State of California

DRAFT

Executive Summary

Proposed Identification of Environmental Tobacco Smoke as a Toxic Air Contaminant

California Environmental Protection Agency
Air Resources Board
Office of Environmental Health Hazard Assessment

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For the "Proposed Identification of Environmental Tobacco Smoke as a Toxic Air Contaminant"

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Introduction

In 1983, the State of California established a program to identify the health effects of toxic air contaminants (TACs) and to reduce exposure to these contaminants to protect the public health (Assembly Bill 1807: Health and Safety Code sections 39650-39674). The program includes a two-step process to address the potential health effects from TACs. The first step involves the evaluation of a substance, by the Air Resources Board (ARB) and the Office of Environmental Health Hazard Assessment (OEHHA), to determine if it is toxic and to estimate public exposure. This step is the risk assessment (or identification) phase. Under state law, the ARB is authorized to identify a substance as a TAC if it determines the substance is "an air pollutant which may cause or contribute to an increase in mortality, in serious illness, or which may pose a present or potential hazard to human health (Health and Safety Code section 39655)."

The second step, determining the need for and appropriate degree of control measures, occurs only if the ARB identifies the substance as a toxic air contaminant. This step is the risk management (or control) phase of the process (Health and Safety Code sections 39665 and 39666). This report does not address the need for control measures to reduce ETS exposure, nor contain any recommendations in that regard.

The ARB and the OEHHA are evaluating environmental tobacco smoke (ETS) as a candidate toxic air contaminant under the State's air toxics identification program. This report presents the information upon which this assessment is based.

What is Contained in This Report?

This report, prepared by the staff of the Air Resources Board (ARB) and the Office of Environmental Health Hazard Assessment (OEHHA), presents an evaluation of exposures to environmental tobacco smoke and the potential health effects associated with these exposures.

Part A of the report, prepared by the staff of the ARB, addresses the exposures to ETS in California. Some of the information in this document is based on data presented in the OEHHA's 1997 report: "Health Effects of Exposure to Environmental Tobacco Smoke." Specifically, Chapter 2 (Exposure Measurement and Prevalence) of the

OEHHA report was updated to include ETS exposure information developed subsequent to the data presented in the report.

Part B of the report, prepared by the staff of the OEHHA, evaluates the potential health impacts from exposures to ETS. In this document, information from their 1997 report, and which was later published by the U.S. National Cancer Institute in 1999, has been updated to include more recent literature. OEHHA's evaluation now includes other comprehensive reviews published as Reports of the Surgeon General, the U.S. Environmental Protection Agency, and the National Research Council, as well as several other published papers on ETS-related health effects since their initial 1997 ETS review.

Together, the Part A and B of this report will serve as the basis for the identification of ETS as a toxic air contaminant (TAC) under the authority of California's TAC Program (Assembly Bill 1807: Health and Safety Code Sections 39660-39662).

How Does the ARB Identify a Substance as a TAC?

With input from the public, industry, and the scientific community, the ARB and the OEHHA gather all of the relevant scientific information on a substance. Under the requirements of law (Health and Safety Code sections 39660-39662), the ARB and OEHHA must answer the following questions:

❶ Is the substance used in California?
❷ Who is exposed to the substance?
❸ How many people are exposed?
❹ How much is emitted into the air?
❺ How long does the substance stay in the air?
❻ How much of a substance can be measured in the air?
❻ Does exposure to the substance cause increased health impacts in children?
❼ Does the substance pose a potential health risk to Californians?

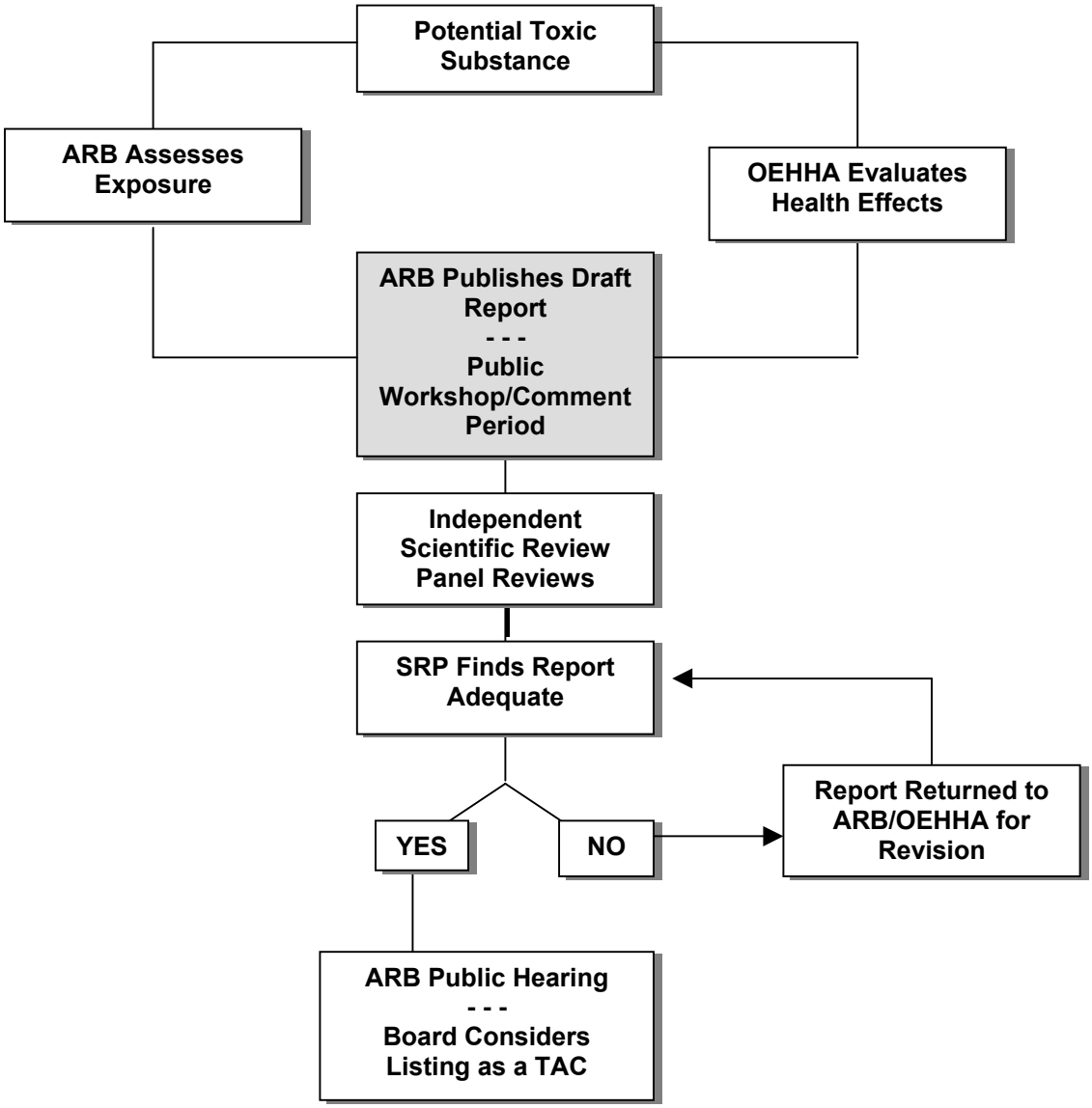
The ARB staff determines the public's potential exposure to the substance while the OEHHA must determine if exposure to the substance poses a potential health risk. Both agencies then prepare a draft report which serves as the basis for identifying a substance.

Once the draft report is released, the public review process begins. The public review is a critical step in identifying a substance. After the release of the report, a workshop is held to discuss the report during a formal comment period. After receiving public comments, both verbal and written, we carefully review all comments, incorporate new information, and revise the report where appropriate.

After the comment period and public workshop, the report is then submitted to the Scientific Review Panel (SRP) on Toxic Air Contaminants. The SRP is an independent group of scientists, who review the report for its scientific accuracy. If the SRP

determines that the report is not based on sound scientific information, it is sent back to the staff for revisions. If the SRP approves the revised report, the SRP prepares its "findings" which are submitted, along with the staff report, to the ARB for consideration at a public hearing. The Board then decides whether to identify a substance as a TAC (see illustration below). If the substance is identified as a TAC, it is listed in Title 17 of the California Code of Regulations under section 93000.

The Identification Process



What Happens When a Substance is Identified as a TAC by the Air Resources Board?

After a substance is identified as a TAC, the ARB is required to conduct a needs analysis to determine if any regulatory action is warranted. Specifically, the law requires the ARB to prepare a report which assesses the need and appropriate degree of control of a TAC, in consultation with the local districts, affected industry, and the public.

Where is Environmental Tobacco Smoke in the Toxic Air Contaminant Process?

This draft report is being released to solicit public comments on the draft version of the report which includes the Executive Summary, Part A (exposure assessment), and Part B (health assessment). This version of the report, along with the comments received and any revisions resulting from the comments, will be reviewed and discussed with the SRP at a noticed public meeting of the SRP.

What is Environmental Tobacco Smoke?

Environmental Tobacco Smoke is a complex mixture of thousands of gases and fine particles emitted by the burning of tobacco products and from smoke exhaled by the smoker. Other minor contributors are from the smoke that escapes while the smoker inhales and some vapor-phase related compounds that diffuse from the tobacco product. The composition will vary depending on the heat of combustion, the tobacco content, additives present, and the type of filter material used.

Many of the substances found in ETS have known adverse health effects. The table below lists some of these compounds.

Some Substances in Environmental Tobacco Smoke with Known Adverse Health Effects

1,3-butadiene	Cadmium
2-Naphthylamine	Chromium VI
4-Aminobiphenyl	Ethyl benzene
4-nitrobiphenyl	Formaldehyde
Acetaldehyde	Hydrazine
Acrolein	Methyl chloride
Aniline	Nickel
Arsenic (inorganic)	Nicotine
Benzene	Phenol
Benz[a]anthracene	Styrene
Benzo[a]pyrene	Toluene

How much ETS is Emitted in California?

The amount of ETS emitted into the environment depends in large part on the smoking public's behavior. However, the source of ETS emissions is from the combustion of individual tobacco products.

For this evaluation, ETS emissions were characterized using the most widely measured components of ETS: nicotine, respirable particulate matter (RSP), and carbon monoxide (CO). Emissions were estimated using data from California Tobacco Surveys, emission rates from the scientific literature, and cigarette consumption data.

2002 California Statewide ETS Emissions (tons/year)

	Cigarettes	Cigars	Total
Nicotine	36	4	40
RSP	335	30	365
CO	1475	432	1907

What is the Prevalence of Smokers in California?

The California Tobacco Survey (CTS), developed by the California Department of Health Services (CDHS), indicates that during the past decade, smoking prevalance among adults (over age 18) and adolescents (12 to 17 years) has gradually decreased.

Starting in 2001, CDHS began measuring adolescent prevalence through their California Student Tobacco Survey (CSTS). The CSTS was incorporated by CDHS since it samples school populations and provides better statistical accuracy. The most recent CTS and CSTS surveys show that both the adult (2002 data) and adolescent (2001 data) smoking prevalence is about 16%. The CSTS data also shows that the range of adolescent smokers varies from 10% in 9th grade to 23% in 12th grade.

How does California Compare to the Rest of the Nation?

Since the passage of Proposition 99 in 1988, the annual adult per capita cigarette consumption has declined by over 60% in California. Adult smoking prevalence in California has dropped at a faster rate relative to the rest of the nation.

Comparison of Reduction in Cigarette Consumption: California versus U.S.

Fiscal Year	1987/1988 (packs per adult)	2001/2002 (packs per adult)	% Decline
California	126.6 packs	47.7 packs	62.3
United States	154.8 packs	99.2 packs	35.9

What is the Prevalence of ETS Exposure in California?

Smoking behavior and other factors that change smoking patterns such as smoking regulations, affect present and future exposure patterns. Information from several smoking behavior related surveys indicate that California's adults, adolescents, and children are exposed to ETS during some time of the day.

According to studies from the late 1980s and the early 1990s, on a given day, 56% of adults (over age 18), 64% of adolescents (12-17 years), and 38% of children (0-11 years), may be exposed to ETS during their daily activity. Actual incidence may be lower today due to decreases in workplace smoking and in public locations such as restaurants, bars, and gaming clubs due to California smoking restrictions.

How do we Measure ETS Exposure in the Environment?

Exposure to ETS is difficult to characterize because it is a complex mixture of substances and the difficulty in determining an appropriate marker that is representative of ETS as a whole. Given its complex nature, it is necessary to select surrogate measure of exposure that is representative of ETS as a whole.

Several components of ETS have been studied as surrogates or markers for ETS. Nicotine has been most widely studied as a potential marker because its only major source is tobacco smoke. Other ETS markers that have been studied include: solanesol, 3-ethenylpyridine (3-EP), carbon monoxide, iso- and anteisoalkanes (C_{29}-C_{34}), PAHs, fluorescing particulate matter, respirable suspended particles, and ultraviolet particulate matter.

Are there Studies of Outdoor Air Concentrations of ETS?

In general, studies measuring outdoor ETS concentrations are limited. Two published studies we are aware of measured outdoor air concentrations outside of California. One study used fine smoke particles to estimate ETS; concentrations ranging from 0.28 to 0.36 microgram of nicotine per cubic meter of air ($\mu g/m^3$). Another study used personal badge monitors to measure ambient nicotine levels. This study reported a 7-day median nicotine concentration in the outdoor environment of 0.025 ug/m^3.

To obtain data on current levels of ETS in ambient air where people spend part of their day, the ARB monitored nicotine concentrations at several outdoor smoking areas in California. The study gathered two 8-hour samples and six 1-hour samples per site tested. Depending on the site location and number of smokers present, the results showed a range of concentrations from 0.013-3.1 $\mu g/m^3$ for the 8-hour samples and 0.016-4.6 $\mu g/m^3$ for the 1-hour measurements. Overall, the results indicate that concentrations of nicotine correspond to the number of smokers in the smoking areas, although factors such as the size of the smoking area and the presence of wind affected the results.

Are There Estimates of Indoor Air Exposure to ETS?

Yes. Several studies have estimated ETS levels in different indoor environments using nicotine and respirable particulate matter (RSP) as markers for ETS exposure. Current indoor concentrations of nicotine in California are estimated to range from 0.5 to 6.0 $\mu g/m^3$ in the home environment, 2-8 $\mu g/m^3$ in offices or public buildings where smoking is permitted, and less than 1 $\mu g/m^3$ in public buildings where smoking is prohibited. However, certain workplaces, such as the documented 20% of free-standing bars that do not comply with California's workplace smoking ban, would likely have higher levels of ETS. Based on measurements from several studies, levels could range from 9.8 $\mu g/m^3$ in betting establishments to 76.0 $\mu g/m^3$ for bingo parlours. RSP concentrations are estimated to range from less than 15 ug/m^3 where smoking is prohibited to about 300 ug/m^3 in the home environment where one cigarette is being smoked.

How do we Estimate the California Public's Exposure to ETS?

An individual's exposure depends on the air concentration of a pollutant in a given environment, and the time they spend in that environment. An individual's total daily exposure is the sum of all the exposures they experience across their 24-hour day, including both indoor and outdoor environments.

A scenario-based approach was used to characterize the range of the public's exposure to ETS during a 24-hour period. The scenario-based exposure method uses the results from ARB's ETS air monitoring study, available indoor ETS concentration data, and scenario-based activity patterns to estimate exposures under different situations. The results show a wide range of possible population subgroup daily exposures. For individuals living in non-smoking homes and having only brief encounters with ETS, their 24-hour exposures are low, about 1 $\mu g\text{-}hr/m^3$. For those living in homes with indoor smokers and experiencing in-vehicle exposures, their integrated 24-hour exposure estimate can range up to 81 $\mu g\text{-}hr/m^3$. Such exposures are especially of concern for young children because they are likely to recur daily and may adversely affect the physiological sensitivity of developing children.

The primary and often the only exposure for individuals that do not spend time near smokers, exposure occurs outdoors in locations over which the individual typically has little control. For non-smokers whose work or other activities bring them into contact with outdoor smokers regularly, 100% of their exposure can be attributable to proximity to outdoor smoking.

Are There Other Methods for Estimating Human Exposure to ETS?

One of the most accurate methods for estimating ETS exposure in a person is through the use of biological markers. Biological markers of ETS exposure are metabolites of tobacco smoke ingredients found in physiological fluids or attached to DNA or proteins. The ability to quantify exposure objectively is an important step in linking exposure to relative risk of adverse outcomes.

Cotinine, a metabolite of nicotine, is the biological marker of choice in most epidemiological studies. Physiological fluid levels correlate very well with ETS exposure documented both by questionnaire and by personal exposure monitoring. Cotinine levels differ between smokers and ETS-exposed non-smokers by 2 to 3 orders of magnitude. From an epidemiological perspective, this difference is useful to determine when people misrepresent their smoking status. Cotinine assays are sensitive enough that individuals without ETS exposure can be distinguished from those persons with low exposure.

The nicotine concentration in hair is emerging as another viable biological marker of ETS exposure. In some instances, hair nicotine has been shown to better correlate with exposure than cotinine.

What is the Persistence of ETS in the Atmosphere?

Gaseous chemicals that are present in ETS can react in the atmosphere with other pollutants and sunlight to form new chemical species. The ETS particles and particle-associated chemicals (those with low vapor pressure that deposit or chemically bind onto the particles) are subject to wet and dry deposition and atmospheric transformation of species adsorbed to the particles.

Nicotine, the principal alkaloid in tobacco, is most commonly found in the gas phase in the environment. In the ambient air, nicotine may react with hydroxyl radicals to have a half-life of approximately one day.

What are the Health Effects Associated with Exposure to ETS?

ETS exposure is causally associated with a number of health effects, including effects on infants and children. ETS has a number of serious impacts on children's health including sudden infant death syndrome (SIDS), exacerbation of asthma, increased respiratory tract infections, increased middle ear infections, low birth weight, and developmental impacts.

Listed in Table ES.1 are the developmental, respiratory, carcinogenic and cardiovascular effects for which there is sufficient evidence of a causal relationship, including fatal outcomes such as sudden infant death syndrome and heart disease mortality, as well as serious chronic diseases such as childhood asthma. There are, in addition, effects for which evidence is suggestive of an association but further research is needed for confirmation. These include spontaneous abortion, cervical cancer, and chronic respiratory symptoms in adults (Table ES.1). Finally, it is not possible to judge on the basis of the current evidence the impact of ETS on a number of endpoints, including congenital malformations, changes in female fertility and fecundability, male reproductive effects, and rare childhood cancers.

Many Californians are exposed to ETS, and the number of people adversely affected may be correspondingly large. Table ES.2 presents morbidity and mortality estimates

for health effects causally associated with ETS exposure. Derivation of these estimates is described further in Part B.

Relative risk estimates associated with some of these endpoints are small, but because the diseases are common the overall impact can be quite large. For example, relative risk estimates in the range of 1.2-1.7 for heart disease mortality in nonsmokers is supported by the collective evidence; this corresponds to approximately 2,000-5,000 deaths annually in California. The relative risk estimate of 1.38 associated with low birthweight implies that ETS may impact fetal growth of 1,577 newborns in California, roughly 1 to 2% of newborns of nonsmokers exposed at home or work. ETS may exacerbate asthma (RR $\approx$ 1.75 to 2.25) in 29,000 to 47,000 children in California. Large impacts are associated with relative risks for respiratory effects in children such as middle ear infection (RR $\approx$ 1.62), and lower respiratory disease in young children (RR $\approx$ 1.5 to 2). Asthma induction (RR $\approx$ 1.75 to 2.25) may occur in as many as 0.5 to 2% of ETS-exposed children. ETS exposure may be implicated in 21 SIDS deaths per year in California (RR $\approx$ 3.5), with a risk of death to 0.1% of infants exposed to ETS in their homes. Lifetime risk of lung cancer death related to ETS-exposed nonsmokers may be about 0.7% (RR $\approx$ 1.2) or higher. For nasal sinus cancers, observed relative risks have ranged from 1.7 to 3.0.

TABLE ES.1
HEALTH EFFECTS ASSOCIATED WITH EXPOSURE TO ENVIRONMENTAL TOBACCO SMOKE

Effects Causally Associated with ETS Exposure

Developmental Effects
Fetal Growth: Low birthweight and decrease in birthweight
Sudden Infant Death Syndrome (SIDS)

Respiratory Effects
Acute lower respiratory tract infections in children (*e.g.,* bronchitis and pneumonia)
Asthma induction and exacerbation in children and adults
Chronic respiratory symptoms in children
Eye and nasal irritation in adults
Middle ear infections in children

Carcinogenic Effects
Lung Cancer
Nasal Sinus Cancer
Breast Cancer

Cardiovascular Effects
Heart disease mortality
Acute and chronic coronary heart disease morbidity
Altered vascular properties

Effects with Suggestive Evidence of a Causal Association with ETS Exposure

Developmental Effects
Spontaneous abortion, preterm delivery, IUGR
Adverse impact on cognition and behavior
Allergic sensitization

Respiratory Effects
Exacerbation of cystic fibrosis
Decreased pulmonary function growth
Chronic respiratory symptoms in adults

Carcinogenic Effects
Cervical cancer
Brain cancer and lymphomas in children

Table ES.2 Attributable Risks Associated with ETS

	Conclusion OEHHA 1997	Conclusion OEHHA 1997	Conclusion Update	Conclusion Update
Outcome	**Excess # in CA**	**Excess # in US**	**Excess # in CA**	**Excess # in US**
Pregnancy: LBW	**1,200-2,200**	**9,700-18,600**	**1,577**	**24,253**[1]
			1,943	**29,590**[1]
Cardiac death (Ischemic heart disease death)	**4,200-7,440**	**35,000-62,000**	**1,713-5,483**[2]	**22,669-69,553**[3]
Lung Cancer Death Incidence	**360**		**411-1,514**[4]	
	3,000			**7,564-26,473**[5]
Asthma (children) New cases			**Episodes**[6]	**Episodes**[7]
	960-3120	**8,000-26,000**	**29,424-46,695**	**438,933-669,295**
Exacerbation	**48,000-120,000**	**400,000-1,000,000**		
Lower respiratory illness	**18,000-36,000**	**150,000-300,000**	**N/A**	**N/A**
Otitis media visits	**78,600-188,700**	**700,000-1,600,000**	**51,690**[8]	**789,712**[9]
SIDS	**120**	**1,900-2,700**	**21**[10]	**431**[11]

[1]Based on adult females reporting exposure to ETS in NHANES III for 1995 (Pirkle et al., 1996)

[2]Based on California Dept Health Services. www.dhs.cs.gov/hisp/chs/OHIR/vssdata/2000data/OOCh5pdf/5_9_Reorg.PDF. Table 5-9 for yr 2000

[3] Based on Anderson and Arias (2003). National Vital Statistics Report. Vol 51(9) Table 2 for yr 2000 Ischemic heart diseases including AMI.

[4]Based on Cancer in California: 1988-1999. California Dept Health Services, Cancer Surveillance Section. Table XIX-1 for yr 1999

[5] Based on Ries et al. (2003) SEER Cancer Statistics Review 1973-2000 National Cancer Institute for yr 2003.

[6] Based on number asthma attacks or episodes in previous 12 months for 0-14 year olds. Calculated from CDC-MMWR 2002 51(SS01); 1-13 assuming 12% of US population lives in CA..

[7] Based on number asthma attacks or episodes in previous 12 months for 0-14 year olds. CDC-MMWR 2002 51(SS01)

[8] Calculated by applying national value (H6) and assuming 12% of US population lives in California

[9] Based on National Center for Health Statistics Series 13 No. 137. Ambulatory Health Care Visits by Children: Principal Diagnosis and Place of Visit for yrs 1993-1995.

[10] Based on California Dept Health Services. www.dhs.ca.gov/hisp/chs/ohir/vssdata/2000data/00ch4pdf/8reorg.pdf. Table 4-8 for yr 2000

[11] Based on National Center for Health Statistics. www.cdc.gov/nchs/fastats/infort.htm for yr 2000

LBW = low birth weight; N/A = data not available; PTD = preterm delivery.

What Perinatal Health Effects have been Observed?

ETS exposure adversely affects fetal growth, with elevated risks of low birth weight or "small for gestational age" observed in numerous epidemiological studies. The primary effect observed, reduction in mean birthweight, is small in magnitude. But if the distribution of birthweight is shifted lower with ETS exposure, as it appears to be with active smoking, infants who are already compromised may be pushed into even higher risk categories. Low birthweight is associated with many well-recognized problems for infants, and is strongly associated with perinatal mortality.

The impact of ETS on perinatal manifestations of development other than fetal growth is less clear. The few studies examining the association between ETS and perinatal death are relatively non-informative. Studies on spontaneous abortion are suggestive of a role for ETS, but further work is needed, particularly as a recent report did not confirm the findings of four earlier studies. Although epidemiological studies suggest a moderate association of severe congenital malformations with paternal smoking, the findings are complicated by the use of paternal smoking status as a surrogate for ETS exposure, since a direct effect of active smoking on sperm cannot be ruled out. In general, the defects implicated differed across the studies, with the most consistent association seen for neural tube defects. At this time, it is not possible to determine whether there is a causal association between ETS exposure and this or other birth defects.

What Postnatal Effects of ETS Exposure have been Observed?

Numerous studies have demonstrated an increased risk of sudden infant death syndrome, or "SIDS," in infants of mothers who smoke. Until recently it has not been possible to separate the effects of postnatal ETS exposure from those of prenatal exposure to maternal active smoking. Recent epidemiological studies now have demonstrated that postnatal ETS exposure is an independent risk factor for SIDS.

Although definitive conclusions regarding causality cannot yet be made on the basis of available epidemiological studies of cognition and behavior, there is suggestive evidence that ETS exposure may pose a hazard for neuropsychological development. With respect to physical development, while small but consistent effects of active maternal smoking during pregnancy have been observed on height growth, there is no evidence that postnatal ETS exposure has a significant impact on growth in otherwise healthy children. Developmental effects of ETS exposure on the respiratory system include lung growth and development, childhood asthma exacerbation, and, in children, acute low respiratory tract illness, middle ear infection and chronic respiratory symptoms.

What are the Effects of ETS Exposure on Female and Male Reproductive Systems?

Active smoking by women has been found to be associated with decreased fertility in a number of studies, and tobacco smoke appears to be anti-estrogenic. The epidemiological data on ETS exposure, though not conclusive are suggestive of

adverse effects on fecundability and fertility. Newer studies reviewed in the update suggest adverse effects of ETS exposure on menstrual cycle disorders. Regarding other female reproductive effects, while studies indicate a possible association of ETS exposure with early menopause, the analytic methods of these studies could not be thoroughly evaluated, and therefore at present, there is not firm evidence that ETS exposure affects age at menopause. Although associations have been seen epidemiologically between active smoking and sperm parameters, conclusions cannot be made regarding ETS exposure and male reproduction, as there is very limited information available on this topic.

What are the Effects on the Respiratory System?

ETS exposure produces a variety of acute effects involving the upper and lower respiratory tract. In children, ETS exposure can exacerbate asthma, and increases the risk of lower respiratory tract illness, and acute and chronic middle ear infection. Eye and nasal irritation are the most commonly reported symptoms among adult nonsmokers exposed to ETS. Odor annoyance has been demonstrated in several studies.

Regarding chronic health effects, there is compelling evidence that ETS is a risk factor for induction of new cases of asthma (in children and adults) as well as for increasing the severity of disease among children and adults with established asthma. In addition, chronic respiratory symptoms in children, such as cough, phlegm, and wheezing, are associated with parental smoking. While the results from all studies are not wholly consistent, there is evidence that childhood exposure to ETS affects lung growth and development, as measured by small, but statistically significant decrements in pulmonary function tests; associated reductions may persist into adulthood. The effect of chronic ETS exposure on pulmonary function in otherwise healthy adults is likely to be small, and unlikely by itself to result in clinically significant chronic disease. However, in combination with other insults (*e.g.*, prior smoking history, exposure to occupational irritants or ambient air pollutants), ETS exposure could contribute to chronic respiratory impairment in adults. In addition, regular ETS exposure in adults has been reported to increase the risk of occurrence of a variety of lower respiratory symptoms.

Children are especially sensitive to the respiratory effects of ETS exposure. Children with cystic fibrosis are likely to be more sensitive than healthy individuals. Several studies of patients with cystic fibrosis, a disease characterized by recurrent and chronic pulmonary infections, suggest that ETS can exacerbate the condition. Several studies have shown an increased risk of atopy (a predisposition to become allergic to common allergens, which can then be manifested as a variety of allergic conditions) in children of smoking mothers, though the evidence regarding this issue is mixed.

What Carcinogenic Effects does ETS have?

The role of ETS in the etiology of cancers in nonsmokers was explored, as smoking has been recognized as an established cause of a number of cancers (lung, larynx, oral cavity, esophagus and bladder), and a probable cause of several others (cervical,

kidney, pancreas, and stomach). Also, ETS contains a number of constituents that have been identified as carcinogens.

Reviews published in the 1986 *Report of the Surgeon General,* by the National Research Council in 1986, and by the U.S. EPA in 1992, as well as the original OEHHA report (CalEPA 1997) concluded that ETS exposure causes lung cancer. Three large U.S. population-based studies and a smaller hospital-based case control study have been published since the completion of the U.S. EPA review. The population-based studies were designed to and have successfully addressed many of the weaknesses for which the previous studies on ETS and lung cancer have been criticized. Results from these studies are compatible with the causal association between ETS exposure and lung cancer already reported by the U.S. EPA, Surgeon General, and National Research Council. The studies examining the effect of ETS exposure on nasal sinus cancers consistently (though not uniformly) show statistically significant associations, presenting strong evidence that ETS exposure increases the risk of nasal sinus cancers in nonsmoking adults. Further study is needed to characterize the magnitude of the risk of nasal sinus cancer from ETS exposure.

Epidemiological studies, supported by animal data, provide evidence consistent with a causal association between ETS exposure and breast cancer in humans, which appears stronger for pre-menopausal breast cancer. Studies assessing the association between passive smoking and breast cancer have generally reported a positive, and often statistically significant association. This risk appears to vary by several factors including menopausal status and timing of exposure; factors not always controlled or analyzed for in studies, including the large U.S. cohort studies. Perhaps for these reasons, in addition to concerns of potential ETS exposure misclassification due to limited or excluded occupational, childhood or total lifetime exposure, the large cohort studies available have not identified significantly elevated increases in breast cancer risk. However, the more recent primary, population-based case-control studies, controlling for several important reproductive, dietary and other potential confounding factors, have consistently identified elevated estimates for residential and occupational exposure, particularly among pre-menopausal women or women exposed early in life. The toxicological data on tobacco smoke constituents continues to strongly support that the cancer risk associated with active smoking and with ETS exposure alone remains highly plausible. In comparison to studies reviewed in the previous OEHHA report (Cal/EPA, 1997), current epidemiological and toxicological data are substantially more indicative of a positive association between ETS exposure and breast cancer risk, particularly in subgroups of women defined by early age of exposure onset, menopausal status, or underlying genetic susceptibility (e.g. for metabolic enzymes). Future studies need to account for these other factors to establish the extent of this exposure-disease relationship. Overall, the weight of evidence (including biomarker, animal and epidemiological studies) is consistent with a causal association between ETS in breast cancer, which appears to be stronger for pre-menopausal breast cancer.

The epidemiological and biochemical evidence suggest that exposure to ETS may increase the risk of cervical cancer. Positive associations were observed in two of three case-control studies and a statistically nonsignificant positive association was observed in the only cohort study conducted. Findings of DNA adducts in the cervical epithelium

as well as nicotine and cotinine in the cervical mucus of ETS-exposed nonsmokers provides biological plausibility.

Precursors of endogenously formed N-nitroso compounds suspected of causing brain tumors are present in high concentrations in ETS. In adults, the epidemiological evidence for an association between ETS exposure and risk of brain tumor remains weak and inadequately researched. More recent studies have focused on the potential association between ETS and childhood brain tumors. In children, recent studies or others not previously reviewed by OEHHA, provide no substantial evidence for an association between maternal smoking and childhood brain tumors, with risk estimates generally near the null. Several studies indicated a slightly stronger association with paternal smoking and brain cancer, although the association is still somewhat weak. The most recent and largest individual study (Filippini et al., 2002) did not consistently observe statistically elevated brain cancer risk. However, the pooled estimate of risk from the Oxford Survey of Childhood Cancers studies (together the largest sample size of the studies reviewed), comparing paternal smokers versus paternal nonsmokers, did find a significantly elevated risk of deaths in offspring of smokers from tumors of the central nervous system (Sorahan et al., 1997b). Overall, the generally positive, but inconsistent, associations reported between paternal smoking and childhood brain tumors, in combination with biologically plausible hypothesis, provide suggestive evidence of an association between ETS and brain cancer in children. Similarly, suggestive evidence of an association between exposure to ETS and childhood cancer is noted for lymphomas and acute lymphocytic leukemia (children of paternal smokers).

For other cancer sites in adults, there has been limited ETS-related epidemiological research in general: there is currently insufficient evidence to draw any conclusion regarding the relationship between ETS exposure and the risk of occurrence of cancer in sites other than lung, nasal cavity, breast, and possibly brain and lymphoma and leukemia. A review of the available literature clearly indicates the need for more research. For example, although compounds established as important in the etiology of stomach cancer are present in tobacco smoke, only a single well designed population based study has been performed for this site. In biochemical studies of nonsmokers, higher levels of hemoglobin adducts of the established bladder carcinogen,

4-aminobiphenyl, have been found in those exposed to ETS. However, no significant increases in bladder cancer were seen in the two epidemiological studies (case-control) conducted to date, although both studies were limited in their ability to detect an effect.

The epidemiological data on ETS exposure and rare childhood cancers provide an inadequate foundation for making conclusions regarding causality. Some studies found small increased risks in children in relation to parental smoking for neuroblastoma, Wilm's tumor, bone and soft-tissue sarcomas, but not for germ cell tumors. Studies to date on these rare cancers have been limited in their power to detect effects. The impact of ETS exposure on childhood cancer would benefit from far greater attention than it has received to date.

What are the Effects on the Cardiovascular System?

The epidemiological data, from prospective and case-control studies conducted in diverse populations, in males and females and in western and eastern countries, support a conclusion that there is a causal association between ETS exposure from spousal smoking and death from coronary heart disease (CHD) in nonsmokers. To the extent possible, estimates of risk were determined with adjustment for demographic factors, and often for other factors related to heart disease, such as blood pressure, serum cholesterol level and obesity index. Risks associated with ETS exposure were almost always strengthened by adjustment for other cofactors. For nonsmokers exposed to spousal ETS compared to nonsmokers not exposed, the risk of CHD mortality is increased by a factor of 1.3. The association between CHD and risk is stronger for mortality than for non-fatal outcomes, including angina. It is also evident that these effects exacerbate or are exacerbated by underlying conditions, and individuals with other chronic conditions such as diabetes, vascular disease or hypertension comprise a susceptible population at even greater risk from ETS exposure.

Data from clinical and animal studies suggest various mechanisms by which ETS causes heart disease. In a number of studies in which nonsmokers were exposed to ETS, carotid wall thickening, lesion formation, aortic distensibility and reactivity, and compromise of endothelial function were similar to, but less extensive than those experienced by active smokers. Other effects observed include impaired exercise performance, altered lipoprotein profiles, enhanced platelet aggregation, and increased endothelial cell counts. These findings may account for both the short- and long-term effects of ETS exposure on the heart. The data reviewed also suggests that the effects of ETS may also contribute to stroke, the etiology of which includes atherosclerosis of the carotid and large arteries of the brain, and degeneration of intracerebral arteries. Research in this area suggests that chronic ETS exposure may increase the risk of stroke by about 82% (Bonita *et al*., 1999).