



**World Health
Organization**

REGIONAL OFFICE FOR **Europe**

**Towards a tool for
assessment of cumulative
risks from indoor air
pollutants in public
settings for children:
the second expert
consultation**

Meeting report

Abstract

Since 2017, the WHO Regional Office for Europe, supported by international experts, has been developing a screening tool for assessment of risks to human health from combined exposure to multiple chemical pollutants in indoor air in public settings for children. The first expert consultation, held on 3–4 December 2018 in Bonn, Germany, agreed on lists of priority chemicals and adverse effect endpoints to be considered in the tool. The second consultation took place in Bonn, Germany, on 23–24 September 2019 and was called to finalize the methodological approach and to agree on collection of the relevant toxicological information. Other topics included the selection of sampling sites; methods for sampling and analysis of chemicals of concern in indoor air in public settings for children; and, an educational course for health-care and public-health professionals on indoor air pollution and children's health. Exposure assessment was discussed alongside the sampling strategy. The main outcomes of the consultation were approaches to the assessment of exposure and handling of toxicological information for the calculation of risks.

KEYWORDS:
RISK ASSESSMENT
HAZARDOUS SUBSTANCES
AIR POLLUTION, INDOOR
ENVIRONMENTAL EXPOSURE

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Acknowledgements

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Abbreviations

ANSES	French Agency for Food, Environmental and Occupational Health and Safety
BMD	benchmark dose
C&L Inventory	Classification and Labelling Inventory
ECHA	European Chemicals Agency
EN	European normative
IARC	International Agency for Research on Cancer
ISO	International Organization for Standardization
LOAEL	lowest-observed-adverse-effect level
NOAEL	no-observed-adverse-effect level
PAH	polycyclic aromatic hydrocarbon
PM	particulate matter
POD	point of departure
PODI	point of departure index
REACH	Registration, Evaluation, Authorization and Restriction of Chemicals
SINPHONIE	Schools Indoor Pollution and Health Observatory Network in Europe
STOT	Specific Target Organ Toxicity
SVOC	semi-volatile organic compound
VOC	volatile organic compound
WHO ECEH	WHO European Centre for Environment and Health

Introduction

In line with priorities of the Parma and Ostrava declarations on environment and health (1,2), the WHO Regional Office for Europe is addressing combined exposures to pollutants in indoor air to improve risk assessment and minimize the effects of hazardous chemicals on children in the places where they live, learn and play.

To facilitate assessment of risks from combined exposure, the WHO European Centre for Environment and Health (ECEH) is developing a screening tool (further – a tool) to support assessment of the risks to children from indoor air pollutants in public settings such as schools, kindergartens and day-care centres, focusing on selected chemicals and health endpoints. This is consistent with the relatively greater exposure of children than adults, based on physiological considerations and behavioural factors, and increasing evidence of health effects in children associated with indoor and outdoor air pollution (3).

The first expert consultation took place on 3–4 December 2018 in Bonn, Germany (4). There, experts discussed the general approach to the development of the tool, which is envisaged to comprise a database of supporting toxicological information for selected chemicals and a spreadsheet to calculate risk of combined exposures based on specified decision rules. The WHO framework for the assessment of risk of combined exposure to multiple chemicals was considered an appropriate construct for the tool.

Experts agreed on the lists of priority chemicals and adverse effect endpoints for consideration in the further development of the tool, and reached consensus on an approach to the collection of toxicological information. Discussions of sampling site selection, sampling and analysis of the most common chemicals in indoor air, and an educational course for public-health and health-care professionals resulted in recommendations on finalizing the relevant documents.

The second expert consultation was organized in Bonn, Germany, on 23–24 September 2019 to finalize the methodological approach and agree on the information needed to make progress on the tool's development. The main objectives were to:

- agree upon the approach to assessing children's exposure to chemicals in the tool;
- review recommendations on the selection of sampling sites, sampling and analysis of chemicals in indoor air, and the document describing a methodological approach to the tool's development;
- examine the educational course for public-health and health-care professionals on chemical pollution of indoor air and its risk for children's health; and
- discuss next steps towards completing and piloting the tool.

The consultation was attended by 17 experts from 14 countries (see Annex 2 for the list of participants). Ms Sani Dimitroulopoulou, Principal Environmental Public Health Scientist at Public Health England, United Kingdom, chaired the meeting. Ms Bilge Danyeli was the rapporteur.

Ms Francesca Racioppi, Head of WHO ECEH, opened the consultation. She highlighted that WHO has prioritized environmental health within school settings. To this end, it is of great importance to understand the risks to which children are exposed and to raise awareness of the links between the environment, health and educational attainment.

Ms Dorota Jarosinska, Programme Manager for Living and Working Environments at WHO ECEH, emphasized the importance of this meeting not only for engaging in methodological discussions but also for ensuring that the tool and associated documentation are clear and communicative to the target audience.

The documents prepared for the second consultations were built on the outcomes of the first expert consultation (4). The draft document describing the methodological approach to the tool's development, an overview of methods for sampling and analysis of the most common chemicals in indoor air, recommendations on the selection of sampling sites and an educational course for public-health and health-care professionals were prepared, following recommendations from the first consultation.

To guide the discussion, invited experts delivered presentations on the agenda topics. These were followed by a detailed discussion of questions raised in the presentations at the plenary and in working groups (see Annex 1 for the programme).

The working groups addressed the four main areas of discussion:

- Group 1. Management of toxicological information, grouping of chemicals and description of the methodological approach
- Group 2. Methods for sampling and analysis of chemicals
- Group 3. Selection of sampling sites
- Group 4: Educational course on chemical pollution of indoor air and its risk for children's health.

Assessment of children's exposure to chemicals in indoor air in public settings (schools, kindergartens, day-care centres)

Calculation of exposure

Three WHO documents guide the calculations and assessment of exposure to chemicals in general and in terms of specific population groups:

- *WHO human health risk assessment toolkit: chemical hazards* (2010) (5)
- *Environmental Health Criteria 237: Principles for evaluation of health risks in children associated with exposure to chemicals* (2006) (6)
- *Environmental Health Criteria 214: Human exposure assessment* (2000) (7).

The basic information needed to assess exposure includes the relevant routes and pathways of exposure, the environmental media expected to contain the chemical, and the duration of exposure. Adjustments related to combined or long-term low-dose exposure may be needed.

Long-term average exposures are considered most relevant for the characterization of risk for developing the tool. Assessment of cancer risk is a special case of long-term exposure for which lifetime average exposure is of interest.

In general, the exposure rate is calculated as the concentration of a chemical in an exposure medium multiplied by the rate at which a person inhales or ingests that medium, divided by their representative body weight. Exposure through inhalation is the concentration of a chemical inhaled during a specified exposure period, calculated based on the inhalation rate of a specific population group.

The plenary discussion focused on consideration of the duration of exposure and possible simplification of exposure calculations for the purpose of combined exposure assessment within the tool. It yielded the following main conclusions.

- The first version of the tool will accept the concept of exposure calculation over 24 h/5 days (one school week) given a potentially equal exposure level in other settings, including households.
- The calculation formula for the inhalation pathway of exposure will be adopted in the development of the tool.

Selection of sampling sites

A questionnaire was developed for the assessment of potential sampling sites to identify places where concentrations of hazardous chemicals are likely to be higher. It was designed for use in schools, kindergartens and day-care centres, and can be completed based on a visual inspection. A set of questions guides the evaluation of factors/sources of pollutants, for which responses are yes or no (scored as 0 or 1).

Discussion of the questionnaire continued in the working group session.

Methods for sampling and analysis of chemicals in indoor air

In preparation for the second expert consultation, the document describing methods for sampling (including both passive and active methods) and analysis of chemicals and the associated database were revised according to the three lists of chemicals agreed during the first consultation (4). The sampling and analysis document outlines practical, commonly used methods that provide adequate quantitative characterization with reasonable detection limit. General considerations for selecting a sampling strategy draw from information in the WHO Regional Office for Europe's meeting report *Methods for monitoring indoor air quality in schools* (8), ISO 16000-1. Indoor air – Part 1: General aspects of sampling strategy (9) and the Schools Indoor Pollution and Health Observatory Network in Europe (SINPHONIE) project (10).

Discussion in the plenary focused on the prioritization of methods for obtaining reliable results and sampling time. Discussion of specific topics related to the analysis of volatile organic compounds (VOCs) and semi-volatile organic compounds (SVOCs) continued in the working group session.

The plenary discussion yielded the following conclusions.

- The priority of methods in decreasing order are: (i) International Organization for Standardization (ISO) and European normative (EN) methods; (ii) national methods authorized according to national rules; and (iii) methods published in peer-reviewed journals.
- Continuous sampling from Monday to Friday (one school week) is recommended, with relevant adjustment of the sampling strategy.
- Accredited laboratories and non-accredited laboratories that have successfully passed the intercomparison exercise should be invited to take part in the analysis of samples; their credibility should be confirmed before a survey starts.
- Alternative methods can be considered in the absence of certain analytical equipment. For example, the method described in EN 14662-5 for sampling VOCs with passive samplers and solvent desorption can be considered if a laboratory does not have thermal desorption equipment recommended by ISO 16017-2.

Management of toxicological information for assessment of risks of combined exposure to multiple chemicals in indoor air

After the first consultation, the collection of toxicological information continued with a focus on the updated lists of chemicals and adverse effect endpoints. Information for five adverse effect endpoints (respiratory, cardiovascular, neurological, carcinogenic effects and irritation) was collected for the 19 chemicals included in the list of priority substances, and for 23 highly prioritized compounds from the list of 36 substances that should be included in the tool when possible (the “wish list”) (4).

For each substance, reference values for inhalation for critical health endpoints and points of departure (PODs) for the five adverse effect endpoints were searched in relevant databases (WHO indoor air quality guidelines (11), the International Toxicity Estimates for Risk Assessments database (12) and the EU-LCI database (13)) and scientific publications). Chemicals were considered to invoke the adverse effect outcome if a relevant lowest-observed-adverse-effect level (LOAEL) or benchmark dose (BMD) for the effect was identified. If a BMD, LOAEL, no-observed-adverse-effect level (NOAEL), tumorigenic concentration or unit risk was/were identified for inhalation, the substance was included in the database. If only (a) NOAEL value(s) for the highest test concentration was/were identified (no LOAEL or BMD), the substance was not assigned to an adverse effect endpoint group.

Identification of chemicals causing respiratory irritation was based on the EU-LCI and Specific Target Organ Toxicity (STOT) SE 3 databases. Thus, if a substance has been categorized as STOT SE 3, it was included. Substances for which any LOAEL for respiratory irritation has been identified were also included.

Regarding the classification of eye irritation, Category 1 of the European Classification and Labelling (C&L) Inventory (14) refers to “causes serious eye damage”, Category 2A refers to

“irritants” and Category 2B refers to “mild irritants”. If a substance has been categorized as Category 1, 2A or 2B in the C&L Inventory, the substance was considered to cause eye irritation assessment. If not categorized as Category 1, 2A or 2B, and if no POD for sensory irritation was available in the database, the substance was not considered to be an irritant.

Classifications for skin corrosion/irritation and respiratory/skin sensitization were considered, but were not taken into account.

Chemicals were considered carcinogenic if tumorigenic concentrations and unit risk values have been identified, and if the substances have been classified in Group 1 by the International Agency for Research on Cancer (IARC) in consistence with identification of the relevant endpoints based on consideration of observational (that is, largely epidemiological) studies in humans. However, additional discussion is needed to finalize the methodological approach in relation to carcinogenicity risks from chemicals in indoor air.

If PODs for non-cancer effects are based on animal data, a point of departure index (PODI) > 100 requires refinement of the assessment or consideration of remedial measures to reduce exposure. If based on human data, a PODI > 10 for any of the effects requires additional refinement or remedial measures.

Several questions were flagged for further discussion in the working group. These concerned the approach for the assessment of carcinogenic effects of polycyclic aromatic hydrocarbons (PAHs), the inclusion of particulate matter (PM) in the tool, the approach for the assessment of cancer risk; the approach for the selection of reference values and PODs for the calculation of risk through the tiers, and adequacy of the margin of exposure.

Discussion of these and other topics continued in the working group session.

A methodological approach to the tool’s development

A draft of the document describing a methodological approach to the tool’s development was prepared following this recommendation from experts at the first consultation: “A document describing in detail the basis for the proposed approach to combined exposure assessment in the tool, with assumptions and limitations and guidance on its practical implementation, should be prepared and accompany the tool” (4). The document was structured as follows:

- Introduction and objectives
- Terminology
- Scope, purpose and limitations of the tool
- Tiered approach
- Chemicals and the basis for their selection
- Health endpoints
- Description and criteria for selection of tiered toxicological information included in the supporting database.

The information included in these chapters was outlined briefly. Several questions were flagged for further discussion. These included decisions on addressing combined exposures to multiple chemicals (not necessarily temporal co-exposure) or mixtures (temporal co-exposures); inclusion of the threshold of toxicological concern to enable expansion of the tool to a broader range of data-poor substances at a later stage; an approach to the calculation of risks for carcinogenicity; the possibility of developing additional criteria for grouping; additional criteria for reference values and/or PODs in the tool; and appropriate filters for the selection of reference values and/or PODs.

Discussion of the document describing the methodology of the tool's development continued in the working group session, which also addressed the collection of toxicological information, formatting of toxicological data and grouping of chemicals for combined exposure assessment.

Building capacity among public-health professionals: an educational course on chemical pollution of indoor air and its risk for children's health

The educational course "Chemical pollution of indoor air and its risk for children's health (with a focus on public settings)" was developed for two main purposes: to train public-health and health-care professionals working at the national level (that is, to train the trainers), and to share information for training/educating public-health professionals at the local level, medical workers such as school nurses and paediatricians, and allied specialists such as teachers. The package consists of the following six modules:

- Introduction
- Sources of chemical in indoor air
- Vulnerability of children
- Indoor air pollution and children's health
- Assessment of risk for children's health from combined exposure to multiple chemicals in indoor air
- Risk communication.

Discussion of the educational course continued in the working group session.

The main outcomes of all working group discussions are summarized in the following session.

Working group session

Group 1. Management of toxicological information, grouping of chemicals and methodological approach

Discussion of these issues yielded the following conclusions.

- Exclude PM from the assessment of combined exposure, which is necessarily restricted to chemicals. Consider the inclusion of PM as a separate, individual compound.
- Accept benzo[a]pyrene as a PAH marker and remove individual PAHs from the list of chemicals for inclusion in the tool. Retain naphthalene due to its presence in gaseous form and inclusion in the WHO guidelines for indoor air quality (15).
- Adopt tumorigenic doses for presentation in the database and application in the tool for consistency with the margin-of-exposure approach for non-cancer effects. Check availability or need for conversion of unit risks. Investigate the impact of including priority substances that are classified in IARC Group 1 versus those classified in Group 1 and Group 2. Describe the basis for the selection of IARC Group 1 in the methodology document. Consider the adequate margin of exposure for carcinogens that act via a mutagenic mode of action according to the European Food Safety Authority and the European Chemicals Agency (ECHA) based on human or animal data.
- Prioritize WHO reference values for hazard index calculations (Tier 0) followed by most recent values. The tool will be designed to permit uploading of national reference values if available.
- For Tier 1, recommend the lowest available NOAEL for both animal and human studies as a default choice for POD selection; if only LOAEL data are available, apply an adjustment factor to the NOAEL using default 3 as suggested by ECHA (14). Provide an option in the tool to override default.
- Include three levels of risks calculation (tiers) in the tool: Tier 0 – hazard index as a sum of acceptable/reference concentrations/values based on critical effect endpoints without grouping of chemicals by adverse effects (conservative); Tier 1, Level 1 – hazard index as a sum of critical effect endpoints with grouping by adverse effects; Tier 1, Level 2 – PODI (if the margin of exposure for Tier 1, Level 2 assessment is not sufficient, seek expert advice on next steps).
- Adjust the exposure scenario of the study to a continuous exposure scenario by applying default adjustment factors as recommended by the Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) guidance (16), except for irritation/upper respiratory tract effects (assumed to be concentration based). Scale human PODs and animal PODs to a common basis (100 for interspecies differences and human variability, 10 for human variability) to have a common metric for hazard to enable comparison with exposure for the margin of exposure.
- Exclude carbon monoxide and ozone from the list of priority chemicals as they are not high priorities for combined exposure assessment for long-term effects. Consider including di(2-ethylhexyl) phthalate, butyl acetate, 1,2,3-trimethyl benzene and 1,4-

dichlorobenzene after double-checking the toxicological information available for these chemicals.

- Check grouping for respiratory irritation against an additional source, such as the French Agency for Food, Environmental and Occupational Health and Safety (ANSES).

Group 2. Methods for sampling and analysis of chemicals

Participants revised the technical document prepared for the consultation. They proposed including a sampling strategy and restructuring the document according to agreement on the list of chemicals for inclusion in the tool.

Group 3. Selection of sampling sites

Participants discussed the approach to evaluating outdoor sources of chemicals (in particular industrial enterprises and car parking places), indoor sources (such as heating systems, building materials and furniture) and the influence of renovations on indoor air pollution. They also addressed issues concerning the labelling of low-emission materials and the definition of rural and urban areas.

Discussion resulted in the following recommendations.

- Revise the list of industrial sources and parking places and propose an estimation of proximity to them.
- Define “rural” and “urban” areas, taking into account existing WHO definitions.
- Add options of materials used for floors, ceilings, wall coverings and window frames.

Group 4. Educational course on chemical pollution of indoor air and its risk for children’s health

Discussion of the content of the educational course yielded the following recommendations for its final revision.

- Revise the infographics on children’s health and sources of chemicals (indoor and outdoor) and the list and graphs of industrial and transport sources of chemicals into indoor air.
- Prioritize data relevant to the WHO European Region rather than global estimates, and include the most recent data if available.
- Double-check the information about health effects on children and reconsider its grouping.
- Include more explanatory information on assessment of risk from combined exposure.
- Include a recommendation on the development of a risk communication strategy.
- Revise key messages to different target groups considering the most recent knowledge about sources of exposure and effectiveness of risk-reduction measures.

Conclusions and next steps

Outcomes of working group discussions were presented and discussed in the plenary. Participants decided on the following next steps.

- Consider the inclusion of PM as an individual-compound risk assessment if not covered by the AirQ+ software tool for risk assessment of outdoor air pollution.
- Revise toxicological information according to the agreements of the working group if possible, and apply the agreed default adjustment factors for risks calculation.
- Prioritize the publication of the educational course after its revision according to the outcomes of the working group discussion, and pilot the course in the trainings planned in Tallinn, Estonia, and Budapest, Hungary, for October 2019.
- Include a sampling strategy in the overview of the methods for sampling and analysis and coordinate it with an approach to the assessment of exposure in the tool.
- Finalize the document describing the methodological approach to the tool's development, taking into account the working group discussions.
- Include in the tool only those chemicals for which toxicological information is available for assessment of risk from combined exposure at three levels of complexity: hazard index without grouping of chemicals according to health effects; hazard index with grouping of chemicals according to health effects; and PODI.
- Consider the inclusion of additional information in the questionnaire for the selection of sampling sites according to working group recommendations.
- Continue the discussion of additional issues using available communication channels (email, WebEx, telephone calls).
- Consider holding a third consultation to test the software when it is developed.

Conclusions of the expert consultation also included lists of chemicals and adverse effect endpoints for final revision for inclusion in the tool, and approaches to the assessment of exposure and management of toxicological information for the calculation of risks.

The following list of chemicals was agreed for a final revision taking into account the availability of toxicological information, as stated above, for inclusion in the tool:

- | | |
|---------------------------|---------------------------------|
| 1. formaldehyde | 11. butyl acetate |
| 2. acetaldehyde | 12. limonene |
| 3. benzene | 13. α -pinene |
| 4. ethylbenzene | 14. tetrachloroethylene |
| 5. o-xylene | 15. trichloroethylene |
| 6. m,p-xylenes | 16. naphthalene |
| 7. styrene | 17. benzo(a)pyrene |
| 8. toluene | 18. nitrogen dioxide |
| 9. 1,2,3-trimethylbenzene | 19. di-n-butyl phthalate |
| 10. 1,4-dichlorobenzene | 20. di(2-ethylhexyl) phthalate. |

Bilateral and multilateral discussions and will continue to finalize the document and to develop the software prototype.

The meeting closed at 17:30 on 24 September 2019.

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Annex 1. Programme

23 September 2019

- 11:30–13:00 Registration
- 13:00–13:20 Opening of the meeting
Ms Dorota Jarosinska, WHO European Centre for Environment and Health (WHO ECEH)
Election of Chair
Tour de table: self-presentation of meeting participants
Adoption of the meeting agenda
- 13:20–13:40 Update on follow-up activities of the first consultation, and scope and expected outcomes of the second consultation
Ms Irina Zastenskaya, WHO ECEH
- 13:40–15:30 **Session 1**
Assessment of children’s exposure to chemicals in indoor air in public settings (schools, kindergartens, day-care centres)
 - an approach to calculating exposure
 - an update on the selection of sampling sites
 - an update on the methods for sampling and analysis of chemicals*Ms Irina Zastenskaya, WHO ECEH*
Mr Alexander Gankin, Scientific Practical Centre of Hygiene, Belarus
Ms Florentina Villanueva, Research Institute for Combustion and Atmospheric Pollution, Spain
Discussion
- 16:00–17:00 **Session 2**
Management of toxicological information for assessment of risks of combined exposure to multiple chemicals in indoor air
 - grouping of toxicological information on points of departure
 - grouping of chemicals according to their adverse effect endpoints*Ms Katleen de Brouwere, VITO, Belgium*
Discussion
- 17:00–18:00 **Session 3**
Methodological approach to the tool’s development: a document accompanying the tool
Ms Bette Meek, University of Ottawa, Canada

18:00 Closure of the day

24 September 2019

9:00–9:30 Wrap-up of the first day

9:30–10:15

Session 4

Building capacity among public health professionals: an educational course on chemical pollution of indoor air and its risk for children's health

Ms Irina Zastenskaya, WHO ECEH

Discussion

10:15–13:00

Working group discussions and finalization of working papers

15:00 – 15:30

Working group reports to the plenary

Discussion

16:00–16:30

Plenary discussion of the meeting outcomes

16:30–17:00

Next steps and closure of the meeting

Annex 2. List of participants

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