HEI
May 1999

Program Summary

Research on Air Toxics

REGULATORY BACKGROUND

Hazardous air pollutants, commonly referred to as "air toxics," are a large group of toxic and potentially toxic compounds emitted from a wide variety of mobile, stationary, and area sources. In the United States, air toxics are not regulated under the National Ambient Air Quality Standards, but are subject to regulations as specified in the Clean Air Act Amendments of 1990 (U.S. Congress 1991). Section 112 of the Clean Air Act lists 188 pollutants[1] or chemical groups as "air pollutants of a hazardous or toxic nature." A hazardous air pollutant is defined as a compound or group of compounds "to which no ambient air standard is applicable and that . . . causes, or contributes to, air pollution which may reasonably be anticipated to result in an increase in mortality or an increase in serious, irreversible, or incapacitating reversible, illness."

Section 112 requires that the U.S. Environmental Protection Agency (EPA) develop a national strategy to control emissions of hazardous air pollutants from urban sources. The strategy must identify at least 30 hazardous air pollutants that account for 90% of the aggregate emissions from area sources, and regulate their emission.

In addition, the Act requires a strategy for substantially reducing the public health risk posed by exposure to hazardous air toxics from all stationary sources, including a 75% reduction in cancer risk attributed to these toxic air pollutants. The focus on cancer as an adverse health endpoint is due to the low exposure concentrations of these air toxics; the EPA's default assumption is that there is no threshold level in the dose-response relation for cancer effects (U.S. Environmental Protection Agency 1986, 1996). Other effects may also be of concern.

Of the 188 hazardous air pollutants, 5 are also listed in Sections 202 and 211 of the Clean Air Act as mobile-source toxic air pollutants; these are defined as the aggregate emissions of acetaldehyde, benzene, 1,3-butadiene, formaldehyde, and polycyclic organic matter (POM), a class of chemicals that includes polycyclic aromatic hydrocarbons. Mobile-source air toxics may account for 21% to 42% of urban air toxics (U.S. Environmental Protection Agency 1998a,b). Section 202 calls for the EPA Administrator to promulgate and, from time to time, revise regulations to control hazardous air pollutants from motor vehicles. At a minimum, the regulations must apply to benzene and formaldehyde. Section 211 of the Clean Air Act requires reductions in emissions of ozone-forming volatile organic compounds and toxic air pollutants.

In response to a set of lawsuits filed in 1995 and 1996 by the Sierra Club, the EPA combined several regulatory efforts that are required by the Clean Air Act concerning air toxics into an Integrated Urban Air Toxics Strategy. The Strategy, released in draft form in August 1998 with a final Strategy due in June 1999, addresses toxic emissions from all outdoor sources, including stationary, area, and mobile sources. Under this strategy, a final rulemaking on mobile-source standards will be issued in 2000, and new area-source standards will be in effect by 2009. The draft Integrated Urban Air Toxics Strategy includes a list of 33 high-priority hazardous air pollutants, including acetaldehyde, acrolein, benzene, 1,3-butadiene, formaldehyde, and POM (see Table 1).

Within the European Union (EU), the Air Quality Framework Directive provides guidelines for future European legislation on air quality. Ambient air quality limit values are being considered for various air toxics. For example, a limit value of 5 $\mu g/m^3$, averaged over the calendar year, has been proposed for benzene. Air toxics are also regulated through the Existing Substances Regulations. All chemical substances placed on the European market must appear in either of the two European inventories: the European Inventory of Existing Commercial Chemical Substances or the European List of Notified (New) Chemicals. Several air toxics have been examined as part of these regulations. For example, the United Kingdom Health and Safety

[1] Section 112(b) originally listed 189 hazardous air pollutants; caprolactam was subsequently removed from this classification.

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Executive, acting as the rapporteur for the rest of the EU, has evaluated human health risks of 1,3-butadiene. They concluded that, although uncertainties still exist about risk, concern is valid, and exposure should be controlled to the lowest practical level. Butadiene is currently classified as a Category 2 carcinogen (a substance that should be regarded as if it is carcinogenic to humans)

In addition, the International Agency for Research on Cancer (IARC), under the World Health Organization, periodically evaluates chemicals for their carcinogenic potential to humans. Several air toxics have been evaluated by IARC working groups (see Table 1).

THE HEI STRATEGY FOR AIR TOXICS RESEARCH

The overall goal of HEI's air toxics research program is to provide information that will reduce uncertainties in evaluating the human health risks associated with exposure to mobile-source air toxics. The assessment of human risk from ambient exposure to a pollutant often relies heavily on data from studies of animals exposed to high concentrations of the pollutant. Regulators must therefore extrapolate (1) from high-level exposures to the lower-level exposures usually present under real-world conditions, and (2) from animal species exposed under controlled experimental conditions to people.

Certain information greatly aids accurate extrapolation across species or exposure levels (see Figure 1), including the exposure level (the concentration of each pollutant a person or animal is exposed to in different microenvironments and the time spent in these microenvironments); the internal dose (the amount of pollutant or its metabolites that is present in the body after exposure); the biologically effective dose (the amount of pollutant or key metabolites that reaches important target sites in the body); the molecular effects (e.g., changes to the structure or function of molecules); and other biological responses potentially associated with the development of clinical disease, such as cancer (formation of some specific DNA adducts, mutations, and chromosomal aberrations). Understanding the relationships among exposure levels, doses, and physiologic effects and responses for various species would improve researchers' ability to determine (1) which species are most similar to humans in their sensitivity to a particular pollutant, and (2) the relationship between exposure level and effects over a wide range of pollutant concentrations. Identifying and documenting these relationships would enable more cost-effective strategies for better controlling exposure and protecting public health.

One tool that can provide information applicable to extrapolation is a biomarker, a biological indicator that can be measured in breath, blood, urine, or tissue. Biomarkers can indicate levels of exposure, dose received in the body or at critical target sites, metabolic pathways for different chemicals, molecular events caused by chemicals or their metabolites, biological effects defined as health endpoints of interest, or indicators of susceptibility to disease. Biomarkers can function as normalizing elements among species or

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Table 1. Regulatory Status of Air Toxics Targeted by HEI's Research Program

	EPA List of Air Toxics					
Chemical	High-Priority Hazardous Air Pollutant	Emitted from Mobile Sources	Carcinogen Classification[a]	IARC Carcinogen Classification[b]	NTP Carcinogen Classification[c]	CARB Air Toxics Classification[d]
Acetaldehyde	Yes	Yes	B2	2B	Reasonably anticipated	IIa
Acrolein	Yes		C			IIa
Benzene	Yes	Yes	A	1	Known	IIa
1,3-Butadiene	Yes	Yes	B2	2A	Reasonably anticipated	IIa
Crotonaldehyde						
Formaldehyde	Yes	Yes	B1	2A	Reasonably anticipated	IIa
Glyoxal						
Methylglyoxal					Reasonably anticipated	IIa/IIIa
POM	Yes	Yes				

[a] EPA: A = human carcinogen (sufficient evidence in humans); B1 = probable human carcinogen (sufficient animal and limited human evidence); B2 = probable human carcinogen (sufficient animal and no human evidence); C = possible human carcinogen (limited animal and no human evidence). (Adapted from U.S. Environmental Protection Agency 1986.)

[b] IARC: 1 = human carcinogen; 2A = probably carcinogenic to humans; 2B = possibly carcinogenic to humans. (Adapted from International Agency for Research on Cancer 1996.)

[c] NTP = National Toxicology Program (U.S.): "Reasonably anticipated" or "known" to be carcinogenic.

[d] CARB = California Air Resources Board: IIa = Toxic Air Contaminant emitted in CA, with one or more health values approved or under development to be reviewed by the Scientific Review Panel; IIIa = Toxic Air Contaminant emitted in CA and nominated for development of health values. (Adapted from California Air Resources Board 1998.)

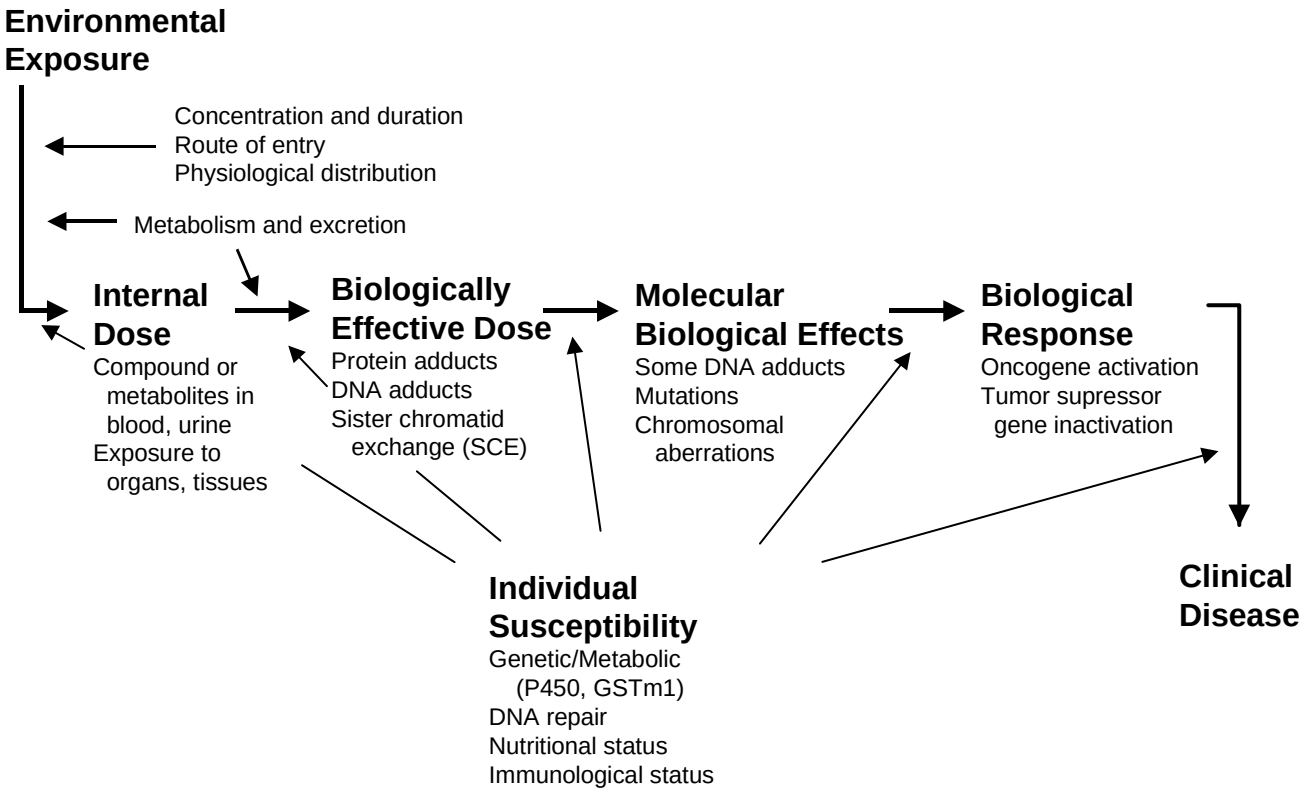

Figure 1. Information useful for extrapolating across species or exposures.

among levels of exposure. For example, a relevant biomarker along the causal pathway of cancer can be compared in rats and mice exposed to different concentrations of a chemical. If this biomarker is also found and validated in occupationally exposed people, it may help us understand the relationship between exposure level and cancer risk in people. In order to study biomarkers feasibly, they must be easily obtained from humans through noninvasive methods and at relatively low expense.

OVERVIEW OF HEI'S AIR TOXICS RESEARCH PROGRAM

Research needs for air toxics were identified at a December 1992 planning workshop organized by HEI with broad participation from individuals in industry, regulatory agencies, and academia. The core of the workshop was five groups of experts who discussed aldehydes, benzene, 1,3-butadiene, POM, and methanol. Recommendations about research needs were published in *Research Priorities for Mobile Air Toxics* (Health Effects Institute 1993b).

Since the 1992 workshop, HEI has funded a number of studies on air toxics (Table 2). The HEI benzene and 1,3-butadiene research programs were established as a result of a Request for Applications (RFA 93-1, *Novel Approaches to Extrapolation of Health Effects for Mobile Source Toxic Air Pollutants*) issued in 1993, and an additional study added in 1994 from HEI's preliminary application process. The RFA targeted issues of both high- to low-dose and cross-species extrapolations. Many of these studies, which have been completed, developed biomarkers for exposure or dose in animals that would eventually be used in human studies.

In an effort to validate in human populations the biomarkers developed in some of the animal studies of benzene and butadiene, HEI issued a Request for Qualifications (RFQ 95-3, *Transitional Epidemiology Studies for Benzene or 1,3-Butadiene Biomarkers*) in late 1995, seeking researchers with access to human populations exposed to benzene or butadiene. HEI invited these researchers to workshops in January 1996, where they met with the researchers who were developing biomarkers under HEI funding. The laboratory investigators described the biomarkers they were developing, and the RFQ respondents described their

Table 2. HEI Air Toxics Studies

Chemical	Recently Completed (Under Review)	Ongoing
Aldehydes	0	4
Benzene	3	2
1,3-Butadiene	5	1
POM	1	1

populations, previous exposure measurements, and exposure-monitoring capabilities. During the workshops the participants began to discuss possible collaborations, and, in the spring of 1996, several groups submitted applications to HEI for collaborative studies to validate the biomarkers in human populations. After scientific review of the applications, two transitional epidemiology studies—led by Drs. Richard Albertini and Qingshan Qu—were selected and are now under way.

HEI has also funded two studies through its preliminary application process that are identifying and characterizing POM of two types: that associated with air particulates, and that modified through atmospheric transformation. These studies are using advanced instrumentation to identify chemicals, and are examining biological endpoints in human cells.

In September 1997, HEI expanded its air toxics research program to include aldehydes with RFA 97-2, *Assessing Personal Exposure to Selected Aldehydes Using Chemical and Biological Techniques*. To evaluate risks to people, more information is needed on exposure to aldehydes, and biomarkers are needed to monitor exposure, dose, or effects in people. The RFA targeted six aldehydes as potentially important toxicologically and representative of aldehydes present in the atmosphere: formaldehyde, acetaldehyde, acrolein, crotonaldehyde, glyoxal, and methylglyoxal.

HEI Benzene Research

Concerns about benzene toxicity come primarily from occupational epidemiologic studies showing that exposure to benzene leads to increased risk of two diseases: aplastic anemia and acute myelogenous leukemia. Aplastic anemia is a form of blood cell toxicity characterized by decreases in the numbers of circulating red and white blood cells and platelets, accompanied by almost complete replacement of many bone marrow cell types with fat and scar tissue. Acute myelogenous leukemia is a form of the progressive, neoplastic disease characterized by anemia, fatigue, weight loss, easy bruising, and deficiency of blood platelets and white blood cells. Assessing risk from benzene exposure for the general population requires extrapolating from the occupational exposures, which range from 2 to 100 parts per million (ppm) of benzene, to typical ambient exposures, which range from < 1 to 3 parts per billion (ppb).

Three areas of uncertainty limit our understanding of benzene-induced leukemia and other possible health effects and thereby limit our ability to assess risk from ambient exposures. First, information about the development of aplastic anemia and the mechanism of leukemogenesis in human populations is incomplete. For example, is aplastic anemia a necessary step in the evolution of leukemia? Benzene research has identified that a threshold exposure level must be reached for benzene to induce aplastic anemia. If aplastic anemia is a necessary stage in the development of leukemia, then leukemia may be seen to have a threshold level of benzene exposure as well.

The second area of uncertainty surrounds the cellular mechanisms of benzene-induced leukemia, especially those steps required in the early stages. At this time, no suitable animal model for benzene-induced leukemia is known, although benzene does produce other types of tumors in mice and rats and has been shown to be toxic to mouse bone marrow (Smith 1996).

The third area of incomplete information is which benzene metabolites are involved in blood stem cell toxicity. Benzene metabolism is complex (Figure 2), and different levels of exposure appear to produce different patterns of metabolites.

HEI's benzene research program has addressed uncertainties associated with the effects of low levels of exposure by focusing on the following general goals:

- Develop sensitive methods to measure metabolites from low-level exposure to benzene;
- Identify markers of exposure, uptake, and metabolism, and validate these markers in an exposed human population;
- Develop exposure-dose-response information on biomarkers so as to evaluate the relationships between exposure levels and levels of metabolites, and between metabolite levels and genetic changes, both within and across species; and
- Make progress toward elucidating the mechanism of benzene toxicity.

This research program was initiated with four studies that investigated the metabolism of benzene after exposure to low concentrations, and developed and evaluated biomarkers of exposure, uptake, metabolism, and effect. Short summaries of these studies, most of which have been completed, can be found in the earlier HEI Program Summary "Research on Benzene and 1,3-Butadiene" (Health Effects Institute 1995b), and in the abstracts presented at HEI's Fourteenth and Fifteenth Annual Conferences (Health Effects Institute 1998, 1999).

The Validation of Biomarkers in Humans Exposed to Benzene

Qingshan Qu, New York University Medical Center, New York, NY

HEI is funding a transitional epidemiologic study, under the direction of Dr. Qingshan Qu, in collaboration with Dr. Guilan Li and others from the National Institute of Occupational Medicine in China. The goal of this study is to validate in an exposed human population several biomarkers for exposure and effects of benzene, which were developed in studies funded from RFA 93-1 (See Table 3).

The first phase of this study involved (1) assessing whether the biomarkers could reliably discriminate between subjects with high-level exposure and unexposed subjects; (2) analyzing the replicability and inter- and intraindividual variability of the biomarkers;

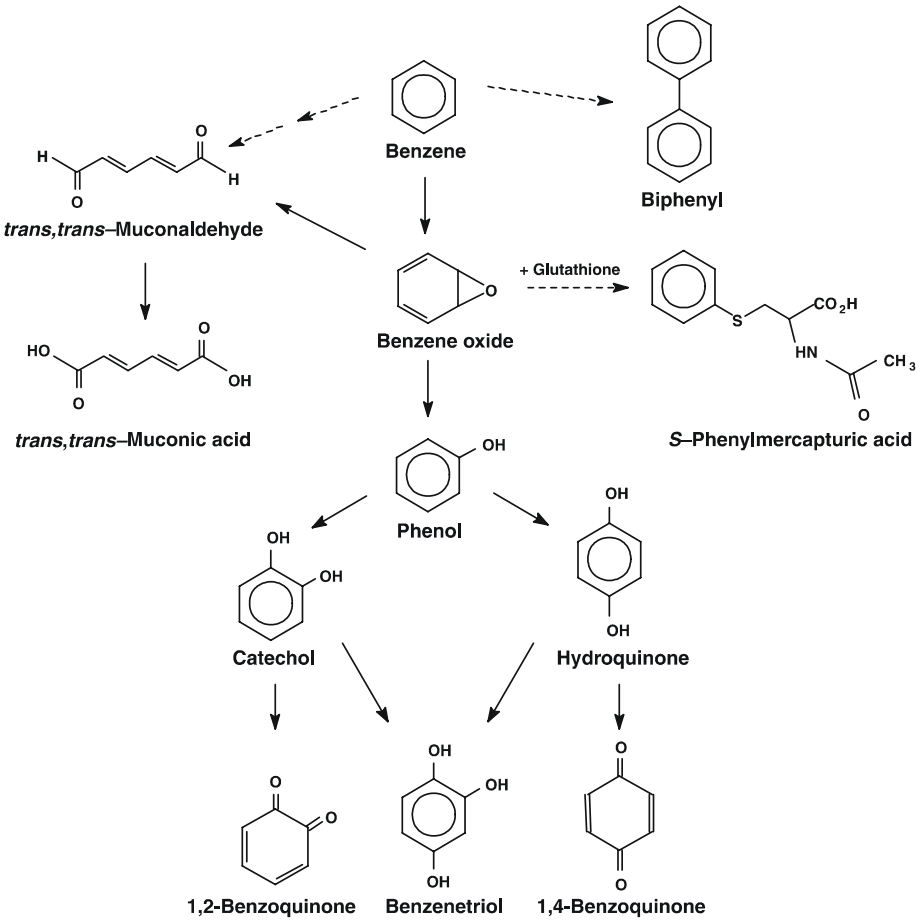

Figure 2. Pathways of benzene metabolism.

and (3) studying the half-lives of biomarkers. This phase examined occupationally exposed subjects in two facilities in Tienjing Province, China, who were selected from a larger cohort of benzene-exposed workers originally identified by the Chinese National Institute of Occupational Medicine. The facilities (a glue factory and a shoe factory) had a suitable range of benzene exposures, ranging from 10 ppm to approximately 140 ppm benzene (mean exposure of 36 ppm). Air concentrations of toluene and xylene were also measured. Control subjects were selected from other industrial facilities in Tienjing Province. Investigators found that several benzene metabolites in the urine, including *S*-phenyl mercapturic acid and *trans,trans*-muconic acid, were higher in exposed workers than in control subjects. These results will be correlated with information regarding blood cell levels.

The ongoing second phase of this study is assessing a dose-response relation for promising biomarkers. Subjects participating in this phase have been exposed to a range of benzene concentrations, including low

Table 3. Biomarkers Being Evaluated in Dr. Qu's Study

Biomarker	Investigator and Institution
Exposure and Dose	
Benzene metabolites in urine Hydroquinone Phenol *S*-Phenyl mercapturic acid 1,2,4-Trihydroxybenzene	Asseih Melikian, American Health Foundation; and Qingshan Qu, New York University Medical Center
Benzene protein adduct in blood *S*-Phenyl cysteine albumin adduct	Stephen Rappaport, University of North Carolina
Effect	
Chromosome aberrations Fluorescent in situ hybridization (FISH) Conventional analysis	David Eastmond, University of California, Riverside

(< 1 ppm), moderate (1.1 to 5 ppm), high (5.1 to 15 ppm), and very high (> 15 ppm).

HEI Butadiene Research

High concentrations of 1,3-butadiene are required before acute toxicity is observed in people or laboratory animals. Until the 1980s, butadiene was considered to be relatively nontoxic, as reflected in permissible occupational exposure limits of 1,000 ppm as an eight-hour time-weighted average. This standard was based on irritation of mucous membranes and narcosis at high levels of exposure (Occupational Safety and Health Administration 1996). However, concern regarding butadiene heightened in the 1980s when laboratory animal studies showed that inhalation of 1,000 ppm butadiene produced tumors in multiple organs in male and female Sprague-Dawley rats (International Institute of Synthetic Rubber Producers 1981). Furthermore, $B6C3F_1$ mice were shown to be much more sensitive than rats; tumors were produced at multiple organ sites at 625 ppm butadiene, the lowest concentration tested (National Toxicology Program 1984). In a follow-up study, inhaled butadiene caused tumor development in mice at very low exposure levels, with lung tumors being produced at concentrations as low as 6.25 ppm butadiene, and hemangiosarcomas of the heart at concentrations as low as 20 ppm. Tumors were induced in multiple organs after only 13 weeks of exposure to 625 ppm butadiene (National Toxicology Program 1993). On the basis of these results, occupational exposure limits were reduced to 1 ppm butadiene as an eight-hour time-weighted average (Occupational Safety and Health Administration 1996).

Although early epidemiologic studies were inconclusive, they suggested a possible risk of cancer of the lymphohematopoietic system in workers exposed to butadiene. A more recent analysis indicates an increased risk of chronic leukemia in long-term workers in the styrene-butadiene rubber (SBR) industry following a 25-year latency period compared with expected rates of leukemia in the general population (Delzell et al. 1996). Furthermore, an increased rate of lymphosarcoma was observed in short-term, highly exposed (wartime) workers in butadiene monomer production. However, no excess risk of chronic leukemia was observed in butadiene monomer production workers (Divine and Hartman 1996). These inconsistencies may reflect the lower time-weighted average butadiene concentrations in the monomer facilities, the smaller number of monomer workers included in the analysis, or the presence of styrene or some other confounding substance, such as the stopping agent dithiocarbamate, in the rubber production facilities. Further analyses of the data are ongoing, including a revised retroactive exposure assessment and characterization of leukemia cell types, and these results may provide important information for regulating exposures to butadiene.

Given the uncertainties in understanding the risk of cancer in exposed workers, risk assessments may need to rely on data from animal studies. However, for butadiene, the results of animal studies present their own uncertainties because mice are much more susceptible to butadiene-induced tumors than rats. Species differences in butadiene metabolism have been proposed as one possible explanation for these different responses.

The general goals of the 1,3-butadiene research program are to:

- Explore the reactivity and mutagenicity of butadiene metabolites to elucidate the mechanisms of carcinogenicity; and
- Identify biomarkers of exposure, dose, and metabolism, and validate these biomarkers in an exposed human population.

The initial butadiene research program funded by HEI consisted of five studies. Summaries of these studies can be found in the earlier HEI Program Summary "Research on Benzene and 1,3-Butadiene" (Health Effects Institute 1995b), and in the abstracts presented at HEI's Fourteenth and Fifteenth Annual Conferences (Health Effects Institute 1998, 1999).

Biomarker Responses in Butadiene-Exposed Czech Workers: A Transitional Epidemiology Study

Richard Albertini, University of Vermont, Burlington, VT

Promising butadiene biomarkers, including several whose development was funded by HEI, are being evaluated in an ongoing multiinvestigator, multinational validation study of a butadiene-exposed human population at industrial facilities near Prague, Czech Republic. Details of the study endpoints and investigators, under the direction of Dr. Richard Albertini, are provided in Table 4. Researchers' goals are to (1) define the optimal conditions for field use of the biomarkers; (2) explore the relationships among exposure levels and biomarkers of exposure, dose, and effects in people; (3) evaluate whether different metabolic genotypes are associated with altered responses; and (4) define the value of measuring butadiene biomarkers in epidemiologic studies.

Subjects for this study were selected from two industrial sites within an industrial complex: a butadiene monomer production unit and the polymerization end of an SBR unit. Control subjects were drawn from the administrative staff within the industrial complex. Substantial information concerning personal and medical histories, as well as information from prior studies involving several of these biomarkers, has already been obtained from the workers at these facilities.

Researchers are measuring butadiene in the general workplace area as well as in the personal spaces of workers; they are also evaluating potential confounders (such as benzene, styrene, and toluene) during a time period relevant to each individual biomarker. Measure-

Table 4. Biomarkers Being Evaluated in Dr. Albertini's Study[a]

Biomarker	Investigator and Institution
Exposure and Dose	
Butadiene metabolites in urine 1,2-Dihydroxy-4-(*N*-acetylcysteinyl)butane (MI) 1-Hydroxy-2-(*N*-acetylcysteinyl)-3-butene (MII) 1,2-Epoxy-3-butene (BDO) 1,2,3,4-Diepoxybutane (BDO_2)	Rogene Henderson, Lovelace Respiratory Research Institute; and Nico van Sittert, Shell International, The Netherlands
Butadiene-hemoglobin adducts in blood *N*-(2-Hydroxylbut-3-en-1-yl) valine *N*-(1-Hydroxylbut-3-en-2-yl) valine 2,3,4-Trihydroxybutyl valine	James Swenberg[b], University of North Carolina, Chapel Hill; and Nico van Sittert, Shell International, The Netherlands
Butadiene-DNA adducts in urine N^7-(2,3,4-Trihydroxybutyl)guanine N^7-(2-Hydroxy-3-buten-1-yl)guanine	Ian Blair[b], University of Pennsylvania Medical School
Sister chromatid exchange	Radim Šrám, Institute of Experimental Medicine, Czech Republic
Effect	
Chromosome aberrations	Radim Šrám, Institute of Experimental Medicine, Czech Republic
hprt Mutations in T lymphocytes	
Autographic assay	Jonathan Ward, University of Texas at Galveston
Cloning assay	A. D. Tates, University of Leiden, The Netherlands
Susceptibility	
Glutathione S–transferase M1 and T1 genotypes	Radim Šrám, Institute of Experimental Medicine, Czech Republic

[a] Samples for air exposure levels were measured by Health and Science Laboratories, U.K.

[b] Biomarker development funded by HEI.

ments of butadiene in an earlier study from this industrial complex averaged 1.7 to 2.9 ppm in the monomer production unit, and 4.5 to 6.3 ppm in the SBR unit. Workers in the SBR unit are also exposed to styrene (mean concentration of 2.4 ppm). Preliminary results of this study can be found in the abstracts presented at HEI's Fifteenth Annual Conference (Health Effects Institute 1999).

HEI Aldehydes Research

Aldehydes are ubiquitous in the environment; they may form in the atmosphere from photochemical oxidation of hydrocarbons, such as those in motor vehicle emissions and exhaust, or may be emitted directly from motor vehicles and other sources. Exposure to aldehydes from automotive sources has increased in recent times with the use of oxygenated fuel additives, especially those derived from methanol and ethanol (Auto/Oil Air Quality Improvement Research Program 1997). Health concerns related to aldehydes include skin, eye, and respiratory tract irritation; asthma; and cancer (reviewed by Leikauf 1992).

The general goals of the current HEI aldehydes research program are to:

- Measure human exposures, in different populations and environments, to several aldehydes including acetaldehyde, acrolein, crotonaldehyde, formaldehyde, glyoxal, and methyl glyoxal; and
- Evaluate biomarkers that may help define dose-response relationships at ambient exposure levels.

Four studies involving aldehydes are currently being funded by HEI (Table 5). Taken together, these studies are examining exposure to various aldehydes, including the six mentioned above (Figure 3), in three types of populations. One population is designed to capture average exposure to aldehydes in the United States; several populations are representative of expo-

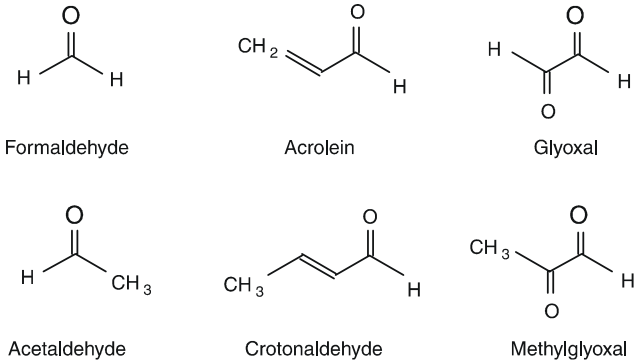

Figure 3. Chemical structure of selected aldehydes.

sures in urban areas with high and moderate pollution levels; and one population is made up of individuals occupationally exposed to aldehydes and other mobile-source air pollutants. Two of the four studies are also evaluating several biomarkers of aldehyde exposure.

Effect of Exposure to Automobile Exhaust on Acrolein- and Crotonaldehyde-Derived DNA Adducts in Human Lymphocyte DNA
Fung-Lung Chung, American Health Foundation, Valhalla, NY

The objective of this study is to measure DNA adducts of crotonaldehyde and acrolein, and assess their utility as biomarkers of exposure in people working in environments where they are expected to come into contact with high concentrations of airborne aldehydes. Levels of aldehyde-specific DNA adducts in blood lymphocytes are being compared to air measurements in the work environment. Exposed populations include workers in diesel repair facilities, garages, and gasoline stations in New York State. All populations include smokers and nonsmokers. In addition, a DNA adduct that may serve as a marker for oxidative damage is being measured.

Characterization of Aldehyde Exposures in the General Population
Lee-Jane Sally Liu, University of Washington, Seattle, WA

This research is assessing personal exposure to several aldehydes in a population representative of the United States. Potential subjects are being contacted by telephone, and 500 individuals are being enrolled in various geographic locations. The geographic distribution of participants mirrors the general distribution of people in the United States (as reflected in the census), and includes a number of housing types and characteristics. Both total exposure to various aldehydes and exposure in specific microenvironments, such as home, workplace, cars, garage, and streets, are being measured using passive personal monitors. Aldehydes and their acid metabolites in breath and urine are being examined as biomarkers of exposure in a subset of highly exposed individuals. This study includes a pilot study examining the sensitivity and stability of passive monitors for the selected aldehydes.

Exposure to Airborne Carbonyls from Motor Vehicle Emissions
Daniel Grosjean, DGA, Inc., Ventura, CA

This investigator is measuring the ambient concentrations of 30 to 60 carbonyl compounds, including a large number of aldehydes, in 11 urban locations, including several U.S. cities with high pollution levels. A possible addition to the study would measure carbonyls in a variety of indoor and commuting locations, and characterize individual people's exposure to these chemicals by examining the amount of time they spend in each location.

Personal and Microenvironmental Measurements of Human Exposures to Multiple Aldehydes in Three Distinct Urban Areas
Junfeng Zhang, Environmental and Occupational Health Sciences Institute, University of Medicine and Dentistry of New Jersey, Piscataway, NJ

This study is assessing exposure to several aldehydes in urban locations in Los Angeles, CA; Houston, TX; and Elizabeth/Bayonne, NJ. This study is part of a project titled "Relationship Between Indoor, Outdoor, and Personal Air" (RIOPA) that HEI is funding jointly with the Mickey Leland National Urban Air Toxics Research Center (NUATRC). RIOPA is studying the relationships among indoor and outdoor sources and total personal exposure to various pollutants, including volatile organic compounds, aldehydes, and $PM_{2.5}$. Dr. Zhang's HEI project extends the NUATRC study by increasing the number of homes where alde-

Table 5. Aldehyde Studies

Investigator and Institution	Aldehyde Species	Population and Locations
Lee-Jane Sally Liu, University of Washington	Formaldehyde, acetaldehyde, acrolein, crotonaldehyde, glyoxal, and methylglyoxal	General population of U.S.
Junfeng Zhang, Environmental and Occupational Health Sciences Institute	Formaldehyde, acetaldehyde, acrolein, crotonaldehyde, glyoxal, and methylglyoxal	Three U.S. urban centers: Los Angeles, CA; Elizabeth/Bayonne, NJ; and Houston, TX
Daniel Grosjean, DGA, Inc.	30 to 60 carbonyls, including formaldehyde, acetaldehyde, acrolein, crotonaldehyde, glyoxal, and methylglyoxal	Ten U.S. urban centers, including Los Angeles, CA, and Houston, TX; plus Mexico City, Mexico
Fung-Lung Chung, American Health Foundation	Acrolein and crotonaldehyde	Occupationally exposed population in New York State

hydes are measured, adding aldehyde exposure measurements in motor vehicles (an important source of exposure to many volatile chemicals), and allowing personal monitoring measurements for all subjects. In addition, this project will develop and field-test a new personal monitor for aldehydes, which may be more sensitive to the low levels of aldehydes present in the environment.

CONCLUSIONS

This Program Summary outlines HEI's current air toxics research program. This program addresses a variety of air toxics, including benzene, 1,3-butadiene, POM, acetaldehyde, formaldehyde, acrolein, and other aldehyde species. Many of these studies have just ended or are due to end during the next year, and should provide useful information to help reduce uncertainties concerning the health effects of air toxics and to address issues laid out in the U.S. EPA's Integrated Urban Air Toxics Strategy. HEI will continue research on air toxics in coming years, and is considering pollutants addressed in this Program Summary and others for future research.

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ABBREVIATIONS

EPA	U.S. Environmental Protection Agency
EU	European Union
IARC	International Agency for Research on Cancer
NUATRC	National Urban Air Toxics Research Center
POM	polycyclic organic matter
$PM_{2.5}$	particulate matter 2.5 μm or smaller
ppb	parts per billion
ppm	parts per million
RIOPA	Relationship Between Indoor, Outdoor, and Personal Air
SBR	styrene-butadiene rubber

HEI HEALTH EFFECTS INSTITUTE

The Health Effects Institute is an independent, nonprofit corporation chartered in 1980 to provide unbiased, timely, relevant, and high-quality scientific information on the health effects of pollutants from motor vehicles and from other sources in the environment. Supported jointly by the U.S. Environmental Protection Agency and industry, HEI has funded over 200 studies and published over 100 Research Reports, producing important research findings on the health effects of a variety of pollutants. Current and planned research programs focus on mobile-source air toxics, particulate pollution, and oxygenates.

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