3. Health-based Guidelines

In this chapter the key air pollutants, also termed "classic" air pollutants - SO_2, NO_2, CO, O_3, SPM and lead - are briefly described with respect to health risk evaluations and recommended guideline values. Particular emphasis is given to PM_{10} and $PM_{2.5}$. The information available for a number of other air pollutants (including inorganic compounds, organic volatile components and certain indoor air pollutants such as radon) is also summarized and presented in a synoptic table. These sections are based upon papers prepared for the updating of the *Air Quality Guidelines for Europe* (WHO 1999a) and exposure information obtained from various regions. A third section considers factors, such as altitude, humidity, temperature, nutritional status, health status, vulnerability etc., that affect the actual health impact of air pollutants on the individual and vulnerable groups.

3.1 Key air pollutants

Sulphur dioxide

Short-period exposures (less than 24 hours)

Most information on the acute effects of SO_2 comes from controlled chamber experiments on volunteers exposed to SO_2 for periods ranging from a few minutes up to one hour (WHO 1999a). Acute responses occur within the first few minutes after commencement of inhalation. Further exposure does not increase effects. Effects include reductions in the mean forced expiratory volume over one second (FEV_1), increases in specific airway resistance (sRAW), and symptoms such as wheezing or shortness of breath. These effects are enhanced by exercise that increases the volume of air inspired, as it allows SO_2 to penetrate further into the respiratory tract.

A wide range of sensitivity has been demonstrated, both among normal subjects and among those with asthma. People with asthma are the most sensitive group in the community. Continuous exposure-response relationships, without any clearly defined threshold, are evident. To develop a guideline value, the minimum concentrations associated with adverse effects in asthmatic patients exercising in chambers have been considered. An example of an exposure-response relationship for asthmatic patients is shown in Figure 3.1, expressed in terms of change in FEV_1 after a 15-minute exposure.

Exposure over a 24-hour period

Information on the effects of exposure averaged over a 24-hour period is derived mainly from epidemiological studies in which the effects of SO_2, SPM and other associated pollutants are considered. Exacerbation of symptoms among panels of selected sensitive patients seems to arise in a consistent manner when the concentration of SO_2 exceeds 250 µg/m^3 in the presence of SPM. Several more recent studies in Europe have involved mixed industrial and vehicular emissions now common in ambient air. At low levels of exposure (mean annual levels below 50 µg/m^3; daily levels usually not exceeding 125 µg/m^3) effects on mortality (total, cardiovascular and respiratory) and on hospital emergency admissions for total respiratory causes and chronic obstructive pulmonary disease (COPD), have been consistently demonstrated. These results have been shown, in some instances, to persist when black smoke and SPM levels were

controlled for, while in others no attempts have been made to separate the pollutant effects. In these studies no obvious threshold levels for SO_2 has been identified.

Long-term exposure

Earlier assessments examined findings on the prevalence of respiratory symptoms, respiratory illness frequencies, or differences in lung function values in localities with contrasting concentrations of SO_2 and SPM, using data from the coal-burning era in Europe. The lowest-observed-adverse-effect level of SO_2 was judged to be at an annual average of 100 µg/m^3, when present with SPM. More recent studies related to industrial sources of SO_2, or to the changed urban mixture of air pollutants, have shown adverse effects below this level. But a major difficulty in interpretation is that long-term effects are liable to be affected not only by current conditions, but also by the qualitatively and quantitatively different pollution of earlier years. However, cohort studies on differences in mortality between areas with contrasting pollution levels indicate that mortality is more closely associated with SPM, than with SO_2.

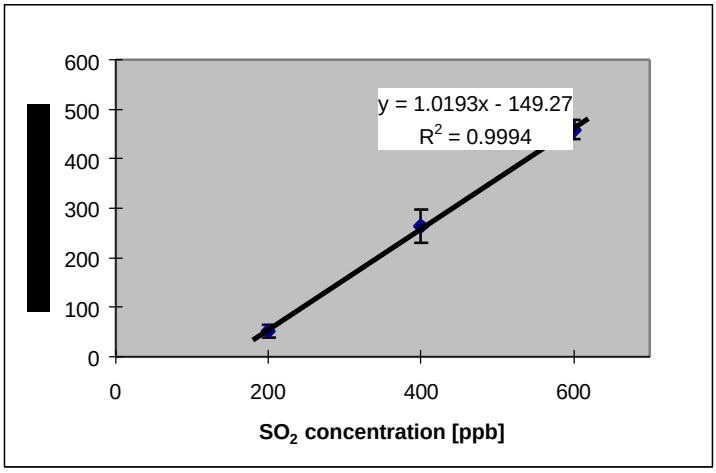

Figure 3.1 Mean change of FEV_1 in asthmatics with changing SO_2 concentrations

Guidelines

Based upon controlled studies with asthmatics exposed to SO_2 for short periods, it is recommended that a value of 500 µg/m^3 (0.175 ppm) should not be exceeded over averaging periods of 10 minutes. Because exposure to sharp peaks depends on the nature of local sources, no single factor can be applied to estimate corresponding guideline values over longer periods, such as an hour. Day-to-day changes in mortality, morbidity, or lung function related to 24-hour average concentrations of SO_2 are necessarily based on epidemiological studies, in which people are in general exposed to a mixture of pollutants; and guideline values for SO_2 have previously been linked with corresponding values for SPM. This approach led to a previous guideline 24-hour average value of 125 µg/m^3 (0.04 ppm) for SO_2, after applying an uncertainty factor of two to the lowest-observed-adverse-effect level. In more recent studies, adverse effects with significant public health importance have been observed at much lower levels of exposure. However, there is still uncertainty as to whether SO_2 is the pollutant responsible for the observed adverse effects, or whether it is a surrogate for SPM with diameters below 10 µm or 2.5µm, or even for some other correlated substance. There is no basis for numerical changes of the 1987 guideline values for SO_2 and thus 125 µg/m^3 for an averaging time of 24 hours and 50 µg/m^3 as an annual mean are recommended. However, the current guideline values are no longer linked

with SPM.

Nitrogen dioxide

Short-term exposure effects

Available data from animal toxicology experiments indicate that acute exposure to NO_2 concentrations of less than 1880 µg/m^3 (1 ppm) rarely produce observable effects. Normal healthy humans, exposed at rest or with light exercise for less than two hours to concentrations above 4700 µg/m^3 (2.5 ppm), experience pronounced decreases in pulmonary function; generally, normal subjects are not affected by concentrations less than 1880 µg/m^3 (1.0 ppm). One study showed that the lung function of subjects with chronic obstructive pulmonary disease is slightly affected by a 3.75-hour exposure to 560 µg/m^3 (0.3 ppm).

A wide range of findings in asthmatics has been reported. Asthmatics are likely to be the most sensitive subjects, although uncertainties exist in the health database. The lowest concentration causing effects on pulmonary function was reported from two laboratories that exposed mild asthmatics for 30-110 minutes to 565 µg/m^3 (0.3ppm) NO_2 during intermittent exercise. However, neither of these laboratories was able to replicate these responses with a larger group of asthmatic subjects. One of these studies indicated that NO_2 can increase airway reactivity to cold air in asthmatic subjects. At lower concentrations, the pulmonary function of asthmatics was not changed significantly.

NO_2 increases bronchial reactivity, as measured by the response of normal and asthmatic subjects following exposure to pharmacological bronchoconstrictor agents, even at levels that do not affect pulmonary function directly in the absence of a bronchoconstrictor. Some, but not all, studies show increased responsiveness to bronchoconstrictors at NO_2 levels as low as 376-565 µg/m^3 (0.2 to 0.3 ppm); in other studies, higher levels had no such effect. Because the actual mechanisms of effect are not fully defined and NO_2 studies with allergen challenges showed no effects at the lowest concentration tested (188 µg/m^3; 0.1 ppm), full evaluation of the health consequences of the increased responsiveness to bronchoconstrictors is not yet possible. Recent studies have shown an increased reactivity to natural allergens in the same concentration range. The results of repetitive exposures of such individuals, or the impact of single exposures on more severe asthmatics, are not known.

Long-term exposure effects

Studies with animals have clearly shown that several weeks to months of exposure to NO_2 concentrations of less than 1880 µg/m^3 (1ppm) causes a range of effects, primarily in the lung, but also in other organs such as the spleen and liver, and in blood. Both reversible and irreversible lung effects have been observed. Structural changes range from a change in cell type in the tracheobronchial and pulmonary regions (at a lowest reported level of 640 µg/m^3), to emphysema-like effects. Biochemical changes often reflect cellular alterations, with the lowest effective NO_2 concentrations in several studies ranging from 380-750µg/m^3.

NO_2 levels of about 940 µg/m^3 (0.5ppm) also increase susceptibility to bacterial and viral infection of the lung. There are no epidemiological studies that can be confidently used to quantify a long-term NO_2 exposure or concentration likely to be associated with the induction of unacceptable health risks in children or adults. Homes with gas cooking appliances have peak levels of NO_2 in the same range as levels causing effects in some animal and human clinical

studies. Epidemiological studies evaluating the effects of NO_2 exposures in such homes have been conducted. In general, epidemiological studies of adults and infants (less than 2years old) show no significant effect of the use of gas cooking appliances on respiratory illness; nor do the few available studies of infants and adults show any associations between pulmonary function changes and gas stove use. However, children 5-12 years old are estimated to have a 20% increased risk for respiratory symptoms and disease for each increase of 28 $\mu g/m^3$ NO_2 (2-week average), where the weekly average concentrations are in the range of 15-128 $\mu g/m^3$ or possibly higher. However, the observed effects cannot clearly be attributed to either the repeated short-term high level peak, or to long-term exposures in the range of the stated weekly averages (or possibly both).

The results of outdoor studies consistently indicate that children with long-term ambient NO_2 exposures exhibit increased respiratory symptoms that are of longer duration, and show a decrease in lung function. However, outdoor NO_2 epidemiological studies, as with indoor studies, provide little evidence that long-term ambient NO_2 exposures are associated with health effects in adults. None of the available studies yields confident estimates of long-term exposure-effect levels, but available results most clearly suggest respiratory effects in children at annual average NO_2 concentrations in the range of 50-75 $\mu g/m^3$ or higher.

Guidelines

Despite the large number of acute controlled exposure studies in humans, several which used multiple concentrations, there is no evidence for a clearly defined concentration-response relationship for NO_2 exposure. For acute exposures, only very high concentrations (>1,000 ppb; 1,990 $\mu g/m^3$) affect healthy people. Based on small changes in lung function, often less than a 5% drop in FEV_1 with NO_2 exposure, and changes in airway responsiveness in studies on asthmatics and patients with chronic obstructive pulmonary disease, a range of 365-565 $\mu g/m^3$ (0.20 to 0.30 ppm) is a clear lowest-observed-effect-level. A 50% margin of safety is proposed because of the reported statistically significant increase in response to a bronchoconstrictor with exposure to 188 $\mu g/m^3$, and because of a meta-analysis suggesting changes in airway responsiveness below 365 $\mu g/m^3$. However, the significance of the response at 188 $\mu g/m^3$ has been questioned on the basis of an inappropriate statistical analysis and a failure to replicate the findings. Based on these human clinical data, a one-hour guideline of 200 $\mu g/m^3$ is proposed. At double this recommended guideline (400 $\mu g/m^3$), there is evidence to suggest possible small effects in pulmonary function of asthmatics. Should the asthmatic be exposed either simultaneously or sequentially to NO_2 and an aero-allergen, the risk of an exaggerated response to the allergen is increased.

Although there is no particular study or set of studies that clearly supports selection of a specific numerical value for an annual average guideline, there is need to protect the public from chronic NO_2 exposures. Based on the studies reviewed, it is not currently possible to select a well-supported value; but a previous review on NO_2 recommended an annual value of 40 $\mu g/m^3$ (WHO 1997c). In the absence of support for an alternative value, this figure is recognized as an air quality guideline.

Carbon monoxide

CO diffuses rapidly across alveolar, capillary and placental membranes. Approximately 80-90 % of the absorbed CO binds with hemoglobin to form carboxyhemoglobin (COHb), which is a

specific biomarker of exposure in blood. The affinity of hemoglobin for CO is 200-250 times that for oxygen. During exposure to a fixed concentration of CO, the COHb concentration increases rapidly at the onset of exposure, starts to level off after 3 hours, and reaches a steady-state after 6-8 hours of exposure. It is noted that the elimination half-life in the fetus is much longer than in the pregnant mother.

The binding of CO with hemoglobin to form COHb reduces the oxygen-carrying capacity of the blood and impairs the release of oxygen from hemoglobin. These are the main causes of tissue hypoxia produced by CO at low exposure levels. At higher concentrations, the rest of the absorbed CO binds with other heme proteins such as myoglobin and with cytochrome oxidase and cytochrome P-450. The toxic effects of CO first become evident in organs and tissues with high oxygen consumption, such as the brain, heart, exercising skeletal muscle and the developing fetus.
Severe hypoxia due to acute CO poisoning may cause both reversible, short-lasting, neurological deficits and severe, often delayed, neurological damage. The neurobehavioural effects include impaired coordination, tracking, driving ability, vigilance and cognitive performance at COHb levels as low as 5.1-8.2%.

In apparently healthy subjects, the maximal exercise performance decreases at COHb levels as low as 5%. The regression between the percentage decrease in maximal oxygen consumption and the percentage increase in COHb concentration appears to be linear, with a fall in oxygen consumption of approximately 1% for each 1% rise in COHb level above 4%.

In controlled studies involving patients with documented coronary artery disease, mean pre-exposure COHb levels of 2.9-5.9% (corresponding to post-exercise COHb levels of 2.0-5.2%) have been associated with a significant shortening in the time to onset of angina, with increased electrocardiographic changes and with impaired left ventricular function during exercise. In addition, ventricular arhythmias may be increased significantly at the higher range of mean post-exercise COHb levels. Epidemiological and clinical data indicate that CO from smoking and environmental or occupational exposures may contribute to cardiovascular mortality and to the early course of myocardial infarction. Current data from epidemiological studies and experimental animal studies indicate that common environmental exposures to CO in the developed world would not have atherogenic effects on humans (WHO 1999a).

During pregnancy, endogenous production of CO is increased so that maternal COHb levels are usually about 20% higher than the non-pregnant values. At steady-state, the fetal COHb levels are as much as 10-15% higher than the maternal COHb levels. There is a well-established and probably causal relationship between maternal smoking and low birth weight at fetal COHb levels of 2-10%. In addition, maternal smoking seems to be associated with a dose-dependent increase in perinatal deaths and with behavioural effects in infants and young children.

Guidelines

Endogenous production of CO results in COHb levels of 0.4-0.7% in healthy subjects. During pregnancy, elevated maternal COHb levels of 0.7-2.5% have been reported, mainly due to increased endogenous production. The COHb levels in non-smoking general populations are usually 0.5-1.5% due to endogenous production and environmental exposures. Non-smoking people in certain occupations (car drivers, policemen, traffic wardens, garage and tunnel workers, firemen etc.) can have long-term COHb levels up to 5%, and heavy cigarette smokers have

COHb levels up to 10% (WHO 1999a). Well-trained subjects engaging in heavy exercise in polluted indoor environments can increase their COHb levels quickly up to 10-20%. Epidemic CO poisonings in indoor ice arenas have been reported.

To protect non-smoking, middle-aged and elderly population groups with documented or latent coronary artery disease from acute ischemic heart attacks, and to protect fetuses of non-smoking pregnant mothers from untoward hypoxic effects, a COHb level of 2.5% should not be exceeded.

The guideline values (ppm values rounded), and periods of time-weighted average exposures, have been determined in such a way that the COHb level of 2.5% is not exceeded, even when a normal subject engages in light or moderate exercise. The guideline values for CO are 100 mg/m^3 (90 ppm) for 15 minutes, 60 mg/m^3 (50 ppm) for 30 minutes, 30 mg/m^3 (25 ppm) for 1 hour, and 10 mg/m^3 (10 ppm) for 8 hours.

Ozone and other photochemical oxidants

O_3 toxicity occurs in a continuum in which higher concentrations, longer exposure duration, and greater activity levels during exposure cause greater effects. Short-term acute effects include pulmonary function changes, increased airway responsiveness and airway inflammation, and other symptoms. These health effects are statistically significant at 160 $\mu g/m^3$ (0.08 ppm) for 6.6 hour exposures in a group of healthy exercising adults, with the most sensitive subjects experiencing a more than 10% functional decrease within 4-5 hours. Controlled exposure of heavily exercising adults, or children to an O_3 concentration of 240 $\mu g/m^3$ (0.l2 ppm) for 2 hours, also produced decreases in pulmonary function. There is no question that substantial acute adverse effects occur during exercise with one hour exposure to concentrations of 500 $\mu g/m^3$ or higher, particularly in susceptible individuals or subgroups.

Field studies in children, adolescents, and young adults have indicated that pulmonary function decrease can occur as a result of short term exposure to O_3 concentrations in the range 120-240 $\mu g/m^3$ and higher. Mobile laboratory studies have observed changes in pulmonary function in children or asthmatics exposed to O_3 concentrations of 280-340 $\mu g/m^3$ (0.14-0.17 ppm) for several hours. Respiratory symptoms, especially coughing, have been associated with O_3 concentrations as low as 300 $\mu g/m^3$ (0.15 ppm). O_3 exposure has also been reported to be associated with increased respiratory hospital admissions and exacerbation of asthma. The effects are observed with exposures to ambient O_3 (and co-pollutants) and with controlled exposures to O_3 alone. This demonstrates that the functional and symptomatic responses can be attributed primarily to O_3.

A number of studies evaluating animals (rats and monkeys) exposed to O_3 for a few hours or days have shown alterations in the respiratory tract, in which the lowest-observed-effect levels were in the range of 160-400 $\mu g/m^3$ (0.08-0.2 ppm). These included the potentiation of bacterial lung infections, inflammation, morphological alterations in the lung, increases in the function of lung enzymes active in oxidant defenses, and increases in collagen content. Long-term exposure to O_3 in the range of 240-500 $\mu g/m^3$ (0.12 to 0.25 ppm) causes morphological changes in the epithelium and interstitium of the centri-acinar region of the lung, including fibrotic changes.

Guidelines

Establishing guidelines for ambient O_3 concentrations is complicated by the fact that detectable responses occur at, or close to, the upper bounds of background concentrations. Thus it is not possible to base the guidelines on a no-observed-adverse-effect level (NOAEL) or LOAEL. At O_3 levels of 200 µg/m^3 and lower (for 1-8 hour exposure periods), there are statistically significant decreases in lung function, airway inflammatory changes, exacerbation of respiratory symptoms, and symptomatic and functional exacerbation of asthma in susceptible people during exercise. Functional changes and symptoms, as well as increased hospital admissions for respiratory causes, are also observed in population studies.

To select a guideline, one must accept the premise that some detectable functional responses are of little or no health concern, and that too few people may respond to the effects of O_3 exposure to warrant designation as a group needing protection from exposure to ambient O_3. In the case of respiratory function responses, a judgement could be made that O_3-related reductions of FEV_1 at, for example, less than 10% were of no clinical concern. The balance of evidence indicates that reductions of FEV_1 of more than 10% occurred at O_3 levels of 160 µg/m^3 and higher. It is generally accepted that the exposure duration to O_3 is important in controlling the response and that exposures to raised concentrations for periods of eight hours are not unlikely. On this basis, a guideline value for ambient air of 120 µg/m^3 for a maximum period of eight hours per day has been established as a level at which acute effects on public health are likely to be small.

For those public health authorities that cannot accept such levels of health risk, an alternative is to explicitly select some other level of acceptable exposure and associated risk using the dose response relationships given in Figures 3.2-3.5. These figures, which are based on corresponding tables in the *Air Quality Guidelines for Europe* (WHO 1999a), summarize the ambient O_3 concentrations that are associated with levels of responses among population subgroups. Although chronic exposure to O_3 may cause effects, quantitative information from humans is inadequate for estimating the degree of protection from chronic effects offered by these *Guidelines*. In any case, the O_3 concentration at which any adverse health outcome is expected will vary with the duration of the exposure and with the volume of air inhaled during the exposure. As there is a strong correlation in field studies between the one-hour and eight-hour O_3 concentration and hospital admissions (Figure 3.5), the reduction in health risk associated with decreasing one-hour or eight-hour O_3 levels should be very similar.

Thus, the amount of time spent outdoors and the typical level of activity are factors which should be considered in risk evaluation. Figures 3.2 and 3.5 summarize the O_3 levels at which two representative adverse health outcomes, based on controlled exposure experiments, may be expected. The dose-response relationships in these figures represent expert judgment based on the collective evidence from numerous studies and linear extrapolation in a few cases where data were limited. Interestingly, these dose-response relationships appear to be non linear.

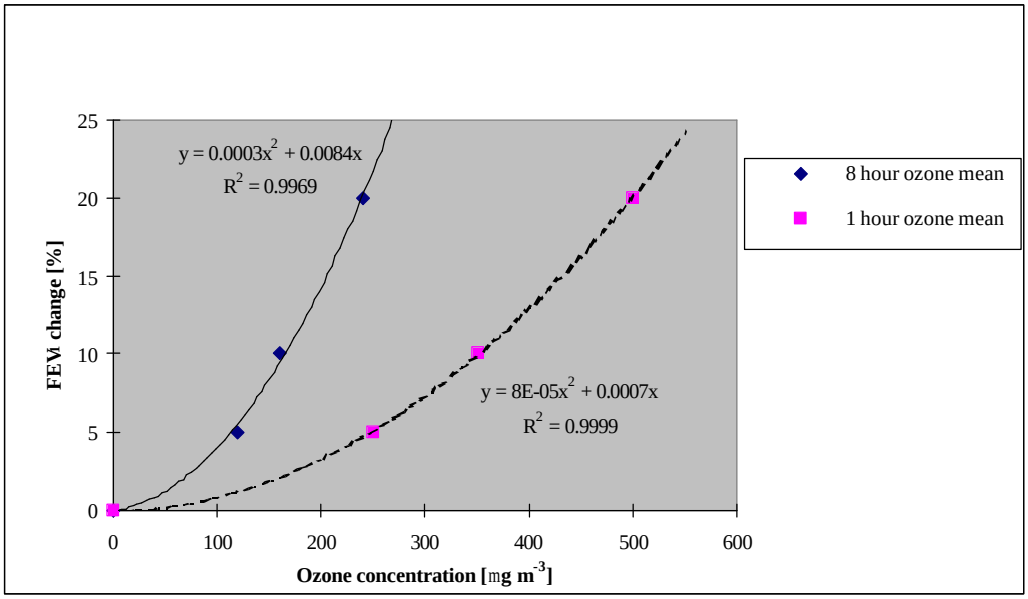

Figure 3.2. Change in FEV_1 as a function of O_3 concentration in the most sensitive 10% of active young adults and children.

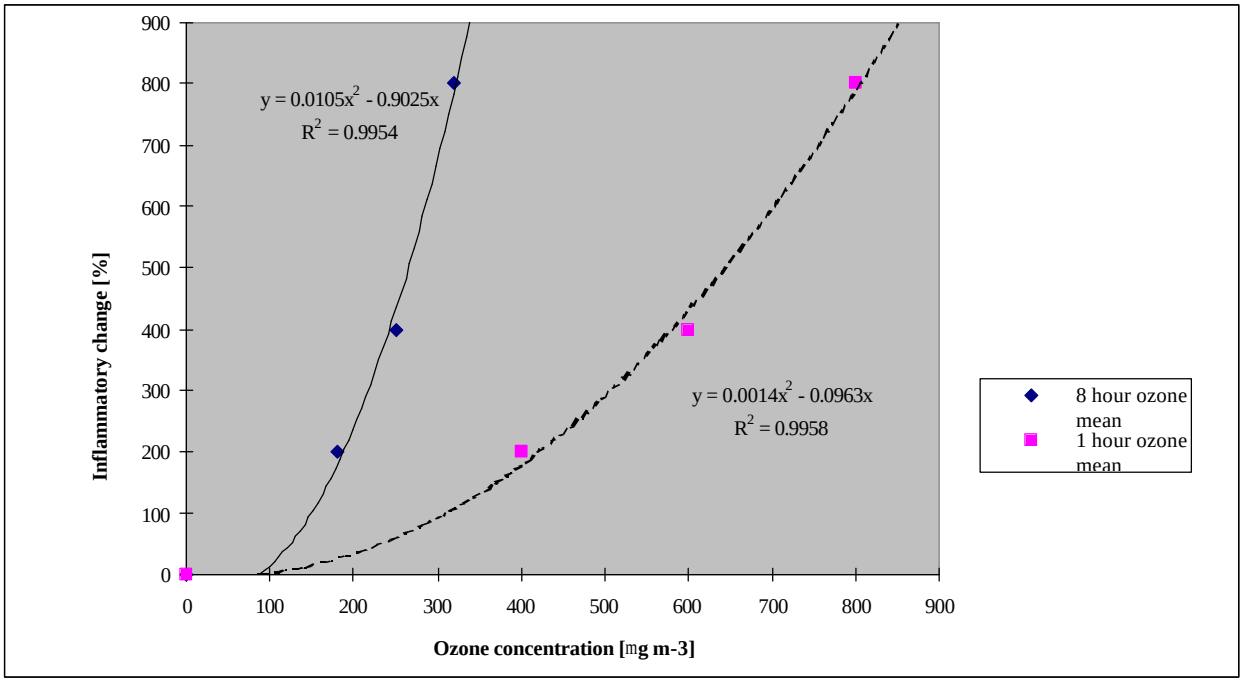

Figure 3.3. Inflammatory change (neutrophil influx in lungs of healthy young adults exercising outdoors at more than 40l/min expiratory volume in the lung) as a function of O_3 concentration.

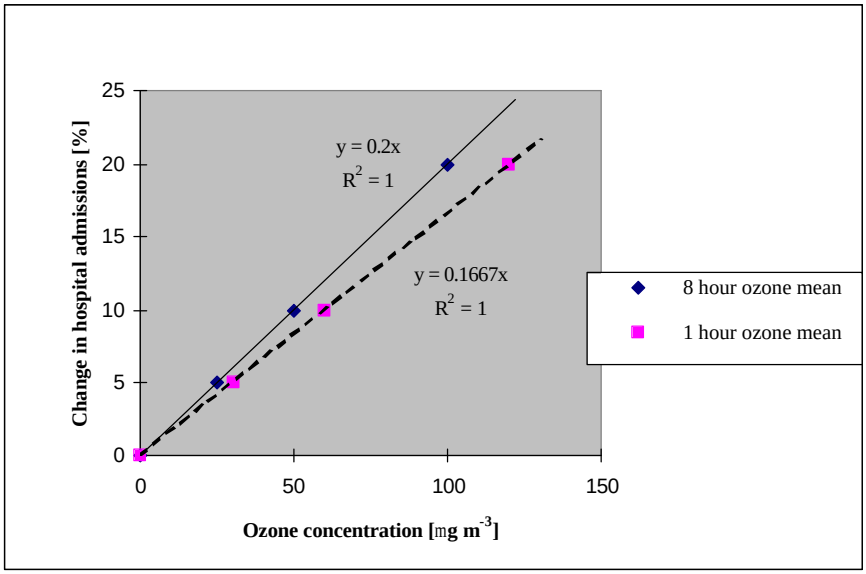

Figure 3.4. Increase in hospital admissions for respiratory conditions as a function of O_3 concentration.

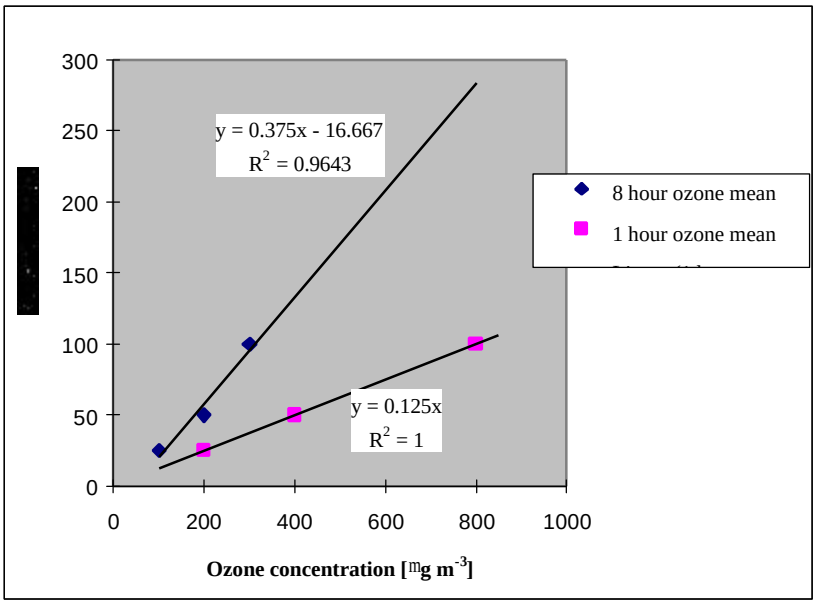

Figure 3.5. Change in symptom exacerbation among adults and asthmatics as a function of O_3 concentration.

Epidemiological data show relationships between changes in various health outcomes and changes in the peak daily ambient O_3 concentration. Two examples of such relationships are shown in Figures 3.4 and 3.5. Short-term increases in levels of ambient O_3 are associated both with increased hospital admissions with a respiratory diagnosis, and with respiratory symptom exacerbation in healthy people and asthmatics. These observations may be used to quantify the expected improvements in health outcomes that may be associated with a lower ambient O_3 concentration. The dose-response relationships presented in Figures 3.4 and 3.5 assume a linear relationship between O_3 concentration and health outcome. However, uncertainties exist concerning the forms of these relationships and it is unclear whether similar response slopes can be expected at widely different ambient O_3 levels. In the event that such relationships are curvilinear (i.e., concave upwards), the benefits of lowering the O_3 concentration are likely to

be greater when the average ambient level is higher. Conversely, if the ambient O_3 concentration is already low, the benefits of lowering the concentration may be less than would be suggested by these figures. Another important area of uncertainty is the degree to which other pollutants influence these relationships.

The previous WHO guidelines (WHO 1987) included a one-hour guideline value of 150-200 $\mu g/m^3$ for O_3. Although recent research does not indicate that this guideline would necessarily be erroneous, the 8-hour guideline would protect against acute one-hour exposures in this range and thus it is concluded that a one-hour guideline value would not be necessary. The health problems of greatest concern are increased hospital admissions, exacerbation of asthma, inflammatory changes in the lung and structural alterations in the lung. These are more appropriately addressed by a guideline value which limits average daily exposure, and consequently inhaled dose and dose rate, rather than addressing the rare short duration deterioration of air quality that may be associated with unusual meteorological conditions.

A guideline for PAN is not warranted at present, as it does not seem to pose a significant health problem at levels that are observed in the environment.

Suspended particulate matter

Health effects of SPM in humans depend on particle size and concentration, and can fluctuate with daily fluctuations in PM_{10} or $PM_{2.5}$ levels. They include acute effects such as increased daily mortality, increased rates of hospital admissions for exacerbation of respiratory disease, fluctuations in the prevalence of bronchodilator use and cough and peak flow reductions. Long-term effects of SPM refer also to mortality and respiratory morbidity, but only few studies on the long-term effects of SPM exist. Air pollution by particulate matter has been considered to be primarily an urban phenomenon, but it is now clear that in many areas of developed countries, urban-rural differences in PM_{10} are small or even absent, indicating that PM exposure is widespread. This is not to imply that exposure to primary, combustion-related PM may not be higher in urban areas.

A variety of methods exist to measure different fractions of particulate matter in air, with different health significance (see Section 2.1.1). This evaluation has tended to focus on studies in which PM exposure was expressed as PM_{10} and $PM_{2.5}$. Health effect studies conducted with various TSP and BS as exposure indicators have provided valuable additional information. However, they are less suitable for deriving exposure-response relationships for PM because TSP includes particles that are too large to be inhaled, or because the health significance of particle opacity as measured by the Black Smoke method is uncertain. Methods for measuring particle concentrations are discussed in section 5.7.

The current time-series epidemiological studies are unable to define a threshold below which no effects occur. Recent studies suggest that even at low levels of PM (less than 100 $\mu g/m^3$), short-term exposure is associated with health effects. At low levels of PM_{10} (0 - 100 $\mu g/m^3$), the short-term exposure-response curve fits a straight line reasonably well (Figures 3.6 to 3.8). However, there are indications from several studies that at higher levels of exposure (several hundreds of $\mu g/m^3$ of PM_{10}), at least for effects on mortality, the curve is flatter than at low levels of exposure. This is discussed later in this section.

Although many studies have obtained acute effect estimates for PM_{10} that are reasonably

consistent, this does not imply that particle composition or size distribution within the PM_{10} fraction is unimportant. Limited evidence from studies on dust storms indicates that such PM_{10} particles are much less toxic than those associated with combustion sources. Recent studies in which PM_{10} size fractions and/or constituents have been measured suggest that the observed effects of PM_{10} are largely associated with fine particles and not with the coarse fraction (PM_{10} minus $PM_{2.5}$). In some areas strong aerosol acidity or sulphate may be the cause of the effects associated with $PM_{2.5}$.

Evidence is also emerging that long-term exposure to low concentrations of PM in air is associated with mortality and other chronic effects, such as increased rates of bronchitis and reduced lung function. Two cohort studies conducted in the U.S.A. suggest that life expectancy may be 2-3 years shorter in communities with high PM than in communities with low PM. This is consistent with earlier cross-sectional studies, which compared age-adjusted mortality rates across a range of long-term average PM concentrations. The results showed that long-term average exposures to low PM levels, starting at about 10 $\mu g/m^3$ of fine particulate matter, were associated with a reduction in life expectancy. Whilst such observations require further corroboration, preferably also from other areas in the world, these new studies suggest that the public health implications of PM exposure may be large.

Figures 3.6-3.8 show summary estimates of the relative increase in various health parameters as a function of PM concentration. These figures are based on data reported in studies in which PM_{10} and/or $PM_{2.5}$ have been measured. They were not inferred from other measures such as Coefficient of Haze, Black Smoke or SPM. The database for parameters other than PM_{10} is still limited, so the evaluation of health effects, especially the short-term effects, is largely expressed in terms of PM_{10}. However, future regulations and monitoring activities should give emphasis to the ultrafine and fine fractions in addition to, or even instead of, PM_{10}.

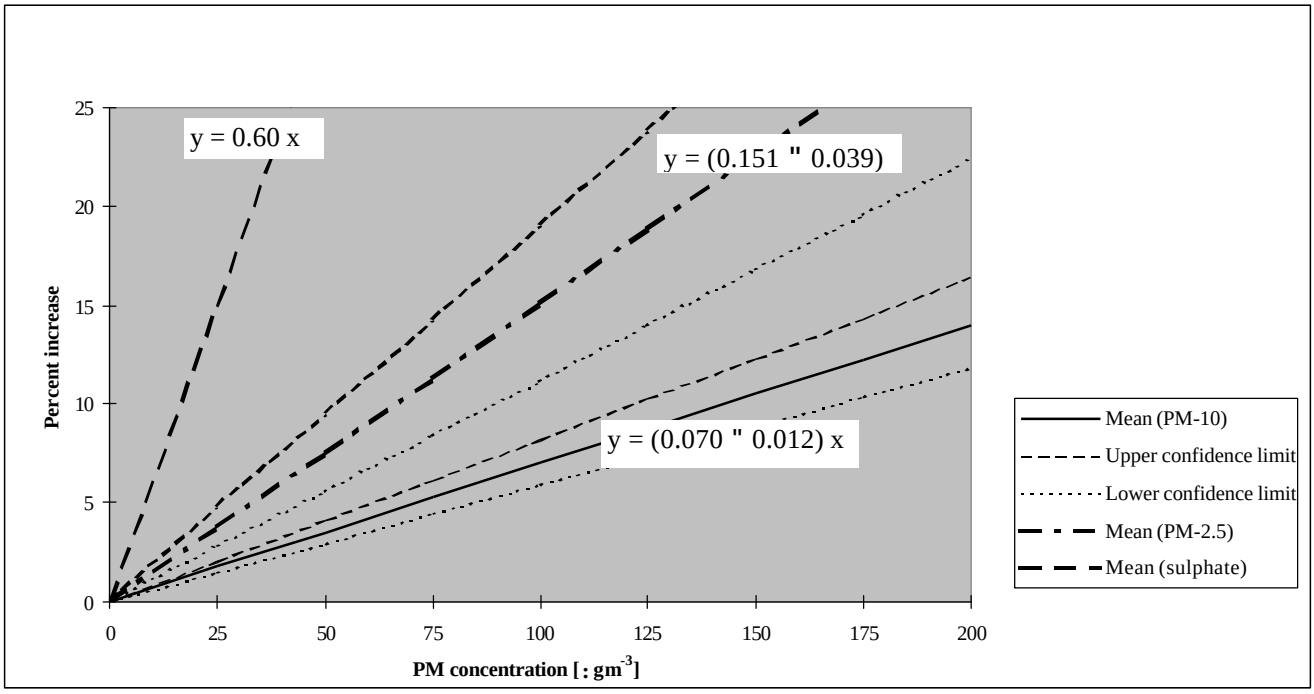

Figure 3.6. Increase in daily mortality as a function of PM concentration.

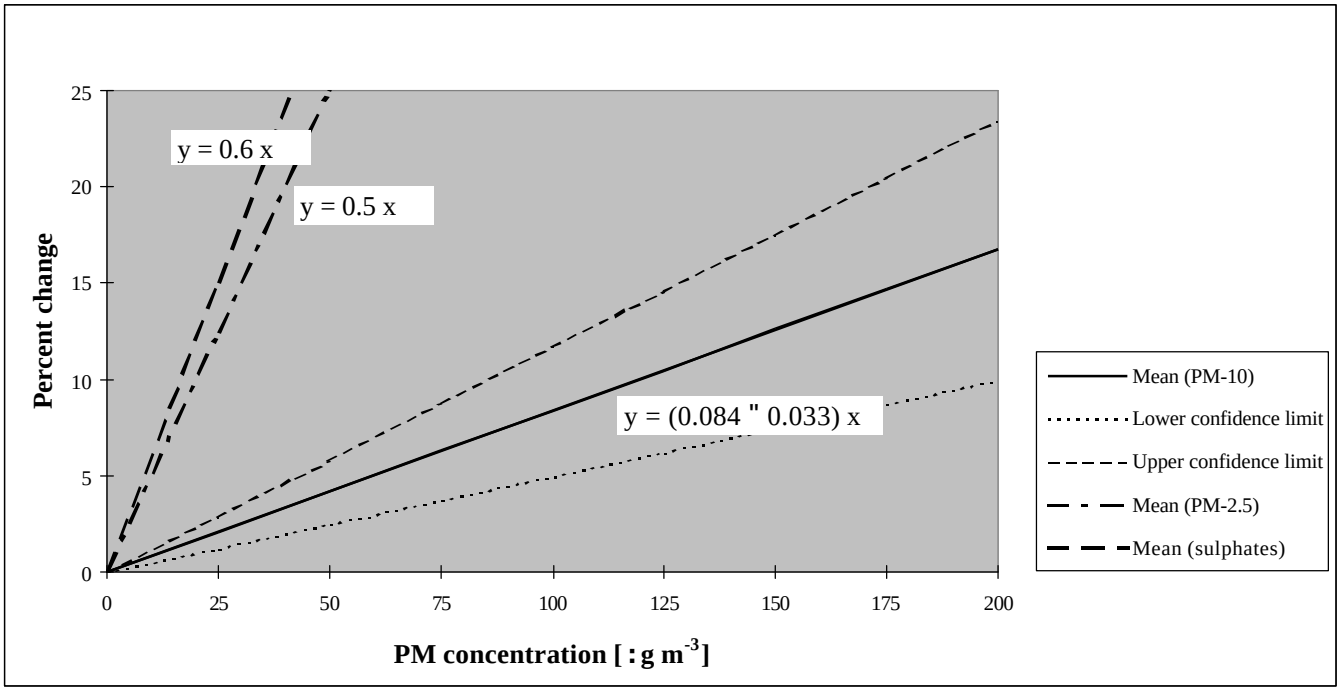

Figure 3.7. Percent change in hospital admissions assigned to PM_{10}, $PM_{2.5}$ and sulphates.

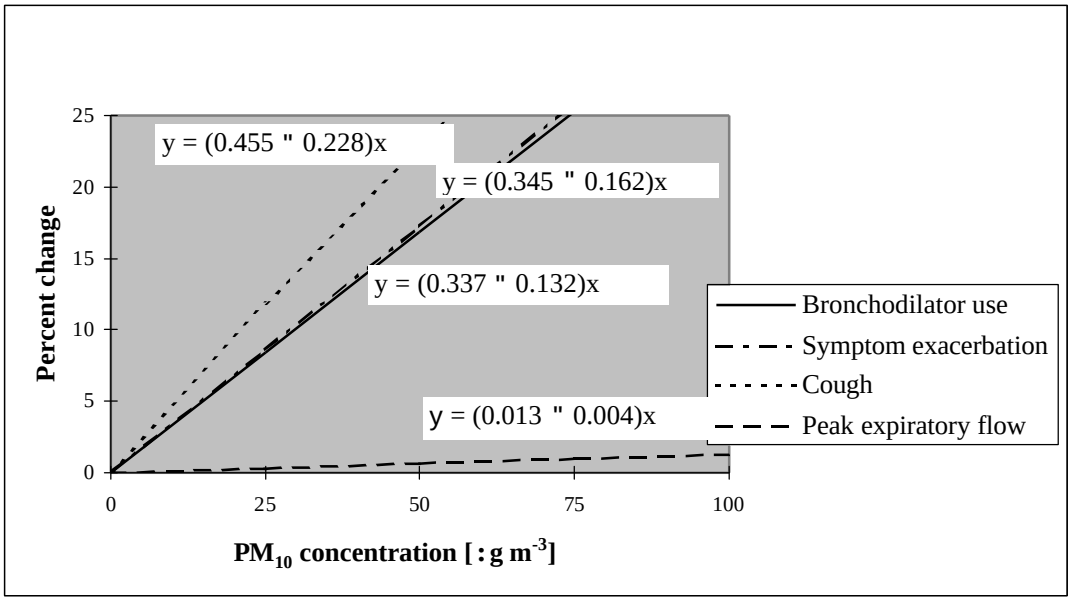

Figure 3.8. Change in health endpoints as a function of PM_{10} concentration.

The following issues should be considered when using these graphs:

(1) The graphs should not be used for PM_{10} concentrations below 20 μg/m^3, or above 200 μg/m^3; or for $PM_{2.5}$ concentrations below 10 μg/m^3, or above 100 μg/m^3. This caution is required as mean 24-hour concentrations outside of the quoted ranges were not used for the risk assessment, and extrapolations beyond them would be invalid.

(2) The areas close to the straight lines in Figures 3.6–3.8 should be considered as 'shaded' areas representing uncertainty, indicated by the 95% confidence intervals (CI).

(3) There is a fundamental difference between the guidelines for PM_{10} or $PM_{2.5}$ and the guideline values for respirable particulate matter derived in the WHO *Air Quality Guidelines for Europe* (WHO 1987). The guidelines for PM_{10} and $PM_{2.5}$ are relationships between a health endpoint and the PM concentration. The percent change is related to the risk of health effects occurring. In consequence, when deriving an air quality standard for PM_{10} or $PM_{2.5}$ using these relationships, it has to be decided which curve should be used and the risk has to be fixed. This is a new situation with respect to the derivation of air quality standard from an air quality guideline value, in which a risk is assumed without it being explicitly stated.

(4) Figures 3.6-3.8 can be used with caution to estimate how many subjects would be affected over a short period of time with increased PM levels, for a population of a given size, mortality and morbidity characteristics. There is need for caution because of variation in results between studies for some effects.

(5) With information on the average number of deaths and the average number of hospital admissions due to respiratory illness in a particular population, the trendlines in Figures 3.6 and 3.7 allow an estimation of the number of subjects that would be affected by an episode of PM_{10}, or $PM_{2.5}$. Similarly, with information on the number of asthmatics using bronchodilators, or experiencing asthma symptoms on a particular day, the trendlines in Figure 3.8 allow an estimate of the expected number of affected subjects. An instructive example is explained in the *Air Quality Guidelines for Europe* (WHO 1999a).

(6) There is little current information to quantify the reduction in life expectancy associated with daily mortality increases related to PM exposure. If effects are restricted to subjects in poor health, effects on age at death may be relatively small.

Guidelines

Evidence from epidemiological studies consistently points to associations between short-term exposure to PM and adverse effects on human health, even at low levels of PM commonly encountered in developed countries. The database does not, however, enable the derivation of specific guideline values at present. Most of the information currently available comes from studies in which particles in air have been measured as PM_{10}. There is now also an increasing body of information on $PM_{2.5}$, and the most recent studies show that, in general, $PM_{2.5}$ is a better predictor of health effects than PM_{10}. Evidence is also emerging that constituents of $PM_{2.5}$, such as sulphates and strongly acidic particles, are sometimes better predictors of health effects than $PM_{2.5}$.

Many studies relate day-to-day variations in PM to day-to-day variations in health parameters. They provide quantitative estimates of effects of PM that are generally consistent. The available information does not allow a judgement to be made of concentrations below which no effects would be expected. For this reason, no guideline value for short-term average concentrations is recommended. Risk managers are referred to the risk estimates provided in the Figures 3.6-3.8 for guidance in setting standards for PM.

There is less information on the long-term effects of PM on health. Some studies have suggested that long-term exposure to PM is associated with reduced survival, and a reduction of life expectancy in the order of 2-3 years. Other recent studies have shown that the prevalence of bronchitis symptoms in children, and of reduced lung function in both children and adults, are associated with PM exposure. For this reason, no guideline value for long-term average concentrations is recommended. Risk managers are referred to the risk estimates provided in Figures 3.6-3.8 for guidance regarding standards for PM.

Lead

The level of lead in blood is the best available indicator of current and recent past environmental exposure and, with stable exposures, may also be a reasonably good indicator of lead body-burden. The biological effects of lead can therefore be related to blood lead levels as an indicator of internal exposure. The relationship between blood lead concentrations and exposure to lead in air exhibits downward curvilinearity where the range of exposures is sufficiently large. At low levels of exposure the deviation from linearity is negligible and linear models of the relationship between intake and blood lead levels are satisfactory approximations.

The LOAEL for hematological and neurological effects of lead in adults and children can be summarized as follows. Frank anemia is exhibited in adults at blood lead levels above 800 µg/l, and in children above about 700 µg/l. Hemoglobin production is reduced in adults at blood lead levels above 500 µg/l and in children above 250-300 µg/l. The presence of lead in the blood also inhibits delta-aminolaevulinic acid dehydrase (ALAD), an enzyme involved in heme biosynthesis, resulting in an accumulation of its substrate, ALA, in blood, plasma and urine (WHO 1987). Urinary ALA and coproporyphyrin are elevated in both adults and children above blood lead levels of about 400 µg/l. Erythrocyte protoporphyrin is found to increase in male adults at blood lead levels above 200-300µg/l, and in female adults and children above 150-200 µg/l. A reduction in vitamin D3 occurs in children at blood lead levels above 100-150 µg/l. Consequently, inhibition of ALAD in adults and children is likely to occur at blood lead levels of about 100 µg/l. However, because of its uncertain biological significance for the functional reserve capacity of the heme biosynthetic system, ALAD inhibition is not treated as an adverse effect here. Encephalopathic signs and symptoms appear not to occur in adults at lead concentrations in blood below 1000-1200 µg/l, and in children below 800-1000 µg/l.

Cognitive effects in lead workers have not been observed at blood lead levels below 500 µg/l, although reductions in nerve conduction velocity were found at concentrations as low as 300 µg/l. Elevation of free erythrocyte protoporphyrin has been observed at blood lead levels of 200-300 µg/l. Central nervous system effects, as assessed by neurobehavioural endpoints, appear to occur in children at levels below 200 µg/l. Consistent effects have been reported for global measures of cognitive functioning, such as the psychometric intelligence quotient, at blood lead levels between 100-150 µg/l. Some epidemiological studies have indicated effects such as hearing impairment at blood lead levels below 100 µg/l. Animal studies provide qualitative support for the claim that lead is a causative agent for hearing impairment.

Guidelines

The guidelines for lead in air are based on the effects of lead in blood. Critical effects to be considered in the adult organism include elevation of free erythrocyte protoporphyrin, whereas for children cognitive deficits, hearing impairment and disturbed vitamin D metabolism are taken

as the decisive effects. All of these effects are considered adverse. A critical level of lead in blood is 100 µg/l. It should be stressed that all of these values are based on population studies yielding group averages, and apply to the individual child only in a probabilistic manner.

For the derivation of a guideline value the following arguments have been considered:

Currently measured "baseline" blood lead levels of minimal anthropogenic origin are probably between 10-30 µg/l.
Various international expert groups have determined that the earliest adverse effects of lead in populations of young children begin at 100-150 µg/l. Although it cannot be excluded that population effects may occur below this range, it is prudent to derive a guideline value based on the lowest value of this range (100 µg/l).
It can be assumed that inhalation of airborne lead is a significant route of exposure for adults (including pregnant women), but it is of less significance for young children, for whom other pathways of exposure such as ingestion are generally more important than inhalation.
It appears that 1 µg Pb/m^3 of air directly contributes approximately 19 µg Pb/l of blood in children and about 16 µg Pb/l of blood in adults, although it is accepted that the relative contribution of lead in air is less significant in children than in adults. These values are approximations, recognizing that the relationships are curvilinear in nature and will apply principally at lower blood lead levels.
It must be taken into account that in typical situations an increase of lead in air also contributes to increased lead uptake by indirect environmental pathways. To correct for uptake by other routes, it is assumed that 1 µg Pb/m^3 in air would contribute to 50 µg Pb/l in blood.
It is recommended that efforts should be undertaken to ensure that at least 98% of an exposed population, including pre-school children, should have blood lead levels that do not exceed 100 µg/l. In this case, the median level of lead in blood would not exceed 54 µg/l. On this basis, the annual average concentration of lead in air should not exceed 0.5 µg/m^3 in blood. These estimates are assumed to also protect adults.
To prevent further increases of lead in soils, and the consequent increases in exposure of future generations, the levels of lead in air should be kept as low as possible.

As both direct and indirect exposure of young children to lead in air occurs, the guidelines for lead in air should be accompanied by other preventive measures. These should specifically take the form of monitoring the lead content of dust and soils arising from the fallout of lead in air. The normal hand-to-mouth behaviour of children necessitates that dust and soil be defined as potentially serious sources of exposure. A specific monitoring value is not recommended. Some data indicate that lead fallout in excess of 250 µg m^{-2}/day will increase blood lead levels.

In summary, the WHO guideline values for the "classic" air pollutants are provided in Table 3.1.

Table 3.1. WHO guideline values for the "classical" air pollutants (WHO 1999a)

Compound	Annual ambient air concentration [μg/m³]	Health endpoint	Observed effect level [μg/m³]	Uncertainty factor	Guideline Value [μg/m³]	Averaging time
Carbon monoxide	500-7000	Critical level of COHb < 2.5%	n.a	n.a.	100 000	15 minutes
					60 000	30 minutes
					30 000	1 hour
					10 000	8 hours
Lead	0.01-2	Critical level of Pb in blood < 100-150 μg Pb/l	n.a.	n.a.	0.5	1 year
Nitrogen dioxide	10-150	Slight changes in lung function in asthmatics	365-565	0.5	200	1 hour
					40	1 year
Ozone	10-100	Respiratory function responses	n.a.	n.a.	120	8 hours
Sulphur dioxide	5-400	Changes in lung function in asthmatics	1000	2	500	10 minutes
		Exacerbations of respiratory symptoms	250	2	125	24 hours
		in sensitive individuals	100	2	50	1 year

n.a. not applicable

3.2 Other air pollutants

This section briefly describes the health-based guidelines for airborne inorganic and organic compounds for non-carcinogenic and carcinogenic health endpoints. Also some compounds relevant for indoor air pollution will be covered. In the process of revising and updating the WHO *Air Quality Guidelines for Europe* and the *Environmental Health Criteria* series, no guideline value and no risk-concentration relationship could be derived for several compounds. The compounds are fluorides and platinum for non-carcinogenic endpoints and 1,3 butadiene and cadmium^{VI} for carcinogenic health endpoints.

Guidelines based on noncarcinogenic health endpoints

In the updated and revised document of the WHO *Air Quality Guidelines for Europe* (WHO 1999a) the following compounds with noncarcinogenic endpoints were considered: cadmium, dichloromethane, fluorides, HCHO, manganese, mercury, styrene, tetrachloroethylene, and toluene.

Data for CS_2 and H_2S were not revised, and the original guidelines (WHO 1987) are still applicable.

In addition, some compounds were not considered in the process of updating and revising the *Air Quality Guidelines for Europe.* The guidelines for these compounds were taken from the published documents of the *Environmental Health Criteria* series (EHC) of the International Programme for Chemical Safety and the Concise International Chemical Assessment Documents (CICAD) of the Inter-Organization programme for the sound Management of Chemicals. For non-carcinogenic health endpoints these include the compounds: acetaldehyde (EHC 167, WHO 1995d); acetone (EHC 207, WHO 1998c); acrolein (EHC 127, WHO 1992b); acrylic acid (EHC 191, WHO 1997d); 2-butoxyethanol (CICAD 10, WHO1998d); carbon tetrachloride (EHC 208, WHO 1999b); chloroform (EHC 163, WHO 1994b); cresol (EHC 128, WHO 1995e); 1,4-dichlorobenzene, monochlorobenzene, and trichlorobenzene (EHC 128, WHO 1991a); di-n-butyl phthalate (EHC 189, WHO 1997e); diesel exhaust (EHC 171, WHO 1996b); 2-ethoxyethanol, 2-ethoxyethanolacetate, and methoxyethanol (EHC 115, WHO 1990a); ethylbenzene (EHC 186, WHO 1996c); hexachlorocyclopentadiene (EHC 120, WHO 1991b); isophorone (EHC 174, WHO 1995f); methanol (EHC 196; WHO 1997f); methyl bromide (EHC 166, WHO 1995g); methylmethacrylate (CICAD 4, WHO 1998e); propanols (EHC 102, WHO 1990b; EHC 103, WHO 1990c); 1,1,1,2-tetrafluoroethane (CICAD 11, WHO 1998f); and xylenes (EHC 190, WHO 1997g).

The starting point for the air quality guidelines for non-carcinogenic air pollutants from the Environmental Health Criteria documents were the concepts of NOEL, NOAEL, LOEL and LOAEL (WHO 1987; WHO 1994c. Uncertainty factors were applied to these values to derive the guidelines. These uncertainty factors take into account intraspecies variation, interspecies variation, quality of data, and extrapolations from LOAEL to NOAEL and from subchronic to chronic effects. Examples for such factors and their application in deriving the guidelines are given in EHC 170 (WHO 1994c). For interspecies (extrapolation from animal to human) variation, usually a factor of 10 was applied. For intraspecies variation a factor of 5–10 was used. For use of an effect level rather than a no-effect level a factor of 2-10 was also applied, depending on the quality of the data. It was usually assumed that an uncertainty factor of 1000, based on interspecies variation (factor of 10), intraspecies variation (factor of 10) and LOAEL to NOAEL extrapolation (factor of 10), also accounted for variations in exposure time and the limitations of the database. If occupational data were the basis of a guideline derivation, a factor accounting for the number of hours per week divided by the number of working hours was applied. The choice of uncertainty factors was subject to individual expertise and judgement.

Some general considerations have to be considered in deriving guideline values in the Environmental Health Criteria (EHC) documents and in their interpretation and use:
A consistent methodology has been used in the derivation of quantitative guideline values for human exposures to chemical substances present in food, drinking-water, air and other media by *ad hoc* IPCS Task Groups (of varying membership) reviewing and evaluating data and finalizing EHC monographs on various chemicals. This approach embodies the concept that, to the extent possible, guidance values for the protection of human health should reflect consideration of total exposure to the substance whether present in air, water, soil, food or other media. Guideline values should be derived for a clearly defined exposure scenario, based on the data for the reference man (as defined in Appendix 4 of WHO 1994c), and therefore might not represent national or local circumstances.

The precision of the guidance values is dependent upon the validity and reliability of the available data. Frequently, there are sources of uncertainty in the derivation of TIs and in their allocation as a basis for guideline values, so that the resulting values represent a best estimate

based on the available data at the time. The description of the derivation of guideline values clearly indicates the nature and sources of uncertainty and the manner in which they have been taken into account in the derivation. The numerical values of guideline values should reflect the precision present in their derivation; usually guideline values are given to only one significant figure.

Establishing tolerable intakes (TIs comprising tolerable daily intakes (TDIs) or acceptable daily intakes (ADIs), in units mg/(kg bw d) or μg/(kg bw d), bw bodyweight) is central to the determination of guidance values. A TDI or ADI is defined as an estimate of the intake of a substance over a lifetime that is considered to be without appreciable health risk. It may have different units depending upon the route of administration upon which it is based and is generally expressed on a daily or weekly basis. Though not strictly an "intake", TIs for inhalation are generally expressed as airborne concentrations (i.e. μg or mg per m^3).

Two areas are critical in the methodology for the derivation of guidance values for human exposures to chemical substances in the environment:

Development of a tolerable intake on the basis of interpretation of the available data on toxicity. For practical purposes, toxic effects are considered to be of two types, threshold and non-threshold. For substances where the critical effect is considered to have a threshold (including non-genotoxic carcinogenesis for which there is adequate mechanistic data), a TI is developed usually on the basis of a NOAEL.

Allocation of the proportions of the tolerable intake to various media. Development on available information, the development of guidance values for compounds present in more than one environmental medium will require the allocation of proportions of the TI to various media (for example, air, food and water). For the derivation of guidance values, the allocation will be based on information on relative exposure via different routes.

Media exposure allocations of TIs for the derivation of guidance values in EHC monographs are based on relative exposure by different routes for a given scenario. Though this is suggested as a practical approach, the use of allocations based on exposure in different media does not preclude the development of more stringent limits. It is also important to recognize that the proportions of total intake from media may vary, based on circumstances. Site- or context-specific guideline values better suited to local circumstances and conditions could be developed from TIs presented in the EHC in situations where relevant data on exposure are available, and particularly where there are other significant sources of exposure to a chemical substance (e.g., in the vicinity of a waste site). Regulatory authorities may also take control to develop risk management strategies appropriate for local circumstances, although the ultimate objective of control should be reduction of exposure from all sources to less than the TIs. In addition, where data on organoleptic thresholds are included in EHC monographs, these can also be considered by relevant authorities in the development of limits.

Polychlorinated dibenzodioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and polychlorinated biphenyls (PCBs) constitute a group of persistent environmental chemicals. A number of dioxin or furan congeners, as well as some co-planar PCBs have been shown to exert a number of toxic responses similar to those of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), the most toxic dioxin. These effects include dermal toxicity, immunotoxicity, reproductive effects and teratogenicity, endocrine disruption and carcinogenicity. For dioxin-like compounds a TDI

was derived in units of toxicity equivalent (TEQ) uptakes (WHO 1998k), which is supposed to represent a tolerable daily intake for life-time exposure. Occasional short-term excursions above the TDI would have no health consequences provided that the averaged intake over long periods is not exceeded. It was stressed that the upper range of the TDI of 4 pg TEQ/kg bw should be considered a maximal tolerable intake on a provisional basis and that the ultimate goal is to reduce human intake levels below 1 pg TEQ/kg bw/day.

The air quality guidelines for non-carcinogenic pollutants can only be applied if the averaging times are specified. The averaging time associated with a guideline value depends on the type of effects that are caused by short-term exposure producing acute effects, or long-term exposure producing chronic effects. Typical averaging times are 30 minutes for odorous pollutants, 24 hours to 1 week for acute exposures and 1 year for chronic health effects. The decision on the averaging time for a guideline needs careful screening of the toxicological and epidemiological findings and expertise in judging the results. As a consequence, the choice of an averaging time can be subjective, as is the choice of an uncertainty factor.

The air quality guidelines for compounds with non-carcinogenic health endpoints are summarized in Table 3.2.

Table 3.2. Guidelines for air quality: compounds with non-carcinogenic health endpoints

Compound	Average ambient air concentration [: g/m^3]	Health endpoint	Observed effect level [mg/m^3]	Uncertainty factor	Guideline Value (GV) or Tolerable Concentr-ation (TC) [: g/m^3]	Averaging time	Source	
Acetaldehyde	5	Irritancy in humans	45 (NOEL)	20	2 000 (TC)	24 hours	WHO 1995d	EHC 167
		Carcinogenicity related irritation in rats	275 (NOEL)	1000	50 (TC)	1 year		
Acetone	0.5-125	Odour annoyance	240 (OT)	n.a.	n.p.	-	WHO 1998c	EHC 207
Acrolein	15	Eye irritation in humans	0.13	n.p.	50 (GV)	30 min	WHO 1992b	EHC 127
		Odour annoyance	0.07	n.a.	-	30 min	WHO 1992b	EHC 127
Acrylic acid	No data	Nasal lesions in mice	15 (LOAEL)	50	54 (GV)	1 year	WHO 1997d	EHC 191
2-Butoxyethanol	0.1-15	Haematoxicity in rats	242 (NOAEL)	10	13100 (TC)	1 week	WHO 1998d	CICAD 10
Cadmium	(0.1-20) . 10^{-3}	Renal effects in the population	n.a.	n.a.	5 x 10^{-3} (GV)	1 year	WHO 1999a	
Carbon disulphide	10-1500	Functional CNS changes in workers	10 (LOAEL)	100	100 (GV)	24 hours	WHO 1987	
		Odour annoyance	0.2 (OT)	n.a.	20 (GV)	30 min	WHO 1987	
Carbon Tetrachloride	0.5-1	Hepatotoxicity in rats	6.1(NOAEL)	1000	6.1 (TC)	1 year	WHO 1999b	EHC 208
1,4 Dichlorobenzene	0.2-3.5	Increase in organ weight and urinary proteins	450 (NOEL)	500	1000 (TC)	1 year	WHO 1991a	EHC 128
Dichloromethane	< 5	COHb formation in normal subjects		n.a.	3000 (GV)	24 hours	WHO 1999a	
Diesel exhaust	1.0 - 10.0	Chronic alveolar inflammation in humans	0.139 (NOAEL)*	25	5.6 (GV)	1 year	WHO 1996b	EHC 171
		Chronic alveolar inflammation in rats	0.23 (NOAEL)*	100	2.3 (GV)	1 year		

***** For diesel exhaust two approaches were applied, which based on a NOAEL of 0.41 mg/m3 in rats. The corresponding levels were converted to a continuous exposure scenario. n.a. not applicable; n.p. not provided.

Table 3.2 Guidelines for air quality: compounds with non-carcinogenic health endpoints (cont.)

Compound	Average Concentration [: g/m^3]	Health endpoint	Observed effect level [mg/m^3]	Uncertainty factor	Guideline Value (GV) or Tolerance Concentration (TC) [: g/m^3]	Averaging time	Source	
2-Ethoxyethanol	No data	Developmental effects in rats	37 (NOEL)	n.p.	n.p.	1 year	WHO 1990a	EHC 115
2-Ethoxyethylacetate	No data	Developmental effects in rats	170 (NOEL)	n.p.	n.p.		WHO 1990a	EHC 115
Ethylbenzene	1-100	Increase of organ weight	2150 (NOEL)	100	22 000 (GV)	1 year	WHO 1996c	EHC 186
Fluorides	0.5 - 3	Effects on livestocks	n.a.	n.a.	1 (GV)	1 year	WHO 1999a	
Formaldehyde	(1-20) . 10^{-3}	Nose, throat irritation in humans	0.1 (NOAEL)	n.a.	100 (GV)	30 min	WHO 1999a	
Hexachlorocyclopentadiene	No data	Inhalation effects in rats	0.45 (NOEL)	n.p.	n.p.	1 year	WHO 1991b	EHC 120
Hydrogen sulphide	0.15	Eye irritation in humans Odour annoyance	15 (LOAEL) (0.2-2.0) x 10^{-3} (OT)	100 n.a.	150 (GV) 7 (GV)	24 hrs 30 min	WHO 1987 WHO 1987	
Isophorone	No data	Odour annoyance	1.14 (OT)	n.a.	-	30 min	WHO 1995f	EHC 174
Manganese	0.01 - 0.07	Neurotoxic effects in workers	0.03 (NOAEL)	200	0.15 (GV)	1 year	WHO 1999a	
Mercury, inorganic	(2-10) . 10^{-3}	Renal tubular effects in humans	0.020 (LOAEL)	20	1 (GV)	1 year	WHO 1999a	
2-Methoxyethanol	No data	Developmental toxicity in rats	31 (NOEL)	n.p.	n.p.		WHO 1990a	EHC 115
Methyl bromide	0.05-0.8	Reduction in fertility index in rats	12 (NOEL)	n.p.	n.p.		WHO 1995g	EHC 166
Methyl Methacrylate	2.4 x 10^{-4}	Degenerate changes in olfactory epithelium in rodents	102.5 (NOEL)	100	200 (TC)	1 year	WHO 1998e	CICAD 4
Monochlorobenzene	0.2-3.5	Decreased food intake, increased organ weight, lesions and changes in blood parameters	341 (LOAEL)	1000	500 (TC)	1 year	WHO 1991a	EHC 128

n.a. not applicable; n.p. not provided.

Table 3.2 Guidelines for air quality: compounds with non-carcinogenic health endpoints (cont.)

Compound	Average ambient air concentration [: g/m^3]	Health endpoint	Observed effect level [mg/m^3]	Uncertainty factor	Guideline Value (GV) or Tolerance concentration (TC) [: g/m^3]	Averaging time	Source	
1-Propanol	0.05	Reproduction in pregnant rats	9001 (NOEL)	n.p.	n.p.		WHO 1990b	EHC 102
2-Propanol	1500-35000	Developmental toxicity in rats	9001 (LOEL)	n.p.	n.p.		WHO 1990c	EHC 103
Styrene	1.0 -20.0	Neurological effects in workers	107 (LOAEL)	40	260 (GV)	1 week	WHO 1999a	
		Odour annoyance	0.07 (OT)	n.a.	7 GV)	30 minutes	WHO 1987	
Tetrachloroethylene	`1 - 5	Kidney effects in workers	102 (LOAEL)	400	250 (GV)	24 hours	WHO 1999a	
		Odour annoyance	8	n.a.	8000 (GV)	30 minutes	WHO 1987	
1,1,1,2-Tetrafluoroethane	No data	Development toxicity in animals	41700 (NOAEL)	n.p.	n.p.		WHO 1998f	CICAD 11
Toluene	5 - 150	Effects on CNS in workers	332 (LOAEL)	1260	260 (GV)	1 week	WHO 1999a	
		Odour annoyance	1 (OT)	n.a.	1000 (GV)	30 minutes	WHO 1987	
1,3,5 Trichlorobenzene	0.5-0.8	Metaplasia and hyzperplasia of respiratory epithelium in rats	100 (NOEL)	500	200 (TC)	1 year	WHO 1991a	EHC 128
1,2,4 Trichlorobenzene	0.02-0.05	Increae in urinary porphyrins in rats	22.3 (NOAEL)	500	50 (TC)	1 year	WHO 1991a	EHC 128
Vanadium	0.05 - 0.2	Respiratory effects in workers	0.02 (LOAEL)	20	1 (GV)	24 hours	WHO 1987	
Xylenes	1 - 100	CNS effects in human volunteers	304 (NOAEL)	60	4800 (GV)	24 hours	WHO 1997g	EHC 190
		Neurotoxicity in rats	870 (LOAEL)	1000	870 (GV)	1 year	WHO 1997g	EHC 190
		Odour annoyance	4.35 (OT)	n.a.	-	30 minutes	WHO 1997g	EHC 190

n.a. not applicable; n.p. not provided.

Table 3.2 Guidelines for air quality: compounds with non-carcinogenic health endpoints (cont.)

Compound	Average ambient air concentration [: g/m^3]	Health endpoint	Observed effect level [mg/kg bw d]	Uncertainty factor	Tolerable Daily intake (TDI orADI) [: g/kg bw d]	Averaging Time (over lifetime)	Source	
Chloroform	0.3-10	Hepatoxicity in beagles	15 (LOEL)	1000	15 (TDI)	24 hours	WHO 1994b	EHC 163
Cresol	1-'10	Reduced body weight and tremors in mice	50 (LOAEL)	300	170 (ADI)	24 hours	WHO 1995e	EHC 168
Di-n-butyl Phthalate	(3-80) . 10^{-3}	Developmental/Reproductive toxicity	66 (LOAEL)	1000	66 (ADI)	24 hours	WHO 1997e	EHC 189
			Estimated human daily intake [pg/kg bw d]		[TEQ/kg bw d]			
Dioxin-like compounds	n.p.	Neurobehavioural effects/ Endometriosis in monkey offspring Decreased sperm count/immune suppression/increase genital malformations in rat offspring	14-37 (LOAEL)*	10	1-4 (TDI)	24 hours	WHO 1998k	

* Estimated from the maternal body burden of exposed rats and monkeys by applying a factor of 2..
kg bw d = kilogramme bodyweight per day

Additional air pollutants were considered for which it was not possible to derive guideline values. For non-carcinogenic health endpoints these compounds include dioxins, fluorides, platinum and other compounds, for which the existing information can be extracted from the EHC series compiled in Appendix 4.

Guidelines based on carcinogenic health endpoints

In the revision of the WHO *Air Quality Guidelines for Europe* (WHO 1999a) the following compounds with carcinogenic endpoints were considered: arsenic, benzene, chromium (VI), man-made vitreous fibres, nickel, PAH, radon, trichloroethylene, and toluene. The data for acrylonitrile and vinylchloride were not revised and updated and the original guidelines are still applicable (WHO 1987). Additional carcinogenic compounds, for which unit risks could be derived from the EHC series publications, are included in the guidelines. These include acetaldehyde (EHC 167, WHO 1995d); bis(chloromethyl)ether (EHC 201, WHO 1998h); 1,2-dichloroethane (CICAD 1, WHO 1998g); diesel exhaust (EHC 171, WHO 1996b); selected non-heterocyclic PAH (EHC 202, WHO 1998i); and 1,1,2,2-tetrachloroethane (CICAD 3, WHO 1998j).

In addition, for some carcinogenic compounds, such as 1,3 butadiene and cadmium, guidelines could not be derived. Existing information on these compounds can be taken from WHO 1999a and, for other compounds, from the published documents of the *Environmental Health Criteria* series compiled in Appendix 4.

Table 3.3 Guidelines for air pollutants with carcinogenic health endpoints

Compound	Average ambient air concentration [μg/m^3]	Health endpoint	Unit risk [μg/m^3]$^{-1}$	IARC classification	Source	
Acetaldehyde	5	Nasal tumours in rats	(1.5-9) x 10^{-7}	2B	WHO 1995d	EHC 167
Acrylonitrile	0.01 - 10	Lung cancer in workers	2 x 10^{-5}	2A	WHO 1987	
Arsenic	(1 - 30) . 10^{-3}	Lung cancer in exposed humans	1.5 x 10^{-3}	1	WHO 1999a	
Benzene	5.0 - 20.0	Leukemia in exposed workers	(4.4-7.5) x 10^{-6}	1	WHO 1999a	
Benzo[a]pyrene		Lung cancer in humans	8.7 x 10^{-2}	1	WHO 1999a	
Bis(chloromethyl)ether	No data	Epitheliomas in rats	8.3 x 10^{-3}	1	WHO 1998h	EHC 201
Chloroform	0.3-10	Kidney tumours in rats	4.2 x 10-7	2B	WHO 1994b	EHC 163
Chromium^{VI}	(5-200) . 10^{-3}	Lung cancer in exposed workers	(1.1-13) x 10^{-2}	1	WHO 1999a	
1,2-Dichloroethane	0.07 - 4	Tumour formation in rodents	(0.5-2.8) x 10^{-6}	2B	WHO 1998g	CICAD 1
Diesel exhaust	1.0 - 10.0	Lung cancer in rats	(1.6-7.1) x 10^{-5}	2A	WHO 1996b	EHC 171

Table 3.3 Guidelines for air pollutants with carcinogenic health endpoints (cont.)

Compound	Average ambient air concentration [μg/m^3]	Health endpoint	Unit risk [μg/m^3]$^{-1}$	IARC classification	Source	
ETS	1-10	Lung cancer in exposed humans	10^{-3}		WHO 1999a	
Nickel	1-180	Lung cancer in exposed humans	3.8×10^{-4}	1	WHO 1999a	
PAH (BaP)	$(1\text{-}10) \cdot 10^{-3}$	Lung cancer in exposed humans	8.7×10^{-2}	1	WHO 1999a	
1,1,2,2-Tetrachloroethane	0.1 - 0.7	Hepatocellular carcinomas in mice	$(0.6\text{-}3.0) \times 10^{-6}$	3	WHO 1998j	CICAD 3
Trichloroethylene	1 -10	Cell tumours in testes of rats	4.3×10^{-7}	2A	WHO 1999a	
Vinychloride	0.1 - 10	Hemangiosarkoma in exposed workers Liver cancer in exposed workers	1×10^{-6}	1	WHO 1987	

For the compounds noted inTable 3.3 estimation of the unit risks is described in the references quoted. Unit risks for mixtures such as petrol exhaust, roofing tar, smokeless and smoky coal, and wood smoke can, in principle, be estimated from the potencies of these mixtures and the unit risk of benzo[a]pyrene (BaP) by use of the formula:

$UR_{mixture}$ = (potency of mixture)/(potency of "coke oven top") x UR_{BaP} x (content of BaP in mixture).

In this relationship the potencies of the mixture and the potency of "coke oven top" are taken fromTable A.I.17 of EHC 202 (WHO 1998i); $UR_{mixture}$ denotes the unit risk of the mixture and UR_{BaP} that of BaP; the unit of the content of BaP in the mixture is microgram per gram of mixture. Table 3.4 reflects the relative potencies of the mixtures, which defined as the potencies of the mixtures divided by the potency of "coke oven top" (see EHC 202, WHO 1998i).

Table 3.4. Relative potencies of certain mixtures

Mixture	Relative potency of mixture
Petrol exhaust	0.736
Roofing tar	0.145
Smokeless coal	0.368
Smoky coal	1.026
Wood smoke	0.759

For example, the BaP content of wood smoke has been estimated to range between 1 and 29 [mg BaP/g of mixture] (Ward 1999). Inserting all quantities into the above equation leads to a unit risk for wood smoke in the range of (0.07-1.9) x 10^{-7} $[\mu g/m^3]^{-1}$. If the BaP content of other mixtures are known the unit risk can be estimated in a similar way.

Using the potencies of other non-heterocyclic polycyclic hydrocarbons relative to BaP (see Table AI.9 of EHC 202, WHO 1998i), unit risks can also be given as a rough estimate for these compounds by using of the formula (results are given in Table 3.5)

$UR_{compound}$ = (potency of compound)/(potency of BaP) x UR_{BaP}

Table 3.5. Estimate of unit risks for several polycyclic aromatic hydrocarbons

Compound	Relative potency range compared to BaP	Unit risk [μg/m^3]$^{-1}$
Anthanthrene	0.28 - 0.32	(2.4 - 2.8) x 10^{-2}
Benz[a]anthracene	0.014 - 0.145	(1.2 - 13) x 10^{-4}
Benzo[a]pyrene	1	8.7 x 10^{-2}
Benzo[b]fluoranthene	0.1 - 0.141	(0.87 - 1.2) x 10^{-2}
Benzo[j]fluoranthene	0.045 - 0.1	(0.4 - 0.87) x 10^{-2}
Benzo[k]fluoranthene	0.01 - 0.1	(8.7 - 87) x 10^{-4}
Chrysene	0.001 - 0.1	(8.7 - 870) x 10^{-5}
Cyclopenta[*cd*]pyrene	0.012 - 0.1	(1 - 8.7) x 10^{-3}
Dibenzo[a,e]pyrene	1	8.7 x 10^{-2}
Dibenz[a,c]anthracene	0.1	8.7 x 10^{-3}
Dibenz[a,h]anthracene	0.89 - 5	(7.7 - 43.5) x 10^{-2}
Dibenzo[a,l]pyrene	100	8.7 x 10^{-0}
Dibenzo[a,e]fluoranthene	1	8.7 x 10^{-2}
Dibenzo[a,h]pyrene	1 - 1.2	(8.7 - 10.4) x 10^{-2}
Dibenzo[a,i]pyrene	0.1	8.7 x 10^{-3}
Fluoranthene	0.001 - 0.01	(8.7 - 87) x 10^{-5}
Indeno[1,2,3,-*cd*]pyrene	0.067 - 0.232	(5.8 - 20.2) x 10^{-3}

Air quality guidelines for man-made vitreous fibres and radon were also revised Man-made vitreous fibre (MMVF) concentrations have been measured in only a few studies and have been found to average about 340 fibres per cubic metre (F/m^3) in ambient air and 570 F/m^3 in indoor air. Maximum values were 2400 F/m^3 in ambient air and 5600 F/m^3 in indoor air. Several types of refractory ceramic fibres were found to be carcinogenic in inhalation studies in animals. The IARC classified ceramic fibres as possibly carcinogenic to humans (Group 2B). From inhalation studies in animals, the unit risk for lung tumours for a lifetime exposure to 1000 F/m^3 was estimated to be 10^{-6} per fibre/m^3 for fibres of length below 5 μm.

Radon is another indoor air pollutant known to cause lung cancer in humans. Average indoor concentrations range between 20 and 200 Bq/m^3. A study of lung cancer in workers showed a linear increase in lung cancer in response to increases in estimated radon exposure (Pershagen et al. 1994). Figure 3.9 shows the estimated proportion of lung cancers that can be attributed to residential radon. This figure can be used to assess the risk of radon exposure.

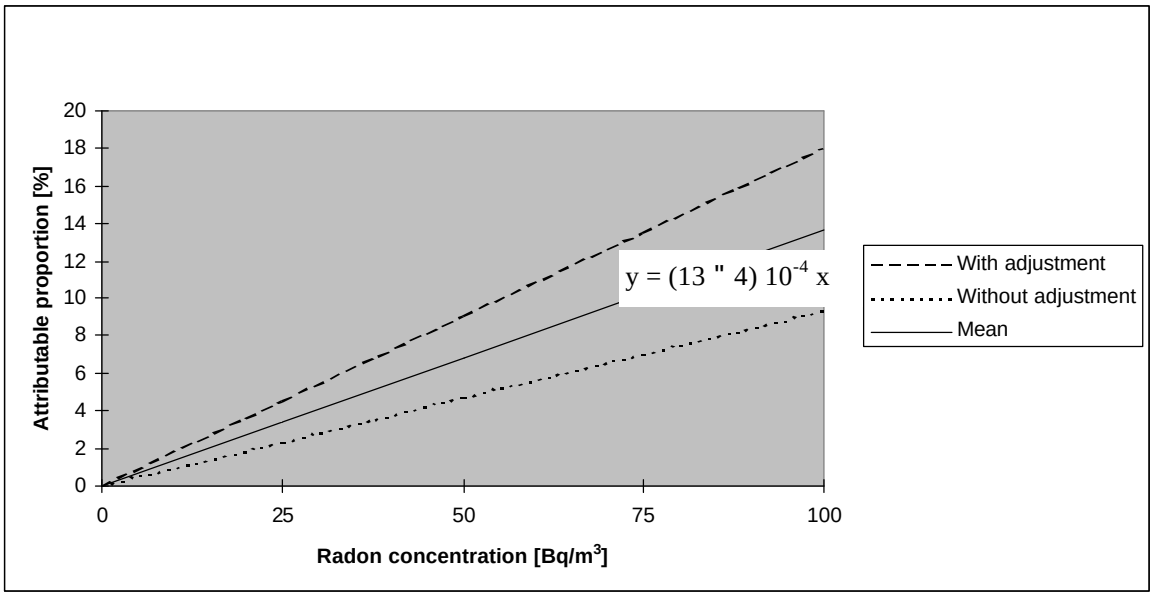

Figure 3.9. The proportion of lung cancers attributable to radon exposure.

3.3 Classical air pollutants: applicability of WHO Air Quality Guidelines for Europe *on a world-wide scale*

In the derivation of the WHO *Air Quality Guidelines for Europe*, assumptions were made for some compounds, which may not be applicable in some parts of the world. For some, but not all, pollutants the importance of different routes of exposure may vary from country to country. It should be understood that if such factors were to be taken into account then different guidelines could be derived. It is important that regulatory authorities should answer the following question before adapting for local use a guideline from the *Air Quality Guidelines for Europe*: Do local circumstances give cause to doubt the likely validity of the guideline set out in the WHO *Air Quality Guidelines* as a basis for setting local guidelines or standards? For a number of pollutants a unit risk assessment has been provided. These assessments are also dependent upon considerations of the comparative importance of different routes of exposure.

3.4 Studies of effects of air pollutants on health in WHO regions

As discussed above, the effects of air pollutants on health vary depending on several factors. These include the level of exposure and the susceptibility of the exposed population. The susceptibility of the population is affected by factors such as the numbers of young children and older people, as well as the proportion of people suffering from asthma and other chronic respiratory conditions. Epidemiological studies reflect this variation in sensitivity by showing different associations between levels of exposure and health effects for different subpopulations. In addition, sources and patterns of exposure, e.g. indoor and outdoor exposures, are likely to differ substantially from region to region. In part this is dependent upon weather conditions.

These factors and the variation in response-concentration relationships are powerful arguments for health studies being undertaken in the different WHO Regions on the effects of air pollutants.

It could be a mistake to simply adopt response-concentration relationships derived from Western European or North American studies for general use.

No general review drawing together the results of epidemiological studies on air pollution across the WHO Regions has been published. Regions differ significantly in terms of the number of studies undertaken and in the quality of those studies. Many, perhaps most, studies are done with the intention of characterising the local problem and quantifying the effects of air pollution on health. Preliminary studies to assess whether there is a problem are common.

Recent developments in our understanding of the effects of air pollutants on health suggest that, at least for particulate matter and O_3, all levels of exposure above zero are associated with effects on health. That pollutants such as sulphur and NO_2 should be regarded as no-threshold compounds seems toxicologically implausible, although such a conclusion is difficult to avoid given the current time-series data.

Sulphur dioxide

Latin America

Few epidemiological studies conducted in Latin America have investigated the effect of SO_2 on health. In a study conducted in Chile close to an industrial area where SO_2 annual means ranged from 101-145 $\mu g/m^3$, and maximum daily averages from 405-1230 $\mu g/m^3$, an increase of 50 $\mu g/m^3$ in the SO_2 daily mean value was related to a 4% increase in cough frequency (95% CI: 1-7%), a 3% increase in phlegm production (95% CI: 0-6%) and a 4% increase in wheeze occurrence (95% CI: 0-11%), with a one-day lag among children with chronic respiratory symptoms (Sanchez-Cortez 1997). A significant change in evening peak flow measurements was also observed. No effects were observed in children without chronic respiratory symptoms. In this study, health effects were observed at levels lower than 125 $\mu g/m^3$ (the WHO guideline) among susceptible children. However, SO_2 may have interacted with PM_{10} levels, which ranged from 5 to 125 $\mu g/m^3$ in this study.

In the same study, when areas with different long-term ambient levels of SO_2 were compared (70 $\mu g/m^3$ vs. 130 $\mu g/m^3$ annual mean over 3 years), the prevalence of chronic respiratory symptoms was higher in the area with the higher SO_2 annual means (30% vs. 14% for chronic cough and 14.3% vs. 6.1% for wheezing). The differences were statistically significant (Sanchez-Cortez 1997). PM_{10} annual means were low in both areas.

Mediterranean Region

Few studies have investigated the effects of air pollution on health in the Eastern Mediterranean region. In one study of residents of the Shoubra El-Kheima industrial area of Egypt results showed that 37.4% of the examined sample (4730 subjects) suffered from chronic obstructive pulmonary diseases (COPD) and the prevalence increased with age (El-Samara et al. 1984). This study found that 1478 students (out of the studied group of 6380 students) were suffering from COPD. A strong positive correlation was recorded between PM_{10} level and incidence of asthma.

Western Pacific Region

Japan

An epidemiological survey in Japan from 1981 to 1983 involved schoolchildren aged 6-12 years (Nitta et al. 1993; Ono et al. 1990; Nakai et al. 1995). Annual mean concentrations in urban areas ranged from 26.8-30.9 $\mu g/m^3$ SO_2. Suburban area levels ranged from 20.5-23.9 $\mu g/m^3$ and background levels from 13.3-22.9 $\mu g/m^3$. Comparison of the effect of SO_2 on human health in the different areas showed that the prevalence of asthmatic symptoms, of chest congestion and of phlegm significantly correlated with annual mean levels of SO_2.

China

Epidemiological investigations in China show short-term exposure to 280 $\mu g/m^3$ SO_2 was correlated with apparent effects on the health of traffic police, whose respiratory function was reduced by 29-64%, and whose incidence of chronic rhinitis and pharyngitis was raised by 30-90%, compared with the control group (BMEPB 1980). Where the annual average air concentration of SO_2 was 260 $\mu g/m^3$, secondary and elementary school students had a much higher incidence of chronic respiratory diseases than in less polluted areas. For example, the incidence of tonsil suppuration was increased 5.1-fold, simple rhinitis by 1.1-fold and nose engorgement by 0.9-fold (BMEPB 1980). Under long exposure to an annual average of 175 $\mu g/m^3$ SO_2 (with 550 $\mu g/m^3$ particulate matter also present), the three-year average mortality from pulmonary heart disease and respiratory diseases in the community was twice that of the control group (GMEPB 1980).

A study was conducted on the influence of SO_2 pollution on lung function of children and women (Chen et al. 1993). It found that at annual average concentration of 140 $\mu g/m^3$ (with 150 $\mu g/m^3$ particulate matter), SO_2 is associated with lower levels of lung function in children at the ages of 10-12, with major decreases in FVC and FEV_1. For each 60 $\mu g/m^3$ increment in annual average concentration of SO_2, there was an average 99 ml drop in the children's FVC and a 70 ml drop in FEV_1. The FVC of women was decreased by 57 ml under the same conditions. In addition, it was found that SO_2 can affect women's non-specific immunity in parts of their respiratory passages, lowering their average concentration of saliva lysozyme by 5.6 µg/ml and specific immuneglobuline by 32 µg/ml (Chen et al. 1995).

South East Asia

The results of epidemiological studies in India indicate that adverse health effects can be associated with ambient air SO_2 at an annual average concentration of 40 $\mu g/m^3$. Interpretation of these findings is complicated by the high co-existing particle levels, as well as by a number of additional local factors. These include high indoor and occupational exposure to air pollutants, below average health conditions and poor nutritional status, unsafe water supply, poor general hygiene etc.

A study of 4129 community residents of three areas of Bombay, representing three grades of air pollution conditions (based on secondary data), and a fourth area 40 km away towards the south-east as a control, found:

i. Higher morbidity in the two more polluted areas for breathing problems, cough and common colds. The city's residents in the polluted zone were the healthiest, even in comparison to rural populations. Other symptoms related to pollution were headache, eye irritation, chest

pain, skin lesions and intermittent cough.

ii. In the urban low pollution area there was a larger prevalence of cardiac complaints.

Table 3.6. Standardised prevalence of selected diseases in Bombay (after Kamat and Doshi 1987)

Disease	Urban SO_2 levels			
	Low (<50 µg/m^3)	Intermediate (51-100 µg/m^3)	High (>100 µg/m^3)	Rural (control)
Dyspnea	3.2	6.0	7.3	5.5
Chronic cough	1.7	2.7	5.1	3.3
Intermittent cough	0.4	5.8	15.6	3.7
Frequent colds	12.1	20.8	18.0	11.0
Chronic bronchitis	2.3	4.5	4.5	5.0
Cardiac disorders	8.2	4.3	6.8	2.7

A study (Kamat et al. 1992) of 4 comparable communities in central and north-eastern Bombay (2 each) among randomly matched 349 subjects in 1988-1989, along with ambient SO_2, NO_2 and SPM air monitoring was carried out in Parel, Maravali, Deonar and Dadar. Air pollutant levels in winter were higher particularly for SO_2 in Parel (up to 584 µg/m^3) and Maravali; Deonar showed lower pollution. Clinical respiratory symptoms were higher in Parel and Maravali (cough 12% and 11.2%, dyspnea 17% and 13.3% respectively). Cardiac problems were commoner in Parel (11.0%). Maravali had a high prevalence for headache and eye irritation (9.5%). Those using kerosene suffered more than those using gas (22.2% as compared to 9.2%) Lung functions (FVC, FEV_1) were lowest in Parel for males and in Maravali for females. Expiratory flow rates were lower at Dadar, followed by Maravali. Despite lower SO_2 pollution, symptoms in Maravali residents were comparable to those in Parel. It was conjectured that this may be due to added effect of diesel exhausts (NO_2, SPM) or other unmeasured chemicals.

Nitrogen dioxide

Latin America

There are few data from Latin America on the impact of outdoor sources of NO_2 exposure on health. As in many Latin American cities, NO_2 levels are usually low (WHO 1998b). However, in a preliminary study conducted in Sao Paulo, Brazil (Saldiva et al. 1995), a 75 µg/m^3 increase in NO_2 was related to a 30% increase in mortality for respiratory illness among children less than five years old.

In Mexico City, a time-series study of hospital emergency visits among children less than 15 years of age found NO_2 daily levels correlated with upper respiratory illnesses (Tellez-Rojo et al. 1999). Stronger associations were observed during the winter months, when NO_2 levels ranged from 40-160 µg/m^3 (mean 90 µg/m^3), and O_3 levels from 82-740 µg/m^3 (mean 368 µg/m^3). The correlation coefficient between pollutants and illness was 0.44. The highest indicated effect of NO_2 was observed with a two-day lag. A 56 µg/m^3 increase in daily NO_2 ambient concentration was associated with a 39% increase in upper respiratory illnesses (95% CI: 28-51%). However, given the mixture of contaminants, and the general low NO_2 levels observed in this study, it is not possible to ascertain that NO_2 is the contaminant responsible for the observed effects.

Western Pacific Region

Japan

From 1992 to 1995, the Japanese Environment Agency surveyed the health effects of air pollutants in about 15 000 schoolchildren (EA 1997). The results showed that the prevalence of asthmatic symptoms was higher at NO_2 levels above 37.6 $\mu g/m^3$ than below this level. In general, however, the levels of NO_2 in Japan are not high enough to demonstrate a clear cause-effect relationship between the prevalence of asthmatic symptoms and NO_2 concentration. But neither are they low enough to rule out a causal relationship.

A survey of respiratory symptoms as a function of distance from roads with heavy traffic showed that the prevalence rate of respiratory symptoms, such as chronic cough and wheezing, was higher in residents nearer roads (Nitta et al. 1993; Ono et al. 1990). When there were no indoor NO_2 sources except for gas cooking stoves, both indoor and individual levels of NO_2 were attributable primarily to automobile exhaust (Nakai et al. 1995).

It has been reported that an interaction between air pollution, especially NO_2, and high temperature, may synergistically increase lung cancer mortality rates, since regional differences in age-adjusted lung cancer rates were explained by an interaction between NO_2 and temperature (Choi et al. 1997).

China

In recent years, epidemiological studies examined NO_2 concentrations in kitchens of 160 city dwellers, as well as urine hydroxyproline (HOP) levels of individuals after 24-hour exposures. The results showed that in liquid petroleum gas (LPG) -fuelled kitchens, NO_2 peak concentrations can reach 990-1,809 $\mu g/m^3$ at the moment of ignition, 17-37.5 -fold higher than the daily average concentration of 50 $\mu g/m^3$ (background concentration). Also, the urine HOP levels of individuals cooking in LPG-fuelled kitchens were higher than those cooking in coal fuelled kitchens (Zhang Jinhiang et al. 1996). In contrast, NO_2 exposures produced by burning coal was significantly higher than those resulting from the burning of LPG.

A survey in four cities showed that the daily average value of indoor NO_2 concentration was 53 $\mu g/m^3$, and elevated levels of SO_2, CO and TSP were recorded. Studies of primary school students aged 10-15 years residing in this environment showed 30-70% suffer from coughing, and 7-40% suffer from phlegm; and the incidence of tonsillitis and hyperplasia of retropharyngeal lymph folliculi are 7-17% and 15-16%, respectively. In addition, effects on immunity indices (such as PHA skin test and saliva lysozyme) were also observed (Wang Jin et al. 1989; Qin Yuhui et al. 1990).

Studies on 60 healthy Beijing children aged 9-11 years, and exposed to NO_2 at a daily average level of 70-110 $\mu g/m^3$, with the peak values of 150-260 $\mu g/m^3$ for two months, reported a negative correlation between NO_2 concentration and peak expiratory flow rates (PEFR). The results indicate that increased NO_2 level could affect children's respiratory function, aggravate air duct blocking and subsequently reduce PEFR (Wang Lihua et al. 1994). Long-term exposure to 50-100 $\mu g/m^3$ NO_2 may significantly affect children's respiratory and immunity systems; and it may have similar effects on sensitive adults.

Australia

Morgan et al. (1998) examined the effects of outdoor air pollutants on daily hospital admissions in Sydney, Australia. A time-series analysis of counts of daily hospital admissions and outdoor air pollutants (1990-1994) showed that an increase in the daily maximum 1-hour concentration of NO_2 from the 10th to the 90th percentile was associated with an increase of 5.29% (95% CI: 1.07% to 9.68%) in childhood asthma admissions and 4.60% (95% CI: -0.17% to 9.61%) in COPD admissions. A similar increase in daily maximum 1-hour particle concentration was associated with an increase of 3.01% (95% CI: -0.38% to 6.52%) in COPD admissions. An increase from the 10th to the 90th percentile in daily maximum 1-hour NO_2 was associated with an increase of 6.71% (95% CI: 4.25% to 9.23%) in heart disease admissions among those 65 years and older. Increases in heart disease, COPD and childhood asthma were associated with increased NO_2 levels.

Carbon monoxide

Mediterranean Region

In Cairo, CO concentrations greater than the WHO *Guidelines for Air Quality* values were recorded in streets having moderate-to-heavy traffic densities in residential areas and in the city centre (Nasralla 1997). These concentrations resulted in high levels of COHb in the blood of traffic policemen, sometimes reaching more than 10%. This study also found a significant direct relationship between ischemic heart disease and COHb level in Cairo traffic policemen (Salem 1990).

Western Pacific Region

China

Chinese middle-school students residing in a relatively low-pollution district of Shenyang, and undergraduate students studying at a relatively low-pollution district of Beijing, had average blood COHb concentrations of 0.8 % and 0.5 % respectively. Research on the effect of indoor CO on children aged 8-13 years showed that for rooms with individual heating the average CO content was 12.4 mg/m^3 and the COHb blood levels in these children was 4.17%. In rooms with central heating, the CO concentration was 6.4 mg/m^3 and the COHb levels in was 1.79% (Liu Jifang et al. 1992). This study also showed that in individually heated rooms the children's saliva lysozyme exhibited lower activity than that in centrally heated rooms; and immunoglobulin G content of the former is less than that of the latter. This phenomenon suggests that CO pollution could result in hypoimmunity for children (Liu Jifang et al. 1992).

Ozone and other photochemical oxidants

Latin America

Several studies conducted in Mexico City have illustrated the association of acute peak daily O_3 concentration with respiratory health. A study conducted among children reported both acute and subacute effects of O_3 on lung functions (Castillejos et al. 1992). A 106 $\mu g/m^3$ rise in the mean 48-hour O_3 levels was associated with a decrease of 2% in FEV_1, and a 7.4% decrease in the forced expiratory flow FEF_{25-75}. A greater decrease in these parameters was observed in children with chronic cough, chronic phlegm or wheeze. In another study, conducted among

school children from Mexico City, that compared quintiles of O_3 concentration, a decrease of 1.43% in FVC and 2.85% in FEV_1 was reported in the highest quintile of O_3 concentration (364-730 µg/m^3) (Castillejos et al.1995). This change in FEV_1 is less than that predicted by Figure 3.2.

In a study conducted among pre-school children, an increase in school absenteeism for respiratory illnesses was observed among children exposed to higher O_3 concentrations (Romieu et al. 1992). Children exposed for two consecutive days to peak daily O_3 levels above 260 µg/m^3 had a 20% increase in risk of respiratory illness. For children exposed for 2 consecutive days to high O_3 levels (above 260 µg/m^3) and the previous day were exposed to low temperature, the risk of respiratory illness reached 40%. It is important to note that in Mexico City, and in some areas of Sao Paulo, levels of 260 µg/m^3 are frequently reached on several consecutive days.

O_3 exposure has also been related to emergency department visits for acute upper respiratory illness among children in Mexico City. An increase of 100 µg/m^3 in the 1-hour daily maximum was related to a 10% increase (95% CI: 7-13%) in upper respiratory illnesses during winter time. An increase of 100 µg/m^3 in the 1-hour daily maximum during 5 consecutive days was related to a 30% increase in upper respiratory illnesses (95% CI: 23-37%) (Tellez-Rojo et al. 1997). In this study a non-linear effect was observed in relation to O_3 levels. The upper respiratory illnesses increased linearly from 160-300 µg/m^3 and then tended to level off. A further increase in risk was observed at levels close to 440 µg/m^3. Effects at low concentrations of O_3 could not be studied.

Asthmatic children may be more susceptible than others to the effects of O_3 exposure. Studies conducted in Mexico City have shown that asthma-related emergency department visits increased 43% (95% CI: 24-66%) for an increase of 50 ppb in the daily 1-hour maximum O_3 level, with a 1-day lag (Romieu et al. 1995). In this study, peak O_3 concentrations ranged from 20-500 µg/m^3, with a mean of 180 µg/m^3.

In panels of asthmatic children, O_3 exposure has been related to a decrease in peak expiratory flow rate and an increase in respiratory symptoms (Romieu et al. 1996; Romieu et al. 1997). In general an increase of 100 µg/m^3 of daily peak O_3 concentrations led to an 11% increase (95% CI: 5-19%) of lower respiratory symptoms and a significant decrease in peak expiratory flow rate.

The decreased respiratory function observed among children exposed to O_3 in Mexico City seems to be smaller than that observed in children who are not chronically exposed to high levels of O_3, suggesting the existence of a phenomenon of "tolerance". This finding supports studies showing that repetitive exposures tend to produce smaller responses (Hackney et al. 1997; Folinsbee 1991). The potential adverse effect of such "tolerance", or functional adaptation, is not known, but the absence of a protective response to O_3 exposure (bronchoconstriction) could lead to a higher exposure of children and therefore a more severe long-term effect. Experimental studies in animals and humans have shown that O_3 increases airway permeability and particle clearance, causes airway inflammation and a decrease in bacterial capacity, causes structural alteration in the lung and accelerate ageing of the lung (Lippmann 1989; and Section 3.1).

Western Pacific Region

China

An investigation has been conducted in China on the effect of short-term O_3 exposure on lung function for male non-smokers. During the test, volunteers undertook a moderate amount of exercise at intervals; and parameters of vital capacity were monitored. The study data showed that under the condition of short-term exposure 180 ± 40 μg/m^3 is the threshold concentration for acute lung dysfunction; and 100μg/m^3 is the threshold concentration for general malaise (Fang Qisheng et al. 1991).

Australia

A time-series analysis of counts of daily hospital admissions and outdoor air pollutants in Sydney (Morgan et al. 1998) found that an increase in the daily maximum 1-hour O_3 concentration was associated with a 2.45% (95% CI: -0.37, 5.35) increase in heart disease admissions among those 65 years and older.

A study of daily mortality in the Brisbane region (Simpson et al. 1997) indicated that O_3 levels (maximum daily O_3 levels were about 240 μg/m^3) were significantly associated with total daily mortality. There was little evidence of interaction between the O_3 effects (mainly in summer) and particles or with SO_2 and NO_2. The associations between O_3 and daily mortality were significant only for individuals who were older than 65 years of age. Positive associations were also found with cardiovascular disease categories and the regression coefficients, when significant, were higher than those for total mortality. The results indicated a possible threshold for O_3 levels.

Suspended Particulate Matter

Latin America

Evaluation of the effects of short-term exposure on morbidity and mortality

Various studies in Latin America have assessed the effect of particulate matter pollution on health. These included mortality studies, and studies of the health effects of particulate matter on respiratory symptoms and functions among children and adults. Studies related to the effects of particulate matter pollution on mortality have been conducted in Brazil, Chile and Mexico. An increase of 10 μg/m^3 PM_{10} in Sao Paulo was related to an increase in daily mortality of 3% among adults older than 65 years of age (Saldiva et al. 1995). In Chile, a 0.8% increase (95% CI: 0.6-1.2%) in daily mortality was reported for an increase of 10 μg/m^3 PM_{10} (Ostro et al. 1999). In Mexico, a 0.5% increase (95% CI: 0.3-0.7%) in daily mortality was found for a similar increase in daily TSP (Borja-Aburto et al. 1997). These results are concordant with similar studies conducted in other parts of the world (Pope et al. 1995).

Studies conducted to determine the impact of particulate matter pollution on respiratory emergencies and medical visits have also suggested a positive association (Molina Esquivel et al. 1989; Ara-Seebla 1990; Arranda et al. 1994). In a study conducted in Santiago, Chile, respiratory-related emergency visits were related to ambient levels of PM_{10} and $PM_{2.5}$ during the winter months. In this study, PM_{10} levels ranged from 16-270 μg/m^3 and $PM_{2.5}$ levels from 10-156 μg/m^3. It was observed that an increase of 63.5 μg/m^3 in PM_{10} (1 quartile of the

distribution) was related to a 2% increase (95% CI: 0.5-3.4%) in respiratory-related emergency department visits, with a 2-day lag during the winter months. A 36.5 $\mu g/m^3$ in $PM_{2.5}$ was related to a 2.2% increase in the number of emergency department visits for acute respiratory illnesses (95% CI: 0.9-3.6%) with a 2-day lag. A similar increase in $PM_{2.5}$ was related to a 5.4% increase in the risk of acute pneumonia (95% CI: 1.9-5.6%) with a 3-day lag, and to a 3.7% increase in the risk of upper respiratory illnesses (95% CI: 1.9-5.6%) with a 2-day lag during winter (Ilabaca Marileo 1996). In this study, the $PM_{2.5}$ daily mean ranged from 10-156 $\mu g/m^3$, and the relation appeared to be linear over the range of concentration studied.

The dose-response curves of this study, for emergency department visits of patients with severe and not-so-severe respiratory diseases related to PM_{10} and $PM_{2.5}$, had smaller slopes than those provided in the WHO Guidelines (Figure 3.7). In fact, for PM_{10} the slope fell below the lower confidence limit provided. For $PM_{2.5}$, the slope was considerably smaller than that shown in the WHO Guidelines. However, when the relationship of $PM_{2.5}$ with pneumonia-related emergency department visits, a severe respiratory illness, was considered, the slope was larger and above the upper limit of the PM_{10} effect predicted by the WHO Guidelines.

Results from a panel study conducted in Punchucavi, Chile, indicated an increase of 5% in cough (95% CI: 1-10%) among children with chronic respiratory symptoms was associated with an increase of 30 $\mu g/m^3$ in the 24-hour average levels of PM_{10} (Sanchez-Cortez 1997).

Studies conducted in Mexico among asthmatic children have documented an increase in respiratory symptoms and a decrease in lung function related to exposure to PM_{10}. During the study, daily PM_{10} ambient levels ranged from 29-363 $\mu g/m^3$, with a mean of 167 $\mu g/m^3$, and daily $PM_{2.5}$ levels ranged from 23-177 $\mu g/m^3$, with a mean of 86 $\mu g/m^3$. The results suggested that an increase of 10 $\mu g/m^3$ in PM_{10} levels was associated with a 4% increase in minor respiratory symptoms, and a 0.35% decrease in peak expiratory flow rate (Romieu et al. 1996). In the same study, an increase of 10 $\mu g/m^3$ in the $PM_{2.5}$ daily mean level was associated with an 8% increase (95% CI: 3-14%) in the incidence of symptoms in the lower respiratory tract. It is important to note that results of this study suggest a synergistic effect of PM_{10} and O_3 exposure on the incidence of symptoms in the lower respiratory tract among these children.

Evaluation of the effects of long-term exposure on mortality and morbidity.

Few studies have investigated the long-term health effects of particulate matter in Latin America. In a study conducted in Rio de Janeiro, an association was found between the annual average TSP levels in different districts of the city and mortality for pneumonia among infants (Penna and Duchiade 1991). For each 10 $\mu g/m^3$ increase in TSP, the infant mortality from pneumonia was estimated to increase by 2.2 per 10,000 population.

Studies conducted in Cubatao, Brazil, have documented the decrease in pulmonary functions among children chronically exposed to high particle levels (Hofmeister 1987; Spektor et al. 1991). Children residing in the most polluted areas had lower pulmonary functions. Studies conducted in Chile (SERPLAC 1989; Arranda et al. 1993) reported a higher incidence of respiratory symptoms and lower pulmonary functions in children resident in Santiago than in a control city. The results suggested an association between cough, nocturnal respiratory symptoms and hoarseness, and PM_{10} levels. However, these studies do not provide sufficient data to quantitatively evaluate the risk.

Mediterranean Region

A study showed a significant increase of chest diseases occurred in schoolchildren living in Kafr El-Elwe (a residential settlement close to a cement company) and Helwan City, as compared with those living in Shebin El-Kom, a more rural area (Hussein 1988; Nasralla 1992). It was found that 29.2% of schoolchildren in the first two settlements have obstructive lung diseases compared to only 9% in Shebin El-Kom. Furthermore, the high rate of mortality due to chest and cardiovascular diseases among the population of Helwan and Maadi was related to the prevalence of high concentrations of suspended particles and SO_2 in the atmosphere (Hussein 1988; Nasralla 1992).

Western Pacific Region

Japan

An epidemiological survey of schoolchildren in Japan showed that the prevalence of asthmatic symptoms, and congestion in chest and phlegm, was significantly correlated with levels of SPM (Nitta et al. 1993; Ono et al. 1990; Nakai et al. 1995). The annual mean concentrations of SPM in urban, suburban and background areas were 45.1-52.7 μg/m^3, 36.5-43.3 μg/m^3 and 27.8-32.4 μg/m^3, respectively. The Japanese Environment Agency surveyed the health effects of air pollutants in about 15,000 schoolchildren (EA 1997). The results revealed a correlation between the prevalence of asthmatic symptoms and SPM at annual mean levels of 25-57 μg/m^3 SPM. An epidemiological study in 185 schoolchildren (Shima and Adachi 1996) has shown that children with high IgE levels appear to be particularly susceptible to the effects of automobile exhaust at annual average concentrations of SPM of about 34 μg/m^3.

A study of the morbidity of allergic rhinitis based on Japan National Health Insurance records showed a three-fold increase in the rate of allergic rhinitis (AR) over 10 years (Miyao et al. 1993). Additionally, results suggested possible correlations between the morbidity of AR and the mean yearly levels of the pollutant components SPM and NO_2.

China

Epidemiological studies in China show that under long-term exposure, there is a correlation between particle concentrations and mortality from lung cancer. An investigation based on data for 50 million people in 26 cities showed that the average PM_{10} pollution in urban districts and in control districts were 460 μg/m^3 and 220 μg/m^3, respectively, and the corresponding average mortality from lung cancer was 14.0% and 7.0% (He Xingzhou et al. 1984; Fang Qisheng et al. 1991). The incidence of respiratory diseases, mainly chronic broncho-pneumonia and emphysema, with symptoms of coughing and dyspnea, increased with increasing particle level. Every 100 μg/m^3 increase in TSP concentration led to a 6.75% increase in the incidence of chronic broncho-pneumonia in this coal-burning area. The results showed that exposure to 200 μg/m^3 of TSP can cause upper-respiratory diseases in children; and that 290-470 μg/m^3 of TSP significantly depressed immune functions in children. TSP concentrations less than 160 μg/m^3 had no obvious effect on the incidence of respiratory tract diseases. Another study found that organic extracts from TSP of different sizes had different strengths of mutagenic effects. The smaller the particle, the stronger its mutagenic effects (Li Xiuyun et al. 1992).

Exposure to TSP (with the daily-average concentration below 150 μg/m^3) produced an increased

frequency of attacks of asthma in some asthma patients. The lung function of children was reduced after short-term exposure to TSP concentrations over 250 μg/m^3. When TSP concentration were higher than 750 μg/m^3, middle-aged and old people, people with respiratory disease, and cardiovascular patients exhibited higher mortality (Li Xiuyun et al. 1992).

Australia

In Sydney, a time-series analysis of counts of daily hospital admissions and outdoor air pollutants (Morgan et al. 1998) showed that an increase in daily maximum 1-hour particle concentration was associated with an increase of 3.01% (95% CI: -0.38% to 6.52%) in hospital admissions for chronic obstructive pulmonary disease. An increase from the 10th to the 90th percentile in daily mean particle concentrations was associated with an increase in heart disease admissions among those 65 years and older of 2.82% (95% CI: 0.90 to 4.77), respectively.

A study of daily mortality in the Brisbane region (Simpson et al. 1997) indicated that the associations between total daily mortality and particle levels that were found in the United States and other countries might also be applicable in Brisbane. The associations between particulate matter and daily mortality were significant only for individuals who were older than 65 years of age; positive associations were also found with cardiovascular disease categories. And the regression coefficients, when significant, were higher than those for total mortality. The results did not indicate a threshold for particle levels.

Africa

A paucity of data exists in Africa about health effects associated with exposure to specific air pollutants. However, numerous studies in South Africa have indicated associations between a variety of respiratory symptoms and air pollution in urban, industrial and informal settlement areas. For example, high prevalence rates for respiratory illness were found in a residential suburb within an industrial area, relative to a suburb further away. Similarly, when compared with areas using cleaner fuel, raised levels of respiratory effects have been identified in informal settlements, where coal and wood were commonly used for domestic purposes (Opperman et al. 1993; Terblanche et al. 1992; Terblanche et al. 1993).

Lead

Latin America

Lead is transported to the fetus across the placenta since there is no metabolic barrier to fetal lead uptake. Parental exposure to lead produces toxic effects on the human fetus including reductions in gestational age, birthweight and mental development. A study conducted in Mexico has shown that the concentration of lead in the bone of a mother was significantly related to low birthweight (Gonzalez-Cossio et al. 1997).

The central nervous system is the primary target organ for lead toxicity in children (Needleman and Galsonis 1990), as discussed in Section 3.3. In agreement with these findings a study, conducted in Mexico City among schoolchildren from low-to-medium social status and aged 9-12 years, showed a strong negative correlation between blood lead level, and intellectual coefficients and teacher grading. There was no evidence of a threshold level (Muñoz et al. 1993).

The intensity of vehicular traffic, as a surrogate for exposure to ambient air lead, has been related to blood lead levels. In a study conducted in Mexico, children residing near a road with high traffic volumes had significantly higher levels of lead in blood than did children residing in a residential neighbourhood with smaller traffic volumes (Romieu et al. 1992). In another study conducted in Mexico among two hundred children younger than five years of age, the concentration of lead in ambient air was a significant predictor of blood lead levels (Romieu et al. 1995). The concentration of lead in ambient air (24-hour average) ranged from 0.20-0.52 $\mu g/m^3$. The correlation coefficient between lead in the blood and lead in ambient air was 0.30. It was estimated that for each increase of 1.5 $\mu g/m^3$ of lead in ambient air, the concentration of lead in blood would increase by 1 µg/dl.

Africa

Studies conducted in Johannesburg indicated that approximately 60% of children have blood lead levels exceeding 10 µg/dl. Children from an informal settlement group, where coal was largely used for cooking purposes, had significantly higher blood lead levels than their inner city and suburban counterparts. In Cape Town, about 13% of coloured pre-school and first-grade children had blood lead levels above 25 µg/dl (Deveaux et al. 1986; von Schirnding 1989; von Schirnding et al 1991).