3. ESTIMATION OF ENVIRONMENTAL TOBACCO SMOKE EXPOSURE

3.1. INTRODUCTION

Environmental tobacco smoke (ETS) is composed of exhaled mainstream smoke (MS) from the smoker, sidestream smoke (SS) emitted from the smoldering tobacco between puffs, contaminants emitted into the air during the puff, and contaminants that diffuse through the cigarette paper and mouth end between puffs (NRC, 1986; U.S. DHHS, 1986; Guerin et al., 1992). These emissions contain both vapor phase and particulate contaminants. SS is the major component of ETS, contributing nearly all of the vapor phase constituents and over half of the particulate matter.

Overall, ETS is a complex mix of over 4,000 compounds. This mix contains many known or suspected human carcinogens and toxic agents. The information necessary to evaluate human exposures to each of the compounds of human health interest in ETS does not exist.

Recognizing that it is impractical to characterize the many individual compounds that make up ETS and to then assess exposures to those compounds, this chapter focuses on the characterization of the complex ETS contaminant mix and exposure to it by nonsmokers. Available data on the physical and chemical properties of sidestream and mainstream smoke are compared to assess the potential for the release of known or suspected human carcinogens and toxic agents into indoor environments where human exposures occur. The available published data are reviewed to determine whether ETS constituents exist in elevated levels in various indoor environments where smoking occurs and whether human exposures ensue. Particular attention is focused upon environmental and biological marker compounds that serve as proxies for the complex ETS mix and the compounds of human health interest.

The available biomarker data for ETS clearly show that levels of ETS contaminants encountered indoors by nonsmokers are of sufficient magnitude to be absorbed and to result in measurable doses. Chapters 6 and 8 and Appendix B use such biomarker data for estimating relative residential and nonresidential ETS exposures in calculating the associated risks for lung cancer and various noncancer respiratory effects.

Epidemiologic studies relating exposure to ETS with lung cancer (Chapter 5) and respiratory disorders other than cancer (Chapter 7) frequently rely on questionnaires to assess level of exposure. This chapter reviews the limited number of studies that have attempted to validate questionnaires with objective measures of exposure. All of these are population surveys and not epidemiologic disease studies. The few studies that compare body cotinine levels with childhood respiratory disease occurrences are discussed in Chapters 7 and 8.

This chapter concludes that (1) MS, SS, and ETS are chemically similar and contain a number of known or suspected human carcinogens and toxic compounds; (2) marker compounds for ETS are measurable in a variety of indoor environments; (3) exposure to ETS is extensive; and (4) there is a measurable uptake of ETS by nonsmokers.

3.2. PHYSICAL AND CHEMICAL PROPERTIES

Over the past several years, there have been a number of reviews of the physical and chemical properties of mainstream and sidestream cigarette smoke (NRC, 1986; U.S. DHHS, 1986; Guerin et al., 1992). A particularly detailed review is contained in the recent book by Guerin et al. (1992). This section summarizes the findings of these reviews to identify the similarities and differences in mainstream and sidestream emissions and to establish that known and suspected human carcinogens and toxic agents are released into occupied spaces from tobacco combustion. Data contained in these reviews, as well as recently published material, are also presented to document that sidestream emissions of notable air contaminants result in measurable increases of these contaminants in indoor locations where individuals spend time.

The physical and chemical characterization of MS air contaminant emissions from cigarettes, cigars, or pipes is derived from laboratory-based studies that have typically utilized standardized testing protocols (FTC, 1990; Guerin et al., 1992). The data available are primarily for tobacco combustion in cigarettes and provide a substantial database on the nature of MS. These protocols employ smoking machines, set puff volumes and frequencies, and standardized air contaminant collection protocols (small chambers, Cambridge filters, chamber air flow rates, etc.). Existing standardized protocols reflect conditions representative of human smoking practices of over 30 years ago for nonfiltered cigarettes and may not reflect current human smoking parameters for today's filtered low-tar cigarettes (NRC, 1986; U.S. DHHS, 1986; Guerin et al., 1992). It has been suggested that current standardized protocols, particularly for filter cigarettes, may underestimate MS deliveries (Guerin et al., 1992). MS air contaminant emission rates determined in these studies using standardized protocols can be affected by a number of factors, such as puff volume, air dilution rate, paper porosity, filter ventilation air flow around the cigarette, and moisture content of the tobacco. Actual smoking habits of individuals can also dramatically alter the MS deliveries. Variability in any of the factors can affect the nature and quantity of the MS emissions.

Standardized testing protocols for assessing the physical and chemical nature of SS emissions from cigarette smoke do not exist, and data on SS are not as extensive as those for MS emissions. Protocols used for the generation and collection of SS emissions typically use standardized MS protocols (smoking machines, puff volumes, etc.) with modifications in the test devices (use of small chambers) that allow for the simultaneous collection of SS emissions for analysis (Dube and Green, 1982; McRae, 1990; Rickert et al., 1984).

The protocols for the collection of SS emissions are such that results can be directly compared to MS emissions and thus provide valuable insights into the physical and chemical nature of ETS. It should be noted, however, that the SS emissions collected under these protocols may be somewhat different from ETS emissions. ETS also contains exhaled MS, which has not yet been characterized. Exhaled MS can contribute from 15% to 43% of the particulate matter in ETS, though little of the gas phase contaminants (Baker and Proctor, 1990). In addition, SS samples are not collected under conditions where the emissions are diluted and "aged," as is ETS. The aging and dilution of the SS emissions can produce changes in phase distribution of the contaminants.

Results of laboratory evaluations have indicated substantial similarities and some differences between MS and SS emissions from cigarettes (NRC, 1986; U.S. DHHS, 1986; Guerin et al., 1992). Differences in SS and MS

emissions are due to differences in the temperature of combustion of the tobacco, Ph, and degree of dilution with air, which is accompanied by a corresponding rapid decrease in temperature. SS is generated at a lower temperature (approximately 600°C between puffs vs. 800-900°C for MS during puffs) and at a higher Ph (6.7-7.5 vs. 6.0-6.7) than MS. Being slightly more alkaline, SS contains more ammonia, is depleted of acids, contains greater quantities of organic bases, and contains less hydrogen cyanide than MS. Differences in MS and SS are also ascribable to differences in the oxygen concentration (16% in MS vs. 2% in SS). SS contaminants are generated in a more reducing environment than those in MS, which will affect the distribution of some compounds--nitrosamines, for example, are present in greater concentrations in SS than in MS.

SS is rapidly diluted in air, which results in a SS particle size distribution smaller than that for MS and in the potential for changes in phase distribution for several constituents. Nicotine, for example, while predominantly in the particle phase in MS, is found predominantly in the gas phase in ETS (Eudy et al., 1985). The shift to gas phase is due to the rapid dilution in SS. SS particle size is typically in the range of 0.01-1.0 μm, while MS particle size is 0.1-1.0 μm. The SS size distribution shifts to small sizes with increasing dilution (NRC, 1986; U.S. DHHS, 1986; Guerin et al., 1992; Ingebrethsen and Sears, 1985). The differences in size distribution for MS and SS particles, as well as the different breathing patterns of smokers and nonsmokers, have implications for deposition of the produced particle contaminants in various regions of the respiratory tract. Estimates of from 47% to more than 90% deposition for MS and of 10% deposition for SS have been reported (U.S. DHHS, 1986).

Despite quantitative differences and potential differences in phase distributions, the air contaminants emitted in MS and SS are qualitatively very similar in their chemical composition because they are produced by the same process. Over 4,000 compounds have been identified in laboratory-based studies of MS (Dube and Green, 1982; Roberts, 1988). In a 1986 IARC monograph evaluating the carcinogenic risk of tobacco smoke to humans (IARC, 1986), 42 individual MS components were identified as carcinogenic in bioassays with laboratory animals, with many of these either known or suspected human carcinogens. Many additional compounds in MS have been identified as toxic compounds. Although SS emissions have not been chemically characterized as completely as MS emissions, many of the compounds found in MS emissions, including a host of carcinogenic agents, are found in SS emissions (NRC, 1986; U.S. DHHS, 1986; Guerin et al., 1992; Dube and Green, 1982; Roberts, 1988) and at emission rates considerably higher than for MS.

Part of the data available from studies of MS and SS emissions is shown in Table 3-1 (extracted from NRC, 1986). These data are for nonfilter cigarettes and represent a summary of data from several sources. It is immediately obvious from Table 3-1 that SS and MS contain many of the same notable air contaminants, including several known or suspected human toxic and carcinogenic agents, and that SS emissions are often considerably higher than MS emissions. For the compounds shown in Table 3-1, 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, several by an order of magnitude or more. For example, *N*-nitrosodimethylamine, a potent animal carcinogen, is emitted in quantities 20 to 100 times higher in SS than in MS. Table 3-1 similarly shows that several toxic compounds found in MS are also

found in SS (carbon monoxide, ammonia, nitrogen oxides, nicotine, acrolein, acetone, etc.). Again, for many of these compounds, SS emissions are higher than MS emissions--in some cases by an order of magnitude or higher.

The SS/MS emission ratios shown in Table 3-1 can be highly variable and potentially misleading because, as noted earlier, a number of factors can have a substantial impact on MS emissions. A filtered cigarette, for example, can substantially reduce MS of total mass well below that shown in Table 3-1, thus resulting in a much higher SS/MS ratio. A number of recent studies (Adams et al., 1987; Guerin, 1987; Higgins et al., 1987; Chortyk and Schlotzhauer, 1989; Browne et al., 1980; Guerin et al., 1992) indicate that, quantitatively, SS emissions show little variability as a function of a number of variables (puff volume, filter vs. nonfilter cigarette, and filter ventilation). The lack of substantial variability in SS emissions is related to the fact that sidestream emissions are primarily related to the weight of tobacco and paper consumed during

Table 3-1. Distribution of constituents in fresh, undiluted mainstream smoke and diluted sidestream smoke from nonfilter cigarettes[1]

Constituent	Amount in MS	Range in SS/MS
Vapor phase:[2]		
Carbon monoxide	10-23 mg	2.5-4.7
Carbon dioxide	20-40 mg	8-11
Carbonyl sulfide	12-42 µg	0.03-0.13
Benzene[3]	12-48 µg	5-10
Toluene	100-200 µg	5.6-8.3
Formaldehyde[4]	70-100 µg	0.1-~50
Acrolein	60-100 µg	8-15
Acetone	100-250 µg	2-5
Pyridine	16-40 µg	6.5-20
3-Methylpyridine	12-36 µg	3-13
3-Vinylpyridine	11-30 µg	20-40
Hydrogen cyanide	400-500 µg	0.1-0.25
Hydrazine[4]	32 ng	3
Ammonia	50-130 µg	3.7-5.1
Methylamine	11.5-28.7 µg	4.2-6.4
Dimethylamine	7.8-10 µg	3.7-5.1
Nitrogen oxides	100-600 µg	4-10
N-Nitrosodimethylamine[4]	10-40 ng	20-100
N-Nitrosodiethylamine[4]	ND-25 ng	<40
N-Nitrosopyrrolidine[4]	6-30 ng	6-30
Formic acid	210-490 µg	1.4-1.6
Acetic acid	330-810 µg	1.9-3.6
MethCyl chloride	150-600 µg	1.7-3.3
1,3-Butadiene[4,6]	69.2 µg	3-6

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Table 3-1. (continued)

Constituent	Amount in MS	Range in SS/MS
Particulate phase:[2]		
Particulate matter[7]	15-40 mg	1.3-1.9
Nicotine	1-2.5 mg	2.6-3.3
Anatabine	2-20 µg	<0.1-0.5
Phenol	60-140 µg	1.6-3.0
Catechol	100-360 µg	0.6-0.9
Hydroquinone	110-300 µg	0.7-0.9
Aniline[4]	360 ng	30
2-Toluidine	160 ng	19
2-Naphthylamine[3]	1.7 ng	30
4-Aminobiphenyl[3]	4.6 ng	31
Benz[a]anthracene[5]	20-70 ng	2-4
Benzo[a]pyrene[4]	20-40 ng	2.5-3.5
Cholesterol	22 µg	0.9
γ-Butyrolactone[5]	10-22 µg	3.6-5.0
Quinoline	0.5-2 µg	3-11
Harman[8]	1.7-3.1 µg	0.7-1.7
N-Nitrosonornicotine[5]	200-3,000 ng	0.5-3
NNK[9]	100-1,000 ng	1-4
N-Nitrosodiethanolamine[4]	20-70 ng	1.2
Cadmium[4]	110 ng	7.2
Nickel[3]	20-80 ng	13-30
Zinc	60 ng	6.7
Polonium-210[3]	0.04-0.1 pCi	1.0-4.0
Benzoic acid	14-28 µg	0.67-0.95
Lactic acid	63-174 µg	0.5-0.7
Glycolic acid	37-126 µg	0.6-0.95
Succinic acid	110-140 µg	0.43-0.62
PCDDs and PCDFs[10]	1 pg	2

(continued on the following page)

Table 3-1. (continued)

[1]Data in this table come from the NRC report (1986), except where noted, which compiled data from Elliot and Rowe, 1975; Schmeltz et al., 1979; Hoffman et al., 1983; Klus and Kuhn, 1982; Sakuma et al., 1983, 1984a, 1984b; and Hiller et al., 1982. Full references are given in NRC, 1986. Diluted SS is collected with airflow of 25 mL/s, which is passed over the burning cone; as presented in the NRC report on passive smoking (1986).
[2]Separation into vapor and particulate phases reflects conditions prevailing in MS and does not necessarily imply same separation in SS.
[3]Known human carcinogen, according to U.S. EPA or IARC.
[4]Probable human carcinogen, according to U.S. EPA or IARC.
[5]Animal carcinogen (Vainio et al., 1985).
[6]Data from Brunnemann et al., 1990.
PCDDs = polychlorinated dibenzo-p-dioxins;
PCDFs = polychlorinated dibenzofurans.
[7]Contains di- and polycyclic aromatic hydrocarbons, some of which are known animal carcinogens.
[8]1-methyl-9*H*-pyrido[3,4-*b*]-indole.
[9]NNK = 4-(*N*-methyl-*N*-nitrosamino)-1-(3-pyridyl)-1-butanone.
[10]Data from Löfroth and Zebühr, 1992. Amount is given as International Toxic Equivalent Factor (I-TEF).

the smoldering period, with little influence exerted by cigarette design (Guerin et al., 1992). More recent summary data on SS emission rates from filtered test cigarettes and commercial cigarettes for many compounds of human health interest are presented by Guerin et al. (1992) and shown, with modifications, in Table 3-2. Much of the data in Table 3-2 is extracted from detailed data presented in an R.J. Reynolds (1988) report. Table 3-2, like Table 3-1, documents that appreciable quantities of important air contaminants are emitted into the air from SS emissions resulting from tobacco combustion. The table demonstrates that SS emissions are reasonably similar across different brands of cigarettes, varying by only a factor of 2-3. So, while MS emissions can vary considerably (Table 3-1), SS emissions are relatively constant (Table 3-2).

In summary, the available data indicate that tobacco combustion results in the emission of a large number of known toxic compounds and that many of these will be released at rates that are higher in SS than in MS. Emphasis in characterizing SS emissions has been placed upon those carcinogens and toxic compounds found in MS. Although not all of the SS emissions have been characterized, the available data showing SS to be enriched in many of the same carcinogens and toxic agents found in MS lead to the conclusion that ETS will contain the same hazardous compounds. This conclusion provides the basis for the toxicological comparison of these complex mixtures in Chapter 4. The enrichment of several known or suspected carcinogens in SS relative to MS suggests that the SS contaminant mix may be even more carcinogenic than the MS mix, per

Table 3-2. Example sidestream cigarette smoke deliveries[1]

Constituent	Kentucky reference[2]	Commercial
	Milligrams per cigarette	
Condensate		36-67
Total particulate matter	16.9	16-36, 20-23
Nicotine	5.6	5.7-11.2, 2.7-6.1
Carbon monoxide	54	41-67
Carbon dioxide	474	
Nitrogen oxides	0.9	
Ammonia	9.1	
Formaldehyde	0.7	
Acetaldehyde	4.2	
Acrolein	1.3, 1.4	0.7-1.0
Propionaldehyde	0.9	
Benzene	0.3, 0.4, 0.7	0.3-0.5
Toluene	0.8, 1.3	0.8-1.1
Styrene		
Pyrrole	0.4	
Pyridine	0.3	
3-Vinylpyridine		
3-Hydroxypyridine		
Limonene	0.3	<0.1-0.4
Neophytadiene		0.1-0.2
Isoprene	2.5, 6.1	4.4-6.5
nC_{27}-nC_{33}	0.2-0.8	
Acetonitrile	1.0, 0.8[3]	
Acrylonitrile	0.2	

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Table 3-2. (continued)

Constituent	Kentucky reference[2]	Commercial
	Micrograms per cigarette	
Hydrogen cyanide	53, 17[3]	
Phenol		44-371
o-Cresol		24-98
m + p-Cresol		59-299
Catechol		46-189
Hydroquinone		26-256
Naphthalene		53-177
Phenanthrene		2.4
Anthracene		0.7
Fluoranthene		0.7
Pyrene		0.5
Benz[a]anthracene	0.2	0.2
Benzo[a]pyrene	0.1	0.1
NNN[4]	0.2	1.7
NNK[4]	0.4	0.4
NAT[4]	0.1	
NAB[4]	<0.1	
DMNA[4]	0.3	0.7-1.0
EMNA[4]		<0.1
DENA[4]		<0.1-0.1
NPYR[4]	0.2	0.2-0.4
2-Naphthylamine		<0.1-1[5]
4-Aminobiphenyl		<0.1-0.2[5]
Nickel		
Cadmium		
Lead		
Chromium		

(continued on the following page)

Table 3-2. (continued)

[1]Table reprinted from Guerin et al. 1992, who compiled data from Browne et al., 1990; Brunnemann et al., 1977, 1978, and 1990; Chortyk and Schlotzhauer, 1989; Grimmer et al., 1987; Guerin, 1991; Higgins et al., 1987; Johnson et al., 1973; O'Neill et al., 1987; R.J. Reynolds, 1988; Rickert et al., 1984; Sakuma et al., 1983, 1984a, 1984b; and Norman et al., 1983. Full references are given in Guerin et al., 1992.
[2]Filter 1R4F unless otherwise specified.
[3]Nonfilter 1R1.
[4]*N*-nitrosonornicotine (NNN), 4-methylnitrosoamino-1-(3-pyridinyl)-1-butanone (NNK), *N*-nitrosoanatabine (NAT), *N*-nitrosoanabasine (NAB), dimethylnitrosamine (DMNA), ethylmethylnitrosamine (EMNA), diethylnitrosamine (DENA), *N*-nitrosopyrrolidine (NPYR).
[5]Calculated from NRC, 1986, SS/MS ratio.

unit tobacco burned. The mouse skin painting bioassays of organic extracts of MS and SS reviewed in Chapter 4 add support to the suggestion that SS is a more potent carcinogen than MS. Furthermore, the incomplete chemical characterization of SS emissions means that there may be additional, as yet unidentified compounds in SS of human health interest.

Detailed chemical characterizations of ETS emissions under conditions more typical of actual smoking conditions (e.g., using smokers rather than smoking machines) are limited. As a result, the impact on ETS of factors such as the rapid dilution of SS emissions, adsorption and remission of contaminants, and exhaled MS is not well understood. Several studies conducted in chambers or controlled environments and using smokers (e.g., Benner et al., 1989; Duc and Huynh, 1989; Leaderer and Hammond, 1991; R.J. Reynolds, 1988; NRC, 1986; U.S. DHHS, 1986; Guerin et al., 1992) have characterized some of the ETS components (total mass, carbon monoxide, nicotine and other selected compounds, including known carcinogenic and toxic substances). These studies indicate that many of the contaminants of interest in SS are measurable in ETS (NRC, 1986; U.S. DHHS, 1986; Guerin et al., 1992) and that several SS contaminants (e.g., total mass, carbon monoxide, nicotine) are easily measurable in ETS. It is not known how the MS and SS air contaminant emission data for specific compounds, generated by the standardized testing protocols utilized, compare to data gathered under conditions more representative of actual smoking in occupied spaces.

3.3. ASSESSING ETS EXPOSURE

In the course of a typical day, an individual spends varying amounts of time in a variety of environments (residences, industrial and nonindustrial workplaces, automobiles, public access buildings, outdoors, etc.). While in these different environments, individuals are exposed to a broad and complex spectrum of organic and inorganic chemicals in gaseous and particle forms, as well as a range of viable particles.

ETS is a major source of indoor air contamination because of the large, though decreasing, number of smokers in the population and the quantity and quality of the contaminants emitted into the environment from tobacco combustion (NRC, 1981, 1986). In a 1990 self-reported smoking survey of a representative sample of the U.S.

civilian, noninstitutionalized population, it was reported that 50.1% (89.9 million) of the adult population were ever-smokers and 25.5% were current smokers (CDC, 1992). The reported average number of cigarettes smoked per day was 19.1, with 22.9% of smokers reporting smoking 25 or more cigarettes per day. From 1965 through 1985, the overall smoking prevalence among U.S. adults declined 0.5% annually, with a 1.1% annual decline between 1987 and 1990.

In another recent survey (CDC, 1991b), 40.3% (46 million) of employed adults ($\geq$ 18 years old) in 1988 (who reported that their workplace was not in their home) worked in locations where smoking was allowed in designated or other areas. Of the nonsmokers (79.2 million), 36.5% (28.5 million) worked at places that permitted smoking in designated (if any) and other areas. Of these nonsmokers, 59.2% (16.9 million) reported that exposure to ETS in their workplace caused them discomfort. The survey highlighted the importance of the workplace as a major source of ETS exposure in addition to the home.

The available data on ETS exposure to children in the home are limited. However, based on the 1988 National Health Interview Survey on Child Health, 42% of children 5 years of age and under are estimated to live in households with current smokers (Overpeck and Moss, 1991). The home environment is clearly an important source of ETS exposure for children.

Nationally based survey data needed to make direct estimates of the frequency, magnitude, and duration of ETS exposure for nonsmoking adults and children and the different indoor environments in which those exposures occur are not available. The survey data available, however, do indicate that due to the ubiquitous nature of ETS in indoor environments, some unintentional inhalation of ETS by nonsmokers is unavoidable.

The combustion of tobacco results in the emission of a particularly complex array of air contaminants into indoor microenvironments. Data on the chemical composition of mainstream and sidestream cigarette emissions as well as measurements in indoor spaces where smoking occurs indicate that exposure to ETS will result in exposure to toxic and carcinogenic agents (Section 3.2). The nature of the ETS contaminant mix and eventual human exposure is the product of the interaction of several interrelated factors associated with the source, transport, chemical transformation, dispersal, removal, and remission from surfaces, as well as human activities. Efforts to determine adverse health effects of ETS must address the issue of exposure to a complex mixture, which can occur in a number of environments. Assessing exposure to ETS, as with any complex air contaminant mix, is inherently complicated in epidemiologic studies (Leaderer et al., 1992).

Because of the many potentially toxic agents in ETS and the various possible toxicological endpoints of interest, it is neither feasible nor desirable to focus on any one contaminant. Rather, the focus is on gathering information on marker or proxy compounds or other indicators of ETS exposure. In assessing these exposures, both direct and indirect methods can be employed. Direct methods include personal monitoring and measurement of biological markers. Indirect methods employ models to estimate exposures. The modeling approach generally makes use of stationary monitoring and questionnaire data.

Stationary monitoring is used to measure concentrations of air contaminants in different environments. These measured concentrations are then combined with time-activity patterns (time budgets) to determine the average exposure of an individual as the sum of the concentrations in each environment weighed by the time spent in that environment. Monitoring of contaminants might also be supplemented with the monitoring of factors in the environment that affect the contaminant levels measured (meteorological variables, primary compounds, ventilation, etc.). Measurement of these factors, in a carefully chosen set of conditions, can lead to models that predict concentrations in the absence of measured concentrations and provide a means of assessing the impact of efforts to reduce or eliminate exposures. Questionnaires are used to determine time-activity patterns of individuals, to provide a simple categorization of potential exposure, and to obtain information on the properties of the environment affecting the measured levels (number of smokers, amounts smoked, etc.).

ETS exposure measurements, whether conducted to support epidemiological studies or to determine the extent of exposure in nonsmoking individuals, have typically employed air monitoring of indoor spaces, personal monitoring, and questionnaires. Modeling of ETS exposures, while useful in estimating, from measured data, the level of exposure in a variety of indoor spaces under varying conditions, is beyond the scope of this report.

3.3.1. Environmental Concentrations of ETS

The SS emission data discussed in Section 3.2 and shown in Tables 3-1 and 3-2 clearly indicate that tobacco combustion will result in the release of thousands of air contaminants into the environments in which smoking occurs. The concentrations of the known and unidentified contaminants in the ETS complex mix in an enclosed space can exhibit a pronounced spatial and temporal distribution. The concentration is the result of a complex interaction of several important variables, including (1) the generation rate of the contaminant(s) from the tobacco (including both SS and exhaled MS emissions), (2) location in the space that smoking occurs, (3) the rate of tobacco consumption, (4) the ventilation or infiltration rate, (5) the concentration of the contaminant(s) in the ventilation or infiltration air, (6) air mixing in the space, (7) removal of contaminants by surfaces or chemical reactions, (8) re-emission of contaminants by surfaces, and (9) the effectiveness of any air cleaners that may be present. Additional considerations relate to the location at which contaminant measurements are made, the time of sample collection, the duration of sampling, and method of sampling.

Variations in any one of the above factors related to introduction, dispersal, and removal of ETS contaminants can have a marked impact on the resultant indoor ETS constituent concentrations. Any one of these parameters can vary by an order of magnitude or more. For example, infiltration rates in residences can range from 0.1 to over 2.0 air changes per hour, and house volumes can range from 100 to over 700 m^3 (Grimsrud et al., 1982; Grot and Clark, 1979; Billick et al., 1988; Koutrakis et al., 1992). Smoking rates and mixing within and between rooms can also show considerable variability. The potential impact on indoor ETS-related respirable suspended particle (RSP) mass concentrations due to variations in these parameters is demonstrated in Figures 3-1 and 3-2 (these figures were taken directly from Figures 5-4 and 5-5 in NRC, 1986). Figures 3-1 and 3-2 are based on the mass

balance model for ETS (NRC, 1986) for a typical range of input parameters encountered in indoor spaces. These figures demonstrate that ETS-generated RSP concentrations in indoor environments can range from less than 20 $\mu g/m^3$ to over 1 mg/m^3 depending upon the location and conditions of smoking.

Numerous field studies in "natural" environments have been conducted to assess the contribution of smoking occupancy to indoor air quality. These studies, summarized in a number of reviews (e.g., NRC, 1986; U.S. DHHS, 1986; Guerin et al., 1992), have measured several ETS-related contaminants of human health concern (e.g., particle mass, carbon monoxide, benzene, nicotine, polycyclic aromatic hydrocarbons, *N*-nitrosamines), in a number of enclosed environments (e.g., residential, office, transportation) and under a variety of smoking and ventilation rates. These studies demonstrate that (1) many of the contaminants of health interest found in SS are also found in ETS; (2) ETS contaminants are found above background level in a wide range of indoor environments in which smoking occurs; and (3) the concentrations of ETS contaminants indoors can be highly variable. These findings can be demonstrated for selected ETS-related compounds presented in Figure 3-3 and in Table 3-3.

Figure 3-3 principally utilizes data summaries presented in reviews of indoor measurements of ETS-related compounds in a variety of indoor spaces (NRC, 1986; U.S. DHHS, 1986; and particularly Guerin et al., 1992). Only the range of average concentrations measured in

Figure 3-1. Diagram for calculating the respirable suspended particle mass (RSP) from ETS emitted into any occupied space as a function of the smoking rate and removal rate (N). The removal rate is equal to the sum of the ventilation or infiltration rate (n_v) and the removal rate by surfaces (n_s) times the mixing factor. The calculated ETS-related RSP mass determined from this figure serves as an input to Figure 3-2 to determine the ETS-related RSP mass concentration in any space in $\mu g/m^3$. Smoking rates (diagonal lines) are given as cigarettes smoked per hour. Mixing is determined as a fraction, and n_v and n_s are in air changes per hour (ach). All three parameters have to be estimated or measured. Calculations were made using the equilibrium form of the mass-balance equation and assume a fixed emission rate of 26 mg/m^3 of RSP.

Shaded area shows the range of RSP emissions that could be expected for a residence with one smoker smoking at a rate of either 1 or 2 cigarettes per hour for the range of mixing, ventilation, and removal rates occurring in residences under steady-state conditions.

Source: NRC, 1986.

Figure 3-2. Diagram to calculate the ETS-associated respirable suspended particle mass (RSP) concentration in $\mu g/m^3$ in a space as a function of total mass of ETS-generated RSP emitted in mg (determined from Figure 3-1) and the volume of a space (diagonal lines). The concentrations shown assume a background level of zero in the space. The particle concentrations shown are estimates during smoking occupancy. The dashed horizontal lines (A, B, C, and D) refer to National Ambient Air Quality Standards (health-related) for total suspended particulates established by the U.S. Environmental Protection Agency. A is the annual geometric mean. B is the 24-hour value not to be exceeded more than once a year. C is the 24-hour air pollution emergency level. D is the 24-hour significant harm level. Shaded area shows the range of concentrations expected (from Figure 3-1) for a range of typical volumes of U.S. residences and rooms in these residences.

Source: NRC, 1986.

Figure 3-3. Range of average indoor concentrations for notable ETS contaminants associated with smoking occupancy for different indoor environments. Ranges of averages are principally from tables presented in Guerin et al. (1992), although other sources were used (NRC, 1986; U.S. DHHS, 1986; Turk et al., 1987). Background levels are subtracted. Maximum recorded values are typically orders of magnitude higher than averages shown.

Table 3-3. Tobacco-specific *N*-nitrosamines in indoor air (ng/m^3)[1]

Site	Approx. # of cigarettes smoked	Collection time (hours)	Flow rate (liters/ min.)	Tobacco-specific *N*-nitrosamines		
				NNN[2]	NAT[2]	NNK[2]
Bar I	25-35	3	3.2	22.8	9.2	23.8
Bar II	10-15	3	3.2	8.3	6.2	9.6
Bar III	10-15	3	3.2	4.3	3.7	11.3
Restaurant[3]	25-30	6	2.15	1.8	1.5	1.4
Restaurant[3]	40-50	8	2.1	ND	ND	3.3
Car[4]	13	3.3	2.15	5.7	9.5	29.3
Train I	50-60	5.5	3.3	ND	ND	4.9
Train II	50-60	6	3.3	ND	ND	5.2
Office	25	6.5	3.3	ND	ND	26.1
Smoker's Home	30	3.5	3.3	ND	ND	1.9

[1]Data corrected for recovery.
[2]NNN = NNN-*N*-nitrosonornicotine; NAT = NAT-*N*-nitrosoanataline;
NNK = NNK-4-methylInitrosoamino-1-(3 pyridinyl)-1-butanone.
[3]Smoking section.
[4]Windows partially open.
ND = not detected (in some cases due to chromatographic interference).

Source: Brunnemann et al., 1992.

different environments is shown. Maximum values, which can range up to two or more orders of magnitude above the averages, are not shown in Figure 3-3. Background levels for nonsmoking conditions have been subtracted. When smoking occurs, concentrations of total polycyclic aromatic hydrocarbons, benzo[a]pyrene, benzene, formaldehyde, toluene, and carbon monoxide will be elevated above background levels in a variety of indoor environments. Figures 3-7 and 3-8 present a similar summary with the same conclusions for two other ETS-related contaminants--respirable suspended particle mass and nicotine.

N-nitrosamines are important constituents of SS because they are considered to be carcinogenic, because they are emitted in much larger quantities in SS than in MS (Table 3-1), and because tobacco combustion is the only identified air source in the nonoccupational indoor environment. Guerin et al. (1992) reviewed the available data on indoor levels of *N*-nitrosamines related to smoking occupancy. They concluded that levels associated with smoking can range from less than detectable to as high as 100 ng/m^3 for nitrosodimethylamine (NDMA) under conditions of heavy smoking. A more typical range of concentrations of NDMA were

< 10-40 ng/m^3. In a recent paper, Brunnemann et al. (1992) demonstrated that exposure to tobacco specific *N*-nitrosamines can occur in a variety of indoor spaces under a range of smoking conditions (Table 3-3).

The potential for high exposures of nonsmokers to carcinogenic components found enriched in SS can be demonstrated in the case of 4-aminobiphenyl (4-ABP). Tables 3-1 and 3-2 show 4-ABP emissions in SS to be approximately 30 times higher than in MS (100-200 μg/cig). Despite the fact that SS emissions of 4-ABP are diluted rapidly in the indoor environment, presumably resulting in considerably less exposure than to smokers, 4-ABP Hb adduct levels in nonsmokers have been found to be 10% to 20% of those in smokers (see Section 3.3.2).

There are important circumstances where concentrations of ETS-related contaminants in indoor spaces may considerably underestimate potential levels of exposure. These circumstances occur when the SS emissions or exhaled MS emissions are in direct proximity to a nonsmoker (e.g., an infant held by a smoking mother or father, or when a nonsmoker is directly downwind of the plume of a smoldering cigarette). While there are no measurements to assess the impact on the nonsmoker's exposure under these conditions, it is an important exposure and will be much higher than would be predicted from existing environmental measurements of more diluted SS and exhaled MS emissions.

The data discussed above represent concentrations measured in selected indoor environments and indicate that exposure will occur for individuals in those spaces. Estimating the actual level of exposure (concentration × time) requires knowledge of the actual time spent in those environments.

3.3.1.1. *Markers for Environmental Tobacco Smoke*

Although ETS is a major source of indoor air contaminants, the actual contribution of ETS to indoor air is difficult to assess due to the background levels of many contaminants contributed from a variety of other indoor and outdoor sources. Relatively few of the individual constituents of the ETS mix have been identified and characterized. In addition, little is known about the role of individual ETS constituents in eliciting the adverse health and nuisance effects observed. However, the issue is not how to fully characterize the exposure to each ETS-related contaminant, but rather how to obtain accurate quantitative measures of exposure to the entire ETS mixture. The measurement of all components in ETS is not feasible, practical, or even desirable due to limitations in knowledge of the mixture components related to the effects of interest, as well as the feasibility and cost of sampling. It is necessary then to identify a marker (also referred to as a tracer, proxy, indicator, or surrogate) for ETS that will, when measured, accurately represent the frequency, duration, and magnitude of exposure to ETS. These markers can be chemicals measured in the air, biomarkers, models, or simple questionnaires.

There are important issues related to the measurement of a given marker compound to represent exposure to ETS. Ideally, an air contaminant marker for ETS should (1) vary with source strength, (2) be unique to the source, (3) be easily detected in air at low concentrations, (4) be similar in emission rates for a variety of tobacco products, (5) occur in a consistent ratio in air to other ETS components in the complex mix, and (6) be easily, accurately, and cost effectively measured (Leaderer, 1990). The marker can be a specific compound (e.g., nicotine) or much less specific

(e.g., respirable suspended particle mass). These criteria for selecting a suitable marker compound are the ideal criteria. In practice, no single contaminant or class of contaminants has been identified that would meet all the criteria. Selection of a suitable marker for ETS is reduced to satisfying as many of the criteria for judging a marker as is practical. In using a marker, it is important to state clearly the role of the marker and to note its limitations.

A number of marker or proxy compounds have been used to represent ETS concentrations in both field and chamber studies. Nicotine, carbon monoxide, 3-ethenylpyridine, nitrogen dioxide, pyridine, aldehydes, nitrous acid, acrolein, benzene, toluene, myosmine, and several other compounds have been used or suggested for use as markers or proxies for the vapor phase constituents of ETS (NRC, 1986; U.S. DHHS, 1986; Hammond et al., 1987; Eatough et al., 1986; Löfroth et al., 1989; Leaderer and Hammond, 1991; Guerin et al., 1992). Tobacco-specific nitrosamines, particle phase nicotine and cotinine, solanesol, polonium-210, benzo[a]pyrene, potassium, chromium, and respirable suspended particle mass (RSP--particle mass $\leq 2.5\ \mu$m) are among the air contaminants used or suggested for use as markers for particle phase constituents of ETS (NRC, 1986; U.S. DHHS, 1986; Leaderer and Hammond, 1991; Benner et al., 1989; Hammond et al., 1987; Rickert, 1984; Guerin et al., 1992). All the markers employed to date have some problems associated with their use. For example, carbon monoxide, nitrogen oxides, benzene, and RSP have many indoor and outdoor sources other than the combustion of tobacco, while other compounds such as nitrosamines and benzo[a]pyrene are sufficiently difficult to measure (e.g., concentrations in smoking environments are low and the cost of collection and analysis of samples is high) that their use is very limited.

At the present time, vapor phase nicotine and respirable suspended particulate matter are widely and most commonly used as markers of the presence and concentration of ETS for a variety of reasons associated with their ease of measurement, existing knowledge of their emission rates from tobacco combustion, and their relationship to other ETS contaminants.

Vapor phase nicotine, the dominant form of nicotine in ETS (Eudy et al., 1985; NRC, 1986; U.S. DHHS, 1986; Hammond et al., 1987; Eatough et al., 1986; Guerin et al., 1992) accounts for approximately 95% of the nicotine in ETS and is a good marker air contaminant for ETS. It is specific to tobacco combustion and is emitted in large quantities in ETS (NRC, 1981, 1986; U.S. DHHS, 1986; Rickert et al., 1984; Eatough et al., 1990; Guerin et al., 1992). Chamber measurements have shown that nicotine concentrations vary with source strength (Rickert et al., 1984; Hammond et al., 1987; Hammond and Leaderer, 1987; Leaderer and Hammond, 1991) and show little variability among brands of cigarettes, despite variations in MS emissions (Rickert et al., 1984; Leaderer and Hammond, 1991). Field studies have shown that weekly nicotine concentrations are highly correlated with the number of cigarettes smoked (Hammond et al., 1987; Mumford et al., 1989; Thompson et al., 1989; Leaderer and Hammond, 1991). One large field study (Leaderer and Hammond, 1991) showed that weekly nicotine concentrations were strongly correlated with measured RSP levels, as well as with reported number of cigarettes smoked. In this study, the slope of the regression line was 10.8 (standard error of ± 0.72), similar to the RSP/nicotine level seen in chamber studies. Also, the RSP intercept was equal to background levels in homes without smoking (17.9 $\mu g/m^3$ ± 1.63) (Leaderer et al., 1990). A comparable study by Miesner et al. (1989) of particulate matter and nicotine in

workplaces found a similar ratio between RSP and nicotine. The utility of nicotine as an ETS marker is enhanced by the fact that recent advances in air sampling have resulted in the development of a variety of validated and inexpensive passive and active monitoring methods for measuring nicotine in indoor air environments and for personal monitoring (Hammond et al., 1987; Hammond and Leaderer, 1987; Eatough et al., 1989a; Koutrakis et al., 1989; Muramatsu et al., 1984; Oldaker and Conrad, 1987).

Nicotine is also an attractive marker for the complex ETS air contaminant mix because it and its metabolites, principally cotinine, can serve as biomarkers of ETS exposure. Nicotine and cotinine have long served as markers for active smoking. Over the past several years, measurements of nicotine and cotinine in blood, urine, and saliva have been used extensively as reasonably sensitive biomarkers indicative of exposure to ETS (see Section 3.3.2).

Nicotine is, however, not an ideal ETS marker. One of the potential drawbacks is that vapor-phase nicotine has a high affinity for indoor surfaces. The high adsorption rate of nicotine could decrease its concentration relative to other ETS constituents, particularly ETS-associated particle mass (Eudy et al., 1986; Rickert et al., 1990; Eatough et al., 1989b). This relative decrease in concentration could lead to an underestimation of ETS exposures. The ratio of nicotine to RSP and possibly other ETS constituents would be expected to be most dynamic as the ETS contaminant mix ages (Eatough et al., 1989a). An additional potential problem is that nicotine may be re-emitted from interior surfaces, resulting in measurable concentrations in the absence of active smoking. There have, however, been a number of field studies (see above and Figures 3-4 and 3-7) where nicotine has been used successfully as an ETS marker. These studies would indicate that the uncertainties associated with nicotine in typical indoor environments under normally encountered smoking rates are relatively small. Levels of nicotine in smoking environments have been measured over several orders of magnitude (Figures 3-4 and 3-7), suggesting that the uncertainty associated with its high adsorption rate is small compared to the concentration range. It should also be noted that other gas phase ETS contaminants may exhibit adsorption and reemission properties similar to that of nicotine. Use of nicotine or any other ETS marker must consider the limitations associated with its use.

The combustion of tobacco results in substantial emissions of RSP. One small chamber study using a smoking machine found the average particle emission rate for 15 Canadian cigarettes to be 24.1 mg/cigarette with a range of 15.8-36.0 mg/cigarette (Rickert et al., 1984). A large chamber study using smokers reported an average particle emission rate of 17.1 mg for 12 brands of American cigarettes (Leaderer and Hammond, 1991). This study noted that emission rates among brands are similar. Included in the RSP are a number of compounds of direct health concern, e.g., many of the polycyclic aromatic hydrocarbons and tobacco-specific *N*-nitrosamines (NRC, 1986; U.S. DHHS, 1986; Guerin et al., 1992; Tables 3-1 and 3-3, Figure 3-3). There are a number of accepted methods to measure personal RSP exposures and concentrations in indoor environments (Ogden et al., 1990). The available methods permit the accurate measurement of RSP for sampling times ranging from seconds to several days.

Numerous studies of personal exposures to RSP and of RSP levels in indoor environments have shown elevated levels of RSP in environments where smoking was reported (NRC, 1986; U.S. DHHS, 1986; Guerin et al., 1992; Leaderer and Hammond, 1991; Turk et al., 1987). One study found a strong correlation between weekly

residential RSP levels and reported number of cigarettes smoked (Leaderer and Hammond, 1991). At low smoking and high ventilation rates, however, it may be difficult to separate out the ETS-associated RSP in a background of RSP from other indoor sources (e.g., kerosene heaters) or even from outdoor sources. In using RSP as a marker for ETS, it is important to account for the background RSP level related to other sources before ascertaining the contribution from ETS. Efforts to model ETS exposures for the purpose of assessing risks and the impact of various mitigation measures have often focused on predicting ETS-associated RSP concentrations (e.g., Repace and Lowrey, 1980).

3.3.1.2. *Measured Exposures to ETS-Associated Nicotine and RSP*

3.3.1.2.1. ***Measurements using stationary monitors.*** In the past several years, numerous studies have been conducted in a variety of indoor environments to determine the impact of tobacco combustion on levels of nicotine and RSP. These studies have employed a variety of protocols that used a diversity of air sampling techniques (passive, active, continuous integrative, etc.), sampled over highly varying timeframes (from minutes to several days), and collected highly variable information on factors affecting the measured concentrations (number of cigarettes smoked, volume of building, ventilation rates, etc.). In an attempt to present an overall view of the contribution of ETS to indoor air quality, only the summary results of the measured concentrations of ETS-associated nicotine and RSP will be discussed here. Several reviews of the studies evaluating the impact of ETS on indoor RSP levels have been conducted over the past few years, and a number of recent reports have discussed measured indoor levels of nicotine (e.g., NRC, 1986; U.S. DHHS, 1986; Guerin et al., 1992; Leaderer and Hammond, 1991). Only the indoor levels measured are discussed and summarized. In order to assess exposures, the time in contact with the concentrations would have to be estimated or measured. The reader is referred to those reports and to the individual study reports to acquire more detailed information.

Measured nicotine concentrations in various indoor environments where smoking was noted are summarized in Figure 3-4. The mean concentration, standard deviation, and the maximum and minimum values recorded are presented. Also given in Figure 3-4 are the number of locations in which the measurements were taken and the references in which the data were reported. Elevated nicotine levels were measured in all microenvironments in which smoking was reported. Measured nicotine levels, as would be expected, were highly variable, covering several orders of magnitude.

The home and workplace may represent the most important environments for exposure to ETS because of the amount of time individuals spend there. For the five studies reporting residential levels, average nicotine concentrations in homes where smoking occurs ranged from less than 1 $\mu g/m^3$ (Leaderer and Hammond, 1991) to over 14 $\mu g/m^3$ (Muramatsu et al., 1984). For two of the studies (Leaderer and Hammond, 1991; Marbury et al., 1990) nicotine concentrations represent weekly averages. Actual concentrations in the homes during nonsleeping occupancy (i.e., while smoking would be occurring) would be considerably higher than the levels presented in the table (a factor of 3 or more higher). Workplace nicotine also demonstrated a wide range of concentrations, from near

zero to over 33 $\mu g/m^3$. In other environments, nicotine concentrations also demonstrated considerable variability. It is important to note that short-term concentrations

Figure 3-4. Mean, standard deviation, and maximum and minimum nicotine values measured in different indoor environments with smoking occupancy. References from which observations are reported and the number of environments monitored are also given.

REFERENCES FOR FIGURES 3-4 AND 3-5

Figure 3-4

1. Leaderer and Hammond, 1991
2. Mumford et al., 1989
3. Marbury et al., 1990
4. Muramatsu et al., 1984
5. Coultas et al., 1990b
6. Weber and Fischer, 1980
7. Vaughan and Hammond, 1990
8. Leaderer, 1989
9. Miesner et al., 1989
10. Hinds and First, 1975
11. Oldaker et al., 1990
12. Coghlin et al., 1989
13. Badre et al., 1978
14. Higgins, 1987
15. Nagda et al., 1990
16. Eatough et al., 1990
17. Mattson et al., 1989
18. Harmsden and Effenberger, 1957
19. Cano et al., 1970

Figure 3-5

1. Brunekreef and Boleij, 1982
2. Hawthorne et al., 1984
3. Moschandreas, 1981
4. Nitschke et al., 1985
5. Parker et al., 1984
6. Spengler et al., 1981
7. Spengler et al., 1985
8. Leaderer et al., 1990
9. Lebret et al., 1990
10. Coultas et al., 1990b
11. Turk et al., 1987
12. Weber and Fischer, 1980
13. Sterling and Sterling, 1983
14. Nelson et al., 1982
15. Quant et al., 1982
16. Repace and Lowery, 1980
17. Repace and Lowery, 1982
18. Leaderer, 1989
19. First, 1984
20. Oldaker et al., 1990
21. Ishizu, 1980
22. Husgafvel-Pursiainen et al., 1986
23. Eatough et al., 1990
24. Neal et al., 1978
25. Nagda et al., 1990
26. U.S. Department of Transportation, 1971
27. Elliot and Rowe, 1975

(on the order of minutes) are likely to show considerably more variability, resulting in considerably higher short-term peak exposures.

A substantial number of studies examining the impact of tobacco combustion on concentrations of RSP in various indoor environments have been reported. Many of these studies have reported outdoor RSP concentrations and indoor RSP levels without smoking as well as concentrations when smoking occurs. These studies are summarized in Figure 3-5. Outdoor and indoor RSP levels for each of the studies as well as the smoking-associated RSP measurements are shown. The sampling time for the presented data ranged from one minute to over several days. A major portion of the data is for the residential indoor environment. Where smoking is reported, RSP levels are considerably higher than RSP levels outdoors or indoors without smoking. RSP levels associated with smoking, like those for nicotine, demonstrated considerable variability ranging from a few $\mu g/m^3$ to over 1 mg/m^3. Workplace RSP levels associated with smoking occupancy are comparable to residential RSP levels.

In one large residential study, both ETS-associated nicotine and RSP levels were found to be highly correlated ($r = 0.84$; $p < 10^{-5}$) with reported number of cigarettes smoked (Leaderer and Hammond, 1991). This study found that, consistent with chamber data, measured nicotine concentrations predicted the contribution to residential RSP levels from tobacco combustion (Figure 3-6). The data in Figure 3-6 might be used to estimate the RSP levels associated with tobacco combustion from the nicotine levels shown in Figure 3-4. The predictive equation, along with the standard errors, is given in the figure and figure legend. In a study of the impact of smoking on residential levels of RSP and nicotine and of urinary cotinine levels in nonsmoking occupants involving 10 homes, a correlation of 0.54 between residential levels of RSP and nicotine was found (Coultas et al., 1990b).

Indoor levels of nicotine and RSP associated with the combustion of tobacco are a function of several factors related to the generation, dispersal, and removal of ETS in enclosed environments (see Section 3.3.1). Thus, measured levels of these air contaminants indicate a wide range of concentrations (Figures 3-1 and 3-2). Figures 3-7 and 3-8 present a summary of the range of nicotine and ETS-associated particle concentrations measured by type of environment. The figures present the range of average values reported for each study and the minimum and maximum values reported. Only studies reporting sampling times over 4 hours were included in the residential and office summaries in Figures 3-7 and 3-8, because the averaging time is more likely to represent the exposures associated with occupancy time (this included most of the studies for residential spaces shown in Figures 3-4 and 3-5). Since occupancy time in other environments (e.g., restaurants) is likely to be much shorter, averaging times on the order of minutes or greater were considered for the other indoor environments presented in the figures. Indoor particulate

Figure 3-5. Mean, standard deviations, and maximum and minimum concentrations of respirable suspended particle mass (RSP) measured in different indoor environments for smoking and nonsmoking occupancy. Also shown are outdoor concentrations. References from which observations are reported and the number of environments monitored are also given.

Figure 3-6. Week-long respirable suspended particle mass (RSP) and nicotine measurements in 96 residences with a mixture of sources. Numbers 1-9 refer to the number of observations at the same concentration.

Source: Leaderer and Hammond, 1991.

Figure 3-7. Range of average nicotine concentrations and range of maximum and minimum values measured by different indoor environments for smoking occupancy from studies shown in Figure 3-4. Only those studies with sampling times of 4 hours or greater are included in the residential and office indoor environment summaries.

Figure 3-8. Range of average respirable suspended particle mass (RSP) concentrations and range of maximum and minimum values measured by different indoor environments for smoking occupancy from studies shown in Figure 3-5. RSP values represent the contribution to background levels without smoking. Background levels were determined by subtracting reported indoor concentrations without smoking. Only those studies with sampling times of 4 hours or greater are included in the residential and office indoor environment summaries.

levels associated with smoking occupancy (Figure 3-8) were calculated by subtracting particle levels for nonsmoking occupancy (presented in the studies) from the smoking occupancy levels. Thus, the increase in particle mass concentrations associated with ETS is presented in Figure 3-8. Indoor RSP levels in residences without smokers are typically in the range of 10-25 $\mu g/m^3$, while background office levels are somewhat lower (Figure 3-5).

The summary nicotine data (Figure 3-7) suggest that average nicotine values in residences with smoking occupancy will range from 2 to approximately 10 $\mu g/m^3$, with high values up to 14 $\mu g/m^3$ and low values down to 0.1 $\mu g/m^3$. Offices with smoking occupancy show a range of average nicotine concentrations similar to that of residences, but with considerably higher maximum values. The data from other indoor spaces suggest considerable variability, particularly in the range of maximum values. The cumulative distribution of weekly nicotine measured in one study (Leaderer and Hammond, 1991) for a sample of 96 homes, with the levels for smoking occupancy emphasized, is shown in Figure 3-9.

Particle mass concentrations in smoker-occupied residences show average increases of from 18 to 95 $\mu g/m^3$, while the individual increases can be as high as 560 $\mu g/m^3$ or as low as 5 $\mu g/m^3$ (Figure 3-8). Figure 3-10 (Leaderer and Hammond, 1991) highlights the distribution of weekly RSP concentrations for residences with smoking occupancy. In that study, smoking residences had RSP concentrations approximately 29 $\mu g/m^3$ higher than nonsmoking homes. Concentrations in offices with smoking occupancy will be on average about the same as those in residences. Interestingly, in a large and possibly the most comprehensive study of particle mass concentrations associated with smoking and nonsmoking sites in office buildings (Turk et al., 1987), the geometric mean concentration for RSP in 32 smoking sites was 44 $\mu g/m^3$ while the geometric mean for 35 nonsmoking sites was 15 $\mu g/m^3$. The difference of 29 $\mu g/m^3$ is the same as that found for smoking and nonsmoking residences (Figure 3-10). Restaurants, transportation, and other indoor spaces with smoking occupancy will result in a considerably wider range of average, minimum, and maximum increases in particle concentrations than the residential or office environments.

As noted earlier, indoor air contaminant concentrations are the result of the interaction of a number of factors related to the generation, dispersal, and elimination of the contaminants. Source use is no doubt the most important factor. Few studies have measured contaminant concentrations as a function of the smoking rate in residences or offices, but some data are available. One study estimated an average weekly contribution to residential RSP of 2-5 $\mu g/m^3$ per cigarette (Leaderer et al., 1990), while another study estimated that a pack-a-day smoker would add 20 $\mu g/m^3$ to residential levels (Spengler et al., 1981). Coultas et al. (1990b) estimated

Figure 3-9. Cumulative frequency distribution and arithmetic means of vapor-phase nicotine levels measured over a 1-week period in the main living area in residences in Onondaga and Suffolk Counties in New York State between January and April 1986.

Source: Leaderer and Hammond, 1991.

Figure 3-10. Cumulative frequency distribution and arithmetic means of respirable suspended particle mass levels by vapor-phase nicotine levels measured over a 1-week period in the main living area in residences in Onondaga and Suffolk Counties in New York State between January and April 1986.

Source: Leaderer and Hammond, 1991.

that one or more smokers in a home added approximately 17 $\mu g/m^3$ to the residential RSP level. Variations in residential RSP levels as a function of the number of smokers and over a period of several months are demonstrated in Figure 3-11 (Spengler et al., 1981). An association between the reported number of cigarettes and weekly residential nicotine and RSP levels for a sample of 96 homes (Leaderer and Hammond, 1991) is shown in Figure 3-12a and 3-12b. Smoking clearly increases indoor concentrations of both nicotine and particle mass, and residential levels of both nicotine and particle mass increase with increasing levels of smoking. Since nicotine and particle mass are proxies for the complex ETS contaminant mix, other ETS air contaminants, including the toxic and carcinogenic contaminants, should, similarly, be elevated with smoking occupancy. This elevation for selected contaminants is shown in Figure 3-3 and Table 3-3, and for a wider range of contaminants in other publications (NRC, 1986; U.S. DHHS, 1986; Guerin et al., 1992; Turk et al., 1987; Brunnemann et al., 1992).

Children have been identified as a particularly sensitive group at health risk from exposure to ETS in the residential indoor environment (NRC, 1986; U.S. DHHS, 1986). One study has measured smoking status of the parents and weekly nicotine concentrations in the activity rooms and bedrooms of 48 children under the age of 2 years (Marbury et al., 1990). The results, shown

Figure 3-11. Monthly mean respirable suspended particle mass (RSP) concentrations in six U.S. cities.

Source: Spengler et al., 1981.

Figure 3-12a. Week-long nicotine concentrations measured in the main living area of 96 residences versus the number of questionnaire-reported cigarettes smoked during the air-sampling period. Numbers 1-9 refer to the number of observations at the same concentrations. Closed circles indicate that cigar or pipe smoking was reported in the houses, with each cigar or pipe smoked set equal to a cigarette. Data from residences in Onondaga and Suffolk Counties in New York State between January and April 1986. For panel (a), the standard errors for the intercept and slope are 0.014 and 0.002, respectively. For panel (b), the standard errors for the intercept and slope are 2.1 and 0.03, respectively.

Source: Leaderer and Hammond, 1991.

Figure 3-12b. Week-long respirable suspended particle mass (RSP) concentrations measured in the main living area of 96 residences versus the number of questionnaire-reported cigarettes smoked during the air-sampling period. Numbers 1-9 refer to the number of observations at the same concentrations. Closed circles indicate that cigar or pipe smoking was reported in the houses, with each cigar or pipe smoked set equal to a cigarette. Data from residences in Onondaga and Suffolk Counties in New York State between January and April 1986. For panel (a), the standard errors for the intercept and slope are 0.014 and 0.002, respectively. For panel (b), the standard errors for the intercept and slope are 2.1 and 0.03, respectively.

Source: Leaderer and Hammond, 1991.

in Table 3-4, indicate that activity and bedroom concentrations of nicotine in the children's homes increase with the number of cigarettes reported smoked in the home by parents. Concentrations also increased with the number of reported smokers in the household. Correlation coefficients over 0.7 were calculated between nicotine concentrations and number of cigarettes smoked. Exposure of children to ETS is covered in greater detail in Chapter 8.

It is important to note that while measurements of nicotine and ETS-associated RSP are good indicators of the contribution of ETS to air contaminant levels in indoor environments, their measurement does not directly constitute a measure of total exposure. The concentrations measured in all indoor environments have to be combined with time-activity patterns in order to determine average exposure of an individual as the sum of the concentrations in each environment weighted by the time spent in that environment. Both the home and the work environment (those without policies restricting smoking) have highly variable ETS concentrations, with the ranges largely overlapping. Which environment is most important in determining total exposure will vary with individual circumstances (e.g., a person who lives in a nonsmoking home but works in an office with smokers will receive most ETS exposure at work, but for those exposed both at home and at work, the home may be more important because, over the course of a week, more time is generally spent at home).

An additional issue to be considered is how well the general indoor concentrations represent exposures of individuals who may be directly exposed to the SS plume of ETS. Small children, particularly infants, held by smoking parents may receive exposures considerably higher than those predicted from concentrations reported for indoor spaces. Special consideration must be given to these significant subpopulations.

3.3.1.2.2. ***Personal monitors.*** Personal monitoring allows for a direct integrated measure of an individual's exposure. Personal air monitoring employs samplers (worn by individuals) that record the integrated concentration of a contaminant to which individuals are exposed in the course of their normal activity for time periods of several hours to several days. The monitors can be active (employing pumps to collect and concentrate the air contaminant) or passive (working on the principal of diffusion). As with biomarkers, personal monitoring provides an integrated measure of exposure to air contaminants across a number of environments where an individual spends time but does not provide direct information on concentrations of the air contaminant of interest in individual environments or on the level of exposure in each environment unless samples are taken in only one environment or are changed with each change of environment. Supplemental

Table 3-4. Weekly average concentrations of each measure of exposure by parental smoking status in the cross-sectional study, Minnesota, 1989

	Smoking status				
	Non-smokers	Light smokers	Father only	Mother only	Both parents
Number of subjects	23	4	8	6	7

Total cigarettes (no./week)	0.9	28.8	68.6	58.8	227.6
Activity room nicotine ($\mu g/m^3$)	0.15	0.32	2.45	5.50	12.11
Bedroom nicotine ($\mu g/m^3$)	-	0.30	1.21	2.66	5.32

information (air monitoring of spaces, time-activity patterns, etc.) is needed to determine the contribution of each microenvironment to total exposure.

Relatively few studies have measured personal exposures to ETS-associated nicotine and RSP for nonsmoking individuals. The few reported studies of personal exposure to nicotine are summarized in Table 3-5. Personal exposures associated with specific indoor environments are presented. Indoor environments include the nonindustrial workplace, homes, restaurants, public buildings, and transportation-related indoor spaces. Table 3-5 highlights the wide range of indoor environments in which ETS exposures take place and the wide range of personal exposures encountered in those environments. It is important to note, however, that relatively few observations are available and that observations for nonworkplace nicotine exposures are dominated by the Japanese data (Muramatsu), which may not be representative of personal exposures in the United States. Because the data are limited, specific conclusions about the contribution of different indoor environments to personal nicotine exposures associated with passive smoking cannot be drawn. The data do indicate, however, that a wide range of exposures to ETS takes place in a variety of indoor environments where smoking is permitted. The data also indicate that occupational and residential environments are important sources of exposure to ETS because of the levels encountered, which are comparable, and the amount of time individuals spend in them.

Studies of personal exposure to RSP of nonsmoking individuals that have attempted to stratify the collected data by ETS exposure are shown in Table 3-6. Three of the five studies represent exposures integrated over several different microenvironments (residential, public

Table 3-5. Studies measuring personal exposure to airborne nicotine associated with ETS for nonsmokers

Study	Setting	Subject	N	Nicotine, µg/m^3 X(±SD)	Nicotine, µg/m^3 Range	Comments
Mattson et al., 1989	Airplane	Attendants	16	4.7 (±4.0)	0.1-10.5	4 atten-dants on 4 flights
Schenker et al., 1990	Railroad	Clerks	40	6.9		Samples collected over work shifts
Coultas et al., 1990a	Workplace	Nonindus-trial	15	20.4 (±20.6)		
Muramatsu et al., 1984	Office	Volunteers	10	21.1		Calculated from data presented
	Laboratory		8	5.8		
	Conference room		5	38.7		
	Home		3	11.2		
	Hospital lobby		1	3.0		
	Hotel lobby		4	11.2		
	Restaurant		15	26.0		
	Transportation		22	21.7		
Muramatsu et al., 1984	Office	Volunteers	3	6.9		Calculated from data presented
	Home		7	7.0		
	Restaurant		15	28.2		
	Car		7	40.0		
	Public transportation		1	11.4		

Table 3-6. Studies measuring personal exposure to particulate matter associated with ETS for nonsmokers

Study	Setting	Number of subjects			Particle mass, µg/m^3		Particle mass due to ETS
		Total	No ETS exp.	ETS exp.	X (±SD)	Range	µg/m^3
Spengler et al., 1981	24-hr. day	45			NR	NR	20[a]
Spengler et al., 1985	24-hr. day	101			NR	NR	
			28		NR	NR	28[a]
				73	NR	NR	
Sexton et al., 1984	24-hr. day	48			NR	NR	
			NR		31.7	NR	18.4[1]
				NR	50.1	NR	
Coultas et al., 1990a	Workplace	15			63.9±41.5	4.0-145.8	
			1		4.0		64[2]
				14	68.2±39.5	14.7-145.8	
Schenker et al., 1990	Workplace				86		[3]

[1]Calculated by authors from the regression line.
[2]Calculated from data presented, after the method of Leaderer and Hammond (1991).
[3]Calculated from nicotine exposure, after the method of Leaderer and Hammond (1991).

NR = not reported.

buildings, occupational, etc.), while two studies report exposures for the workplace only. Individuals reporting exposure to ETS have substantially higher integrated exposures to RSP than those reporting no exposure. Passive smoke exposure resulted in increases in personal RSP exposures of 18-64 $\mu g/m^3$. It is difficult to assess the ETS contribution to personal RSP levels for each indoor environment for the 24-hour RSP personal exposures. The contribution of each indoor environment must be substantially higher than the 24-hour averages presented, because exposures presumably did not occur during sleeping hours or in all microenvironments. Table 3-6 demonstrates that the contribution of ETS-related RSP in the work environment to personal exposure is important and variable.

The most extensive study of personal exposure to RSP clearly demonstrates the impact on RSP levels from ETS (Spengler et al., 1985). In this study, outdoor, indoor, and personal 24-hour concentrations of RSP (particle diameter $\leq 3.5\ \mu m$) were obtained for a sample of 101 nonsmoking individuals. Of the 101 nonsmokers, 28 persons reported some exposure to ETS in either the home or workplace, while 73 reported no ETS exposure. The cumulative frequency distributions of RSP for the ETS-exposed and non-ETS-exposed individuals and measured outdoor levels are shown in Figure 3-13. Those reporting ETS exposure had mean personal RSP levels 28 $\mu g/m^3$ higher than those reporting no ETS exposure (Table 3-6). A larger variation in RSP concentrations was also seen for those reporting ETS exposure.

Figure 3-13. Cumulative frequency distribution of respirable suspended particle mass (RSP) concentrations from central site ambient and personal monitoring of smoke-exposed and nonsmoke-exposed individuals.

Source: Spengler et al., 1985.

3.3.2. Biomarkers of ETS Exposure

Biomarkers of exposure are actually measures of dose or uptake and hence indicators that an exposure has taken place. Biomarkers, within the context of assessing exposure to air contaminants, refer to cellular, biochemical, or molecular measures obtained from biological media such as human tissues, cells, or fluids that are indicative of human exposure to air contaminants (NRC and Committee on Biological Markers, 1986; NRC, 1986; Hulka et al., 1990). The relationship between the biomarker and exposure, however, is complex and varies as a function of several factors, including environmental factors and the uptake, distribution, metabolism, and site and mode of action of the compound or compounds of interest.

Ideally, a biomarker of exposure for a specific air contaminant should be chemically specific, have a long half-life in the body, be detectable in trace quantities with high precision, be measurable in samples easily collected by noninvasive techniques, be inexpensive to assay, be either the agent associated with the effects or strongly associated with the agent of interest, and be quantitatively relatable to a prior exposure regimen. Ideal biomarkers for air contaminants, like markers for complex mixtures, do not exist.

Numerous biomarkers have been proposed as indicators for ETS (e.g., thiocyanate, carboxyhemoglobin, nicotine and cotinine, *N*-nitrosoproline, aromatic amines, protein or DNA adducts) (NRC, 1986; U.S. DHHS, 1986). While these biomarkers demonstrate that an exposure has taken place, they may not be directly related to the potential for developing the adverse effect under study (i.e., not the contaminant directly implicated in the effect of interest), they can show considerable variability from individual to individual, and they represent only fairly recent exposure (potentially inadequate for chronic outcomes). Furthermore, some of these markers may not be specific to ETS exposure (e.g., carboxyhemoglobin) while others (e.g., thiocyanate) may not be sensitive enough for ETS exposures.

Nicotine and its metabolite, cotinine, in the saliva, blood, and urine are widely used as biomarkers of active smoking and exposure to ETS and are valuable in determining total or integrated short-term dose to ETS across all environments (NRC, 1986; U.S. DHHS, 1986). Nicotine and cotinine are specific to tobacco and are accurately measured by gas chromatography, radioimmunoassay, or high pressure liquid chromatography in concentrations down to 1 ng/mL. Nicotine has a half-life of about 2 hours in the blood and is metabolized to cotinine and excreted in the urine. The short half-life of nicotine makes it a better indicator of very recent exposures than of integrated exposure.

Cotinine in saliva, blood, and urine is the most widely accepted biomarker for integrated exposure to active smoking or ETS (NRC, 1986; U.S. DHHS, 1986). Cotinine is the major metabolite of nicotine, is specific to tobacco, and has a longer half-life for elimination from the body. The elimination half-life in smokers is approximately 20 hours (range of 10 to 37 hours), but it is typically longer in nonsmokers with ETS exposure, particularly in children (Figure 3-14) (Collier et al., 1990; Elliot and Rowe, 1975; Goldstein et al., 1987; Etzel et al., 1985; Greenberg et al., 1984). The half-life of cotinine makes it a good indicator of integrated ETS exposure over the previous day or two. Laboratory studies of nonsmokers exposed to acute high levels of ETS over varying times have shown significant

uptake of nicotine by the nonsmokers and increases in their cotinine levels (NRC, 1986; U.S. DHHS, 1986; Hoffman et al., 1984; Russell and Feyerabend, 1975).

Cotinine, however, is not an ideal biomarker for ETS, and caution in its use has been suggested (Idle, 1990). Cotinine is only one of the metabolites of nicotine (trans-3′-hydroxycotinine has recently been identified as the major metabolite [Neurath et al., 1988]), and it shows considerable intersubject variability in controlled nicotine exposure studies (Idle, 1990). The assumption that nicotine is specific to tobacco has recently been questioned (Idle, 1990; Sheen, 1988; Castro and Monji, 1986; Davis et al., 1991). Plant sources other than tobacco, primarily from the Solanaceae family, which are common dietary components have been suggested as sources (e.g., eggplant, tomato, and green pepper). It has been suggested that nicotine in food is a natural defense against bacteria, fungi, insects, and animals (Ames, 1983).

Figure 3-14. Average cotinine $t_{1/2}$ by age groups.

Source: Collier et al., 1990.

Tea has been identified as a particularly high source of dietary nicotine (Sheen, 1988). The impact of dietary nicotine, particularly tea, on cotinine levels of nonsmokers was evaluated in a study of 3,383 men and women 40-59 years of age as part of the Scottish Heart Health Study (Tunstall-Pedoe et al., 1991). The study found a small but inconsistent effect on serum cotinine levels with consumption of 10 or more cups of tea per day with no effect for consumption rates at fewer than 10 cups per day. The authors concluded that "cotinine levels in true nonsmokers reflect far more the nicotine in inhaled ambient tobacco smoke than they do nicotine in tea."

In the most detailed evaluation of nicotine in food, Davis et al. (1991) measured nicotine in a number of teas and foods. They found nicotine levels ranging from less than detectable to 285 ng/g wet weight. The authors calculated that with consuming average quantities of tomatoes, potatoes, cauliflower, and black tea, the average

contribution to urinary cotinine levels would be 0.6 ng/mL. High consumption of the foods and tea might result in a maximum urinary cotinine level of 6.2 ng/mL. The average contribution of dietary nicotine intake to urinary cotinine levels might be expected to be below 1 ng/mL and somewhat higher under conditions of high consumption of nicotine-containing foods.

Several population-based studies examined cotinine levels in smokers, nonsmokers reporting passive smoke exposure, and nonsmokers reporting no passive smoke exposure (NRC, 1986; U.S. DHHS, 1986; Greenberg et al., 1984; Wald et al., 1984; Wald and Ritchie, 1984; Jarvis et al., 1985; Coultas et al., 1987; Riboli et al., 1990; Cummings et al., 1990; Tunstall-Pedoe et al., 1991). These studies found that exposure to ETS is highly prevalent even among those living with a nonsmoker (e.g., Cummings et al., 1990). Saliva, serum, and urine cotinine levels in ETS-exposed nonsmokers are generally higher than those in nonsmokers reporting no ETS exposure, and levels of cotinine are considerably higher in smokers than those in nonsmokers passively exposed (e.g., Table 3-7). Cotinine levels in nonsmokers exposed to ETS are approximately 1% of the levels in active smokers. Cotinine levels of nonsmokers have been found to increase with self-reported ETS exposure (e.g., Figures 3-15 and 3-16).

In a 10-country study of ETS exposure of 1,369 nonsmoking women (Riboli et al., 1990), average urinary levels of cotinine/creatinine by country ranged from approximately 2.5 ng/mg for Shanghai to approximately 14 ng/mg for Trieste. Eighty percent of those sampled had a detectable level of cotinine. Statistically significant differences were observed between centers with lowest values observed in Honolulu, Shanghai, and Chandigarh and the highest values in Trieste, Los Angeles, and Athens. This study also found an increase in cotinine/creatinine levels from the group of women reporting no ETS exposure either at home or work (lowest exposure) to the group reporting ETS exposure both at home and at work, the highest exposure group

Table 3-7. Approximate relations of nicotine as the parameter between nonsmokers, passive smokers, and active smokers

Nicotine/cotinine	Nonsmokers without ETS exposure (N = 46)		Nonsmokers with ETS exposure (N = 54)		Active smokers (N = 94)
	Mean value	% of active smokers' value	Mean value	% of active smokers' value	Mean value
Nicotine (ng/mL):					
in plasma	1.0	7.0	0.8	5.5	14.8
in saliva	3.8	0.6	5.5	0.8	673
in urine	3.9	0.2	12.1[1]	0.7	1,750
Cotinine (ng/mL):					
in plasma	0.8	0.3	2.0[1]	0.7	275
in saliva	0.7	0.2	2.5[2]	0.8	310
in urine	1.6	0.1	7.7[2]	0.6	1,390

[1]Differences between nonsmokers exposed to ETS compared with nonsmokers without exposure: $p < 0.01$.
[2]Differences between nonsmokers exposed to ETS compared with nonsmokers without exposure: $p < 0.001$.

Source: Jarvis, 1987.

Figure 3-15. Distribution of individual concentrations of urinary cotinine by degree of self-reported exposure to ETS. Horizontal bars indicate median values.

Source: Jarvis and Russell, 1985.

Figure 3-16. Urinary cotinine concentrations by number of reported exposures to tobacco smoke in the past 4 days among 663 nonsmokers, Buffalo, New York, 1986.

Source: Cummings et al., 1990.

(Figure 3-17). The group of women reporting ETS exposure only at home had cotinine/creatinine levels approximately 60% of those who reported exposure both at home and at work.

Urinary cotinine levels also were found to increase with the number of questionnaire-reported ETS exposures in a group of 663 never-smokers and ex-smokers (Cummings et al., 1990). In that study, 76% of the subjects reported passive smoke exposure in the 4-day period preceding the sampling. Of the total sample, 91% had detectable cotinine levels. Among the 76% reporting ETS exposure, 28% reported exposure at work, 27% at home, 16% in restaurants, 11% at social gatherings, 10% in a car or airplane, and 8% in public buildings. Cotinine levels in this study were also found to vary by month, with the winter months being associated with higher levels and corresponding to higher reported exposures.

Cotinine values in smokers and nonsmokers measured in both the laboratory or field setting show considerable variability due to individual differences in the uptake, distribution, metabolism, and elimination of nicotine. Another issue to be considered in interpreting the field data is that exposure status is determined by respondent self-reporting. This can lead to a misclassification error, which tends to reduce the differences in cotinine levels measured in the ETS-exposed versus non-ETS-exposed groups and to increase the variability in the levels within any exposure category. Within the exposed group, this misclassification error could either increase or decrease the average cotinine levels measured.

It is important to recognize that nicotine and cotinine are actually proxy biomarkers. They may not be the active agents in eliciting the adverse effect under study but merely indicative of the level of passive smoke exposure. Using these measures to estimate cigarette equivalents or determine equivalent active smoking exposure could result in over- or underestimating exposure to individual or classes of compounds that may be more directly related to the health or nuisance effect of concern. Use of different biomarker proxies (e.g., protein adducts) could result in estimates of much larger cigarette equivalent doses.

Nevertheless, nicotine and cotinine levels in ETS-exposed nonsmokers measured in laboratory and field studies have been used to estimate cigarette equivalent exposures and to equate ETS exposures with active smoker exposures (NRC, 1986; U.S. DHHS, 1986; Jarvis, 1989). On an equivalent cigarette basis, an upper-bound estimate of nicotine dose of 2.5 mg/day for a passive smoke exposure has been proposed (Jarvis, 1989). This would translate into the equivalent of about one-fifth of a cigarette per day or about 0.7% of the average smoker's dose of nicotine (cigarette equivalent dose of other toxins or carcinogens would be different--see above). Comparisons of cotinine values in ETS-exposed nonsmokers with those measured in smokers ranged from 0.1% to 2%. One analysis proposed that, on average, nonsmokers' cotinine levels are 0.5%-0.7% of those found in cigarette smokers (Jarvis, 1989). It should be noted that these

Figure 3-17. Average cotinine/creatinine levels for subgroups of nonsmoking women defined by sampling categories of exposure or by self-reporting exposure to ETS from different sources during the 4 days preceding collection of the urine sample.

Source: Riboli et al., 1990.

estimations are based on a number of assumptions that may not hold (e.g., the half-life of nicotine and cotinine in smokers and nonsmokers being the same).

One of the protein adducts used as a biomarker of active and passive smoking is the 4-aminobiphenyl adduct of hemoglobin. One advantage of hemoglobin adducts is that their half-life is quite long and they will persist through the life of a red blood cell, which is approximately 120 days. Therefore, levels of 4-ABP-Hb adducts reflect exposures over the past several weeks, rather than the day or two of exposure integration reflected by cotinine measurements.

Tobacco smoke is the primary environmental source of 4-aminobiphenyl (its use in the dye industry was discontinued decades ago), and smokers have between 5 and 8 times as much 4-ABP-Hb adducts as nonsmokers (Hammond et al., 1990; Perera et al., 1987; Maclure et al., 1989). That nonsmokers appear to have approximately 10-20% the adduct level as smokers may at first appear to be contradictory to the urinary cotinine ratios of about 1%, but in fact both results are quite consistent with our knowledge of the emissions of various contaminants in mainstream and sidestream smoke. Approximately twice as much nicotine is emitted in sidestream as in mainstream smoke, but about 31 times as much 4-ABP is emitted in SS as in MS. Thus, compared to MS, SS is 15 times more enriched in 4-ABP than in nicotine. Similarly, the ratio of biomarkers in those exposed to ETS compared with smokers is roughly 15 times greater for the biomarker 4-ABP-Hb adducts than for the biomarker cotinine, a metabolite of nicotine.

The above discussions indicate that the cigarette equivalent dose of those exposed to ETS varies with the compound, so that a passive smoker may receive 1% as much nicotine as an active smoker but 15% as much 4-ABP. These examples demonstrate the importance of careful interpretation of biomarkers in estimating doses.

3.3.3. Questionnaires for Assessing ETS Exposures

Questionnaires are the most commonly used method to assess exposure to ETS in both retrospective and prospective studies of acute and chronic effects. They are the least expensive method to obtain ETS exposure information for large populations. They can be used to provide a simple categorization of ETS exposure, to determine time-activity patterns of individuals (e.g., how much time is spent in environments where smoking occurs), and to acquire information on the factors or properties of the environment affecting ETS concentrations (e.g., number of cigarettes smoked, size of indoor environments, subjective evaluation of level of smokiness). The time-activity pattern information is combined with measured or estimated concentrations of ETS in each environment to provide an estimate of total exposure. Information on the factors affecting ETS concentrations is used to model or predict ETS levels in those environments.

Questionnaires are used most extensively to provide a simple categorization of potential ETS exposure (e.g., do you live with a smoker?, are you exposed to ETS at your place of work?, how many hours a week are you exposed to ETS?) and to obtain information on possible confounders (e.g., occupational history, socioeconomic status). When used simply to determine a dichotomous exposure (ETS-exposed vs. unexposed), any misclassification tends to bias measures of association toward the null. Thus, any effect that may be present will be underestimated or even may not

be detectable. If there are more than two exposure categories (e.g, light, medium, or heavy exposure), the intermediate categories of exposure may be biased either away from or toward the null. Misclassification errors may arise from respondents' (1) lack of knowledge, (2) biased recall, (3) memory failure, and (4) intentional alteration of information. Additionally, there are investigator-based sources of misclassification. Errors may arise if semiquantitative levels are incorrectly imputed to answers; e.g., even if house exposures are higher than occupational exposures on average, for any given individual the ranking may well be reversed from that of the average.

In using questionnaires to assess exposure categories to ETS, to determine time-activity patterns, and to acquire information on the factors affecting concentrations, it is important to minimize the uncertainty associated with the estimate and to characterize the direction and magnitude of the error.

Unlike for active smoking assessment, standardized questionnaires for assessing ETS exposures in prospective or retrospective studies of acute or chronic health or nuisance effects do not exist. Lebowitz et al. (1989) reported on an effort to develop a standardized questionnaire to assess ETS exposure in various indoor environments. This questionnaire, however, has not yet been validated. Questionnaires used to assess ETS exposure typically have been developed for specific studies and have not been validated for general use. There is no "gold standard" with which to validate the questionnaires. Various strategies, however, have been used to assess the validity of diverse types of questionnaires used to assess ETS exposure. Efforts to validate questionnaires have used survey data, air monitoring of nicotine in various microenvironments, and nicotine or cotinine in body fluid samples.

A recent study (Leaderer and Hammond, 1991) of 96 homes using a questionnaire to assess residential smoking and a passive nicotine air monitor found that 13% of the residences reporting no smoking had measurable levels of nicotine while 28% of the residences reporting smoking had nondetectable levels of nicotine. A good level of agreement between questionnaire-reported number of cigarettes smoked and residential levels of ETS-related RSP and nicotine was observed in this study (Figures 3-12a and 3-12b).

Studies (Marbury et al., 1990; Coghlin et al., 1989; Coultas et al., 1987, 1990a, 1990b; Riboli et al., 1990; Cummings et al., 1990) comparing various measures of ETS exposure (location of exposure, intensity of exposure, duration of exposure, number of cigarettes smoked, etc.) with cotinine levels measured in physiological fluids generally meet with only moderate success (explained variations on the order of 40% or less). The largest such study (Riboli et al., 1990) was a collaborative effort conducted in 10 countries; correlations in the range of 0.3 to 0.51 ($p < 0.01$) were found between urinary cotinine levels and various measures of exposure derived from questionnaire data. Using cotinine as a biomarker of exposure, studies indicated that a substantial percentage of those reporting no ETS exposure by questionnaire do have measurable exposure. Differences in the uptake, metabolism, and excretion of nicotine among individuals make it difficult to use this measure as a "gold standard" in validating questionnaires. Also, the recent exposure (previous 1-2 days) that is measured by cotinine may differ from usual exposure.

In a study involving 10 homes with 20 nonsmoking and 11 homes with smoking residents, the variability of four markers of ETS exposure (questionnaires, cotinine in saliva and urine, respirable suspended particle mass in air, and nicotine in air) was assessed (Coultas et al., 1990b). Questionnaire-reported exposures explained less than 10%

of the variability in air concentrations of suspended particle mass and nicotine, 8% of the variability in urinary cotinine, and 23% of the variability in saliva cotinine. The authors concluded that multiple exposure assessment measurement tools were needed to assess ETS exposure in the home.

In one effort to develop a validated questionnaire (Coghlin et al., 1989), 53 subjects were asked detailed questions about their exposures to ETS, including location of exposures, number of smokers, ventilation characteristics, number of hours exposed, proximity of smokers, and intensity of ETS. They then wore a passive sampler for nicotine for 7 days and recorded the same information regarding each exposure episode in daily diaries. Formulae were developed to score the exposures on both the questionnaire and the diary, and these scores were then correlated to the average nicotine concentrations measured over the 7-day period. Excellent correlation was found (r^2 = 0.83 for the questionnaire and 0.90 for the diary). However, the simple questions that have been used most frequently in epidemiologic studies, such as whether a subject lived with a smoker or the number of hours the subject was exposed, were not nearly as well correlated with the measured exposures. These results indicate that reliable questionnaires can be developed, but that those used in most studies in the past will lead to some random misclassification of exposure, and, hence, underestimation of any effect that may be present.

More recently, epidemiologic studies of acute and chronic respiratory effects in children associated with ETS exposure have utilized questionnaires in combination with measurements of cotinine levels in physiologic fluids (Ehrlich et al., 1992; Reese et al., 1992; Etzel et al., 1992). The studies provide more of a direct link between questionnaire-assessed exposures and objective measures of exposure and disease. Such studies, discussed in Chapter 8, not only provide a means of validating questionnaires but also provide data to establish validation of the risk models used in Chapter 8.

ETS exposures take place across a number of environments, with an individual's total exposure being a function of the amount of time spent in each environment and the concentration in that environment. Questionnaires need to assess exposures across indoor environments. Personal air monitoring provides a method to validate ETS exposure assessment questionnaires and to assess the contribution of each environment to total current exposure.

Personal air monitoring and cotinine measurements in combination with questionnaires have highlighted the importance of obtaining information on spouses' smoking status, smoking at home, smoking at work, smoking in various other indoor environments (social settings, vehicles, public places, etc.), amount of time in environments where smoking occurs, and the intensity of the exposure (Marbury et al., 1990; Coghlin et al., 1989; Coultas et al., 1987, 1990a, 1990b; Riboli et al., 1990; Cummings et al., 1990).

3.4. SUMMARY

ETS is a major source of indoor air contaminants. The ubiquitous nature of ETS in indoor environments indicates that some unintentional inhalation of ETS by nonsmokers is virtually unavoidable. ETS is a dynamic complex mixture of over 4,000 chemicals found in both vapor and particle phases. Efforts to characterize the physical and chemical properties of SS emissions, the principal component of ETS, have found that: (1) MS and SS emissions

are qualitatively very similar in their chemical composition, containing many of the same carcinogenic and toxic compounds, (2) several of these compounds, including five known human carcinogens, nine probable human carcinogens, three animal carcinogens, and several toxic agents, are emitted at higher levels in SS than MS smoke (sometimes by an order of magnitude or more); (3) SS emissions of these notable air contaminants demonstrate little variability among brands of cigarettes. The enrichment of several known or suspected carcinogens in SS relative to MS smoke suggests that the SS contaminant mix may be even more carcinogenic than the MS mix, per unit of tobacco burned.

Sidestream emissions, while enriched in several notable air contaminants, are quickly diluted into the environment where ETS exposures take place. Air sampling conducted in a variety of indoor environments has shown that nonsmoker exposure to ETS-related toxic and carcinogenic substances will occur in indoor spaces where there is smoking occupancy. Individuals close to smokers (e.g., an infant in a smoking parent's arms) may be directly exposed to the plume of SS or exhaled MS, and thus be more heavily exposed than indoor measurements from stationary air monitors might indicate.

Given the complex nature of ETS, it is necessary to identify marker or proxy compounds that when measured will allow for the quantification of exposure to ETS. Vapor phase nicotine and respirable suspended particle mass are two such markers that are suitable indicators of exposure to ETS. Nicotine and RSP have been measured in personal monitoring studies and in studies of a variety of indoor environments. The results of these studies clearly demonstrate that reported exposure to ETS, even under the conditions of low frequency, duration, and magnitude, will result in RSP and nicotine values above background. These studies indicate that ETS exposures take place in a wide range of environments (residences, workplaces, restaurants, airplanes, etc.,) where smoking occurs. Indoor levels of RSP and vapor phase nicotine have been shown to vary in a linear fashion with reported tobacco consumption. Nicotine levels measured indoors have ranged from less than 1 $\mu g/m^3$ to over 500 $\mu g/m^3$, while RSP levels have ranged from less than 5 $\mu g/m^3$ to over 1 mg/m^3. Nicotine exposures greater than 100 $\mu g/m^3$ are exceedingly rare; most environments measured have ranged from less than 0.3 (smoke free) to 30 $\mu g/m^3$; bars and smoking sections of planes may reach 50-75 $\mu g/m^3$. Thus, the normal range of ETS exposures is approximately 100-fold: 0.3 to 30 $\mu g/m^3$ for nicotine and from 5 to 500 $\mu g/m^3$ for RSP.

In residences with smoking occupancy, average daily or weekly nicotine values might typically range from less than 1 to 10 $\mu g/m^3$, varying principally as a function of number of smokers or number of cigarettes smoked. Average daily or weekly residential concentrations of ETS-associated RSP could be expected to increase from 18 to 95 $\mu g/m^3$ (added to background levels) in homes where smoking occurs. Like nicotine, ETS-associated RSP increases with increased smoking. Average levels of nicotine and RSP in offices with smoking occupancy are roughly comparable to those in homes.

Cotinine in saliva, blood, and urine, while not an ideal biomarker, is the most widely accepted biomarker of ETS exposure. Cotinine is an excellent indicator that ETS exposure has taken place. It also establishes the link between exposure and uptake. Studies show that cotinine levels correlate with levels of ETS exposure. The available

data also indicate that as many as 80% of nonsmokers are exposed to ETS and that there is variability in average exposure levels among nonsmokers in different geographical regions.

Although average cotinine levels are a useful indicator of relative doses of ETS among different groups of nonsmokers, the ratio of cotinine levels in nonsmokers versus smokers may not be indicative of the exposure ratio for the active agents in ETS and MS responsible for the adverse effects. For example, while comparisons of cotinine levels in smokers and nonsmokers have led to estimates that ETS-exposed nonsmokers receive from 0.1 to 0.7% of the dose of nicotine of an average smoker, ETS-exposed nonsmokers may receive 10-20% of the dose of 4-ABP that smokers inhale.

Questionnaires are the most commonly used method to assess exposure to ETS in both retrospective and prospective studies of acute and chronic effects. They have been used not only to establish simple categories of ETS exposure but also to obtain information on activity patterns of exposed individuals and on environmental factors affecting concentrations in different indoor environments. No standardized or validated questionnaires have yet been developed for assessing ETS exposure. A number of studies have compared questionnaire responses to measured air concentrations of nicotine and RSP and to cotinine levels. These efforts have indicated that a significant percentage of individuals reporting no exposure had actually been exposed. In general, questionnaires had moderate success in assessing exposure status and level of exposure. Misclassification errors must be addressed when using questionnaires to assess ETS exposure.

In summary, ETS represents an important source of toxic and carcinogenic indoor air contaminants. The available data suggest that exposure to ETS is widespread, with a wide range of exposure levels.