WHO Expert Consultation:

Available evidence for the future update of the WHO Global Air Quality Guidelines (AQGs)

Meeting report
Bonn, Germany
29 September-1 October 2015

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ABSTRACT

WHO Air Quality Guidelines (AQGs) are used as a reference tool to help decision-makers across the world in setting standards and goals for air quality management. Their regular update is essential to continue protecting populations from the adverse health effects of air pollution.

In the last years, new evidence has emerged on the health effects of ambient air pollutants. In September 2015 WHO organized a global consultation meeting to seek expert opinion on the latest available evidence on the health effects of several ambient air pollutants and on interventions to reduce air pollution. The results from this consultation will contribute to the thinking behind the future update of the AQGs.

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1. Background

Air pollution, both indoor and outdoor, is a recognized threat to human health, even at low doses, and has been convincingly associated with increased mortality and morbidity worldwide. WHO estimated that 3.7 million persons died prematurely in 2012 due to the effects of ambient air pollution, with the Western Pacific and South East Asian regions bearing most of the burden (WHO 2012). These premature deaths are to a large extent due to ischaemic heart disease, stroke, COPD, lower respiratory tract infections and lung cancer, diseases which ranked among the top ten causes of death in the world in 2012.

Rather than decreasing, recent studies show that the burden of disease attributable to ambient air pollution has increased steadily worldwide since 1990, and that the global risk factor of ambient particulate matter in terms of attributable DALYs increased by 6% between 2000 and 2013 (Forouzanfar et al. 2015). This underscores the importance and the growing need to establish effective public policies that mitigate the environmental determinants of these complex diseases.

1.1. The 2015 World Health Assembly and the need to update existing air quality guidelines

The sixty-eighth World Health Assembly (WHA), the decision-making body of the WHO, adopted in May 2015 a resolution under the title *"Health and the Environment: Addressing the health impact of air pollution"* which was endorsed by 194 Member States (MSs) (WHO 2015). This resolution stated the need to redouble the efforts of MSs and WHO to protect populations from the health risks posed by air pollution.

MSs are urged to raise public and stakeholder awareness on the impacts of air pollution on health, provide measures to reduce or avoid exposure and facilitate relevant research, along with developing policy dialogue, strengthen multisector cooperation at national, regional and international levels and take effective steps to reduce health inequities related to air pollution.

This resolution for the first time recognized the role of WHO air quality guidelines (AQGs) for both ambient air quality and indoor air quality in providing guidance and recommendations for clean air that protect human health. In particular, it requested the Director-General to strengthen WHO capacities in the field of air pollution and health through the development and regular update of WHO AQGs in order to facilitate effective decision making, and to provide support and guidance to MS in their efficient implementation.

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1.2.   Scope of the consultation

As a response to the WHA resolution, and considering the conclusions from a recent review of the scientific evidence on health aspects of air pollution conducted as part of the WHO REVIHAAP Project (2013) (WHO 2013), WHO organized an expert consultation in Bonn, Germany, from the 29th of September to the 1st of October 2015, as a preliminary step in the process of the future update of the global AQGs.

The objective of this consultation was to obtain expert opinion and guidance in order to identify and discuss the latest available evidence on health effects of ambient air pollutants and interventions to reduce air pollution, to contribute to the thinking behind the future update of the AQGs. To this end, WHO convened 28 participants with a global geographic representation (from all six WHO regions) and a wide array of expertise in relation to air pollution from the fields of epidemiology, toxicology and clinical evidence, risk and exposure assessment, atmospheric chemistry, methodology, policy implications, and accountability research/intervention studies. Representatives from WHO Headquarters, WHO Regional Office for the Eastern Mediterranean, WHO Regional Office for Europe, and the International Agency for Research on Cancer (IARC) were also in attendance. Annex 1 presents a full list of the meeting participants.

Experts were asked to identify and discuss the available scientific evidence on a number of ambient air pollutants, as well as methodological issues and implications of recent research and intervention studies for the future update of the ambient AQGs. The outcome of this expert consultation will serve as a basis for further planning of WHO work on this topic.

Financial and in-kind support for the organization of this meeting was obtained from the Federal Office for the Environment, Switzerland, the Federal Ministry for the Environment, Nature Conservation, Building and Nuclear Safety, Germany, and the Environmental Protection Agency, United States of America (US EPA).

1.3.   Organization

A background document, accompanied by two annexes, was made available to participants prior to the expert meeting providing an overview of the latest WHO air quality guidelines, a summary of the current state of evidence in relation to the exposure levels and health effects for the different air pollutants and preliminary results from an ongoing systematic review on the effectiveness of interventions to reduce air pollution (see Annex 2 for list of supporting documentation and authorship). Key questions to help guide expert discussions were also provided as part of the background material.

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The latest evidence for the classical air pollutants particulate matter (PM), ozone (O_3), nitrogen dioxide (NO_2) and sulfur dioxide (SO_2), in addition to the relevance of interventions in the context of guideline update were discussed in plenary (days 1 and 3). A number of other organic and inorganic air pollutants (listed in Table 1 of this report) were discussed in smaller working groups and then consensus on expert recommendations was reached in plenary (day 2). The final program of the meeting is provided in Annex 3 to the present report.

All experts filled in the WHO Declaration of Interest Form prior to the meeting. Their review by WHO assured the lack of circumstances that could give rise to experts´ potential conflict of interest related to the subject of the consultation.

The meeting was chaired by Martin Williams and Nadia Vilahur acted as meeting rapporteur. The three working groups were chaired by Francesco Forastiere, Tom Luben and Lidia Morawska, while Pierpaolo Mudu, Marie-Eve Héroux and Nadia Vilahur acted as group rapporteurs.

2. Process of guideline development

The development and update of guidelines is a time-consuming task requiring a substantial effort from the scientific community under WHO coordination. Any WHO-produced guideline must be based on a comprehensive and objective assessment of the available scientific evidence. In addition, and especially when guidelines are intended for worldwide use such as the AQGs, also heterogeneity on technological feasibility, economic development and other political factors must be recognized and considered when interventions (such as, for example, to reduce air pollution) are recommended.

A summary of the process of producing a WHO guideline was presented. This follows internationally recognized standards and methods adopted since 2007, and is published in the *WHO Handbook for Guideline Development* (WHO 2014b), as a guidance manual on how to plan, develop and publish a WHO guideline, ensuring that it is free from biases and meets public health needs.

The process of guideline development consists of 3 stages: planning, development and publishing/updating, as summarized in Figure 1 from the above-mentioned manual.

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Table 1.1. The guideline development process at WHO

Stage/primary contributor	Step	Chapter
Planning		
WHO Member State, WHO country office or public/private entity	Request guidance on a topic	1
WHO technical unit	Determine if a guideline is needed; review existing WHO and external guidelines	2
	Obtain approval for guideline development from the director of the relevant technical unit at WHO	2
	Discuss the process with the GRC Secretariat and with other WHO staff with experience in developing guidelines	2
	Form the WHO guideline steering group	3
	Identify sufficient resources; determine the timeline	2
WHO guideline steering group	Draft the scope of the guideline; begin preparing the planning proposal	2,4
	Identify potential members of the GDG and its chair	3
	Obtain declaration of interests and manage any conflicts of interest among potential GDG members	6
WHO guideline steering group and GDG	Formulate key questions in PICO format; prioritize outcomes	5, 7
WHO guideline steering group	Finalize the planning proposal and submit it to the GRC for review	4
GRC	Review and approve the planning proposal	4
Development		
Systematic review team	Perform systematic reviews of the evidence for each key question	8
	Evaluate the quality of the evidence for each important outcome, using GRADE as appropriate	9
WHO guideline steering group	Convene a meeting of the GDG	10,11
GDG	Formulate recommendations using the GRADE framework	10,11
WHO steering group	Draft the guideline document	10,11
External review group	Conduct external peer review	12
Publishing and updating		
WHO guideline steering group and editors	Finalize the guideline document; perform copy-editing and technical editing; submit the final guideline to the GRC for review and approval	12
GRC	Review and approve the final guideline	12
WHO guideline steering group and editors	Finalize the layout; proofread	12
	Publish (online and in print as appropriate)	12
WHO technical unit and programme manager	Disseminate, adapt, implement, evaluate	13
WHO technical unit	Update	12

GDG: guideline development group; GRADE: Grading of Recommendations Assessment, Development and Evaluation; GRC: Guideline Review Committee; PICO: population, intervention, comparator, and outcome.

This expert consultation represents the initial step within the planning stage, with the aim of discussing new evidence in order to determine the need of updating the existing WHO AQGs.

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3. Existing WHO air quality guidelines

The series of existing WHO AQGs are used as a reference tool to help decision-makers across the world in setting standards and goals for air quality management that ultimately protect human health, and have been widely adopted by risk assessment institutions worldwide.

3.1. History

An overview of the history of the WHO AQGs was presented, based on a review conducted by Robert L Maynard and collaborators (Maynard in preparation).

WHO work on air quality dates back as far as 1958, when a first report was produced, in which the potential adverse effects on health from exposure to several air pollutants at low levels was already mentioned, although no or very little evidence was available at that time. Further WHO expert publications (1964, 1972, 1976 and 1984), including the International Program on Chemical Safety (IPCS) Environmental Health Criteria monographs, set the basis for the first edition of the WHO AQGs in 1987 (WHO 1987).

This first volume, covering 28 air pollutants classified in organic and inorganic[1], clearly stated that compliance with guideline values did not guarantee absence of health effects, due to other causes including combined exposure, multiple routes of exposure or sensitive groups. Different approaches were used to deal with carcinogenic (i.e. unit risk factors) and non-carcinogenic-health endpoints (i.e. LOAEL and protection factors), and SO_2 and PM were considered jointly. The second edition of the WHO AQGs was published in 2000 (WHO 2000), as a response to the compelling evidence of health effects occurring at lower levels of exposure, and represented a starting point for the derivation of legally binding limit values in the framework of the EU Air Quality Directive in Europe (EC 1996). This volume covered 35 air pollutants, with additional assessments for 3 organic air pollutants (butadiene, polychlorinated biphenyls and polychlorinated dibenzodioxins and dibenzofurans), and a section on indoor air pollutants including radon, environmental tobacco smoke and man-made vitreous fibres. However, a few of the pollutants in the 2000 AQGs were not re-evaluated and the previous assessment from 1987 was retained (i.e. acrylonitrile, carbon disulfide, hydrogen sulfide, 1,2-dichloroethane, asbestos, vinyl chloride and vanadium). To note, no numerical guidelines were provided for PM, but instead risk estimates were given for an increase in PM concentrations.

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[1] **Organic:** Acrylonitrile, Benzene, Carbon disulphide, 1,2-Dichloroethane, Dichloromethane, Formaldehyde, Polynuclear aromatic hydrocarbons, Styrene, Tetrachloroethylene, Toluene, Trichloroethylene, Vinyl chloride; **Inorganic:** Arsenic, Asbestos, Cadmium, Carbon monoxide, Chromium, Hydrogen sulphide, Lead, Manganese, Mercury, Nickel, Nitrogen dioxide, Ozone, Radon, Sulfur dioxide, Particulate Matter and Vanadium.

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The latest WHO AQGs *"WHO Air Quality Guidelines, Global Update 2005"* included a first part on application of AQGs for policy development and risk reduction followed by a comprehensive risk assessment for the four classical air pollutants PM, O_3, NO_2 and SO_2. In addition to numerical guidelines, in most cases it also proposed interim targets above the guideline value to promote steady progress in different regions of the world towards meeting WHO guidelines (WHO 2006).

In addition, WHO has published a series of indoor AQGs on Dampness and Mould (2009), Selected Pollutants (2010) and Household Fuel Combustion (2014) (WHO 2009, 2010b, 2014a).

3.2.   Identification of ambient air pollutants for expert consultation

Based on the previous editions of the WHO ambient AQGs, and in preparation for this consultation, 32 air pollutants were selected for expert discussion during the meeting (Table 1), according to the following:

- o   All air pollutants which were addressed, at least once, in published WHO ambient AQGs (1987, 2000 and/or 2006 editions) were included.
- o   Pollutants explicitly classified as indoor air pollutants in the 2000 AQGs edition were excluded (i.e. radon, environmental tobacco-smoke and man-made vitreous fibres).
- o   Pollutants assessed in the WHO indoor AQGs for selected chemicals (2010) were included only if they were already covered in previous AQGs as an ambient air pollutant (naphthalene, therefore, was not included).

A summary table of the latest WHO air quality guidelines for these 32 ambient air pollutants, extracted from the background meeting document, is provided as Annex 4 to the present report. This table contains additional information on their carcinogenicity classification from the WHO International Agency for Research on Cancer (IARC) and the existence of additional WHO assessments or guidelines (i.e. Concise International Chemical Assessment Documents (CICAD), WHO Guidelines for Drinking Water (GDWQ), and Joint FAO/WHO Expert Committee on Food Additives (JECFA)).

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Table 1. Air pollutants considered for discussion during the expert consultation

organic pollutants	*inorganic pollutants*	*classical pollutants*
Acrylonitrile	Arsenic	Nitrogen dioxide
Benzene	Asbestos	Ozone
Butadiene	Cadmium	Particulate matter
Carbon disulfide	Chromium	Sulfur dioxide
Carbon monoxide	Fluoride	
1,2-Dichloroethane	Hydrogen sulfide	
Dichloromethane	Lead	
Formaldehyde	Manganese	
PAHs	Mercury	
PCBs	Nickel	
PCDDs/PCDFs	Platinum	
Styrene	Vanadium	
Tetrachloroethylene		
Toluene		
Trichloroethylene		
Vinyl chloride		

PAHs:Polycyclic aromatic hydrocarbons, PCBs:Polychlorinated biphenyls, PCDDs:
Polychlorinated dibenzodioxins PCDFs:Polychlorinated dibenzofurans.

4. Discussions and expert advice

A series of introductory presentations on the classical air pollutants (PM, O_3, NO_2, and SO_2) were provided during the first meeting day, before starting the discussion in plenary on the latest health evidence for these pollutants and whether it justified their re-evaluation in the context of the WHO AQGs. Speakers provided a summary of the current guidelines, main conclusions and recommendations from the 2013 WHO REVIHAAP Project and other recent assessments along with the most informative results from selected critical new studies since the publication of the last WHO AQGs for these pollutants.

Meeting participants were asked to discuss the new available evidence on exposure or health effects of relevance for guideline development, and to comment specifically on:

o The shape of the concentration-response function (CRF), identification of thresholds and effects at very low or very high pollutant levels.

o Effects at different exposure duration times (long-term, short-term).

o Considerations regarding vulnerable sub-groups or windows of susceptibility.

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o Causality and independence of effects (including multi-pollutant effect estimates as a basis for joint health impact assessment).

Additionally, for PM:

o On the sources, particle size and composition (in particular for black and/or elemental carbon and ultrafine particles).

The available evidence for the remaining 28 air pollutants was discussed during the second day of the meeting, first in small working groups and then conclusions from the small groups were presented by chairs in plenary session, discussed and finally agreed on.

Experts were asked to discuss the newly available evidence on exposure through air and related health outcomes for the pollutants and comment on the need and relevance for re-evaluation of this evidence in the context of the update of the WHO air quality guidelines.

As a result of the discussions held among participants during the meeting, the 32 air pollutants were categorized in 4 groups as shown in Table 2, to reflect the need for systematic review of the evidence in the context of the process of updating the existing WHO Air Quality Guidelines. However, it has to be acknowledged that more evidence might become available during the process development that might change the current expert's view on this proposed classification.

Table 2. Summary of expert pollutant advice

Recent evidence justifies re-evaluation *(Group 1)*	*Recent evidence justifies re-evaluation* *(Group 2)*	*Recent evidence justifies re-evaluation* *(Group 3)*	*Recent evidence does not justify need for re-evaluation* *(Group 4)*
Particulate Matter	Cadmium	Arsenic	Mercury
Ozone	Chromium	Manganese	Asbestos
Nitrogen dioxide	Lead	Platinum	Formaldehyde
Sulfur dioxide	Benzene	Vanadium	Styrene
Carbon monoxide	PCDDs & PCDFs	Butadiene	Tetrachloroethylene
	PAHs*	Trichloroethylene	Carbon disulfide
		Acrylonitrile**	Fluoride
		Hydrogen sulfide	PCBs
		Vinyl chloride	1,2-dichloroethane
		Toluene	Dichloromethane
		Nickel	

*PAHs were assigned to Group 2 (taking benzo[a]pyrene as a reference compound), on the basis of availability of new evidence since 2010 regarding non-cancer health endpoints (i.e. cardiovascular, neurodevelopment effects, lower birth weight etc.) and conclusions from ongoing health risk assessments that have included non-cancer health effects from benzo[a]pyrene and reference concentration values for inhaled PAHs.
**Acrylonitrile was classified in Group 3 with possible reclassification to Group 2 depending on the results from updated cohort analyses in the USA that are expected to be available in the near term..

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Group 1: Pollutants included in Group 1 are those that, according to the expert's opinion, should be considered of greatest importance in the process of updating the WHO AQGs. The large body of new health-related evidence for these pollutants justifies the need for their systematic re-evaluation, with a special consideration of interactions among pollutants, and a close scrutiny at results from multipollutant models. Experts advised WHO to establish a specific working group for that purpose at a later stage of the process.

Group 2: Pollutants in Group 2 are those for which, according to experts, a systematic revision of the existing evidence is strongly recommended, due to their widespread presence in ambient air and the large amount of new evidence available regarding adverse health effects, which may lead to changes to the existing guideline values. Whether this should be framed as a secondary stage of this process was outside the specific scope of this consultation.

Group 3: A systematic re-evaluation of the new evidence existing for air pollutants included in Group 3 is warranted according to experts, although with less urgency than for pollutants included in the two previous groups. Some of the pollutants in this group need to be regarded as part of the PM mixture.

Group 4: According to experts, recent evidence available for pollutants in Group 4 does not justify the imminent need for their reassessment in the context of updating the WHO ambient AQGs, and should therefore be kept for future consideration. In addition, some of these pollutants are currently addressed in occupational setting guidelines, and/or through water guidelines or other types of management processes. However, this classification does not imply invalidation of the existing WHO AQGs for these pollutants.

The discussions and the expert conclusions for the air pollutants included in each group are summarized below:

4.1.   Air pollutants included in Group 1

There was a general agreement among experts with the REVIHAAP project conclusions on the classical pollutants, which stated that there is a need to revisit the current guidelines for PM, O_3, NO_2, and SO_2 as the evidence base for the association between short- and long-term exposure to these pollutants and health effects has become much larger and broader since 2006. Further, experts concluded that carbon monoxide (CO) is another airpollutant for which a large amount of new evidence is available, that should be reviewed at the same time as the classical pollutants mentioned before.

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PM

PM $_{2.5}$

Since the publication of the latest WHO guidelines, new studies have emerged showing associations between both short- and long-term exposure including mortality and cardiovascular disease morbidity at levels below the existing WHO guideline values (Crouse et al. 2012; Shi et al. 2016; Thurston et al. 2015). Also, IARC has recently classified ambient air pollution and the PM mixture as carcinogenic, with evidence of increased risk for cancer also at levels below the current $PM_{2.5}$ guideline. These findings support the need for re-evaluation of the evidence base considered in the latest $PM_{2.5}$ guidelines.

Experts emphasized the need for a re-evaluation of the existing concentration response function (CRF) for $PM_{2.5}$, based on observations of changes in risk at low and very high concentrations, that suggest a steeper exposure–response relationship at lower levels and flattening-off at higher concentrations (observed both for cancer and non-cancer health endpoints). This implies that extrapolation from studies conducted in European and North American cities might not be applicable in countries such as India or China. New studies are being conducted in countries with higher levels of exposure, and their results should be closely examined. Experts also mentioned the usefulness of developing CRFs for other identified health endpoints than mortality. In this regard, there are a growing number of health endpoints that have been subject to research (Alzheimer's disease and other neurological endpoints, cognitive impairment, diabetes, systemic inflammation, aging, etc.). Previous air quality guidelines focussed on the most studied health outcomes (often mortality), but experts noted the importance of describing and summarizing this wide morbidity spectrum for which evidence is increasing, before narrowing down to a selected fewer health endpoints for risk assessment and formulation of AQGs purposes. This should be based on a set of criteria such as the strength of the association and clarity of the evidence, as well as understanding of the biological mechanisms. Ongoing health risk assessment processes, including the US EPA Integrated Science Assessment (ISA) on PM (a first draft is currently planned for release by the end of 2017), among others, could greatly contribute to this task. Finally, experts pointed out that WHO might need to consider a review of the available evidence for various averaging times for $PM_{2.5}$ exposure, especially in relation to short-term exposure (e.g. 1-hour), as emerging evidence suggests adverse health effects at much shorter timescales than previously considered.

PM $_{10}$

Meeting participants raised the suggestion that it might be relevant to investigate the health outcomes related to coarse particles ($PM_{2.5} - PM_{10}$) instead of PM_{10} as a whole. Coarse particles should be

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reviewed in terms of mass, composition and health effects (especially from short-term exposure, since the evidence of effects on cardiorespiratory health and mortality has increased substantially), as well as in the context of sources.

With respect to carcinogenicity, it was noted that the risks estimated for PM_{10} by IARC are virtually the same as for $PM_{2.5}$ (possibly triggered by the fact that one is contained within the other), and that the carcinogenicity attributed to PM_{10} could be a result of carcinogenicity due to other chemicals present in the mixture, such as polycyclic aromatic hydrocarbons (PAHs).

Experts agreed on the importance of understanding the specific health effects of natural source coarse components including windblown road and desert dust, which can lead to extremely high air concentrations of PM_{10} in some regions, although these sources cannot be controlled easily and more research evidence needs to be generated to support risk assessment.

Other PM metrics or components

Recent reviews of evidence conclude that it is not possible to clearly differentiate those constituents (or sources) that are more closely related to specific health outcomes (EPA 2009b). Although PM mass continues to be the best indicator to characterize the risk, experts agreed in that the different components of the PM mixture should not be overlooked and advised a systematic evaluation of their health effects to be conducted during the upcoming guideline review process (taking into consideration the multiplicity of sources and varying particle composition around the world), which will inform the need to develop guidance for specific particle components.

The following PM metrics or components were particularly discussed:

PM_1: Experts agreed that to date there is no standardized and validated methodology for a reliable quantification in terms of mass, and a lack of substantial epidemiological evidence for guideline development purposes.

Black carbon (BC): A number of studies consistently show associations between exposure to BC and health effects, including recent large Chinese studies published since 2013 (Janssen N 2012; Kim et al. 2014). However, different methods are used to measure BC in air and experts raised their concern on the importance of ensuring a consistent and reliable measurement in order to quantitatively estimate health effects. In addition, monitoring of BC worldwide is limited, although experts acknowledged that the recommendation of a guideline for BC could influence the expansion of its monitoring in many regions of the world. There are high correlations between BC and both NO_2 and ultrafine particles, and this should be taken into account, especially in the developed world where the main source of BC is traffic coming from diesel powered vehicles. Finally, sources of BC vary widely

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across the world with biomass burning being very relevant developing countries (where fewer epidemiological studies are available).

Overall, there was a general consensus among experts that the available body of scientific evidence needs to be reviewed for BC, which might provide a better CRF and/or more evidence from epidemiological and toxicological studies to support causality. Whether a guideline should be produced, or some other form of recommendation that would stimulate more research and monitoring of BC, is something that should be discussed as an outcome of the revision of the AQGs at a later stage.

Ultrafine particles (UFP): Some recent studies are pointing towards effects of UFP on health outcomes such as CV mortality independent of PM mass (Su et al. 2015), but existing evidence seems yet insufficient to consider developing AQGs for UFP. Experts are unaware of the existence of studies on health effects from long-term exposure for UFP, which would enable the derivation of a guideline value. Experts recommended that WHO reviews the emerging evidence for UFPs, noting that there are methodological challenges for the assessment of UFPs to overcome for guideline development purposes, and pointed out the importance of considering that specific components such as metals or PAHs might be underlying some of the adverse health effects attributed to UFPs.

Ozone

A considerable number of studies on the health effects of ozone have been published since the latest WHO AQGs in 2006, including more short- and long-term exposure studies, at lower concentrations and in regions of the world other than North America and Europe (mostly meta-analyses in China).

Short term:

Experts agreed that the process should review the accumulated new evidence, as there is mixed evidence of effects at levels below 100 µg/m³ for an average 8-hour mean exposure (Dai et al. 2015; Pascal et al. 2012; Pattenden et al. 2010). Additional short-term averaging times could be considered if evidence is sufficient. Importantly, multipollutant models should be closely looked at, since the negative correlations existing among ozone and other pollutants might affect the CRF and threshold determination, especially at the lower end of the distribution of measured concentrations, as observed in a recent report by the UK Committee on the Medical Effects of Air Pollutants (COMEAP) (COMEAP 2015). Finally, the general expert's view was that the SOMO35 (sum of mean ozone values over 35 ppb) indicator does not necessarily need to be discussed in the context of the guidelines, unless as part of a section addressing management issues.

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Long term:

Experts agreed with the conclusions of the recent REVIHAAP project, in that new evidence of adverse health effects due to long-term exposure to ozone published since the latest WHO AQGs warrants consideration in future revision of the guidelines. This is in line with the 2013 US EPA ISA for Ozone and Related Photochemical Oxidants (EPA 2013a), reporting *"likely to be a causal relationship between long-term exposure to O_3 and respiratory effects"*. Additionally, the ISA determined that *"the evidence was suggestive of a causal relationship for long-term exposure to O_3 and cardiovascular effects, reproductive and developmental effects, cancer, and total mortality"*. Experts recognized that this is a relevant research area and therefore researchers should be encouraged to examine the effects of long-term exposure to ozone on health outcomes as part of existing or future large cohort studies. Moreover, it was strongly agreed that WHO should review this accumulating evidence, which might lead to the development of a numerical guideline for long-term exposure to ozone. This might have large downstream policy implications, including the need to address global emissions of ozone precursors, and impact on other areas such as climate change mitigation and ecosystems. Experts pointed out the importance during this process of addressing confounding due to multipollutant exposures (most importantly PM and NO_2), considerations on seasonality effects (summer versus winter averages), and effects due to repeated peaks of exposure versus chronic exposure to inform the long-term ozone recommendation form.

Finally, in considering evidence of health effects from other photochemical oxidants such as peroxyacetyl nitrate (PAN), participants agreed that the current body of evidence in the context of health effects is too limited to recommend a systematic revision for guideline development, although more examination of such complex reaction products is warranted in the future.

NO_2

Since the publication of the latest WHO AQGs, new studies have emerged, reporting associations with both short-term and long-term exposure to NO_2.

Short term

Experts agreed that the new evidence should be re-evaluated in order to provide an epidemiologically-based short term recommendation, considering new time-series studies providing CRFs with wider ranges of exposure including concentrations below the current guideline value of 200µg/m³. Moreover, there was a general consensus that, in view of recently available report from the French Agency for Food, Environmental and Occupational Health and Safety (ANSES 2013b) and/or ongoing (yet unpublished) assessments from the COMEAP, Health Canada (HC) or US EPA, the evidence of a causal relationship of short-term NO_2 with respiratory outcomes has strengthened, while

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it remains suggestive for cardiovascular disease and mortality. Therefore, experts suggested that in terms of setting guidelines, the process might consider focusing on respiratory effects, for which evidence of causality seems more robust from different type of studies (time-series, chamber, panel, toxicological…), and strongly emphasized that this process will require a careful scrutiny of the multi-pollutant models including not only $PM_{2.5}$ but other pollutants present in the traffic mixture (mainly CO, EC and BC, but also PAHs) in order to disentangle NO_2 and ozone related health effects. In addition, a careful examination of the specific monitoring locations and the exposure assessment methodology used in the available studies was advised, due to the very strong spatial gradients in NO_2 concentrations.

Long term

There was a general consensus among the participants on REVIHAAP recommendations to update the current WHO AQG for NO_2 based on the amount and quality of the new evidence from cohort studies, which might result in a numerical recommendation below the current annual 40µg/m³ guideline value. These new studies, as well as results from recent meta-analyses and upcoming reports of which experts were aware of (e.g. a COMEAP report to be published by the first half of 2016), show associations of long-term NO_2 exposure with different health outcomes such as children's respiratory symptoms or lung function, and provide more evidence in relation to mortality (respiratory, cardiovascular and all cause), as well as some indication for lung carcinogenicity. Few existing studies have considered two or more pollutant models, but experts emphasized that, particularly in the context of long-term exposure, the fact that NO_2 may represent other constituents in the mixture of traffic-related air pollutants needs to be addressed when reviewing the evidence.

Nitric oxide

Nitric oxide often shares its main sources with NO_2, especially in urban settings, where it can reach very high concentrations under specific atmospheric circumstances.

Experts were aware of some literature showing adverse effects of NO following drastic changes in exposure in the context of its therapeutic use, mainly in chronic obstructive pulmonary disease (COPD) patients and at higher doses than what is commonly found in ambient air (Barbera et al. 1996; Weinberger et al. 2001). Experts recognized that there are a number of methodological challenges in exposure assessment of NO due to its high correlation with NO_2. There was a general agreement that the upcoming process should consider the existing evidence for NO, specifically in the context of effects in the general population due to ambient air exposure, to conclude on whether there is enough basis for developing a health based recommendation separate from NO_2.

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SO$_2$

Since the 2005 global update of the WHO air quality guidelines, some new studies on the health effects of SO$_2$ have been published, especially time-series but also toxicological studies. Ambient levels of SO$_2$ have decreased over time in some regions of the world, but increased in others.

Short term and Long term:

Experts concluded that, in agreement with the outcome of the REVIHAAP Project and considering the high levels measured in some countries, the available evidence for SO$_2$ should be looked at again in relation to very short (10 min) and short-term (24 hours) exposure, but also likely for long-term exposure, for which there is currently no guideline value (with subsequent impacts at a global scale, such as acidification of the environment). This systematic review can benefit from newly/upcoming information from recent national assessments from USA and Canada, which are expected to provide additional evidence of very short/short-term SO$_2$ exposure and respiratory effects based on chamber studies, and suggest mixed evidence for long-term exposure and adverse health effects. Further, new available studies conducted in regions of the world that present higher concentrations of SO$_2$ should be considered (Lai et al. 2013; Shang et al. 2013).

Experts were of the view that an effort should be made as part of the process to recommend a CRF for SO$_2$, to have a quantitative tool that would allow comparison of the level of protection achieved with WHO guidelines across different pollutants, and agreed that WHO might need to revisit the feasibility of providing interim targets for SO$_2$ in the updated guidelines.

CO

Carbon monoxide is ubiquitously found in ambient air, particularly in developing countries, where emissions can be high. CO is widely monitored in ambient air and there is substantial new evidence since the latest WHO AQGs on associations between long-term exposure to low concentrations and a wide range of health effects including reproductive outcomes, or short-term exposure and mortality. There is also increasing understanding that CO mechanisms of action are not only based on hypoxia induced by formation of carboxyhaemoglobin (on which the current guideline is based) (Piantadosi 2008; Reboul et al. 2012). US EPA completed an ISA for this pollutant in 2010 (EPA 2010) and the WHO indoor air quality guidelines (2010) included recommendations for CO (WHO 2010b), and as the exposure profile differs significantly between indoor and outdoor environments, experts advise WHO to systematically reevaluate CO as an ambient air pollutant, along with the classical pollutants as part of the AQGs update process.

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4.2.   Air pollutants included in Group 2

Benzene: Ambient air exposure is widespread and relevant worldwide. Sources include biomass burning, the use of compressed petroleum gas and its presence in gasoline and high emissions in several countries including China, due to high concentrations of aromatic compounds in gasoline. A recent health assessment suggested a different unit risk for cancer than WHO (ANSES 2014), and new studies, both for short- and long-term exposure, show associations of benzene with non-cancer health endpoints (e.g. neurological effects), and report higher risks at lower levels of exposure. Experts agreed that all this body of new evidence should be re-evaluated.

Cadmium: Experts agreed with the conclusions of the REVIHAAP project, in that present levels of cadmium in air are too high to obtain a cadmium balance in soils (suggesting that the cadmium dietary intake of the population will not decrease). In addition, strong evidence is available on new health effects due to cadmium exposure in the general population especially on bone, but also on hormone-related cancer, cardiovascular disease, and fetal growth (Akesson et al. 2014; Larsson and Wolk 2015; Tellez-Plaza et al. 2013).

Chromium: Current WHO recommendations include a reasonably high unit risk for inhaled chromium VI using lung cancer as a critical effect. In addition, some evidence suggests a relationship with respiratory irritation; lung function and dermal and reproductive effects (IPCS 2013). Exposure to chromium is ubiquitous, mainly as a result from burning of fossil fuels in addition to natural sources and, similar to other pollutants, chromium accumulates in soils and water via atmospheric wet and dry deposition. The US EPA is currently updating an assessment for chromium VI that is anticipated to be released for external peer review in 2017.

Lead: There was a general expert consensus with the conclusions of the REVIHAAP Project in that the current WHO AQGs for lead need to be re-evaluated. New evidence consistently shows that effects on the central nervous system in children and on the cardiovascular system in adults occur at, or below, the existing guideline levels (EFSA 2013; EPA 2013b). Furthermore, direct inhalation of lead (present from historical emissions) contributes to the blood levels in children, in addition to the indirect exposure through soil deposition**.** Experts pointed out the need to coordinate with other activities on lead that might be conducted by WHO.

Polychlorinated dibenzodioxins and dibenzofurans (PCDDs and PCDFs): Concentrations in ambient air are generally low, but experts recognized the importance of the current emissions and increasing trends of dioxins/furans as byproducts from open combustion of plastic and other types of waste (e.g. medical), which could affect a large part of the population (Weichenthal et al. 2015). New evidence is available due to long-term exposure on cancer, reproductive (hormonal), immune,

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developmental and fetal effects (Yi-Hsuan Shih et al. 2015). Although overall limited information might be available for PCDDs and PCDFs in air from the last 15 years, experts agreed that a re-evaluation of the new evidence existing for these chemicals, for which no numerical guideline is currently provided in the WHO AQGs, should be conducted, with further downstream policy benefits. Additionally, there was a general consensus among participants that this assessment should include planar PCBs.

Polycyclic aromatic hydrocarbons (PAHs): PAHs in air come mostly from combustion of carbonaceous material, including biomass and wood, diesel and coal, often leading to peaks of exposure of public health concern during the winter months. Experts acknowledged the difficulty of quantitatively assessing the health effects due to PAH mixtures, and recognized that, for guideline purposes, a focus on benzo(a)pyrene as an indicator for deriving a quantitative guideline for PAHs is still appropriate. IARC reclassified benzo(a)pyrene in 2005 as a Group 1 carcinogen, but experts also discussed the emerging recent evidence on non-cancer health end-points such as the cardiovascular system, neurodevelopment or effects on birth weight. Upcoming US EPA assessments, currently under peer review, will provide non-cancer toxicity values for benzo[a]pyrene and updated relative potency factors for PAHs. Also, considering that the current EU air quality target value for benzo(a)pyrene of 1 ng/m^3 annual mean (leading to a somewhat high lifetime cumulative risk for cancer of 1 x 10^{-4}) is significantly exceeded in many EU Member States, and in view of the increase in the emission trends of benzo(a)pyrene in several European countries (EEA 2015), experts concluded that the new health evidence should be re-evaluated.

4.3.   Air pollutants included in Group 3

Acrylonitrile: Worldwide production of acrylonitrile is very high, and exposure of the general population in ambient air could be of concern, especially for those living near industrial emission sources such as acrylic fiber or chemical manufacturing plants, rubber production facilities and wastes, or near major populations centers (Fritz 2015), but also as a result of plastic production and its use as a pesticide (fumigation), mainly in developing countries. Acrylonitrile is a potentially toxic chemical, with limited evidence of carcinogenicity in humans and evidence of multiple tumor sites in experimental animals (IPCS 2002). Updated cohort analyses are currently ongoing in the USA. Results from these studies may provide additional useful information to WHO on this pollutant in terms of need for reevaluation as part of this process.

Arsenic: Experts agreed with the conclusions of the REVIHAAP project, in that the new evidence available for arsenic might not lead to a substantial change to the unit risk currently recommended in the WHO AQGs. In addition, exposure through diet (food, water) is more relevant than air. However, non-carcinogenic effects should be looked at, and ongoing evidence assessments conducted by US

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EPA as well as the European Food Safety Authority might provide new useful information on this regard.

Butadiene: Main sources of butadiene in ambient air include motor vehicle exhaust, manufacturing and processing facilities of styrene-butadiene rubber, forest fires or other combustion processes. The implementation of catalytic converters has led to a decrease in the levels of this pollutant in developed countries. This compound is classified by IARC as a Group 1 carcinogen, and experts were not aware of a new substantial or critical body of evidence regarding additional health outcomes.

Hydrogen sulfide: This air pollutant is ubiquitous near sources, mainly related to petroleum and natural gas production, as well as pulp and paper mills and waste management. However, the majority is emitted from natural sources often related to anaerobic biological processes. Although the average ambient concentrations might be relatively low and there is no evidence of health concerns in humans at those low levels other than nuisance odor, health risk assessments conducted after the year 2000 provided lower reference values (based on animal studies) than the current WHO AQG from 1987 (ATSDR 2014c).

Manganese: Main sources of manganese are industrial and in the use of manganese-containing fuel additives, in addition to natural sources. There is new evidence suggesting neurotoxic and neurologic effects due to exposure via inhalation, with increased susceptibility in children and elderly population (HC 2010). A higher inhalation standard than the existing WHO guidelines was published by ATSDR in 2012 (EPA 2012a). An ongoing US EPA review on this pollutant might provide new useful information.

Nickel: The levels in ambient air are generally low (except for some hot spots). Carcinogenicity (lung and nasal sinus) observed in occupational cohorts was the critical health endpoint used in the existing WHO AQGs to derive a unit risk for nickel (subsulfide and dust nickel). More recently, potential associations of nickel exposure through air and cardiovascular disease and inflammation have been described, but experts agreed with the REVIHAAP project conclusion that more epidemiological and experimental studies are needed in this regard. A report on health risks from nickel in food and drinking water has been recently published by EFSA (EFSA 2015). Experts raised the issue that nickel speciation is also fundamental for guideline purposes, with current AQGs likely focusing on nickel dust and subsulfide. Nickel is an important constituent of the PM mixture and some studies suggest that it could contribute to some extent to the health effects attributed to fine PM (Bell et al. 2009).

Platinum: Concentrations in ambient air are overall very low, and this poses monitoring and analytical challenges. As a result, limited knowledge on the geographical distribution of the

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compound in air is available. There is evidence of acute allergic sensitization effects and exacerbation of asthma, mainly from worker studies and inhalation animal studies. No numerical guideline for platinum is provided in the current AQGs, and experts pointed out that an existing US EPA 2009 draft assessment for halogenated platinum (not finalized and archived) could be helpful to WHO in providing a characterization of the scientific literature available at that time (EPA 2009a). Also, halogenated platinum was considered in a WHO IPCS draft report on "Guidance for immunotoxicity risk assessment for chemicals" in relation to sensitization and allergic response (WHO 2010a).

Toluene: Levels in air in North America and EU countries are decreasing, but will potentially increase in other regions, especially as a result of efforts towards decreasing benzene levels in fuels. Concentrations measured in air in road traffic sites can be up to three times higher than those for benzene. However, the current WHO guideline value from 2000 is consistent or even lower than the values proposed by more recent assessments from US EPA (EPA 2005, 2012b), HC (HC 2011) or ANSES (ANSES 2010b).

Tetrachloroethylene: Sources of exposure are mainly indoors, including occupational (from dry-cleaning industries). Outdoor air exposure might be relevant for people residing near contaminated sites. A future decrease in concentrations is expected in the USA due to phase-out of this chemical. This pollutant has been addressed in 2010 by the WHO guidelines for indoor air quality, using effects in the kidney indicative of early renal disease as a critical endpoint (WHO 2010b). There is evidence that tetrachloroethylene may be carcinogenic to humans (IARC Group 2A) and recent health risk assessments are available from US EPA (2012) and ATSDR (2014) on non-cancer effects with lower reference values based on color vision impairment and cognitive effects (ATSDR 2014b; EPA 2012c).

Trichloroethylene: This compound is potentially relevant in the context of ambient air exposure. It is ubiquitous, even though air levels are generally higher in urban than in rural areas, with the highest concentrations found in commercial/industrial areas. Experts agreed that more data on monitoring in ambient air would be needed. This pollutant is addressed by the 2010 WHO guidelines for indoor air quality (WHO 2010b). While no guideline value was provided, the unit risk estimate might need reevaluation, since it is of one order of magnitude lower than the unit risk provided by a later assessment conducted by US EPA in 2011 (EPA 2011). Other recent assessments for this pollutant are available from ATDSR (providing a reference value for chronic exposure) and from ANSES (ANSES 2013a; ATSDR 2014a).

Vanadium: Vanadium pentoxide is the compound of more concern in relation to air exposure, and it is mainly emitted by the steel industry. However, vanadium is also present in liquid fuels, particularly marine diesel. Experts agreed with the REVIHAAP project conclusion that in addition to the studies

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on occupationally exposed workers, an evaluation based on more recent data about effects in the general population would be appropriate (considering additional health endpoints, such as airway response). Vanadium pentoxide is classified as possibly carcinogenic to humans (IARC Group 2B), and no concentration-response function for this compound is available. Assessments for this compound have recently been conducted (ATSDR 2012) or are currently ongoing (US EPA). Additionally, vanadium is an important constituent of the PM mixture and some studies suggest that it could contribute to some extent to the health effects attributed to fine PM.

Vinyl chloride: Production of this chemical is high, but exposure in air worldwide still needs to be fully evaluated and characterized. High concentrations in air are likely surrounding the sources of emission. It has been classified as a Group 1 carcinogen from the IARC (2012), and health effects other than cancer have been reported in relation to both short and long-term exposure (ATSDR 2006).

4.4.   Air pollutants included in Group 4

Asbestos: Asbestos related health effects have been extensively documented previously and unit risks are available as part of existing AQGs. WHO recommendations clearly state that the most efficient way to eliminate asbestos-related diseases is to stop using all types of asbestos. Exposure is mainly occupational, but open cut mines could affect population living around them. In such situations, guidance for mitigation can be provided as part of separate WHO activities.

Carbon disulfide: A main source in air comes from natural gas production. However, ambient air levels of CS_2 are extremely low and hard to measure (except in specific workplaces where it is used). There is no evidence for carcinogenicity for this compound and, in general, toxicity levels are rather low. The current WHO AQGs guidelines (from 1987) are more protective than values provided by later assessments conducted by the US EPA, HC or the California Office of Environmental Health Hazard Assessment (OEHHA) (EPA 1966; HC 2000; OEHHA 2002).

1,2-Dichloroethane: Concentrations in ambient air have decreased worldwide as a result of the ban on leaded gasoline. Currently, a predominant source in ambient air comes from the manufacture of vinyl chloride, particularly affecting population near point sources. It is classified by the IARC as a possibly carcinogenic compound to humans (Group 2B), and an assessment published in 2009 by ANSES established a relatively low unit risk of cancer (ANSES 2009). As such, experts agreed that a reduction of this pollutant could be achieved indirectly through setting vinyl chloride guidelines.

Dichloromethane: This pollutant is widespread in industrial uses, but in general concentrations in air are low. The current IARC classification as Group 2B (possibly carcinogenic) is currently under review for reclassification in Group 2A. There is not a substantial body of new evidence pointing

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towards additional health endpoints in humans. A WHO drinking water guideline from 2011 exists for this pollutant (WHO 2011).

Fluoride: The main exposure source of fluoride is water; only 0.001% of the body burden in the general population comes from air. Except from occupational exposure, inhalation exposure is considered negligible. There are no carcinogenicity data available for this compound (IARC Group 3, 1987). A WHO drinking water guideline from 2011 already exists for this pollutant (WHO 2011).

Formaldehyde: This compound is found at higher concentrations in indoor than in outdoor environments, as a result of combustion in indoor environments (wood stoves, kerosene heaters and cigarette), off-gassing from manufactured wood products in new and renovated homes, carpets, paints and varnishes and when used as a disinfectant. This pollutant has been addressed in 2010 by the WHO guidelines for indoor air quality, using sensory irritation as a critical outcome (WHO 2010b), and it is classified as carcinogenic Group 1 by the IARC since 2012.

Mercury: Experts agreed with the conclusions of the REVIHAAP Project in that there is little new evidence on the health effects of air emissions of mercury that would have an impact on the current guideline. Considering the limited new health evidence from inorganic mercury, the relatively low direct contribution to human exposure through air (levels of inorganic mercury in air are extremely low), and that a UN convention exists specifically addressing mercury (Minamata Convention on Mercury: http://www.mercuryconvention.org/), experts agreed in the context of this process that there is no need for immediate re-evaluation of the evidence.

Polychlorinated biphenyls (PCBs): The main sources of PCBs are diet and indoor air. No guideline value was proposed for this compound in the 2000 WHO AQGs, since inhalation was estimated to constitute only a small proportion of the daily intake (1-2%), which mainly comes from food. There is strong evidence for associations with neurotoxicity, reproductive toxicity, developmental toxicity, hepatotoxicity, and immunotoxicity, but experts recognized that risk management approaches or guidelines other than ambient AQGs exist that would best address this chemical.

Styrene: Levels of styrene monitored in ambient air are generally below the current AQGs, and also lower than values reported in indoor environments. The current WHO AQGs is based on carcinogenicity. Some re-assessments of this pollutant have been conducted by the ATDSR and ANSES (ANSES 2010a; ATSDR 2010). Overall, experts concluded that the reevaluation of the limited new body of evidence for styrene may not lead to a lower guideline value than the existing one.

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5. Interventions in the context of AQGs

Previous editions of the AQGs have mainly focussed on providing guidance in the form of pollutant-exposure specific recommendations, usually as 'not to be exceeded' concentration levels of air pollutants. Some informative text on application of guidelines in policy formulation, including risk management and implementation of the guidelines, has also been proposed; however this has largely been done without a systematic review of the underlying scientific evidence evaluating their effectiveness.

For the next update of the guidelines, it may be possible to formulate recommendations concerning specific measures or interventions shown to decrease the levels of air pollutants and improve health. These recommendations could be useful to countries, policy makers or other end-users of the guidelines on how to progress towards meeting the WHO goals. If and to what extent the available scientific evidence justifies including this particular topic as part of the updated AQGs was discussed during the third day of the expert meeting.

Jacob Burns from the University of Munich presented the study design and preliminary results of an ongoing Cochrane systematic review, conducted in collaboration with researchers from the Health Effects Institute (HEI), assessing the effectiveness of interventions in improving air quality (mostly $PM_{2.5}$ and PM_{10}) and/or health effects. This review includes evidence from 47 studies in 18 countries across the world, categorized according to the source of PM as vehicular, industrial, residential or multiple sources; and assesses the effect of these interventions on both non-health (i.e. mainly changes in pollutant concentrations) and health outcomes (i.e. mortality, hospital admissions due to cardiovascular or respiratory events, emergency department admissions and pre-term birth weight). Modelling studies were not included in the review as the project did not have the scope to evaluate the quality of the models.

The expected publication date of the review is spring 2016, but preliminary results suggested a general decrease in pollution levels ($PM_{2.5}$ and PM_{10}) following the interventions assessed. However, some particular challenges in the overall assessment of this type of studies were raised, such as how to ensure that measured changes are due to the intervention, what constitutes an intervention versus a control site, how to deal with study uncertainties and how to meaningfully summarize the very heterogeneous group of studies.

The main expert opinions from discussion on this topic were the following:

- o Accountability research (i.e. research aimed at providing evidence that air quality regulations improve public health) can provide convincing arguments to motivate governments to address

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local, specific sources, and can provide necessary evidence that air quality and health improve as a result of interventions, even in areas with low air pollution.

o   Intervention studies are an important part of the evidence to be considered for the guidelines. The mapping of the existing evidence on interventions provided in the Cochrane review is essential to identify areas in which general recommendations can be developed. However, the evidence retrieved is still limited and there is a need to continue improving the design of this type of studies, especially regarding sources of counfounding (an outstanding issue especially when evaluating the long-term effectiveness of interventions) and improving assessment of the exposure to decrease study uncertainty. Therefore, it is not expected that the findings of the Cochrane review will provide strong evidence on the basis of health endpoints that can be used to recommend specific interventions. This is not to imply that successful interventions to reduce air pollutant concentrations (and therefore probably improve health) do not exist. Also, not all policy evaluations are presented as formal intervention studies and many may appear in the grey literature, such as in Government reports. Further, they may be based on a collective body of evidence published in separate articles on monitoring trends, atmospheric modelling, emissions factors etc.

o   As such, experts underlined that the focus of the guidelines on pollutant-specific risk assessment is still appropriate. The next update of the guidelines could provide general risk management principles and best practices, including examples on how AQGs can be used in policy formulation, especially in developing countries, while in depth evaluation of policies and effectiveness of interventions should most appropriately be conducted as part of a process separate to that of the update of the AQGs.

o   The effectiveness of other types of interventions, for example individual interventions (e.g. use of masks) has not been included in the ongoing Cochrane systematic review, and has not been systematically evaluated before. ANSES is currently assessing the efficiency of using masks under different scenarios, to be completed by the end of 2016. The outcome of this assessment could support further thinking on whether recommendations on this topic could be provided by WHO in the updated guidelines or as part of other processes.

6.   Conclusions

Experts agreed on the need for WHO to start the process of updating the current ambient AQGs. It was unanimously recognized that all the 32 ambient air pollutants addressed during this consultation are relevant in that there is evidence that they can all pose health hazards to human populations, and therefore should be carefully followed by WHO and monitored by countries worldwide. There is a need to regularly review and update existing WHO AQGs. However, this task can be challenging if

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evidence has to be retrieved to support a large number of existing recommendations. In this situation, it is essential to give priority to the more important areas, or those in which substantial new evidence has emerged in relation to ambient air. After a careful review and discussion of the available evidence for the future update of the WHO AQGs, experts agreed that these immediate priorities concern the air pollutants included in Group 1 (PM, O_3, NO_2, SO_2, and CO).

6.1.   Additional expert opinions

This section summarizes additional considerations relevant to the global update process of WHO AQGs raised by the expert community during the meeting:

o   Experts consulted identified several air pollutants, which are not covered by existing WHO AQGs, and that could be relevant to consider as part of future AQGs (i.e. copper, iron, silicate, antimony, ammonia, aldehydes, and NO). However, in the spirit of transparency, a suggestion was made for WHO to consider establishing a structured system for enlarging the scope of the future AQGs with additional pollutants, similar to the open solicitations procedure existing in other agencies. As an example, the IARC process encourages the general public, the scientific community, national health agencies, and other organizations to nominate agents for carcinogenicity review by submitting online a nomination form for the pollutant summarizing the basis for the request along with a WHO declaration of interest. These nominations are then evaluated and prioritized by an international and interdisciplinary Advisory Group.

o   Some compounds from the BTEX group (i.e. ethylbenzene and xylenes) in addition to styrene were not included in the list for discussion during the expert consultation since no previous WHO AQG for these pollutants was available. Taking into account the available evidence from recent reviews from other organizations (EPA 2009c, 2012d, e, f), experts agreed that the immediate need for evaluation of this pollutants was not apparent.

o   A transparent, systematic and accountable process will need to be developed to assess the large amount of available evidence, with clear methodology on how to conduct the systematic reviews and grade the quality of the evidence. It is expected that in some cases this process will consist of a review of recent existing reviews and/or available assessments by national agencies. Experts encourage WHO to join forces with experienced institutions or commitees that have well established methods and criteria for selection and decision making, in addition to comprehensive sources of open data from which WHO could benefit. It would be advantageous for the guideline update process to consider the creation of a working group for that purpose, including relevant experts from US EPA, IARC, collaborators involved in the Global Burden of Disease (GBD) project or the UK COMEAP, along with institutions with

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extensive experience in managment of large databases on air pollution and health such as for example the Air Pollution Epidemiology Database (APED) at St. George's University of London, UK, or the Air Pollution and Health (LUDOK) database at the Swiss Tropical and Public Health Institute (TPH) in Basel, Switzerland.

o   In order to inform the future update of the WHO AQGs and ensure that it meets the needs of the main end-users, it may be useful for WHO to critically assess the implementation and usefulness of the existing WHO AQGs in different countries. Such an effort was attempted in 2007 by means of a survey, but results were limited as this was conducted too shortly after the publication of the latest edition of the guidelines (Vahlsing and Smith 2012).

o   The evidence on effects of acute exposure (short-term peaks) to classical pollutants should be reviewed, as there are data available showing harmful effects due to very short exposures at high concentrations (e.g. for PM and NO_2), which might support the development of guidelines for additional, shorter exposure times.

o   Additionally, it will be important to ensure that recommendations are relevant globally and apply to the whole range of air concentrations measured worldwide. Epidemiological data available from studies conducted in regions of the world with higher levels of air pollution are critical for proper assessment of the risk and communication to policy makers and other end-users in areas of the world where air pollutant levels may be higher than in Europe or North America.

o   Finally, experts emphasized the importance of establishing a conceptual approach to address the multipollutant confounding existing across the various air pollutants. Additionally, conducting a health risk assessment for the mixture of urban pollutants would be of high relevance, but framed outside of the direct scope of guideline development.

6.2.   Follow up actions

Expert advice obtained during this consultation and summarized in the present report will be used by WHO along with additional inputs as a basis to develop the planning proposal, that will be submitted for approval to the WHO Guideline Review Committee before formally starting the process of updating the AQGs.

As such, next steps of the planning process will consist of drafting the scope of the update, including an initial list of priority topics and key issues and the formulation of questions to be answered in the guidelines following a specific format, taking into account inequity/human rights and gender considerations. Various guideline groups with specific tasks will be established (WHO Steering Group, Guideline Development Group, Systematic Review Team, External Peer-review Group). The

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specific format and content of the updated AQGs will be defined at a later stage of the process with inputs from the different expert groups, and was outside the scope of the present expert consultation.

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Annex 1: Final list of participants

World Health Organization

**WHO Expert Meeting: Consultation on available evidence for the
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**Bonn, Germany
29 September – 1 October 2015**

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Annex 2: List of background material

The following documents were prepared as supporting material to the expert consultation meeting. The background document was developed by WHO (Marie-Eve Héroux and Nadia Vilahur, Regional Office for Europe), Annex 1 was prepared in collaboration with US EPA (Tom Luben, George Woodall, Lynn Flowers and collaborators), and Annex 2 was produced by the authors of the ongoing Cochrane systematic review on interventions in air pollution, Jacob Burns (University of Munich), Eva Rehfuess, Hanna Boogaard, and Annemoon van Erp (Health effects Institute).

Background document:

"Available evidence for the future update of the WHO Global Air Quality Guidelines"

Annex 1:

"Individual air pollutant summaries: Latest information available and critical issues to consider for future update of WHO Air Quality Guidelines"

Annex 2:

"Effective interventions to reduce air pollutant levels and improve public health."

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Annex 3: Final Programme

**WHO Expert Meeting: Consultation on available evidence for
the future update of the WHO Global Air Quality Guidelines**

**Bonn, Germany
29 September – 1 October 2015**

29 September 2015

8:30	Registration open
9:00	Opening of the meeting (*WHO*)
9:15	Introduction of participants, appointment of chairpersons and rapporteur, adoption of agenda and programme
9:45	Objectives of the meeting and proposed plan for discussion (*Marie-Eve Héroux*)
10:00	Global and regional perspectives for air quality and context for update of guidelines (*Marie-Eve Héroux; Nadia Vilahur*)
10:20	History of WHO air quality guidelines (*Michal Krzyzanowski*)
10:45	Coffee break
11:15	Classical pollutants: available evidence for the future update of the WHO Global Air Quality Guidelines
	Presentation on PM and ozone (*Bert Brunekreef*)
	Discussion in plenary
12:30	Lunch break
13:30	Classical pollutants: available evidence for the future update of the WHO Global Air Quality Guidelines
	Discussion in plenary (*continued*)
15:00	Coffee break
15:30	Classical pollutants: available evidence for the future update of the WHO Global Air Quality Guidelines
	Presentation on NO_2 and SO_2 (*Heather Walton*)
	Discussion in plenary (*continued*)
17:25	Short introduction to the next sessions in working groups

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17:30   End of day 1

30 September 2015

9:00   Discussion in 3 working groups on available evidence for the future update of the WHO Global Air Quality Guidelines

> Pollutant Group 1: PAHs and metals (Arsenic, Cadmium, Chromium, Lead, Manganese, Mercury, Nickel, Platinum, Vanadium)
> (*Chair: Francesco Forastiere*)
>
> Pollutant Group 2: Asbestos, Benzene, Butadiene, Carbon monoxide, Formaldehyde, Styrene, Tetrachloroethylene, Trichloroethylene, Toluene
> (*Chair: Lidia Morawska*)
>
> Pollutant Group 3: Acrylonitrile, Carbon disulfide, Fluoride, 1-2-Dichloroethane, Dichloromethane, Hydrogen sulphide, PCBs, PCDDs and PCDFs, Vinyl chloride
> (*Chair: Tom Luben*)

10:30   Coffee break

11:00   Discussion in 3 working groups on available evidence for the future update of the WHO Global Air Quality Guidelines (continued)

13:00   Lunch break

14:00   Plenary reporting and general discussion on available evidence
> Chair Group 1
> Chair Group 2
> Chair Group 3

15:30   Coffee break

16:00   Plenary reporting and general discussion on available evidence (continued)

17:30   End of day 2

19:00   Social dinner (location to be confirmed)

1 October 2015

9:00   Recap from previous day's meeting

9:15   Plenary discussion on any additional air pollutants and outstanding issues

10:00   Best practices, interventions and accountability measures: available evidence for the future update of the WHO Global Air Quality Guidelines
> Presentation (*Jacob Burns*)
> Discussion in plenary

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11:30	Coffee break
12:00	General summary of plenary discussion; identification of relevant air pollutants and interventions for future update of the WHO Global Air Quality Guidelines
13:00	Agreement on recommendations for follow-up actions and next steps
13:30	Concluding remarks: other WHO activities on air quality, and use of scientific evidence in guideline development (*Carlos Dora*)
13:55	Closure of the meeting
14:00	Lunch

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Annex 4: Summary Table of WHO Air Quality Guidelines

Summary of existing WHO air quality guidelines and additional WHO guidelines and assessments for ambient air pollutants

		Averaging Time	*Time-Weighted Average*	*Year of Latest WHO AQGs**	*Health Endpoints used for AGQ development*	*IARC Group Classification (Year)*	*Other WHO Health Risk Assessments (Year)***
Classical pollutants							
1	PM_{10}	Annual	20 µg/m^3	2006	Total, cardiopulmonary and lung cancer mortality	1 (2013)	
	PM_{10}	24 h	50 µg/m^3	2006	Total, cardiopulmonary and lung cancer mortality		
2	$PM_{2.5}$	Annual	10 µg/m^3	2006	Total, cardiopulmonary and lung cancer mortality	1 (2013)	
	$PM_{2.5}$	24 h	25 µg/m^3	2006	Total, cardiopulmonary and lung cancer mortality		
3	O_3	8h daily max	100 µg/m^3	2006	Daily mortality	n/a	
4	NO_2	Annual	40 µg/m^3	2010	Respiratory effects in children	n/a	
		1 h daily max	200 µg/m^3	2010	Bronchial responsiveness in asthmatics	n/a	
5	SO_2	24 h	20 µg/m^3	2006	All age mortality and childhood respiratory disease	3 (2001)	
		10 min	500 µg/m^3	2006	Respiratory symptoms in asthmatics		

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		Averaging Time	*Time-Weighted Average*	*Year of Latest WHO AQGs**	*Health Endpoints used for AGQ development*	*IARC Group Classification (Year)*	*Other WHO Health Risk Assessments (Year)***
Organic Pollutants							
5	Acrylonitrile	n/a	No safe level	2000	Carcinogenicity (lung)	2B (1999)	CICAD (2002)
6	Benzene	n/a	No safe level	2010	Carcinogenicity (myeloid leukaemia) and genotoxicity	1 (2012)	
7	Butadiene	n/a	No safe level	2000	Carcinogenicity (multisite)	1 (2012)	CICAD (2001)
8	Carbon disulfide	24 h	100 µg/m^3	1987	Neurological, coronary heart disease and endocrine disturbance	n/a	CICAD (2002)
		30 min	20 µg/m3	1987	Sensory effects or annoyance reactions	n/a	
9	1,2-Dichloroethane	24 h	0.7 mg/m^3	2000	Histological changes in the liver (animal studies)	2B (1999)	
10	Dichloromethane	24 h	3 mg/m^3	2000	Production of carboxyhaemoglobin (COHb)	2A *(in preparation)*	GDWQ (2011)
11	Formaldehyde	30 min	100 µg/m^3	2010	Sensory irritation	1 (2012)	
12	Polycyclic aromatic hydrocarbons	n/a	No safe level	2010	Carcinogenicity (lung)	1 B[a]P (2012)	
13	Polychlorinated biphenyls	n/a	No guideline	2000	n/a	1 (2012)	CICAD (2003)

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		Averaging Time	Time-Weighted Average	Year of Latest WHO AQGs*	Health Endpoints used for AGQ development	IARC Group Classification (Year)	Other WHO Health Risk Assessments (Year)**
			value				
14	Polychlorinated dibenzodioxins and dibenzofurans	n/a	No guideline value	2000	n/a	3 (1997)	JECFA (2002)
15	Styrene	Weekly	0.26 mg/m³	2000	Carcinogenicity (lymphatic and hematopoietic)	2B (1987)	GDWQ (2011)
		30 min	70 µg/m³	2000	Odour detection threshold		
16	Tetrachloroethylene	Annual	0.25 mg/m³	2010	Kidney alterations	2A (2014)	
		30 min	8 mg/m³	2010	Sensory effects or annoyance reactions	2A (2014)	
17	Toluene	Weekly	0.26 mg/m³	2000	Central Nervous System (CNS) effects (also developmental)	3 (1999)	GDWQ (2011)
		30 min	1 mg/m³	2000	Odour detection threshold	3 (1999)	
18	Trichloroethylene	n/a	No safe level	2010	Carcinogenicity and genotoxicity	1 (2014)	
19	Vinyl chloride	n/a	No safe level	2000	Carcinogenicity (liver and other sites)	1 (2012)	

Inorganic pollutants

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		Averaging Time	*Time-Weighted Average*	*Year of Latest WHO AQGs**	*Health Endpoints used for AGQ development*	*IARC Group Classification (Year)*	*Other WHO Health Risk Assessments (Year)***
20	Arsenic	n/a	No safe level	2000	Carcinogenicity (lung)	1 (2012)	JECFA (2011)
21	Asbestos	n/a	No safe level	2000	Carcinogenicity (lung and mesothelioma)	1 (2012)	
22	Cadmium	Annual	5 ng/m³	2000	Carcinogenicity (lung)	1 (2012)	JECFA (2013)
23	Carbon monoxide	15 min	100 mg/m³	2010	COHb levels in non-smokers blood below 2%	n/a	
		1 h	35 mg/m³	2010	Same as above	n/a	
		8 h	10 mg/m³	2010	Same as above	n/a	
		24 h	7 mg/m³	2010	Same as above	n/a	
24	Chromium	n/a	No safe level	2000	Carcinogenicity (lung)	1, Chromium VI compounds (2012); 3, Chromium metallic (1990)	CICAD (2013)
25	Fluoride	n/a	No guideline value	2000	Impairment of pulmonary function and skeletal fluorosis	3 (1987)	EHC (2002)
26	Hydrogen sulphide	24 h	150 µg/m³	2000	Serious eye damage	n/a	CICAD (2003)
		30 min	7 µg/m³	2000	Odour detection threshold	n/a	

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		Averaging Time	*Time-Weighted Average*	*Year of Latest WHO AQGs**	*Health Endpoints used for AGQ development*	*IARC Group Classification (Year)*	*Other WHO Health Risk Assessments (Year)***
27	Lead	Annual	0.5 µg/m³	2000	Free erythrocyte protoporphyrin levels in adults; cognitive deficits, hearing impairment and disturbed vitamin D metabolism in children	2B (1987), inorganic lead 2A (2006), organic lead 3 (2006)	JECFA (2011)
28	Manganese	Annual	0.15 µg/m³	2000	Neurotoxic effects in workers, developmental effects in children	n/a	
29	Mercury	Annual	1 µg/m³	2000	Effects on kidney and CNS	mercury and inorganic mercury compounds 3 (1993); methylmercury compounds 2B (1993)	JECFA (2011) and CICAD (2003) for elemental mercury
30	Nickel	n/a	No safe level	2000	Carcinogenicity (lung and nasal sinus)	nickel, metallic and alloys 2B (1990); nickel compounds 1 (2012)	GDWQ (2011)
31	Platinum	n/a	No guideline value	2000	Sensitization reactions	n/a	
32	Vanadium pentoxide	24 h	1 µg/m³	1987	Chronic upper respiratory tract symptoms	2B (2006)	CICAD (2001)

*2010 indicates WHO indoor air quality guidelines for selected chemicals, while the remaining years (1987, 2000 and 2006) refer to WHO ambient air quality guidelines; **CICAD: Concise International Chemical Assessment Documents; GDWQ: WHO Guidelines for Drinking Water; JECFA: Joint FAO/WHO Expert Committee on Food Additives.

WHO Air Quality Guidelines (AQGs) are used as a reference tool to help decision-makers across the world in setting standards and goals for air quality management. Their regular update is essential to continue protecting populations from the adverse health effects of air pollution.

In the last years, new evidence has emerged on the health effects of ambient air pollutants. In September 2015 WHO organized a global consultation meeting to seek expert opinion on the latest available evidence on the health effects of several ambient air pollutants and on interventions to reduce air pollution. The results from this consultation will contribute to the thinking behind the future update of the AQGs.