APPENDIX III

PROPOSED IDENTIFICATION OF ENVIRONMENTAL TOBACCO SMOKE AS A TOXIC AIR CONTAMINANT

AS APPROVED BY THE SCIENTIFIC REVIEW PANEL ON JUNE 24, 2005

Under Separate Cover:

Executive Summary
Part A – Exposure Assessment
Part B – Health Effects
Part C – Public Comments and ARB/OEHHA Staff Responses

State of California
AIR RESOURCES BOARD

APPENDIX III

PROPOSED IDENTIFICATION OF ENVIRONMENTAL TOBACCO SMOKE AS A TOXIC AIR CONTAMINANT

EXECUTIVE SUMMARY

As Approved by the Scientific Review Panel
On June 24, 2005

The SRP approved Executive Summary is a supporting technical document which is incorporated by reference in the Initial Statement of Reasons (Staff Report)

State of California

Proposed Identification of Environmental Tobacco Smoke as a Toxic Air Contaminant

Executive Summary

As Approved
by the Scientific Review Panel
on June 24, 2005

California Environmental Protection Agency

Air Resources Board

Part A- Exposure Assessment

Office of Environmental Health Hazard Assessment

Part B- Health Effects

EXECUTIVE SUMMARY

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

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

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, which was later published by the U.S. National Cancer Institute in 1999, has been updated to include more recent literature. OEHHA's evaluation includes numerous published papers on ETS-related health effects since their initial 1997 ETS review.

Part C of the report, prepared by both ARB and OEHHA staff, addresses the comments received on the first public version of the report. The Part C document contains the staff responses to comments and the comment letters.

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?
❼ Does exposure to the substance cause increased health impacts in children?
❽ Does the substance pose a potential health risk to Californians?

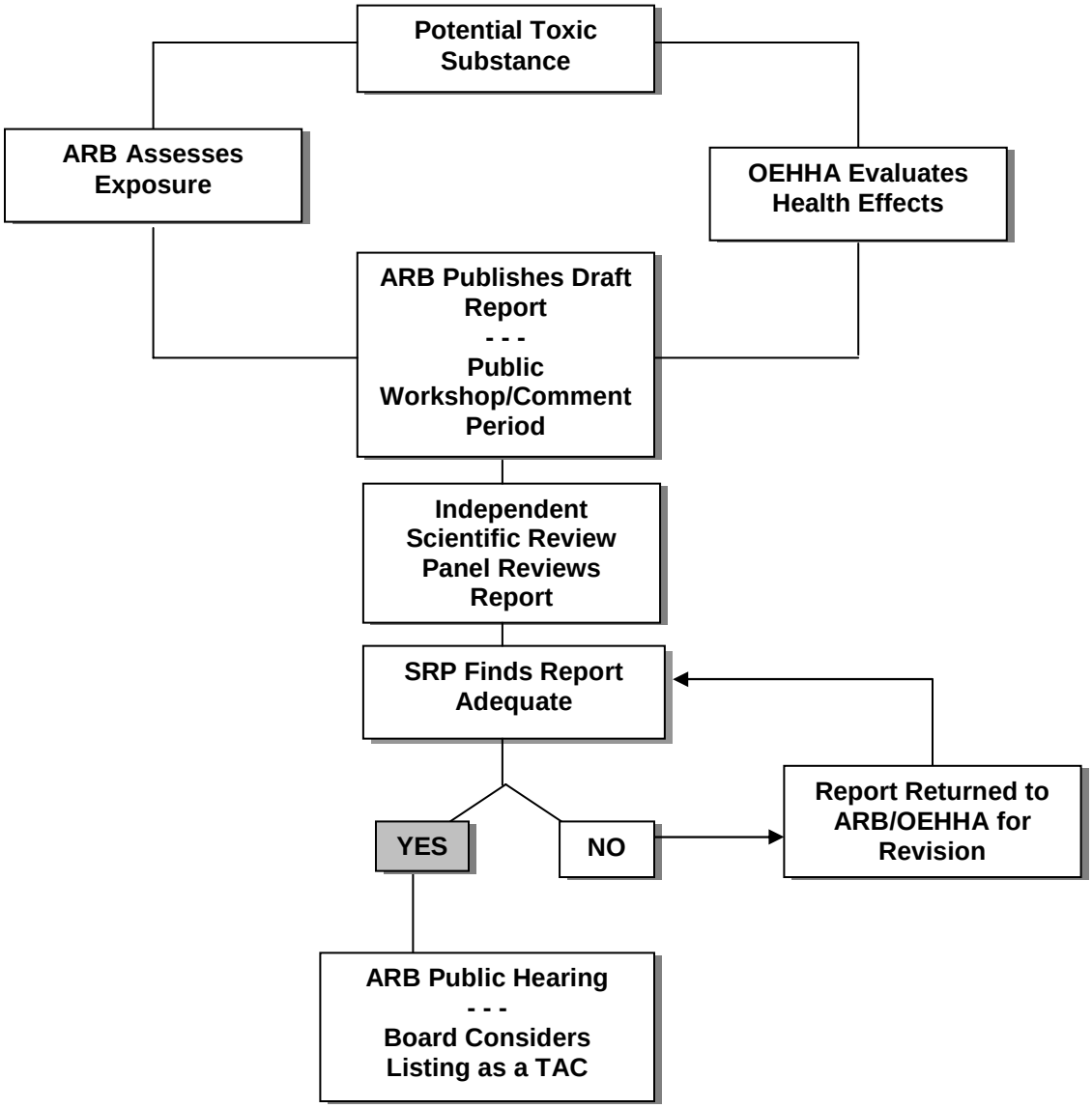
The ARB staff determines the public's potential exposure to the substance while the OEHHA must determine if exposure to the substance poses a potential health risk. Both agencies then prepare a draft report which serves as the basis for identifying a substance.

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 Health and Safety Code provides for the development of 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?

Environmental Tobacco Smoke has undergone a thorough and extensive evaluation since it entered the identification program in June 2001. In December 2003, the draft report, which included the Executive Summary, Part A (exposure assessment), and Part B (health assessment), was released to the public for a three month comment period. In March 2004, a public workshop was held to discuss the report. On November 30, 2004, the SRP held a meeting to discuss the report and the comments received on the draft report (Part C - responses to public comments). The meeting was continued on January 6, 2005 and on March 14, 2005. On June 24, 2005, the SRP held a fourth meeting to discuss and approve the revised draft report. The SRP findings recommend that the ARB take the necessary steps to list ETS as a TAC. Furthermore, the SRP recommends to OEHHA that ETS, once listed, be added to the list of toxic air contaminants that may disproportionately impact children (pursuant to Health and Safety Code section 39669.5(c)). As indicated by the preceding graphic, the next step in the toxic air contaminant process is to notice a public hearing of the Air Resources Board.

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

The size of ETS particles range from 0.01 to about 1 µm. Freshly produced ETS undergoes complex atmospheric changes such as coagulation, evaporation, dilution and condensation. However, ETS fine particles essentially remain below 1 µm in size.

What are the Total ETS Emissions in California?

ETS emissions were characterized using the most widely measured components of ETS: nicotine, respirable particulate matter (RSP), and carbon monoxide (CO). Total emissions, as a result of combustion of tobacco products, were estimated using data from the California Tobacco Surveys, emission rates from the scientific literature, and cigarette sales data from the State Board of Equalization.

2002 California Statewide ETS Emissions (tons/year)

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

How much ETS is Emitted Outdoors in California?

The amount of ETS emitted into the outdoor environment depends in large part on the smoking public's behavior. Outdoor ETS emissions include direct emissions from outdoor smoking, plus ETS emissions generated indoors which eventually ventilate outside. Apportioning ETS emissions as either outdoor or indoor emissions is difficult to determine due to limited information. However, existing information shows that most smoking in California occurs outdoors. This is demonstrated by the fact that most workplaces (including bars and restaurants) in California, through the enactment of Assembly Bill 13 (AB13) in 1998, are now smoke-free. In addition, data from the 2002 California Adult Tobacco Survey (CATS), shows that over 80% of all California homes

with children are now smokefree and that about 50% of California smokers report that they do not smoke in their own homes. For ETS generated indoors, building ventilation studies show that 50 – 80 percent of ETS (including ETS constituents) is exchanged with outdoor air over a given time period. From all of the available information, the ARB staff estimates that at least 80% of total ETS emissions (including those directly emitted outdoors and emissions ventilated from indoors) are emitted to the outdoor environment.

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 prevalence 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 many of 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), reported exposure to ETS during their daily activity. Actual incidence is assumed to 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. However, up to 20% of adolescents may still be exposed to ETS in their homes.

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. Due to its complex nature, it is necessary to select a 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 source is primarily tobacco smoke. Other ETS markers that have been studied include: solanesol, 3-ethenylpyridine (3-EP), carbon monoxide, iso- and anteisoalkanes (C_{29}-C_{34}), polycyclic aromatic hydrocarbons, fluorescing particulate matter, respirable suspended particles, and ultraviolet particulate matter.

Are there Studies that have Determined Outdoor Air Concentrations of ETS in California?

Yes. There are studies that have either measured or modeled outdoor air concentrations of ETS constituents. One study estimated concentrations of fine smoke particles in the Los Angeles air using tobacco-specific iso- and anteisoalkanes. Using the measurements from these marker compounds, the annual average ambient fine (less than 2.5 microns) ETS particles in the Los Angeles air was estimated to range from 0.28 to 0.36 microgram of ETS particle per cubic meter of air ($\mu g/m^3$). The levels were based on annual measurement data from 1982. Another study used personal badge monitors to measure personal nicotine levels. This study reported a 7-day median nicotine concentration in the outdoor environment of 0.025 $\mu g/m^3$, based on those study participants who reported no indoor exposure.

One study used a chemical mass balance receptor model based on organic compounds to estimate source contributions to fine particle mass concentrations in the Los Angeles air. The modeled annual average concentration for the Los Angeles air was estimated to be 0.21 $\mu g/m^3$ fine ETS particulate matter in 1982.

Has the ARB Measured Outdoor Concentrations of ETS in California?

Yes. 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 nicotine 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 corresponded mainly to the number of smokers in the smoking areas, the size of the smoking area and meteorological conditions.

What are the Outdoor Air Levels of ETS that Most Californians Breathe?

The scenario-based approach used to characterize the range of the public's exposure to ETS in this report showed that Californians who neither smoke nor associate with many smokers will have very limited ETS exposure. In this case, individuals will likely experience the majority of their lifetime ETS exposure from background levels of ETS which result from occasional or steady state near-source emissions. Since most Californians live and work in urban areas, the ARB staff has estimated an outdoor annual average ambient ETS particle concentration for the Los Angeles air for 2003. The staff used the two Los Angeles studies discussed above as a basis for this estimate. The staff applied an adjustment factor to the 1982 fine particle estimates presented in the two Los Angeles studies to reflect reductions in cigarette sales and cigarette emission rates that have occurred since 1982. The results show that estimated annual average fine ETS particle concentrations in Los Angeles in 2003 likely decreased to between 0.06 to 0.10 µg/m^3. The table below summarizes the outdoor air concentration data for ETS nicotine and fine particles from all outdoor estimates.

Estimates of ETS Outdoor Ambient Concentrations

Method/Reference	Data Year	Concentrations (µg/m^3)	
		Fine $PM_{2.5}$	Nicotine
Fine PM – Source Apportionment Schauer *et al*., 1996	1982	0.21 µg/m^3 annual average	*0.026 µg/m^3 annual average
Iso- and anteisoalkanes – measurement Rogge *et al*., 1994	1982	–	*0.035 – 0.044 µg/m^3 annual average
Nicotine – measurement Eisner *et al*., 2001	2001	*0.20 µg/m^3 7-day median conc.	0.025 µg/m^3 7-day median conc.
Nicotine – measurement ARB, 2003	2003	*0.11 – 25 µg/m^3 8-hour range *0.073 – 0.97 µg/m^3 8-hour background	0.013 – 3.1 µg/m^3 8-hour range 0.009 – 0.12 µg/m^3 8-hour background
Los Angeles background - Estimate ARB, 2004	2003	–	*0.008 - 0.013 µg/m^3 annual average

* Calculated value using: PM2.5/Nicotine concentration = 8

Are There Estimates of Indoor Air Exposure to ETS?

Yes. A number of studies have estimated ETS levels in different indoor environments using nicotine and respirable particulate matter (RSP), and other markers for ETS exposure. Current typical indoor concentrations of nicotine in California are estimated to range from near zero to about 6.0 µg/m^3 in the home environment. Because of California's workplace smoking ban, California office buildings will generally have very

low smoking concentrations. However, certain workplaces, such as the small (but documented) percentage of free-standing bars that still do not comply with California's workplace smoking ban, would likely have higher levels of ETS. Based on measurements from several studies, average nicotine levels could be as high as 76.0 µg/m^3 for bars and bingo parlors where smoking still occurs.

RSP concentrations in certain entertainment venues (such as casinos and bingo parlors) are estimated to range from less than 15 µg/m^3, where smoking is prohibited, up to 350 µg/m^3, where smoking is allowed. In the home environment, short-term peak RSP levels have been found up to 300 µg/m^3, where just one cigarette was smoked. Likewise, in-vehicle ETS RSP concentrations are estimated to range from about 90 µg/m^3 to well over 1,000 µg/m^3, depending on ventilation and position of windows.

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 average 24-hour exposure concentrations are low, and are estimated to be less than 0.01 µg/m^3. For those living in homes with indoor smokers and experiencing in-vehicle exposures, the average exposure concentration to which they are exposed to over 24-hours can easily range up to 7.4 µg/m^3, and up to 19.4 µg/m^3 in a realistic, "maximally exposed" situation. Such exposures are especially of concern for developing young children because they are likely to recur daily and may result in serious health consequences.

This approach differs from previous TAC exposure assessments, which were based on California population-weighted exposures to outdoor average ambient concentrations. That approach was appropriate for TACs emitted from area-wide or region-wide sources such as motor vehicles and industrial plants. However, cigars and cigarettes, the primary sources of ETS, are smaller sources that emit pollutants near people. As a result, the highest exposures to ETS are very localized. Therefore, because exposures are localized and ETS is not monitored at ambient monitoring stations, we believe the scenario-based approach provides better and more informative estimates of public exposure to ETS.

The primary and often the only exposure for individuals who do not spend time near smokers is outdoors in locations over which the individual typically has little control. For nonsmokers 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 nonsmokers 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, especially where exposure is highly episodic.

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), induction and exacerbation of asthma, increased respiratory tract infections, increased middle ear infections, and causes developmental toxicity resulting in low birth weight, and impaired lung function growth, predisposition to SIDS (to the extent that this is a developmental effect), and other 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 SIDS, heart disease mortality and lung cancer death, as well as serious chronic diseases, such as childhood asthma. There are a number of effects for which evidence is suggestive of a causal association, but further research is needed for confirmation, including spontaneous abortion, decreased lung function growth, cervical cancer, and chronic respiratory symptoms in adults. 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, adverse 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. For lung cancer, where certain California-specific data are unavailable, estimates are derived from figures published for the U.S. population, assuming that the number affected in California would be 12% of the total. The estimates for cardiovascular disease, middle ear infection, asthma episodes, SIDS, pre-term delivery, and low birth weight were derived using information on prevalence of ETS exposure in California and the U.S.

Relative risk estimates associated with some of these endpoints are small, but because the diseases are common and ETS exposure is frequent and widespread, the overall impact can be quite large. The relative risk is a measure of the relation between exposure to a substance and the incidence of a disease. A relative risk of 1.0 indicates no relationship. For ETS, a relative risk estimate of 1.2-1.7 for heart disease mortality in nonsmokers is supported by the collective evidence; this corresponds to approximately 1,700-5,500 deaths annually in California. The relative risk estimate of 1.38 associated with low birth weight implies that ETS may impact fetal growth of 1,600 newborns in California. It is estimated that at least 31,000 children in California experience one or more ETS-related asthma episodes (new onset or exacerbation) each year. Large impacts are also associated with relative risks for respiratory effects in children such as middle ear infection (RR $\approx$ 1.62) (about 50,000 children annually), and lower respiratory infection in young children (RR $\approx$ 1.5 to 2) (18,000 to 36,000 children annually). ETS exposure is implicated in 21 SIDS deaths per year in California (RR $\approx$ 3.5). About 400 to 1,100 lung cancer deaths in California are ETS-related. For nasal sinus cancers, observed relative risks have ranged from 1.7 to 3.0. This is as high as or higher than the relative risks observed for lung cancer. Finally, for breast cancer, when evaluating younger, primarily premenopausal women at diagnosis, a pooled risk estimate of 1.68 is derived in the meta-analysis, and when restricted to the studies with better exposure assessment, an estimate of 2.20 is obtained (see Table 1). These estimates of association could represent a significant number of cases as this is a relatively common cancer in women. Adding the mid-point of the ranges for lung cancer deaths and heart disease deaths, and including the SIDS point estimate, one can attribute about 50,000 deaths per year in the U.S. and 4,000 deaths per year in California from ETS-associated disease. This does not include the estimates for other ETS-associated cancer deaths.

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

Effects Causally Associated with ETS Exposure

Developmental Effects
Fetal growth: Low birth weight and decrease in birth weight
Sudden Infant Death Syndrome (SIDS)
Pre-term Delivery

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 in younger, primarily premenopausal women

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

Reproductive and Developmental Effects
Spontaneous abortion, Intrauterine Growth Retardation
Adverse impact on cognition and behavior
Allergic sensitization
Decreased pulmonary function growth
Adverse effects on fertility or fecundability

Cardiovascular and Hematological Effects
Elevated risk of stroke in adults

Respiratory Effects
Exacerbation of cystic fibrosis
Chronic respiratory symptoms in adults

Carcinogenic Effects
Cervical cancer
Brain cancer and lymphomas in children
Nasopharyngeal cancer
All cancers – adult and child

Table ES.2 Attributable Risks Associated with ETS

	Conclusion OEHHA 1997	Conclusion OEHHA 1997	Conclusion Update	Conclusion Update
Outcome	**Annual Excess # in CA**	**Annual Excess # in US**	**Annual Excess # in CA**	**Annual Excess # in US**
Pregnancy: Low birth weight Pre-term delivery	1,200-2,200	9,700-18,600	1,600 [1] 4,700 [1]	24,500 [2] 71,900 [2]
Asthma (in children):				
# Episodes [3]			31,000 [4]	202,300 [5]
# New cases	960-3120	8,000-26,000	N/A	N/A
#Exacerbations	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	50,200	790,000 [6]
SIDS	120	1,900-2,700	21 [7]	430 [8]
Cardiac death (Ischemic heart disease death)	4,200-7,440	35,000-62,000	3,600 (range: 1,700-5,500) [9]	46,000 (range: 22,700-69,600) [10]
Lung cancer death	360	3000	400 [11]	3400
Breast cancer – diagnosis in younger, primarily premenopausal women			All studies: OR 1.68 (95% CI 1.31-2.15) [12] Best studies: OR 2.20 (95% CI 1.69-2.87) Approximate 68-120% increased risk	

1 Based on California Dept Health Services (CDHS, 2000a), Table 2-6, Number and percent of live births with selected medical characteristics by race/ethnic group of mother, California 2000, and Gilpin *et al.* (2001).

2 Based on CDC (2002b) National Vital Statistics Report. Vol 51(2) 2002. Births: Final data for 2001, and on adult females reporting exposure to ETS in NHANES III for 1995 (Pirkle *et al.*, 1996).

3 The data to distinguish number of new cases from number of exacerbations were not available for the updated calculations; thus, OEHHA considered that these estimates were best described as number of episodes.

4 Based on number of asthma attacks or episodes in previous 12 months for 0-17 year olds. Calculated from California Health Interview Survey for 2001.

5 Based on number of asthma attacks or episodes in previous 12 months for 0-14 year olds in Mannino *et al.* (2002b) CDC-MMWR 51(SS01)).

6 Based on Freid *et al.* (1998) 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.

7 Based on California Dept Health Services (CDHS, 2000b), Table 4-10 for yr 2000 Leading causes of infant death by race/ethnic group of child, California 2000.

8 Based on CDC (2002a) National Center for Health Statistics (2002). www.cdc.gov/nchs/fastats/infort.htm for yr 2000.

9 Based on California Dept Health Services (CDHS, 2000c), Table 5-7, Deaths, death rates, and age-adjusted death rates for leading causes by sex, California, 1999- 2000.

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

11 Assuming California exposure and death rates are similar to national rates and California population is 12% of national population.

12 OEHHA is unable at this time to calculate an attributable risk as it is not possible to account accurately for the portion attributable to other known risk factors. The OR for all studies is based on our meta-analysis of all studies with risk estimates for younger primarily premenopausal women. The OR for best studies is based on the OR for studies which evaluated younger primarily premenopausal women and which did a better job of ascertaining exposure – see Part B Section 7.4.1.3.2 and Table 7.4.1l.

N/A = data not available.

Citations for documents cited in above table appear in Part B Chapter 1 references.

What Perinatal Health Effects have been Observed?

ETS causes developmental toxicity. 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 birth weight, is small in magnitude. But if the distribution of birth weight 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 birth weight is associated with many well-recognized problems for infants, and is strongly associated with perinatal mortality. ETS is also associated with pre-term delivery. Premature babies are also at higher risk for a number of health problems.

The impact of ETS on perinatal manifestations of development other than fetal growth and pre-term delivery 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. Although epidemiological studies suggest an 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.

What Postnatal Developmental 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, and many of these studies demonstrated a dose-response gradient.

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. As discussed in greater detail below, developmental effects of ETS exposure on the respiratory system include childhood asthma induction and possibly adverse effects on lung growth and development.

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 active tobacco smoking appears to be anti-estrogenic. The epidemiological data on ETS exposure, though not conclusive, are suggestive of adverse effects on fecundability and fertility, and possibly on menstrual cycle disorders, although not many studies are available on this endpoint. 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 adolescents/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 develop IgE antibodies against 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, because active smoking has been recognized as an established cause of cancers in a number of organs including: lung, larynx, oral cavity, naso-, oro-,and hypo-pharynx, nasal cavity and sinuses, esophagus, kidney, urinary bladder and ureter, uterine cervix, pancreas, liver, bone marrow (myeloid leukemia), and stomach (IARC, 2004). Also, ETS contains a number of constituents that have been identified as carcinogens in animals and humans.

Reviews published in the 1986 *Report of the Surgeon General* (U.S. DHHS, 1986), by the National Research Council (NRC, 1986g), and by the United States Environmental Protection Agency (U.S. EPA) (1992i), as well as the original OEHHA report (Cal/EPA, 1997) concluded that ETS exposure causes lung cancer. Since the previous OEHHA review (Cal/EPA, 1997), numerous epidemiological studies and several meta-analyses have examined the association between passive smoking and lung cancer. 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 non-smoking adults. Finally, studies suggest an association between ETS exposure and elevated risks of nasopharyngeal cancers.

Many population-based case-control studies (as well as three cohort studies), controlling for several important reproductive, dietary and other potential confounding factors, have identified elevated breast cancer risks for residential and occupational exposure overall or in individual strata. Higher risks were noted in several studies for breast cancer diagnosed in women under age fifty (primarily premenopausal), or with long duration or high intensity exposure. The toxicological data on carcinogenicity of tobacco smoke constituents strongly support that the risk associated with ETS exposure is highly plausible. Overall, the weight of evidence (including toxicology of ETS constituents, epidemiological studies, and breast biology) is consistent with a causal association between ETS exposure and breast cancer in younger, primarily premenopausal women. In contrast to the findings in younger women, in studies which reported statistics for women diagnosed with breast cancer after menopause, risk estimates cluster around a null association (see Figure 7.4.4). There are, however, elevated risk estimates in some studies for postmenopausal women either overall or in specific strata. The evidence to date for older/postmenopausal women is, therefore, considered inconclusive. Further research indicating a positive association would be necessary prior to altering this finding.

The epidemiological and biochemical evidence suggest that exposure to ETS may increase the risk of cervical cancer. Positive associations were observed in three of four case-control studies and a statistically nonsignificant positive association was observed in the only cohort study conducted. A new population-based cross-sectional

study found statistically significant elevated risks for cervical cancer. Findings of DNA adducts in the cervical epithelium as well as nicotine and cotinine in the cervical mucus of ETS-exposed nonsmokers supports biological plausibility.

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. Overall, the generally positive, but inconsistent, associations reported between paternal smoking and childhood brain tumors, in combination with biological plausibility, 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). These observed associations may reflect an effect of pre-conceptional paternal smoking on sperm, rather than an effect of ETS exposure.

For other cancer sites in adults, there has been limited ETS-related epidemiological research in general. The evidence to date 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, is inconclusive. 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 case-control studies and one cohort study conducted to date, although both studies were limited in their ability to detect an effect.

The epidemiological data are insufficient to assess potential associations between ETS exposure and rare childhood cancers. 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 coronary heart disease (CHD) mortality 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 confounders. 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.