this Paper, the health effects literature is described and evaluated using conventional standards of evidence accepted by the scientific community, and in relation to any specific standards that have been developed for the purposes of regulating environmental or occupational hazards. Those standards, in general, appropriately allow action to be taken with lesser information, and do not necessarily require extensive epidemiologic evidence. For instance, proof of adverse health effects in well designed animal experiments, coupled with evidence that people are exposed to an agent, is sufficient to trigger regulatory action under a number of statutes (e.g., Occupational Safety and Health Act; Federal Food, Drug, and Cosmetic Act; Clean Air Act).

CHARACTERIZING PASSIVE EXPOSURE TO TOBACCO SMOKE

It has been relatively easy to approximate relative exposure levels among smokers to cigarette smoke as the number of cigarettes smoked per day and the number of years that the person has smoked. Quantifying passive exposure of nonsmokers to cigarette smoke is more difficult. One part of the effort to characterize exposure of nonsmokers has been to measure the concentrations of cigarette smoke constituents in indoor environments and to determine the contributions of "sidestream" and "mainstream" smoke to "environmental" tobacco smoke. There have been about two dozen investigations of environmental tobacco smoke constituents, including both controlled studies in special experimental chambers and measurements in the air of smoky restaurants, bars, and nightclubs, and other smoky, enclosed spaces. A second and more recent thrust has been to test the body fluids--blood, urine, and saliva--of passively exposed nonsmokers for elevated levels of tobacco smoke constituents or their metabolizes (smoke constituents modified within the body to become different chemical entities).

Mainstream, Sidestream, and Environmental Smoke

Mainstream smoke is the tobacco smoke that is generated during a puff and is drawn

through the butt end into the smoker's respiratory system. Sidestream smoke comes directly from the burning end of the cigarette, cigar, or pipe. Environmental tobacco smoke refers to what passive smokers are actually exposed to. Smokers, of course, are exposed to both mainstream and environmental smoke.

A smoker's exposure results primarily from the mainstream smoke drawn into the lungs. Non-smokers are exposed primarily to sidestream smoke (nearly 85 percent of the smoke in a room is sidestream smoke) and to smaller amounts of exhaled mainstream smoke, smoke that comes from the nonburning end of the cigarette but is not inhaled by the smoker, and smoke that diffuses through the paper wrapper of the cigarette.

Researchers have designed laboratory apparatus to measure the amounts of the various substances contained in sidestream and mainstream smoke. The instruments measure the concentrations in the smoke immediately after it leaves the butt end (mainstream smoke) or the burning end (sidestream smoke) of the cigarette. Measured in this fashion, the concentrations of many toxic substances in captured sidestream smoke are greater than those found in mainstream smoke, e.g., tar, nicotine, benzo[a]pyrene (for a detailed discussion of this topic, see NRC, 1981). This is because different amounts of tobacco are burned when producing mainstream and sidestream smoke, the tobacco's burning temperature is different during puffing compared to when it is only smoldering, and some substances are absorbed by the tobacco and filter as the mainstream smoke passes through.

Because smoke is diluted by air in a room, the exposures of nonsmokers are much less than the measured concentrations of toxic substances in sidestream or mainstream smoke as they emerge directly from the cigarette. In addition to the effects of dilution, environmental tobacco smoke differs somewhat from mainstream and sidestream smoke as a result of chemical and physical changes that occur as mainstream and sidestream smoke cool and react in the air. A number of researchers, including, notably, Repace and Lowrey and their colleagues, over the

years, have documented the significant contribution of environmental tobacco smoke to indoor air pollution in studies in enclosed spaces (summarized in Repace and Lowrey, 1985b).

For example, the largest particles in sidestream smoke tend to settle out of the air and some gases react to form different substances. While the differences between what smokers and nonsmokers are exposed to have been frequently emphasized, they are not so great as to require a conclusion that sidestream smoke is dramatically different from mainstream smoke.

Measurements of Specific Constituents of Environmental Tobacco Smoke

More than 2,000 constituents of environmental tobacco smoke have been identified; many of these substances cause cancer in experimental animals (NRC, 1981). The National Research Council Committee on Indoor Pollution concluded that passive smoking constituted the "principal source of exposure to many of these compounds" for many people (NRC, 1981). The most frequently-measured products of cigarette smoke in indoor air are carbon monoxide and particulate; other constituents such as dimethylnitrosamine, benzo[a]pyrene, and nicotine, have been measured less frequently. Polonium 210, a radioactive isotope, is also present in environmental tobacco smoke. This literature is reviewed in the 1981 National Research Council study, *Indoor Pollutants* (NRC, 198 1), and in the 1984 Surgeon General's Report on Chronic Obstructive Lung Disease (USDHHS,1984).

Measurements of environmental tobacco smoke usually distinguish between the gaseous phase and the particulate phase, which consists not only of particles, but some other compounds that adhere to the particles. Investigations with the aim of characterizing levels of exposure, rather than the makeup of the smoke, have chosen to measure one or more compounds thought to be representative of smoke levels. The appropriate constituents to measure differ for particulate, which tend to settles out more quickly, and the gaseous phase, which remains for

relatively long periods. The characteristics of enclosed spaces, such as their size and particularly their ventilation, affect the fate of cigarette smoke and therefore the opportunity for passive **exposure** to smoke.

Carbon monoxide is an easily measured combustion product of burning tobacco, and the most frequently quantified component of the gaseous phase. Carbon monoxide is generated by sources of combustion other than burning tobacco, such as automobiles and gas cooking. The Occupational Safety and Health Administration has set a workplace permissible exposure limit of 50 parts per million (ppm) averaged over eight hours. In 1972, the National Institute for Occupational Safety and Health recommended a 10-hour average limit of 35 ppm, and a ceiling limit of 200 ppm. The Environmental Protection Agency National Primary Ambient-Air Quality Standard one-hour limit for carbon monoxide in outdoor air is 35 ppm, and their eight-hour standard, an average limit, is 9 ppm; both limits may be exceeded only once per year.

Carbon monoxide levels in areas where people have been smoking are consistently higher than in "control" areas, which can be outdoors in some cases or indoor spaces where there has been no smoking. Levels of between 10 ppm and 20 ppm often occur in areas such as nightclubs, taverns, and automobiles. Most measurements reported in restaurants are in the range of 5 to 10 ppm. Control levels range from 1 to 3 ppm.

Acrolein is the gaseous constituent responsible for most of the odor associated with cigarette smoke, and also may cause eye and throat irritation. Levels of acrolein found in enclosed spaces under conditions of heavy smoking have exceeded the levels recommended in industrial conditions (NRC, 1981).

Nicotine is found in both the gaseous phase and the particulate phase, and is technically difficult to measure. A few studies have quantified nicotine concentrations, however, showing significant increases over background levels.

A more common measurement has been of total particulates, which also are elevated in areas where people have been smoking. In one study of 69 homes in six cities, average particulate concentrations were 43 micrograms per cubic meter (ug/m^3) of air in homes with one cigarette smoker; 75 ug/m^3 in homes with two or more smokers; compared with 24 ug/m^3 in homes without smokers and 22 ug/m^3 outdoors (Spengler et al., 1981, cited in NRC, 1981). Measures of total particulate may include a great deal of material not associated with tobacco smoke, however, and are influenced by a wide variety of factors, including the number of people in a room. A measure of total particulate, therefore, may not be as useful as some of the more specific indicators of the level of environmental tobacco smoke.

Other gaseous constituents that have been measured and found elevated in smoky conditions are nitrogen oxides, nitrosamines, carbon dioxide, methane, acetylene, ammonia, hydrogen cyanide, methylfuran, acetonitrile, and pyridine. Tar, water, toluene, phenol, methylnaphthalene, pyrene, benzo[a]pyrene, aniline and naphthylamine, constituents of the particulate phase, also are elevated in smoky conditions.

Biologic Markers of Passive Exposure to Tobacco Smoke

Certain constituents of tobacco smoke are measurable, some easily so, in the blood, urine, and saliva of smokers. These indicators have been used, for instance, to verify self-reported smoking status, especially among people who claimed to have stopped smoking. In nonsmokers, these same indicators have been used in a number of studies to estimate exposure levels of nonsmokers to varying amounts of environmental tobacco smoke. This is an area of continuing development.

When carbon monoxide is inhaled, it enters the bloodstream via the lungs. Carbon monoxide has an extremely strong affinity for the hemoglobin molecules contained in red blood cells, more than 200 times stronger than the affinity of oxygen molecules for hemoglobin, and

competes successfully with oxygen for carriage on the hemoglobin molecule. (At very high doses, carbon monoxide is lethal, as it displaces so much oxygen that the tissues become oxygen-starved.) The combination of carbon monoxide and hemoglobin is a molecule called "carboxyhemoglobin," which can be measured in blood. Studies have shown increases in carboxyhemoglobin after exposure to environmental tobacco smoke, which are, as expected, smaller than changes recorded after direct smoking. With a half life of about four hours in blood, carboxyhemoglobin is a good indicator of acute exposure to cigarette smoke (or other types of combustion), but is not a good indicator of chronic exposure (USDHHS, 1984).

Serum thiocyanate (SCN), the metabolize of hydrogen cyanide, a constituent of tobacco smoke, has also been used to verify self-reported smoking status, and has been used in a few studies of nonsmokers' environmental smoke exposure. The value of SCN measurements is limited by many factors unrelated to smoke exposure that influence levels of thiocyanate in the blood.

Nicotine is the most tobacco-specific constituent in smoke that occurs in relatively large quantities. It is possible to measure nicotine in body fluids, but its half life of about 30 minutes makes nicotine unsuitable for estimating chronic exposure. Nicotine has been measured in the blood, urine, and saliva of nonsmokers under both experimental (Russell and Feyerabend, 1975, cited in Feyerabend, Higenbottam, and Russell, 1982) and in typical workplace conditions (Feyerabend, Higenbottam, and Russell, 1982). Under workplace conditions, Feyerabend, Higenbottam, and Russell (1982) found that all nonsmokers had detectable levels of nicotine in saliva and urine. Those nonsmokers who reported exposure to cigarette smoke had significantly higher levels than those who reported no exposure. There was some overlap of nicotine levels of exposed nonsmokers and levels in light smokers in the sample (smokers who had smoked three or fewer cigarettes before the sample was taken), but most of the overlap was with smokers who had not yet smoked a cigarette on the day the urine sample was taken.

Cotinine appears to be the most promising marker of passive smoke exposure (USDHHS, 1984; Jarvis et al., 1985). Cotinine, the major metabolize of nicotine, has a half life of 20 to 30 hours, so consistent, daily exposure to tobacco smoke should result in elevated levels of cotinine, as measured in blood, urine, or saliva (USDHHS, 1983). Cotinine levels have been measured in the blood and urine of smokers since the late 1970's, and correlate well with levels of smoking. A recent study in smokers (Sepkovic and Haley, 1985) indicates good correlation of cotinine levels and nicotine content of cigarettes smoked, and of changes in smoking habits. That study also points out that cotinine levels in blood, urine, and saliva may change at different rates over time and are not equally sensitive to changes in exposure.

Recently, studies of urine cotinine in nonsmokers have been carried out in attempts to measure passive exposure to cigarette smoke (Wald et al., 1984; Matsukura et al., 1984; Jarvis et al., 1985). Matsukura and colleagues (1984) found higher levels of urinary cotinine in Japanese nonsmokers passively exposed to tobacco smoke at home, at work, or in both locations, and the effects were dose related in both settings. They also compared cotinine levels in nonsmokers from rural areas with those from urban areas, and found that, for nonsmokers who did not live with smokers, levels were significantly lower for rural compared with urban dwellers. Nonsmokers with the highest urine cotinine levels were those exposed to the smoke of more than 40 cigarettes per day at home; those individuals had cotinine levels similar to those of smokers of up to three cigarettes per day. Jarvis and colleagues (1985) studied saliva cotinine in British schoolchildren, aged 11 to 16. They found a strong, statistically significant relationship between the smoking status of parents and cotinine levels in children, with the highest levels in children of two smoking parents.

Summary: Characterizing Passive Exposure

There is no doubt that tobacco smoking indoors contributes chemical and physical