

# **TOWARDS A TOOL FOR ASSESSMENT OF CUMULATIVE RISKS FROM INDOOR AIR POLLUTANTS IN PUBLIC SETTINGS FOR CHILDREN: THE FIRST EXPERT CONSULTATION**

**Meeting report  
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## ABSTRACT

The WHO Regional Office for Europe has initiated the development of a tool to facilitate assessments of the risk to human health from combined exposures to hazardous chemicals in indoor air, especially in public settings for children. In December 2018 an expert consultation was held to share knowledge, expertise and experience in the area of children's health and indoor air quality, with the aim of assisting and advising WHO in developing the tool. A wide range of topics was discussed including the methodological approach to the development of the tool, collection of toxicological information, identification of chemicals and health end-points of highest priority and development of recommendations for sampling and analysis of indoor air pollutants and training for paediatricians and public health professionals. The main outcomes were agreement on the list of chemicals for inclusion in the tool, the adverse health effects to be considered, advice on the revision of technical documents on the methods for sampling and analysis of chemicals, and prioritization of sampling sites for planning national monitoring programmes for indoor air quality.

### Keywords

RISK ASSESSMENT  
HAZARDOUS SUBSTANCES  
AIR POLLUTION, INDOOR  
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## Abbreviations

ISO	International Organization for Standardization
LOAEL	lowest observed adverse effect level
NOAEL	no observed adverse effect level
PAH	polycyclic aromatic hydrocarbons
PM	particulate matter
SINPHONIE	Schools Indoor Pollution and Health Observatory Network in Europe
VOC	volatile organic compounds
WHO ECEH	WHO European Centre for Environment and Health

## Introduction

Interactions of chemical pollutants in the indoor environment may pose special risks to children owing to their greater potential for intake based on physiological considerations and behavioural factors (1). A number of health disorders in children can be linked with outdoor and indoor air quality, including respiratory diseases, neurodevelopmental disorders and impairment of functions of the immune system (2). The chemical risk to children from indoor air pollutants has not been well assessed. A substance-by-substance approach to risk assessment could underestimate the true risk from co-exposure to multiple chemicals in the indoor air. A WHO framework for assessing the risks of combined exposure to multiple chemicals provides a basis for assessment of combined exposure risks (3).

Improvement of indoor air quality is one of the environment and health priorities recognized at the global and regional levels, for example, in the United Nations 2030 Agenda for Sustainable Development, goal 3.9 (to reduce the number of deaths and illnesses from hazardous chemicals) and 4.a (to build educational facilities that provide safe learning environments). Its importance is also recognized in WHO's 2016 *Road map for an enhanced global response to the adverse health effects of air pollution* (4) and 2017 *Road map to enhance health sector engagement in the Strategic Approach to International Chemicals Management towards the 2020 goal and beyond* (5) and, in Europe, in the Ostrava Declaration on Environment and Health (2017) (6).

To address this challenge and to provide support to Member States, the WHO Regional Office for Europe, European Centre for Environment and Health (WHO ECEH), has undertaken a project to develop a tool to assess the health risks to children from combined exposure to indoor air pollutants, with priority given to public settings for children such as schools, kindergartens, and day-care centres.

As part of this process, a consultation was organized in Bonn, Germany on 3 and 4 December 2018, with financial support from the German Federal Ministry for the Environment, Nature Conservation and Nuclear Safety. This first expert consultation aimed to assist and advise the WHO through sharing the knowledge, expertise and experience in assessing the risks of combined exposure to chemicals and indoor air quality. Participants were to agree on the approach for developing the tool, create a list of chemicals and adverse effects of concern, and give advice on the use of available toxicological information. In addition, to provide advice on planning and designing indoor air quality monitoring programmes, recommendations on prioritizing sampling sites and choosing methods of sampling and analysis.

Ms Dorota Jarosinska, Programme Manager, Living and Working Environments, WHO ECEH, opened the meeting and welcomed the participants. WHO ECEH has valuable experience in developing and applying tools to support decision-making, such as AirQ+ tool<sup>1</sup> to calculate the health effects of exposure to ambient air pollution, or CaRBonH tool<sup>2</sup> to quantify the co-benefits of reducing greenhouse gas emissions. The new tool will benefit two areas, indoor air quality and

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<sup>1</sup> Available at <http://www.euro.who.int/en/health-topics/environment-and-health/air-quality>

<sup>2</sup> Available at <http://www.euro.who.int/en/health-topics/environment-and-health/Climate-change/publications/2018/achieving-health-benefits-from-carbon-reductions-manual-for-carbonh-calculation-tool-2018>

chemicals management, and might be used by specialists in chemicals risk assessment and indoor air quality.

The meeting continued with a series of presentations prepared by consultants invited by the WHO ECEH followed by the discussion (programme in Annex 1). The topics, discussed during the meeting included the health effects of indoor air pollutants, a list of chemicals of concern (Annex 2), a database of toxicological information on chemicals of concern, and monitoring of indoor air quality in public settings for children.

In preparation for the consultation, WHO ECEH had initiated and coordinated the development of several technical documents. These were shared with the experts and underpinned the discussion during the meeting. These included:

- a list of priority chemicals (30 substances) identified on the basis of a review of studies of air quality in schools and kindergartens in Europe;
- a systematic review of the likelihood of co-exposure to hazardous chemicals in indoor air globally;
- a compilation of information on the toxicity of chemicals (30 chemicals);
- a proposal for prioritizing sampling sites for national monitoring programmes drafted on the basis of analysis of potential sources of chemicals to indoor environment; and
- an overview of methods for sampling and analysis of indoor air pollutants.

The meeting was attended by 18 experts from 14 countries and a representative of the European Commission (list of participants in Annex 3). The meeting was chaired by Ms Irina Zastenskaya, WHO ECEH.

## **Introduction of the methodological concept of a tool for assessment of the health risks from combined exposure to hazardous chemicals in the indoor air**

Evidence of the negative impact of indoor air pollution in schools and other public settings for children is increasing. Participants of a training workshop on *Multiple exposures and risks: evidence review, knowledge transfer and policy implications training workshop* (held in Bonn, Germany, 16–18 October 2013) identified assessment of risk from combined exposures to chemical pollutants in the indoor environment as a priority area for application of the WHO framework for assessment of risks of combined exposures to multiple chemicals (3). In 2017, the WHO ECEH initiated development of a tool for assessing the risks of multiple indoor air pollutants, based on application of the Tier 0 and Tier 1 approaches in the WHO framework (3). Key components of exposure were identified, and the likelihood of co-exposure within a relevant timeframe was demonstrated through the systematic review commissioned by the WHO ECEH. Consistent with the WHO framework, a concept of a tool is based on dose-additivity. The tool will initially cover exposure to gaseous forms of chemicals and focus on public settings for children such as kindergartens, day-care centres and schools. In the future, the tool could be extended for assessing indoor air-related risks for children and other population groups in other indoor settings, depending on chemicals of concern, and of other forms of chemicals.

The plenary discussion focused on the prioritization of settings for assessment of the risks of combined exposures, and the availability of toxicological information. This included considerations on how to most effectively use information collected through regional and

national projects in the area of indoor air quality. For example, in Germany, the work is advancing to derive thresholds of chemicals of health concern in indoor air. The outcomes of this national project could contribute to the collection of toxicological information needed for the tool.

In order to develop a workable tool, participants proposed to create a manageable list of chemicals to be addressed, and to establish a limited number of indoor air pollution-related health end-points, for which health-based guideline values are available (from WHO and other reliable sources). The possibility of using other points of departure at a later stage, such as benchmark doses as well as information on modes of action, where available, was also discussed.

A document, which describes the methodological aspects of the development of the tool, is needed to facilitate understanding of the proposed approach. This could include: (i) terminology; (ii) scope and limitations of the tool in terms of the chemicals and guidance values included; and (iii) the approach to structuring information/input data according to the WHO's methodological framework, and prioritization of supporting information sources (international databases and national guidance values).

The participants concluded that:

- WHO's methodological framework is relevant for the development of the tool;
- a document describing the overall methodological approach should accompany the tool;
- at the initial stage, the tool will cover priority adverse effects and chemicals.

## **Health effects from exposure to chemicals in indoor air**

An overview of reported studies of associations between indoor air pollution and children's health was presented to support a discussion of the adverse health effects that could potentially be priorities for a combined exposure risk assessment. At the request of WHO, and based on existing information on the effects of air pollution on health, information on a limited number of adverse effects: respiratory, cardiovascular, neurological, immune system, endocrine disruption and carcinogenicity was compiled in a technical document prepared for the meeting.

Evidence of the effects of indoor air pollution on children's health is growing (7–9). Both short- and long-term effects have been associated with measured or estimated concentrations of indoor air pollutants (10–12). Several national and international research projects (the School Environment and Respiratory Health of Children study, the Interventions on Health Effects of School Environment study and the Schools Indoor Pollution and Health Observatory Network in Europe (SINPHONIE)) investigated associations between exposure to air pollutants and health outcomes in children in public settings. In most of these studies the relationship between air quality and one or more health outcomes was observed (13, 14).

Environment-related health effects generally result from a complex interaction between external factors related to the environment and factors inherent in humans (15). The external factors include types of pollutants, their numbers and concentrations resulting from emissions from outdoor and indoor sources, their distribution between gaseous and particulate phases and the duration of exposure. Factors inherent to humans such as genetic susceptibility, physiological characteristics and lifestyle, are important but will not be considered in the tool.



In most studies, effects of chemicals in the indoor air on respiratory systems were reported. Respiratory tract irritation, influenza-like symptoms, cough and shortness of breath are the most common symptoms of acute exposure to chemicals in indoor air (16 -20). Longer exposure could lead to reduction of lung function capacity, exacerbation of asthma and increased risks of other chronic respiratory diseases later in life (21-23).

In a number of studies, associations between chemicals in indoor air and effects on the nervous system in children have been reported. Headaches, dizziness, diminished learning abilities and memory functions as well as cognitive disorders are some of the well-known symptoms of exposure to neurotoxic chemicals and some endocrine disruptors (24-26). There is much less evidence about cardiovascular disorders and impacts on the immune system in children, due to exposure to indoor air pollutants. Immune system disorders include the development of allergies and the dysfunction of the immune system and autoimmune processes (27,28).

Associations between some long-term health effects at later life-stages and indoor air pollution have also been reported. The estimated life-time risk of cancer may be increased due to exposure to volatile organic compounds (VOC) in schools (29). The delayed effects of certain chemicals, including those in indoor air, such as disorders of the reproductive, neurological and cardiovascular systems can be diagnosed later in life (25,30-33).

Several studies have been conducted to assess the risks of combined exposure to airborne chemicals in schools using different methodologies: maximum cumulative ratio and hazard index for chemical groups, and the chemical-by-chemical approach, using a hazards quotient or excess risk method (30,34,35).

The discussion focused on the creation of a list of potential target systems and organs for hazardous chemicals in indoor air for grouping them for assessment of risks from combined exposure. In addition to the initial short list of target systems and organs proposed by WHO (respiratory, cardiovascular and nervous systems), the experts proposed that a number of other target end-points should be included in the list for discussion in the working group: liver and kidneys, local irritation (skin, eye, nose), hematotoxicity, genotoxicity and carcinogenicity, sensitization, the endocrine disruption, and ocular and dermatological effects.

The participants concluded that:

- the target end-points to be discussed in the working groups included adverse effects on the respiratory, nervous, cardiovascular, immune, endocrine, and ocular systems, liver and kidneys disorders, hematotoxicity, carcinogenicity, irritation and sensitization and dermatological effects;
- given a wide list of the possible end-points, the discussion of priorities addressed the following considerations: exposure by inhalation; adverse effects of principal concern; coordination with a priority list of chemicals; and the availability of toxicological information related to certain chemicals and adverse effects.

## Collection of toxicological information on the most common chemical pollutants in indoor air

Information on the toxicological characteristics of chemicals is critical both, for a single chemical risk assessment, and for a risk assessment from combined exposure to chemicals. In the preparatory stage for the first expert consultation, information on the toxicity of 30 chemicals identified from the initial list of 96 substances (see below on p. 6), selected based on the analysis of chemicals observed in studies of the indoor air quality in Europe, since 2011.

Consistent with data requirements for Tier 0 and Tier 1 assessments in the WHO Framework, risk values for threshold and non-threshold critical end-points and no observed adverse effect levels (NOAELs) for three health end-points (respiratory effects, cardiovascular effects and neurological effects) focusing on the inhalation pathway of exposure had been retrieved from the existing databases. Priority was given to WHO sources, although other sources were consulted when necessary, including the Toxicology Data Network (TOXNET), the Agency for Toxic Substances and Disease Registry (ATSDR), the United States Environmental Protection Agency and its Integrated Risk Information System (IRIS). Where the NOAELs or lowest observed adverse effect levels (LOAELs) (see next paragraph) for chronic exposure were not available, NOAELs or LOAELs for intermediate and acute exposure were considered. Results from searches in the databases of the European Chemicals Agency and the European Union Lowest Concentration of Interest<sup>3</sup> were also included.

A tabular summary of the results was presented to the experts. NOAELs derived in the best available study were included in the table. If the databases included no judgement on the best available study, the lowest NOAEL was reported. If there was no NOAEL, the LOAEL was included. For the majority of the substances investigated for three end-points (respiratory, cardiovascular and neurotoxic effects), specific NOAELs were retrieved based on the search strategy. For some substances, however, it was not possible to identify the NOAEL and LOAEL for one or more adverse effect end-points. For example, NOAELs are not established for some endocrine-disrupting and carcinogenic chemicals; there are indications that, for certain substances, NOAELs /LOAELs for the selected end-points are very high in comparison with prevailing levels in indoor air and their use is not reasonable; information on the NOAEL/LOAEL for some emerging substances is not available in the prioritized databases. NOAEL was also not available for PM.

A tool developed for the Flemish government by the Flemish Institute for Technological Research (VITO) for assessing the risks of individual chemicals was presented as an example of calculating risks of individual chemicals.

The participants proposed that:

- for the purpose of the tool, thresholds, NOAEL data should be used; the LOAEL can be considered, if there is no information about NOAEL;
- the approach to collecting and compiling toxicological information for combined exposure assessment and the development of the tool should be clarified in the document describing the methodological approach to the development of the tool.

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<sup>3</sup> Available at [https://ec.europa.eu/growth/sectors/construction/eu-lci/values\\_en](https://ec.europa.eu/growth/sectors/construction/eu-lci/values_en)

## **The most common chemicals in indoor air in public buildings for children and the likelihood of combined exposure to them**

At the request of the WHO ECEH and based on a literature review, a list of common chemical pollutants in the indoor air in public settings for children was developed. Two criteria were applied, the first being the measurements of chemicals in indoor air in schools and other settings for children between 2012 and 2017, and the geographical location limited to Europe as the second criterion. A list of 96 chemicals was developed and reduced to 30 chemicals according to the frequency of their detection in studies in public settings for children and given available resources to ensure the feasibility of collecting toxicological information for the development of the tool.

The likelihood of co-exposure to chemicals in indoor air was assessed based on the frequency of detection in the indoor air of public settings for children worldwide. If a group of chemicals was detected in 100% of samples, co-exposure was confirmed; if a result was less than 100%, a chemical was considered not systematically present in the indoor air samples. The review followed the PRISMA protocol (36). Publications from January 2014 to October 2018 in three databases were considered: Science Direct, PubMed and Google Scholar. Studies that presented data on at least two indoor chemicals measured simultaneously in pre- or elementary schools and day-care centres or kindergartens were included in the assessment. Radon and carbon monoxide were excluded. A database was created based on the assessment of the publications, including: years of measurements; geographical location (country); type of environment (rural, urban, industrialized); type of building (school, kindergarten); number of buildings; number of rooms; number of air samples; compounds measured; corresponding Chemical Abstracts Service (CAS) number; and frequency of detection of measured compounds. When detection frequencies were not reported, an estimate was indicated (based on the centiles given in the publication). In total, 1658 publications were identified in the selected data sources. After screening titles and abstracts, 1585 studies were excluded because non-indoor air was investigated (relative to outdoor air, dust or comfort assessment), only CO<sub>2</sub> and temperature were measured, only one pollutant was analysed, or air was sampled in other types of building (households, hospitals). Full text screening resulted in exclusion of another 43 studies. In 37 of these, no detection of frequency or distribution of concentrations was provided; in five, an environment not used by children was investigated (such as a university teacher's room); and in one case the full text was not available. In studies performed in 16 countries worldwide, 177 chemicals were investigated. More than two chemicals were detected in 100% of studies that confirmed a high level of probability of combined exposures to chemicals.

The list of 30 chemicals was discussed in a working group to ensure that chemicals of highest priority that could feasibly be included in the tool were listed.

The following factors were taken into further account:

- the inclusion of a reasonable and manageable number of chemicals at the outset; with options to increase the number of chemicals to be addressed at a later stage (depending on the availability of toxicological information);
- availability of high confidence information on the respective adverse effects;

- critical consideration in relation to chemical emissions from outdoor and indoor sources (such as building materials or furniture) and what is measured in indoor air in public health buildings;
- availability of standardized sampling and analytical methods;
- availability of chemicals guideline values in the WHO's *Indoor air quality guidelines* and at national level in many countries as well as chemicals that were assessed in harmonized studies as SINPHONIE.

## Setting monitoring programmes for indoor air quality

To assist countries in planning and designing surveys for collecting information on exposure for both individual chemical risk assessment and assessments of risk from combined exposure, recommendations on prioritizing sampling sites and the selection of methods for sampling and analysis of chemicals in indoor air were developed for consideration by the participants. Adoption of a harmonized approach to collection of information on exposure is likely to increase the comparability of results of the assessment of indoor air pollution and combined exposure across WHO Europe as well as identification of the chemicals that drive risks and their sources.

Two technical documents compiled at the request of the WHO ECEH at the preparatory stage for the expert consultation were discussed regarding the development of national and local monitoring programmes in terms of methods for sampling and analysis of chemicals in indoor air and the selection and/or prioritization of sampling sites.

## Methods for sampling and analysis of chemicals in indoor air

Thirty chemicals included in the list compiled by WHO were organized by chemical group as a basis to select appropriate methods for sampling and analysis. Information on available methods was collected from relevant publications, European normative documents and the database of the International Organization for Standardization (ISO). ISO and/or European standardized methods are available for the most chemicals in the list. Both passive and active sampling were considered. The main focus was on passive sampling given its advantages including: no need for a pumping system and energy supply; silent operation; low cost; no need for a high level of expertise and special training of personnel; and the possibility of defining a sampling period based on preliminary information on the concentration of pollutants. For some compounds (such as semi-volatile organic compounds), the required sampling period is quite long and the assessments are semi-quantitative, while the calibration of passive samplers for selected semi-volatile organic compounds is still very limited in indoor air. Passive sampling for VOCs also has limitations. For example, for 1,4-dichlorobenzene,  $\alpha$ -pinene and limonene, the adsorbent is not specified in ISO 16017-2 and the sampling rates are not calculated. Commercial samplers would, therefore, have to be used. For PM, gravimetric methods or optical instruments are needed for the sampling and analysis of concentrations. In addition to the description of methods, the document includes information about general principles, quality assurance procedures and the quality control programme with reference to relevant ISO documents. A database of methods for sampling and analysis was developed and included in the technical document prepared for the meeting participants.

The participants agreed that the document describing methods for sampling and analysis should be revised according to the lists of chemicals drawn up during the meeting.

## **Prioritization of sampling sites**

A monitoring programme is needed to collect information for assessment of exposures and the respective health risks. A simple prioritization system was developed to guide the collection of information on exposure to facilitate identification of sampling sites with potentially higher levels of chemical contamination of indoor air. Information about the main outdoor and indoor sources of chemicals into indoor air was summarized and weighting criteria were proposed to reflect the potential levels of emissions and characteristics of chemical contamination of indoor air. Outdoor factors included location of the building (rural, urban), proximity to industrial enterprises, distance from busy roads and weather conditions, including the predominant wind direction. The proposed score for assessment ranged from 0 to 3, with the highest score for buildings located near busy roads and industrial facilities. Indoor factors included building characteristics, such as the age of a building and terms of operation. Room characteristics included materials used for decorating walls and ceilings, floor coverings, and furniture and equipment and the density thereof. The proposed score varied from 0 to 4.

The participants stressed the importance of recommendations for identifying sampling sites where higher concentrations of air pollutants were expected, although this is a challenging task. They described examples based on their own research experience of factors such as floor covering materials and ventilation. An approach to assess information on solvent-based paints, energy-saving routines, the ageing of schools and other public settings for children and influence of outdoor sources of pollution was also discussed.

The experts advised to build on experiences gathered in the SINPHONIE project and in other projects. Examples were the recently published guidance by the United Kingdom Department of Education on ventilation, thermal comfort and indoor air quality in schools (37) and the outcomes of a project on the indoor environment in schools implemented by the Estonian Health Board.

The need for assessments of odours and their possible incorporation in the combined exposure risk assessment using odour thresholds was mentioned. Further discussion is, however, needed to decide if it is feasible to assess combined risks for odour.

The experts made the following recommendations for further work on the document on prioritization of sampling sites:

- a questionnaire should be created as a checklist or other type of format, allowing yes/no answers in as simple a form as possible;
- questions on sources of chemicals should be linked to the list of pollutants selected for the tool for assessment of risks of combined exposure to chemicals;
- rural and urban schools should be distinguished according to their location;
- wind direction in relation to outdoor sources of air pollution – upstream and downstream, should be included;
- yes/no questions should be formulated about the presence of industrial enterprises and high-traffic roads, and options provided for characterizing types of industry (such as a

power plant, waste management plant or chemicals plant) nearby or dominant upwind of the school;

- the ranking of energy-efficient versus conventional buildings should be reconsidered and a question formulated regarding the mode of ventilation;
- the age of a building or time since it was reconstructed should be reconsidered/excluded as a factor influencing indoor air pollution;
- an option for ranking two categories of flooring and ceiling materials (low-emission and high-emission) should be included to guide an assessor on how to consider a level of emission, for example, when collecting information on labelling and on emissions from different materials;
- new materials such as ceramic should be included in prioritization of floor coverings, and an explanation of what materials are included in the category “natural wood-based”; it should not be forgotten that wall-to-wall carpets are still used in some countries;
- as regards cleaning activities and the use of rooms, the following questions can be asked: “how often is the room cleaned using cleaning materials”, “is cleaning commonly done before or after classes”; “is the room used for other activities (for example, in the evenings, during weekends, what types of activity)”;
- complaints from children, teachers and other school personnel and parents should be included in the questionnaire for prioritization of sampling sites.

## **Education of health care professionals about indoor air pollution and its impact on children’s health: revision of educational materials**

The educational module had been prepared as a supplementary document for the tool. It addresses the need for public health professionals to improve their understanding of chemical risks and the risk arising from mixtures of hazardous chemicals in indoor air. It is expected that a training course, using this material, would advance the understanding of potential risk and its mitigation among public health professionals. The module consists of around 70 slides, covering: the policy framework in the WHO European Region; information available from WHO sources; the relevance of indoor air pollution to children’s health; the sources of chemicals in indoor air and sources of exposure of children; risk assessment as an approach for collecting information to plan risk mitigation measures; the characteristics of some common chemicals in relation to the health disorders they can cause; the availability of toxicological information for risk assessment; specific vulnerability of children; monitoring of indoor air quality and obtaining of data on exposure to chemicals; risk mitigation measures; and assessment of risks from combined exposures to multiple chemicals.

The participants highlighted the importance of training and sharing experience of good practices. They proposed that case studies should be included, such as of the assessment of risks of exposure to multiple indoor air pollutants versus the assessment of individual chemical risks, or examples from clinical practice. Practical exercises would be useful for understanding how knowledge can be used in everyday work. In addition to webinars and on-line training courses, the face-to-face training the trainers, would be an option to facilitate risk assessment from combined exposure to multiple chemicals and use of the tool. Courses could be pilot-tested and

discussed in countries participating in the development of the tool. An educational module for public health professionals on risk communication should accompany the risk assessment module. This should provide advice and an explanation on how to communicate risk to teachers, school administrations, parents, decision-makers and children. It Key messages for different audiences should be included in the educational modules/leaflets/other materials for promoting risk assessment from combined exposure to chemicals in indoor air.

To ensure that such training courses are effective, the participants advised that:

- an education module on risk communication should be developed, targeting different stakeholders, including policy-makers;
- if possible, a pilot train-the-trainers session should be organized on the assessment of combined exposure risks using the tool and the training modules;
- key messages for parents and children should be included in the risk communication educational module for the above categories.

## Discussion in working groups

Participants discussed the list of chemicals and the available sampling and analysis methods, as well as a list of adverse effects end-points.

### Working group 1. A list of chemicals and methods for their sampling and analysis

The short list of chemicals (30 compounds) served as a basis for compiling a list of chemicals for considering in the tool development. It was agreed that the list should contain chemicals, which are considered priorities for health concern as a basis to calculate the risk of combined exposures.

Three lists of chemicals were drawn up:

- (i) a list of substances included in the *WHO Indoor air quality guidelines*, chemicals investigated in the SINPHONIE project and some chemicals that are controlled in many European countries; the short list of priority chemicals includes 19 priority substances (plus radon which cannot be included in the combined exposure risk assessment and was excluded from the list);
- (ii) a “wish list” in which optional compounds are included (36 substances and groups of substances), organized according to priority: phthalates in group 1 – highest priority; synthetic musks in group 2; polycyclic aromatic hydrocarbons (PAH) in group 3; and brominated and organophosphate flame retardants and chlorinated paraffins in groups 4 and 5, respectively (lowest priority); the groups were prioritized not only according to their importance for exposure to children but also taking into account the relative availability of analytical methods of reasonable costs and the lack of standardized methods;
- (iii) a list of additional chemical compounds that can be measured using the same sampling and analytical methods as for chemicals from the short and the optional lists (the agreed lists of chemicals are in Annex 2).

Participants also discussed the possibility of using the calculated maximum cumulative ratio. This ratio offers an opportunity both to extend the list of chemicals (if a methodology exists), and to identify which compounds determine risk and drive risk assessment.

The use of harmonized methods for sampling and analysis facilitates the acquisition of reliable and comparable results, both temporally and geographically. The participants discussed the methods summarized in the technical document prepared for the meeting, reaching consensus on the following points.

- The use of ISO 16017-2 (thermal desorption) for VOCs can be recommended, given that the thermal desorption technique avoids the use of hazard solvents to extract the chemicals in the laboratory. For  $\alpha$ -pinene, limonene and 1,4-dichlorobenzene, however, this standard does not provide the sampling rates and commercial passive samplers are needed.
- In addition, poly (2,6-diphenyl-p-phenylenoxid) (Tenax) could be used as an adsorbent but the sampling rates for limonene,  $\alpha$ -pinene, 1,4-dichlorobenzene and trichloroethylene are not included in ISO 16017-2. Some commercial brands offer passive samplers with adsorbents such as graphitized charcoal that provide sampling rates for all VOCs of interest except naphthalene. Additional investigation of the possibility of calculating the naphthalene sampling rate is needed. Tenax can also be used as adsorbent if the sampling rates for all compounds of interest are provided.
- PAH, phthalates and musks could be sampled using low volume air sampling according to ISO 16000-12 and 16000-13. Phthalates could also be sampled according to ISO 16000-33:2017.
- Since passive sampling presents limitations (only the gas phase can be sampled), semi-VOCs should be measured by means of active samplers.
- The “method” document should stress that the indoor air temperature needs to be measured to correct the sampling rates for, for example, VOCs.
- It was decided to check the possibility of using optical instruments or microsensors for monitoring PM. The technique has a number of advantages such as ease of use, time resolution, more data provision and the possibility of measuring PM<sub>10</sub> and PM<sub>2.5</sub> using the same instrument. These measurements are not, however, standardized. The work on the use of microsensors for ambient air quality monitoring, which in the future might be applicable for indoor air pollution, including on chemicals is ongoing.
- Carbon monoxide is usually measured in indoor air by automatic portable sensors that can also measure CO<sub>2</sub>. Participants proposed that CO<sub>2</sub> should be measured in schools for calculating ventilation rates.

## **Working group 2. Adverse effect end-points for gathering toxicological information**

Participants discussed a broad list of end-points for potential adverse effects, including both those proposed by WHO and those proposed during the plenary discussion. The final list for the group discussion included the effects on respiratory system, nervous system, and immune system, hematotoxicity, sensitization, toxicity for the renal system, hepatotoxicity, respiratory



irritation, skin irritation, carcinogenicity, endocrine-system disruption and disorders of the ocular system.

The following criteria guided the discussion to identify adverse effect end-points of priority concern:

- evidence of the health impact of hazardous chemicals in indoor air;
- inhalation as a pathway of exposure;
- effects described in toxicological and epidemiological studies;
- availability of information on toxicological characteristics, including points of departure and modes of action;
- conformity with the list of chemicals.

Skin irritation was excluded because it is not a common effect from the inhalation pathway of exposure. The kidney and liver play a role in the detoxification and elimination of a majority of chemicals and while they are commonly target organs for toxicity via the oral route, levels of inhaled chemicals that can cause kidney and liver damage are commonly higher than those observed in indoor air.

Occasionally, hematotoxic effects are critical for a limited number of chemicals in low concentrations, such as benzene, but this is not common. Allergy will be partly covered under risks for respiratory irritation or for other respiratory system disorders. The toxicological information needed for the assessment of risks from endocrine-disrupting chemicals and effects on the immune system is limited and inclusion of these end-points is considered premature at present.

In conclusion, effects on the following systems or end-points related to long- and short-term exposure were agreed for initial consideration for inclusion in the tool:

- respiratory system;
- nervous system;
- cardiovascular system – assessment of risks of PM (optional);
- carcinogenicity – depending on the list of chemicals and based on assessments from the International Agency for Research on Cancer;
- respiratory irritation – depending on the list of chemicals.

## **Uncertainties and limitations of the tool for assessment of the risk from combined exposure to indoor air pollutants**

The value 100 (adjustment factor (AF) 10 for intraspecies and AF 10 for interspecies) for animal studies can be considered as a benchmark for considering the adequacy of margin of exposure for the purposes of the tool. The rationale for interpreting margins of exposure including those based on epidemiological studies needs to be explained in a methodological document accompanying the tool.

Other topics discussed before closure of the meeting included:

- application of different points of departure for risk assessment;
- prioritization of toxicological datasets for toxicological information collection;
- relevant toxicological information to enable higher tiered assessment for combined exposures;
- how to incorporate the maximum cumulative ratio for hazardous chemicals in indoor air when possible;
- use of information from animal and human studies.

Participants decided that discussion of these issues should continue with key experts, and the results should be reported to the second expert consultation.

## Conclusions and next steps

This first expert consultation resulted in a number of conclusions relevant for further development of the tool and the supplementary documents. The most important are listed below.

- The WHO framework for assessment of risk from combined exposure to hazardous chemicals provides an appropriate construct for the development of the tool. Health-based guideline values and other points of departure, such as NOAELs and LOAELs, can be used for Tier 0 and Tier 1, respectively, of the framework for assessment of risk of combined exposure to multiple chemicals in indoor air.
- A limited number of adverse effects end-points for grouping chemicals were agreed, including respiratory and nervous disorders, carcinogenicity and respiratory irritation, if confirmed after screening assessment in accordance with the list of priority chemicals, and the option to assess cardiovascular risks from PM.
- Two lists of chemicals were agreed: a priority list of 19 chemicals and an optional list for future consideration in the tool (36 substances in addition) (Annex 2).
- The description of methods for sampling and analysis of chemicals in indoor air should be revised according to the agreed lists of chemicals.
- Recommendations or guidance on prioritizing sampling sites should be simplified as much as possible but should be sufficiently specific to pose questions, which require only binary responses (yes/no).
- Document describing in detail the basis for the proposed approach to combined exposure assessment in the tool, with assumptions and limitations and a manual for use of the tool, should be prepared and accompany the tool.

The second expert consultation will be organized once a final list of chemicals grouped according to their health effects has been produced.

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## *Annex 1*

### PROGRAMME

#### **3 December 2018**

- 13.00–13:30 Opening of the Meeting  
*Dorota Jarosinska, Programme Manager, WHO ECEH*
- 13:30–13:45 Scope and expected outcomes of the consultation  
*Irina Zastenskaya, WHO ECEH*
- 13:45 - 14:30 Assessment of health risks from mixtures of chemical pollutants in indoor environment: introduction of the concept of a tool for assessment of risks of exposure to chemical mixture in indoor environment  
*Irina Zastenskaya, WHO ECEH*  
Discussion
- 14:30–15:15 Health effects and end-points of exposure to mixtures of indoor air pollutants to be included in the tool  
*Szigeti Tamás, National Public Health Centre, Budapest, Hungary*  
Discussion
- 15:45–17:00 Availability and approaches to collection of toxicological information on most common chemical pollutants in the indoor air  
*Katleen de Brouwere, VITO health, Belgium*  
Discussion
- 17:00–17:45 The most common chemicals in indoor air in public buildings for children and the likelihood of combined exposure to them  
*Corinne Mandin, Scientific and Technical Centre for Building, France*  
Discussion

#### **4 December 2018**

- 9:00–10:30 Setting monitoring programmes for indoor air quality including selection of methods for chemical pollutants sampling and analysis  
Prioritization of public settings for children for planning of a national monitoring programme for indoor air quality  
*Alexander Gankin, Scientific Practical Centre of Hygiene, Belarus*  
Methods for sampling and analysis of the most common chemical pollutants in indoor air  
*Florentina Villanueva, Research Institute for Combustion and Atmospheric Pollution, Spain*  
Discussion
- 11:00–12:30 Working groups to finalize the document on national monitoring programmes (prioritization system and methods)
- 13:30–15:30 Education of health care professionals on indoor air pollution and its impact on children's health: revision of educational materials  
*Dr Irina Zastenskaya, WHO ECEH*  
Discussion
- 15:50–16:30 Uncertainties and limitations of the tool for assessment of cumulative risk of indoor pollutants  
*Irina Zastenskaya, WHO ECEH*  
Discussion
- 16.30–17.00 Wrap up, next steps and closure of the Meeting

## Annex 2

### LISTS OF CHEMICALS

Table 1. List of priority substances

No.	Chemical family		Substance	CAS number	
1	Aldehydes		formaldehyde	50-00-0	
2			acetaldehyde	75-07-0	
3	VOCs	Aromatic hydrocarbons	benzene	71-43-2	
4			ethylbenzene	100-41-4	
5			o-xylenes	95-47-6	
6			m,p-xylenes	108-38-3 / 106-42-3	
7			styrene	100-42-5	
8			toluene	108-88-3	
9			Terpenes	limonene	138-86-3
10				$\alpha$ -pinene	80-56-8
11		Chlorinated hydrocarbons	tetrachloroethylene	127-18-4	
12			trichloroethylene	79-01-6	
13	Semi-VOCs	PAH	Naphthalene	91-20-3	
14			Benzo(a)pyrene	50-32-8	
15	PM		PM <sub>10</sub>	-	
16			PM <sub>2.5</sub>	-	
17	Inorganic compounds		CO	630-08-0	
18			NO <sub>2</sub>	10102-44-0	
19			O <sub>3</sub>	10028-15-6	

Table 2. List of chemicals that should be included in the tool when possible (a “wish” list)

No.	Order of priority		Substances	CAS Number
1	1	Phthalates	diethyl phthalate (DEP)	84-66-2
2			diisobutyl phthalate (DiBP)	84-69-5
3			di-n-butyl phthalate (DnBP)	84-74-2
4	2	Musks	galaxolide	1222-05-5
5			tonalide	21145-77-7
6	3	PAHs	Acenaphthene	83-32-9
7			Acenaphthylene	208-96-8
8			Phenanthrene	85-01-8
9			Anthracene	120-12-7
10			benz[a]anthracene	56-55-3
11			Benzo[b]fluoranthene	205-99-2
12			benzo[ j ]fluoranthene	205-82-3
13			benzo[e]pyrene	192-97-2
14	Benzo[ghi]perylene	191-24-2		

No.	Order of priority		Substances	CAS Number
15			Benzo[k]fluoranthene	207-08-9
16			Chrysene	218-01-9
17			Dibenz[a,h]anthracene	53-70-3
18			Dibenzo[a,l]pyrene	191-30-0
20			Fluoranthene	206-44-0
21			Fluorene	86-73-7
22			Indeno[1,2,3-cd]pyrene	193-39-5
23			Pyrene	129-00-0
24	4	Brominated flame retardants (BFRs)	BDE 47	5436-43-1
25			BDE 209	1163-19-5
26			BDE 99	60348-60-9
27			BDE 100	189084-64-8
28			BDE 153	68631-49-2
29			BDE 183	207122-16-5
30			BDE 28	41318-75-6
31			DBE-DBCH (4-(1,2-dibromoethyl)-1,2-dibromocyclohexane)	3322-93-8
32		Organophosphates (OPs)	tributylphosphate	126-73-8
33			tri-(2-butoxyethyl)-phosphate (TBEP)	78-51-3
34			tris(1-chloro-2-propyl) phosphate (TCPP)	13674-84-5
35			tris(2-chloroethyl) phosphate (TCEP)	115-96-8
36	5	Chlorinated paraffins		

Table 3. Additional chemical compounds that can be determined using the same analytical methods

Chemical family		Substances	CAS Number
VOCs	Aldehydes	butyraldehyde	123-72-8
		hexaldehyde	66-25-1
	Aromatic hydrocarbons	1,2,3-Trimethylbenzene	526-73-8
		1,4-dichlorobenzene	106-46-7
		n-butyl benzene	104-51-8
		Alcohols	1-butanol
	esters	ethylacetate	141-78-6
		methylacetate	79-20-9
		butyl acetate	123-86-4
	Alkans	heptane	142-82-5



### *Annex 3*

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## The WHO Regional Office for Europe

The World Health Organization (WHO) is a specialized agency of the United Nations created in 1948 with the primary responsibility for international health matters and public health. The WHO Regional Office for Europe is one of six regional offices throughout the world, each with its own programme geared to the particular health conditions of the countries it serves.

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The WHO Regional Office for Europe has initiated the development of a tool to facilitate assessments of the risk to human health from combined exposures to hazardous chemicals in indoor air, especially in public settings for children. In December 2018 an expert consultation was held to share knowledge, expertise and experience in the area of children's health and indoor air quality, with the aim of assisting and advising WHO in developing the tool. A wide range of topics was discussed including the methodological approach to the development of the tool, collection of toxicological information, identification of chemicals and health end-points of highest priority and development of recommendations for sampling and analysis of indoor air pollutants and training for paediatricians and public health professionals. The main outcomes were agreement on the list of chemicals for inclusion in the tool, the adverse health effects to be considered, advice on the revision of technical documents on the methods for sampling and analysis of chemicals, and prioritization of sampling sites for planning national monitoring programmes for indoor air quality.

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