can be used to study differences in lung cancer risk. As Geoffrey Rose said, "the hardest cause to identify is one that is universally present." This is certainly the case for gasoline exhaust. Another major challenge is that gasoline exhaust has many of the same constituents as other mobile source emissions, such as diesel exhaust, such that possible surrogates of gasoline exhaust exposure may not be unique. Both diesel and gasoline, along with a range of other sources, contribute to $PM_{2.5}$, which is the metric that has been used to characterize exposure for the study of lung cancer risk in some well-known prospective cohort studies. In addition, if studies mis-specify the time-period during which exposure acts to cause disease, then they may not be able to accurately estimate the relationship between air pollution and lung cancer. In most cases they will underestimate any effect that may exist. We do not know the relevant time period for gasoline exhaust, nor indeed for most pollutants.

There is a large body of evidence that shows that urban air pollution is associated with lung cancer. Three recent prospective cohort studies have measured associations between air pollution and lung cancer – the Harvard Six Cities study, the American Cancer Society study and the Seventh Day Adventist study. In the Six Cities study, the measure of exposure to air pollution was $PM_{2.5}$. This study found a 40% increase in the risk of mortality from lung cancer. The other studies have shown some variation in the relative increases, but generally the increases have been about of that magnitude. The increases were found after controlling for most major risk factors, including cigarette smoke, occupation and prior health data. The studies have used various indices of exposure, including SO_4, O_3, $PM_{2.5}$, PM_{10}, NO_2 and SO_2, none of which are specific for gasoline or

even mobile sources in general. The same general results are seen for the case control studies conducted over the last 20 years.

Other evidence for the association between air pollution and lung cancer comes from biomarker studies that looked at the relationship between air pollution exposure and PAH DNA adducts. The results are consistent, but not specific to a particular source.

The Nyberg *et al.* population-based case control study from Sweden that is in press was discussed in some detail. The study is large with over one thousand lung cancer cases between 1950 and 1990 and controlled for all important risk factors in a very detailed way. They also tried to construct historical estimates of exposure to air pollution based on long-term records of NO_2, to characterize mobile sources, and SO_2, to characterize stationary sources. For the 30-year duration of exposure, the relative risk of traffic-related air pollution is about 1.3. When latency of 21 to 30 years is accounted for, the relative risk is 1.6. No associations were found for stationary sources, unlike other studies.

In terms of a specific association between gasoline exhaust and health effects, there have been some relevant studies. Studies of bridge and tunnel workers have been negative. A study of turnpike workers in Massachusetts found no association between pulmonary function and air pollution, predominately automobile exhaust. The International Agency for Research on Cancer (IARC) reviewed the available evidence in 1989. Two studies were discussed that were considered to involve predominant exposure to gasoline engine exhaust; these studies were inconclusive for lung cancer.

Recent studies include a large case-control study in Montreal and a study of the respiratory health of children in the Netherlands. The Montreal study looked at many occupational risk factors for a variety of cancers. The study included 900 lung cancer cases, which were classified according to occupational exposure to diesel exhaust and gasoline emissions. This study observes the same relative risks for diesel exhaust and lung cancer that have been observed in virtually every previous similar study. For gasoline, there was no significant increase.

There is a series of studies in the Netherlands looking at respiratory health in children. The study reported by Brunekreef *et al.* (1999) included 24 schools, located near freeways with varying traffic density, with health measurements taken in approximately 2500 children aged seven to twelve years old. The study measured indoor and outdoor $PM_{2.5}$, black smoke, NO_2, and benzene. EC, PAH and elements were analyzed in selected samples. The study found elevations of 1.5-2-fold in the prevalence of a variety of chronic respiratory symptoms associated with truck traffic. The results for cars showed slight increases for some symptoms, but nothing like the increases observed for trucks.

The major conclusions of the talk were:

- Urban air pollution is associated with an increased risk of lung cancer
- There is limited evidence that mobile source air pollution is associated with increased lung cancer risk in the general population
- Additional research is required to examine the contribution, if any, of gasoline exhaust

Question Period for Cohen

1. In the Nyberg study, how was the mobile source determined and classified?

Cohen: They had long-term history of NO_2 for periods of 30 years. They used geographical methods to map the concentrations to the residences. For a small period of the total exposure, they modeled the concentrations in the absence of measured data.

2. One reason that might explain the lower risk for gasoline exposure in an occupational setting is the great care taken to address carbon monoxide exposure, which is higher for cars. Diesel vehicles tend to be left running, because it is harder to start a diesel vehicle, and the CO concentrations are lower than those for cars.

Cohen: Part of it also has to do with classification of the occupation as "mostly exposed to gasoline" versus "mostly exposed to diesel. The occupations considered mostly exposed to gasoline included things like route drivers and delivery people, not people working in garages, who would be expected to have the most intense exposures.

3. Another obvious confounder is the residential exposure to gasoline, which you have no data on. This would not explain the difference between gasoline and diesel, but it may confound the gasoline results entirely. Those who are not exposed to gasoline at work may be exposed on the way to and from work and at home.

Cohen: Yes that could be an explanation, although you could say the same for diesel (response was that diesel exposures are somewhat more limited geographically).

4. What about the association of gasoline to cancers other than lung cancer?

There are reports for other cancers of associations with mobile source derived air pollution. The most consistent has been bladder cancer and diesel exhaust. However, there is some suggestion that methodological problems may have biased the results, which would explain the association. The situation is even less clear for other cancers.

Childhood Cancer and Traffic – An Ecological Study

Peggy Reynolds, California Department of Health Services

Reynolds began by reviewing the available literature on traffic and childhood cancer, which largely consists of case control studies originally designed to look at electromagnetic fields (EMF) and cancer. The case control study by Savitz found a significant association between traffic and cancer. Pearson and Associates reanalyzed the data using a more refined measure of traffic exposure and found a higher point estimate. A study in Sweden used nitrogen dioxide in outdoor air as a proxy for traffic, finding an elevated but not significant odds ratio. A study in Arizona, the only one that was not an EMF study, looked at leukemia and found no association with traffic. In an ecologic study, Knox and Gilman reported a case excess in proximity to motorways, but did not provide quantification. In a second ecologic study in Sweden, Norlinder reported an association between car density and higher rates of acute myelogenous leukemia (AML).

The approach taken in this study was to use the Geographic Tracking Information System technology to layer demographic profiles of population and health outcomes onto information related to streets and traffic data. The patterns of health effects rates by neighborhood were examined. A neighborhood was defined at the 1990 census block level, which contains an average of about one thousand people. There were 21,000 block groups in California in 1990. The study included all cancers diagnosed in California among children under the age of 15, from 1988-1994, which amounted to 7000 cancers. The analysis strategy was to look at rate ratios, by using Poisson regression to adjust for age, race, sex, socioeconomic status and urbanization.

It is not clear what to use as an indirect indicator of exposure when conducting an epidemiological study focused on traffic. Automobile hydrocarbon emissions for a 20-mile trip include contributions from the start, running, stop and diurnal phases. The running itself accounts for only 31% of the emissions under these conditions. Thus, vehicle density may be more relevant than traffic or street density.

This study selected three metrics as indirect measures of exposure: vehicle density, road density, and traffic density. There were a number of difficulties in assigning density values based on Caltrans data to the various block groups. A large effort went into looking for methods to address these difficulties. For vehicle density, as expected, there is higher ownership in the largest population centers. The other two metrics, road and traffic density, produced very similar maps.

The indirect measures of exposure were compared to 1990 data from the 20 California Air Resources Board monitoring sites on the annual median concentration of benzene and 1,3-butadiene. There was little or no relationship to measures of vehicle or road density, but some positive correlation with the traffic density measures.

The metrics were examined in terms of relationship to population characteristics: age group, race/ethnicity, and socioeconomic status. There does not appear to be differences

between age groups living in the block groups with the highest traffic density. For racial/ethnic groups, a disproportionately higher percentage of children of color live in the highest traffic density areas. There is also a dramatic relationship between a combined socioeconomic status (SES) score and high traffic areas, with people with the lowest SES most likely to live in the highest traffic density blocks.

Childhood cancer rate ratios were estimated for each exposure metric. There was little or no evidence for a risk relationship between childhood cancer and vehicle, road or traffic density.

There are a number of limitations to the study. First, it is an ecologic study, with all the attendant problems. Second, there are a number of sources of measurement error. There were no available data on residential history, nor data on other risk factors.

The advantages to the study are that it is population-based, large, demographically diverse, geographically diverse, and employed consistent ascertainment methods in characterizing both the exposure metrics and the outcomes of interest.

The major conclusions of the study were:

- Traffic metrics are not necessarily correlated with air monitoring data
- Traffic density is higher in more urban and lower SES neighborhoods
- High traffic neighborhoods do not have a pattern of higher childhood cancer rates

Question Period for Reynolds

1. What specific SES indicators did you control for?

Reynolds: In this particular analysis, we were controlling for median family income, but the various SES indicators look like they have a similar profile.

2. Did you analyze for specific cancers, such as leukemia?

Reynolds: Yes, we looked at all childhood leukemias and did not see anything different.

3. Did you look at a correlation analysis between traffic density and NO_2 and PM_{10}?

Gunier: We looked at carbon monoxide; the correlation coefficient was similar to those for benzene and 1,3-butadiene.

4. Which of the pollutants would you expect to be related to leukemia measures?

Reynolds: It's hard to say. Benzene comes to mind because that has been associated with adult leukemias. We know very little about causes of childhood leukemia.

5. Are you going to be able to do analysis based on individual data?

Reynolds: This was the ecologic study. We are following up with a case-control study where we will have some individual level data, such as maternal address at birth. We are also collaborating on a population based childhood leukemia study in the greater Bay Area and Central Valley where we will have individual risk factor information.

6. Did your regression analysis take account of the fact that both the occurrence rates and the various covariates are spatially correlated? One of the things that emerged from a reanalysis of the Six Cities Study was the importance of accounting for spatial autocorrelation.

Reynolds: We have not examined that formally in the data, but it did not make any difference in the analysis.

7. Hertz-Picciotto: We did a study in which we looked at low birth weight in relationship to proximity to carbon monoxide monitors. There was initially a strong relationship between the CO measurements and low birth weight, after adjusting for race. After accounting for individual data on SES, however, the association disappeared.

Reynolds: There has been no evidence for an association between SES and childhood cancer, but we will look at that.

8. In 1990, the air monitors were intentionally sited away from the source of pollution. So the fact that there was little or no correlation means that they sited them well. The minor correlation in one measure was probably just a reflection that the monitors were in areas with population.

Reynolds: Epidemiology is a blunt instrument. We wanted to do some sort of external validation. It was surprising to find any correlation in one of the measures.

Strategies for Risk Assessment of Carcinogenic Complex Mixtures

Irva Hertz-Picciotto, University of North Carolina

The standard regulatory procedure for estimating risk is to calculate the risks of individual constituents and add them up to get total risk of a mixture. The total risk for cigarette smoke is known, providing an opportunity to test whether adding the risks of the individual constituents produced a plausible estimate of the total risk. There are very good epidemiologic studies on the risk of lung and bladder cancer and leukemia for people who smoke versus people who don't smoke. Cigarette smoke contains some of the same compounds found in other agents such as air pollution. Compounds are present that cause mutations, induce enzymes, disrupt the endocrine system, cause chromosomal damage, cell proliferation, apoptosis and so on. In general, exposures associated with cigarette smoke are low compared to occupational settings or animal carcinogenesis

bioassays. So the additivity assumption will be tested for this mixture of low level exposures.

There have been many papers arguing that the cancer testing program undertaken in the U.S. leads to gross overestimation of risks at low exposures, because the doses are at the maximum tolerated dose (MTD) or half the MTD. The body's defense mechanisms may be totally overwhelmed at these doses, making the results not relevant at low doses. If this were the case, then when we add up the individual risks of the components of cigarette smoke we might expect to find risks that are five, ten, 30 or even 100-fold higher than the actual risks we see in smokers. We might find that only a few components are responsible for the overestimate, while other components result in more believable estimates. On the other hand, we might see that we have accounted for a lot of the carcinogenic components and then obtained a sum that was too small. In that scenario, it may be that major components are missing, or that we need to look at a nonadditive way to combine risks from multiple exposures in a mixture.

The first steps were to identify the carcinogenic components of cigarette smoke, determine the dose of each of those compounds in cigarette smoke, and identify or derive cancer potencies. This was done based on literature data. From this information, the predicted deaths were determined and summed up for all the individual components. The predicted deaths were compared with the attributable risks based on observed mortality from cigarette smoking.

The chemicals classified as Groups 1, 2A, and 2B by the International Agency for Research on Cancer (IARC) were considered carcinogens in this project. In terms of doses, the initial document used was an IARC monograph on carcinogens in cigarette smoke. Newer literature was used to update that information. Attempts were made to get mean or midpoint dose estimates for both mainstream and sidestream smoke. Preference was given to U.S. produced cigarettes. In a few cases, nothing at all was available.

The smoker was assumed to inhale 100% of the compound in the mainstream smoke, and 3.3% of the compound in the sidestream smoke. The risks were presented with and without the estimates from sidestream smoke, since there were so many compounds that did not have sidestream information available. A light smoker was defined as smoking 20 cigarettes per day from the age of 15 up to the age of 75, while a heavy smoker was defined as smoking 40 cigarettes per day. In determining potency, the preference was given to using human data if they were available. In the absence of human data, the most sensitive animal species was used. The same cancer site in humans and animals was selected if possible. The choice to focus on site specificity was the major deviation from regulatory policy, as the typical approach is to use the most sensitive site in animals. Potency in animals was derived using the multistage model, while potency based on human data was derived using linear relative risk models. PAHs were characterized as a group, using the benzo(a)pyrene potency as a surrogate.

The results of the analysis indicate that PAHs alone may be responsible for between 15 and 38% of the lung cancer deaths from cigarette smoke. The nitrosamines are a much smaller contributor, only around 3%. Vinyl chloride is negligible.

Turning to leukemia, based on a quadratic dose response curve, only about 0.07% of leukemia deaths would be due to benzene for a light smoker. This dose-response curve is not plausible, since there are not a large number of known leukemogens in cigarette smoke and benzene would therefore be expected to be responsible for a greater percentage of leukemia deaths. Based on a linear model, somewhere between 8 and 70% of the deaths would be due to benzene.

For bladder cancer, there were no data at all from human studies or from inhalation studies in animals, only ingestion studies. The aromatic amines are expected to be big players in cigarette smoke in terms of bladder cancer, along with arsenic. The results of the analysis suggest, however, that the aromatic amines contribute very little to the bladder cancer deaths. This leads to the question of why was there such a severe underestimation? There are at least three plausible explanations, possibly more. First, it may be that the assumption of additivity does not apply in this case. There may be some sort of potentiation with other particles, which may not themselves produce a bladder effect, but may result in a higher delivery of dose. Or there may be actual potentiation or synergism going on. Second, there may be underestimation of the individual risks. It may be that linearity is not conservative enough for the aromatic amines or that animals are not a good model for human carcinogenicity for those compounds. Third, there may be unidentified bladder carcinogens in cigarette smoke, which may be even more potent than the identified ones.

The major conclusions of this study are that under the assumption of additivity:

- A slight underestimation of lung cancer risks occurred; and
- A gross underestimation of bladder cancer risk occurred.

Question period for Hertz-Picciotto

Questions were deferred until the morning question period.

A Comparative Approach to Assessing Cancer Risk for Gasoline Exhaust Particles

Joellen Lewtas, U.S. Environmental Protection Agency

Dr. Lewtas discussed complex mixture risk assessment, with a specific focus on evaluating cancer risk associated with particulate matter. The research looked at comparative potency of various mixtures. Certain combustion related mixtures had good epidemiologic data and an estimate of human cancer potency. For example, coke oven emissions, cigarette smoke and coal tar related exposures had all been studied as to lung cancer risk. These mixtures were collected, the particles extracted, the extractable organic mass measured, human exposure simulated, and in vitro and animal cancer bioassays carried out. The purpose of this was to determine whether the relative potency hypothesis held up; that is, that there is a constant relative potency across bioassay systems (*e.g.*, human and rodent) such that:

$$\left(\frac{\text{Human potency carcinogen}_1}{\text{Human potency carcinogen}_2}\right) = k \times \left(\frac{\text{Bioassay potency carcinogen}_1}{\text{Bioassay potency carcinogen}_2}\right)$$

The bioassays were compared to one another and then to the human risk estimates. For this talk, the results from the mouse skin tumor assay were discussed. Most of the studies conducted were initiation/promotion, but there were also some complete carcinogenesis studies conducted. Fives doses were used with 40 male and 40 female Sencar mice. Papillomas per mouse were scored. There was also a mouse skin tumor study of three types of exposure in China, where an epidemiologic cancer study was conducted simultaneously, in order to provide more data for validation purposes. There are numerous publications describing the results.

A plot of the mouse skin tumor initiation potency against the human lung cancer risk was constructed initially for cigarette smoke, roofing tar emissions and coke oven emissions. There was a high correlation between these two measures. Later, points for diesel exhaust and smoky coal from China were added, and those fell along the same correlation line. The points tended to be clustered together, with the exception of cigarette smoke, so additional points would be useful in that region. Correlations between human lung cancer risk and other measures, such as the Ames assay, were also examined. The best correlation was for the mouse skin tumor assay. For other mixtures, then, it is possible to run the mouse skin tumor assay, and use the correlation to obtain an estimate of the human lung cancer risk. This extrapolation was done for woodstove emissions and gasoline automobile exhaust. The estimated human cancer risk for gasoline engine exhaust was somewhat lower than that for diesel exhaust.

Work has also been published on the chemistry of the emissions and the relationship between the PAHs in the mixtures and the tumor potency of the mixtures.

Additional work was presented on the formation of DNA adducts for these mixtures. In general, those complex mixtures that are very potent in the tumor assays tend to be more potent in forming DNA adducts. However, all of these mixtures are genotoxic

carcinogens, which act by a mechanism involving DNA adducts. This relationship would not necessarily hold up for other constituents of gasoline.

Morning Question Period

1. Do you have thoughts on how tumor promoters would factor into the comparative potency model?

Lewtas: The promoters and initiators are present together in particle bound mixtures. In doing a complete carcinogenesis assay, like the newborn mouse assay, it accounts for initiation and promotion. The results for the complete carcinogenesis assay agreed well with the tumor initiation assay, which suggests that for these mixtures, the initiators are driving the relative potency.

Hertz-Picciotto: An important consideration is timing of exposure. If both the initiator and promoter will be present for a long period of time, then you are interested in the total impact of initiation and promotion. With any mixture, there are multiple initiators and promoters, so the question is how useful is it to keep breaking things down into the components rather than look at the mixture as a whole. The project I presented was necessary to do, because testing is done on a one-by-one basis. However, we should really be thinking of combined exposures. The experimental situation should be modeled more like human exposures, with all the confounders present in a controlled way. This would be very expensive, but the data would be more useful for extrapolating to humans.

Cohen: This has been done for PM in animal models designed to reflect the most sensitive groups.

Lewtas: Risk assessment has so many assumptions that the more approaches we take the better.

Witschi: In 1972, an experiment was done in which mice were exposed to cigarette smoke and then filtered cigarette smoke. The observed tumorigenicity was the same. So with essentially no particles, the results were the same.

3. The potential for antagonism should not be overlooked. For example, cadmium is carcinogenic, but if the animal is exposed to nickel at the same time, the two are antagonistic instead of additive.

4. Could you comment on the use of DNA and protein adducts as biomarkers?

Lewtas: Based on studies done to date, the protein adducts have not been sensitive enough. They have a much longer half-life, but there is no observable difference in adduct levels between very high occupational exposures versus environmental exposures. It might be possible to observe differences with more sensitive protein adducts. In the DNA adduct studies done for ambient air, the DNA adduct levels seem to correlate well

with particle exposures. DNA adducts are a short-lived exposure measure, and don't accumulate dose over the whole exposure period.

Session 2 Panel Questions and Discussion

1. Referring to the preliminary list of chemicals, do you have other suggestions of potentially carcinogenic compounds or compounds that may cause chronic respiratory health effects that should be included in this phase of the project? Are there other compounds that may be suspected toxicants that should be monitored for future consideration?

The panel emphasized the importance of looking at exposure to sources and mixtures, as opposed to individual chemicals. For example, it would be useful to look at natural gas burning vehicles as a source in order to compare the merits of those vehicles to diesel vehicles in public transportation.

2. Can the toxicity of gasoline PM be attributed to specific compounds? What is your opinion on the possibility that there are additional unidentified chemical species in the particulate phase that may be important toxicologically? What size fraction of gasoline PM contains the toxicologically important compounds?

One size category that may be most relevant would be ultrafine particles, those that are less than 1 micron in diameter. These particles are also still important when they coalesce into larger particles, not only because that actually can make them more respirable, more likely to be deposited out of the air stream, but also because they have a significant surface area. Ultrafine particles have a tremendous surface area per volume ratio. They can serve as an important vehicle for carrying other toxicants into the lung.

3. What other health endpoints should be included in future phases of the research, either in a chemical-by-chemical assessment, or for evaluating by group of compounds (*e.g.*, neurotoxicants)?

There is a whole range of effects that have biologic plausibility: overall mortality, respiratory disease, cardiovascular disease, SIDS, asthma, ear infections, low birth weight.

4. What is known about the potential for toxicological interaction between gasoline-related compounds at relevant exposure levels?

In most cases the toxicity of the mixture is related to the toxicity of its most abundant compounds. More often than not, things will be additive. There are very few examples, but they do exist, where something in a mixture can counteract the effects of other agents.

There are probably some antagonisms among compounds in gasoline and ambient air pollution. The project on cigarette smoke suggested that whatever the antagonisms are they seem to be outweighed by some synergisms. In fact the most abundant compounds

certainly did NOT account for the majority of lung and bladder cancers or leukemias in smokers. Before the study, it was thought that overestimation of risk would occur, that there would be antagonisms going on, but they did not show up statistically in the overall picture.

In a study at U.C. Davis of ETS, even at high levels, there were no effects at the morphologic cellular level in mouse lung. But with subsequent exposure to ozone, there was a potentiation of the effects of ozone. Data in the literature indicates that the interactions between hydrocarbons and benzene occurred only at very high levels. There probably isn't interaction occurring at the levels occurring in ambient air.

5. Are there noncarcinogenic compounds/particles associated with gasoline that could potentiate the effects of the carcinogenic components?

The panel members were not aware of specific compounds. A potential problem can occur if a compound leads to chronic or persistent irritation especially to the epithelial lining of the airways or in the gas exchange regions, which leads to cell turnover or constant inflammation, and may then lead to enhanced carcinogenesis.

6. What lessons learned from carrying out risk assessments of other complex mixtures (*e.g.*, cigarette smoke, air pollution in general) can be applied to the current assessment of gasoline-related exposures?

The lesson from the smoking example is that we cannot fully account for the effects of cigarette smoking on cancer risk simply by looking at the individual constituents. It's a very tough question, how to deal with mixtures. It is not necessarily fruitful to look at the individual components. Epidemiologic studies of the whole mixture may really be the best way to look at this, particularly for short induction time outcomes, assuming they can be done and done well.

It is important to pay attention to social class, which is clearly a modifier of the effect of air pollution on total mortality.

Children should be studied further. During our early years, the lungs are undergoing tremendous changes. Children really represent a different population. The studies of children and their vicinity to freeways currently underway in California should be very enlightening.

7. The toxicological database for the majority of gasoline-related compounds is sparse. What should be done to evaluate these compounds in the absence of data?

The panel suggested applying a probabilistic approach using Crystal Ball. The panel also noted that for some of the constituents in gasoline fairly sophisticated structure activity relationships are available.

8. Population exposure estimates based on annual average ambient air concentrations traditionally assume 24-hour outdoor exposure at the place of residence. For a risk assessment of gasoline-related compounds, what other approaches to assessing exposure should be considered (e.g., consideration of exposures while commuting)?

The panel highlighted commuting exposures, noting that exposure in private cars to much higher concentrations than what is measured in the ambient freeway air can be one of the bigger risk factors.

9. How can the results of studies of exposures and health effects associated with traffic in general be interpreted in terms of the relative contribution from gasoline-powered vehicles?

Some studies do not have sufficient information to make that distinction. The studies in the Netherlands and California were mentioned as some that could distinguish between the effects of light-duty versus heavy-duty emissions. The California study discussed by Reynolds used different street types as indicators for different types of traffic, but so far large differences have not been detected. Further study was recommended.

10. Which is likely to be more significant for public health in California: chronic health impacts associated with gasoline-related exposures or acute health impacts?

This depends on the definition of acute. Daily mortality is acute, but there has been an attempt by Joel Schwartz to tease out the day-to-day effects versus time periods where you have some averaging of effects over time. Defining what is acute and what is chronic is not entirely easy to do. You may call respiratory infections an acute response, but they might be affecting people who are chronically undernourished or with weakened immune systems. In this case, chronic effects are contributing to the impact of acute exposures.

Is an acute repeated exposure different than a chronic exposure? If you are exposed to carbon monoxide every day and you have a certain level of carboxyhemoglobin, that will produce impacts over the long term.

What is it that defines a chronic exposure? Is it the repeated acute relatively high concentrations, is it the low to moderate levels, or is it a combination of the two. It depends on the outcome of interest. We also should expand our view of the outcome issue, as some of the subclinical changes may have important long-term effects. As our ability to measure some of these relevant biomarkers improves we have the opportunity to expand our perspective on outcome.

11. Which sensitive sub-populations should be considered in an assessment of gasoline-related exposures (e.g., asthmatics)?

The panel agreed that children are an important subpopulation. Other subpopulations of potential concern noted by the panel included fetuses, individuals with lower

socioeconomic status, the elderly, individuals who are heavily medicated, and individuals with cardiovascular disease.

12. Are there any chemicals that are currently regulated as acute toxicants (e.g., ozone) that should be considered in a risk assessment of chronic effects of gasoline-related compounds?

Ozone is a good example. There are several studies that suggest potential long-term effects on the development of lungs from chronic ozone exposure. This also has relevance to cancer. Decline in lung function and diagnosis of chronic respiratory disease is associated with increased mortality overall and also with increased incidence of lung cancer and mortality from lung cancer.

Nitrogen dioxide and NO_x are also important, based on results from the children's health study in Southern California, which has followed 5000 children over 8 years. In the first four years, the lung function was significantly lower in those children most exposed to NO_x, and NO_2 specifically, and PM secondarily. Nitrogen dioxide is showing a stronger effect than that of ozone.

PM can have both acute and chronic effects, so it can't be placed in one bin over another.

Other Discussion Questions/Issues Raised by the Audience or Panel

1. How do you do a risk assessment to address cars driving along a road next to a new project or the added cars that the project would bring? For example, suppose a school is being built and it's possible to build it away from the road but it costs more to do so. How do you figure out the benefit in terms of risk reduction? Could the diesel cancer potency be applied to the concentration of elemental carbon?

Some of the options available for assessing diesel are not available for gasoline, and even for diesel the assessment was controversial. There are no epidemiologic studies that could provide estimates for gasoline PM. In terms of using the diesel potency in combination with the elemental carbon, that is a possible option but would be controversial. The panel noted that there are other important health effects for particulates besides cancer. There are solid data regarding daily mortality and acute morbidity, both quantitative and qualitative. The panel emphasized again the importance of looking at children's health, including asthma.

2. Could the panel comment on applicability of older studies to understanding the situation in California?

A panel member discussed some of the relevant issues. Some things have changed and some things are the same. Given the fact that we do not know which of those things is important, it's hard to say that you shouldn't use the information that is available. One example from Europe illustrates this to some degree. A city in Eastern Germany had extensive data going back to the mid 80's. Post reunification there were profound

changes in the nature of air pollution and individual diseases. It went from industrial pollution to more Western style mobile pollution. So the air pollution patterns changed significantly. Yet one could still measure the relative increases in daily mortality associated with indices of particulate air pollution under both conditions….Don't want to imply that we shouldn't do research as air pollution and fuel change. We ought to look at health effects that have short induction times, so you don't have to wait long to see an effect. If we wanted to see the effect on cancer of changing fuels now, we would have to wait a long time. Effects on exacerbation of asthma, hospital emissions or daily mortality would show up more quickly. This argues that it is very important to have in place approaches for studying how those sentinel events might change in response to technological innovation.

3. Metals in gasoline

Most concentrations of metals are low. Some metal may come from the catalytic converter. The use of fuel borne catalysts to reduce emissions has been discussed for diesel but not gasoline (though an early proposal to use manganese was scrapped).

Very little trace element information is available in the speciation data for gasoline and diesel. About 95% of directly emitted PM is carbonaceous, with the remainder being trace amounts of other things. One metal that shows up is iron, probably from the engine and possibly from lube oil.

Metal additives are strictly regulated and it would be very difficult to add anything to gasoline that is not made from carbon, hydrogen or nitrogen.

4. Does the panel know of any exposure data regarding alkylates or whether there are any substitutes for alkylates?

Isooctane is a typical example of an alkylate, which is a wide range of C7-C9 highly branched paraphenic or alkane molecules. Increases in that type of compound in fuel have been observed between 1995 and 1996. This would be expected to be reflected in ambient air.

In comparison to alkanes with the same carbon number and same size, alkylates are less reactive and remain in the atmosphere for longer. Isooctane is about 2.5-3 times less reactive than octane. The reaction products should be similar to alkanes, but the branching will likely make the reaction scheme more complex and the final list of reaction products are not known. Only one study is available for isooctane and that has not yet been published.

5. How well characterized are emissions during the cold start period?

There is a tremendous range in cold start emissions for different vehicles. High emitters will have higher cold start emissions. There is also actually a correlation between average emission rates and income. In normal well-maintained vehicles under driving

conditions similar to the Federal Test Procedure (FTP) conditions, almost all of the PM comes out in cold start.

6. Air pollution is a nuisance. Eye irritation, odors, and limited visibility do impact the quality of life. These issues are high on the public's radar screen. We also do not pay enough attention to impacts on plants. If the air pollution increases at the same rate in the Central Valley, California is predicted to lose 20-25% of its crops.