



**Economic and Social  
Council**

Distr.  
GENERAL

EB.AIR/WG.1/2003/11  
17 June 2003

Original: ENGLISH

---

**ECONOMIC COMMISSION FOR EUROPE**

EXECUTIVE BODY FOR THE CONVENTION ON  
LONG-RANGE TRANSBOUNDARY AIR POLLUTION

Working Group on Effects  
(Twenty-second session, Geneva, 3-5 September 2003)  
Item 4 (g) of the provisional agenda

MODELLING AND ASSESSMENT OF THE HEALTH IMPACT  
OF PARTICULATE MATTER AND OZONE

Summary report prepared by the joint Task Force on the Health Aspects of Air Pollution of the World Health Organization/European Centre for Environment and Health and the Executive Body

I. INTRODUCTION

1. At its twentieth session the Executive Body for the Convention invited the Task Force on the Health Aspects of Air Pollution to evaluate and assess the health effects of long-range transboundary air pollution and to report to the Working Group on Effects in 2003 on a preliminary assessment of the health risk of particulate matter and ozone.

2. The sixth meeting of the Task Force on the Health Aspects of Air Pollution was held from 22 to 23 May 2003 in Bonn (Germany). It was attended by 21 experts from 12 Parties to the Convention, the World Health Organization's European Centre for Environment and Health, Bonn Office (WHO/ECEH), the European Commission (EC), the European Environment Agency (EEA), the EMEP Meteorological Synthesizing Centre-West (MSC-W), the Centre for Integrated Assessment Modelling (CIAM), and the Oil Companies' European Organization for Environment, Health and Safety (CONCAWE).

Documents prepared under the auspices or at the request of the Executive Body for the Convention on Long-range Transboundary Air Pollution for GENERAL circulation should be considered provisional unless APPROVED by the Executive Body.

3. The main objectives of the meeting were to:

(a) Review, on the basis of new knowledge and, in particular, the recent findings of the WHO project “Systematic review of health aspects of air pollution in Europe”, the availability of methods for health impact assessments for ozone and particulate matter from long-range transboundary air pollution which might be used in the forthcoming review of the Gothenburg Protocol; and

(b) Formulate recommendations concerning the process of health impact assessment and its details.

4. Mr. J. Schneider (WHO) summarized the results of the project “Systematic review of health aspects of air pollution in Europe” implemented by the WHO/ECEH Bonn Office to support the Clean Air for Europe (CAFE) programme of the European Commission (<http://europa.eu.int/comm/environment/air/cafе/index.htm>). This project finalized the hazard assessment for particulate matter, ozone and nitrogen dioxide in March 2003. The results were extensively reviewed by WHO experts and presented at a meeting of the CAFE Steering Group. The full WHO document presenting the results of the assessment is available at: <http://www.euro.who.int/document/e79097.pdf>.

5. Mr. A. Zuber (European Commission) informed the Meeting that the CAFE secretariat had prepared a set of additional questions which were addressed by WHO as part of the systematic review project.

6. The review by WHO/ECEH Bonn Office reaffirmed the health relevance of exposure to fine particulate matter and ozone at concentrations commonly present in Europe. Long-range transport of these pollutants contributed significantly to population exposure and related health effects.

7. The Task Force took note of the report and stressed the importance of its results for the work under the Convention and the CAFE programme. It agreed that a summary of the key findings of this hazard assessment should be communicated without any delay to the Working Group on Effects and to the Executive Body. It therefore decided to annex the “Summary of the WHO review” to this report, which summarizes the discussions of the sixth meeting of the Task Force and its conclusions and recommendations. This summary, presented in the form of questions and answers, provides concise information on the current scientific understanding of the health effects of particulate matter, ozone and nitrogen dioxide.

## II. PARTICULATE MATTER

8. Mr. M. Amann (CIAM) presented a working document on a methodology for including particulate matter (PM) related mortality into the integrated assessment modelling framework of the RAINS model. This document included a number of crucial assumptions, which the Task Force discussed in detail. The Task Force used the conclusions of the recent WHO/ECEH review to: (i) assume a causal relationship between PM exposure and mortality; and (ii) use the annual mean of PM<sub>2.5</sub> (PM<sub><2.5</sub> µm) as an indicator for PM-related mortality. The Task Force noted that some data suggested that different components that contributed to PM<sub>2.5</sub> mass might not be

equally hazardous. In particular, the discussion focused on the role of the secondary inorganic aerosols (including nitrates and sulphates). It concluded that, due to the absence of compelling toxicological data about different PM components acting in a complex mixture, it was not possible to quantify the relative importance of the main PM components for effects on human health at this stage.

9. For exposure assessment, the RAINS model would use PM concentration estimates and information on the place of residence of the population. On the regional scale, the PM estimates in the RAINS model were based on the results from the unified EMEP atmospheric dispersion model (<http://www.emep.int>), which provided PM concentrations at a scale of 50 km x 50 km. Concentrations and subsequent human exposure in urban background areas would be estimated using results from the City Delta project (<http://rea.ei.jrc.it/netshare/thunis/citydelta/>). It was noted that the unified EMEP model currently underestimated the observed PM concentrations, partly due to the fact that mineral dust and secondary organic aerosols were not yet included in the model. The Task Force stressed the importance of including secondary organic aerosols in the atmospheric modelling. It welcomed the new draft monitoring strategy of EMEP for PM and reiterated the potential usefulness of detailed PM data (including composition) for health studies. The Task Force also recognized that the overall uncertainty of the exposure estimates (including stochastic uncertainties) would be a necessary element for a comprehensive uncertainty analysis of the health impact assessment.

10. The Task Force endorsed the decision to apply the relative risk for all causes of mortality estimated for the average exposure level in the extended American Cancer Society (ACS) cohort study as described by Pope et al. (2002).<sup>1</sup> It was felt that this risk coefficient was a more appropriate choice than the estimates specific to the PM levels in the initial or final period of the follow-up in the ACS study, since there were indications that for some health end points, such as cardiopulmonary mortality, recent exposure was relevant, while for others, such as lung cancer, it could be assumed that exposure dating from both periods of exposure was important. Some participants noted that this choice was possibly biased towards underestimating the effects, since the population in the cohorts followed had an educational status above average in the United States, while the risk was higher for those with lower education. In addition, it was also noted that the estimate for relative risk from the ACS study was lower than from another available cohort study (the Six City Study). CIAM was invited to conduct sensitivity analysis using the relative risk based on the initial exposure level reported by Pope et al.

11. The Task Force concluded that it was appropriate to extrapolate the concentration-response function linearly to higher concentrations than those of the evidentiary population. It was assumed that this choice would not influence the results of the scenario analysis strongly, since it was expected that PM<sub>2.5</sub> concentrations at urban background locations would exceed the upper range of the ACS data only in a few cities in 2010 and onwards. CIAM was invited to conduct a sensitivity analysis using a log linear concentration-response relationship.

---

<sup>1/</sup> Pope C.A. et al. Lung cancer, cardiopulmonary mortality and long-term exposure to fine particulate air pollution. Journal American Medical Association, 2002; 287:1132-1141.

12. For the analysis of different emission reduction scenarios, the Task Force recommended using only the anthropogenic contribution to PM<sub>2.5</sub> mass; for this anthropogenic contribution, no no-effect level was assumed. The Task Force also agreed that both the reduction in life expectancy and the total number of years of life lost were relevant informative end points to be used in the scenario analysis.

13. The relative risk coefficient would be applied only to the population older than 30 years, which also meant some underestimation of the total health effects, since possible impacts of pollution on infant mortality was omitted from the calculation.

14. The Task Force also noted that the approach - while appropriate for including the effects of PM on human health into the integrated assessment framework - did not yield an overall quantification of all effects related to exposure to PM. Important effects which were currently not covered, but should eventually be taken into account in any cost benefit analysis, included infant mortality and morbidity outcomes.

15. The WHO/ECEH Bonn Office was invited to prepare in close collaboration with CIAM a note summarizing the reasoning for the choices mentioned, based on the discussions of the Task Force. CIAM was also invited to assess the robustness of the critical assumptions made and the underlying uncertainties and to report the result of this analysis back to the Task Force at its next meeting.

16. The Task Force noted with concern that the 6<sup>th</sup> Research Framework Programme of the European Union provided only limited possibilities for funding large multi-city studies to investigate some of the outstanding issues on the health effects of air pollution, which could potentially reduce the uncertainty. There was also a need for more studies on human exposure.

### III. OZONE

17. The Task Force noted that the AOT60 concept used previously within the RAINS model might no longer be appropriate to account for the effects of ozone on human health in the light of the findings of the review published by the WHO/ECEH Bonn Office and summarized in the annex. In particular, the WHO review had concluded that effects might occur at levels below 60 ppb, which was the current threshold level used to calculate AOT60, and a possible threshold, if any, might be close to background levels and not determinable. This review had also indicated that the effects of ozone on mortality and some morbidity outcomes were independent of those of PM.

18. The Task Force invited CIAM to propose a methodology to include the effects of ozone on mortality into integrated assessment modelling. Such a methodology should:

(a) Allow for calculations of attributable deaths, based on information from a meta-analysis of time-series studies. Mr. R. Anderson (United Kingdom) informed the Task Force that such a meta-analysis was currently being conducted by St. George's Hospital in London, as part of the WHO/ECEH systematic review project. He explained that the meta-analysis would make use of an extensive database of time-series studies which was continuously updated at St. George's Hospital;

- (b) Base its exposure assessment on urban background ozone concentrations for urban populations (mean of daily eight-hour maximum values). These concentrations would also be provided by the unified EMEP model and results from the City Delta project;
- (c) Be robust in relation to key assumptions. In particular, CIAM was requested to investigate the influence of hemispheric ozone background concentrations on the selected approach;
- (d) Include in the sensitivity analysis the study of consequences of limiting the analysis of impacts to the summer season using the summer-specific relative risk coefficients;
- (e) Be presented at the next meeting of the Task Force.

19. CIAM was also invited to suggest some indicative comparisons of attributable deaths from short-term exposure to ozone and PM, and from long-term exposure to PM. The estimation of the number of attributable deaths from the short-term exposures to both ozone and PM should be based on the above-mentioned meta-analysis of time-series studies conducted by St. George's Hospital, London.

#### IV. MORBIDITY

20. The current RAINS model framework and other regional or global health impact assessments lacked an appropriate methodology to include effects on morbidity. This was due to various reasons such as the lack of data on baseline rates, the differences in baseline rates, the differences and non-uniformity in health and effects reporting, etc. Inclusion of morbidity end points in health impact assessments was however important to estimate the contribution to health effects in terms of the number of attributable cases as well as to the total burden of disease and the cost and benefits of reducing the pollution.

21. Mr. L. van Bree (Netherlands) informed the Task Force on a proposal to establish a stepwise harmonized methodology to include morbidity end points into health impact assessments. He explained the current difficulties as described above and suggested a feasibility study with specific data (e.g. from studies in the Netherlands). The Task Force took note of the work and concluded that it was premature to include morbidity as a health outcome explicitly into the RAINS integrated assessment framework. It invited Mr. L. van Bree to report back on the progress of the feasibility study.

#### V. GENERAL RECOMMENDATIONS

22. The Task Force discussed the need to present the (un)certainty of the estimated health impacts and possible changes due to the reduction of the population exposure to the pollution. It concluded that maintaining the clarity of presentation and of the action-related results of the modelling was an essential prerequisite. However, an assessment of the sensitivity of the applied methodology to the assumptions was a necessary element of the analysis. An important part of this analysis was a demonstration of the impacts of the key assumptions made in the health impact assessment analysis on the proposed pollution abatement strategies. It was recommended that a formal approach to uncertainty analysis should be developed as an integral part of the overall health impact assessment. Such an approach should be prepared by CAIM in close collaboration with WHO/ECEH Bonn Office.

## VI. WORK-PLAN

23. The next meeting of the Task Force would be held in early 2004 in Bonn (Germany). This meeting would review the preliminary results obtained with the RAINS model to estimate the impacts of the health effects of PM and ozone, and would provide an opportunity to formulate final comments on specific assumptions and the approach taken.

24. The Task Force invited the WHO/ECEH Bonn Office to propose a more detailed work-plan for 2004 and beyond. Potential issues for an in-depth assessment included the carcinogenic potential of certain air pollutants, work on source-related health risks (such as traffic), a reassessment of the importance of different PM fractions, possible impacts and relationships with climate change, and health gains from (past) emissions abatement.

Annex<sup>2</sup>**HEALTH ASPECTS OF AIR POLLUTION WITH PARTICULATE MATTER,  
OZONE AND NITROGEN DIOXIDE**Summary of the WHO review

(<http://www.euro.who.int/document/e79097.pdf>)

In 2001, WHO agreed with the European Commission to provide the Clean Air For Europe (CAFE) programme of DG Environment of the European Commission with a systematic, periodic, scientifically independent review of the health aspects of air quality in Europe. The CAFE Steering Group, which advises DG Environment of the European Commission on the strategic direction of the CAFE programme, has formulated specific questions to be addressed by the WHO process and decided that the review should focus on: particulate matter (PM), nitrogen dioxide (NO<sub>2</sub>) and ozone (O<sub>3</sub>). These questions were forwarded to WHO and then restructured to enable a harmonized approach to be taken for the review of all three pollutants.

Elaboration of the answers to the questions involved ca. 50 experts from Europe and North America preparing and reviewing consecutive drafts. The final text of the answers was agreed by a WHO Working Group meeting, held from 13 to 15 January 2003 in Bonn, Germany. Besides the answers, the Working Group prepared a rationale to each answer, providing essential references and justifying decisions taken by the reviewers evaluating the scientific evidence. This summary presents full text of the answers only. The rationale, as well as all other information prepared by the review process, can be found in the WHO document "Health Aspects of Air Pollution with Particulate Matter, Ozone and Nitrogen Dioxide", WHO/Euro, 2003 (<http://www.euro.who.int/document/e79097.pdf>).

**I. PARTICULATE MATTER (PM)**

1) Is there new scientific evidence to justify reconsideration of the current WHO Guidelines for the pollutant?

The current WHO Air quality guidelines (AQC) provide exposure-response relationships describing the relation between ambient PM and various health end points. No specific guideline value was proposed as it was felt that a threshold could not be identified below which no adverse effects on health occurred. In recent years, a large body of new scientific evidence has emerged that has strengthened the link between ambient PM exposure and health effects (especially cardiovascular effects), justifying reconsideration of the current WHO PM Air quality guidelines (AQGs) and the underlying exposure-response relationships.

The present information shows that fine particles (commonly measured as PM<sub>2.5</sub>) are strongly associated with mortality and other end points such as hospitalization for cardio-pulmonary disease, so that it is recommended that Air quality guidelines for PM<sub>2.5</sub> be further developed.

---

2 The annex is reproduced as received by the secretariat.

Revision of the PM<sub>10</sub> WHO AQGs and continuation of PM<sub>10</sub> measurement is indicated for public health protection. A smaller body of evidence suggests that coarse mass (particles between 2.5 and 10 µm) also has some effects on health, so a separate guideline for coarse mass may be warranted. The value of black smoke as an indicator for traffic-related air pollution should also be re-evaluated.

- 2) Which effects can be expected of long-term exposure to levels of PM observed currently in Europe (include both clinical and pre-clinical effects, e.g. development of respiratory system)?

Long-term exposure to current ambient PM concentrations may lead to a marked reduction in life expectancy. The reduction in life expectancy is primarily due to increased cardio-pulmonary and lung cancer mortality.

Increases are likely in lower respiratory symptoms and reduced lung function in children, and chronic obstructive pulmonary disease and reduced lung function in adults.

- 3) Is there a threshold below which no effects on health of PM are expected to occur in all people?

Epidemiological studies on large populations have been unable to identify a threshold concentration below which ambient PM has no effect on health. It is likely that within any large human population, there is such a wide range in susceptibility that some subjects are at risk even at the lowest end of the concentration range.

- 4) Are effects of the pollutant dependent upon the subjects' characteristics such as age, gender, underlying disease, smoking status, atopy, education etc? What are the critical characteristics?

In short-term studies, elderly subjects, and subjects with pre-existing heart and lung disease were found to be more susceptible to effects of ambient PM on mortality and morbidity. In panel studies, asthmatics have also been shown to respond to ambient PM with more symptoms, larger lung function changes and with increased medication use than non-asthmatics.

In long-term studies, it has been suggested that socially disadvantaged and poorly educated populations respond more strongly in terms of mortality. PM also is related to reduced lung growth in children.

No consistent differences have been found between men and women, and between smokers and non-smokers in PM responses in the cohort studies.

- 5) To what extent is mortality being accelerated by long- and short-term exposure to the pollutant (harvesting)?

Cohort studies have suggested that life expectancy is decreased by long-term exposure to PM. This is supported by new analyses of time-series studies that have shown death being advanced by periods of at least a few months, for causes of death such as cardiovascular and chronic pulmonary

disease.

- 6) Is the considered pollutant per se responsible for effects on health?

Ambient PM per se is considered responsible for the health effects seen in the large multi-city epidemiological studies relating ambient PM to mortality and morbidity such as NMMAPS and APHEA. In the Six Cities and ACS cohort studies, PM but not gaseous pollutants with the exception of sulphur dioxide was associated with mortality. That ambient PM is responsible per se for effects on health is substantiated by controlled human exposure studies, and to some extent by experimental findings in animals.

- 7) For PM: which of the physical and chemical characteristics of particulate air pollution are responsible for health effects?

There is strong evidence to conclude that fine particles ( $< 2.5 \mu\text{m}$ ,  $\text{PM}_{2.5}$ ) are more hazardous than larger ones (coarse particles) in terms of mortality and cardiovascular and respiratory end points in panel studies. This does not imply that the coarse fraction of  $\text{PM}_{10}$  is innocuous. In toxicological and controlled human exposure studies, several physical, biological and chemical characteristics of particles have been found to elicit cardiopulmonary responses. Amongst the characteristics found to be contributing to toxicity in epidemiological and controlled exposure studies are metal content, presence of PAHs, other organic components, endotoxin and both small ( $< 2.5 \mu\text{m}$ ) and extremely small size ( $< 100 \text{nm}$ ).

- 8) What is the evidence of synergy / interaction of the pollutant with other air pollutants?

Few epidemiological studies have addressed interactions of PM with other pollutants. Toxicological and controlled human exposure studies have shown additive and in some cases, more than additive effects, especially for combinations of PM and ozone, and of PM (especially diesel particles) and allergens. Finally, studies of atmospheric chemistry demonstrate that PM interacts with gases to alter its composition and hence its toxicity.

- 9) What is the relationship between ambient levels and personal exposure to the pollutant over the short term and long term (including exposures indoors)? Can the differences influence the results of studies?

Whereas personal exposure to PM and its components is influenced by indoor sources (such as smoking) in addition to outdoor sources, there is a clear relationship on population level between ambient PM and personal PM of ambient origin over time, especially for fine combustion particles. On a population level, personal PM of ambient origin 'tracks' ambient PM over time, thus measurements of PM in ambient air can serve as a reasonable 'proxy' for personal exposure in time-series studies.

The relationship between long-term average ambient PM concentrations and long-term average personal PM exposure has been studied less. Contributions to personal PM exposure from smoking and occupation need to be taken into account. However, the available data suggest that imperfect relations between ambient and personal PM do not invalidate the results of the long-

term studies.

10) Which are the critical sources of the pollutant (or, for PM, its components) responsible for health effects?

Short-term epidemiological studies suggest that a number of source types are associated with health effects, especially motor vehicle emissions, and also coal combustion. These sources produce primary as well as secondary particles, both of which have been associated with adverse health effects. One European cohort study focused on traffic-related air pollution specifically, and suggested the importance of this source of PM. Toxicological studies have shown that particles originating from internal combustion engines, coal burning, residual oil combustion and wood burning have strong inflammatory potential. In comparison, wind-blown dust of crustal origin seems a less critical source.

11) Have positive impacts on public health of reductions of emissions and/or ambient concentrations of the pollutant been shown?

Positive impacts of reductions in ambient PM concentrations on public health have been shown in the past, after the introduction of clean air legislation. Such positive impacts have also been reported more recently in a limited number of studies. Toxicological findings also suggest that qualitative changes in PM composition could be of importance for the reduction of PM-induced adverse health effects.

12) What averaging period (time pattern) is most relevant from the point of view of protecting human health?

As effects have been observed from both short-term and long-term ambient PM exposures, short-term (24 hours) as well as long-term (annual average) guidelines are recommended.

## II. OZONE (O<sub>3</sub>)

1) Is there new scientific evidence to justify reconsideration of the current WHO Guidelines for ozone (O<sub>3</sub>)?

The current WHO Air quality guidelines (AQG) (WHO, 2000) for O<sub>3</sub> provide a guideline value of 120µg/m<sup>3</sup> (60 ppb), based on controlled human exposure studies, for a maximum 8-hour concentration. The AQG also provide two concentration-response tables, one for health effects estimated from controlled human exposure studies and one from epidemiological studies. No guideline for long-term effects was provided. Since the time these guidelines were agreed, there is sufficient evidence for their reconsideration. Issues to be considered are: the averaging time(s) for the short-term guidelines and their associated levels, the concentration-response functions used in the tables, the outcomes included in the concentration-response tables, whether a long-term guideline and/or complementary guidelines (e.g. restricting personal activity) should be adopted.

Recent epidemiological studies have strengthened the evidence that there are short-term O<sub>3</sub> effects on mortality and respiratory morbidity and provided further information on exposure-response

relationships and effect modification. There is new epidemiological evidence on long-term O<sub>3</sub> effects and experimental evidence on lung damage and inflammatory responses. There is also new information on the relationship between fixed site ambient monitors and personal exposure, which affects the interpretation of epidemiological results.

2) Which effects can be expected of long-term exposure to levels of O<sub>3</sub> observed currently in Europe (both clinical and pre-clinical effects)?

There are few epidemiological studies on the chronic effects of ozone on human health. Incidence of asthma, a decreased lung function growth, lung cancer and total mortality are the main outcomes studied. At levels currently observed in Europe, the evidence linking O<sub>3</sub> exposure to asthma incidence and prevalence in children and adults is not consistent. Available evidence suggests that long-term O<sub>3</sub> exposure reduces lung function growth in children. There is little evidence for an independent long-term O<sub>3</sub> effect on lung cancer or total mortality.

The plausibility of chronic damage to the human lung from prolonged O<sub>3</sub> exposure is supported by the results of a series of chronic animal exposure studies.

3) Is there a threshold below which no effects on health are expected to occur in all people?

There is little evidence from short-term effect epidemiological studies to suggest a threshold at the population level. It should be noted that many studies have not investigated this issue. Long-term studies on lung function do not indicate a threshold either. However, there may well be different concentration-response curves for individuals in the population, since in controlled human exposure and panel studies there is considerable individual variation in response to O<sub>3</sub> exposure. From human controlled exposure studies, which generally do not include especially sensitive subjects, there is evidence for a threshold for lung damage and inflammation at about 60 to 80 ppb (120-160 µg/m<sup>3</sup>) for short-term exposure (6.6 hours) with intermittent moderate exercise. Where there are thresholds, they depend on the individual exercise levels.

4) Are effects of O<sub>3</sub> dependent on subjects' characteristics such as age, gender, underlying disease, smoking status, atopy, education, etc.?

Individuals vary in their O<sub>3</sub> responsiveness for different outcomes, for reasons which remain largely unexplained but appear to be partly based on genetic differences. There is some evidence that short-term O<sub>3</sub> effects on mortality and hospital admissions increase with age. Gender differences are not consistent. It appears that the effects of O<sub>3</sub> exposure on symptoms are greater in asthmatic children. Lung function decrements are more consistent in asthmatic children, especially those with low birth weight.

One important factor modifying the effect of O<sub>3</sub> on lung function is ventilation rate. As tidal volume increases, O<sub>3</sub> penetrates deeper into the lungs. Duration of exposure is also a critical factor: Ozone effects accumulate over many hours but after several days of repeated exposures there is adaptation in functional but not inflammatory responses. The effects of O<sub>3</sub> exposure on lung function, symptoms and school absences are larger in children who exercise more or spend more time outdoors.

- 5) To what extent is mortality being accelerated by long- and short-term exposure to O<sub>3</sub> (harvesting)?

Long-term O<sub>3</sub> effects have been studied in two cohort studies. There is little evidence of an independent long-term O<sub>3</sub> effect on mortality so that no major loss of years of life is expected. The issue of harvesting, i.e. the advancement of mortality by only relatively few days, has not been addressed in short-term exposure studies of O<sub>3</sub>.

- 6) Is O<sub>3</sub>, per se, responsible for effects on health?

In short-term studies of pulmonary function, lung inflammation, lung permeability, respiratory symptoms, increased medication usage, morbidity and mortality, O<sub>3</sub> appears to have independent effects (especially in the summer). For long-term effects the results are not entirely consistent. When particle acidity was studied, O<sub>3</sub> effects were partly explained. A few studies in North America found effects of O<sub>3</sub> on asthma incidence and functional changes independent of other classical pollutants, but acidity was not taken into account.

Experimental studies show the potential of O<sub>3</sub> to cause these health effects.

- 7) For PM: which of the physical and chemical characteristics of particulate air pollution are responsible for health effects?

Not relevant for ozone.

- 8) What is the evidence of synergy/interaction of O<sub>3</sub> with other air pollutants?

Epidemiological studies show that short-term effects of O<sub>3</sub> can be enhanced by particulate matter and vice versa. Experimental evidence from studies at higher O<sub>3</sub> concentrations shows synergistic, additive or antagonistic effects, depending on the experimental design, but their relevance for ambient exposures is unclear. O<sub>3</sub> may act as a primer for allergen response.

- 9) What is the relationship between ambient levels and personal exposure to O<sub>3</sub> over short and long periods (including exposures indoors)? Can the differences influence the results of studies?

Personal exposure measurements are not well correlated with ambient fixed site measurements. To account for that, in some studies, additional information (e.g., activity patterns) was used to improve personal exposure estimates based on fixed site measurements. Being a highly reactive gas, O<sub>3</sub> concentrations indoors are generally lower (less than 50%) than those in ambient air. There are very few indoor sources in most homes (such as xerographic copiers, electrostatic air cleaners). Outdoor O<sub>3</sub> levels vary across city areas because O<sub>3</sub> is scavenged in the presence of NO. Early morning and late night exposures outdoors are lower because of the diurnal cycle of ambient O<sub>3</sub>. Thus, for O<sub>3</sub>, cumulative daily or long-term average exposures are largely determined by exposures occurring outdoors in the afternoon. The studied effects of exposure misclassification are in the direction of underestimation of O<sub>3</sub> exposure effects and may conceal real effects.

- 10) Which are the critical sources of the pollutant responsible for health effects?

Ozone is a secondary pollutant produced by photochemical activity in the presence of precursors. The working group felt that it was beyond its core competence to give a detailed description of ozone formation and dispersion patterns.

- 11) Have positive impacts on public health of reductions of emissions and/or ambient concentrations of O<sub>3</sub> been shown?

There are very few opportunities to evaluate O<sub>3</sub> reduction per se. One study of intra-state migrants showed a beneficial effect on lung function in children who moved to lower PM and O<sub>3</sub> areas. A decrease in O<sub>3</sub> during the 1996 Olympics was associated with a reduction of asthma admissions. The interpretation of these findings is unclear.

- 12) What averaging period (time pattern) is most relevant from the point of protecting human health?

For short-term exposure, it is clear that the effects increase over multiple hours (e.g., 6-8 hours for respiratory function effects and lung inflammation). Thus, an 8-hour averaging time is preferable to a 1-hour averaging time. The relationship between long-term O<sub>3</sub> exposure and health effects is not yet sufficiently understood to allow for establishing a long-term guideline.

### III. NITROGEN DIOXIDE (NO<sub>2</sub>)

- 1) Is there new scientific evidence to justify reconsideration of the current WHO Guidelines for nitrogen dioxide (NO<sub>2</sub>)?

The current WHO guideline values for NO<sub>2</sub> are a 1-hour level of 200 µg/m<sup>3</sup> and an annual average of 40 µg/m<sup>3</sup>. Since the previous review, only a small number of additional human exposure studies have been carried out. These do not support the need to change the 1-hour guideline value. With regard to the annual average, there have been some new epidemiological studies reporting associations of longer-term exposure with lung function and respiratory symptoms. The former group that proposed the annual guideline value of 40 µg/m<sup>3</sup> acknowledged that “although there is no particular set of studies that clearly support the selection of a specific numerical value for an annual average guideline the database nevertheless indicates a need to protect the public from chronic nitrogen dioxide exposures.” Because of a lack of evidence, the former group selected a value from a prior WHO review. The new evidence does not provide sufficient information to justify a change in the guideline value. Given the role of NO<sub>2</sub> as a precursor of other pollutants and as a marker of traffic-related pollution, there should be public health benefits from meeting the current guidelines. Thus the present working group did not find sufficient evidence to reconsider the current 1-hour and annual WHO guidelines for NO<sub>2</sub>.

- 2) Which effects can be expected of long-term exposure to levels of NO<sub>2</sub> observed currently in Europe (both pre-clinical and clinical effects)?

The epidemiological studies provide some evidence that long-term NO<sub>2</sub> exposure may decrease lung function and increase the risk of respiratory symptoms.

- 3) Is there a threshold below which no effects of NO<sub>2</sub> on health is expected to occur in all people?

The evidence is not adequate to establish a threshold for either short- or long-term exposure. While a number of epidemiological studies have described concentration-response relationships between ambient NO<sub>2</sub> and a range of health outcomes, there is no evidence for a threshold for NO<sub>2</sub>.

- 4) Are effects of NO<sub>2</sub> dependent upon the subjects' characteristics such as age, gender, underlying disease, smoking status, atopy, education, etc.? What are the critical characteristics?

In general, individuals with asthma are expected to be more responsive to short-term exposure to inhaled agents, when compared to individuals without asthma. Controlled human exposure studies of short-term responses of persons with and without asthma to NO<sub>2</sub> have not been carried out. There is limited evidence from epidemiological studies that individuals with asthma show steeper concentration-response relationships. Small-scale human exposure studies have not shown consistent effects of NO<sub>2</sub> exposure on airways reactivity in persons with asthma, even at exposure levels higher than typical ambient concentrations. As for other pollutants, children can reasonably be considered to be at increased risk. There is limited evidence for influence of the other listed factors on the effects of NO<sub>2</sub>.

- 5) To what extent is mortality being accelerated by long- and short-term exposure to the pollutant (harvesting)?

Methodological limitations constrain identification of harvesting due to NO<sub>2</sub> itself. The few long-term studies have not shown evidence for association between NO<sub>2</sub> and mortality. Associations have been observed between NO<sub>2</sub> and mortality in daily time-series studies, but on the basis of present evidence these cannot be attributed to NO<sub>2</sub> itself with reasonable certainty.

- 6) Is the considered pollutant per se responsible for effects on health?

The evidence for acute effects of NO<sub>2</sub> comes from controlled human exposure studies to NO<sub>2</sub> alone. For the effects observed in epidemiological studies, a clear answer to the question cannot be given. Effects estimated for NO<sub>2</sub> exposure in epidemiological studies may reflect other traffic related pollutants, for which NO<sub>2</sub> is a surrogate. Additionally there are complex interrelationships among the concentrations of NO<sub>2</sub>, PM and O<sub>3</sub> in ambient air.

- 7) For PM: which of the physical and chemical characteristics of particulate air pollution are responsible for health effects?

Not relevant for nitrogen dioxide.

- 8) What is the evidence of synergy / interaction of the pollutant with other air pollutants?

There have been few controlled human exposure studies on interactions with other chemical pollutants, although several studies show that NO<sub>2</sub> exposure enhances responses to inhaled pollens. Some epidemiological studies have explored statistical interactions of NO<sub>2</sub> with other pollutants, including particles, but the findings are not readily interpretable.

- 9) What is the relationship between ambient levels and personal exposure to the pollutant over the short term and long term (including exposures indoors)? Can the differences influence the result of studies?

In any particular setting the answer will depend on the relative contributions of outdoor and indoor sources and on personal activity patterns. A direct relationship between personal exposure and outdoor concentrations is found in the absence of exposure to indoor sources such as unvented cooking or heating appliances using gas, and tobacco smoking. However, since outdoor NO<sub>2</sub> is subject to wide variations caused by differences in proximity to road traffic and local weather conditions, the relationship of personal exposure to measurements made at outdoor monitoring stations is variable. Results of epidemiological studies relying on outdoor NO<sub>2</sub> concentrations may be difficult to interpret if account is not taken of exposure to indoor sources.

- 10) Which are the critical sources of the pollutant responsible for health effects?

In most urban environments in Europe, the principal source of NO<sub>2</sub> is NO<sub>x</sub> from motor vehicles of all types and energy production in some places.

- 11) Have positive impacts on public health of reduction of emissions and/or ambient concentrations of NO<sub>2</sub> been shown?

No recent peer-reviewed publication could be found to answer this question.

- 12) What averaging period (time pattern) is the most relevant from the point of view of public health and would additional protection be provided by setting standards for more than one averaging period for NO<sub>2</sub>?

With regard to protection against acute health effects, either the peak-hour average or 24hr (daily) average NO<sub>2</sub> concentrations can be used as a measure of direct short-term exposure, since they are highly correlated in urban areas. Having a longer-term guideline value is also supported by the evidence on possible direct effects of NO<sub>2</sub>, and on its indirect consequences through the formation of secondary pollutants.