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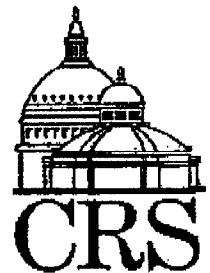
CRS Report for Congress

Environmental Tobacco Smoke and Lung Cancer Risk

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ENVIRONMENTAL TOBACCO SMOKE

This section of the report briefly describes the chemical and physical characteristics of mainstream and sidestream smoke (the two major components of ETS) and discusses studies which have measured indoor ETS levels, and estimated ETS exposure and uptake among nonsmokers. Researchers have concluded that ETS contains most, if not all, of the carcinogenic and toxic compounds that are present in mainstream smoke. The studies also indicate that there is widespread exposure to ETS, and some measurable uptake of ETS by nonsmokers.

MAINSTREAM AND SIDESTREAM SMOKE¹²

Environmental tobacco smoke is a combination of mainstream smoke (MS) exhaled by smokers and sidestream smoke (SS) released directly from the burning tip of cigarettes. It is typically highly diluted. Mainstream smoke is comprised of small particles averaging 0.35-0.4 μm in diameter¹³ (particle phase) and a mixture of gases (vapor phase). The particle phase includes several metals (e.g., cadmium and zinc) and a variety of non-volatile organic compounds of high molecular weight. The vapor phase includes numerous highly volatile compounds such as carbon monoxide and hydrogen cyanide.

Nicotine and many other semi-volatile constituents of tobacco smoke occur both in the particle phase and the vapor phase depending on their volatility and the prevailing conditions. These compounds tend to be present in the particle phase of highly concentrated inhaled MS, but evaporate into the vapor phase as exhaled MS rapidly dilutes during the formation of ETS.

Sidestream smoke is the primary contributor to ETS, providing most of the vapor phase and over half of the particles. It is produced by the same fundamental processes as MS and consists of the same chemical compounds including many known or suspected human carcinogens. However, SS is generated at lower temperatures and at a higher pH than MS, and as a result it has a different relative chemical composition.

Table 1 lists the concentrations of various compounds in both phases of MS delivered by unfiltered cigarettes, as measured by a standard smoking machine. The table also compares the amount of each compound delivered in MS and in SS by computing a SS/MS ratio.¹⁴ These ratios indicate that, with the

¹² For a more comprehensive discussion of the physical and chemical characteristics of mainstream and sidestream smoke, see M.R. Guerin et al. *The Chemistry of Environmental Tobacco Smoke: Composition and Measurement*, 1992, Lewis Publishers, Inc., Chelsea, Michigan.

¹³ One micron (μm) = 1/1000 millimeter (mm).

¹⁴ There is no standard method for collecting and analyzing SS, unlike MS. Researchers have used a variety of small chambers in which to confine the burning cigarette and collect the SS. These devices produce a somewhat artificial smoking environment compared to that associated with human smoking, and, of course, do not take into account the dilution that occurs during the

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exception of hydrogen cyanide and organic acids, the majority of compounds are

TABLE 1. Comparison of Mainstream and Sidestream Smoke Deliveries for Selected Compounds		
Constituent	Mainstream per Cigarette ^a	SS/MS Ratio
Mainstream vapor phase		
Carbon monoxide	10-23 mg	2.5-4.7
Carbon dioxide	20-40 mg	8-11
Benzene ^b	12-48 g	5-10
Acetone	100-250 g	2-5
Hydrogen cyanide	400-500 g	0.1-0.25
Ammonia	50-130 g	40-170
Pyridine	16-40 g	6.5-20
Nitrogen oxides	100-600 g	4-10
N-Nitrosodimethylamine ^c	10-40 ng	20-100
Mainstream particle phase		
Nicotine	1-2.5 mg	2.6-3.3
Phenol	60-140 g	1.6-3.0
2-Naphthylamine ^b	1.7 ng	30
4-Aminobiphenyl ^b	4.6 ng	31
Cadmium ^c	100 ng	7.2
Nickel ^b	20-80 ng	13-30
Lactic acid	63-174 g	0.5-0.7
Succinic acid	110-140 g	0.43-0.62

^a The units are in milligrams (1 mg = 1/1000 g), micrograms (1 g = 1/1000 mg), and nanograms (1 ng = 1/1000 g).

^b Known human carcinogen, according to EPA or IARC.

^c Probable human carcinogen, according to EPA or IARC.

Source: National Research Council, 1986. Table 2-2.

released in greater quantities in SS than in MS. In its analysis of MS and SS emissions data, EPA found that all of the five known human carcinogens, nine probable human carcinogens, and three animal carcinogens are emitted at higher levels in SS than in MS, often by a factor of ten or more.

formation of ETS.

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ETS COMPOSITION AND MEASUREMENT¹⁵

There is limited information on the chemical composition of ETS. Exhaled MS, which can contribute between 15 percent and 43 percent of the particulate matter in ETS, has yet to be characterized. There is also little data on the impact of dilution on SS emissions. During ETS formation, both SS and exhaled MS are diluted by many orders of magnitude and subsequently undergo physical transformation and alterations in chemical composition.

Numerous studies of the impact of smoking occupancy on indoor air quality have measured several ETS-related compounds of human health concern, including known and suspected carcinogens, in a variety of settings (e.g., residential, office, transportation, etc.). Researchers have concluded (1) that many of the potentially harmful compounds in SS are also present in ETS, and (2) that these ETS contaminants are found above background levels in a wide range of indoor environments in which smoking occurs. These studies indicate that the composition of ETS can be highly variable depending on the smoking rates, the amount and type of ventilation, contact with indoor surfaces, and a host of other environmental conditions.

Given that ETS is a complex mixture of thousands of compounds, many of which change chemically and physically over time, it is necessary to identify a chemical marker to represent the frequency, duration, and magnitude of ETS exposure. An ideal marker would be a compound that is specific to tobacco smoke, easy to measure, and that behaves similarly to ETS as a whole. Several markers have been identified, though none meets all these criteria. However, vapor phase nicotine and respirable suspended particles (RSP)¹⁶ are both suitable indicators of exposure to ETS.

A variety of methods have been used to measure indoor nicotine and RSP levels in order to assess ETS exposure. Air sampling devices may be placed at specific indoor locations for varying periods of time (stationary sampling) or worn by individuals (personal monitoring). Researchers have also measured chemicals (biomarkers) in the blood and urine of ETS-exposed nonsmokers.

Tobacco combustion produces significant emissions of respirable suspended particles (RSP). There are a number of accepted methods that permit accurate measurement of RSP concentrations in indoor environments for sampling times ranging from seconds to several days. Studies have shown that RSP levels in smoking environments are usually higher than in non-smoking environments. Leaderer and Hammond conducted a large chamber study using smokers and

¹⁵ For more information on the chemistry of ETS and on chemical markers for ETS, see EPA Report, chapter 3, and Guerin et al., 1992.

¹⁶ Respirable suspended particles (RSP) refers to particles that are small enough to reach the deepest recesses of the lungs during inhalation. There is some disagreement among researchers as to the upper size limit for RSP. Some investigators use a conservative value of 3 μ m, others use values of 10 or 15 μ m. However, if one is using RSP as a marker for ETS, choosing among these values is largely irrelevant, because most ETS particles are less than 1 μ m.

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reported an average RSP emission rate per cigarette of 17.1 mg.¹⁷ RSP emission rates among different brands of cigarettes were similar.

Respirable suspended particles are also generated by other types of combustion. At low smoking and high ventilation rates, it might be difficult to distinguish ETS-associated RSP from a background of RSP from other indoor sources (e.g., kerosene heaters) or even outdoor sources. However, studies by Repace indicate that the fraction of indoor RSP attributable to smoking is typically 80 to 90 percent of the total RSP.¹⁸

Vapor phase nicotine is the most common ETS marker. Nicotine is unique to tobacco and can be reliably measured using a variety of methods. Average indoor air concentrations typically range from 1 to 10 micrograms per cubic meter ($\mu\text{g}/\text{m}^3$). Several studies have shown that weekly nicotine concentrations are highly correlated with the number of cigarettes smoked. One of these studies also reported a strong correlation between weekly nicotine concentrations and RSP levels in smoking households.¹⁹ The RSP-to-nicotine ratio in this study was approximately 10:1, which is similar to the ratio seen in chamber studies and other field studies, including a recent California State report.²⁰

Nicotine is not an ideal ETS marker because it is readily adsorbed onto surfaces, thus reducing its concentration relative to other ETS components as ETS ages. Some studies have demonstrated that vapor phase nicotine is depleted from a smoking environment more rapidly than the particulate portion of ETS. This could lead to an underestimation of ETS exposures. Nicotine also evaporates from surfaces onto which it has been adsorbed, which results in measurable concentrations even in the absence of active smoking. The affinity of nicotine for surfaces may limit its use as an ETS marker in environments where ETS concentrations are very low. However, under normally encountered smoking rates, the uncertainties associated with nicotine's high adsorption rate are likely to be small.

ETS INDOOR AIR CONCENTRATIONS AND EXPOSURE

Numerous studies have measured concentrations of nicotine and RSP in a variety of indoor environments. These studies employed a range of sampling devices, sampled over varying timeframes (from minutes to days), and included highly variable information on various factors affecting the measured

¹⁷ Leaderer, B.P. and S.K. Hammond. *Environ. Sci. Technol.*, Vol. 25, 1991, p. 770-771.

¹⁸ See, for example: Repace, J.L. Tobacco Smoke Pollution. In *Nicotine Addiction, Principles and Management*. Orleans, T. and A.H. Lowrey, eds. Oxford University Press, New York, 1993.

¹⁹ Leaderer, B.P. and S.K. Hammond, 1991.

²⁰ The California Air Resources Board report, *Toxic Volatile Organic Compounds in ETS: Emissions Factors for Modeling Exposures of Californian Populations*, was prepared by the Lawrence Berkeley Laboratory and concluded that nicotine and ETS-RSP behave similarly.

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concentrations, such as number of cigarettes smoked and ventilation rates. EPA summarized much of this information in its report, to which the reader is referred for more detailed information.²¹

Stationary Air Samplers

Most of the studies used stationary air samplers. Although the results were highly variable, nicotine and RSP concentrations in smoking environments were consistently higher than in non-smoking environments. Table 2 shows the range of average values obtained in these studies. The minimum and maximum values are also presented in parentheses. Only studies reporting sampling times over four hours were included in the data on residential and office settings so as to more closely approximate occupancy time. Since occupancy time in restaurants is likely to be shorter than four hours, data from studies using shorter sampling times were included in the table.

TABLE 2. Indoor Nicotine and RSP Concentrations with Smoking Occupancy: Range of Average Values Reported (Min - Max Values)		
Location	Nicotine ($\mu\text{g}/\text{m}^3$)	RSP ($\mu\text{g}/\text{m}^3$)*
Residential	2-11 (<1-14)	18-95 (5-560)
Office	1-13 (<1-35)	<5-62 (<5-90)
Restaurant	6-18 (<1-70)	35-986 (10-1370)

* RSP levels associated with smoking occupancy were calculated by subtracting background RSP levels associated with non-smoking occupancy.

Source: Figures 3-7 and 3-8, EPA, 1992.

The summary nicotine data in the table indicate that average concentrations in residences with smoking occupancy range from 2 $\mu\text{g}/\text{m}^3$ to 11 $\mu\text{g}/\text{m}^3$, with high values up to 14 $\mu\text{g}/\text{m}^3$ and low values down below 1 $\mu\text{g}/\text{m}^3$. Offices with smoking occupancy have average nicotine concentrations that are similar to those in residences, but with significantly higher maximum values. The data from restaurants show even higher maximum values. With regard to RSP concentrations, there is also broad overlap in the average values obtained from residential and office environments. However, the data from restaurants show a much wider range of values.

In a recently published study, Hammond and coworkers measured average weekly nicotine concentrations at 25 diverse worksites including fire stations, newspaper publishers, textile dyeing plants, and a variety of manufacturing

²¹ EPA Report, chapter 3.

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companies.²² Between 15 and 25 samplers were placed in each worksite. Worksite smoking policy had a significant effect on the nicotine concentration. The median²³ nicotine level in open-plan offices that allowed smoking was $8.6 \mu\text{g}/\text{m}^3$, but only $1.3 \mu\text{g}/\text{m}^3$ in worksites that restricted smoking to designated areas. In worksites that banned smoking, the median nicotine level was $0.3 \mu\text{g}/\text{m}^3$.

Guerin and Jenkins measured the concentrations of ETS constituents, including nicotine and RSP, in "typically encountered" residential and occupational indoor settings and found that low-level concentrations were much more common than higher-level concentrations.²⁴ These results reflect the fact that the researchers included a significant number of non-smoking and smoking-restricted sites. Very high concentrations were generally found in enclosed areas designated for smoking, and in poorly ventilated areas where smoking intensity was high.

Personal Monitors

Measurement of indoor air concentrations of ETS components indicates the potential for exposure, but actual exposure also depends on the amount of time spent in a particular environment. The amount of exposure will depend on the individual's circumstances. A woman who lives with a nonsmoker but works in an office with smokers will receive most of her ETS exposure at work, whereas someone who lives and works with smokers may receive the majority of her exposure in the home where more time is spent.

Personal monitoring allows researchers to estimate individual exposure. Study participants wear a monitor that continuously samples and records the concentration of air contaminants to which individuals are exposed in the course of their daily activities. If subjects use different monitors in different indoor environments (e.g. home vs. workplace) and record the amount of time spent in each setting, then researchers can calculate the contribution of each environment to total exposure.

To date, few studies have measured ETS exposure to nicotine and RSP using personal monitors. Limited published data on nicotine show a wide range of ETS exposures in indoor environments with smoking occupancy, with average concentrations ranging from less than $5 \mu\text{g}/\text{m}^3$ up to $40 \mu\text{g}/\text{m}^3$. Other personal

²² Hammond, S.K. et al. *J. American Medical Association*, v. 274, no. 12, 1995, p. 956-960.

²³ The median value is the mid-point of a range of measurements. Half of the values are less than the median, half are greater than the median.

²⁴ For more information, see Guerin et al., 1992; Guerin, M.R. and R.A. Jenkins. *Recent Advances in Tobacco Science*, Vol. 18, 1992, p.95-114; and Guerin, M.R. Environmental Tobacco Smoke Exposure Assessment. Paper presented at Japan Indoor Air Research Society, April 1993. Sponsored by U.S. Dept. of Energy. NTIS/DE93015521.

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monitor studies found that ETS exposure increased RSP levels between 18 $\mu\text{g}/\text{m}^3$ and 64 $\mu\text{g}/\text{m}^3$.²⁵

It is difficult to assess the ETS contribution to nicotine and RSP levels for each indoor environment using these data. In many cases, study participants wore the same monitor for 24 hours, and the reported nicotine and RSP levels represent 24-hour average values. These values may underestimate the contribution of some non-residential indoor environments as they include home sleeping hours when presumably there was little if any ETS exposure.

Unpublished data from a recent multi-city study using personal monitors suggest that typical exposures are low relative to estimates obtained using stationary air samplers. This large study, conducted jointly by Oak Ridge National Laboratory and R.J. Reynolds Tobacco Company, recruited approximately 100 nonsmokers in each of 16 cities nationwide. Study participants were provided with two monitors — one to wear at work and the other for the remainder of the 24-hour period — and required to keep a detailed written record of their activities. In addition to nicotine and RSP, the monitors measured five other ETS constituents.

The average nicotine concentration in 415 smoker-occupied homes was 2.16 $\mu\text{g}/\text{m}^3$, with a median level of 0.68 $\mu\text{g}/\text{m}^3$, indicating that most participants received relatively little ETS exposure. The average and median nicotine levels in workplaces without smoking restrictions were 2.77 $\mu\text{g}/\text{m}^3$ and 0.58 $\mu\text{g}/\text{m}^3$, respectively. Researchers calculated total daily exposure to nicotine in each indoor environment by multiplying the average nicotine concentration by duration of exposure and breathing rate. Total daily nicotine exposure in smoker-occupied homes was 6.8 μg per day ($\mu\text{g}/\text{day}$), compared to a value of 5.8 $\mu\text{g}/\text{day}$ for workplaces without smoking restrictions.

The study's authors suggested two explanations for the fact that average nicotine concentrations recorded in this study lie at the bottom end of the ranges reported in earlier studies. First, fewer smokers are lighting up in the presence of nonsmokers, a response to changing societal attitudes toward smoking. Second, nonsmokers are spending less time in obviously smoky environments. Nonsmokers who come in contact with smokers may receive relatively little exposure depending on their proximity to the smoker and the length of time spent in that indoor environment.

Noting the tobacco industry's involvement in the study, critics claim that it underrepresented the amount of ETS exposure among nonsmokers. The study sampled a disproportionately low number of smoker-occupied workplaces. Out of 1,356 workplaces sampled, only 168 (12.4 percent) allowed smoking without restriction. National estimates of workplace smoking prevalence suggest that a significantly higher percentage of workplaces allow smoking (see later section on occupational ETS exposure). However, it is not possible to determine whether the recruitment procedures used in the study led to the

²⁵ EPA Report, tables 3-5 and 3-6.

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selection of participants whose ETS exposure in smoker-occupied indoor environments was significantly below average exposure levels for nonsmokers nationwide.

Biomarkers

The presence of a biomarker in the blood or urine provides direct evidence of ETS exposure and uptake. The relationship between the biomarker and exposure is complex due to many environmental and physiological factors. The most commonly used and widely accepted ETS biomarker is cotinine, the major metabolite of nicotine inside the body. Nicotine has a half-life of about 2 hours in the blood and is metabolized to cotinine and excreted in the urine. Cotinine has a half-life of approximately 20 hours in smokers, somewhat longer in ETS-exposed nonsmokers, which makes it a good indicator of ETS exposure and uptake over the previous two days.

Studies show that blood and urine cotinine levels in ETS-exposed nonsmokers are generally higher than those in nonsmokers reporting no ETS exposure, but far lower than the levels of cotinine in smokers. Comparisons of cotinine levels in smokers and nonsmokers indicate that ETS-exposed nonsmokers receive approximately 0.7 percent of the nicotine dose of an average smoker.²⁶ Cotinine levels in nonsmokers have also been found to increase with self-reported ETS exposure. There is considerable variation in cotinine levels among smokers and ETS-exposed nonsmokers because of individual differences in the uptake, metabolism, and elimination of nicotine.

ETS CANCER RISK

The EPA classified ETS as a carcinogen based on the chemical similarities between inhaled MS and ETS, and evidence of ETS exposure and uptake by nonsmokers. Studies indicate that tobacco smoke is a lung carcinogen even at the smallest exposures to active smoking, and the risk increases with exposure, as measured either by number of cigarettes smoked per day, or years of cigarette smoking. According to the EPA, exposure to ETS, which is qualitatively similar to MS, therefore, should also increase the risk of lung cancer, and the evidence of widespread exposure to, and uptake of, ETS components in the general population is sufficient to conclude that ETS is a lung-cancer hazard.²⁷

A few researchers have challenged the classification of ETS as a known human carcinogen based on its relationship to MS. They point to the fact that MS contains chemicals at concentrations of up to one million times those found in ETS, and that more of the chemicals are in the particle (tar) phase of MS. Differences between passive smoking (normal inhalation) and active smoking

²⁶ Jarvis, M.J. *Mutation Research*, Vol. 222, 1989, p. 101-110.

²⁷ See, for example, testimony presented by Dr. Douglas Dockery, Harvard School of Public Health, on July 21, 1993, before the House Committee on Agriculture, Subcommittee on Specialty Crops and Natural Resources.

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(deep inhalation) also affect the degree of exposure to vapor phase constituents and the deposition of particles inside respiratory passageways. Based on these considerations, an ETS chemist concluded that the evidence for ETS carcinogenicity remains questionable.²⁸

Asserting that ETS is a lung carcinogen leaves unanswered the question: How great a cancer risk does passive smoking pose? Researchers have used nicotine measurements to calculate ETS exposure in terms of cigarette equivalents, by estimating the number of cigarettes one would have to smoke to receive the same amount of nicotine as breathing ETS in a particular environment for a given period of time.²⁹ For example, the amount of nicotine inhaled by a nonsmoker working in a relatively smoky restaurant for eight hours is equivalent to smoking one-eighth of a cigarette.³⁰

Cigarette equivalents calculated for some of the known carcinogens in ETS yield much higher values because these compounds are emitted at higher levels in SS than in MS (see Table 1). About three times as much nicotine is emitted in SS as in MS, whereas approximately 30 times as much 4-aminobiphenyl (4-ABP). Thus, a description of exposure in nicotine cigarette equivalents underestimates exposure to a known carcinogens in tobacco smoke by a considerable margin.³¹

The cigarette equivalent approach can also be applied to cotinine data. If, as stated above, cotinine levels in ETS-exposed nonsmokers average 0.7 percent of the levels found in smokers, and if one assumes that the average smoker smokes 19 cigarettes a day,³² then the amount of nicotine to which the average ETS-exposed nonsmoker is exposed is roughly equivalent to smoking one-eighth of a cigarette a day.

There are significant uncertainties in using cigarette equivalents to try to quantify ETS cancer risk. Estimates of ETS exposure using cigarette equivalents vary enormously depending on the compound chosen. Researchers

²⁸ Testimony presented by Dr. Michael Guerin, Oak Ridge National Laboratory, at the July 21 ETS hearing.

²⁹ The formula for cigarette equivalents = amount from ETS exposure/amount from smoking one cigarette.

³⁰ Assumes an average nicotine concentration of 18 $\mu\text{g}/\text{m}^3$. Exposures longer than 8 hours would lead to proportionately higher cigarette equivalents, as would higher breathing rates resulting from physical exertion at work. Based on calculations presented in Hammond et al., 1996.

³¹ Recent newspaper advertisements by R.J. Reynolds Tobacco Company stated that nonsmokers are exposed to only slightly more than one "cigarette equivalent" a month in the workplace. However, this statement is misleading as it refers to nicotine cigarette equivalents and therefore underestimates exposure to many other toxic and carcinogenic compounds in ETS.

³² U.S. Centers for Disease Control. *Morbidity and Mortality Weekly Report*, Vol. 41, 1992. p. 354.

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do not know how the levels of these individual compounds relate to overall ETS exposure, or exposure to those ETS constituents that may be linked to lung cancer. Indeed, they do not know which ETS constituents are responsible for lung cancer and other health effects attributed to ETS exposure. Although 4-ABP is a bladder carcinogen, it does not appear to be associated with lung cancer. Finally, the contrasting breathing patterns of active and passive smokers may strongly influence the degree of exposure and uptake of various tobacco smoke constituents in the lungs of smokers and nonsmokers.

In order to estimate ETS lung cancer risk using cigarette equivalents researchers assume that there is a linear relationship between exposure (number of cigarettes smoked a day) and cancer risk that extends from the relatively intense exposures typical of active smoking down to the much lower exposures associated with passive smoking. EPA uses this type of straight-line extrapolation from high exposures down to zero exposure in all its cancer-risk assessments but researchers do not know the actual shape of the exposure-risk relationship for passive smoking and lung cancer.