CONTRA COSTA TIMES

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California approves new ozone-level limits

By Gillian Flaccus
ASSOCIATED PRESS

LOS ANGELES - The state Air Resources Board unanimously adopted a new limit on ozone levels Thursday that gives California the toughest guidelines in the nation -- a standard that critics argue is largely symbolic.

Supporters estimate that, if fully effective, the new standard could save Californians millions of dollars each year in medical costs and productivity losses linked to smog-induced illness.

They insist that while it may take years for the state to meet the new standard, its existence will force individual air quality districts to implement long-term strategies to reduce pollution.

"It's definitely a goal that the air district will strive for," said Luna Salaver, spokeswoman for the Bay Area Air Quality Management District.

The majority of the state currently doesn't meet the less-stringent federal standard.

The eight-member board met for nearly 21/2 hours before approving the new limit. California has no authority to impose sanctions for violations of the rules.

Several board members said they supported the change but expressed concerns about the as-yet-unknown cost of implementing it statewide.

nie Holmes-Gen, spokeswoman for the American Lung Association of California, said the new ozone standard is based on the latest esearch.

New evidence suggests pollution can cause a host of illnesses -- heart and lung disease, asthma, premature death -- and can exacerbate the symptoms of diabetes, she said.

Before the vote, she stressed to board members that they should only consider public health -- not expense -- when considering the new guideline.

"Today your job is to determine the level at which public health is protected," she said. "We should not settle for anything less."

Ozone pollution occurs when hydrocarbons and nitrogen oxides -- released as fossil fuels burn or chemicals evaporate -- combine with heat and sunlight.

Clean-air advocacy groups hope the upgraded California standard will influence new ozone standards currently under review at the federal level.

California is the only state that's allowed to have its own air pollution standards because it had emissions requirements in place before the federal Clean Air Act was passed in 1971, said Sonya Lunder, spokeswoman for the Environmental Working Group.

Other states can choose to follow the federal standards or California's tougher standards, she said.

The new standard passed Thursday calls for an average ozone level that doesn't exceed .07 parts per million over an eight-hour period. The federal eight-hour standard is .08 parts per million.

nty percent of California counties didn't meet the federal eight-hour standard between 2000-2003, said Lunder, and an estimated 92 nt of counties would fail the state standard, if implemented. The state already has a one-hour standard for ozone that is stricter than federal rule.

The Environmental Protection Agency can withhold federal transportation funds from states that don't meet their ozone standards, but most states have until 2021 to fully comply, state officials said.

A coalition of groups representing the interests of the automobile and technology industries had opposed the new state eight-hour

guideline.

Bruce Magnani, legislative advocate for the California Chamber of Commerce, said the proposed standard is so restrictive, it approaches limiting the amount of ozone pollution to what occurs naturally in the air -- .04 parts per million.

"I think it could only have negative impacts on the economy, because it's so strict. No one knows how they're going to implement this, Magnani said.

Steven Douglas of the Alliance of Automobile Manufacturers said he was worried about a lack of information on the cost associated with the new standard. He also said he wanted to know how much the state would have to reduce ozone emissions to reach the new target.

"The very essence of good public policy is trying to find the balance between the costs and the benefits," Douglas said. "There isn't any discussion of the cost (here)."

Staff scientists said evaluating that cost would likely take at least until 2007 and possibly longer for areas around Los Angeles.

Air Resources Board

State of California

Governor Arnold Schwarzenegger

Review of the California Ambient Air Quality Standard For Ozone

Volume I of IV

Chapters 1-2

Appendix A—Proposed Amendments

Staff Report

Initial Statement of Reasons for Proposed Rulemaking

March 11, 2005

California Environmental Protection Agency

Air Resources Board

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Disclaimer

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http://www.arb.ca.gov/research/aaqs/ozone-rs/ozone-rs.htm

This staff report, the Notice of Public Hearing to consider Amendments to Regulations for the State Ambient Air Quality Standard for Ozone, and all subsequent regulatory documents, including the FSOR, when completed, are available on the ARB Internet site for this rulemaking at www.arb.ca.gov/regact/ozone05/ozone05.htm
Electronic copies on compacts discs or paper copies of this report may be obtained from the Public Information Office, Air Resources Board, 1001 I Street, Visitors and Environmental Services Center, 1st Floor, Sacramento, CA 95814, (916) 322-2990.

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Abbreviations and Definitions

abscission	the normal separation, involving a layer of specialized cells, of flowers, fruits and leaves of plants
AOT40	accumulated exposure over threshold of 40 ppb ozone
AQDA	air quality data action
ARB	Air Resources Board
AVG	aminoethoxyvinyl glycine
BSA	Broader Sacramento Area
Ca^{2+}	calcium ion
canopy	a cover of foliage that forms when the leaves on the branches trees in a forest overlap during the growing season
CEC	controlled environment chamber
CFR	Code of Federal Regulations
CO_2	carbon dioxide
COPD	chronic obstructive pulmonary disease
d	day
edaphic	the physical, chemical, and biological characteristics of soil
ESPACE	European Stress Physiology and Climate Experiment
FACE	Free Air Carbon Enrichment system, a chamber-free, open-air fumigation design
FEF25-75%	forced expiratory flow rate between 25 and 75% of forced vital capacity
FEM	federal equivalent method (for air monitoring)
FEV1	forced expiratory volume in one second
fine roots	roots with a diameter between 0.5 to 3 mm
foliar	of or referring to a plant leaf
FRM	federal reference method (for air monitoring)
full-sib	seedlings that have the same parents, but not necessarily from seed produced in the same year
FVC	forced vital capacity
g	gram
GBVAB	Great Basin Valleys Air Basin
gdw	gram dry weight
GIS	geographic information system

gfw	gram fresh weight
hr	hour
ha	hectare (= 10,000 m^2; an area that is 100 m x 100 m)
half-sib	seedlings that have one parent in common
hm	hourly mean
HNO_3	nitric acid
homeostasis	the tendency toward maintaining physiological stability within an organism (plant or animal)
H&SC	Health and Safety Code
IPM	Integrated Pest Management.
Jeffrey pine	*Pinus jeffreyi* Grev. and Balf.
k	allometric growth coefficient describing the distribution of dry weight gain between competing plant parts, defined as the ratio of the relative growth rates of the competing plant parts
K^+	potassium ion
kg	kilogram (= 1,000 g = 2.205 pounds)
km	kilometer (= 1,000 m = 0.6214 miles)
L	liter
LCAB	Lake County Air Basin
LST	local standard time
LTAB	Lake Tahoe Air Basin
m	meter (= 3.28 feet)
m^2	square meter, an area that is 1 m x 1 m
MCAB	Mountain Counties Air Basin
MDAB	Mojave Desert Air Basin
mesophyll cells	the internal cells of a leaf, distinct from cells at the leaf surface or from cell layers immediately adjacent to the leaf surface
mixed conifer	forests with a tree-layer dominated by a mixture of conifer species
montane	of or relating to a mountain or mountainous area
mRNA	messenger RNA (ribonucleic acid)
mycorrhizae	a biological association of a fungus (e.g., *Pisolithus tinctorius*) with the root cells of a plant (e.g., ponderosa pine tree)
mycorrhizal trees	trees with roots associated a mycorrhizae fungus

n	sample size
NARSTO	a public/private partnership to coordinate research in Canada, Mexico and the United States on tropospheric air pollution (formerly the North American Research Strategy for Tropospheric Ozone)
NCAB	North Coast Air Basin
NCCAB	North Central Coast Air Basin
NCLAN	National Crop Loss Assessment Network, a national study of ozone impacts on crops, undertaken during the 1980s
NEPAB	Northeast Plateau Air Basin
ng	nanogram (= 0.000000001 g = 10^{-9} g)
NH_4N_3	ammonium nitrate
nL	nanoliter (10^{-9} L)
nm	nanometer, or one billionth of a meter
NO	nitric oxide, the primary nitrogen-containing by-product of combustion
NO_2	nitrogen dioxide
NO_X	nitrogen oxides (or oxides of nitrogen)
ns	not statistically significant at p =0.05
O_3	ozone; triatomic oxygen
OII	ozone injury index
OTC	open top field exposure chamber
PAR	photosynthetically active radiation (400 – 700 nm)
phloem	the plant tissue through which sugars and other organic materials are transferred to different parts of the plant
photosynthesis	the production by green plants of organic compounds from water and carbon dioxide using energy absorbed from sunlight
Pisolithus tinctorius	a mycorrhizae-forming fungus that forms root-associations with a wide variety of pine and other tree species
ppb	parts per billion by volume
ppb-hr	parts per billion hours (i.e., sum of concentration times duration), a measure of exposure to ozone
ppm	parts per million by volume
ppm-hr	parts per million hours (i.e., sum of concentration times duration), a measure of exposure to ozone

process rates	the degree or amount at which specific actions or activities occur (e.g., water vapor loss from leaves of plants)
QAS	Quality Assurance Section (of ARB)
R:S	ratio of root biomass (dry weight) to shoot biomass
RGR	relative growth rate, defined as the difference in the dry weight of a plant or plant part over a time period, divided by the initial dry weight and the length of the time period
RH	relative humidity
RuBisCO	ribulose bisphosphate carboxylase-oxygenase
RuBP	ribulose bisphosphate
SCCAB	South Central Coast Air Basin
SCOIAS	Sierra Cooperative Ozone Impact Assessment Study
SDAB	San Diego Air Basin
senescence	the onset of aging -- a phase in plant development from maturity to the complete loss of organization and function in plants
SFBAAB	San Francisco Bay Area Air Basin
shoot	the aboveground portion of the plant (e.g., leaves, stems, flowers, and fruits)
sieve cells	the primary type of cell found in the phloem of plants
SIP	State Implementation Plan
SJVAB	San Joaquin Valley Air Basin
SoCAB	South Coast Air Basin
SSAB	Salton Sea Air Basin
sucrose	a disaccharide (with 12 carbon atoms) commonly found in plants
(sucrose) translocation	the movement of sucrose (or other soluble organic food materials) through plant tissues – most commonly from leaves to stems/roots
SUM06	an ozone exposure metric involving concentration weighting, defined as the sum of all hourly mean ozone concentrations equal to or greater than 70 ppb
terrain-effect winds	air currents influenced by the geographic features of the land that it passes over
TREEGRO	a physiologically based computer simulation model of tree growth and development

Ulmus americana	the scientific name for "American Elm"
UN-ECE	United Nations Economic Commission for Europe
USD	United States dollars
USDA	United States Department of Agriculture
USDI	United States Department of the Interior
USEPA	United States Environmental Protection Agency
USV	Upper Sacramento Valley
V_d	deposition velocity, defined as deposition flux of ozone divided by its concentration in air (usually in cm/s or m/s)
VPD	vapor pressure deficit, a measure of evaporative demand of air
whorl	the arrangement of leaves, petals, etc., at about the same place on a stem
wk	week
yr	year
ZAP	zonal application system, a chamber-free, open-air exposure system
µg	microgram (= 0.000001 g = 10^{-6} g)
µm	micrometer or micron (= 0.000001 m = 10^{-6} m)

1 Executive Summary

The California Health and Safety Code in section 39606, requires the Air Resources Board to adopt ambient air quality standards at levels that adequately protect the health of the public, including infants and children, with an adequate margin of safety. Ambient air quality standards are the legal definition of clean air. In December 2000, as a requirement of the Children's Environmental Health Protection Act (Senate Bill 25, Escutia, Stats. 1999, Health and Safety Code 39606 (d)(1)), the Air Resources Board (ARB or Board), approved a report, "Adequacy of California Ambient Air Quality Standards" (ARB and OEHHA, 2000) that contained a brief review of all of the existing health-based California ambient air quality standards.

Following this review, the standard for ozone, currently set at 0.09 parts per million (ppm) for one hour, was prioritized to undergo full review after review of the standards for particulate matter and sulfates. Staff from ARB and the Office of Environmental Health Hazard Assessment (OEHHA) have reviewed the scientific literature on public exposure, atmospheric chemistry, health effects of exposure to ozone, and welfare effects. This Staff Report or Initial Statement of Reasons (Staff Report) presents the findings of the review and the staff recommendations to revise the ozone standard in order to adequately protect public health. The proposed amendments to the ambient air quality standard for ozone are based on the health effects review contained in Volume III of this Report and the recommendation of OEHHA, as required by Health and Safety Code section 39606(a)(2).

1.1 Summary of the Staff Report/Initial Statement of Reasons

1.1.1 Health Effects of Ozone

Scientific studies show that exposure to ozone can result in reduced lung function, increased respiratory symptoms, increased airway hyperreactivity, and increased airway inflammation. Exposure to ozone is also associated with premature death, hospitalization for cardiopulmonary causes, emergency room visits for asthma, and restrictions in activity.

In controlled human exposure studies (see Chapter 9), exercising individuals exposed for 1 hour (hr) to an ozone concentration as low as 0.12 parts per million (ppm) or for 6.6 hours to a concentration as low as 0.08 ppm experienced lung function decrements and symptoms of respiratory irritation such as cough, wheeze, and pain upon deep inhalation. The lowest ozone concentrations at which airway hyperreactivity (an increase in the tendency of the airways to constrict in reaction to exposure to irritants) has been reported are 0.18 ppm ozone following 2-hour exposure in exercising subjects, 0.40 ppm following 2-hour exposure in resting subjects, and 0.08 ppm ozone in subjects exercising for 6.6 hr. Airway inflammation has been reported following 2-hour exposures to 0.20 ppm ozone and following 6.6-hour exposure to 0.08 ppm ozone.

Additional support for the exposure/response relationship for ozone health effects is derived from animal toxicological studies, which have shown that chronic ozone exposure can induce morphological (tissue) changes throughout the respiratory tract, particularly at the junction of the conducting airways and the gas exchange zone in the deep lung. In addition, the magnitude of ozone-induced effects is related to the inhaled dose (ozone concentration times breathing rate times exposure duration). Of these three factors ozone concentration is the most significant in predicting the magnitude of observed effects, followed by ventilation rate. Exposure duration has the least influence of the three factors.

Epidemiological studies (see Chapter 10) have shown positive associations between ozone levels and several health effects, including decreased lung function, respiratory symptoms, hospitalizations for cardiopulmonary causes, emergency room visits for asthma, and premature death. Children may be more affected by ozone than the general population due to effects on the developing lung and to relatively higher exposure than adults. There is little information available on the effects of ozone exposure on infants. Also, asthmatics may represent a sensitive sub-population for ozone. Since most California residents are exposed to levels at or above the current State ozone standard during some parts of the year, the statewide potential for significant health impacts associated with ozone exposure is large and wide-ranging.

1.1.2 Summary of Non-health Issues

The Staff Report contains reviews and discussions of non-health topics to provide a context for the health review and the staff recommendations for the State ozone standard. Almost all of the ozone in California's atmosphere results from reactions between substances emitted from sources including motor vehicles and other mobile sources, power plants, industrial plants, and consumer products. These reactions involve volatile organic compounds (VOC) and oxides of nitrogen (NO_X) in the presence of sunlight (Chapter 3). Ozone is a regional pollutant, as the reactions forming it take place over time, and downwind from the sources of the emissions. As a photochemical pollutant, ozone is formed only during daylight hours under appropriate conditions, but is destroyed throughout the day and night. Thus, ozone concentrations vary depending upon both the time of day and the location. Even in pristine areas there is some ambient ozone that forms from natural emissions that are not controllable (Chapter 4). This is termed "background" ozone. The average "background" ozone concentrations near sea level are in the range of 0.015 to 0.035 ppm, with a maximum of about 0.04 ppm.

The Staff Report includes an overview of statewide ozone precursor emissions that are involved in the formation of ozone (Chapter 5). The Staff Report also includes a discussion of the current ultraviolet photometry monitoring method, and a listing of approved samplers (Chapter 6). Although there are two measurement methods for ozone approved for use in the U.S. by the U.S. Environmental Protection Agency (USEPA), the method based on ultraviolet photometry is almost universally used in practice and is approved for use in California for state air quality standards.

The Staff Report includes a summary of current air quality in California, as well as long-term trends in statewide ozone concentrations (Chapter 7). Ozone is monitored continuously at approximately 175 sites in California. The highest number of exceedance days for both the State and federal 1-hour standards occurred in the San Joaquin Valley Air Basin and the South Coast Air Basin. Both areas had more than 115 State standard exceedance days and 31 or more federal standard exceedance days during each of the three years from 2001 through 2003. The Sacramento Metro Area, Mojave Desert Air Basin, and Salton Sea Air Basin all averaged more than 50 State standard exceedance days and averaged 6 or more federal standard exceedance days during 2001 through 2003. The remaining five areas (Mountain Counties Air Basin, San Diego Air Basin, San Francisco Bay Area Air Basin, South Central Coast Air Basin, and the Upper Sacramento Valley) averaged from 12 to 45 State standard exceedance days. The Upper Sacramento Valley area had no exceedances of the federal standard while the Mountain Counties Air Basin, San Diego Air Basin, San Francisco Bay Area Air Basin, and South Central Coast Air Basin each averaged 1 to 2 federal standard exceedance days for the three-year period.

The range of the measured maximum 1-hour concentrations tends to follow a similar pattern. The South Coast Air Basin showed the highest values, with measured concentrations of 0.169 ppm or higher during 2001 through 2003. The next highest 1-hour ozone concentrations occurred in the Salton Sea Air Basin and San Joaquin Valley Air Basin, which had concentrations of 0.149 ppm or higher during all three years. During 2001 through 2003, neither the State nor federal 1-hour standard was exceeded in the Lake County Air Basin, North Coast Air Basin, or Northeast Plateau Air Basin. Data for four additional areas, Great Basin Valleys Air Basin, Lake Tahoe Air Basin, North Central Coast Air Basin, and the Upper Sacramento Valley show exceedances of the State standard, but not the federal 1-hour standard (as described earlier, representative data for the Northeast Plateau Air Basin and Great Basin Valleys Air Basin are available for 2002 and 2003 only). Both the State and federal 1-hour standards were exceeded during at least two of the three years in all other areas.

Californians' indoor and personal exposures to ozone are largely determined by the outdoor ozone concentrations in their community. Nonetheless, some Californians experience a substantial exposure to ozone indoors, due to the increasing use of certain types of appliances and equipment that emit ozone. Children and those who are employed in outdoor occupations or exercise heavily outdoors, experience substantially greater exposures to ozone than the rest of the population, because they spend time outdoors during peak ozone periods.

A review of welfare effects, including effects of ozone on forest trees, agricultural crops, and materials is also discussed in this report (Chapter 8). Elevated concentrations of ozone can cause adverse effects on agricultural crops, forest trees and materials at current ambient levels, and the proposed health-based ozone standards should also provide protection to crops, forests and materials. In broad terms, impacts to crops are generally more severe than for forest trees owing to their inherently more vigorous rates of growth. Discussed in the

subsection on crops and the methods used to expose plants to ozone. This is followed by an examination of the physiological basis of ozone damage to plants, with special emphasis on carbon metabolism and the resulting impacts on crop growth and yield. Data collected since the 1950s on mixed conifer forests in the San Bernardino Mountains and the Sierra Nevada indicate that increasing numbers of ponderosa and Jeffrey pines exhibit ozone-specific needle damage due to the pollutant's cumulative effects. Also discussed are the impacts of ozone on materials, including building materials, rubber, paint, and fabrics. Although the proposed ozone standards are based on human health effects, progress toward attaining the proposed standards will provide welfare benefits.

1.2 Staff Recommendations for the Ozone Standard

California ambient air quality standards are defined in the Health and Safety Code section 39014, and 17 Cal. Code Regs. section 70101, and comprise four elements: (1) a definition of the air pollutant, (2) an averaging time, (3) a pollutant concentration, and (4) a monitoring method to determine attainment of the standard. The current California ambient air quality standard for ozone is 0.09 ppm averaged over one hour and was set by the Board in 1988. The data indicate that the current standard alone is not sufficiently protective of human health. Based on the review of the scientific literature and recommendations by OEHHA, the staff recommends that the following revisions be made to the California ambient air quality standard for ozone:

1. Ozone will continue to be the pollutant addressed by the standard.
2. Ozone 1-hour-average Standard – retain the current 1-hour-average standard for ozone at **0.09 ppm, not to be exceeded.**
3. Ozone 8-hour-average Standard – establish a new 8-hour-average standard for ozone at **0.070 ppm, not to be exceeded.**
4. Ozone Monitoring Method: retain the current monitoring method for ozone which uses the ultraviolet (UV) photometry method for determining compliance with the State ambient air quality standard for ozone. Incorporate by reference (17 Cal. Code Regs. section 70101) all federally approved UV methods (i.e., samplers) for ozone as "California Approved Samplers". This will result in no change in air monitoring equipment practices, but will align state monitoring requirements with federal requirements.

These recommendations are based on the following findings:

a. Reduced lung function and increased respiratory or ventilatory symptoms following 1-hour exposure to 0.12 ppm ozone with moderate to heavy exercise.

b. Increased airway hyperreactivity following 2-hour exposure to 0.18 ppm in exercising subjects.

c. Airway inflammation following 2-hour exposure to 0.20 ppm ozone in exercising subjects

d. Reduced lung function, increased respiratory and ventilatory symptoms, increased airway hyperreactivity, and increased airway inflammation following 6.6 to 8-hour exposure to 0.08 ppm ozone.

e. Evidence from epidemiological studies of several health endpoints including premature death, hospitalization, respiratory symptoms, and restrictions in activity and lung function.

f. Evidence from epidemiological studies of emergency room visits for asthma suggesting a possible threshold concentration between 0.075 and 0.11 ppm from analyses based on a 1-hour averaging time, and a possible threshold concentration between 0.070 and 0.10 ppm from analyses based on an 8-hour averaging time.

g. There is no evidence that children and infants respond to lower ozone concentrations than adults. Their risk is primarily related to their greater ventilation rate and greater exposure duration.

h. The dose-rate of ozone inhalation influences the magnitude of observed effects.

1.3 Other Recommendations

In light of the adverse health effects observed at current ambient concentrations and the lack of a demonstrated effect threshold for the population as a whole, staff makes the following comments:

1. Fund additional research investigating the responses of human subjects to multi-hour exposures to ozone concentrations between 0.04 and 0.08 ppm.
2. The standards should be revisited within five years, in order to re-evaluate the evidence regarding the health effects associated with ozone exposure.
3. In any air basin in California that currently attains the ambient air quality standards for ozone, air quality should not be degraded from present levels.

1.4 Estimated Health Benefits

Staff estimates that attainment of the proposed ozone standards throughout California would avoid a significant number of adverse health effects each year, specifically:

- 580 (290 – 870, probable range) premature deaths for all ages.
- 3,800 (2,200 – 5,400, 95% confidence interval (CI)) hospitalizations due to respiratory diseases for all ages.
- 600 (360 – 850, 95% CI) emergency room visits for asthma for children under 18 years of age.
- 3.3 million (430,000 – 6,100,000, 95% CI) school absences for children 5 to 17 years of age.

- 2.8 million (1.2 million – 4.6 million, 95% CI) minor restricted activity days for adults above 18 years of age.

As discussed in Appendix B, there are a several important assumptions and uncertainties in this analysis. Some have to do with study design, statistical methods, and choice of epidemiological studies used to develop the concentration-response (CR) functions used in the analysis. Few studies have investigated the shape of the CR function, or whether there is a population response threshold for health endpoints other than emergency room visits for asthma. Further uncertainty is added by assumptions in the statewide exposure assessment. It should also be noted that since several health effects related to acute exposure, and effects of chronic ozone exposure, are not included in the estimates, the health benefits associated with lowering ozone exposure are likely underestimated.

1.5 Public and Peer Review of the Staff Recommendations

The draft version of this Staff Report was released to the public on June 21, 2004 and presented for review and comment at public workshops during 2004 on July 14 in Sacramento, July 15 in El Monte, July 16 in Fresno, and August 25 in Sacramento.

The draft Staff Report was peer reviewed by the Air Quality Advisory Committee (AQAC). AQAC is a scientific peer review committee, appointed by the University of California, to independently evaluate the scientific basis of staff findings and recommendations in the draft Staff Report for revising the California ambient air quality standard for ozone. The AQAC held a public meeting to discuss its review of the draft Staff Report, comments submitted by the public, and staff responses to those comments. AQAC concluded that the report was well written and researched, and that the proposed revision to the State ozone standard was adequately supported. AQAC findings, public comments, and staff responses can be found in Appendices C-E. Following the meeting of the Air Quality Advisory Committee (AQAC), staff revised the draft Staff Report based on comments received from AQAC and the public.

1.6 Environmental and Economic Impacts

The proposed ambient air quality standards will in and of themselves have no environmental or economic impacts. Standards simply define clean air. Once adopted, local air pollution control or air quality management districts are responsible for the adoption of rules and regulations to control emissions from stationary sources to assure their achievement and maintenance. The ARB is responsible for adoption of emission standards for mobile sources and consumer products. A number of different implementation measures are possible, and each could have its own environmental or economic impact. These impacts must be evaluated when the control measure is proposed. Any environmental or economic impacts associated with the imposition of future measures will be considered if and when specific measures are proposed.

1.7 Environmental Justice Considerations

State law defines environmental justice as the fair treatment of people of all races, cultures, and incomes with respect to the development, adoption, implementation, and enforcement of environmental laws, regulations, and policies. The available literature suggests there appears to be no special vulnerability related to race, ethnicity or income level, although there may be higher exposure. Ambient air quality standards define clean air; therefore, all of California's communities will benefit from the proposed health-based standards.

1.8 Comment Period and Board Hearing

Release of this Staff Report opens the official 45-day public comment period required by the Administrative Procedure Act prior to the public meeting of the Air Resources Board to consider the staff's recommendations. Please direct all comments to either the following postal or electronic mail address:

Clerk of the Board
Air Resources Board
1001 "I" Street, 23rd Floor
Sacramento, California 95814
ozone05@listserve.arb.ca.gov

To be considered by the Board, written submissions not physically submitted at the hearing must be received at the ARB no later than 12:00 noon, April 27, 2005. Public workshops will be scheduled for April 2005 to present the final staff recommendations and receive public input on the Staff Report. Information on these workshops, as well as summaries of the presentations from past workshops and meetings are available by calling 1-916-445-0753 or at the following ARB website:
http://www.arb.ca.gov/research/aaqs/ozone-rs/ozone-rs.htm.

An oral report summarizing the staff recommendations for revising the ozone standard will be presented to the Board at a public hearing scheduled for April 28, 2005.

The staff recommends that the Board adopt the proposed amendments to the ambient air quality standards for ozone as stated above. The proposed amendments and their basis are described in detail in this Staff Report, which contains the findings of ARB and OEHHA staff's full review of the public health, scientific literature, and exposure pattern data for ozone in California. Due to the extensive nature of the literature review and the hundreds of studies reviewed, the Staff Report is divided into four volumes. Volume I contains the Executive Summary, Overview and Staff Recommendations, and Appendix A, the proposed amendments to the California Code of Regulations (amended regulatory text). Volumes II through IV present more detailed discussions of the material that is summarized in Volume I. Volume II includes background material on non-health topics, including chemistry of ozone formation and deposition, ozone precursor sources and emissions, ozone exposure and background levels, measurement methods, and welfare effects of ozone exposure. Volume III contains a summary

of ozone health effects and an in-depth discussion of the basis for the staff recommendation. Volume IV includes several appendices, including an analysis of the estimated health benefits associated with attainment of the proposed standards, summaries of Air Quality Advisory Committee and public comments and staff responses, and supplemental animal toxicologic data.

1.9 References

Air Resources Board and Office of Environmental Health Hazard Assessment (2000). Adequacy of California Ambient Air Quality Standards: Children's Environmental Health Protection Act. Staff Report. Sacramento, CA. Available at http://www.arb.ca.gov/ch/programs/sb25/airstandards.htm.

2 Overview and Staff Recommendations

Ozone (O_3) can damage human cells upon contact, and has been implicated in a variety of adverse health effects. Scientific studies show that exposure to ozone can result in reduced lung function, increased respiratory symptoms, increased airway hyperreactivity, and airway inflammation. Exposure to ozone is also associated with premature death, hospitalization for cardiopulmonary causes, emergency room visits for asthma, and restrictions in activity. Ozone forms in the atmosphere as the result of reactions involving sunlight and two classes of directly emitted precursors. One class of precursors includes nitric oxide (NO) and nitrogen dioxide (NO_2), collectively referred to as nitrogen oxides or NO_X. The other class of precursors includes volatile organic compounds (VOCs, also called reactive organic gases or ROG), such as hydrocarbons. Ozone forms in greater quantities on hot, sunny, calm days. In metropolitan areas of California and areas downwind, ozone concentrations frequently exceed existing health-protective standards in the summertime. The current California ambient air quality standard for ozone is 0.09 ppm for one hour.

The sources of ozone precursor emissions within California have been grouped into three major categories: point sources, which are distinct facilities such as power plants and factories; mobile sources, which includes cars, trucks, and off-road mobile equipment; and area-wide sources, which include agricultural and construction activities, and consumer products. VOCs are emitted from vehicles, factories, fossil fuels combustion, evaporation of paints, and many other sources. NO_X is emitted from high-temperature combustion processes, such as at power plants or in motor vehicle exhaust .

The concentrations of ozone measured in the air vary both regionally and seasonally throughout California. For example, the Los Angeles area and the San Joaquin Valley experience highest ozone levels in the state. Ozone concentrations are typically higher during the summer months than the winter months.

To help understand which sources contribute to high ozone levels, the ARB has developed and maintains detailed facility and source specific estimates of the overall estimated ozone precursor emissions. Only the precursor gases are estimated. As a complement to emission inventory and routinely collected air quality monitoring data, the ARB conducts atmospheric modeling, using these precursor emission inventories and other appropriate information, to estimate ozone levels

2.1 Setting California Ambient Air Quality Standards

Ambient air quality standards (AAQS) represent the legal definition of clean air. They specify concentrations and durations of exposure to air pollutants that reflect the relationships between the intensities and composition of air pollution and undesirable effects (Health and Safety Code section 39014). The objective of an AAQS is to provide a basis for preventing or abating adverse health or welfare effects of air pollution (17 Cal. Code Regs. section 70101).

Health and Safety Code section 39606(a)(2) authorizes the Air Resources Board (Board) to adopt standards for ambient air quality "in consideration of public health,

safety, and welfare, including, but not limited to, health, illness, irritation to the senses, aesthetic value, interference with visibility, and effects on the economy." Standards represent the highest pollutant concentration for a given averaging time that is estimated to be without adverse effects for most people. Standards are set to ensure that sensitive population sub-groups are protected from exposure to levels of pollutants that may cause adverse health effects. A margin of safety is added to account for possible deficiencies in the data and measuring methodology. Health-based standards are based on the recommendation of the Office of Environmental Health Hazard Health Assessment (OEHHA).

Recent legislation requires that infants and children be given special consideration when ambient air quality standards are adopted. As part of its recommendation to the ARB, the statute requires OEHHA to use current principles, practices, and methods used by public health professionals to assess the following considerations for infants and children:

1. Exposure patterns among infants and children that are likely to result in disproportionately high exposure to ambient air pollutants in comparison to the general population.
2. Special susceptibility of infants and children to ambient air pollutants in comparison to the general population.
3. The effects on infants and children of exposure to ambient air pollutants and other substances that have a common mechanism of toxicity.
4. The interaction of multiple air pollutants on infants and children, including the interaction between criteria air pollutants and toxic air contaminants.

The law also requires that the scientific basis or the scientific portion of the method used to assess these considerations be peer reviewed (Health and Safety Code section 39606(c)). The draft Staff recommendations and their bases, including OEHHA's assessment and recommendation, is peer reviewed by the Air Quality Advisory Committee (AQAC). AQAC is an external peer review committee established in accordance with section 57004 of the Health and Safety Code and appointed by the President of the University of California a University of California. The AQAC meets to independently evaluate the scientific basis of draft recommendations for revising the California ambient air quality standards.

Ambient air quality standards should not be interpreted as permitting, encouraging, or condoning degradation of present air quality that is superior to that stipulated in the standards. Rather, they represent the minimum acceptable air quality. An AAQS adopted by the Board is implemented, achieved, and maintained by numerous rules and regulations that limit pollution from specific sources of ozone precursors. These rules and regulations are primarily, though not exclusively, emission limitations established by the regional and local air pollution control and air quality management districts for stationary sources, and by the Board for vehicular sources and consumer products (see generally, Health and Safety Code sections 39002, 40000, and 40001).

2.2 Current California Ambient Air Quality Standard for Ozone

The current California ambient air quality standard for ozone, established in 1988, is 0.09 ppm (180 $\mu g/m^3$) for a one-hour average. This value is not to be exceeded. This standard was established based on the following most relevant effects, which are listed in the table of standards (17 Cal. Code Regs. section 70200):

a. Short-term exposures:

(1) Pulmonary function decrements and localized lung edema in humans and animals.

(2) Risk to public health implied by alterations in pulmonary morphology and host defence in animals.

b. Long-term exposures: Risk to public health implied by altered pulmonary morphology in animals after long-term exposures and pulmonary function decrements in chronically exposed humans.

c. Welfare effects:

(1) Yield loss in important crops and predicted economic loss to growers and consumers.

(2) Injury and damage to native plants and potential changes in species diversity and number.

(3) Damage to rubber and elastomers and to paints, fabric, dyes, pigments, and plastics.

The US EPA has set national ambient air quality standards, as noted in the table below. The federal one-hour standard will be phased out beginning in June 2005. The Federal Clean Air Act gives California authority to set its own ambient air quality standards in consideration of statewide concerns. California has the largest number of exceedances of the Federal 8-hour ozone standard in the United States, supporting California's need to address a significant statewide public health issue.

Current Ambient Air Quality Standards for Ozone

Averaging Time	California Standard	Federal Standard
1 Hour	0.09 ppm (180 $\mu g/m^3$)	0.12 ppm (235 $\mu g/m^3$)
8 Hour	—	0.08 ppm (157 $\mu g/m^3$)

2.3 History of Ozone/Oxidant Standards

The first state oxidant standard was set in December 1959 by the state Department of Public Health (DPH), which had the responsibility for setting air pollution standards before the creation of the ARB. This standard was set at 0.15 ppm, averaged for one hour. The standard was for oxidant, rather than ozone, because the monitoring method available at that time, the potassium iodide (KI) method, measured all ambient oxidant

gases, including ozone and other oxidants such as peroxyacetyl nitrate (PAN) nitrogen dioxide, photochemical aerosols, and other unknown oxidants.

In 1969, the newly-created ARB reviewed the oxidant standard set by DPH and revised the standard to a concentration of 0.10 ppm, averaged over one hour, not to be equaled or exceeded. The information considered by the Board in 1969 included adverse effects upon: (1) the health of humans and animals; (2) vegetation; (3) materials; and (4) visibility. Eye irritation was listed as the most relevant effect of oxidant.

In 1974, the Board introduced ultraviolet photometry as the monitoring method for the standard. However, since ultraviolet photometry measures only ozone, the Board changed the designation of the standard from "oxidant" to "oxidant (as ozone)." Because only ozone was to be measured, the Board changed the most relevant effect from: "eye irritation" (which is caused primarily by peroxyacyl nitrates or PANs) to "aggravation of respiratory disease" (which is caused primarily by ozone).

In 1988, the Board changed the designation of the standard from "oxidant (as ozone)" to "ozone", and revised the standard to a concentration of 0.09 ppm, averaged over one hour, to reflect that the listed relevant effects were related to ozone exposure, rather than to oxidants in general.

For comparison, in 2000, the World Health Organization established a guideline value for ozone in ambient air of 120 $\mu g/m^3$ (0.061 ppm) for a maximum period of 8 hours per day (WHO 2000).

2.4 Review of the California Ambient Air Quality Standards

The Children's Environmental Health Protection Act (Senate Bill 25, Escutia, Stats. 1999, ch. 731) required the ARB, in consultation with the OEHHA, to evaluate all health-based standards by December 31, 2000, to determine whether the standards were adequately protective of the health of the public, including infants and children (Health and Safety Code section 39606 (d)). At its December 7, 2000 meeting, the Board approved a report, "Adequacy of California Ambient Air Quality Standards: Children's Environmental Health Protection Act" (ARB, et al., 2000), prepared by ARB and OEHHA staffs. The Adequacy Report concluded that health effects may occur in infants and children and other potentially susceptible subgroups exposed to ozone at or near levels corresponding to the current standard. The report identified the standard for ozone as having the second highest priority for further detailed review and possible revision. The standard for PM10 (including sulfates) had the highest priority and was reviewed and revised in 2002, including establishment of a new standard for PM2.5.

2.5 Findings of the Standard Review

2.5.1 Chemistry and Physics

Most of the ozone in California's air results from reactions between substances emitted from sources including motor vehicles, power plants, industrial plants, consumer products, and vegetation. These reactions involve volatile organic compounds (VOCs, which the ARB also refers to as reactive organic gases or ROG) and oxides of nitrogen (NO_X) in the presence of sunlight. Ozone is a regional pollutant, as the reactions

forming it take place over time, and downwind from the precursor sources. As a photochemical pollutant, ozone is formed only during daylight hours under appropriate conditions, but is destroyed throughout the day and night. Thus, ozone concentrations vary depending upon both the time of day and the location. Ozone concentrations are higher on hot, sunny, calm days. In metropolitan and downwind areas of California, ozone concentrations frequently exceed regulatory standards during the summer.

2.5.2 Ozone Background

Even in pristine areas there is some ambient ozone that forms from natural emissions that are not controllable. This is termed "background" ozone. Overall, it appears that "background" ozone in California is dominated by natural tropospheric and stratospheric processes. The effects of occasional very large biomass fires and anthropogenic emissions are secondary factors. The foregoing discussion indicates that average "natural background" ozone near sea level is in the range of 0.015 to 0.035 ppm, with a maximum of about 0.04 ppm. Exogenous enhancements to "natural" levels generally are small (about 0.005 ppm), and are unlikely to alter peak concentrations.

At altitudes above 2 km stratospheric intrusions can push peak ambient concentrations to 0.045 to 0.050 ppm. The timing, spatial extent, and chemical characteristics of stratospheric air mass intrusions makes these events recognizable in air quality records, providing that the affected region has a fairly extensive monitoring network and that multiple air quality parameters (CO, VOC, PM, RH) are being measured as well.

Intermittent episodes of "natural" ozone from very large biomass fires in boreal forests (Alaska, Canada, Siberia) can produce short-lived pulses of ozone up to 0.020 ppm that may arrive during the North American ozone season. Present understanding suggests that these are infrequent events at latitudes below about 50N. There are no data documenting such an event in California. Long range transport of anthropogenic ozone may grow as Asian energy consumption increases the continent's NO_X emissions. Model studies indicate that the Asian ozone increment in North America could double over the next few decades. Assuming the temporal pattern of transport remains unchanged, such an impact could increase mean ozone concentrations by 0.002 to 0.006 ppm. The potential effect on peak transport events is unknown at this time.

2.5.3 Ozone Precursor Emissions

Ozone is an oxidant gas that forms photochemically in the atmosphere when nitrogen oxides (NO_X) and reactive organic gases (ROG) are present under appropriate atmospheric conditions (see Chapter 5). Carbon monoxide (CO) is also an ozone precursor. Both ROG and NO_X are emitted from mobile sources, point sources, and area-wide sources. ROG emissions from anthropogenic sources result primarily from incomplete fuel combustion, and from the evaporation of solvents and fuels, while NO_X and CO emissions result almost entirely from combustion processes.

2.5.4 Monitoring Method

Two measurement methods for ozone are approved for use in the U.S. by the USEPA: one is based on the chemiluminescence that occurs when ozone and ethylene react, and the other on the attenuation of ultraviolet (UV) radiation by ozone. The method based on UV spectrometry is almost universally used in practice. Specifications and

criteria for both methods exist in federal regulation. The UV photometry-based method is approved for use in California for state air quality standards. Both state and federal requirements are applied directly by the ARB and the air districts in the ozone monitoring network in California.

2.5.5 Exposure

During 2001 through 2003, neither the State nor federal 1-hour standard was exceeded in the Lake County Air Basin, North Coast Air Basin, or Northeast Plateau Air Basin. Data for four additional areas, Great Basin Valleys Air Basin, Lake Tahoe Air Basin, North Central Coast Air Basin, and the Upper Sacramento Valley show exceedances of the State standard, but not the federal 1-hour standard (as described earlier, representative data for the Northeast Plateau Air Basin and Great Basin Valleys Air Basin are available for 2002 and 2003 only). Both the State and federal 1-hour standards were exceeded during at least two of the three years in all other areas.

The highest 8-hour average values were found in the South Coast Air Basin and San Joaquin Valley Air Basin. Maximum 8-hour concentrations in the South Coast Air Basin ranged from 0.144 ppm to 0.153 ppm during 2001 through 2003, while maximum 8-hour concentrations in the San Joaquin Valley ranged from 0.120 ppm to 0.132 ppm during the same three-year period. Three other areas, the Mojave Desert Air Basin, the Sacramento Metro Area, and the Salton Sea Air Basin also had a maximum 8-hour concentration above 0.120 ppm during at least one of the three years.

With respect to the federal 8-hour ozone standard, Lake County Air Basin and North Coast Air Basin showed no exceedance days during 2001 through 2003. One area, the Lake Tahoe Air Basin, averaged only one exceedance day for the three-year period, while the North Central Coast Air Basin averaged three 8-hour exceedance days. In contrast, the San Joaquin Valley Air Basin showed the highest average number of exceedance days (123), followed by the South Coast Air Basin (99). The Sacramento Metro Area, Mojave Desert Air Basin, Mountain Counties Air Basin, and Salton Sea Air Basin each averaged between 42 and 68 exceedance days during 2001 through 2003. The remaining four areas averaged between 7 and 25 federal 8-hour exceedance days during the three-year period.

Californians' indoor and personal exposures to ozone are largely determined by the outdoor ozone concentrations in their community. Nonetheless, some Californians experience a substantial exposure to ozone indoors, due to the increasing use of certain types of appliances and equipment that emit ozone. Others, such as many children and those who are employed in outdoor occupations, may experience substantially greater exposures to ozone than the rest of the population, because they spend time outdoors during peak ozone periods.

2.5.6 Welfare Effects

A review of welfare effects, including effects of ozone on forest trees, agricultural crops, and materials is also discussed in this report (Chapter 8). Elevated concentrations of ozone can cause adverse effects on agricultural crops, forest trees and materials at current ambient levels, and the proposed health-based ozone standards should also provide protection to crops, forests and materials. In broad terms, impacts to crops are

generally more severe than for forest trees owing to their inherently more vigorous rates of growth. Discussed in the subsection on crops and the methods used to expose plants to ozone. This is followed by an examination of the physiological basis of ozone damage to plants, with special emphasis on carbon metabolism and the resulting impacts on crop growth and yield. Data collected since the 1950s on mixed conifer forests in the San Bernardino Mountains and the Sierra Nevada indicate that increasing numbers of ponderosa and Jeffrey pines exhibit ozone-specific needle damage due to the pollutant's cumulative effects. Also discussed are the impacts of ozone on materials, including building materials, rubber, paint, and fabrics. Although the proposed ozone standards are based on human health effects, progress toward attaining the proposed standards will provide welfare benefits.

2.5.7 Health Effects

Review of the controlled human exposure, animal toxicology and epidemiologic literature led to the following conclusions as to the health effects of ozone exposure:

1. The lowest ozone concentration at which reduced lung function and increased respiratory and ventilatory symptoms have been observed following 1-hour exposure is 0.12 ppm with moderate to heavy exercise.
2. The lowest ozone concentration at which increased airway hyperreactivity following 2-hour exposure has been reported is 0.18 ppm in exercising subjects.
3. The lowest ozone concentration at which airway inflammation following 2-hour exposure has been reported is 0.20 ppm ozone in exercising subjects
4. Reduced lung function, increased respiratory and ventilatory symptoms, increased airway hyperreactivity, and increased airway inflammation have been reported following 6.6- to 8-hour exposure to 0.08 ppm ozone.
5. Evidence from epidemiological studies of several health endpoints including premature death, hospitalization, respiratory symptoms, and restrictions in activity and lung function.
6. Evidence from epidemiological studies of emergency room visits for asthma suggests a possible threshold concentration between 0.075 and 0.11 ppm from analyses based on a 1-hour averaging time, and a possible threshold concentration between 0.070 and 0.10 ppm from analyses based on an 8-hour averaging time.
7. There is no evidence that children and infants respond to lower ozone concentrations than adults. Their risk is primarily related to their greater ventilation rate and greater exposure duration.
8. The dose-rate of ozone inhalation influences the magnitude of observed effects.

2.6 Summary of Recommendations

Following a detailed review of the scientific literature on the health and welfare effects of ozone, staff is proposing to revise the ambient air quality standard for ozone. The recommended ozone standards are based on scientific information about the health impacts associated with ozone exposure, recognizing the uncertainties in these data. The definition of California ambient air quality standards assumes a threshold below

which effects do not occur. However, the extremely wide range of individual responsiveness to ozone makes identification of a threshold on a population level somewhat problematic. In addition, the Children's Environmental Health Protection Act [Senate Bill 25, Escutia; Stats. 1999, Ch. 731, H&SC section 39606(d)(2)] requires a standard that "adequately protects the health of the public, including infants and children, with an adequate margin of safety." Recognizing the uncertainties in the database, staff makes the following recommendations.

1. Ozone will continue to be the pollutant addressed by the standard.

2. One-hour ambient air quality standard: staff recommends retaining the current 1-hour ozone standard at a concentration of **0.09 ppm**, not to be exceeded, based on several factors. First, at 0.12 ppm, in several studies 10 - 25% of the subjects experienced a decline of 10% of more in FEV1. In one study, these lung function changes were accompanied by increases in cough. At 0.24 ppm, increases were also observed in shortness of breath and pain on deep breath. These lung function and symptom outcomes have been demonstrated and replicated in several carefully controlled human exposure studies. The population at risk for these effects includes children and adults engaged in active outdoor exercise and workers engaged in physical labor outdoors. Thus, a margin of safety is necessary to account for variability in human responses. In addition, the chamber studies, by design, do not include potentially vulnerable populations (e.g., people with moderate to severe asthma, Chronic Obstructive Pulmonary Disease or COPD, and heart disease) who may be incorporated in the epidemiologic studies.

   Second, chamber studies indicate that bronchial responsiveness and pulmonary inflammation occur with 1-hour exposure to 0.18 to 0.20 ppm. Bronchial responsiveness can aggravate pre-existing chronic respiratory disease. The ultimate impact of the inflammatory response is unclear but repeated exposures to high ozone levels may result in restructuring of the airways, fibrosis, and possibly permanent respiratory injury. These latter outcomes are supported by animal toxicology studies, which also suggest the possibility of decreases in lung defense mechanisms.

   Third, epidemiological studies completed over the last 10 years indicate the potential for severe adverse health outcomes including premature death, hospitalizations, and emergency room visits. These studies include concentrations to which the public is currently being exposed. It is possible that some of these associations are due to relatively short-term exposures, for example less than two hours, since people at risk of experiencing these endpoints are unlikely to be engaged in multi-hour periods of moderate or heavy work or exercise outdoors. However, since there is high temporal correlation between 1-, 8-, and 24-hour average ozone concentrations, the averaging time of concern cannot be discerned from these studies.

   Viewing all of the evidence, staff recommends retention of the 1-hour standard of 0.09 ppm, not to be exceeded, as being protective of public health with an adequate margin of safety.

3. Eight-hour ambient air quality standard: We recommend establishing a new 8-hour average standard of **0.070 ppm**, not to be exceeded. Our recommendation for the 8-

hour standard is based primarily on the chamber studies that have been conducted over the last 15 years, supported by the important health outcomes reported in many of the epidemiologic studies. With exposure for 6.6 to 8-hours to an ozone concentration of 0.08 ppm, several studies have reported statistically significant group effects on lung function changes, ventilatory and respiratory symptoms, airway hyperresponsiveness, and airway inflammation in healthy, exercising individuals. A substantial fraction of subjects in these studies exhibited particularly marked responses in lung function and symptoms. Consequently, a concentration of 0.08 ppm ozone for an 8-hour averaging time can not be considered adequately protective of public health, and does not include any margin of safety, based on the definitions put forth in State law. The one published multi-hour study investigating a concentration below 0.08 ppm showed no statistically significant group mean decrement in lung function or symptoms at 0.04 ppm compared to a baseline of clear air. In addition, all individual subjects had changes in FEV1 of less than 10%. One unpublished multi-hour study at 0.06 ppm (Adams 1998) reported no statistically significant group mean changes, relative to clean air, in either lung function or symptoms including pain on deep inhalation and total symptom score. Therefore, staff has recommended an 8-hour concentration of 0.070 ppm. Many of the studies, and issues and concerns associated with the epidemiological studies listed above concerning the 1-hour standard are also relevant to the 8-hour standard. As discussed above, it may be that the health effects, often correlated with 1-hour exposures in the epidemiologic studies, are actually associated with 8-hour (or other) average exposures. Therefore, these epidemiologic findings were factored into the margin of safety for the 8-hour average.

It should be noted that the recommended 8-hour average concentration has three rather than two decimal places. Staff initially considered selection of 0.07 ppm. However, rounding conventions applied to air quality data (see Section 7.1.4) are such that any measured value up to and including 0.074 ppm would round down to 0.07 ppm. The available data suggested that selection of 0.07 ppm would not include an adequate margin of safety, as required by State law. The one available study at 0.06 ppm did not find a group mean effect. Staff is recommending that the 8 hour average standard have three decimal places, 0.070 ppm, to ensure an adequate margin of safety. Section 6.3 discusses issues related to precision and accuracy of the monitored data.

4. Monitoring method for ozone: Staff recommends retention of the current monitoring method for ozone which uses the ultraviolet (UV) absorption method for determining compliance with the state Ambient Air Quality Standard for ozone. Incorporate by reference all federally approved UV methods for ozone as California Approved Samplers for ozone. This will not change current air monitoring practices, but will align state monitoring requirements with federal requirements.

2.6.1 Consideration of Infants and Children

The Children's Environmental Health Protection Act [Health and Safety Code section 39606 (b)] requires that air pollution effects on children and infants be specifically considered in selection of ambient air quality standards. Children have a higher ventilation rate relative to body weight at rest and during activity than adults. Children

also tend to spend more time outside and be more active than adults. Consequently, virtue of their higher ventilation rates and outdoor behavior patterns, they are likely to inhale larger total doses of ozone than the general population. However, the chamber studies of exercising children suggest that they have responses generally similar to adults, pointing to a similar degree of responsiveness. Epidemiologic studies that have examined both children and adults do not show clear evidence for greater sensitivity in children. Studies in animals at high exposure concentrations (0.5 ppm and higher, 8 hrs/day for several consecutive days) indicate that developing lungs of infant animals are adversely affected by ozone. The recommended standards are well below that level of exposure. Two studies have shown evidence of lower lung function in young adults raised in high ozone areas (Kunzli et al. 1997; Galizia and Kinney 1999). The study by Kunzli et al. (1997) suggested that exposure to ozone prior to age 6 was associated with lower attained lung function. Examination of data for the Los Angeles basin from the early 1980s, show summer averages of the 1-hour maximum to be above 0.10 ppm. This is considerably above present levels and above the recommended 1-hour standard. There is also evidence that children who play three or more sports are at higher risk of developing asthma if they also live in high ozone communities in Southern California. This study needs to be repeated before the effect can be attributed to ozone exposure with greater certainty, but the finding is of concern. The warm season daily 8-hour maximum concentrations of ozone measured in these high ozone areas, over the four years of study, was 0.084 ppm. The proposed 8-hour standard of 0.070 ppm, therefore, should protect most children from asthma induction that may be associated with ozone exposure. Collectively, this body of evidence suggests that although children appear to be similarly responsive to a given dose of ozone as adults, they are at greater risk than adults of experiencing adverse responses to ozone by virtue of their higher level of outdoor activity, and consequently greater total exposure.

2.7 Estimated Health Benefits

It is estimated that attainment of the proposed ozone standards throughout California would avoid a significant number of adverse health effects each year, specifically:

- 580 (290 – 870, probable range) premature deaths for all ages.
- 3,800 (2,200 – 5,400, 95% confidence interval (CI)) hospitalizations due to respiratory diseases for all ages.
- 600 (360 – 850, 95% CI) emergency room visits for asthma for children under 18 years of age.
- 3.3 million (430,000 – 6,100,000, 95% CI) school absences for children 5 to 17 years of age.
- 2.8 million (1.2 million – 4.6 million, 95% CI) minor restricted activity days for adults above 18 years of age.

As discussed in Appendix B, there are a several important assumptions and uncertainties in this analysis. Some concern the study design, statistical methods, and choice of epidemiological studies used to develop the concentration-response (CR) functions used in the analysis. Few studies have investigated the shape of the CR function, or whether there is a population response threshold for health endpoints other

than emergency room visits for asthma. Further uncertainty is added by assumptions in the statewide exposure assessment. It should also be noted that since several health effects related to acute exposure, and effects of chronic ozone exposure, are not included in the estimates noted above, the health benefits associated with lowering ozone exposure are likely underestimated.

2.8 Public Outreach and Review

A draft Staff Report containing staff's preliminary findings was released to the public on June 21, 2004 titled, "Review of California Ambient Air Quality Standard for Ozone". Public outreach for the standard review involved dissemination of information through various outlets to include the public in the regulatory process. In an ongoing effort to include the public in the review of the ozone standard, the ARB and OEHHA integrated outreach into public meetings, workshop presentations, electronic "list serve" notification systems, and various web pages. Notification of release of the Staff Report, the schedule for public meetings and workshops, and invitations to submit comments on the Staff Report were made through the "list serve" notification system. Public workshops on the proposed ozone standard were held on July 14 – 16, 2004 in Sacramento, El Monte, and Fresno. An additional public workshop was held on August 24, 2004 in Sacramento.

Individuals or parties interested in signing up for an electronic e-mail "list serve" notification on the PM standards, as well as any air quality-related issue, may self-enroll at the following location: www.arb.ca.gov/listserv/aaqs/aaqs.htm. Additional information on the standards review process is also available at the ozone standards review schedule website at: www.arb.ca.gov/research/aaqs/ozone-rs/ozone-rs.htm.

2.9 Air Quality Advisory Committee Review

The Air Quality Advisory Committee, an external scientific peer review committee that was appointed by the President of the University of California, met January 11 and 12, 2005, in Berkeley, California to review the initial Staff Report and public comments, and to ensure that the scientific basis of the recommendations for the ozone standard are based upon sound scientific knowledge, methods, and practices. The AQAC held a public meeting, which provided time for oral public comments, and discussed their review of the draft Staff Report and the draft recommendations, and provided comments for improving the draft Staff Report. Final findings were received on February 24, 2005.

The AQAC determined that the staff recommendations were well founded on the scientific literature, and voted to endorse them. The Committee made suggestions for minor changes to the draft Staff Report to increase clarity, requested more detailed discussion of several topics, and inclusion of several additional scientific papers. The AQAC findings is included in this Initial Statement of Reasons as Appendix C, in Volume IV.

2.10 Environmental and Economic Impacts

The proposed ambient air quality standards are scientific in nature, and will in and of themselves have no environmental or economic impacts. Standards simply define clean air. Once adopted, local air pollution control or air quality management districts are

responsible for the adoption of rules and regulations to control emissions from stationary sources to assure their achievement and maintenance. The Board is responsible for adoption of emission standards for mobile sources. A number of different implementation measures are possible, and each could have its own environmental and/or economic impact. These impacts must be evaluated when the control measure is proposed. Any environmental or economic impacts associated with the imposition of future measures will be considered if and when specific measures are proposed.

2.11 Environmental Justice

State law defines environmental justice as the fair treatment of people of all races, cultures, and incomes with respect to the development, adoption, implementation, and enforcement of environmental laws, regulations, and policies (Senate Bill 115, Solis; Stats 1999, Ch. 690; Government Code §65040.12(c)). The Board established a framework for incorporating environmental justice into the ARB's programs consistent with the directives of State law (ARB, 2001). The policies developed apply to all communities in California, but recognize that environmental justice issues have been raised more in the context of low-income and minority communities, which sometimes experience higher exposures to some pollutants as a result of the cumulative impacts of air pollution from multiple mobile, commercial, industrial, areawide, and other sources.

Because ambient air quality standards simply define clean air, all of California's communities will benefit from the proposed health-based standards, as progress is made to attain the standards. Over the past twenty years, the ARB, local air districts, and federal air pollution control programs have made substantial progress towards improving the air quality in California. However, some communities continue to experience higher exposures than others as a result of the cumulative impacts of air pollution from multiple mobile and stationary sources and thus may suffer a disproportionate level of adverse health effects. Since the same ambient air quality standards apply to all regions of the State, these communities will benefit by a wider margin and receive a greater degree of health improvement from the revised standards than less affected communities, as progress is made to attain the standards. Moreover, just as all communities would benefit from new, stricter standards, alternatives to the proposed recommendations, such as not proposing an eight-hour ozone standard, would adversely affect many communities.

While it is possible that residents in environmental justice communities may be particularly sensitive to ozone, only one study investigated whether socioeconomic status (SES) alters responses to ozone exposure, and those results were difficult to explain. Hence, the study did not allow inferences as to whether socioeconomic status impacts on sensitivity to ozone. Moreover, other controlled studies investigating whether gender, ethnicity or environmental factors contribute to the responses to ozone exposure could not convincingly demonstrate a link with responsiveness. Therefore, the database is insufficient to conclude whether differences in ozone susceptibility exist in environmental justice communities. These studies are discussed in more detail in Section 9.6.8.

Once ambient air quality standards are adopted, the ARB and the local air districts will

propose emission standards and other control measures designed to result in a reduction of ambient ozone levels. The environmental justice aspects of each proposed control measure will be evaluated in a public forum at this time.

As additional relevant scientific evidence becomes available, the ozone standards will be reviewed again to make certain that the health of the public is protected with an adequate margin of safety.

2.12 References

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Appendix A

PROPOSED AMENDMENTS TO CALIFORNIA CODE OF REGULATIONS

AND

AIR MONITORING QUALITY ASSURANCE MANUAL VOLUME IV, PARTS A, B, & C (DOCUMENT INCORPORATED BY REFERENCE)

[PROPOSED] REGULATION ORDER

Section 70100. Definitions

~~(g) Oxidant. Oxidant is a substance that oxidizes a selected reagent that is not oxidizable by oxygen under ambient conditions. For the purposes of this section, oxidant includes ozone, organic peroxides, and peroxyacyl nitrates but not nitrogen dioxide. Atmospheric oxidant concentrations are to be measured with ozone as a surrogate by ultraviolet photometry, or by an equivalent method.~~

(g~~h~~) Carbon Monoxide ...

(h~~i~~) Sulfur Dioxide ...

(i~~j~~) Suspended Particulate Matter (PM10). Suspended particulate matter (PM10) refers to atmospheric particles, solid and liquid, except uncombined water as measured by a (PM10) sampler which collects 50 percent of all particles of 10 mm aerodynamic diameter and which collects a declining fraction of particles as their diameter increases and an increasing fraction of particles as their diameter decreases, reflecting the characteristics of lung deposition. ~~Suspended particulate matter (PM10) is to be measured by a California Approved Sampler (CAS) for PM10, for purposes of monitoring for compliance with the Suspended Particulate Matter (PM10) standards. Approved samplers, methods, and instruments are listed in Section 70100.1(a) below. A CAS for PM10 includes samplers, methods, or instruments determined by the Air Resources Board or the Executive Officer to produce equivalent results for PM10 with the Federal Reference Method (40 CFR, part 50, Appendix M, as published in 62 Fed. Reg. 38763, July 18, 1997).~~

(j~~k~~) Fine Suspended Particulate Matter (PM2.5). Fine suspended particulate matter (PM2.5) refers to suspended atmospheric particles solid and liquid, except uncombined water as measured by a PM2.5 sampler which collects 50 percent of all particles of 2.5 mm aerodynamic diameter and which collects a declining fraction of particles as their diameter increases and an increasing fraction of particles as their diameter decreases, reflecting the characteristics of lung deposition. ~~Fine suspended particulate matter (PM2.5) is to be measured by a California Approved Sampler (CAS) for PM2.5 for purposes of monitoring for compliance with the Fine Particulate Matter (PM2.5) standards. Approved samplers, methods, and instruments are listed in Section 70100.1(b) below. A CAS for PM2.5 includes samplers, method, and instruments determined by the Air Resources Board or the Executive Officer to produce equivalent results for PM2.5 with the Federal Reference Method (40 CFR, part 50, Appendix L, as published in 62 Fed. Reg. 38763, July 18, 1997).~~

(kl) Visibility Reducing Particles ...

(lm) Hydrogen Sulfide ...

(mn) Nitrogen Dioxide ...

(no) Lead (particulate) ...

(op) Sulfates ...

(pq) Vinyl Chloride ...

(qr) Ozone ...

(rs) Extinction Coefficient ...

Section 70100.1. Methods, Samplers, and Instruments for Measuring Pollutants.

a) PM10 Methods. The method for determining compliance with the PM10 ambient air quality standard shall be the Federal Reference Method for the Determination of Particulate Matter as PM10 in the Atmosphere (40 CFR, Chapter 1, part 50, Appendix M, as published in 62 Fed. Reg., 38753, July 18, 1997). California Approved Samplers for PM10 are set forth in "Air Monitoring Quality Assurance Manual Volume IV, Part A: Monitoring Methods for PM10", adopted [insert date], which is incorporated by reference herein. Samplers, methods, or instruments determined in writing by the Air Resources Board or the Executive Officer to produce equivalent results for PM10 shall also be California Approved Samplers for PM10. These include those continuous samplers that have been demonstrated to the satisfaction of the Air Resources Board to produce measurements equivalent to the Federal Reference Method. ~~The following samplers, methods, and instruments are California Approved Samplers for PM10 for the purposes of monitoring for compliance with the Suspended Particulate Matter (PM10) standards:~~

~~(1) The specific samplers approved are:~~

~~(A) Andersen Model RAAS10-100 PM10 Single Channel PM10 Sampler, U.S. EPA Manual Reference Method RFPS-0699-130, as published in 64 Fed. Reg., 33481, June 23, 1999.~~

~~(B) Andersen Model RAAS10-200 PM10 Single Channel PM10 Audit Sampler, U.S. EPA Manual Reference Method RFPS-0699-131, as published in 64 Fed. Reg., 33481, June 23, 1999.~~

~~(C) Andersen Model RAAS10-300 PM10 Multi Channel PM10 Sampler, U.S. EPA Manual Reference Method RFPS-0669-132, as published in 64 Fed. Reg., 33481, June 23, 1999.~~

~~(D) Sierra (currently known as Graseby) Andersen/GMW Model 1200 High Volume Air Sampler, U.S. EPA Manual Reference Method RFPS-1287-063, as published in 52 Fed. Reg., 45684, December 1, 1987 and in 53 Fed. Reg., 1062, January 15, 1988.~~

~~(E) Sierra (currently known as Graseby) Andersen/GMW Model 321B High Volume Air Sampler, U.S. EPA Manual Reference Method RFPS-1287-064, as published in 52 Fed. Reg., 45684, December 1, 1987 and in 53 Fed. Reg., 1062, January 15, 1988.~~

~~(F) Sierra (currently known as Graseby) Andersen/GMW Model 321-C High Volume Air Sampler, U.S. EPA Manual Reference Method RFPS-1287-065, as published in 52 Fed. Reg., 45684, December 1, 1987.~~

~~(G) BGI Incorporated Model PQ100 Air Sampler, U.S. EPA Manual Reference Method RFPS-1298-124, as published in 63 Fed. Reg., 69624, December 17, 1998.~~

~~(H) BGI Incorporated Model PQ200 Air Sampler, U.S. EPA Manual Reference Method RFPS-1298-125, as published in 63 Fed. Reg., 69624, December 17, 1998.~~

~~(I) Rupprecht & Patashnick Partisol Model 2000 Air Sampler, U.S. EPA Manual Reference Method RFPS-0694-098, as published in 59 Fed. Reg., 35338, July 11, 1994.~~

~~(J) Rupprecht & Patashnick Partisol-FRM Model 2000 PM10 Air Sampler, U.S. EPA Manual Reference Method RFPS-1298-126, as published in 63 Fed. Reg., 69625, December 17, 1998.~~

~~(K) Rupprecht & Patashnick Partisol Plus Model 2025 PM10 Sequential Air Sampler, U.S. EPA Manual Reference Method RFPS-1298-127, as published in 63 Fed. Reg., 69625, December 17, 1998.~~

~~(L) Tisch Environmental Model TE-6070 PM10 High Volume Air Sampler, U.S. EPA Manual Reference Method RFPS-0202-141, as published in 67 Fed. Reg., 15566, April 2, 2002.~~

~~(2) Continuous samplers:~~

~~(A) Andersen Beta Attenuation Monitor Model FH 62-C14 equipped with the following components: louvered PM10 inlet, volumetric flow controller, automatic filter change mechanism, automatic zero check, and calibration control foils kit*.~~

~~(B) Met One Beta Attenuation Monitor Model 1020 equipped with the following components: louvered PM10 size selective inlet, volumetric flow controller, automatic filter change mechanism, automatic heating system, automatic zero and span check capability*.~~

~~(C) Rupprecht & Patashnick Series 8500 Filter Dynamics Measurement System equipped with the following components: louvered PM10 size selective inlet, volumetric flow control, flow splitter (3 liter/min sample flow), sample equilibration system (SES) dryer, TEOM sensor unit, TEOM control unit, switching valve, purge filter conditioning unit, and palliflex TX40, 13 mm effective diameter cartridge*.~~

b) PM2.5 Methods. The method for determining compliance with the PM2.5 ambient air quality standard shall be the Federal Reference Method for the Determination of Particulate Matter as PM2.5 in the Atmosphere, 40 CFR, Chapter 1, part 50, Appendix L, as published in 62 Fed. Reg., 38714, July 18, 1997 and as amended in 64 Fed. Reg., 19717, April 22, 1999. The samplers listed in the Federal Reference Method must use either the WINS impactor or the U.S. EPA-approved very sharp cut cyclone (67 Fed. Reg., 15566, April 2, 2002) to separate PM2.5 from PM10. California Approved Samplers for PM2.5 are set forth in "Air Monitoring Quality Assurance Manual Volume IV, Part B: Monitoring

Methods for PM2.5", adopted [insert date], which is incorporated by reference herein. Samplers, methods, or instruments determined in writing by the Air Resources Board or the Executive Officer to produce equivalent results for PM2.5 shall also be California Approved Samplers for PM2.5. These include those continuous samplers that have been demonstrated to the satisfaction of the Air Resources Board to produce measurements equivalent to the Federal Reference Method. ~~The following samplers, methods, and instruments are California Approved Samplers for PM2.5 for the purposes of monitoring for compliance with the Fine Particulate Matter (PM2.5) standards:~~

~~(1) The specific samplers approved are:~~

~~(A) Andersen Model RAAS 2.5-200 PM2.5 Ambient Audit Air Sampler, U.S. EPA Manual Reference Method RFPS-0299-128, as published in 64 Fed. Reg., 12167, March 11, 1999.~~

~~(B) Graseby Andersen Model RAAS 2.5-100 PM2.5 Ambient Air Sampler, U.S. EPA Manual Reference Method RFPS-0598-119, as published in 63 Fed. Reg., 31991, June 11, 1998.~~

~~(C) Graseby Andersen Model RAAS 2.5-300 PM2.5 Sequential Ambient Air Sampler, U.S. EPA Manual Reference Method RFPS-0598-120, as published in 63 Fed. Reg., 31991, June 11, 1998.~~

~~(D) BGI Inc. Models PQ200 and PQ200A PM2.5 Ambient Fine Particle Sampler, U.S. EPA Manual Reference Method RFPS-0498-116, as published in 63 Fed. Reg., 18911, April 16, 1998.~~

~~(E) Rupprecht & Patashnick Partisol FRM Model 2000 Air Sampler, U.S. EPA Manual Reference Method RFPS-0498-117, as published in 63 Fed. Reg., 18911, April 16, 1998.~~

~~(F) Rupprecht & Patashnick Partisol Model 2000 PM 2.5 Audit Sampler, as described in U.S. EPA Manual Reference Method RFPS-0499-129, as published in 64 Fed. Reg., 19153, April 19, 1999.~~

~~(G) Rupprecht & Patashnick Partisol Plus Model 2025 PM 2.5 Sequential Air Sampler, U.S. EPA Manual Reference Method RFPS-0498-118, as published in 63 Fed. Reg., 18911, April 16, 1998.~~

(H) Thermo Environmental Instruments, Incorporated Model 605 "CAPS" Sampler, U.S. EPA Manual Reference Method RFPS-1098-123, as published in 63 Fed. Reg., 58036, October 29, 1998.

(I) URG-MASS100 Single PM2.5 FRM Sampler, U.S. EPA Manual Reference Method RFPS-0400-135, as published in 65 Fed. Reg., 26603, May 8, 2000.

(J) URG-MASS300 Sequential PM2.5 FRM Sampler, U.S. EPA Manual Reference Method RFPS-0400-136, as published in 65 Fed. Reg., 26603, May 8, 2000.

(K) BGI Inc. Model PQ200 VSCC PM2.5 Sampler, U.S. EPA Manual Equivalent Method EQPM-0202-142, as published in 67 Fed. Reg., 15567, April 2, 2002.

(L) BGI Inc. Model PQ200A VSCC PM2.5 Sampler, U.S. EPA Manual Equivalent Method EQPM-0202-142, as published in 67 Fed. Reg., 15567, April 2, 2002.

(M) Rupprecht & Patashnick Partisol FRM Model 2000 PM2.5 FEM Air Sampler, U.S. EPA Manual Equivalent Method EQPM-0202-143, as published in 67 Fed. Reg., 15567, April 2, 2002.

(N) Rupprecht & Patashnick Partisol Model 2000 PM2.5 FEM Audit Sampler, U.S. EPA Manual Equivalent Method EQPM-0202-144, as published in 67 Fed. Reg., 15567, April 2, 2002.

(O) Rupprecht & Patashnick Partisol Plus Model 2025 PM-2.5 FEM Sequential Sampler, U.S. EPA Manual Equivalent Method EQPM-0202-145, as published in 67 Fed. Reg., 15567, April 2, 2002.

(2) Continuous samplers:

(A) Andersen Beta Attenuation Monitor Model FH 62 C14 equipped with the following components: louvered PM10 size selective inlet, very sharp cut or

~~sharp-cut cyclone, volumetric flow controller, automatic filter change mechanism, automatic zero check, and calibration control foils kit*.~~

~~(B) Met One Beta Attenuation Monitor Model 1020 equipped with the following components: louvered PM10 size selective inlet, very sharp cut or sharp cut cyclone, volumetric flow controller, automatic filter change mechanism, automatic heating system, and automatic zero and span check capability*.~~

~~(C) Rupprecht & Patashnick Series 8500 Filter Dynamics Measurement System equipped with the following components: louvered PM10 size selective inlet, very sharp cut or sharp cut cyclone, volumetric flow control, flow splitter (3 liter/min sample flow), sample equilibration system (SES) dryer, TEOM sensor unit, TEOM control unit, switching valve, purge filter conditioning unit, and palliflex TX40, 13 mm effective diameter cartridge*.~~

~~*Instrument shall be operated in accordance with the vendor's instrument operation manual that adheres to the principles and practices of quality control and quality assurance as specified in Volume I of the "Air Monitoring Quality Assurance Manual", as printed on April 17, 2002, and available from the California Air Resources Board, Monitoring and Laboratory Division, P.O. Box 2815, Sacramento CA 95814, incorporated by reference herein.~~

(c) Ozone Methods. The method for determining compliance with the ozone ambient air quality standard shall be the Federal Equivalent Method for the Determination of Ozone in the Atmosphere (40 CFR, part 53). California Approved Samplers for ozone are set forth in "Air Monitoring Quality Assurance Manual Volume IV, Part C: Monitoring Methods for Ozone", as adopted [insert date]. Samplers, methods, or instruments determined in writing by the Air Resources Board or the Executive Officer to produce equivalent results for ozone shall also be California Approved Samplers for ozone.

NOTE

Authority cited: Sections 39600, 39601 and 39606, Health and Safety Code. Reference: Sections 39014, 39606, 39701 and 39703(f), Health and Safety Code.

Section 70200. Table of Standards ***

Substance	Concentration and Methods*	Duration of Averaging Periods	Most Relevant Effects	Comments
Ozone	0.09 ppm**	1 hour	a. Short-term exposures: (1) ~~Pulmonary function decrements and localized lung edema in humans and animals.~~ One-hour and multi-hour exposures: lung function decrements, and symptoms of respiratory irritation such as cough, wheeze, and pain upon deep inhalation. (2) Multi-hour exposures: airway hyperreactivity and airway inflammation. ~~(2) Risk to public health implied by alterations in pulmonary morphology and host defence in animals.~~ (3) excess deaths, hospitalization, emergency room visits, asthma exacerbation, respiratory symptoms and restrictions in activity	a. The standard is intended to prevent adverse human health effects.
	0.070 ppm**	8 hour		
	ultraviolet photometry using California Approved Sampler as set forth in section 70100.1 (c)		b. Long-term exposures: ~~Risk to public health implied by altered pulmonary morphology in animals after long-term exposures and pulmonary function decrements in chronically exposed humans.~~ Ozone can induce tissue changes in the respiratory tract, and is associated with decreased lung function and emergency room visits for asthma.	b. The standard, when achieved, will not prevent all injury to crops and other types of vegetation, but is intended to place an acceptable upper limit on the amount of yield and economic loss, as well as on adverse environmental impacts.
			c. Welfare effects: (1) Yield loss in important crops and predicted economic loss to growers and consumers. (2) Injury and damage to forests ~~native plants and potential changes in species diversity and~~ number. ~~(3) Damage to rubber and elastomers and to paints, fabric, dyes, pigments, and plastics.~~	

Suspended Particulate Matter (PM10)	50 µg/m^3 PM10** 20 µg/m^3 PM10** using California Approved Sampler as set forth in section 70100.1(a)	24 hour sample 24 hour samples, annual arithmetic mean	Prevention of excess deaths, illness and restrictions in activity from short-and long-term exposures. Illness outcomes include, but are not limited to, respiratory symptoms, bronchitis, asthma exacerbation, emergency room visits and hospital admissions for cardiac and respiratory diseases. Sensitive subpopulations include children, the elderly, and individuals with pre-existing cardiopulmonary disease.	This standard applies to suspended mater as measured by PM10 sampler, which collects 50% of all particles of 10 µm aerodynamic diameter and collects a declining fraction of particles as their diameter increases, reflecting the characteristics of lung deposition.

* The list of California Approved Samplers may be obtained from the Air Resources Board, Monitoring and Laboratory Division, P.O. Box 2815, Sacramento, CA 95814. Any equivalent procedure which can be shown to the satisfaction of the Air Resources Board to give equivalent results at or near the level of the air quality standard may be used.

** These standards are violated when concentrations exceed those set forth in the body of the regulation. All other standards are violated when concentrations equal or exceed those set forth in the body of the regulation.

*** Applicable statewide unless otherwise noted.

****These standards are violated when particle concentrations cause measured light extinction values to exceed those set forth in the regulations.

NOTE

Authority cited: Sections 39600, 39601(a) and 39606, Health and Safety Code. Reference: Sections 39014, 39606, 39701 and 39703(f), Health and Safety Code; and Western Oil and Gas Ass'n v. Air Resources Bd. (1984) 37 Cal.3d 502.

HISTORY

1. Amendment filed 9-18-89; operative 10-18-89 (Register 89, No. 39). For prior history, see Register 88, No. 27.
2. Amendment filed 6-29-92; operative 7-29-92 (Register 92, No. 27).
3. Amendment filed 6-5-2003; operative 7-5-2003 (Register 2003, No. 23).

(1) The method for determining compliance with the State PM10 ambient air quality standard shall be the Federal Reference Method (FRM) for the Determination of Particulate Matter as PM10 in the Atmosphere (40 CFR, Chapter 1, part 50, Appendix M, as published in 62 Fed. Reg., 38753, July 18, 1997). When employed according to the FRM, the following are California Approved Samplers:

(A) Andersen Model RAAS10-100 PM10 Single Channel PM10 Sampler, U.S. EPA Manual Reference Method RFPS-0699-130, as published in 64 Fed. Reg., 33481, June 23, 1999.

(B) Andersen Model RAAS10-200 PM10 Single Channel PM10 Audit Sampler, U.S. EPA Manual Reference Method RFPS-0699-131, as published in 64 Fed. Reg., 33481, June 23, 1999.

(C) Andersen Model RAAS10-300 PM10 Multi Channel PM10 Sampler, U.S. EPA Manual Reference Method RFPS-0669-132, as published in 64 Fed. Reg., 33481, June 23, 1999.

(D) Sierra (currently known as Graseby) Andersen/GMW Model 1200 High-Volume Air Sampler, U.S. EPA Manual Reference Method RFPS-1287-063, as published in 52 Fed. Reg., 45684, December 1, 1987 and in 53 Fed. Reg., 1062, January 15, 1988.

(E) Sierra (currently known as Graseby) Andersen/GMW Model 321B High-Volume Air Sampler, U.S. EPA Manual Reference Method RFPS-1287-064, as published in 52 Fed. Reg., 45684, December 1, 1987 and in 53 Fed. Reg., 1062, January 15, 1988.

(F) Sierra (currently known as Graseby) Andersen/GMW Model 321-C High-Volume Air Sampler, U.S. EPA Manual Reference Method RFPS-1287-065, as published in 52 Fed. Reg., 45684, December 1, 1987.

(G) BGI Incorporated Model PQ100 Air Sampler, U.S. EPA Manual Reference Method RFPS-1298-124, as published in 63 Fed. Reg., 69624, December 17, 1998.

(H) BGI Incorporated Model PQ200 Air Sampler, U.S. EPA Manual Reference Method RFPS-1298-125, as published in 63 Fed. Reg., 69624, December 17, 1998.

(I) Rupprecht & Patashnick Partisol Model 2000 Air Sampler, U.S. EPA Manual Reference Method RFPS-0694-098, as published in 59 Fed. Reg., 35338, July 11, 1994.

(J) Rupprecht & Patashnick Partisol-FRM Model 2000 PM10 Air Sampler, U.S. EPA Manual Reference Method RFPS-1298-126, as published in 63 Fed. Reg., 69625, December 17, 1998.

(K) Rupprecht & Patashnick Partisol-Plus Model 2025 PM10 Sequential Air Sampler, U.S. EPA Manual Reference Method RFPS-1298-127, as published in 63 Fed. Reg., 69625, December 17, 1998.

(L) Tisch Environmental Model TE-6070 PM10 High-Volume Air Sampler, U.S. EPA Manual Reference Method RFPS-0202-141, as published in 67 Fed. Reg., 15566, April 2, 2002.

(2) The following continuous Californian Approved Samplers have been demonstrated to the satisfaction of the Air Resources Board to produce measurements equivalent to the FRM:

(A) Andersen Beta Attenuation Monitor Model FH 62 C14 equipped with the following components: louvered PM10 inlet, volumetric flow controller, automatic filter change mechanism, automatic zero check, and calibration control foils kit*.

(B) Met One Beta Attenuation Monitor Model 1020 equipped with the following components: louvered PM10 size selective inlet, volumetric flow controller, automatic filter change mechanism, automatic heating system, automatic zero and span check capability*.

(C) Rupprecht & Patashnick Series 8500 Filter Dynamics Measurement System equipped with the following components: louvered PM10 size selective inlet, volumetric flow control, flow splitter (3 liter/min sample flow), sample equilibration system (SES) dryer, TEOM sensor unit, TEOM control unit, switching valve, purge filter conditioning unit, and palliflex TX40, 13 mm effective diameter cartridge*.

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*Instrument shall be operated in accordance with the vendor's instrument operation manual that adheres to the principles and practices of quality control and quality assurance as specified in Volume I of the "Air Monitoring Quality Assurance Manual", as printed on April 17, 2002, and available from the California Air Resources Board, Monitoring and Laboratory Division, P.O. Box 2815, Sacramento CA 95814, incorporated by reference herein.

(1) The method for determining compliance with the State PM2.5 ambient air quality standard shall be the Federal Reference Method (FRM) for the Determination of Particulate Matter as PM2.5 in the Atmosphere, 40 CFR, part 50, Appendix L, as published in 62 Fed. Reg., 38714, July 18, 1997 and as amended in 64 Fed. Reg., 19717, April 22, 1999. These must use either the WINS impactor or the U.S. EPA-approved very sharp cut cyclone (67 Fed. Reg., 15566, April 2, 2002) to separate PM2.5 from PM10. When employed according to the FRM, the following are California Approved Samplers:

(A) Andersen Model RAAS 2.5-200 PM2.5 Ambient Audit Air Sampler, U.S. EPA Manual Reference Method RFPS-0299-128, as published in 64 Fed. Reg., 12167, March 11, 1999.

(B) Graseby Andersen Model RAAS 2.5-100 PM2.5 Ambient Air Sampler, U.S. EPA Manual Reference Method RFPS-0598-119, as published in 63 Fed. Reg., 31991, June 11, 1998.

(C) Graseby Andersen Model RAAS 2.5-300 PM2.5 Sequential Ambient Air Sampler, U.S. EPA Manual Reference Method RFPS-0598-120, as published in 63 Fed. Reg., 31991, June 11, 1998.

(D) BGI Inc. Models PQ200 and PQ200A PM2.5 Ambient Fine Particle Sampler, U.S. EPA Manual Reference Method RFPS-0498-116, as published in 63 Fed. Reg., 18911, April 16, 1998.

(E) Rupprecht & Patashnick Partisol-FRM Model 2000 Air Sampler, U.S. EPA Manual Reference Method RFPS-0498-117, as published in 63 Fed. Reg., 18911, April 16, 1998.

(F) Rupprecht & Patashnick Partisol Model 2000 PM-2.5 Audit Sampler, as described in U.S. EPA Manual Reference Method RFPS-0499-129, as published in 64 Fed. Reg., 19153, April 19, 1999.

(G) Rupprecht & Patashnick Partisol-Plus Model 2025 PM-2.5 Sequential Air Sampler, U.S. EPA Manual Reference Method RFPS-0498-118, as published in 63 Fed. Reg., 18911, April 16, 1998.

(H) Thermo Environmental Instruments, Incorporated Model 605 "CAPS" Sampler, U.S. EPA Manual Reference Method RFPS-1098-123, as published in 63 Fed. Reg., 58036, October 29, 1998.

(I) URG-MASS100 Single PM2.5 FRM Sampler, U.S. EPA Manual Reference Method RFPS-0400-135, as published in 65 Fed. Reg., 26603, May 8, 2000.

(J) URG-MASS300 Sequential PM2.5 FRM Sampler, U.S. EPA Manual Reference Method RFPS-0400-136, as published in 65 Fed. Reg., 26603, May 8, 2000.

(K) BGI Inc. Model PQ200-VSCC PM2.5 Sampler, U.S. EPA Manual Equivalent Method EQPM-0202-142, as published in 67 Fed. Reg., 15567, April 2, 2002.

(L) BGI Inc. Model PQ200A-VSCC PM2.5 Sampler, U.S. EPA Manual Equivalent Method EQPM-0202-142, as published in 67 Fed. Reg., 15567, April 2, 2002.

(M) Rupprecht & Patashnick Partisol-FRM Model 2000 PM2.5 FEM Air Sampler, U.S. EPA Manual Equivalent Method EQPM-0202-143, as published in 67 Fed. Reg., 15567, April 2, 2002.

(N) Rupprecht & Patashnick Partisol Model 2000 PM2.5 FEM Audit Sampler, U.S. EPA Manual Equivalent Method EQPM-0202-144, as published in 67 Fed. Reg., 15567, April 2, 2002.

(O) Rupprecht & Patashnick Partisol-Plus Model 2025 PM-2.5 FEM Sequential Sampler, U.S. EPA Manual Equivalent Method EQPM-0202-145, as published in 67 Fed. Reg., 15567, April 2, 2002.

(2) The following continuous samplers have been demonstrated to the satisfaction of the Air Resources Board to produce measurements equivalent to the FRM:

(A) Andersen Beta Attenuation Monitor Model FH 62 C14 equipped with the following components: louvered PM10 size selective inlet, very sharp cut or sharp cut cyclone, volumetric flow controller, automatic filter change mechanism, automatic zero check, and calibration control foils kit*.

(B) Met One Beta Attenuation Monitor Model 1020 equipped with the following components: louvered PM10 size selective inlet, very sharp cut or sharp cut cyclone, volumetric flow controller, automatic filter change mechanism, automatic heating system, and automatic zero and span check capability*.

(C) Rupprecht & Patashnick Series 8500 Filter Dynamics Measurement System equipped with the following components: louvered PM10 size selective inlet, very sharp cut or sharp cut cyclone, volumetric flow control, flow splitter (3 liter/min sample flow), sample equilibration system (SES) dryer, TEOM sensor unit, TEOM control unit, switching valve, purge filter conditioning unit, and palliflex TX40, 13 mm effective diameter cartridge*.

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*Instrument shall be operated in accordance with the vendor's instrument operation manual that adheres to the principles and practices of quality control and quality assurance as specified in Volume I of the "Air Monitoring Quality Assurance Manual", as printed on April 17, 2002, and available from the California Air Resources Board, Monitoring and Laboratory Division, P.O. Box 2815, Sacramento CA 95814, incorporated by reference herein.

Part C: Monitoring Methods for Ozone

The method for determining compliance with the State ozone ambient air quality standard shall be the Federal Equivalent Method (FEM) for the Determination of Ozone in the Atmosphere (40 CFR, part 53). The FEM (ultraviolet photometry) is considered equivalent to the Federal Reference Method (chemiluminescence) as described in 40 CFR, Chapter 1, Part 50, Appendix D as published in FR 62, 38895, July 18, 1997. When employed according to the FEM (40 CFR, part 53), the following are California Approved Samplers:

(A) Dasibi Models 1003-AH, 1003-PC, or 1003-RS Ozone Analyzers, USEPA Automated Equivalent Method EQOA-0577-019, as published in FR 42, 28571, June 03, 1977.

(B) Dasibi Models 1008-AH, 1008-PC, or 1008-RS Ozone Analyzers, USEPA Automated Equivalent Method EQOA-0383-056, as published in FR 48, 10126, March 10, 1983.

(C) DKK-TOA Corp. Model GUX-113E Ozone Analyzer, USEPA Automated Equivalent Method EQOA-0200-134, as published in FR 65, 11308, March 02, 2000.

(D) Environics Series 300 Ozone Analyzer, USEPA Automated Equivalent Method EQOA-0990-078, as published in FR 55, 38386, September 18, 1990.

(E) Environnement S.A. Model $O_3$41M UV Ozone Analyzer, USEPA Automated Equivalent Method EQOA-0895-105, as published in FR 60, 39382, August 02, 1995.

(F) Environnement S.A. Model $O_3$42M UV Ozone Analyzer, USEPA Automated Equivalent Method EQOA-0206-148, as published in FR 67, 42557, June 24, 2002.

(G) Environnement S.A. SANOA Multigas Longpath Monitoring System, USEPA Automated Equivalent Method EQOA-0400-137, as published in FR 65, 26603, May 08, 2000.

(H) Horiba Instruments Models APOA-360 and APOA-360-CE Ozone Monitor, USEPA Automated Equivalent Method EQOA-0196-112, as published in FR 61, 11404, March 20, 1996.

(I) Monitor Labs/Lear Siegler Model 8810 Ozone Analyzer, USEPA Automated Equivalent Method EQOA-0881-053, as published in FR 46, 52224, October 26, 1981.

(J) Monitor Labs/Lear Siegler Models ML9810, ML9811, or ML9812, Monitors Labs Model ML9810B, or Wedding & Associates Model 1010 Ozone Analyzers, USEPA Automated Equivalent Method EQOA-0193-091, as published in FR 58, 6964, February 03, 1993.

(K) Opsis Model AR 500 and System 300 Open Path Ambient Air Monitoring Systems for Ozone, USEPA Automated Equivalent Method EQOA-0495-103, as published in FR 60, 21518, May 02, 1995.

(L) PCI Ozone Corporation Model LC-12 Ozone Analyzer, USEPA Automated Equivalent Method EQOA-0382-055, as published in FR 47, 13572, March 31, 1982.

(M) Philips PW9771 O3 Analyzer, USEPA Automated Equivalent Method EQOA-0777-023, as published in FR 42, 38931, August 01, 1977; FR 42, 57156, November 01, 1977.

(N) Teledyne-Advanced Pollution Instrumentation, Inc. Model 400E Ozone Analyzer, Advanced Pollution Instrumentation, Inc. Model 400/400A Ozone Analyzer, USEPA Automated Equivalent Method EQOA-0992-087, as published in FR 57, 44565, September 28; 1992, FR 63, 31992, June 11, 1998; FR 67, 57811, September 12, 2002.

(O) Thermo Electron/Thermo Environmental Instruments Models 49, 49C, USEPA Automated Equivalent Method EQOA-0880-047, as published in FR 45, 57168, August 27, 1980

PROPOSITION 65 STATUS REPORT SAFE HARBOR LEVELS:

No Significant Risk Levels for Carcinogens and Maximum Allowable Dose Levels for Chemicals Causing Reproductive Toxicity

September 2003

Reproductive and Cancer Hazard Assessment Section
Office of Environmental Health Hazard Assessment
California Environmental Protection Agency

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Proposition 65 Safe Harbor Levels Development

The Office of Environmental Health Hazard Assessment (OEHHA) of the California Environmental Protection Agency is the lead agency for the implementation of the Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65 or the Act). In that role, OEHHA has developed Proposition 65 safe harbor levels -- no significant risk levels (NSRLs) for carcinogens and maximum allowable dose levels (MADLs) for chemicals that cause reproductive toxicity. The NSRL is the daily intake level calculated to result in one excess case of cancer in an exposed population of 100,000, assuming lifetime (70-year) exposure at the level in question. The MADL is the level at which the chemical would have no observable adverse reproductive effect assuming exposure at 1,000 times that level. The NSRLs and MADLs are promulgated in Title 22, California Code of Regulations, (CCR) Sections 12705 and 12805 respectively to assist interested parties in determining whether warnings are required for exposures to listed chemicals, and whether discharges to sources of drinking water are prohibited.

Safe harbor levels may be based on risk assessments conducted outside OEHHA, as provided for in 22 CCR 12705(b), 12705(c), and 12805. In some cases, this can expedite safe harbor development. However, it should be noted that the process of review and consideration of existing risk assessments can be a lengthy one, and will depend on the complexity of the scientific information underlying the assessment, as well as on available resources.

This document provides the status of the development and adoption of intake levels calculated for all chemicals on the Proposition 65 list. In units of micrograms per day (µg/day), Part A reports NSRLs adopted in regulation for carcinogens and Part B reports MADLs adopted in regulation for chemicals that cause reproductive toxicity.

Parts C and D of this document give priority levels for development of dose response assessments for chemicals that cause cancer and reproductive toxicity, respectively. Interested parties are invited to recommend changes in priority levels. OEHHA retains the right to change priorities in response to the nature and availability of scientific information, and resources available, and requests from the public and the Attorney General's office.

Parts C and D also give draft levels, some of which have been available since the early 1990's and others of which have been updated recently. OEHHA will continue to review the basis for draft numbers and update analyses as needed, before proposing or finalizing levels for formal adoption in regulation.

This status report will be updated on a regular basis.

A. No Significant Risk Levels (NSRLs) Adopted in Regulation for Carcinogens

The table below lists NSRLs for Proposition 65 carcinogens in regulation (22 CCR §12705 and §12709). These levels are intended to provide "safe harbors" for persons subject to the Act, and do not preclude the use of alternative levels that can be demonstrated by their users as being scientifically valid.

A three-tiered procedure for development of NSRLs is currently in place. NSRLs may be based on a *de novo* dose response assessment conducted or reviewed by OEHHA (22 CCR §12705(b)), an assessment conducted by another state or federal agency (22 CCR §12705(c)), or an expedited process conducted by OEHHA (22 CCR §12705(d)). The last column of the table below indicates which of these processes was used to develop the NSRL for each chemical. NSRLs represent the daily intake level calculated to result in a cancer risk of one excess case of cancer in 100,000 individuals exposed over a 70-year lifetime.

NSRLs for chemicals in underline have been adopted since the last Status Report. As chemicals are removed from the Proposition 65 list, the regulatory process to remove the safe harbor level from regulation will be initiated.

Carcinogen	Level (µg/day)	22 CCR Section
A-alpha-C (2-Amino-9H-pyrido[2,3-b]indole)	2	12705(d)
Acetaldehyde	90 (inhalation)	12705(c)
Acetamide	10	12705(d)
2-Acetylaminofluorene	0.2	12705(d)
Acrylamide	0.2	12705(c)
Acrylonitrile	0.7	12705(b)
Actinomycin D	0.00008	12705(d)
AF-2; [2-(2-furyl)-3(5-nitro-2-furyl)acrylamide]	3	12705(d)
Aldrin	0.04	12705(b)
2-Aminoanthraquinone	20	12705(d)
o-Aminoazotoluene	0.2	12705(d)
4-Aminobiphenyl	0.03	12705(d)
3-Amino-9-ethylcarbazole hydrochloride	9	12705(d)
1-Amino-2-methylanthraquinone	5	12705(d)
2-Amino-5-(5-nitro-2-furyl)-1,3,4-thiadiazole	0.04	12705(d)
Amitrole	0.7	12705(d)
Aniline	100	12705(c)
o-Anisidine	5	12705(d)
o-Anisidine hydrochloride	7	12705(d)
Aramits	20	12705(d)
Arsenic	0.06 (inh) 10 (except inh)	12705(b) 12709
Asbestos NSRL for fibers ≥ 5 micrometers (mm) long and 0.3 wide, with a length/width ratio ≥ 3:1 as measured by phase contrast microscopy.	100 fibers/day (inh)	12705(b)
Auramine	0.8	12705(d)

Carcinogen	Level (µg/day)	22 CCR Section
Azaserine	0.06	12705(d)
Azathioprine	0.4	12705(d)
Azobenzene	6	12705(c)
Benzene	7	12705(b)
Benzidine	0.001	12705(b)
Benzofuran	1.1	12705(b)
Benzo[a]pyrene	0.06	12705(c)
Benzyl chloride	4	12705(c)
Benzyl violet 4B	30	12705(d)
Beryllium	0.1	12709
Beryllium oxide	0.1	12705(c)
Beryllium sulfate	0.0002	12705(c)
Bis(2-chloroethyl)ether	0.3	12705(b)
Bis(chloromethyl)ether	0.02	12705(b)
Bromodichloromethane	5	12705(c)
1,3-Butadiene	0.4	12705(c)
Butylated hydroxyanisole	4000	12705(b)
beta-Butyrolactone	0.7	12705(d)
Cadmium	0.05 (inh)	12705(b)
Captafol	5	12705(d)
Captan	300	12705(d)
Carbazole	4.1	12705(d)
Carbon tetrachloride	5	12705(b)
N-Carboxymethyl-N-nitrosourea	0.70	12705(b)
Chlorambucil	0.002	12705(d)
Chlordane	0.5	12705(c)
Chlordecone (Kepone)	0.04	12705(d)
Chlorendic acid	8	12705(d)
Chlorinated paraffins (Ave. chain length C12; approx. 60% chlorine by weight)	8	12705(d)
Chloroethane (Ethyl chloride)	150	12705(b)
Chloroform	20 (oral)	12705(c)
	40 (inh)	12705(c)
Chloromethyl methyl ether (technical grade)	0.3	12705(d)
3-Chloro-2-methylpropene	5	12705(d)
4-Chloro-ortho-phenylenediamine	40	12705(d)
Chlorothalonil	200	12705(d)
p-Chloro-ortho-toluidine	3	12705(d)
p-Chloro-*o*-toluidine, hydrochloride	3.3	12705(d)
Chlorozotocin	0.003	12705(d)
Chromium (hexavalent)	0.001 (inh)	12705(b)
C.I. Basic Red 9 monohydrochloride	3	12705(d)
Cinnamyl anthranilate	200	12705(d)
Coke oven emissions	0.3	12705(c)
p-Cresidine	5	12705(d)
Cupferron	3	12705(d)
Cyclophosphamide (anhydrous)	1	12705(d)
Cyclophosphamide (hydrated)	1	12705(d)

Carcinogen	Level (µg/day)	22 CCR Section
D&C Red No. 9	100	12705(d)
Dacarbazine	0.01	12705(d)
Daminozide	40	12705(d)
Dantron (Chrysazin; 1,8-Dihydroxyanthraquinone)	9	12705(d)
DDT, DDE, DDD (in combination)	2	12705(b)
DDVP (Dichlorvos)	2	12705(c)
2,4-Diaminoanisole	30	12705(d)
2,4-Diaminoanisole sulfate	50	12705(d)
4,4'-Diaminodiphenyl ether (4,4'-Oxydianiline)	5	12705(d)
2,4-Diaminotoluene	0.2	12705(d)
Dibenz[a,h]anthracene	0.2	12705(d)
1,2-Dibromo-3-chloropropane	0.1	12705(b)
p-Dichlorobenzene	20	12705(b)
3,3'-Dichlorobenzidine	0.6	12705(b)
1,1-Dichloroethane	100	12705(d)
1,2-Dichloroethane (Ethylene dichloride)	10	12705(b)
Dichloromethane (Methylene chloride)	200 (inh)	12705(b)
Dieldrin	50	12705(c)
Di(2-ethylhexyl)phthalate (DEHP)	0.04	12705(b)
Diethylstilbesterol	310	12705(b)
Diglycidyl resorcinol ether (DGRE)	0.002	12705(d)
Dihydrosafrole	0.4	12705(d)
3,3'-Dimethoxybenzidine (o-Dianisidine)	20	12705(d)
3,3'-Dimethoxybenzidine dihydrochloride	0.15	12705(b)
4-Dimethylaminoazobenzene	0.19	12705(b)
trans-2-[(Dimethylamino)methylimino]-5-[2-(5-nitro-2-furyl)vinyl]-1,3,4-oxadiazole	0.2	12705(d)
7,12-Dimethylbenz(a)anthracene	2	12705(d)
3,3'-Dimethylbenzidine (o-Toluidine)	0.003	12705(d)
3,3'-Dimethylbenzidine dihydrochloride	0.044	12705(b)
Dimethylcarbamoyl chloride	0.059	12705(b)
1,2-Dimethylhydrazine	0.05	12705(d)
Dimethylvinylchloride	0.001	12705(d)
2,4-Dinitrotoluene	20	12705(d)
1,4-Dioxane	2	12705(c)
Direct Black 38 (technical grade)	30	12705(b)
Direct Blue 6 (technical grade)	0.09	12705(d)
Direct Brown 95 (technical grade)	0.09	12705(d)
Disperse Blue 1	0.1	12705(d)
Epichlorohydrin	200	12705(d)
Estradiol 17b	9	12705(b)
Ethyl-4,4'-dichlorobenzilate (Chlorobenzilate)	0.02	12705(d)
Ethylene dibromide	7	12705(d)
Ethylene oxide	0.2 (oral)	12705(b)
Ethylene thiourea	3 (inh)	12705(b)
Ethyleneimine	2	12705(b)
Folpet	20	12705(d)
	0.01	12705(d)
	200	12705(c)

Carcinogen	Level (µg/day)	22 CCR Section
Formaldehyde (gas)	40	12705(c)
2-(2-Formylhydrazino)-4-(5-nitro-2-furyl)thiazole	0.3	12705(d)
Furmecyclox	20	12705(c)
Glu-P-1 (2-Amino-6-methyldipyrido[1,2-a:3',2'-d]imidazole)	0.1	12705(d)
Glu-P-2 (2-Aminodipyrido[1,2-a:3',2'-d]-imidazole)	0.5	12705(d)
Gyromitrin (Acetaldehyde methylformylhydrazone)	0.07	12705(d)
HC Blue 1	10	12705(d)
Heptachlor	0.2	12705(c)
Heptachlor epoxide	0.08	12705(c)
Hexachlorobenzene	0.4	12705(b)
Hexachlorocyclohexane		
alpha isomer	0.3	12705(c)
beta isomer	0.5	12705(c)
gamma isomer	0.6	12705(c)
technical grade	0.2	12705(b)
Hexachlorodibenzodioxin	0.0002	12705(b)
Hexachloroethane	20	12705(d)
Hydrazine	0.04	12705(c)
Hydrazine sulfate	0.2	12705(c)
Hydrazobenzene (1,2-Diphenylhydrazine)	0.8	12705(d)
IQ (2-Amino-3-methylimidazo[4,5-f]quinoline)	0.5	12705(d)
Isobutyl nitrite	7.4	12705(d)
Lasiocarpine	0.09	12705(d)
Lead	15 (oral)	12705(b)
Lead acetate	23 (oral)	12705(b)
Lead phosphate	58 (oral)	12705(b)
Lead subacetate	41 (oral)	12705(b)
Me-A-alpha-C (2-Amino-3-methyl-9H-pyrido[2,3-b]indole)	0.6	12705(d)
MeIQ (2-amino-3,4-dimethylimidazo-[4,5-*f*]quinoline)	0.46	12705(d)
MeIQx (2-Amino-3,8-dimethylimidazo[4,5-*f*]quinoxaline)	0.41	12705(d)
Melphalan	0.005	12705(d)
2-Methylaziridine (Propyleneimine)	0.028	12705(b)
Methyl carbamate	160	12705(d)
3-Methylcholanthrene	0.03	12705(d)
4,4'-Methylene bis(2-chloroaniline)	0.5	12705(d)
4,4'-Methylene bis(N,N-dimethyl)benzeneamine	20	12705(c)
4,4'-Methylene bis(2-methylaniline)	0.8	12705(d)
4,4'-Methylenedianiline	0.4	12705(d)
4,4'-Methylenedianiline dihydrochloride	0.6	12705(d)
Methylhydrazine	0.058 (oral)	12705(b)
	0.090 (inhalation)	12705(b)
Methylhydrazine sulfate	0.18	12705(b)
Methyl methanesulfonate	7	12705(d)
2-Methyl-1-nitroanthraquinone (of uncertain purity)	0.2	12705(d)
N-Methyl-N'-nitro-N-nitrosoguanidine	0.08	12705(d)
Methylthiouracil	2	12705(d)

Carcinogen	Level (µg/day)	22 CCR Section
Michler's ketone	0.8	12705(d)
Mirex	0.04	12705(d)
Mitomycin C	0.00009	12705(d)
Monocrotaline	0.07	12705(d)
5-(Morpholinomethyl)-3-[(5-nitrofurfurylidene)-amino] -2-oxazolidinone	0.18	12705(b)
MX (3-chloro-4-(dichloromethyl)-5-hydroxy-2(*5H*)-furanone)	0.11	12705(b)
Nalidixic acid	28	12705(d)
2-Naphthylamine	0.4	12705(d)
Nickel refinery dust	0.8	12705(c)
Nickel subsulfide	0.4	12705(c)
Nitrilotriacetic acid	100	12705(d)
Nitrilotriacetic acid, trisodium salt monohydrate	70	12705(d)
5-Nitroacenaphthene	6	12705(d)
5-Nitro-o-anisidine	10	12705(d)
Nitrofen (technical grade)	9	12705(d)
Nitrofurazone	0.5	12705(d)
1-[(5-Nitrofurfurylidene)-amino]-2-imidazolidinone	0.4	12705(d)
N-[4-(5-Nitro-2-furyl)-2-thiazolyl]acetamide	0.5	12705(d)
N-Nitrosodi-n-butylamine	0.06	12705(b)
N-Nitrosodiethanolamine	0.3	12705(c)
N-Nitrosodiethylamine	0.02	12705(b)
N-Nitrosodimethylamine	0.04	12705(b)
p-Nitrosodiphenylamine	30	12705(d)
N-Nitrosodiphenylamine	80	12705(b)
N-Nitrosodi-n-propylamine	0.1	12705(b)
N-Nitroso-N-ethylurea	0.03	12705(b)
4-(N-Nitrosomethylamino)-1-(3-pyridyl)-1-butanone	0.014	12705(d)
N-Nitrosomethylethylamine	0.03	12705(c)
N-Nitroso-N-methylurea	0.006	12705(b)
N-Nitroso-N-methylurethane	0.006	12705(d)
N-Nitrosomorpholine	0.1	12705(d)
N-Nitrosonornicotine	0.5	12705(d)
N-Nitrosopiperidine	0.07	12705(d)
N-Nitrosopyrrolidine	0.3	12705(c)
Pentachlorophenol	40	12705(c)
Phenacetin	300	12705(d)
Phenazopyridine	4	12705(d)
Phenazopyridine hydrochloride	5	12705(d)
Phenesterin	0.005	12705(d)
Phenobarbital	2	12705(d)
Phenoxybenzamine	0.2	12705(d)
Phenoxybenzamine hydrochloride	0.3	12705(d)
o-Phenylenediamine	26	12705(d)
o-Phenylenediamine dihydrochloride	44	12705(d)
Phenyl glycidyl ether	5.0	12705(b)
Phenylhydrazine	1.0	12705(b)
Phenylhydrazine hydrochloride	1.4	12705(b)
o-Phenylphenate, sodium	200	12705(d)

Carcinogen	Level (µg/day)	22 CCR Section
Polybrominated biphenyls	0.02	12705(b)
Polychlorinated biphenyls	0.09	12705(c)
Polygeenan	1200	12705(b)
Ponceau MX	200	12705(d)
Ponceau 3R	40	12705(d)
Potassium bromate	1	12705(d)
Procarbazine	0.05	12705(d)
Procarbazine hydrochloride	0.06	12705(d)
1,3-Propane sultone	0.3	12705(d)
beta-Propiolactone	0.05	12705(d)
Propylthiouracil	0.7	12705(d)
Reserpine	0.06	12705(d)
Safrole	3	12705(d)
Sterigmatocystin	0.02	12705(d)
Streptozotocin	0.006	12705(d)
Styrene oxide	4	12705(d)
Sulfallate	4	12705(d)
Tetrachlorodibenzo-p-dioxin	0.000005	12705(b)
1,1,2,2-Tetrachloroethane	3	12705(d)
Tetrachloroethylene	14	12705(c)
Tetranitromethane	0.059	12705(b)
Thioacetamide	0.1	12705(d)
4,4'-Thiodianiline	0.05	12705(d)
Thiourea	10	12705(d)
Toluene diisocyanate	20	12705(d)
ortho-Toluidine	4	12705(d)
ortho-Toluidine hydrochloride	5	12705(d)
Toxaphene	0.6	12705(b)
Trichloroethylene	50 (oral)	12705(b)
	80 (inh)	12705(b)
2,4,6-Trichlorophenol	10	12705(b)
Trimethyl phosphate	24	12705(d)
Tris(1-aziridinyl)phosphine sulfide (Thiotepa)	0.06	12705(d)
Tris(2,3-dibromopropyl)phosphate	0.3	12705(d)
Trp-P-1 (Tryptophan-P-1)	0.03	12705(d)
Trp-P-2 (Tryptophan-P-2)	0.2	12705(d)
Urethane (Ethyl carbamate)	0.7	12705(b)
Vinyl chloride	3	12705(b)
Vinyl trichloride (1,1,2-Trichloroethane)	10	12705(d)
2,6-Xylidine	110	12705(b)

B. Maximum Allowable Dose Levels (MADLs) Adopted in Regulation for Chemicals Causing Reproductive Toxicity

The following table is a compilation of MADLs in regulation (22 CCR §12805) for Proposition 65 chemicals that cause reproductive toxicity. These levels represent the no observable effect level (NOEL) for the chemical, divided by 1,000. NOELs are set in accordance with procedures specified in 22 CCR §12803. MADLs for chemicals in underline have been adopted since the last Status Report.

Chemical Listed as Causing Reproductive Toxicity	Level (µg/day)
Benzene	24 (oral)
	49 (inhalation)
Cadmium	4.1 (oral)
2,4-DB (2,4-dichlorophenoxybutyric acid)	910
m-Dinitrobenzene	38
Ethylene oxide	20
Hydramethylnon	120 (oral)
Lead	0.5
Linuron	460
N-Methylpyrrolidone	3200 (inhalation)
	17000 (dermal)
Quizalofop-ethyl	590
Toluene	7000[a]

[a] Level represents absorbed dose (rounded from 6,525 µg/day). Since 100% of ingested toluene is absorbed, oral dose is equivalent to administered dose. It is assumed that roughly 50% of the dose administered by the inhalation route is absorbed. Therefore the MADL for inhaled toluene is 13,000 µg/day (rounded from 13,050 µg/day), corresponding to an absorbed dose of 6,525 µg/day.

C. Priority List for the Development of NSRLs for Proposition 65 Carcinogens

OEHHA has developed the following priority list, which classifies into four priorities carcinogens for which dose-response assessments have not been completed. Priority levels reflect the availability and quality of scientific data for dose-response assessments, potential for exposure, resources available to perform the assessment, commitments made in settlement of the case of AFL-CIO v. Deukmejian (Sacramento Superior Court No. 3481295) and input from the public and Attorney General's office. OEHHA anticipates proposing NSRLs for the majority of chemicals in the first priority group within the next two years, and for second priority chemicals within the next two to four years. It is unlikely that NSRLs for third and fourth priority chemicals would be released within the next three years.

Any interested party may submit recommendations to OEHHA for revising the priority assignment for any of the chemicals listed. Recommendations should be accompanied by appropriate documentation supporting the alternative priority assignment suggested. OEHHA expects changes in priorities resulting from the availability of scientific information and resources, and requests from the public and Attorney General's office.

A three-tiered procedure for development of NSRLs is currently in place. NSRLs may be based on a *de novo* dose response assessment conducted or reviewed by OEHHA (22 CCR §12705(b)), an assessment conducted by another state or federal agency (22 CCR §12705(c)), or an expedited process conducted by OEHHA (22 CCR §12705(d)). The table below lists draft NSRLs and their year of release, along with the subsection of 12705 indicating the procedure used to develop the value. OEHHA will review the basis for draft numbers and update analyses as needed, before proposing or finalizing levels for formal adoption in regulation. Chemicals in bold font have been added to the Proposition 65 list or changed in priority status since the last Status Report.

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1. First Priority for NSRL Development

Acetochlor	(1992 draft NSRL: 70 µg/day [12705(c)])
Acifluorfen	(1992 draft NSRL: 20 µg/day [12705(c)])
Alachlor	(1992 draft NSRL: 9 µg/day [12705(c)])
1-Amino-2,4-dibromoanthraquinone	
Aniline hydrochloride	
Antimony oxide	
Azacitidine	
Benz[a]anthracene	(2003 draft oral NSRL: 0.033 µg/day [12705(b)])
Benzo[b]fluoranthene	(2003 draft oral NSRL: 0.096 µg/day [12705(b)])
Benzo[j]fluoranthene	(2003 draft oral NSRL: 0.11 µg/day [12705(b)])
Benzo[k]fluoranthene	
Benzotrichloride	(1993 draft oral NSRL: 0.05 µg/day [12705(c)])
	(1993 draft NSRL: 0.0002 µg/day [12705(b)])
2,2-Bis(bromomethyl)-1,3-propanediol	
Bromate	
Bromoform	(2003 draft NSRL: 64 µg/day [12705(b)])
Chlordimeform	(1992 draft NSRL: 0.5 µg/day [12705(c)])
p-Chloroaniline	
p-Chloroaniline hydrochloride	
Chrysene	(2003 draft oral NSRL: 0.35 µg/day [12705(b)])
C. I. Acid Red 114	
C.I. Direct Blue 15	
C.I. Direct Blue 218	

C.I. Solvent Yellow 14	
Dibenz[a,h]acridine	
Dibenz[a,j]acridine	
7H-Dibenzo[c,g]carbazole	(2003 draft oral NSRL: 0.0030 µg/day [12705(b)])
Dibenzo[a,e]pyrene	
Dibenzo[a,h]pyrene	(2003 draft oral NSRL: 0.0054 µg/day [12705(b)])
Dibenzo[a,i]pyrene	(2003 draft oral NSRL: 0.0050 µg/day [12705(b)])
Dibenzo[a,l]pyrene	
3,3'-Dichlorobenzidine dihydrochloride	
1,2-Dichloropropane	
1,3-Dichloropropene	(1993 draft oral NSRL: 4 µg/day [12705(b)])
	(1993 draft inhalation NSRL: 20 µg/day [12705(c)])
Diepoxybutane	
Diethyl sulfate	(1993 draft NSRL: 0.7 µg/day [12705(b)])
Dimethyl sulfate	(1993 draft NSRL: 0.05 µg/day [12705(b)])
1,1-Dimethylhydrazine (UDMH)	(1992 draft NSRL: 0.3 µg/day [12705(b)])
1,6-Dinitropyrene	(1993 draft NSRL: 0.02 µg/day [12705(b)])
1,8-Dinitropyrene	(1993 draft NSRL: 0.01 µg/day [12705(b)])
2,6-Dinitrotoluene	
Estragole	
Ethinylestradiol	
Furan	
Glycidol	(1992 draft NSRL: 0.4 µg/day [12705(b)])
Griseofulvin	(1992 draft NSRL: 50 µg/day [12705(b)])
Hexamethylphosphoramide	(1992 draft NSRL: 0.01 µg/day [12705(b)])
Indeno[1,2,3-cd]pyrene	
Isoprene	
Lactofen	(1992 draft NSRL: 4 µg/day [12705(c)])
5-Methylchrysene	(2003 draft oral NSRL: 0.0084 µg/day [12705(b)])
Methyleugenol	
Methylmercury compounds*	
N-Methylolacrylamide	(1992 draft NSRL: 2 µg/day [12705(b)])
Metronidazole	(1992 draft NSRL: 4 µg/day [12705(b)])
Nafenopin	
Naphthalene	
Nickel carbonyl	
o-Nitroanisole	
Nitrobenzene	
4-Nitrobiphenyl	
6-Nitrochrysene	(1993 draft NSRL: 0.002 µg/day [12705(b)])
2-Nitrofluorene	(1993 draft NSRL: 0.09 µg/day [12705(b)])
2-Nitropropane	(1993 draft inhalation NSRL: 30 µg/day [12705(b)])
1-Nitropyrene	(1993 draft NSRL: 0.6 µg/day [12705(b)])
4-Nitropyrene	(1993 draft NSRL: 0.03 µg/day [12705(b)])
N-Nitrosomethylvinylamine	(1993 draft NSRL: 0.004 µg/day [12705(b)])
N-Nitrososarcosine	(1993 draft NSRL: 5 µg/day [12705(b)])
Ochratoxin A	(1992 draft NSRL: 0.03 µg/day [12705(b)])
Oxazepam	
o-Phenylphenol	
PhiP	
Progesterone	
Pronamide	

* For explanation of priority levels see discussion above.

Pyridine
Selenium sulfide
1,2,3-Trichloropropane
Tris(2-chloroethyl)phosphate
Vinyl bromide (1992 draft oral NSRL: 1 µg/day [12705(b)])
(1992 draft inhalation NSRL: 4 µg/day [12705(b)])
4-Vinylcyclohexene

It is anticipated that changes to NSRLs currently in regulation will be proposed or adopted during the next year for the following chemicals:

Acrylamide
Benzene (2003 draft oral NSRL: 6.4 µg/day [12705 (b)])
(2003 draft inhalation NSRL: 13 µg/day [12705 (b)])
Chromium (VI)
Ethylene thiourea
o-Phenylphenate, sodium
Pentachlorophenol
Safrole
Tetrachloroethylene

2. Second Priority for NSRL Development

Aflatoxins (1992 draft NSRL: 0.02 µg/day [12705(b)])
p-Aminoazobenzene
Bis(2-chloro-1-methylethyl)ether, technical grade
Bromoethane
Cacodylic acid
Catechol
Ceramic fibers (airborne particles of respirable size)
1-Chloro-4-nitrobenzene
Chloroprene
5-Chloro-o-toluidine and its strong acid salts
Cobalt metal powder
Cobalt [II] oxide
Cobalt sulfate heptahydrate
Diaminotoluene (mixed)
2,3-Dibromo-1-propanol
Dichloroacetic acid
1,4-Dichloro-2-butene
Diesel engine exhaust
Di-n-propyl isocinchomeronate (MGK Repellent 326)
Diuron
Ethoprop
Fenoxycarb
Indium phosphide
Iprodione
Isoxaflutole
Isosafrole
Metham sodium
Methyl iodide
1-Naphthylamine
Nickel and certain nickel compounds
Nitromethane

o-Nitrotoluene
Oxadiazon
Oxythioquinox
Polychlorinated dibenzo-p-dioxins
Primidone
Propachlor
Quinoline and its strong acid salts
Radionuclides
Salicylazosulfapyridine
Silica, crystalline (airborne particles of respirable size)
Testosterone and its esters
p-a,a,a-Tetrachlorotoluene
Tetrafluoroethylene
2,4,5-Trimethylaniline and its strong acid salts
Triphenyltin hydroxide
Trypan blue (commercial grade)
4-Vinyl-1-cyclohexene diepoxide

3. Third Priority for NSRL Development

Adriamycin (Doxorubicin hydrochloride)
Benzidine-based dyes
N,N-Bis(2-chloroethyl)-2-naphthylamine
Bischloroethyl nitrosourea (BCNU) (Carmustine)
1,4-Butanediol dimethanesulfonate (Busulfan)
Carbon black (airborne, unbound particles of respirable size)
Chloramphenicol
1-(2-Chloroethyl)-3-cyclohexyl-1-nitrosourea (CCNU)
1-(2-Chloroethyl)-3-(4-methylcyclohexyl)-1-nitrosourea
Chlorotrianisene
Ciclosporin (Cyclosporin A; Cyclosporine)
Cidofovir
Cisplatin
Clofibrate
Daunomycin
N,N'-Diacetylbenzidine
3,3'-Dichloro-4,4'-diaminodiphenyl ether
Dienestrol
1,2-Diethylhydrazine
Diisopropyl sulfate
2,4-/2,6-Dinitrotoluene mixture
Diphenylhydantoin (Phenytoin)
Diphenylhydantoin (Phenytoin), sodium salt
Estrone
Estropipate
Ethyl acrylate
Furazolidone
Fusarin C
Ganciclovir sodium
Gasoline engine exhaust (condensates/extracts)
Gemfibrozil
Glasswool fibers (airborne particles of respirable size)
Glycidaldehyde
Mancozeb

Maneb
Medroxyprogesterone acetate
Merphalan
Mestranol
Metiram
Mustard Gas
Niridazole
Nitrogen mustard (Mechlorethamine)
Nitrogen mustard hydrochloride (Mechlorethamine HCl)
Norethisterone (Norethindrone)
Oxymetholone
Panfuran S
Polychlorinated dibenzofurans
Procymidone
Propargite
Propylene oxide (1991 draft oral NSRL: 3 µg/day [12705(c)])
(1991 draft inhalation NSRL: 60 µg/day [12705(c)])
Spironolactone
Stanozolol
Strong inorganic acid mists containing sulfuric acid
Tamoxifen and its salts
Terrazole
Thiodicarb
Thorium dioxide
Treosulfan
Trichlormethine (Trimustine hydrochloride)
Uracil mustard
Vinclozolin
Vinyl fluoride
Zileuton

4. Fourth Priority for NSRL Development

Alcoholic beverages
2-Aminofluorene
4-Amino-2-nitrophenol
Analgesic mixtures containing phenacetin
Betel quid with tobacco
Bitumens, extracts of steam-refined
Bracken fern
Caffeic acid
Carbon-black extracts
Certain combined chemotherapy for lymphomas
Citrus Red No. 2
Conjugated estrogens
Creosotes
Cycasin
Cytembena
D&C Orange No. 17
D&C Red No. 8
D&C Red No. 19
3,7-Dinitrofluoranthene
3,9-Dinitrofluoranthene
Erionite

Ethyl methanesulfonate
Iron dextran complex
Lynestrenol
8-Methoxypsoralen with ultraviolet A therapy
5-Methoxypsoralen with ultraviolet A therapy
Methylazoxymethanol
Methylazoxymethanol acetate
Nitrogen mustard N-oxide
Nitrogen mustard N-oxide hydrochloride
3-(N-Nitrosomethylamino)propionitrile
Norethynodrel
Oil Orange SS
Oral contraceptives, combined
Oral contraceptives, sequential
Palygorskite fibers
Phenolphthalein
Residual (heavy) fuel oils
Shale-oils
Soots, tars, and mineral oils
Talc containing asbestiform fibers
Tobacco, oral use of smokeless products
Tobacco smoke
Tris(aziridinyl)-para-benzoquinone (Triaziquone)
Unleaded gasoline (wholly vaporized)

D. Priority List for the Development of MADLs for Chemicals Causing Reproductive Toxicity

OEHHA has developed the following priority list, which divides chemicals causing reproductive toxicity for which dose-response assessments have not been completed into three priorities. Priority levels reflect the availability and quality of scientific data for dose-response assessments, potential for exposure, resources available to perform the assessment, and input from the public and the Attorney General's office. OEHHA anticipates proposing MADLs for the majority of chemicals in the first priority group within the next two years, and for several chemicals in the second priority within the next two to four years. It is unlikely that MADLs for chemicals in the third priority group would be released within the next three years.

Any interested party may submit recommendations to OEHHA on revising the priority assignment for any of the chemicals listed. Recommendations should be accompanied by appropriate documentation supporting the alternative priority assignment suggested. OEHHA expects changes in priorities resulting from the availability of scientific information and resources and requests from the public and Attorney General's office..

Also given below are draft levels available and year of release. OEHHA will review the basis for draft numbers and update analyses as needed, before proposing or finalizing levels for formal adoption in regulation. Chemicals in bold font have been added to the Proposition 65 list or changed in priority status since the last Status Report.

1. First Priority for MADL Development

Arsenic (inorganic oxides)	(2003 draft oral MADL: 0.10 µg/day)
Carbon disulfide	(1994 draft oral MADL: 600 µg/day) (1994 draft inhalation MADL: 1000 µg/day)
1,2-Dibromo-3-chloropropane (DBCP)	(1994 draft MADL: 5 µg/day)
Ethylene glycol monoethyl ether	
Ethylene glycol monomethyl ether	
Ethylene glycol monoethyl ether acetate	
Ethylene glycol monomethyl ether acetate	
Mercury and mercury compounds*	
Metham sodium	
Methyl bromide as a structural fumigant	(1994 draft MADL: 1000 µg/day)
Methyl mercury*	(1994 draft MADL: 0.3 µg/day)
Nicotine	
Thiophanate-methyl	
Triphenyl tin hydroxide	
Vinclozolin	

2. Second Priority for MADL Development

Amitraz
Bromacil lithium salt
Bromoxynil
Bromoxynil octanoate
Chinomethionat (Oxythioquinox)
Chlorsulfuron
Cocaine

* For explanation of priority levels see discussion above.

Cycloate
Dichlorophene
Diclofop methyl
Disodium cyanodithioimidocarbonate
Ethyl dipropylthiocarbamate
Ethylene thiourea
Fenoxaprop ethyl
Fluazifop butyl
Fluvalinate
Methazole
Metiram
Myclobutanil
Nabam
Nitrapyrin
Oxadiazon
Oxydemeton methyl
Potassium dimethyldithiocarbamate
Propargite
Resmethrin
Sodium dimethyldithiocarbamate
Sodium fluoroacetate
Terbacil
2,3,7,8-Tetrachlorodibenzo-para-dioxin (TCDD)
Triadimefon
Tributyltin methacrylate
Triforine

3. Third Priority for MADL Development

Acetazolamide
Acetohydroxamic acid
Actinomycin D
All-trans retinoic acid
Alprazolam
Altretamine
Amantadine hydrochloride
Amikacin sulfate
Aminoglutethimide
Aminoglycosides
Aminopterin
Amiodarone hydrochloride
Amoxapine
Anabolic steroids
Angiotensin converting enzyme (ACE) inhibitors
Anisindione
Aspirin
Atenolol
Auranofin
Azathioprine
Barbiturates
Beclomethasone dipropionate
Benomyl
Benzphetamine hydrochloride
Benzodiazepines

Bischloroethyl nitrosourea (BCNU) (Carmustine)
Butabarbital sodium
1,4-Butanediol dimethanesulfonate (Busulfan)
Carbamazepine
Carbon monoxide
Carboplatin
Chenodiol
Chlorambucil
Chlorcyclizine hydrochloride
Chlordecone (Kepone)
Chlordiazepoxide
Chlordiazepoxide hydrochloride
1-(2-Chloroethyl)-3-cyclohexyl-1-nitrosourea (CCNU) (Lomustine)
Cidofovir
Cladribine
Clarithromycin
Clobetasol propionate
Clomiphene citrate
Clorazepate dipotassium
Codeine phosphate
Colchicine
Conjugated estrogens
Cyanazine
Cycloheximide
Cyclophosphamide (anhydrous)
Cyclophosphamide (hydrated)
Cyhexatin
Cytarabine
Dacarbazine
Danazol
Daunorubicin hydrochloride
o,p'-DDT
p,p'-DDT
Demeclocycline hydrochloride (internal use)
Diazepam
Diazoxide
Dichlophenamide
Dicumarol
Diethylstilbestrol (DES)
Diflunisal
Dihydroergotamine mesylate
Diltiazem hydrochloride
o-Dinitrobenzene
p-Dinitrobenzene
2,4-Dinitrotoluene
2,6-Dinitrotoluene
Dinitrotoluene (technical grade)
Dinocap
Dinoseb
Diphenylhydantoin (Phenytoin)
Doxorubicin hydrochloride
Doxycycline (internal use)
Doxycycline calcium (internal use)
Doxycycline hyclate (internal use)

Doxycycline monohydrate (internal use)
Endrin
Epichlorohydrin
Ergotamine tartrate
Estropipate
Ethionamide
Ethyl alcohol in alcoholic beverages
Ethylene dibromide
Etodolac
Etoposide
Etretinate
Filgrastim
Flunisolide
Fluorouracil
Fluoxymesterone
Flurazepam hydrochloride
Flurbiprofen
Flutamide
Fluticasone propionate
Ganciclovir sodium
Gemfibrozil
Goserelin acetate
Halazepam
Halobetasol propionate
Haloperidol
Halothane
Heptachlor
Hexachlorobenzene
Hexamethylphosphoramide
Histrelin acetate
Hydroxyurea
Idarubicin hydrochloride
Ifosfamide
Iodine-131
Isotretinoin
Leuprolide acetate
Levodopa
Levonorgestrel implants
Lithium carbonate
Lithium citrate
Lorazepam
Lovastatin
Mebendazole
Medroxyprogesterone acetate
Megestrol acetate
Melphalan
Menotropins
Meprobamate
Mercaptopurine
Methacycline hydrochloride
Methimazole
Methotrexate
Methotrexate sodium
Methyl chloride

Methyltestosterone
Midazolam hydrochloride
Minocycline hydrochloride (internal use)
Misoprostol
Mitoxantrone hydrochloride
Nafarelin acetate
Neomycin sulfate (internal use)
Netilmicin sulfate
Nickel carbonyl
Nifedipine
Nimodipine
Nitrofurantoin
Nitrogen mustard (Mechlorethamine)
Nitrogen mustard hydrochloride (Mechlorethamine hydrochloride)
Norethisterone (Norethindrone)
Norethisterone acetate (Norethindrone acetate)
Norethisterone (Norethindrone)/Ethinyl estradiol
Norethisterone (Norethindrone)/Mestranol
Norgestrel
Oxazepam
Oxymetholone
Oxytetracycline (internal use)
Oxytetracycline hydrochloride (internal use)
Paclitaxel
Paramethadione
Penicillamine
Pentobarbital sodium
Pentostatin
Phenacemide
Phenprocoumon
Pimozide
Pipobroman
Plicamycin
Polybrominated biphenyls
Polychlorinated biphenyls
Pravastatin sodium
Prednisolone sodium phosphate
Procarbazine hydrochloride
Propylthiouracil
Pyrimethamine
Quazepam
Retinol/retinyl esters, when in daily dosages in
excess of 10,000 IU, or 3,000 retinol equivalents.
Ribavirin
Rifampin
Secobarbital sodium
Sermorelin acetate
Streptomycin sulfate
Streptozocin (streptozotocin)
Sulfasalazine
Sulindac
Tamoxifen citrate
Temazepam
Teniposide

Testosterone cypionate
Testosterone enanthate
Tetracycline (internal use)
Tetracyclines (internal use)
Tetracycline hydrochloride (internal use)
Thalidomide
Thioguanine
Tobacco smoke (primary)
Tobramycin sulfate
Triazolam
Trientine hydrochloride
Trilostane
Trimethadione
Trimetrexate glucuronate
Uracil mustard
Urethane
Urofollitropin
Valproate (Valproic acid)
Vinblastine sulfate
Vincristine sulfate
Warfarin
Zileuton

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September 1997

Public Health Statement for Benzene

CAS# 71-43-2

This Public Health Statement is the summary chapter from the Toxicological Profile for benzene. It is one in a series of Public Health Statements about hazardous substances and their health effects. A shorter version, the ToxFAQs™, is also available. This information is important because this substance may harm you. The effects of exposure to any hazardous substance depend on the dose, the duration, how you are exposed, personal traits and habits, and whether other chemicals are present. For more information, call the ATSDR Information Center at 1-888-422-8737.

This public health statement tells you about benzene and the effects of exposure.

The Environmental Protection Agency (EPA) identifies the most serious hazardous waste sites in the nation. These sites make up the National Priorities List (NPL) and are the sites targeted for long-term federal cleanup. Benzene has been found in at least 816 of the 1,428 current or former NPL sites. However, it's unknown how many NPL sites have been evaluated for this substance. As more sites are evaluated, the sites with benzene may increase. This information is important because exposure to this substance may harm you and because these sites may be sources of exposure.

When a substance is released from a large area, such as an industrial plant, or from a container, such as a drum or bottle, it enters the environment. This release does not always lead to exposure. You are exposed to a substance only when you come in contact with it. You may be exposed by breathing, eating, or drinking the substance or by skin contact.

If you are exposed to benzene, many factors determine whether you'll be harmed. These factors include the dose (how much), the duration (how long), and how you come in contact with it. You must also consider the other chemicals you're exposed to and your age, sex, diet, family traits, lifestyle, and state of health.

1.1 What is benzene?

Benzene, also known as benzol, is a colorless liquid with a sweet

Priority List of Hazardous Substances

Division of Toxicology

odor. Benzene evaporates into air very quickly and dissolves slightly in water. Benzene is highly flammable. Most people can begin to smell benzene in air at 1.5–4.7 parts of benzene per million parts of air (ppm) and smell benzene in water at 2 ppm. Most people can begin to taste benzene in water at 0.5–4.5 ppm. Benzene is found in air, water, and soil.

Benzene found in the environment is from both human activities and natural processes. Benzene was first discovered and isolated from coal tar in the 1800s. Today, benzene is made mostly from petroleum sources. Because of its wide use, benzene ranks in the top 20 in production volume for chemicals produced in the United States. Various industries use benzene to make other chemicals, such as styrene (for Styrofoam® and other plastics), cumene (for various resins), and cyclohexane (for nylon and synthetic fibers). Benzene is also used for the manufacturing of some types of rubbers, lubricants, dyes, detergents, drugs, and pesticides. Natural sources of benzene, which include volcanoes and forest fires, also contribute to the presence of benzene in the environment. Benzene is also a natural part of crude oil and gasoline and cigarette smoke.

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1.2 How might I be exposed to benzene?

Benzene is commonly found in the environment. Industrial processes are the main sources of benzene in the environment. Benzene levels in the air can increase from emissions from burning coal and oil, benzene waste and storage operations, motor vehicle exhaust, and evaporation from gasoline service stations. Since tobacco contains high levels of benzene, tobacco smoke is another source of benzene in air. Industrial discharge, disposal of products containing benzene, and gasoline leaks from underground storage tanks can release benzene into water and soil.

Benzene can pass into air from water and soil surfaces. Once in the air, benzene reacts with other chemicals and breaks down within a few days. Benzene in the air can attach to rain or snow and be carried back down to the ground.

Benzene in water and soil breaks down more slowly. Benzene is slightly soluble in water and can pass through the soil into underground water. Benzene in the environment does not build up in plants or animals.

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1.3 How can benzene enter and leave my body?

Most people are exposed to a small amount of benzene on a daily basis. You can be exposed to benzene in the outdoor environment, in the workplace, and in the home. Exposure of the general population to benzene is mainly through breathing air that contains benzene. The major sources of benzene exposure are tobacco

smoke, automobile service stations, exhaust from motor vehicles, and industrial emissions. Vapors (or gases) from products that contain benzene, such as glues, paints, furniture wax, and detergents can also be a source of exposure. Auto exhaust and industrial emissions account for about 20% of the total nationwide exposure to benzene. About 50% of the entire nationwide exposure to benzene results from smoking tobacco or from exposure to tobacco smoke. The average smoker (32 cigarettes per day) takes in about 1.8 milligrams (mg) of benzene per day. This is about 10 times the average daily intake of nonsmokers.

Measured levels of benzene in outdoor air have ranged from 0.02 to 34 parts of benzene per billion parts of air (ppb) (1 ppb is 1,000 times less than 1 ppm). People living in cities or industrial areas are generally exposed to higher levels of benzene in air than those living in rural areas. Benzene levels in the home are usually higher than outdoor levels. People living around hazardous waste sites, petroleum refining operations, petrochemical manufacturing sites, or gas stations may be exposed to higher levels of benzene in air.

For most people, the level of exposure to benzene through food, beverages, or drinking water is not as high as through air. Typical drinking water contains less than 0.1 ppb benzene. Benzene has been detected in some bottled water, liquor, and food. Leakage from underground gasoline storage tanks or from landfills and hazardous waste sites containing benzene can result in benzene contamination of well water. People with benzene-contaminated tap water can be exposed from drinking the water or eating foods prepared with the water. In addition, exposure can result from breathing in benzene while showering, bathing, or cooking with contaminated water.

Individuals employed in industries that make or use benzene may be exposed to the highest levels of benzene. As many as 238,000 people may be occupationally exposed to benzene in the United States. These industries include benzene production (petrochemicals, petroleum refining, and coke and coal chemical manufacturing), rubber tire manufacturing, and storage or transport of benzene and petroleum products containing benzene. Other workers who may be exposed to benzene because of their occupations include steel workers, printers, rubber workers, shoe makers, laboratory technicians, firefighters, and gas station employees.

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1.4 How can benzene affect my health?

Benzene can enter your body through your lungs when you breathe contaminated air. It can also enter through your stomach and intestines when you eat food or drink water that contains benzene. Benzene can enter your body through skin contact with

benzene-containing products such as gasoline.

When you are exposed to high levels of benzene in air, about half of the benzene you breathe in leaves your body when you breathe out. The other half passes through the lining of your lungs and enters your bloodstream. Animal studies show that benzene taken in by eating or drinking contaminated foods behaves similarly in the body to benzene that enters through the lungs. A small amount will enter your body by passing through your skin and into your bloodstream during skin contact with benzene or benzene-containing products. Once in the bloodstream, benzene travels throughout your body and can be temporarily stored in the bone marrow and fat. Benzene is converted to products, called metabolites, in the liver and bone marrow. Some of the harmful effects of benzene exposure are believed to be caused by these metabolites. Most of the metabolites of benzene leave the body in the urine within 48 hours after exposure.

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1.5 What levels of exposure have resulted in harmful health effects?

To protect the public from the harmful effects of toxic chemicals and to find ways to treat people who have been harmed, scientists use many tests.

One way to see if a chemical will hurt people is to learn how the chemical is absorbed, used, and released by the body; for some chemicals, animal testing may be necessary. Animal testing may also be used to identify health effects such as cancer or birth defects. Without laboratory animals, scientists would lose a basic method to get information needed to make wise decisions to protect public health. Scientists have the responsibility to treat research animals with care and compassion. Laws today protect the welfare of research animals, and scientists must comply with strict animal care guidelines.

After exposure to benzene, several factors determine whether harmful health effects will occur and if they do, what the type and severity of these health effects might be. These factors include the amount of benzene to which you are exposed and the length of time of the exposure. Most data involving effects of long-term exposure to benzene are from studies of workers employed in industries that make or use benzene. These workers were exposed to levels of benzene in air far greater than the levels normally encountered by the general population. Current levels of benzene in workplace air are much lower than in the past. Because of this reduction, and the availability of protective equipment such as respirators, fewer workers have symptoms of benzene poisoning.

Brief exposure (5–10 minutes) to very high levels of benzene in air (10,000–20,000 ppm) can result in death. Lower levels (700–

3,000 ppm) can cause drowsiness, dizziness, rapid heart rate, headaches, tremors, confusion, and unconsciousness. In most cases, people will stop feeling these effects when they stop being exposed and begin to breathe fresh air.

Eating foods or drinking liquids containing high levels of benzene can cause vomiting, irritation of the stomach, dizziness, sleepiness, convulsions, rapid heart rate, coma, and death. The health effects that may result from eating foods or drinking liquids containing lower levels of benzene are not known. If you spill benzene on your skin, it may cause redness and sores. Benzene in your eyes may cause general irritation and damage to your cornea.

Benzene causes problems in the blood. People who breathe benzene for long periods may experience harmful effects in the tissues that form blood cells, especially the bone marrow. These effects can disrupt normal blood production and cause a decrease in important blood components. A decrease in red blood cells can lead to anemia. Reduction in other components in the blood can cause excessive bleeding. Blood production may return to normal after exposure to benzene stops. Excessive exposure to benzene can be harmful to the immune system, increasing the chance for infection and perhaps lowering the body's defense against cancer.

Benzene can cause cancer of the blood-forming organs. The Department of Health and Human Services (DHHS) has determined that benzene is a known carcinogen. The International Agency for Cancer Research (IARC) has determined that benzene is carcinogenic to humans, and the EPA has determined that benzene is a human carcinogen. Long-term exposure to relatively high levels of benzene in the air can cause cancer of the blood-forming organs. This condition is called leukemia. Exposure to benzene has been associated with development of a particular type of leukemia called acute myeloid leukemia (AML).

Exposure to benzene may be harmful to the reproductive organs. Some women workers who breathed high levels of benzene for many months had irregular menstrual periods. When examined, these women showed a decrease in the size of their ovaries. However, exact exposure levels were unknown, and the studies of these women did not prove that benzene caused these effects. It is not known what effects exposure to benzene might have on the developing fetus in pregnant women or on fertility in men. Studies with pregnant animals show that breathing benzene has harmful effects on the developing fetus. These effects include low birth weight, delayed bone formation, and bone marrow damage.

The health effects that might occur in humans following long-term exposure to food and water contaminated with benzene are not known. In animals, exposure to food or water contaminated with benzene can damage the blood and the immune system and can

even cause cancer.

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1.6 Is there a medical test to determine whether I have been exposed to benzene?

Several tests can show if you have been exposed to benzene. Some of these tests may be available at your doctor's office. All of these tests are limited in what they can tell you. The test for measuring benzene in your breath must be done shortly after exposure. This test is not very helpful for detecting very low levels of benzene in your body. Benzene can be measured in your blood. However, since benzene disappears rapidly from the blood, measurements may be accurate only for recent exposures. In the body, benzene is converted to products called metabolites. Certain metabolites of benzene, such as phenol, muconic acid, and S-phenyl-N-acetyl cysteine (PhAC) can be measured in the urine. The amount of phenol in urine has been used to check for benzene exposure in workers. The test is useful only when you are exposed to benzene in air at levels of 10 ppm or greater. However, this test must also be done shortly after exposure, and it is not a reliable indicator of how much benzene you have been exposed to, since phenol is present in the urine from other sources (diet, environment). Measurement of muconic acid or PhAC in the urine is a more sensitive and reliable indicator of benzene exposure. The measurement of benzene in blood or of metabolites in urine cannot be used for making predictions about whether you will experience any harmful health effects. Measurement of all parts of the blood and measurement of bone marrow are used to find benzene exposure and its health effects.

For people exposed to relatively high levels of benzene, complete blood analyses can be used to monitor possible changes related to exposure. However, blood analyses are not useful when exposure levels are low.

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1.7 What recommendations has the federal government made to protect human health?

The federal government develops regulations and recommendations to protect public health. Regulations can be enforced by law. Federal agencies that develop regulations for toxic substances include the Environmental Protection Agency (EPA), the Occupational Safety and Health Administration (OSHA), and the Food and Drug Administration (FDA). Recommendations provide valuable guidelines to protect public health but cannot be enforced by law. Federal organizations that develop recommendations for toxic substances include the Agency for Toxic Substances and Disease Registry (ATSDR) and the National Institute for Occupational Safety and Health (NIOSH).

Regulations and recommendations can be expressed in not-to-

exceed levels in air, water, soil, or food that are usually based on levels that affect animals, then they are adjusted to help protect people. Sometimes these not-to-exceed levels differ among federal organizations because of different exposure times (an 8-hour workday or a 24-hour day), the use of different animal studies, or other factors.

Recommendations and regulations are also periodically updated as more information becomes available. For the most current information, check with the federal agency or organization that provides it. Some regulations and recommendations for benzene include the following:

EPA has set the maximum permissible level of benzene in drinking water at 5 parts per billion (ppb). Because benzene can cause leukemia, EPA has set a goal of 0 ppb for benzene in drinking water and in water such as rivers and lakes. EPA estimates that 10 ppb benzene in drinking water that is consumed regularly or exposure to 0.4 ppb benzene in air over a lifetime could cause a risk of one additional cancer case for every 100,000 exposed persons. EPA recommends a maximum permissible level of benzene in water of 200 ppb for short-term exposures (10 days) for children.

EPA requires that the National Response Center be notified following a discharge or spill into the environment of 10 pounds or more of benzene.

The Occupational Safety and Health Administration (OSHA) regulates levels of benzene in the workplace. The maximum allowable amount of benzene in workroom air during an 8-hour workday, 40-hour workweek is 1 part per million (ppm). Since benzene can cause cancer, the National Institute for Occupational Safety and Health (NIOSH) recommends that all workers likely to be exposed to benzene wear special breathing equipment.

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1.8 Where can I get more information?
If you have any more questions or concerns, please contact your community or state health or environmental quality department or:

Agency for Toxic Substances and Disease Registry
Division of Toxicology
1600 Clifton Road NE, Mailstop F-32
Atlanta, GA 30333

Information line and technical assistance:

Phone: 888-422-8737
FAX: (770)-488-4178

ATSDR can also tell you the location of occupational and environmental health clinics. These clinics specialize in recognizing, evaluating, and treating illnesses resulting from exposure to hazardous substances.

To order toxicological profiles, contact:

National Technical Information Service
5285 Port Royal Road
Springfield, VA 22161
Phone: 800-553-6847 or 703-605-6000

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References

Agency for Toxic Substances and Disease Registry (ATSDR). 1997. Toxicological profile for benzene. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service.

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ToxFAQs™

July 1999

Public Health Statement for Ethylbenzene

CAS# 100-41-4

This Public Health Statement is the summary chapter from the Toxicological Profile for ethylbenzene. It is one in a series of Public Health Statements about hazardous substances and their health effects. A shorter version, the ToxFAQs™, is also available. This information is important because this substance may harm you. The effects of exposure to any hazardous substance depend on the dose, the duration, how you are exposed, personal traits and habits, and whether other chemicals are present. For more information, call the ATSDR Information Center at 1-888-422-8737.

This public health statement tells you about ethylbenzene and the effects of exposure.

The Environmental Protection Agency (EPA) identifies the most serious hazardous waste sites in the nation. These sites make up the National Priorities List (NPL) and are the sites targeted for long-term federal cleanup activities. Ethylbenzene has been found in at least 720 of the 1,467 current or former NPL sites. However, the total number of NPL sites evaluated for this substance is not known. As more sites are evaluated, the sites at which ethylbenzene is found may increase. This information is important because exposure to this substance may harm you and because these sites may be sources of exposure.

When a substance is released from a large area, such as an industrial plant, or from a container, such as a drum or bottle, it enters the environment. This release does not always lead to exposure. You are exposed to a substance only when you come in contact with it. You may be exposed by breathing, eating, or drinking the substance or by skin contact.

If you are exposed to ethylbenzene, many factors determine whether you'll be harmed. These factors include the dose (how much), the duration (how long), and how you come in contact with it. You must also consider the other chemicals you're exposed to and your age, sex, diet, family traits, lifestyle, and state of health.

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Toxicological Profiles
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MMGs
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1.1 What is ethylbenzene?

Ethylbenzene is a colorless liquid that smells like gasoline. You can smell ethylbenzene in the air at concentrations as low as 2 parts of ethylbenzene per million parts of air by volume (ppm). It evaporates at room temperature and burns easily. Ethylbenzene occurs naturally in coal tar and petroleum. It is also found in many products, including paints, inks, and insecticides. Gasoline contains about 2% (by weight) ethylbenzene. Ethylbenzene is used primarily in the production of styrene. It is also used as a solvent, a component of asphalt and naphtha, and in fuels. In the chemical industry, it is used in the manufacture of acetophenone, cellulose acetate, diethylbenzene, ethyl anthraquinone, ethylbenzene sulfonic acids, propylene oxide, and -methylbenzyl alcohol. Consumer products containing ethylbenzene include pesticides, carpet glues, varnishes and paints, and tobacco products. In 1994, approximately 12 billion pounds of ethylbenzene were produced in the United States.

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1.2 What happens to ethylbenzene when it enters the environment?

Ethylbenzene is most commonly found as a vapor in the air. This is because ethylbenzene moves easily into the air from water and soil. Once in the air, other chemicals help break down ethylbenzene into chemicals found in smog. This breakdown happens in less than 3 days with the aid of sunlight. In surface water such as rivers and harbors, ethylbenzene breaks down by reacting with other compounds naturally present in the water. In soil, the majority of ethylbenzene is broken down by soil bacteria. Since ethylbenzene binds only moderately to soil, it can also move downward through soil to contaminate groundwater. Near hazardous waste sites, the levels of ethylbenzene in the air, water, and soil could be much higher than in other areas.

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1.3 How might I be exposed to ethylbenzene?

There are a variety of ways you may be exposed to this chemical. If you live in a highly populated area or near many factories or heavily traveled highways, you may be exposed to ethylbenzene in the air. Releases of ethylbenzene into these areas occur from burning oil, gas, and coal and from discharges of ethylbenzene from some types of factories. The median level of ethylbenzene in city and suburban air is about 0.62 parts of ethylbenzene per billion parts (ppb) of air. In contrast, the median level of ethylbenzene measured in air in country locations is about 0.01 ppb. Indoor air has a higher median concentration of ethylbenzene (about 1 ppb) than outdoor air. This is because ethylbenzene builds up after you use household products such as cleaning products or paints.

Ethylbenzene was found in only one of ten U.S. rivers and

streams tested in 1982 and 1983. The average level measured was less than 5.0 ppb. Ethylbenzene gets into water from factory releases, boat fuel, and poor disposal of waste. Background levels in soils have not been reported. Ethylbenzene may get into the soil by gasoline or other fuel spills and poor disposal of industrial and household wastes.

Some people are exposed to ethylbenzene in the workplace. Gas and oil workers may be exposed to ethylbenzene either through skin contact or by breathing ethylbenzene vapors. Varnish workers, spray painters, and people involved in gluing operations may also be exposed to high levels of ethylbenzene. Exposure may also occur in factories that use ethylbenzene to produce other chemicals.

You may be exposed to ethylbenzene if you live near hazardous waste sites containing ethylbenzene or areas where ethylbenzene spills have occurred. Higher-than-background levels of ethylbenzene were detected in groundwater near a landfill and near an area where a fuel spill had occurred. No specific information on human exposure to ethylbenzene near hazardous waste sites is available.

You may also be exposed to ethylbenzene from the use of many consumer products. Gasoline is a common source of ethylbenzene exposure. Other sources of ethylbenzene exposure come from the use of this chemical as a solvent in pesticides, carpet glues, varnishes and paints, and from the use of tobacco products. Ethylbenzene does not generally build up in food. However, some vegetables may contain very small amounts of it.

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1.4 How can ethylbenzene enter and leave my body?

When you breathe air containing ethylbenzene vapor, it enters your body rapidly and almost completely through your lungs. Ethylbenzene in food or water can also rapidly and almost completely enter your body through the digestive tract. It may enter through your skin when you come into contact with liquids containing ethylbenzene. Ethylbenzene vapors do not enter through your skin to any large degree. People living in urban areas or in areas near hazardous waste sites may be exposed by breathing air or by drinking water contaminated with ethylbenzene. Once in your body, ethylbenzene is broken down into other chemicals. Most of it leaves in the urine within 2 days. Small amounts can also leave through the lungs and in feces. Liquid ethylbenzene that enters through your skin is also broken down. Ethylbenzene in high levels is broken down slower in your body than low levels of ethylbenzene. Similarly, ethylbenzene mixed with other solvents is also broken down more slowly than ethylbenzene alone. This slower breakdown will increase the time it takes for ethylbenzene to leave your body.

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1.5 How can ethylbenzene affect my health?

To protect the public from the harmful effects of toxic chemicals and to find ways to treat people who have been harmed, scientists use many tests.

One way to see if a chemical will hurt people is to learn how the chemical is absorbed, used, and released by the body; for some chemicals, animal testing may be necessary. Animal testing may also be used to identify health effects such as cancer or birth defects. Without laboratory animals, scientists would lose a basic method to get information needed to make wise decisions to protect public health. Scientists have the responsibility to treat research animals with care and compassion. Laws today protect the welfare of research animals, and scientists must comply with strict animal care guidelines.

At certain levels, exposure to ethylbenzene can harm your health. People exposed to high levels of ethylbenzene in the air for short periods have complained of eye and throat irritation. Persons exposed to higher levels have shown signs of more severe effects such as decreased movement and dizziness. No studies have reported death in humans following exposure to ethylbenzene alone. However, evidence from animal studies suggests that it can cause death at very high concentrations in the air (about 2 million times the usual level in urban air). Whether or not long-term exposure to ethylbenzene affects human health is not known because little information is available. Short-term exposure of laboratory animals to high concentrations of ethylbenzene in air may cause liver and kidney damage, nervous system changes, and blood changes. The link between these health effects and exposure to ethylbenzene is not clear because of conflicting results and weaknesses in many of the studies. Also, there is no clear evidence that the ability to get pregnant is affected by breathing air or drinking water containing ethylbenzene, or coming into direct contact with ethylbenzene through the skin. Two long-term studies in animals suggest that ethylbenzene may cause tumors. One study had many weaknesses, and no conclusions could be drawn about possible cancer effects in humans. The other, a recently completed study, was more convincing, and provided clear evidence that ethylbenzene causes cancer in one species after exposure in the air to concentrations greater than 740 ppm that were approximately 1 million times the levels found in urban air. At present, the federal government has not identified ethylbenzene as a chemical that may cause cancer in humans. However, this may change after consideration of the new data.

There are no reliable data on the effects in humans after eating or drinking ethylbenzene or following direct exposure to the skin. For this reason, levels of exposure that may affect your health after

eating, drinking, or getting ethylbenzene on your skin are estimated from animal studies. There are only two reports of eye or skin exposure to ethylbenzene. In these studies, liquid ethylbenzene caused eye damage and skin irritation in rabbits. More animal studies are available that describe the effects of breathing air or drinking water containing ethylbenzene.

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1.6 How can ethylbenzene affect children?

This section discusses potential health effects from exposures during the period from conception to maturity at 18 years of age in humans. Potential effects on children resulting from exposures of the parents are also considered.

Since ethylbenzene is contained in many consumer products (including gasoline, paints, inks, pesticides, and carpet glue), it is possible for children to be exposed to ethylbenzene, especially by inhalation. Children might also be exposed to ethylbenzene from hazardous waste. Ethylbenzene vapors are heavier than air, and children generally spend more time on the floor or ground than do adults. We do not know whether children would be different than adults in their weight-adjusted intake of ethylbenzene.

No data describe the effect of exposure to ethylbenzene on children or immature animals. It is likely that children would show the same health effects as adults. Respiratory and eye irritation and dizziness are the most prevalent signs of exposure to high levels of ethylbenzene in adults, and children would probably also exhibit these effects. We do not know whether children differ in their susceptibility to the effects of ethylbenzene. We do not know whether ethylbenzene causes birth defects in people. Minor birth defects have occurred in newborn animals whose mothers were exposed by breathing air contaminated with ethylbenzene.

We do not know whether ethylbenzene can cross the placenta to an unborn child or accumulate significantly in breast milk.

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1.7 How can families reduce the risk of exposure to ethylbenzene?

Ethylbenzene is found in the blood, urine, breath, and some body tissues of exposed people. Urine is most commonly tested to determine exposure to ethylbenzene. The test measures the presence of substances formed following an exposure to ethylbenzene. These substances are formed by the breakdown of ethylbenzene. You should have this test done within a few hours after exposure occurs because these substances leave the body very quickly. Although this test can prove your exposure to ethylbenzene, it cannot yet predict the kind of health effects that might develop from that exposure.

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1.8 Is there a medical test to determine whether I have ben exposed to ethylbenzene?

If your doctor finds that you have been exposed to significant amounts of ethylbenzene, ask your doctor if children may also be exposed. When necessary your doctor may need to ask your state public heath department to investigate.

Ethylbenzene is found in consumer products including gasoline, pesticides, carpet glues, varnishes, paints, and tobacco products. Exposure to ethylbenzene vapors from household products and newly installed carpeting can be minimized by using adequate ventilation. Household chemicals should be stored out of reach of young children to prevent accidental poisonings. Always store household chemicals in their original labeled containers; never store household chemicals in containers children would find attractive to eat or drink from, such as old soda bottles. Gasoline should be stored in a gasoline can with a locked cap. Keep your Poison Control Center's number by the phone. To minimize exposure, children should be kept out of areas where products that contain ethylbenzene are being used. Sometimes older children sniff household chemicals in an attempt to get high. Your children may be exposed to ethylbenzene by inhaling products containing it, such as paints, varnishes, or gasoline. Talk with your children about the dangers of sniffing chemicals.

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1.9 What recommendations has the federal government made to protect human health?

The federal government develops regulations and recommendations to protect public health. Regulations can be enforced by law. Federal agencies that develop regulations for toxic substances include the Environmental Protection Agency (EPA), the Occupational Safety and Health Administration (OSHA), and the Food and Drug Administration (FDA). Recommendations provide valuable guidelines to protect public health but cannot be enforced by law. Federal organizations that develop recommendations for toxic substances include the Agency for Toxic Substances and Disease Registry (ATSDR) and the National Institute for Occupational Safety and Health (NIOSH).

Regulations and recommendations can be expressed in not-to-exceed levels in air, water, soil, or food that are usually based on levels that affect animals; then they are adjusted to help protect people. Sometimes these not-to-exceed levels differ among federal organizations because of different exposure times (an 8-hour workday or a 24-hour day), the use of different animal studies, or other factors.

Recommendations and regulations are also periodically updated as

more information becomes available. For the most current information, check with the federal agency or organization that provides it. Some regulations and recommendations for ethylbenzene include the following:

The federal government has developed regulatory standards and guidelines to protect you from possible health effects of ethylbenzene in the environment. EPA's Office of Drinking Water (ODW) set 700 ppb (this equals 0.7 milligrams ethylbenzene per liter of water or mg/L) as the acceptable exposure concentration of ethylbenzene in drinking water for an average weight adult. This value is for lifetime exposure and is set at a level that is expected not to increase the chance of having (noncancer) adverse health effects. The same EPA office (ODW) set higher acceptable levels of ethylbenzene in water for shorter periods (20 ppm or 20 mg/L for 1 day, 3 ppm or 3 mg/L for 10 days). EPA has determined that exposures at or below these levels are acceptable for small children. If you eat fish and drink water from a body of water, the water should contain no more than 1.4 mg ethylbenzene per liter.

EPA requires that a release of 1,000 pounds or more of ethylbenzene be reported to the federal government's National Response Center in Washington, D.C.

OSHA set a legal limit of 100 ppm ethylbenzene in air. This is for exposure at work for 8 hours per day.

NIOSH also recommends an exposure limit for ethylbenzene of 100 ppm. This is for exposure to ethylbenzene in air at work for up to 10 hours per day in a 40-hour work week. NIOSH also set a limit of 125 ppm for a 15-minute period.

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1.10 Where can I get more information?

If you have any more questions or concerns, please contact your community or state health or environmental quality department or:

Agency for Toxic Substances and Disease Registry
Division of Toxicology
1600 Clifton Road NE, Mailstop F-32
Atlanta, GA 30333

Information line and technical assistance:

Phone: 888-422-8737
FAX: (770)-488-4178

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August 1995

Public Health Statement for Xylene

CAS# Mixed Xylene 1330-20-7

This Public Health Statement is the summary chapter from the Toxicological Profile for xylene. It is one in a series of Public Health Statements about hazardous substances and their health effects. A shorter version, the ToxFAQs™, is also available. This information is important because this substance may harm you. The effects of exposure to any hazardous substance depend on the dose, the duration, how you are exposed, personal traits and habits, and whether other chemicals are present. For more information, call the ATSDR Information Center at 1-888-422-8737.

This Statement was prepared to give you information about xylene and to emphasize the human health effects that may result from exposure to it. The Environmental Protection Agency (EPA) has identified 1,408 hazardous waste sites as the most serious in the nation. These sites comprise the "National Priorities List" (NPL): those sites which are targeted for long-term federal cleanup activities. Xylene has been found in at least 658 of the sites on the NPL. However, the number of NPL sites evaluated for xylene is not known. As EPA evaluates more sites, the number of sites at which xylene is found may increase. This information is important because exposure to xylene may cause harmful health effects and because these sites are potential or actual sources of human exposure to xylene.

When a substance is released from a large area, such as an industrial plant, or from a container, such as a drum or bottle, it enters the environment. This release does not always lead to exposure. You can be exposed to a substance only when you come in contact with it. You may be exposed by breathing, eating, or drinking substances containing the substance or by skin contact with it.

If you are exposed to a substance such as xylene, many factors will determine whether harmful health effects will occur and what the type and severity of those health effects will be. These factors include the dose (how much), the duration (how long), the route or pathway by which you are exposed (breathing, eating, drinking, or

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skin contact), the other chemicals to which you are exposed, and your individual characteristics such as age, gender, nutritional status, family traits, life-style, and state of health.

1.1 What is xylene?

In this report, the terms xylene, xylenes, and total xylenes will be used interchangeably. There are three forms of xylene in which the methyl groups vary on the benzene ring: *meta*-xylene, *ortho*-xylene, and *para*-xylene (*m*-, *o*-, and *p*-xylene). These different forms are referred to as isomers. The term total xylenes refers to all three isomers of xylene (*m*-, *o*-, and *p*-xylene). Mixed xylene is a mixture of the three isomers and usually also contains 6–15% ethylbenzene. Xylene is also known as xylol or dimethylbenzene. Xylene is primarily a synthetic chemical. Chemical industries produce xylene from petroleum. Xylene also occurs naturally in petroleum and coal tar and is formed during forest fires. It is a colorless, flammable liquid with a sweet odor.

Xylene is one of the top 30 chemicals produced in the United States in terms of volume. It is used as a solvent (a liquid that can dissolve other substances) in the printing, rubber, and leather industries. Along with other solvents, xylene is also used as a cleaning agent, a thinner for paint, and in varnishes. It is found in small amounts in airplane fuel and gasoline. Xylene is used as a material in the chemical, plastics, and synthetic fiber industries and as an ingredient in the coating of fabrics and papers. Isomers of xylene are used in the manufacture of certain polymers (chemical compounds), such as plastics.

Xylene evaporates and burns easily. Xylene does not mix well with water; however, it does mix with alcohol and many other chemicals. Most people begin to smell xylene in air at 0.08–3.7 parts of xylene per million parts of air (ppm) and begin to taste it in water at 0.53–1.8 ppm.

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1.2 What happens to xylene when it enters the environment?

Xylene is a liquid, and it can leak into soil, surface water (creeks, streams, rivers), or groundwater, where it may remain for months or more before it breaks down into other chemicals. However, because it evaporates easily, most xylene (if not trapped deep underground) goes into the air, where it stays for several days. In the air, the xylene is broken down by sunlight into other less harmful chemicals.

Xylene can enter the environment when it is made, packaged, shipped, or used. Most xylene that is accidentally released evaporates into the air, although some is released into rivers or lakes. Xylene can also enter soil, water, or air in large amounts after an accidental spill or as a result of an environmental leak

during storage or burial at a waste site.

Xylene very quickly evaporates into the air from surface soil and water. Xylene stays in the air for several days until it is broken down by sunlight into other less harmful chemicals.

Most xylene in surface water evaporates into the air in less than a day. The rest of it is slowly broken down into other chemicals by small living organisms in the water. Only very small amounts are taken up by plants, fish, and birds. We do not know exactly how long xylene stays in water, but we do know that it stays longer in underground water than in lakes and rivers, probably because it can evaporate from the latter.

Xylene evaporates from soil surfaces. Xylene below the soil surface stays there for several days and may travel down through the soil and enter underground water (groundwater). Small living organisms in soil and groundwater may transform it into other less harmful compounds, although this happens slowly. It is not clear how long xylene remains trapped deep underground in soil or groundwater, but it may be months or years. Xylene stays longer in wet soil than in dry soil. If a large amount of xylene enters soil from an accidental spill, a hazardous waste site, or a landfill, it may travel through the soil and contaminate drinking water wells. Only a small amount of xylene is absorbed by animals that live in water contaminated with xylene.

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1.3 How might I be exposed to xylene?

You may be exposed to xylene because of its distribution in the environment. Xylene is primarily released from industrial sources, in automobile exhaust, and during its use as a solvent. Hazardous waste disposal sites and spills of xylene into the environment are also possible sources of exposure. You are most likely to be exposed to xylene by breathing it in contaminated air. Levels of xylene measured in the air of industrial areas and cities of the United States range from 1 to 88 parts of xylene per billion parts of air (a part per billion [ppb] is one thousandth of a part per million [ppm]; one ppm equals 1,000 ppb). Xylene is sometimes released into water and soil as a result of the use, storage, and transport of petroleum products. Surface water generally contains less than 1 ppb, although the level may be higher in industrial areas. You can also be exposed to xylene by drinking or eating xylene-contaminated water or food. Levels of xylene in public drinking water supplies have been reported to range from 0 to 750 ppb. Little information exists about the amount of xylene in food. Xylene levels ranging from 50 to 120 ppb have been found in some fish samples. Xylene has been found in chicken eggs and in the polystyrene packaging in which they are sold.

You may also come in contact with xylene from a variety of

consumer products, including cigarette smoke, gasoline, paint, varnish, shellac, and rust preventives. Breathing vapors from these types of products can expose you to xylene. Indoor levels of xylene can be higher than outdoor levels, especially in buildings with poor ventilation. Skin contact with products containing xylene, such as solvents, lacquers, paint thinners and removers, and pesticides may also expose you to xylene.

Besides painters and paint industry workers, others who may be exposed to xylene include biomedical laboratory workers, distillers of xylene, wood processing plant workers, automobile garage workers, metal workers, and furniture refinishers also may be exposed to xylene. Workers who routinely come in contact with xylene-contaminated solvents in the workplace are the population most likely to be exposed to high levels of xylene.

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1.4 How can xylene enter and leave my body?

Xylene is most likely to enter your body when you breathe xylene vapors. Less often, xylene enters the body through the skin following direct contact. It is rapidly absorbed by your lungs after you breathe air containing it. Exposure to xylene may also take place if you eat or drink xylene-contaminated food or water. The amount of xylene retained ranges from 50% to 75% of the amount of xylene that you inhale. Physical exercise increases the amount of xylene absorbed by the lungs. Absorption of xylene after eating food or drinking water containing it is both rapid and complete. Absorption of xylene through the skin also occurs rapidly following direct contact with xylene. Absorption of xylene vapor through the skin is lower than absorption of xylene vapor by the lungs. However, it is not known how much of the xylene is absorbed through the skin. At hazardous waste sites, breathing xylene vapors, drinking well water contaminated with xylene, and direct contact of the skin with xylene are the most likely ways you can be exposed. Xylene passes into the blood soon after entering the body.

In people and laboratory animals, xylene is broken down into other chemicals especially in the liver. This process changes most of the xylene that is breathed in or swallowed into a different form. Once xylene breaks down, the breakdown products rapidly leave the body, mainly in urine, but some unchanged xylene also leaves in the breath from the lungs. One of the breakdown products of xylene, methylbenzaldehyde, is harmful to the lungs of some animals. This chemical has not been found in people exposed to xylene. Small amounts of breakdown products of xylene have appeared in the urine of people as soon as 2 hours after breathing air containing xylene. Usually, most of the xylene that is taken in leaves the body within 18 hours after exposure ends. Storage of xylene in fat or muscle may prolong the time needed for xylene to leave the body.

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1.5 How can xylene affect my health?

Short-term exposure of people to high levels of xylene can cause irritation of the skin, eyes, nose, and throat; difficulty in breathing; impaired function of the lungs; delayed response to a visual stimulus; impaired memory; stomach discomfort; and possible changes in the liver and kidneys. Both short- and long-term exposure to high concentrations of xylene can also cause a number of effects on the nervous system, such as headaches, lack of muscle coordination, dizziness, confusion, and changes in one's sense of balance. People exposed to very high levels of xylene for a short period of time have died. Most of the information on long-term exposure to xylene is from studies of workers employed in industries that make or use xylene. Those workers were exposed to levels of xylene in air far greater than the levels normally encountered by the general population. Many of the effects seen after their exposure to xylene could have been caused by exposure to other chemicals that were in the air with xylene.

Results of studies of animals indicate that large amounts of xylene can cause changes in the liver and harmful effects on the kidneys, lungs, heart, and nervous system. Short-term exposure to very high concentrations of xylene causes death in animals, as well as muscular spasms, incoordination, hearing loss, changes in behavior, changes in organ weights, and changes in enzyme activity. Long-term exposure of animals to low concentrations of xylene has not been well studied.

Information from animal studies is not adequate to determine whether or not xylene causes cancer in humans. Both the International Agency for Research on Cancer (IARC) and EPA have found that there is insufficient information to determine whether or not xylene is carcinogenic and consider xylene not classifiable as to its human carcinogenicity.

Exposure of pregnant women to high levels of xylene may cause harmful effects to the fetus. Studies of unborn animals indicate that high concentrations of xylene may cause increased numbers of deaths, decreased weight, skeletal changes, and delayed skeletal development. In many instances, these same concentrations also cause damage to the mothers. The higher the exposure and the longer the exposure to xylene, the greater the chance of harmful health effects. Lower concentrations of xylene are not so harmful.

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1.6 Is there a medical test to determine whether I have been exposed to xylene?

Medical tests are available to determine if you have been exposed to xylene at higher-than-normal levels. Confirmation of xylene exposure is determined by measuring some of its breakdown

products eliminated from the body in the urine. These urinary measurements will determine if you have been exposed to xylene. There is a high degree of agreement between exposure to xylene and the levels of xylene breakdown products in the urine. However, a urine sample must be provided very soon after exposure ends because xylene quickly leaves the body. Alcohol or aspirin may produce false positive test results. Medical tests have been developed to measure levels of xylene in blood by the National Center for Environmental Health Laboratory and in exhaled breath by EPA's Total Exposure Assessment Methodology. These tests may be available in certain doctors' offices. Available tests can only indicate exposure to xylene; they cannot be used to predict which health effects, if any, will develop.

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1.7 What recommendations has the federal government made to protect human health?

EPA estimates that, for an adult of average weight, exposure to 10 milligrams of xylene per liter (mg/L or ppm) of water each day for a lifetime (70 years) is unlikely to result in harmful noncancerous health effects. For a long-term but less-than-lifetime exposure (about 7 years), 27.3 ppm is estimated to be a level unlikely to result in harmful health effects in an adult.

Exposure to 12 ppm xylene in water for 1 day or to 7.8 ppm of xylene in water for 10 days or longer is unlikely to present a health risk to a small child. EPA has proposed a recommended maximum level of 10 ppm xylene in drinking water.

To protect people from the potential harmful health effects of xylene, EPA regulates xylene in the environment. EPA has set a legally enforceable maximum level of 10 mg/L (equal to 10 ppm) of xylene in water that is delivered to any user of a public water system. The Occupational Safety and Health Administration (OSHA) has set an occupational exposure limit of 100 ppm of xylene in air averaged over an 8-hour workday and a 15-minute exposure limit of 150 ppm. These regulations also match recommendations (not legally enforceable) of the American Conference of Governmental Industrial Hygienists. The National Institute for Occupational Safety and Health (NIOSH) has recommended an exposure limit (not legally enforceable) of 100 ppm of xylene averaged over a workday up to 10 hours long in a 40-hour workweek. NIOSH has also recommended that exposure to xylene not exceed 150 ppm for longer than 15 minutes. NIOSH has classified xylene exposures of 10,000 ppm as immediately dangerous to life or health.

EPA and the Food and Drug Administration (FDA) specify conditions under which xylene may be used as a part of herbicides, pesticides, or articles used in contact with food. The EPA has a

chronic drinking water health advisory of 27.3 ppm for an adult and 7.8 ppm for a 10-kilogram child.

EPA regulations require that a spill of 1,000 pounds or more of xylene or used xylene solvents be reported to the Federal Government National Response Center.

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1.8 Where can I get more information?

If you have any more questions or concerns, please contact your community or state health or environmental quality department or:

Agency for Toxic Substances and Disease Registry
Division of Toxicology
1600 Clifton Road NE, Mailstop F-32
Atlanta, GA 30333

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5285 Port Royal Road
Springfield, VA 22161
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U.S. Environmental Protection Agency

Lead in Paint, Dust, and Soil

Basic Information

Did you know the following facts about lead?

FACT: Lead exposure can harm young children and babies even before they are born.

FACT: Even children who seem healthy can have high levels of lead in their bodies.

FACT: You can get lead in your body by breathing or swallowing lead dust, or by eating soil or paint chips containing lead.

FACT: You have many options for reducing lead hazards. In most cases, lead-based paint that is in good condition is not a hazard.

FACT: Removing lead-based paint improperly can increase the danger to your

family.

If you think your home might have lead hazards, read on to learn about lead and some simple steps to protect your family.

Health Effects of Lead

In the United States, about 900,000 children ages 1 to 5 have a blood-lead level above the level of concern.

Even children who appear healthy can have dangerous levels of lead in their bodies.

- People can get lead in their body if they:
  - Put their hands or other objects covered with lead dust in their mouths.
  - Eat paint chips or soil that contains lead.
  - Breathe in lead dust (especially during renovations that disturb painted surfaces).
- Lead is even more dangerous to children than adults because:
  - Babies and young children often put their hands and other objects in their mouths. These objects can have lead dust on them.
  - Children's growing bodies absorb more lead.
  - Children's brains and nervous systems are more sensitive to the damaging effects of lead.
- If not detected early, children with high levels of lead in their bodies can suffer from:
  - Damage to the brain and nervous system
  - Behavior and learning problems (such as hyperactivity)
  - Slowed growth
  - Hearing problems
  - Headaches
- Lead is also harmful to adults. Adults can suffer from:
  - Difficulties during pregnancy
  - Other reproductive problems (in both men and women)
  - High blood pressure
  - Digestive problems
  - Nerve disorders
  - Memory and concentration problems
  - Muscle and joint pain

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Where Lead is Found

*In general, the older your home, the more likely it has lead-based paint. *

- Paint. Many homes built before 1978 have lead-based paint. The

federal government banned lead-based paint from housing in 1978. Some states stopped its use even earlier. Lead can be found:
    - In homes in the city, country, or suburbs.
    - In apartments, single-family homes, and both private and public housing.
    - Inside and outside of the house.
- In soil around a home. (Soil can pick up lead from exterior paint, or other sources such as past use of leaded gas in cars.)
- Household dust. (Dust can pick up lead from deteriorating lead-based paint or from soil tracked into a home.)
- Drinking water. Your home might have plumbing with lead or lead solder. Call your local health department or water supplier to find out about testing your water. You cannot see, smell, or taste lead, and boiling your water will not get rid of lead. If you think your plumbing might have lead in it:
    - Use only cold water for drinking and cooking.
    - Run water for 15 to 30 seconds before drinking it, especially if you have not used your water for a few hours.
- The job. If you work with lead, you could bring it home on your hands or clothes. Shower and change clothes before coming home. Launder your work clothes separately from the rest of your family's clothes.
- Old painted toys and furniture.
- Food and liquids stored in lead crystal or lead-glazed pottery or porcelain.
- Lead smelters or other industries that release lead into the air.
- Hobbies that use lead, such as making pottery or stained glass, or refinishing furniture.
- Folk remedies that contain lead, such as "greta" and "azarcon" used to treat an upset stomach.

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Where Lead is Likely to be a Hazard

Lead from paint chips, which you can see, and lead dust, which you can't always see, can be serious hazards.

- Peeling, chipping, chalking, or cracking lead-based paint is a hazard and needs immediate attention.
- Lead-based paint may also be a hazard when found on surfaces that children can chew or that get a lot of wear-and-tear. These areas include:
    - Windows and window sills.
    - Doors and door frames.
    - Stairs, railings, and banisters.
    - Porches and fences.

Note: Lead-based paint that is in good condition is usually not a hazard.

- Lead dust can form when lead-based paint is dry scraped, dry sanded, or heated. Dust also forms when painted surfaces bump or rub together. Lead chips and dust can get on surfaces and objects that people touch. Settled lead dust can re-enter the air when people vacuum, sweep, or walk through it.

- Lead in soil can be a hazard when children play in bare soil or when people bring soil into the house on their shoes. Contact the National Lead Information Center (NLIC) to find out about testing soil for lead.

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Checking Your Family and Home for Lead

Get your children and home tested if you think your home has high levels of lead.

Just knowing that a home has lead-based paint may not tell you if there is a hazard.

To reduce your child's exposure to lead, get your child checked, have your home tested (especially if your home has paint in poor condition and was built before 1978), and fix any hazards you may have.

- Your Family
  - Children's blood lead levels tend to increase rapidly from 6 to 12 months of age, and tend to peak at 18 to 24 months of age.
  - Consult your doctor for advice on testing your children. A simple blood test can detect high levels of lead. Blood tests are important for:
    - Children at ages 1 and 2.
    - Children and other family members who have been exposed to high levels of lead.
    - Children who should be tested under your state or local health screening plan.
  - Your doctor can explain what the test results mean and if more testing will be needed.
- Your Home
  - You can get your home checked in one of two ways, or both:
    - A paint inspection tells you the lead content of every different type of painted surface in your home. It won't tell you whether the paint is a hazard or how you should deal with it.
    - A risk assessment tells you if there are any sources of serious lead exposure (such as peeling paint and lead dust). It also tells you what actions to take to address these hazards.
  - Have qualified professionals do the work. There are standards in place for certifying lead-based paint professionals to ensure the work is done safely, reliably, and effectively. Contact the National Lead Information Center (NLIC) for a list of contacts in your area.
  - Trained professionals use a range of methods when checking your home, including:
    - Visual inspection of paint condition and location.
    - A portable x-ray fluorescence (XRF) machine.
    - Lab tests of paint samples.
    - Surface dust tests.

Note: Home test kits for lead are available, but studies suggest that they are not always accurate. Consumers should not rely on these tests before doing renovations or to assure safety.

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What You Can do to Protect Your Family

- If you suspect that your house has lead hazards, you can take some immediate steps to reduce your family's risk:
  - If you rent, notify your landlord of peeling or chipping paint.
  - Clean up paint chips immediately.
  - Clean floors, window frames, window sills, and other surfaces weekly. Use a mop, sponge, or paper towel with warm water and a general all-purpose cleaner or a cleaner made specifically for lead. REMEMBER: NEVER MIX AMMONIA AND BLEACH PRODUCTS TOGETHER SINCE THEY CAN FORM A DANGEROUS GAS.
  - Thoroughly rinse sponges and mop heads after cleaning dirty or dusty areas.
  - Wash children's hands often, especially before they eat and before nap time and bed time.
  - Keep play areas clean. Wash bottles, pacifiers, toys, and stuffed animals regularly.
  - Keep children from chewing window sills or other painted surfaces.
  - Clean or remove shoes before entering your home to avoid tracking in lead from soil.
  - Make sure children eat nutritious, low-fat meals high in iron and calcium, such as spinach and dairy products. Children with good diets absorb less lead.
- In addition to day-to-day cleaning and good nutrition:
  - You can temporarily reduce lead hazards by taking actions such as repairing damaged painted surfaces and planting grass to cover soil with high lead levels. These actions (called "interim controls") are not permanent solutions and will need ongoing attention.
  - To permanently remove lead hazards, you must hire a certified lead "abatement" contractor. Abatement (or permanent hazard elimination) methods include removing, sealing, or enclosing lead-based paint with special materials. Just painting over the hazard with regular paint is not enough.
  - Always hire a person with special training for correcting lead problems—someone who knows how to do this work safely and has the proper equipment to clean up thoroughly. Certified contractors will employ qualified workers and follow strict safety rules set by their state or the federal government.
  - Contact the National Lead Information Center(NLIC) for help with locating certified contractors in your area and to see if financial assistance is available.

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Are You Planning to Buy or Rent a Home Built Before 1978?

Many houses and apartments built before 1978 have paint that contains lead (called lead-based paint). Lead from paint, chips, and dust can pose serious health hazards if not taken care of properly.

Federal law requires that individuals receive certain information before renting

or buying a pre-1978 housing:

- Residential Lead-Based Paint Disclosure Program
  - LANDLORDS have to disclose known information on lead-based paint and lead-based paint hazards before leases take effect. Leases must include a disclosure form about lead-based paint.
  - SELLERS have to disclose known information on lead-based paint and lead-based paint hazards before selling a house. Sales contracts must include a disclosure form about lead-based paint. Buyers have up to 10 days to check for lead hazards.
  - More information on the disclosure program.

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Remodeling or Renovating a Home with Lead-Based Paint

If not conducted properly, certain types of renovations can release lead from paint and dust into the air.

Many houses and apartments built before 1978 have paint that contains lead (called lead-based paint). Lead from paint, chips, and dust can pose serious health hazards if not taken care of properly.

- Federal law requires that contractors provide lead information to residents before renovating a pre-1978 housing:
  - Pre-Renovation Education Program (PRE)
    - RENOVATORS have to give you a pamphlet titled "Protect Your Family from Lead in Your Home", before starting work.
    - More information on the Pre-Renovation Education Program.
- Take precautions before your contractor or you begin remodeling or renovations that disturb painted surfaces (such as scraping off paint or tearing out walls):
  - Have the area tested for lead-based paint.
  - Do not use a belt-sander, propane torch, heat gun, dry scraper, or dry sandpaper to remove lead-based paint. These actions create large amounts of lead dust and fumes.
  - Lead dust can remain in your home long after the work is done.
  - Temporarily move your family (especially children and pregnant women) out of the apartment or house until the work is done and the area is properly cleaned. If you can't move your family, at least completely seal off the work area.
  - Follow other safety measures to reduce lead hazards. You can find out about other safety measures in the EPA brochure titled "Reducing Lead Hazards When Remodeling Your Home". This brochure explains what to do before, during, and after renovations.
  - If you have already completed renovations or remodeling that could have released lead-based paint or dust, get your young children tested and follow the steps outlined to protect your family.

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Additional Resources

- Documents and Brochures
  - Lead in Your Home: A Parent's Reference Guide
  - Testing Your Home for Lead in Paint, Dust, and Soil
  - Finding a Qualified Lead Professional for Your Home
  - Lead Poisoning and Your Children (English)
  - Lead Poisoning and Your Children (En Español)
  - Protect Your Family From Lead in Your Home (English)
  - Protect Your Family From Lead in Your Home (En Español)
  - Reducing Lead Hazards When Remodeling Your Home (English)
  - Reducing Lead Hazards When Remodeling Your Home (En Español)
  - Ten Tips to Protect Children from Pesticide and Lead Poisonings around the Home
  - The Lead-Based Paint Pre-Renovation Education Rule: A Handbook for Contractors, Property Mangers, and Maintenance Personnel
  - Lead Paint Safety: A Field Guide for Painting, Home Maintenance, and Renovation Work
- Other Lead Resources

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OFFICE OF THE SCIENCE ADVISOR

GUIDANCE

CHAPTER 7

ASSESSMENT OF HEALTH RISKS FROM INORGANIC LEAD IN SOIL

ABSTRACT

This guidance describes a mathematical model for estimating blood lead concentration resulting from contact with lead-contaminated environmental media. A lead concentration of concern of ten micrograms per deciliter of whole blood is established. A distributional approach is used, allowing estimation of various percentiles of blood lead concentration associated with a given set of inputs. The method has been adapted to a computer spreadsheet.

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Assessment of Health Risks From Inorganic Lead in Soil

1 INTRODUCTION

1.1 Purpose

The purpose of this guidance is to provide a methodology for evaluating exposure and the potential for adverse health effects resulting from exposure to lead in the environment.

1.2 Application

Since most human health effects data are based on blood lead (Pb) concentration, this guidance presents a blood Pb concentration of concern for the protection of human health, and an alogrithm for estimating blood Pb concentrations in children and adults based on a multi-pathway analysis.

1.3 Limitations

It is anticipated that this guidance will be periodically revised to reflect the changing state of the science.

2 PRINCIPLES

2.1 Blood Lead Concentration Of Concern

The Pb concentration of concern in children and adults is ten micrograms (ug) per deciliter (dl) of whole blood. The point of departure for risk management is a 0.01 risk of exceeding this value.

2.2 Lead Exposure Pathways--Blood Lead Calculation

This method can be used to estimate blood lead concentrations resulting from exposure via the five pathways listed below. Each pathway is represented by an equation relating incremental blood lead increase to a concentration in a medium, using contact rates and empirically determined ratios. The contributions via the five pathways are added to arrive at an estimate of median blood lead concentration resulting from the multipathway exposure. Ninetieth, ninety-fifth, ninety-eighth, and ninety-ninth percentile concentrations are estimated from the median by assuming a log-normal distribution with a geometric standard deviation (GSD) of

1.42. The method has been adapted to a computer spreadsheet.

3 METHODS

Generalized equations describing uptake via the five exposure pathways are as follows:

Dietary Intake Equation

Pbb = dietary Pb * contact rate * dietary constant

where:

dietary Pb (ug Pb/kg diet) = (9.45 + 0.025 * mg Pb/kg soil) [1]
contact rate, adults = 2.2 kg diet/day [2]
contact rate, children = 1.3 kg diet/day [2]
dietary constant, children = 0.16 (ug Pb/dl blood)/(ug Pb/day) [3]
dietary constant, adults = 0.04 (ug Pb/dl blood)/(ug Pb/day) [4]

Drinking Water Intake Equation

Pbb = water Pb * contact rate * dietary constant

where:

drinking water Pb (ug Pb/l water) is a site-specific, measured value [5]
contact rate, adults = 1.4 l water/day [6]
contact rate, children = 0.4 l water/day [6]
dietary constant, children = 0.16 (ug Pb/dl blood)/(ug Pb/day) [3]
dietary constant, adults = 0.04 (ug Pb/dl blood)/(ug Pb/day) [4]

Soil and Dust Ingestion Intake Equation

Pbb = soil Pb * contact rate * soil constant

where:

soil Pb (ug/g) is a site-specific, measured value [15]
contact rate, children = 0.055 g/day [7]
contact rate, adults = 0.025 g/day [8]
soil constant, children = 0.07 (ug Pb/dl blood)/(ug ingested Pb/day) [9]
soil constant, adults = 0.018 (ug Pb/dl blood)/(ug ingested Pb/day) [9]

Inhalation Intake Equation

Pbb = atmospheric Pb * inhalation constant

where:

atmospheric Pb = local or regional ambient Pb (ug/m3) + (airborne dust * soil Pb)10
inhalation constant, children = 1.92 (ug/dl)/(ug/m3)11
inhalation constant, adults = 1.64 (ug/dl)/(ug/m3)11
airborne dust (g/m3) is a site-specific, measured value with a default value

of 0.00005.

Dermal Contact Intak e Equation

Pbb = soil Pb * contact rate * soil constant
where:

soil Pb (ug Pb/gm soil) is a site-specific, measured value
contact rate, children = 1.4 gm soil/day [12]
contact rate, adults = 1.85 gm soil/day [13]
soil constant = 0.0001 (ug Pb/dl blood)/(ug dermal Pb/day) [14]

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1 Derived as follows: (0.945 * 10 ug/kg) + (0.055 * 0.00045 * soil Pb in mg/kg * 1000 ug/mg). Assumes that 5.5% of the diet consists of home-grown produce with the other 94.5% supplied by a homogeneous source with a lead content of 10 ug/kg. If food production on the site can be ruled out, use 10 ug/kg for dietary lead (EPA, 1989b, Bolger, et.al., 1990). Home-grown produce is assumed to contain 0.045% of the lead level in the soil.

2 Based on a report by Pennington (1983). For this method, a one-year-old child shall represent all children, based on the assumption that protecting the one-year-old child will protect all children.

3 Based on a study by Ryu, et.al. (1983)

4 Based on a report by FDA (1990)

5 Pb concentrations in local water supplies as consumed. If site-specific data are unavailable, a value of 15 ug/l may be used.

6 EPA (1989b)

7 Based on Calabrese (1990). Deliberate soil ingestion (soil pica) is represented as 0.00079 kg soil/day average.

8 For residential exposures and most occupational exposures, based on Calabrese (1990). Occupations with a high potential for soil ingestion (such as construction) should be represented as 0 .00005 kg soil/day average.

9 These values are 44% of tha t for lead ingested with food or water, based on a study in rats which compared the bioavailability of lead acetate mixed with the diet to that of soil-bound lead (Chaney et.al., 1990).

10 The ambient air Pb concentration data are available from the California Air Resources Board, Technical Support Division. Data for the most recent year for the nearest monitoring station should be used. If monitoring data collected within the same air basin are unavailable, a value of 0.18 ug/m3 may be used, or consult with the DTSC project manager. Respirable airborne dust is assumed to be 0.00005 g/m3 unless site-specific data are available.

11 Based on EPA (1986)

12 Based on a soil adherence of 5 g/m2 and 0.28 m2 of exposed skin (EPA, 1989b).

13 Based on a soil adhere nce of 5 g/m2 and 0.37 m2 of exposed skin (EPA, 1989b).

14 This value is derived by multiplying the Pb ingestion:blood concentration ratio for adults (0.018 ug/dl per ug/day) by the ratio of dermal absorption [0.06% (Moore, et. al., 1980)] to oral absorption [11% (ATSDR, 1990)].

15 Developed according to Chapter 2 of this Guidance.

4 COMMENTS

4.1 Blood Lead Concentration Of Concern

The traditional reference dose approach to toxic chemicals is not applied to Pb because most human health effects data are based on blood Pb concentrations rather than external dose. Blood Pb concentration is an integrated measure of internal dose, reflecting total exposure from site-related and background sources. A clear no-observed-effect concentration has not been established for such Pb-related endpoints as birth weight, gestation period, heme synthesis and neurobehavioral development in children and fetuses, and blood pressure in middle-aged men. Dose-response curves for these endpoints appear to extend down to 10 ug Pb/dl or less (ATSDR, 1990).

4.2 Estimating Blood Lead Concentrations From Environmental Concentrations

Total Pb is generally used as the measure of Pb in various media, even though the disposition of Pb may differ according to its form. Insufficient data are available to justify differential treatment of different forms of inorganic Pb. However, if the lead at a particular site has been shown, in studies acceptable to DTSC, to be less bioavailable than the assumed values, lower bioavailability factors may be substituted for the default factors. Organic Pb is more readily absorbed through the skin and other membranes than inorganic Pb, and it must therefore be treated separately. Since it is less stable in the environment, it is usually a minor source of exposure.

In the absence of specific information about the population of interest, background exposures are estimated using norms developed from survey data.

4.3 Derivation Of Model Parameters

Unless the potential for on-site gardening can be ruled out, it is assumed that 5.5% of the diet consists of home-grown produce, based on EPA guidance (USEPA, 1991). Pb concentration in home-grown produce is calculated as 0.045% of that in the soil, based on plant uptake studies (Chaney, et.al., 1982). Background dietary Pb concentration (10 ug/kg) is based on a 1990 report based on FDA data (Bolger, et.al., 1990). The default drinking water Pb concentration is based on the federal action concentration of 15 ug/l at the tap (USEPA, 1991b).

The distribution of blood Pb concentrations for a given set of environmental inputs is a critical factor in protecting sensitive members of the population.

Based on a review of data from NHANES II and from several published studies of blood Pb concentrations in children living near point sources of lead, EPA concluded that blood Pb was generally log-normally distributed, that the geometric standard deviation (GSD) for children was between 1.3 and 1.53, and that 1.42 was a representative value for the GSD (USEPA, 1989c). Adult GSDs ranged from 1.34 to 1.40, which we do not consider to be sufficiently different from the range for children to justify using a different value for adults. The model assumes a log-normal distribution with a GSD of 1.42 and uses this information to estimate the fiftieth, ninetieth, ninety-fifth, ninety-eighth, and ninety-ninth percentile blood Pb concentration for a set of inputs. Since this distribution reflects the physiologic and behavioral variables including soil consumption, using upper bound values for contact rates would distort the percentiles corresponding to blood Pb concentrations.

The availability of Pb ingested with soil is based on a study which compared the absorption of soil Pb and Pb acetate incorporated into the diet of rats (Chaney, et.al., 1990). While the authors found a direct relationship between the Pb concentration in the soil and Pb bioavailability, the data did not define the shape of the concentration/ bioavailability curve sufficiently to allow extrapolation beyond the range studied. The highest observed bioavailability for soil lead concentrations less than 1000 ppm was 44% of that observed for Pb acetate, and this guideline adopts this value as a conservative estimate of bioavailability. To accurately assess the matrix effect, a variety of variables, including lead species, particle size, and soil type would have to be systematically examined at various Pb concentrations in soil.

The daily soil adherence to skin of 5 g/m2 (0.5 mg/cm2) is based on Driver et.al (1989). The dermal absorption factor of 0.0001 ug Pb/dl blood per ug dermal Pb/day was developed by multiplying the Pb ingestion:blood concentration ratio for adults (0.018 ug/dl per ug/day) by the ratio of dermal absorption [0.06% (Moore, et. al., 1980)] to oral absorption [(11% (ATSDR, 1990)]. Based on data in the Exposure Factors Handbook (USEPA, 1989b), the median skin area of arms, hands, feet, and legs of 1-year-old boys is estimated to be 0.28 m2, and the median skin area of arms and hands of men is estimated to be 0.37 m2.

The ratio of 0.16 ug/dl per ug/day ingested by children is a value derived from studies in infants by Ryu et.al. (1983). The ratio of 0.04 ug/dl per ug/day ingested by adults is an empirically-determined value recommended by EPA (1986) and FDA (1990). The default value for inadvertent soil/dust ingestion by children , 55 mg/day, is based on tracer studies reviewed by Calabrese, et.al. (1991). Adult soil consumption is 25 mg/day, based on EPA (1991a). DTSC uses soil consumption rates of 200 and 100 mg/day in calculating a reasonable maximum exposure for children and adults,

respectively. However, reasonable maximum inputs are not recommended for use with the lead model because the model already considers the distribution of blood lead, which reflects variation in soil ingestion along with other variables. Soil consumption representing pica is 0.79 g/day, based on estimates by Calabrese et.al. (1991).

The slopes of 1.92 and 1.64 ug/dl of blood per ug/m3 of continuously-breathed air at atmospheric Pb concentrations <5 ug/m3 are based on results of experimental exposures and epidemiological studies which adjusted for airborne lead contributions to pathways other than inhalation. These studies found slopes ranging from 1.52 to 2.46 ug/dl per ug/m3 in children and 1.25 to 2.14 in adults (USEPA, 1986). The default airborne lead concentration is the highest monthly mean 24-hour value recorded in California in 1990.

4.4 Using This Guidance

This guidance may be implemented using a computer spreadsheet, which may be obtained from DTSC. The spreadsheet is based on DTSC Guidance, Volume 4, Chapter 1, which should be consulted for more general aspects of spreadsheet application. For this spreadsheet, soil concentration in mg/kg (ppm w/w) is entered in cell E7. The spreadsheet uses it in each calculation that is affected by soil Pb. Atmospheric Pb is entered in cell B6. Drinking-water Pb is entered in cell B8. If omission of the site-grown produce pathway can be justified, a "0" is entered in cell E9. Airborne dust level is entered in cell E10. The remainder of the cells are protected and should not be altered without approval of DTSC. Any such changes will require sufficient justification and must be documented.

4.5 Other Standards And Guidance

USEPA (1991c) considers lead to be a class B-2 carcinogen, with sufficient evidence in animals and inadequate evidence in humans. A carcinogenic potency has not been assigned. The federal MCL is 15 ug/l maximum at the tap with a maximum of 5 ug/l as a system-wide average (USEPA, 1991b). The Centers for Disease Control has stated that prevention activities should be directed at reducing children's blood Pb concentrations at least to below 10 ug/dl (CDC, 1991). The EPA has set 1.5 ug/m3 as the Pb concentration limit for ambient air (quarterly average) (USEPA, 1978). California's standard is also 1.5 ug/m3, but is based on a monthly average. The threshold limit value is 50 ug/m3 for workplace air (ACGIH, 1989).

FDA (1990) considers the Lowest Observable Adverse Effect Level (LOAEL) to be 10 ug/dl in children and fetuses, and 30 ug/dl in adults. They use empirically-derived ratios of 0.16 and 0.04 ug/dl per ug/day ingested to predict concentrations in young children and adults, respectively. Applying an uncertainty factor of ten results in provisional

tolerable intake levels of 6 ug/day for children six or less, 15 ug/day for children over six, 25 ug/day for pregnant women, and 75 ug/day for men.

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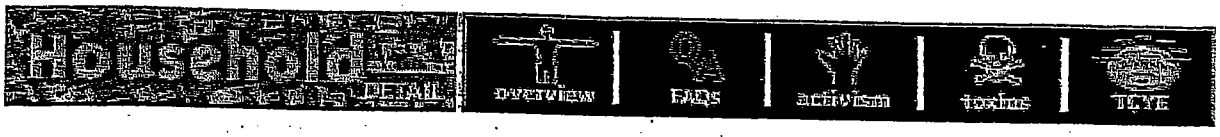

■ General information

Lead: health effects and sources of exposure

WHAT ARE THE SOURCES?

The main sources are petrol and paint. The main pathway of children's exposure is ingestion of contaminated dust and soil via normal hand-to-mouth activity.

TRANSPORT SOURCES

Lead functions as an octane enhancer and valve lubricant for pre-1986 petrol vehicles. It is also used in lead acid batteries and some aviation fuels. The use of leaded petrol has contributed to approximately 90% of lead in air pollution worldwide. In Australia, emissions from motor vehicle exhausts remain a major source of exposure for young children and the major source of chronic (long-term mild to moderate) lead poisoning through contamination of dust, soil and, to a lesser extent, water and food.

PAINT SOURCES

Because of renovation involving lead-containing paint, contaminated homes and yards are the major source of acute (short-term high-dose) lead poisoning. All old (pre-1970s) paints (including on metal surfaces) should be assumed to contain lead unless tests prove otherwise.

INDUSTRY

Lead mining, smelting and to a lesser extent, manufacturing industries, are other major sources of acute poisoning for those in the nearby community. Problems include atmospheric fallout and contaminated effluent and sewage sludge.

FOOD SOURCES

Contamination can occur in eggs, and fruit and vegetables grown near traffic or smelting or mining activity, and lead-soldered tinned acidic foods and ham. The average two-year old gets 60% of their food lead from whole grain foods, possibly due to the use of lead-contaminated fertilisers.

DRINKING WATER

Atmospheric input to surface waters can contribute

about 15% of the lead in drinking water. Water which is acidic and low in dissolved salts can leach substantial quantities in the first five years from PVC pipes, brass or bronze fittings or (illegal) lead solder. Lead-lined holding tanks in water coolers and other containers are further sources of contamination.

OTHER SOURCES

These include contaminated soil from previous use of lead arsenic pesticides; lead crystal; exposure to fumes in glassmaking or lead lighting; swallowing of fishing sinkers, lead shot, bullets or small electronic parts; herbal remedies containing lead, and cosmetics; emissions and ash from incinerators or crematoria; burning lead-painted wood or coal; and seepage from landfill sites.

WHAT ARE THE HEALTH EFFECTS?

The most sensitive parts of the body are the kidneys, the blood and the central nervous system. Because children are developing, they are more susceptible to the effects of even low levels, once thought to be safe. These effects include birth defects, reduced IQ, learning disabilities, stunted growth, hearing loss and behaviour problems.

LEAD AND CHILDREN

Children absorb lead efficiently - up to 50% of ingested lead, which compares to 10-15% in adults (the rest is excreted). Even a moderate amount can contribute significantly to a child's lead uptake. Children are most at risk between the ages of one and four when hand-to-mouth activity is greatest.

The US definition of childhood lead poisoning is a blood lead level over 10 micrograms per decilitre (10 ug/dL). If your blood lead result is in micromoles per litre (umol/L) multiply the number by 20.7 to convert it to ug/dL. In 1993 the National Health and Medical Research Council (NH&MRC) of Australia set the goal of a blood level of less than 10 ug/dl for every Australian.
An American research team found on average that for each three microgram drop there was a corresponding one-point improvement in the children's performance on IQ tests.

Blood lead levels in children from rural areas are lower than in urban areas. A 1994 NSW Health Department study estimates that around 70,000 NSW children aged between 0 and 4 years suffer from lead poisoning.

Symptoms of long-term exposure in adults and children include lower IQ, difficulties with visual motor functions and reaction times, psychological impairment, tiredness, inability to concentrate and low overall functioning. Because these symptoms may only become evident years after the child has been lead poisoned, regular checks on young children's blood lead levels and due care are the only way to monitor lead poisoning and take avoidance action.

HOW LEAD POISONING OCCURS

It can be inhaled, ingested or absorbed through skin which is wet with sweat or saliva. The main sources for young children are leaded petrol fallout and paint, via ingestion of dust and soil.

Children in homes undergoing renovation are between 2 and 12 times more likely to have blood lead levels over 15 ug/dL. When leaded paint is removed from houses, bridges or cars by dry removal techniques, it disperses into the atmosphere as flakes, dust, ash or fumes. However in urban areas, up to 90% of lead in the air is due to leaded petrol exhaust fumes. Fallout from leaded petrol is a major source of contamination in house dusts and soil.

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Toxic Chemicals in Your Environment
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UPDATED VERSION OF THE CALIFORNIA EPA LEAD RISK ASSESSMENT SPREADSHEET MODEL FOR PREDICTING BLOOD LEAD IN CHILDREN AND ADULTS

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ABSTRACT

The California Department of Toxic Substances Control has revised and updated its lead risk assessment spreadsheet model (LeadSpread) for predicting distributions of blood lead for adults and for children 1-2 years old. Inputs to LeadSpread are central tendency values; output is converted to a lognormal distribution via an assumed geometric standard deviation. We increased this geometric standard deviation to 1.60, according to White et al. (1998). We decreased food consumption to 1.1 kg/day for children and 1.9 kg/day for adults (Bolger, 1996) and decreased our estimate of lead in the diet to 2.8 µg/kg of food for children and 1.6 µg/kg of food for adults (USFDA, 1996-97). Based on EPA guidance (USEPA, 1997), we increased soil ingestion rates to 100 mg/day for children and 50 mg/day for adults, decreased the ventilation rate for children to 6.8 m^3/day, and changed exposed skin surface to 2,900 cm^2 for children and 5,800 cm^2 for adults. Using recent guidance on dermal risk assessment (USEPA, 1998), we decreased soil-to-skin adherence from 1 mg/cm^2 for children and adults to 0.2 mg/cm^2 for children and 0.07 mg/cm^2 for adults. Using data from California Air Resource Board (CARB, 1999), we decreased our estimates of lead in air to 0.028 µg/m^3. Airborne respirable particulates were estimated at 1.5 µg/m^3, using emission modeling. Assuming 20 mg Pb/kg in soil and 15 µg Pb/L in drinking water, these revised inputs to LeadSpread predict a geometric mean blood lead concentration of 1.7 µg/dL for children 1-2 years old, with a 99th percentile of 5.2 µg/dL. The National Health and Nutrition Examination Survey III, Phase 2 (NHANES III; USDHHS, 1996) found the geometric mean blood lead concentration in the Western U.S. to be 2.2 for children 1-6 years old and 2.6 in children 1-2 years old. Restricting the data from NHANES III to children living in post-1973 housing, geometric mean blood lead concentration decreased to 1.7 and 1.9 µg/dL for children 1-6 and 1-2 years old, respectively. Thus, LeadSpread with its revised inputs agrees well with NHANES III data for children either 1-2 or 1-6 years old in post-1973 housing. We also predicted blood lead concentrations using LeadSpread with various combinations of possible site-specific inputs.

LEADSPREAD REVISIONS

The California Department of Toxic Substances Control maintains a lead risk assessment spreadsheet model (LeadSpread) for predicting distributions of blood lead concentration in adults and in children 1-2 years old. Inputs to LeadSpread are central tendency values; output is converted to a lognormal distribution via an assumed geometric standard deviation. The Department has recently revised the model by reformatting the spreadsheet and by replacing several default input parameters to reflect more recent information. The revised model parameters are shown below.

DEFAULT INPUT PARAMETER VALUES

General Parameters	Units	Previous	Revised	Reference
Geometric Std. Deviation	Unitless	1.42	1.60	White et al., 1998
Background airborne lead	µg/m^3	0.18	0.028	CARB,1999
Source-specific airborne dust	µg/m^3	50	1.5	Cowherd, 1985
Lead in drinking water	µg/L	15	15	MCL
% Diet home-grown (resident)	%	5.5	7	USEPA, 1997
% Diet home-grown (worker)	%	0	0	

Child Parameters	Units	Previous	Revised	Reference
Daily food consumption	kg/day	1.3	1.1	Bolger, 1996
Dietary lead	µg/kg	10	2.8	USFDA, 1996-97
Soil ingestion	mg/day	55	100	USEPA, 1997
Soil ingestion, pica child	mg/day	790	200	USEPA, 1997
Ventilation rate	m^3/day	10	6.8	USEPA, 1997
Exposed skin area	cm^2	2,800	2,900	USEPA, 1997
Soil-to-skin adherence	mg/cm^2	1	0.2	USEPA, 1998

Adult Parameters	Units	Previous	Revised	Reference
Daily food consumption	kg/day	2.2	1.9	Bolger, 1996
Dietary lead	µg/kg	10	1.6	USFDA, 1996-97
Soil ingestion	mg/day	25	50	USEPA, 1997
Exposed skin area, resid.	cm^2	3,700	5,800	USEPA, 1997
Soil-to-skin adherence	mg/cm^2	1	0.07	USEPA, 1998

RESULTS USING REVISED MODEL

We ran LeadSpread with various combinations of possible site-specific inputs to illustrate its responses to changes in key variables. The following tables illustrate some of these predictions. In each table, the non-default model inputs are highlighted. Poster 342 shows model response to stepwise changes in key input parameters.

TYPICAL CHILD

INPUTS					OUTPUTS			
					Blood lead (µg/dL)		Soil concentration (mg/kg) Corresponding to 10 µg/dL	
Lead in soil (mg/kg)	Home-grown food (% diet)	Lead in water (µg/L)	Airborne Lead (µg/m³)	PM_{10} (µg/m³)	95th percentile	99th percentile	95th percentile	99th percentile
20	7%	15	0.028	1.5	3.8	5.2	247	146
1000	7%	15	0.028	1.5	30.6	42.3	247	146
20	0%	15	0.028	1.5	3.6	5.0	435	255
20	7%	5	0.028	1.5	2.4	3.3	298	197
20	7%	15	0.1	1.5	4.0	5.5	240	139
20	7%	15	0.028	50	3.8	5.2	246	145

PICA CHILD

INPUTS					OUTPUTS			
					Blood lead (µg/dL)		Soil concentration (mg/kg) Corresponding to 10 µg/dL	
Lead in soil (mg/kg)	Home-grown food (% diet)	Lead in water (µg/L)	Airborne Lead (µg/m³)	PM_{10} (µg/m³)	95th percentile	99th percentile	95th percentile	99th percentile
20	7%	15	0.028	1.5	4.1	5.7	159	94
1000	7%	15	0.028	1.5	45.8	63.3	159	94
20	0%	15	0.028	1.5	3.9	5.4	218	128
20	7%	5	0.028	1.5	2.4	3.3	191	126
20	7%	15	0.1	1.5	4.3	5.9	154	89
20	7%	15	0.028	50	4.1	5.7	158	94

ADULT (RESIDENTIAL EXPOSURE)

INPUTS					OUTPUTS			
					Blood lead (µg/dL)		Soil concentration (mg/kg) Corresponding to 10 µg/dL	
Lead in soil (mg/kg)	Home-grown food (% diet)	Lead in water (µg/L)	Airborne Lead (µg/m³)	PM_{10} (µg/m³)	95th percentile	99th percentile	95th percentile	99th percentile
20	7%	15	0.028	1.5	2.5	3.5	1062	676
1000	7%	15	0.028	1.5	9.6	13.2	1062	676
20	0%	15	0.028	1.5	2.5	3.4	3793	2407
20	7%	5	0.028	1.5	1.3	1.8	1230	844
20	7%	15	0.1	1.5	2.8	3.8	1026	640
20	7%	15	0.028	50	2.5	3.5	1037	660

ADULT (OCCUPATIONAL EXPOSURE)

INPUTS				OUTPUTS			
				Blood lead (µg/dL)		Soil concentration (mg/kg) Corresponding to 10 µg/dL	
Lead in soil (mg/kg)	Lead in water (µg/L)	Airborne Lead (µg/m³)	PM_{10} (µg/m³)	95th percentile	99th percentile	95th percentile	99th percentile
20	15	0.028	1.5	2.4	3.3	5,452	3,468
1000	15	0.028	1.5	3.8	5.2	5,452	3,468
20	5	0.028	1.5	1.2	1.7	6,320	4,335
20	15	0.1	1.5	2.6	3.6	5,322	3,337
20	15	0.028	50	2.4	3.3	5,011	3,187

VALIDATION

We compared the revised LeadSpread predictions under baseline conditions (20 mg Pb/kg soil; 15 µg Pb/L drinking water) with National Health and Nutrition Examination Survey (NHANES III) regional survey data (USDHHS, 1996). The results, shown below, indicate reasonable agreement between LeadSpread predictions and NHANES III data for children 1-2 or 1-6 years of age living in post-1973 housing in the Western United States.

Indicator	Median Blood lead concentration (µg/dL)
LeadSpread with 20 mg Pb/kg soil and 15 µg Pb/L drinking water	1.7
NHANES III data for the Western United States:	
Children 1-6 years	2.2
Children 1-2 years	2.6
Children 1-6 living in post-1973 housing	1.7
Children 1-2 living in post-1973 housing	1.9

CONCLUSIONS

The California DTSC has revised its lead risk assessment spreadsheet model (LeadSpread) for predicting distributions of blood lead concentration in adults and in children 1-2 years old. The revised model predicts slightly lower blood lead concentrations with all parameters set at default values. Blood lead predictions using the revised version of LeadSpread agree reasonably well with NHANES III data for children 1-2 or 1-6 years of age living in post-1973 housing in the Western United States.

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SAMPLE SPREADSHEETS

Although the basic equations remain essentially the same, version 7 of the spreadsheet, employs new formatting and layout. It also collapses multiple terms into "pathway exposure factors" (PEF), and removes embedded factors from equations, making them visible in dedicated cells. The two versions of the spreadsheet are compared below.

Leadspread Version 6

LEAD RISK ASSESSMENT SPREADSHEET
CALIFORNIA DEPARTMENT OF TOXIC SUBSTANCES CONTROL

INPUT		OUTPUT							
MEDIUM	LEVEL		Percentiles					PRG-92	PRG-95
LEAD IN AIR (ug/m^3)	0.15		50th	80th	85th	88th	95th	(ug/g)	(ug/g)
LEAD IN SOIL (ug/g)	400.0	BLOOD Pb, ADULT (ug/dl)	2.1	4.5	5.5	6.4	7.1	946.4	1254.0
LEAD IN WATER (ug/l)	15	BLOOD Pb, CHILD (ug/dl)	7.0	10.5	12.4	14.3	15.8	121.7	254.2
PLANT UPTAKE? (YES=1, NO=0)	1	BLOOD Pb, PICA CHILD (ug/dl)	27.7	42.4	48.2	55.5	62.6	15.8	31.6
RESPIRABLE DUST (ug/m^3)	50	BLOOD Pb, INDUSTRIAL (ug/dl)	2.6	3.4	3.9	4.3	4.8	4203.1	6241.1

EXPOSURE PARAMETERS

	units	residential			industrial
		adults	children	children with pica	adults
General					
Days per week	days/wk	7	7	7	5
Dermal Contact					
Skin area	cm^2	5700	2800	2800	5800
Soil adherence	mg/cm^2	0.5	0.5	0.5	0.5
Route-specific constant	(ug/dl)/(ug/day)	0.000111	0.000111	0.000111	0.000111
Soil ingestion					
Soil ingestion	mg/day	25	85	750	25
Route-specific constant	(ug/dl)/(ug/day)	0.0175	0.0704	0.0704	0.0175
Inhalation					
Breathing rate	m^3/day	20	10	10	20
Route-specific constant	(ug/dl)/(ug/day)	0.082	0.192	0.192	0.082
Water Ingestion					
Water ingestion	l/day	1.4	0.4	0.4	1.4
Route-specific constant	(ug/dl)/(ug/day)	0.04	0.15	0.15	0.04
Food Ingestion					
Food ingestion	kg/day	2.2	1.3	1.3	2.2
Route-specific constant	(ug/dl)/(kg/day)	0.04	0.15	0.15	0.04
Dietary concentration	ug/kg	15.4	15.4	15.4	15.5
Lead in produce	ug/kg	180.0	180.0	180.0	

PATHWAYS, ADULTS

Pathway	Residential		Industrial		Concentration in medium
	Blood Pb ug/dl	percent of total	Blood Pb ug/dl	percent of total	
SOIL CONTACT:	0.05	3%	0.09	4%	400 ug/g
SOIL INGESTION:	0.75	5%	0.13	6%	400 ug/g
INHALATION:	0.33	10%	0.23	11%	0.20 ug/m^3
WATER INGESTION:	0.84	27%	0.84	39%	15 ug/l
FOOD INGESTION:	1.70	54%	0.85	40%	15.4 ug Pb/kg diet

PATHWAYS, CHILDREN

Pathway	Typical		with pica		Concentration in medium
	Blood Pb ug/dl	percent of total	Blood Pb ug/dl	percent of total	
SOIL CONTACT:	0.05	1%	0.05	0%	400 ug/g
SOIL INGESTION:	1.55	22%	22.25	80%	400 ug/g
INHALATION:	0.35	5%	0.35	1%	0.20 ug/m^3
WATER INGESTION:	0.85	14%	0.85	3%	15 ug/l
FOOD INGESTION:	4.02	58%	4.02	15%	15.4 ug Pb/kg diet

LeadSpread Version 7

LEAD RISK ASSESSMENT SPREADSHEET
CALIFORNIA DEPARTMENT OF TOXIC SUBSTANCES CONTROL

USER'S GUIDE to version7

INPUT	
MEDIUM	LEVEL
Lead in Air (µg/m³)	0.028
Lead in Soil/Dust (µg/g)	200
Lead in Water (µg/l)	15
% Home-grown Produce	7%
Respirable Dust (µg/m³)	1.5

OUTPUT							
	Percentile Estimate of Blood Pb (ug/dl)					PRG-99	PRG-95
	50th	80th	95th	88th	99th	(µg/g)	(µg/g)
Blood Pb, adult	1.2	2.1	2.5	3.1	3.5	676	1083
Blood Pb, child	1.8	3.2	3.8	4.6	5.2	146	247
Blood Pb, pica child	1.9	3.5	4.1	5.0	5.7	94	159
Blood Pb, occupational adult	1.1	2.0	2.4	2.9	3.3	3475	5464

EXPOSURE PARAMETERS			
	units	adults	children
Days per week	days/wk	7	
Days per week, occupational		5	
Geometric Standard Deviation		1.6	
Blood lead level of concern (µg/dl)		10	
Skin area, residential	cm²	5700	2800
Skin area occupational	cm²	2800	
Soil adherence	µg/cm²	70	200
Dermal uptake constant	(µg/dl)/(µg/day)	0.0001	
Soil ingestion	mg/day	50	100
Soil ingestion, pica	mg/day		200
Ingestion constant	(µg/dl)/(µg/day)	0.04	0.15
Bioavailability	unitless	0.44	
Breathing rate	m³/day	20	8.8
Inhalation constant	(µg/dl)/(µg/day)	0.08	0.182
Water ingestion	l/day	1.4	0.4
Food ingestion	kg/day	1.9	1.1
Lead in market basket	µg/kg	3.1	
Pb in home-grown produce	µg/kg	9.0	

PATHWAYS						
ADULTS	Residential			Occupational		
	Pathway contribution			Pathway contribution		
Pathway	PEF	µg/dl	percent	PEF	µg/dl	percent
Soil Contact	3.8E-5	0.00	0%	1.4E-5	0.00	0%
Soil Ingestion	8.8E-4	0.02	2%	6.3E-4	0.01	1%
Inhalation, bkgrnd		0.05	4%		0.03	3%
Inhalation	2.5E-6	0.00	0%	1.8E-6	0.00	0%
Water Ingestion		0.84	72%		0.84	75%
Food Ingestion, bkgrnd		0.22	19%		0.23	21%
Food Ingestion	2.4E-3	0.05	4%			0%

CHILDREN	typical			with pica		
	Pathway contribution			Pathway contribution		
Pathway	PEF	µg/dl	percent	PEF	µg/dl	percent
Soil Contact	5.6E-5	0.00	0%		0.00	0%
Soil Ingestion	7.0E-3	0.14	8%	1.4E-2	0.25	15%
Inhalation	2.0E-6	0.00	0%		0.00	0%
Inhalation, bkgrnd		0.04	2%		0.04	2%
Water Ingestion		0.96	55%		0.96	51%
Food Ingestion, bkgrnd		0.50	28%		0.50	27%

PROGRAM IN ARSENIC HEALTH EFFECTS RESEARCH

School of Public Health and

Center for Occupational and Environmental Health

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CONTENTS

I. INTRODUCTION

The purpose of this document is to present the Program in Arsenic Health Effects Research based at the University of California, Berkeley. These research activities began nearly ten years ago with a risk assessment for arsenic in drinking water. The realization that potential risks were high led to a program of arsenic research, including epidemiologic studies of various designs which are being undertaken among exposed populations in several countries.

II. MAJOR ACCOMPLISHMENTS

- Provided definitive evidence (from studies conducted in Argentina and Chile) that arsenic is a potent cause of human bladder cancer.

- Provided definitive evidence (from studies conducted in Argentina and Chile) that arsenic is a potent cause of human lung cancer.

- Demonstrated results which indicate that epidemiological and experimental human data do not support the methylation hypothesis.

- Showed that with exposure to water containing around 600 μg/L, 1 in 10 adult cancer deaths may be due to arsenic-caused cancers, the highest environmental cancer risk ever reported.

- Identified a dose-response relationship between arsenic exposure and bladder cell micronuclei, a genotoxic marker of effect.

- Identified a preliminary dose-response relationship between arsenic concentration in well water in India and the occurrence of keratoses and hyperpigmentation.

- Studies currently underway in India, Chile and the US, will allow projection of cancer risks with individual exposure data.

III. COLLABORATING INSTITUTIONS AND RESEARCH SCIENTISTS

United States

University of Washington, Seattle. *Professor David A. Kalman*, Director, Environmental Health Laboratory and Trace Organics Analysis Center, Department of Environmental Health.

University of California, San Francisco. *Professor Frederic Waldman*, Department of Laboratory Medicine, Division of Molecular Cytometry, and *Professor John K. Wiencke*, Department of Epidemiology and Biostatistics.

University of Colorado, Denver. *Professor Michael J. Kosnett*, Division of Clinical Pharmacology and Toxicology, Health Sciences Center.

Chile
Instituto de Salud Pública, Santiago, Chile. Ing. *Nella Marchetti*, Depto. de Salud Ocupacional y Contaminación Ambiental (currently at the Comisión Nacional del Medio Ambiente).

Dra. Catterina Ferreccio, Universidad Catolica, Santiago, Chile.

Servicio de Salud Antofagasta, Chile. *Dr. Mario Goycolea Chaparro and Dr. Alex Arroyo Meneses* (currently Secretario Regional del Ministerio de Salud in Region II).

Argentina
Universidad Católica de Córdoba, *Professor Ruben Sambuelli, Dean Esteban Trakal*.

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IV. FUNDING SOURCES

The main source of funding, which initiated the research program, has been the National Institute of Environmental Health Sciences (NIEHS) Superfund Basic Research Program at the University of California, Berkeley (Professor Martyn Smith, Director). NIEHS has funded the completed projects in Nevada and Chile and is currently funding the Argentina projects, No. P42-ES04705.

Seed funding for several projects has been provided through the NIEHS Center at Berkeley (Professor Bruce Ames, Director). No. P30-ES01896.

The initial risk assessment project was supported by the California Department of Health Services (Now the California Environmental Protection Agency or Cal/EPA).

The Nevada/California bladder cancer case-control study is funded by NIEHS Grant No: ES07459.

The planning of low exposure epidemiological studies was funded by the American Water Works Association Research Foundation (AWWARF).

The collaborative work with the Post Graduate Medical Institute in analysis of the cross-sectional study of arsenic-caused skin lesions was supported in part by the U.S. Environmental Protection Agency (EPA) National Center for Environmental Assessment.

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The first planning of the Nevada/California bladder cancer case-control study was funded by a grant from the U.S. EPA.

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IV. CURRENT RESEARCH PROJECTS

1. Bladder cancer case-control study in Córdoba, Argentina

This study is in progress with an office and staff based in Villa María, Córdoba. The study is defined by 3 major components; 1) Arsenic and bladder cancer dose-response: Bladder cancer cases and age-sex matched population controls from the County of Unión are being interviewed in detail including lifelong residential histories, sources of drinking water and smoking histories. Water samples are being collected from both the current residences and previous residences where possible. Historical data on arsenic measurements in public water supplies are also being collected. We will conduct dose-response analyses incorporating individual exposure data, and examine the possible synergistic effect of cigarette smoking. 2) Metabolism: First-morning urine samples are being collected from cases and controls. Analysis of inorganic arsenic and its methlyated metabolites will be conducted in the laboratory of Professor David Kalman, University of Washington. Cases and controls will be compared to see if they differ in arsenic methylation patterns. 3) Molecular epidemiology: Tumor DNA is being analyzed for genetic alterations using a three-tiered approach: First, screening of the entire genome for gains and losses using comparative genomic hybridization (CGH); Second, specific analyses of chromosomes 9 and 17p for loss of heterozygosity using PCR-based methods; Third, analysis of the p53 gene for mutations using polymerase chain reaction-single-strand conformation (PCR-SSCP). The frequency and pattern of these genetic alterations in bladder tumors of arsenic

exposed and unexposed cases is being compared, and the potential synergistic action of arsenic on genotoxic effects of cigarette smoking is being assessed. In addition, susceptibility differences between cases and controls is being investigated by identifying the presence or absence of the glutathione S-transferases GSTM1 and GSTT1 null genotypes in buccal cells and by comparing urinary arsenic methylation patterns.

2. Bladder cancer case-control study in Nevada and California

The California/Nevada bladder cancer study is a population-based, case-control study that will examine the hypothesis that bladder cancer is caused by ingestion of arsenic in drinking water at relatively low concentrations. The study population includes residents of Kings County in California, and six counties in Nevada (Churchill, Mineral, Lyon, Douglas, Storey and Carson). These counties were chosen because they include water supplies containing close to 100 μg/L of arsenic, the highest level of arsenic found in major water supplies in the U.S.. Other water supplies in the study region contain less than 10 μg/L and thus provide a marked contrast in exposure. Two hundred bladder cancer cases diagnosed between 1994 and 2000 will be identified from the California and Nevada Tumor Registries. Random digit dial (RDD) will be used to identify 400 controls who will be frequency matched to cases by sex and 5-year age groups. Structured personal telephone interviews will be administered to obtain lifetime residential history and detailed information on current and past water consumption patterns. Information will also be obtained regarding cigarette smoking (which may be synergistic with arsenic in causing bladder cancer), chlorination of drinking water, diet, and occupational history. Although carcinogenicity of arsenic at 100 μg/L is uncertain, this study has over 90% statistical power to detect a relative risk of 2.0 which was predicted by linear extrapolation of data from studies in Taiwan.

3. Argentina mortality study

Mortality from internal cancers was identified in areas of the Province of Córdoba, Argentina, which in the past had high levels of arsenic in drinking water. The results concerning bladder cancer have been published (see publication 15). The analyses concerning mortality from other cancers is completed and a manuscript describing the results has been published (see publication 26). Increased rates of kidney and lung cancer were found in the exposed areas, as were the already reported increases in bladder cancer.

4. Dose-response study of arsenic-caused skin lesions in West Bengal, India

Research is being conducted in collaboration with Professor D.N. Guha Mazumder and his research team at the Institute of Post Graduate Education and Research (IPGMER) in Calcutta, India. Our group collaborated with the analysis of data from a large cross-sectional survey of about 7000 people in an arsenic-exposed region in West Bengal. The dose-response analysis linking cases of skin keratoses and hyperpigmentation to arsenic water levels has been recently published (see publication 27). The next phase is a case-control study nested in the same survey, which focuses on participants with skin lesions who had drinking water arsenic levels of less than 500 μg/L. Detailed interviews concerning water sources and fluid consumption, diet,

smoking and medical history are being completed for each participant. Water samples are obtained from all drinking water sources. Each participant receives a physical examination for skin lesions and other signs, portable spirometry, and blood and urine samples are obtained to assess micronutrients and arsenic metabolism. The study is funded by the U.S. EPA.

V. RESEARCH PUBLICATIONS WITH SUMMARIES OF KEY FINDINGS

1. Frost F, Harter L, Milham S, Royce R, Smith AH, Hartley J, Enterline P. Lung cancer among women residing close to an arsenic-emitting copper smelter. Arch Env Health 42:148-52, 1987.

Lung cancer mortality. This project was conducted with the Chronic Disease Epidemiology Section of the Washington State Division of Health. Overall lung cancer mortality rates were not increased among women living near the smelter. However, case-control analysis using an index of exposure based on distance of residence from the smelter showed increasing lung cancer odds ratios from 1 up to 1.6 for those in the highest quintile of potential exposure. The results are consistent with a small elevated lung cancer risk for women who resided close to the smelter for a period of over 20 years. (Note: There is an error in Table 6 - the lines for cases and controls are transposed).

2. Hertz-Picciotto I, Smith AH, Holzman D, Lipsett M, Alexeef G. Synergism between occupational arsenic exposure and smoking in the induction of lung cancer. Epidemiol 3:23-31, 1992.

Synergy. Data were assembled from epidemiological studies concerning inhalation of inorganic arsenic and cigarette smoking. It was concluded that the evidence for synergism between the two exposures was compelling. Various potential mechanisms for synergy were discussed.

3. Smith AH, Hopenhayn-Rich C, Bates MN, Goeden HM, Hertz-Picciotto I, Duggan HM, Wood R, Smith MT, Kosnett MJ. Cancer risks from arsenic in drinking water. Env Health Persp 97:259-67, 1992.

Risk assessment. Evidence that ingestion of inorganic arsenic in drinking water might cause bladder, kidney, lung and liver cancer was examined, and potential cancer risks were calculated for various levels of exposure. It was estimated that at the current standard of 50μg/L, the lifetime risk of dying from one of these cancers could be as high as 13 per 1000 persons. It was noted that existing studies did not support a threshold based on arsenic methylation. It was concluded that although further research was needed to validate the findings of the risk assessment, measures should be taken to reduce arsenic levels in drinking water.

4. Bates MN, Smith AH, Hopenhayn-Rich C. Arsenic ingestion and internal cancers: a review. Am J Epidemiol 135:462-76, 1992.

Internal cancers. A detailed review of epidemiological studies concerning arsenic ingestion and internal cancers was presented. The most informative studies were from Taiwan and it was concluded that these and other studies strongly suggest that ingested inorganic arsenic does cause cancers of the bladder, kidney, lung and liver, and possibly other sites.

5. Hopenhayn-Rich C, Smith AH, Goeden H. Human studies do not support the methylation threshold hypothesis for the toxicity of inorganic arsenic. Env Res 60:161-77, 1993.

Metabolism. The validity of the methylation threshold hypothesis was examined on the basis of published studies. The results indicated that epidemiological and experimental human data does not support the inorganic arsenic methylation threshold hypothesis. Regardless of the absorbed dose of inorganic arsenic, there was always some unmethylated inorganic arsenic present in the urine, even at background exposure levels. It was noted that lack of evidence for a methylation threshold based on the human exposure levels studied did not exclude the possibility of other threshold mechanisms. In addition, the considerable variation in methylation of inorganic arsenic observed between individuals was noted to warrant further study.

6. Hertz-Picciotto I, Smith AH. Observations on the dose-response curve for arsenic exposure and lung cancer. Scand J Work Env Health 19: 217-26, 1993.

Lung cancer dose-response. Information from published studies concerning arsenic inhalation and lung cancer risks was analyzed. It was found that all of the studies with quantitative data were consistent with a supralinear dose-response relationship. Various factors which might be distorting the true biological dose-response were assessed. These included the fact that the workers thought to be most highly exposed might actually have had lower exposures than previously quantified by air sampling as a result of non-random sampling and the possible use of respirators when air levels were highest. It was noted that there was a linear dose-response relationship in one study, which used urine arsenic measurements to assess exposure.

7. Smith AH, Hopenhayn-Rich C, Warner M, Biggs ML, Moore L, Smith MT. Rationale for selecting exfoliated bladder cells micronuclei as potential biomarkers for arsenic genotoxicity. J Toxicol Env Health 40: 223-34, 1993.

Molecular epidemiology. Biological markers of effect of toxic human exposures have the potential to allow exploration of dose-response relationships at levels of exposure lower than those which can be assessed by traditional epidemiological studies involving the ultimate disease end-point. In this paper we give reasons for proposing that exfoliated bladder cell micronuclei might be a good marker for carcinogenic effects of ingestion of inorganic arsenic. Based on studies in Taiwan, it was noted that the highest internal cancer relative risks involved bladder

cancer. Bladder cells can be collected from urine, and originate from a target organ of particular importance for arsenic effects. We described several studies from our group, which used bladder cell micronuclei as biomarkers, noting the important potential contribution of intervention studies incorporating cessation of exposure.

8. Warner M, Moore L, Smith MT, Kalman D, Fanning E, Smith AH. Increased micronuclei in exfoliated bladder cells of persons who chronically ingest arsenic contaminated water in Nevada. Cancer Epidemiol Biom & Prev 3:583-90, 1994.

Molecular epidemiology. This study involved 18 subjects in Nevada whose well water contained on average 1312 µg/L of arsenic, and 18 age and sex matched controls whose well water averaged 16 µg/L. Exposed subjects had a 1.8 fold increase in bladder cell micronuclei, but the differences were largely confined to males. The absence of findings for females was thought to be due to the fact that women exfoliate large numbers of cells into urine, while men exfoliate predominantly transitional cells, which are the cells involved in bladder cancer. No increase was found in buccal cell micronuclei among the arsenic exposed group.

9. Engel RR, Hopenhayn-Rich C, Receveur O, Smith AH. Vascular effects of chronic arsenic exposure: a review. Epidemiol Rev 16:184-209, 1994.

Vascular disease. Existing literature concerning vascular effects from chronic exposure to inorganic arsenic was reviewed in this publication containing 177 citations. It was concluded that there was good epidemiologic evidence indicating that chronic arsenic consumption at high levels is a cause of severe peripheral vascular disease with resulting gangrene and amputations of the limbs. We hypothesized that marginal zinc status might explain the differential occurrence of these conditions in populations ingesting large doses of arsenic. It was also concluded that it was plausible, though epidemiologic evidence is limited, that arsenic might cause increases in vascular mortality beyond that found in patients with severe peripheral vascular disease.

10. Engel RR, Smith AH. Arsenic in drinking water and mortality from vascular disease: an ecologic analysis in 30 U.S. counties. Arch Environ Hlth 49: 418-27, 1994.

Vascular disease. An investigation was made of the ecological relationship between arsenic concentrations in drinking water and mortality from circulatory disease in 30 U.S. counties from 1968 to 1984. Mean arsenic levels ranged from 5.4 to 91.5 µg/L. The standardized mortality ratios (SMRs) for diseases of arteries, arterioles, and capillaries for counties exceeding 20 µg/L were 1.9 (90% CI 1.7-2.1) for females and 1.6 (CI 1.5-1.8) for men. The SMRs for congenital anomalies of the heart and circulatory system were also elevated. Possible problems with the ecological study design and explanations for potentially spurious results were discussed. It was concluded that further investigation of vascular effects of arsenic exposure was warranted.

11. Smith AH, Hopenhayn-Rich C, Biggs ML, Moore L, Dale J, Warner M, Bates M, Engel R. Epidemiological study designs to address potential high bladder cancer risks from arsenic in drinking water. In: Chappell WR, Abernathy CO, Cothern CR, eds. Arsenic: Exposure and Health. Northwood: Science and Technology Letters, 109-17, 1994.

Epidemiological study designs. Various study designs were described which could be used to further investigate effects of arsenic ingestion from drinking water, including ecological studies, cohort studies, and biomarker studies. It was noted that small biomarker studies could be conducted relatively rapidly, and that the effect of interventions could be assessed for biomarkers in cells with short half-lives. However, interpretation of biomarker studies is difficult, consequently, traditional epidemiological study designs have an important role. It was concluded that the potential risks of bladder cancer from ingesting inorganic arsenic in drinking water warranted a concerted epidemiological approach using a variety of different study designs.

12. Bates MN, Smith AH, Cantor KP. Case-control study of bladder cancer and arsenic in drinking water. Am J Epidemiol 141: 523-30, 1995.

Bladder cancer. Cases and controls from the National Bladder Cancer Study were used in this project, which was conducted in collaboration with Dr. Ken Cantor of the National Cancer Institute. Information concerning arsenic levels in drinking water was added to this dataset for respondents from Utah. Water levels ranged from 0.5 to 160 μg/L, but only three towns were served with water containing over 20 μg/L of arsenic. There was no overall association of inorganic arsenic with the risk of bladder cancer at these levels of exposure. However, among cigarette smokers, time window analysis yielded some evidence for a dose-response relationship for exposure to arsenic in drinking water 10-39 years prior to diagnosis with bladder cancer. The possibility was raised that smoking potentiates the effect of arsenic in causing bladder cancer. However, the discrepancy between these findings at such low exposure levels, and predictions based on studies in Taiwan and England, also raised the possibility of bias in the data. It was concluded that further carefully conducted studies in exposed populations were needed.

13. Smith AH, Hopenhayn-Rich C, Biggs ML, Kalman D. Re: Arsenic risk assessment (letter). Env Health Persp 103:13-15, 1995.

Risk assessment. Heather Carlson-Lynch, Barbara Beck and Pamela Boardman of McLaren/Hart Environmental Engineering Corporation and Gradient Corporation wrote a letter which was highly critical of two of our published studies (Hopenhayn-Rich et al, 1993, and Smith et al, 1992, above). In the letter to the editor, we demonstrated that none of the criticisms raised was valid.

14. **Moore L, Smith AH, Hopenhayn-Rich C, Biggs ML, Warner ML, Kalman D, Smith MT. Increased bladder cell micronuclei found in two populations environmentally exposed to arsenic in drinking water. Clin Chem 41:1915-17, 1995.**

Molecular epidemiology. Summary findings from the Nevada bladder cell micronucleus study, with preliminary results from the Chile study, were reported. It was concluded that results from both the North and South American studies provided evidence that arsenic is genotoxic to human bladder epithelium. Further details are given in Warner et al, 1994 (publication 13) and Moore et al. 1997 (publication 15).

15. **Hopenhayn-Rich C, Biggs ML, Fuchs A, Bergoglio R, Tello E, Nicolli H, Smith AH. Bladder cancer mortality associated with arsenic in drinking water in Argentina. Epidemiol. 7:117-124, 1996.**

Bladder cancer. Bladder cancer mortality for the years 1986-1991 was investigated in Córdoba, Argentina in an ecological study comparing counties categorized as previously having high, medium and low water levels of arsenic. The average water arsenic level in the two high exposure counties for arsenic contaminated water sources was 178 μg/L. Clear trends in bladder cancer mortality were shown up to standardized mortality ratios (SMRs) of 2.14 for men (95% CI 1.78-2.53) and 1.82 for women (95% CI 1.19-2.64) in the two high exposure counties. The clear trends found in a population with a different ethnic composition and a high protein diet support the evidence from Taiwan that arsenic in drinking water is a cause of human bladder cancer. While it was made clear that exposure was not uniform within counties, it was noted the findings were roughly consistent with risks which might be predicted from the Taiwan studies.

16. **Hopenhayn-Rich C, Biggs ML, Fuchs A, Bergoglio R, Tello E, Nicolli H, Smith AH. Arsenic and bladder cancer mortality. The Authors Reply. Epidemiol 7:557-58, 1996.**

Bladder cancer. Kenneth G. Brown and Barbara D. Beck wrote a letter critical of the above study in which we were accused of making incorrect assumptions, errors and unwarranted conclusions. In this reply, we noted that we were surprised by their accusations of errors that did not, indeed, exist. However, we agreed with their statement, "the study does affirm the association of high concentrations of inorganic arsenic with increased mortality from bladder cancer, in this instance among the ethnically mixed Córdoba population, in the absence of nutritional deficiency or evidence of other substances such as humic or fluorescent substances".

17. **Moore L, Warner ML, Smith AH, Kalman D, Smith MT. Use of the fluorescent micronucleus assay to detect the genotoxic effects of radiation and arsenic in human exfoliated epithelial cells. Env and Molecular Mutagen 27:176-84, 1996.**

Molecular epidemiology. A new rapid method was used, which involves fluorescent in situ hybridization (FISH) to determine the mechanism of micronucleus formation in epithelial tissues

exposed to carcinogenic agents (as previously described in Titenko-Holland N, Moore LE, Smith MT. Measurement and characterization of micronuclei in exfoliated human cells by fluorescence in situ hybridization with a centromeric probe. Mutat Res 271:69-77, 1992.) The findings concerning micronuclei in exfoliated bladder cells obtained from arsenic-exposed subjects in Nevada suggested that arsenic may have both clastogenic and weak aneuploidogenic properties.

18. Hopenhayn-Rich C, Biggs ML, Smith AH, Kalman D, Moore LE. Methlyation study in a population environmentally exposed to high arsenic water. Env Health Persp 104:620-28, 1996.

Metabolism. Arsenic methylation patterns were investigated in this cross-sectional study of two towns in Chile. One hundred and twenty two people exposed to high levels of arsenic were compared to 98 people in a neighboring town with low levels of arsenic. Arsenic levels in drinking water were 600 ug/L and 15ug/L, respectively. The corresponding mean urinary arsenic levels were 580 µg/L and 60 µg/L, of which 18.4% and 14.9% were inorganic arsenic respectively. The main differences were found in the monomethyarsonate (MMA) to dimethylarsinate (DMA) ratio; high exposure, smoking, and being male were associated with higher MMA/DMA, while longer residence in the exposed town, Atacameno ethnicity, and being female were associated with lower MMA/DMA. Overall, there was no evidence of a threshold for methylation capacity, even at very high exposures. This study, which is the largest study conducted involving metabolites of arsenic to date, confirmed conclusions made in our earlier publications that the methylation threshold hypothesis was not valid.

19. Hopenhayn-Rich C, Biggs ML, Kalman D, Moore LE, Smith AH. Arsenic methylation patterns before and after changing from higher to lower concentrations of arsenic in drinking water. Env Health Persp 104:1200-07, 1996.

Metabolism. Presented are the results of an intervention study of 73 participants (from the above cross-sectional study in Chile), who were provided with water of lower arsenic content (45 µg/L) for two months. Total urinary arsenic levels fell from an average of 636 µg/L to 166 µg/L. There was a small decrease from 17.8% to 14.6% in the percent of urinary arsenic in inorganic form consistent with what might be predicted from the cross-sectional study. Other factors such as smoking, gender, age, years of residence, and ethnicity were associated mainly with changes in the MMA/DMA ratio. The main difference was found for smokers, where practically all of the smokers showed a decrease in the MMA/DMA ratio, while much more variability was seen for non-smokers. It was noted that the changes in the observed percent inorganic arsenic and in the MMA/DMA ratio did not support an exposure based threshold for arsenic methylation in humans. The last two studies (cross-sectional and intervention) also indicate that most of the inter-individual variability in the distribution of urinary metabolites remains unexplained.

20. Wright C, Lopipero P, Smith AH. Meta-analysis and Risk Assessment. In: Topics in Environmental Epidemiology. Eds. Steenland K and Savitz DA, Oxford University Press, 1996.

Risk assessment. Although arsenic is not discussed in this chapter, it is pertinent here because it includes issues and methods concerning the use of epidemiologic studies to estimate population risks at low levels of exposure. It was noted that apparent nonlinearity at low exposure points in studies can be fitted with statistical models that have a profound impact on risk extrapolations to lower doses. However, the empirical evidence for nonlinearity may be extremely weak, and there are often no good biological reasons for rejecting linearity. For these and other reasons, we stated that it would be preferable to use the linear relative risk model for quantitative risk assessment using epidemiologic data, *unless there are good reasons to reject it* (i.e. clear evidence of nonlinearity).

21. Moore LE, Smith AH, Hopenhayn-Rich C, Biggs ML, Kalman DA, Smith MT. Micronuclei in exfoliated bladder cells among individuals chronically exposed to arsenic in drinking water. Cancer Epidemiol Biom & Prev 6:31-6, 1997.

Molecular epidemiology. Using the same towns as the methylation study in Chile described in the previous publication summary, this cross-sectional study was confined to male participants in view of the extensive exfoliation of squamous cells as well as transitional bladder cells which occurs in females. There were 70 high-exposure participants (average urinary arsenic 616 µg/L) and 55 low-exposure participants (average urinary arsenic 66 µg/L). The prevalence of micronuclei increased three-fold (95% CI 1.9-4.6) from the lowest exposure quintile (less than 53.8 µg/L arsenic in urine) to those in the second highest exposure quintile (414-729 µg/L urinary arsenic). Surprisingly, those in the highest exposure quintile (more than 729 µg/L urinary arsenic) did not have any increase in micronucleus prevalence. This finding is not fully explained, but could be due to cytostasis or cytotoxicity at these high exposure levels. The centromeric probe classification of micronuclei suggested that chromosome breakage was the major cause of micronucleus formation. It is noteworthy that the prevalence of micronuclei in bladder cells was elevated even in the second to lowest quintile of exposure (urinary arsenic levels between 53.9 and 137.3 µg/L, prevalence ratio 2.1, 95% CI 1.4-3.4), which raises the possibility that arsenic has genotoxic effects on bladder cells at relatively low levels of exposure.

22. Biggs ML, Kalman DA, Moore LE, Hopenhayn-Rich C, Smith MT, Smith AH. Relationship of urinary arsenic to intake estimates and a biomarker of effect, bladder cell micronuclei. Mut Res 386:185-95, 1997.

Exposure assessment. The primary purpose of this study was to investigate methods for ascertaining arsenic exposure for use in biomarker studies. The study population was the same as the population in the metabolism and bladder cell micronucleus study conducted in Chile. Exposures were assessed by an interviewer-administered questionnaire concerning volumes and sources of fluid intake. Urinary inorganic arsenic measurements including methylated species

were measured in first-morning samples. Creatinine was measured to allow for adjustment for overly concentrated urine. As expected, creatinine adjusted urinary arsenic concentrations had a stronger relationship with the questionnaire-based estimates of arsenic intake than the unadjusted urinary concentrations. Interestingly, the unadjusted urinary arsenic measures had the stronger relationship with bladder cell micronucleus prevalence. This finding is plausible since the unadjusted urinary arsenic concentrations may better reflect target site dose to the bladder, which is exposed to the actual concentration of arsenic in urine.

23. Aposhian HV, Arroyo A, Cebrian M, Del Razo LM, Hurlbut KM, Dart RC, Gonzalez-Ramirez D, Kreppel H, Speiske H, Smith AH, et al. DMPS-Arsenic Challenge Test: I-Increased Urinary Excretion of Monomethylarsonic Acid in Humans Given Dimercaptopropane Sulfonate. J Pharm Exp Ther 282:192-200, 1997.

Chelation study. Directed by Professor Vasken Aposhian of the University of Arizona, this study involved a small subset of participants from our studies in Chile: 13 from the high-exposure town and 11 from the low-exposure town. Each participant was given 300 mg of the chelating agent 2,3-dimercaptone-1-sulfonic acid (DMPS). As expected, urinary arsenic concentrations increased in the 24-hour period after taking DMPS. Interestingly, the increase was considerably more pronounced for MMA than for inorganic arsenic and DMA. In our view, it is difficult to interpret these findings, since the tissue binding strengths of the various arsenic species may vary, and they may have different affinities for the chelating agent. For these and other reasons, urinary arsenic levels in chronically exposed persons remain the best indicators of body dose.

24. Moore, LE, Smith AH, Hopenhayn-Rich C, Biggs ML, Kalman DA, Smith MT. Decrease in bladder cell micronucleus prevalence after intervention to lower the concentration of arsenic in drinking water. Cancer Epidemiol Biomark and Prev 6:1051-6, 1997.

Molecular epidemiology. Water low in arsenic content (45 μg/L) was provided to 34 highly exposed participants in the cross-sectional study in Chile (publication 21 above). Mean urinary arsenic levels in this sub-group decreased from 742 to 225 μg/L during the intervention. Bladder cell micronucleus (MNC) prevalence decreased from 2.63/1000 to 1.79/1000 cells post-intervention ($p<0.05$). When the analysis was limited to individuals previously having subcytotoxic urinary arsenic levels (<700 μg/L), the change between pre- and post-intervention MNC was more pronounced: from 3.54 to 1.47/100 cells respectively ($p=0.002$). The primary changes occurred among smokers, suggesting that smoker's bladder cells could be more susceptible to genotoxic damage caused by arsenic. The reduction in bladder cell MNC prevalence with reduction in inorganic arsenic intake provides further evidence that arsenic is genotoxic to bladder cells.

25. Smith AH, Goycolea M, Haque R, Biggs ML. Marked increase in bladder and lung cancer mortality in a region of Northern Chile due to arsenic in drinking water. Am J Epidemiol, 147:660-69, 1998.

Cancer mortality. Studies in Taiwan and Argentina suggest that ingestion of inorganic arsenic from drinking water results in increased risks of internal cancers, in particular bladder and lung cancer. The authors investigated cancer mortality in a population of around 400,000 people in a region of Northern Chile (Region II) exposed to high arsenic levels in drinking water in past years. Arsenic concentrations from 1950 to the present were obtained. Population-weighted average arsenic levels reached 570 μg/L between 1955 to 1969, and decreased to less than 100 μg/L by 1980. Standardized mortality ratios (SMRs) were calculated for the years 1989 to 1993. Increased mortality was found for bladder, lung, kidney and skin cancer. Bladder cancer mortality was markedly elevated with an SMR of 6.0 [95% confidence interval 4.8-7.4] for men, and 8.2 [6.3-10.5] for women. Lung cancer SMRs were 3.8 [3.5-4.1] for men, and 3.1 [2.7-3.7] for women. Smoking survey data and mortality rates from chronic obstructive pulmonary disease provided evidence that smoking did not contribute to the increased mortality from these cancers. The findings provide additional evidence that ingestion of inorganic arsenic in drinking water is indeed a cause of bladder and lung cancer. It was estimated that arsenic might account for 7% of all deaths among those aged 30 and over. If so, the impact of arsenic on the population mortality in Region II of Chile is greater than any reported to date from environmental exposure to a carcinogen in a major population.

26. Hopenhayn-Rich C, Biggs ML, Smith AH. Lung and kidney cancer mortality associated with arsenic in drinking water in Cordoba, Argentina. Int J Epidemiol 27: 561-69, 1998.

Bladder cancer. Studies in Taiwan have found dose-response relations between arsenic ingestion from drinking water and cancers of the skin, bladder, lung, kidney and liver. To investigate these associations in another population, we conducted a study in Cordoba, Argentina, which has a well-documented history of arsenic exposure from drinking water. Mortality from lung, kidney, liver and skin cancers during the period 1986-1991 in Cordoba's 26 counties was investigated, expanding the authors' previous analysis of bladder cancer in the province. Counties were grouped a priori into low, medium and high arsenic exposure categories based on available data. Standardized mortality ratios (SMRs) were calculated using all of Argentina as the reference population. We found increasing trends for kidney and lung cancer mortality with arsenic exposure, with the following SMRs, for men and women respectively: kidney cancer, 0.87,1.33, 1.57 and 1.00, 1.36, 1.81; lung cancer, 0.92,1.54,1.77 and 1.24, 1.34, 2.16 (in all cases, $p<0.001$ in trend tests), similar to the previously reported bladder cancer results (0.80, 1.28, 2.14 for men, 1.22, 1.39, 1.81, for women). There was a small positive trend for liver cancer but mortality was increased in all three exposure groups. Skin cancer mortality was elevated for women in the high-exposure group, while men showed a puzzling increase in the low-exposure group. The results add to the evidence that arsenic ingestion increases the risk of lung and kidney cancers. In this study, the association between arsenic and mortality from liver and skin cancers was not clear.

27. Guha Mazumder DN, Haque R, Gosh N, De BK, Santra A, Chakraborty D, Smith AH. Arsenic levels in drinking water and the prevalence of skin lesions in West Bengal, India. Int J Epidemiol 27:871-77, 1998.

Skin lesions. A cross-sectional survey was conducted investigating the arsenic-caused skin lesions of keratoses and hyperpigmentation in West Bengal, India. There were 7683 participants who were examined and interviewed, and whose drinking water arsenic levels were measured. Water concentrations ranged up to 3400 ug/L of arsenic but over 80% of participants were consuming water containing less than 500 ug/L. The prevalence of keratoses was strongly related to water arsenic levels rising to 8.5 per 100 for females, and 10.7 per 100 for men, drinking water containing over 800 ug/L. However 12 cases with keratoses (2 females and 10 males) were drinking water containing less than 100 ug/L of arsenic. Findings were similar for hyperpigmentation with strong dose-response relationships, and with 29 cases drinking water containing less than 100ug/L. Calculation by dose per body weight showed that men had roughly two to three times the prevalence of both keratoses and hyperpigmentation compared to women ingesting the same dose of arsenic from drinking water. Subjects who were below 80% of the standard body weight for their age and sex had 1.6 fold increase in prevalence of keratoses, and a 1.2 fold increase in prevalence of hyperpigmentation suggesting that malnutrition might play a small role in increasing susceptibility. The surprising findings concerning cases with apparently low exposure need to be confirmed in studies with more detailed exposure assessment. Further research is also needed concerning susceptibility factors which might be present in the exposed population.

28. Steinmaus C, Moore LE, Hopenhayn-Rich C, Biggs ML, Smith AH. Arsenic in drinking water and bladder cancer. Cancer Invest. In press 1998.

Millions of people throughout the world are drinking water containing inorganic arsenic. Although initially controversial, the association between high exposures to ingested arsenic and bladder cancer is now well established. Unfortunately, the dose-response relationship, especially at low to moderate doses such as those found in the U.S., remains unclear. Attempts to define these risks and establish new drinking water regulations have been controversial, primarily due to questions regarding the risk assessment process used to establish these standards. Epidemiological studies involving low- to moderate- dose exposures will help to define these risks and aid in the establishment of appropriate drinking water regulations. In addition, genetic biomarker studies may provide information on the mechanistic and susceptibility issues of arsenic induced carcinogenesis, and thus may also help elucidate dose-response relationships at low doses. However, until a new arsenic drinking water standard is implemented, most evidence suggests that populations currently exposed to arsenic in drinking water will continue to have substantially elevated cancer risks. Waiting for more precise data before a new standard is applied will only prolong these risks. Therefore, until further research can be completed, an interim drinking water arsenic standard similar to the World Health Organization recommendation of 10 µg/L, may be appropriate.