

EU Forum

The INDEX project: executive summary of a European Union project on indoor air pollutants

The prevalence of allergies, asthma and other respiratory diseases in large populations has increased in recent decades. Among other factors, this phenomenon has been connected to adverse health effects of air pollution. Although some causal links between occupational exposures and their health effects are shown, still little is known about the health risks of lifelong exposure to indoor air pollutants. To assess the health risks of indoor air pollutants at prevailing concentration levels in Europe, the Joint Research Centre of the European Commission carried out a project called “Critical Appraisal of the Setting and Implementation of Indoor Exposure Limits in the EU” (INDEX). The aims of the project were: (1) to assess health risks of indoor-originated chemical pollutants that might be regulated in the EU and (2) to provide suggestions and recommendations on potential exposure limits or other risk management measures. The results of the INDEX project should contribute to the development of an EU strategy for the management of indoor air quality. The highest priority was given in this study to: formaldehyde, nitrogen dioxide, carbon monoxide, benzene and naphthalene. Exposure limits, recommendations and management options were also given to minimize the health risks for these compounds.

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Poor air quality causes adverse health effects in large populations, both in developed and developing countries. For example, allergies, asthma and other respiratory diseases have increased dramatically in recent years (1). It is obvious that air pollution has affected this development. In the last years, indoor air pollution has been recognized as an emerging environmental health issue, since people spend typically about 90% of their time indoors (2–5). People are exposed to a variety of pollutants with known health effects, which are emitted not only from outdoor sources but they can also have their sources in the indoor environment. While the air quality guidelines and standards are widely used in outdoor air quality management, systematic science-based approaches for indoor air quality (IAQ) are lacking. Management of IAQ requires different approaches to those applicable to outdoor air. Therefore, strategy and guidelines for IAQ management are needed. This need was demonstrated, for example, in the THADE

(‘Towards Healthy Air in Dwellings in Europe’) project calling for urgent actions to develop a strategy at international level to manage health risks related to indoor air pollution (6). To be able to develop a strategy and guidelines for selected pollutants that pose the highest health risks, critical health risk assessment and prioritization of the pollutants are necessary.

Because there are now results of large-scale population-based exposure studies available in Europe also for indoor air pollutants, it is possible to assess the potential health risks of indoor air pollutants at the European level. Guidelines for indoor air pollutants, however, have not been set in the EU, in particular, because a systematic health risk assessment for these pollutants was not available yet.

Indoor combustion is a source of pollution causing severe burden to health, especially for children and women in developing countries. In developed countries, IAQ in residences, day-care centres, in homes of elderly

people and other special environments affects population groups that are especially susceptible because of their health status or age. Indoor air pollution has been associated with several allergic diseases and asthma (6, 7). Indoor air pollutants can sensitize humans to allergens and on the contrary, people having allergy, asthma or other chronic pulmonary diseases are especially susceptible to air pollutants. Strong evidence on health effects of air pollution comes from outdoor air studies (8, 9), but indoor air concentrations typically differ from ambient levels, and also additional compounds might be present in indoor air because of emissions from indoor sources. There are many potentially hazardous chemicals released indoors because of combustion, emissions from building materials, household equipment and consumer products. Microbial pollution comes from hundreds of species of bacteria, fungi and moulds growing indoors. IAQ management is made difficult not only by the large number and variation of indoor spaces, but also the complex relations of IAQ and the building design, materials, operation and maintenance, ventilation and behaviour of the building users.

Air quality guidelines have been up-to-now mainly oriented on outdoor air pollution (10). In recent years, indoor air has been recognized first time as an essential part of a complete integrated strategy on air pollution. WHO (11) recognized IAQ as a fundamental human right declaring that "... everyone has the right to breathe healthy indoor air". In 2003, the European Commission (12) adopted a Strategy on Environment and Health. The overall aim of the strategy is to reduce diseases caused by environmental factors in Europe. This strategy was followed by the EU Action Plan on Environment and Health (13). In addition, in the recent update of the WHO Air Quality Guidelines (14, 15), development of guidelines for IAQ was recommended.

Before the INDEX project, the European Union had published risk assessment reports (RAR) for some of the chemicals that were also reviewed in INDEX. Final RARs were available for naphthalene (16), styrene (17), toluene (18) and a draft report for benzene (19) during the course of the INDEX project. Those reports were used as a data source in this project, when applicable to IAQ issues.

This paper illustrates the methods applied in assessing the health risks related to the prevailing residential indoor air exposures in Europe and dose-response factors for the selected compounds in the frame of the INDEX (Critical Appraisal of the Setting and Implementation of Indoor Exposure Limits in the EU) project. It also presents the groups of compounds prioritized according to their health risks, and finally, gives recommendations and management options for the compounds posing the highest health risks.

The final report of the INDEX project (20) is available at <http://web.jrc.ec.europa.eu/pce/pce-documentation.html>.

Methods

Objectives

The INDEX project (*Critical Appraisal of the Setting and Implementation of Indoor Exposure Limits in the EU*) was carried out from December 2002 to December 2004. The project was funded by the DG SANCO of the European Commission (EC) and it was coordinated by the Joint Research Centre of the EC in collaboration with a steering committee of leading European experts on indoor air exposure assessment and on toxicology and epidemiology to assess the health effects of air pollutants.

The scope of INDEX was to: (1) identify priorities of indoor air pollutants based on their health risks, (2) give recommendations to manage those risks and (3) to assess the need of a community strategy for indoor air pollution.

The key issues that were addressed within the project were:

- To set up a list of compounds to be measured and regulated in indoor environments with priority, on the basis of health impact criteria,
- To provide suggestions and recommendations on potential exposure limits or other management options for these compounds, and
- To provide information on links between existing knowledge, ongoing studies, legislation etc., on a world-scale.

Framework of the risk assessment

In order to implement strategies aimed at preventing health effects related to indoor air pollution, a key element is to carry out a systematic risk analysis based on prevailing levels of indoor air pollutants and on their health effects. In the current project, a highly qualified expert group carried out risk analyses for indoor air pollutants in Europe. Population exposures to indoor air pollutants were assessed by collecting results from major European population-based studies. These data represent mostly indoor exposure levels in urban environments. Similarly, health effects of the selected pollutants were collected from the worldwide scientific literature. A framework for risk and exposure assessment in the current study has been adopted following the paradigms of NAS (21) and the EC Directive 93/67/EEC (22). According to the EC Directive 93/67/EEC, formal risk assessment is divided into four activities, which are defined as 'Hazard identification', 'Dose (concentration) – response (effect) assessment', 'Exposure assessment' and 'Risk characterization'. Figure 1 shows the main steps followed by the execution of the INDEX project.

Literature review. In the first phase, a literature review was carried out to collect information about candidate pollutants to be assessed in the later stages of the project. The scientific literature of the indoor air pollutants was reviewed by using several search engines in the Internet and by searching from the relevant journals. In addition to electronic search, numerous study reports concerning indoor air pollutants were reviewed. The main focus of the review was on recent population-based studies to be able to evaluate current population exposures to selected pollutants in Europe. Simultaneously, dose-response factors were collected from the scientific world literature.

Hazard identification. Hazard identification of the indoor air pollutants was assessed combining information on the prevalence of pollutants in European homes with the available knowledge of adverse health effects of these compounds reported in toxicological

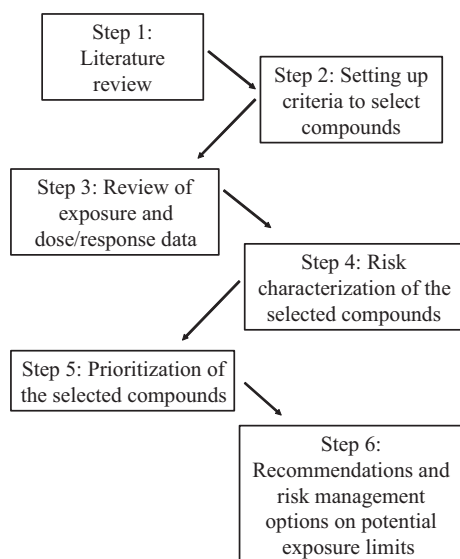


Figure 1. The main steps of the INDEX project.

or epidemiological studies. If a compound was present in indoor air and it has known health effects, it was considered as a potential hazard to European populations and was thus included in the risk assessment process. After the hazard identification of the compounds summarized in the literature review, “a long list” of compounds was created meeting the selection criteria (Fig. 2, phase 1). These compounds were taken to the next phase of the risk analysis.

Selection criteria of the compounds included in the risk analyses. Considering the fact that no new data could be generated during the project, the steering committee defined the following criteria for selection of the pollutants for risk analysis:

1. Only single compounds were considered,
2. The compound should have strong indoor sources, which determine the exposure of a significant fraction of the population, and
3. The compound should have known health effects.

The second requirement was assessed by comparing indoor concentrations to outdoor concentration at the same site if possible. It was also decided that compounds, which have been regulated by specific guidelines or regulations would be excluded from these

Phase 1

1-Butanol
2-Butoxyethanol
2-Ethyl-1-hexanol
2-Methyl-1-propanol
3-Carene
Acetaldehyde
Acetone
Ammonia
 α -Pinene
Benzaldehyde
Benzene
Benzo[a]pyrene
Cadmium
Carbon monoxide
Decane
Dichloromethane
Diisocyanate
d-Limonene
Ethylbenzene
Formaldehyde
Hexaldehyde
Lead
m & p-Xylene
Mercury
Methyl-ethyl-ketone
Naphthalene
Nitrogen dioxide
Nonane
o-Xylene
Pentachlorophenol
Phenol
Propionaldehyde
Propylbenzene
Styrene
Tetrachloroethylene
Toluene
Trichloroethylene
Trimethylbenzenes
Tris-(2-chloroethyl) phosphate
Undecane

Phase 2

1-Butanol
2-Ethyl-1-hexanol
3-Carene
Acetaldehyde
Ammonia
 α -Pinene
Benzaldehyde
Benzene
Cadmium
Carbon monoxide
Dichloromethane
Diisocyanate
d-Limonene
Formaldehyde
Hexaldehyde
m & p-Xylene
Naphthalene
Nitrogen dioxide
o-Xylene
Styrene
Tetrachloroethylene
Toluene
Trichloroethylene
Tris-(2-chloroethyl) phosphate

Phase 3

Acetaldehyde	
Ammonia	1. priority
α -Pinene	
Benzene	Formaldehyde
Carbon monoxide	Carbon monoxide
d-Limonene	Nitrogen dioxide
Formaldehyde	Benzene
m & p-Xylene	Naphthalene
Naphthalene	
Nitrogen dioxide	
o-Xylene	
Styrene	
Toluene	

Figure 2. Indoor-originated compounds that were assessed and considered the most hazardous in the three phases of the hazard identification process.

analyses. For example, radon and tobacco smoke were excluded from the risk assessment process because of the aforementioned criteria.

In the second phase of the selection process, the reviewed data were assessed and more detailed information for the previously selected compounds was collected if available. More compounds were excluded using the following criteria:

- No expressed concerns for health at present levels (for example, acetone, decane, ethylbenzene, phenol, propylbenzene, trimethylbenzene),
- Compound already regulated by use restrictions for indoor materials (pentachlorophenol),
- Incomplete or no dose-response data available at present levels (methyl-ethyl-ketone, propionaldehyde), and
- Main route/media of exposure to the compound in question is other than indoor air (lead, mercury).

After a detailed review and discussion of the available information, 25 compounds were selected for more detailed risk analyses (Fig. 2, phase 2).

In the third phase of the project, also odour threshold values were considered important and thus, these data were included in the analyses. The standardized human odour threshold values were taken from Devos et al. (23). On the basis of the available information and after an extensive discussion on the preselected 25 chemical substances, the steering committee finally decided to conduct a detailed assessment for 14 compounds (Fig. 2, phase 3).

Flame-retardants were regarded as an emerging issue, which will require further consideration in the future. *Tris*-(2-chloroethyl)-phosphate belongs to this group, but because reliable data on its sources and occurrence in indoor environments, exposure routes and on toxicological properties were lacking, the compound was not included in the evaluation procedure in this project.

Exposure assessment. Exposure to selected indoor air pollutants was evaluated by collecting exposure data from scientific literature, from available databases, and by personal communications. The aim of this work was to summarize the prevailing indoor air and personal exposure concentrations of these compounds in European populations. These reviews were mainly focussed on indoor air and exposure concentrations measured recently in European population-based studies such as EXPOLIS (5), German Environmental Surveys, GerES (24), the German study on Indoor Factors and Genetics in Asthma, INGA (25, 26) and a national survey of air pollutants in English homes (27). In addition, some preliminary results of the French National Survey (28, 29) were available during the project. Comparisons have been carried out with regard to the TEAM (30) and the NHEXAS (31, 32) studies carried out in the USA. Results from population-based studies were used to be able to generalize the results from studied individuals to larger populations, targeting to get a picture of indoor exposures all over Europe.

Mean concentrations give us a general picture of the exposure levels, but because of the presence of subpopulations that are exposed to much higher concentrations, the whole exposure distributions were used if this information was available. Indoor air pollutants were linked to their main emission sources if possible.

Dose-response assessment. When preparing the dose-response assessment fact-sheets for the selected chemicals, information was retrieved from scientific literature, mainly by electronic search, comprehensive toxicological reviews of leading health organizations, risk evaluation documents and available databases. In addition, Toxline and Medline were searched for relevant scientific communications.

Nearly all key-studies referred to in the present assessment establishing effect levels for appropriate toxicological endpoints, were those selected by health organizations for the derivation of health-based limits of exposure (ELs) or among risk assessment requirements. Although not specifically addressing the health hazards and risks associated with indoor air exposure, i.e., not being designed for the expression of effects at lowermost exposure concentrations, nearly all studies were aimed at identifying the most sensitive endpoint considered to be of relevance to humans. Where relevant, studies conducted on susceptible subpopulations (e.g., asthmatics, infants, children, pregnant etc.) were quoted and taken into consideration in the risk characterization.

Key-studies were summarized treating effects of short- and long-term exposures. One-page fact-sheets resuming the most relevant toxicological properties were created for each compound. In addition, key-study tables were written, where the reported concentration measures (average, adjusted etc.) were assigned to health-effect levels (NOAELs and LOAELs), stating on whether occupational average levels or experimental concentrations were quoted, or identifying the extrapolation process applied for the given value.

Risk characterization. In the final step of the general risk assessment process, the incidence of health hazards and risks in the European populations, associated with indoor exposure to individual compounds, was evaluated. It should be underlined that the assessment of risk is based on scientific considerations, and has been kept separate from any consideration regarding the risk management process, including the setting or the proposal of Indoor Exposure Limits. Namely, an important uncertainty, not accounted for in the assessment, is the possibility of antagonistic and synergistic effects arising from the exposure to mixtures of chemicals, since little scientific information exists in this area. Multiple contaminants are typically occurring in indoor environments (although at low concentrations) and the resulting uncertainty (uncontrolled factor) should be taken into consideration for the management of risk. Nevertheless, ELs have to be established for individual chemicals, following inhalation exposure in indoor environments, for both short-term (indoor-activity related) and long-term exposures (background indoors). An EL was derived for each compound on the basis of key-studies (critical-study) describing the appropriate toxicological endpoints (among those selected by health organizations for the derivation of health-based reference concentrations). Uncertainty factors (here named assessment factors, AF) applied in the present assessment are the product of the individual factors outlined in Table 1.

For all compounds, threshold-level of action could be identified, enabling a "no-observed-adverse-effect level (NOAEL)/assessment factor (AF)" approach, i.e. EL derived by dividing the critical-effect level by the AF, with the AF based on appropriate scientific evidence. Where no NOAEL observation was documented, a lowest-observed-adverse-effect level (LOAEL) was taken into consideration and an additional assessment factor of 10 used for EL derivation. For one compound only (benzene), the characterization was based on the evaluation of risk for cancer for the entire population than on EL.

In those cases where large differences in sensitivity for different susceptible groups were documented, a bimodal distribution of population responses was supposed to exist and a tenfold difference in sensitivity, usually accepted as higher than the encountered range, was taken into account in the AF derivation. Susceptible subpopulations considered in the present characterization were: asthmatic individuals, infants, children, individuals with heart

Table 1. Elements considered for the derivation of Uncertainty (Assessment) Factors (AS)

Description	Detail	Factor
Extrapolation from an LOAEL to an NOAEL	When in the critical study, no NOAEL could be observed	10
Inter-species extrapolation	Critical study = experimental animal study (no human study available or appropriate)	10
Inter-individual (intra-species) variability in humans	Always, unless the critical study was performed on individuals of the subpopulation considered susceptible	10
Susceptible population	Asthmatic individuals, infants, children, individuals with heart diseases, individuals with (hereditary) enzyme deficiencies, pregnant women	10, 3, 2
Adequacy or quality of toxicological data	Old study	2
Extrapolation from sub-acute to chronic	Deficiencies in toxicological database	10
Extrapolation from sub-acute to acute	Deficiencies in toxicological database	10

diseases, individuals with (hereditary) enzyme deficiencies and pregnant women.

Results and discussion

Based on the conclusions of the risk characterization and on the completeness of individual databases, the compounds were categorized into three groups according to their health risks assessed in this project. Three categories were formed from 14 chemicals listed in Fig. 2, phase 3.

High-priority pollutants

Formaldehyde. Formaldehyde is the most important sensory irritant among the pollutants assessed in the present study. It is considered a chemical of concern at levels exceeding $1 \mu\text{g}/\text{m}^3$, a concentration more or less corresponding to the background level in rural areas. Results from available exposure data, although limited, confirm that almost the entire population is exposed indoors at levels (median level $\pm$ SD of six studies: $26 \pm 6 \mu\text{g}/\text{m}^3$; 90th (percentile) $\pm$ SD: $59 \pm 7 \mu\text{g}/\text{m}^3$; higher than this background level, here established as the limit of exposure, with at least 20% of the European population exposed at levels exceeding the no-observed-adverse-effect-level (NOAEL: $30 \mu\text{g}/\text{m}^3$). Within the concentration range measured, mild irritation of the eyes could be experienced by the general population as well as the odour perceived starting from about $30 \mu\text{g}/\text{m}^3$.

Reported formaldehyde concentrations were lower (99th percentile $< 150 \mu\text{g}/\text{m}^3$) than a presumed threshold for cytotoxic damage to the nasal mucosa and hence considered low enough to avoid any significant risk of upper respiratory tract cancer in humans. The last statement could be subjected to changes because of the current IARC revision of the carcinogenicity of formaldehyde.

Carbon monoxide. Available exposure data confirm that carbon monoxide (CO) sources in EU-residences are contributing to short-term rather than to long-term exposures. Personal exposure outcomes averaged over

1-h were considered of moderate concern even for the most susceptible subpopulations. Nevertheless, uncertainties resulting from the predictive capabilities of the CFK-model [the physiologically based pharmacokinetic model of Coburn, Forster and Kane (33)] in individuals exposed at low CO concentrations and its applicability to sensitive subpopulations, suggest that about 10% of the general nonsmoking population experiences CO levels which could be hazardous for individuals with heart diseases. Increased exposures could be expected for residences in the vicinity of busy city streets. In addition, there is no evidence that long-term CO exposures in EU residences contribute to carboxyhaemoglobin levels in blood higher than the baseline levels resulting from endogenous production in normal, nonsmoking individuals.

On the contrary and in contrast with all other chemicals assessed in the present study, carbon monoxide causes a considerable number of deaths and acute poisonings in the general population (with complications and late sequel). In addition, individuals suffering from CO poisoning are often unaware of their exposure because symptoms are similar to those associated with viral illness or clinical depression. In indoor environments, these health risks are nearly completely associated with the incorrect use of combustion devices or faulty, unvented gas appliances.

Nitrogen dioxide. Reported maximum nitrogen dioxide (NO_2) levels associated with the use of gas appliances in homes (gas cooking and heating) are in the range of 180–250 $\mu\text{g}/\text{m}^3$. Exposure at these levels could generate effects in the pulmonary function of asthmatics, considered to be the subjects most susceptible to acute NO_2 exposure, with the lower end of the range approximating the WHO (34) guideline (200 $\mu\text{g}/\text{m}^3$, 1-h average), established for the protection of asthmatic individuals and the upper end starting to affect health in normal individuals.

For long-term exposures, increased respiratory symptoms and lung function decreases in children were documented to be the most sensitive effects in the general population. Measured background levels in European homes indicate that a remarkable portion of the population is exposed at NO_2 levels higher than the current

guideline values protecting from respiratory effects in children. In up to 25% of the investigated residences (45% in an Italian study), NO₂ levels exceeded the German indoor-related guideline value (GV II: 60 µg/m³, 1-week average), that would have resulted in immediate action, i.e., the examination of the situation with regard to a need for control measures. On the contrary, safe levels in homes, i.e., <40 µg/m³ (following the WHO-recommended annual (mean) value), are not likely to be achievable everywhere (e.g., in areas with intense automotive traffic), given that ventilation alone may introduce outdoor air containing such concentrations.

Benzene. Benzene is ubiquitous in the atmosphere, mainly because of anthropogenic sources (90%), with concentrations in the European continental pristine air ranging from 0.6 to 1.9 µg/m³. It is a genotoxic carcinogen and hence no safe level of exposure could be recommended. Results from nine monitoring surveys indicate that the European population is experiencing in their homes an increased risk, with respect to the estimated background lifetime risk of seven to eight cases per one million people (considering the WHO (35) unit risk factor). Based on the available exposure data (median levels ± SD of nine studies: 4.2 ± 3.2 µg/m³; 90th percentile levels ± SD: 11.5 ± 11.1 µg/m³), two main scenarios could be described as follows:

- 1) People living in highly trafficked urban areas are expected, on an average, to experience an estimated 6- to 30-fold increase in contracting benzene-induced leukaemia during their life, the benzene levels encountered in these areas not being expected to produce chronic effects other than cancer, in particular haematological effects, nor acute sensory effects such as odour perception (odour threshold: 1.2 mg/m³) and sensory irritation. In addition, a reduced contribution of specific indoor sources is likely to be expected, given that ventilation alone may introduce increased outdoor benzene levels, and
- 2) People living in rural areas or in towns with low traffic density were expected, on an average, to experience an estimated 1- to 5-fold increase in contracting benzene-induced leukaemia during their lifetime, this factor depending principally on the presence of indoor sources.

Naphthalene. With regard to the general population a long-term exposure limit has been set at 10 µg/m³, according to the assumption that nasal effects observed in mice are consistent with the health effects reported among exposed workers. Available exposure data indicate that, on average, the European population is exposed to naphthalene levels 10 times lower than this EL, although an important exception resulted from a survey held in Athens, where levels exceeding the EL were measured in nearly all residences. It is assumed that

increased residential exposures originate from the use of naphthalene-based moth-repellents, a widespread use occurring in certain countries of the Mediterranean area.

An important source of uncertainty in establishing safe exposure limits is the potentially greater sensitivity of certain subpopulations to naphthalene toxicity, including infants and neonates, and individuals deficient in glucose-6-phosphate dehydrogenase (G6PD), with the prevalence of this inherited deficiency reported to be 2–20% in defined Mediterranean subpopulations. In these latter cases, manifested the effects are haemolytic anaemia and its sequel.

In relation to carcinogenicity, naphthalene is not genotoxic in vivo and thus tumour development, observed in rodents, is considered to arise via a non-genotoxic mechanism. In addition, the underlying mechanism for the development of nasal tumours in the rat is considered to be the chronic inflammatory damage seen at this site. It follows that prevention of local tissue damage would prevent subsequent development of tumours.

Low priority pollutants

Acetaldehyde. The results from only three indoor air monitoring surveys allow a crude estimate of average acetaldehyde concentrations in European residences. Median concentrations (10–20 µg/m³) are one order of magnitude lower than the Exposure Limit set here at 200 µg/m³ and are within the same range of concentrations occurring in exhaled breath following its endogenous production in the general population, not taking into account increases resulting from the consumption of alcoholic beverages. Considering that exogenous acetaldehyde peak exposures are mainly associated with tobacco smoke, concentrations in the order of the Exposure Limit could be expected following intense cigarette consumption.

Assuming that the available exposure data are indicative of the population residential exposure, it is concluded that people in Europe do not experience increased health hazards associated with acetaldehyde levels in their homes, although additional work should be warranted for a better characterization of exposure and dose-response.

In addition, measured indoor levels are lower than a presumed threshold for cytotoxic damage to the nasal mucosa, and hence considered low enough to avoid any significant risk of upper respiratory tract cancer in humans.

Toluene. Human effects on the central nervous system are considered as the most sensitive effect in both short- and long-term inhalation exposures to toluene. Available exposure data indicate that the European population is not experiencing health effects of concern resulting from the exposure to toluene in their homes. Results from 10

monitoring surveys show that toluene levels in the order of the established exposure limit of $300 \mu\text{g}/\text{m}^3$ could be reached under worse-case conditions and in a limited number of urban residences. On an average, median concentrations (90th percentile) were found to be 16 (5) times lower than the EL. In addition, short-term exposures associated with human indoor activities are not expected to exceed the acute EL set here at $15,000 \mu\text{g}/\text{m}^3$.

Xylenes. A chronic exposure limit of $200 \mu\text{g}/\text{m}^3$ has been derived based on generally mild adverse effects associated with central nervous system and increase in the prevalence of eye irritation and sore throat. The results of eight monitoring surveys indicate that background levels of xylenes in European residences are of no concern to human health since median (90th percentile) levels are, on an average, 20 (6) times lower than the EL established. Acute exposure data indicate that it is very unlikely that xylene emissions associated with human indoor activities would generate levels in the order of the proposed short-term EL of $20 \text{ mg}/\text{m}^3$, considered protective for irritation effects in the general population.

Although human exposure most likely occurs to the mixture of xylene isomers, animal and human toxicity data suggest that mixed xylenes and the different xylene isomers produce similar effects.

Styrene. A long-term exposure limit (EL) of $250 \mu\text{g}/\text{m}^3$ has been derived based on the assumption that neurological effects are probably the most sensitive indicator of styrene toxicity. When examining the results of eight monitoring surveys, it can be concluded that background styrene concentrations in European residences are of no concern to human health since median levels are, on an average, two orders of magnitude below the established EL. Although no acute exposure data were available, it is unlikely that styrene emissions associated with human indoor activities would generate levels up to the proposed short-term EL of $2000 \mu\text{g}/\text{m}^3$, considered protective for irritation effects in asthmatics.

Although genotoxic effects in humans have been observed at relatively low concentrations, they were not considered as critical endpoints for the derivation of the exposure limit, in view of the equivocal evidence for the carcinogenicity of styrene in humans (36).

Pollutants requiring further research with regard to human exposure or dose-response

For some pollutants, it was not possible to assess their health risks because of lacking information on exposure or health effects. Therefore, these compounds could not be prioritized as high- or low-risk compounds, but the research needs for these pollutants could be identified.

Ammonia. There is a lack of knowledge concerning indoor concentrations and exposures to ammonia. Expo-

sure data are limited on only one monitoring survey describing concentrations of ammonia in Finnish homes with and without known IAQ problems. In both cases, measured concentrations were within the same order of magnitude with both exposure limits here established for short- and long-term effects (70 and $100 \mu\text{g}/\text{m}^3$, respectively), relating to irritating effects and pulmonary functions and taking into account the particular susceptibility of asthmatic subjects. It is assumed that exposure concentrations in the order of the short-term EL could easily be attained during domestic activities making use of ammonia-containing household products.

Limonene. An attempt has been carried out in deriving an exposure limit (EL) for long-term effects associated with limonene exposure by referring to a study on volunteers exposed at subacute (2 h) inhalation doses. When comparing this EL ($450 \mu\text{g}/\text{m}^3$) with the results from seven indoor surveys it is concluded that no neurological effects would be expected at background limonene levels encountered in European homes, with median (90th percentile) levels at least 10 (3) times lower than the proposed EL. It is assumed that at 10-fold the level set as the EL, health effects could be expected following acute exposure. Because of its widespread use as a flavouring agent in numerous consumer products, short-term exposures at levels in the order of some milligram per cubic metre could not be excluded, although significant exposure data are lacking.

An exacerbation of effects (no-better defined) could be expected following the concomitant presence of ozone indoors. The reaction of limonene with ozone leads to the formation of volatile compounds and possibly of radicals with irritating properties.

α -Pinene. An attempt has been carried out in deriving an exposure limit (EL) for long-term effects associated with α -Pinene exposure by referring to a study on volunteers exposed at subacute (2 h) inhalation doses. When comparing this EL ($450 \mu\text{g}/\text{m}^3$) with the results from six indoor surveys it is concluded that no irritating effects to the eyes, nose and throat would be expected at background α -pinene levels encountered in European homes, with median (90th percentile) levels at least 40 (10) times lower than the proposed EL. It is assumed that at 10-fold the level set as the EL, health effects could be expected following acute exposure. Because of its widespread use as a flavouring agent in numerous consumer products, short-term exposures at levels in the order of some milligram per cubic metre could not be excluded, although proper exposure data are lacking.

An exacerbation of effects (not better defined) could be expected following the concomitant presence of ozone indoors. α -Pinene reacts with ozone-forming chemicals and possibly radicals with irritating properties.

Recommendations and management options for the high-priority pollutants

The recommendations and management options proposed would – according to present knowledge – protect the general population and most individuals most of the time, but they will not prevent all cancer from indoor exposures nor protect the most susceptible individuals in all conditions, such as individuals with serious respiratory or cardiovascular disease, highly reactive asthmatics, genetically predisposed individuals developing haemolytic anaemia from naphthalene etc.

In addition to the specific recommendations reported below, the following general recommendations and management options apply to most or many indoor air contaminants in the high- and low-priority lists:

- Use appropriate ventilation practices based on the well-defined standards for indoor environments according to the recommendations of the relevant professional organizations,
- Ban tobacco smoking in all indoor spaces under public jurisdiction. Raise public awareness on the hazards of tobacco smoke, and discourage smoking in private residences, particularly in the presence of children, and
- Develop building codes to restrict the construction of attached garages, and to isolate the garages from living and working quarters (closing the doorways, sealing the structures and ensuring proper air-pressure difference between garage and other indoor spaces).

High-priority pollutants

Five pollutants were considered bearing high health risks in the European population. Those pollutants include formaldehyde, nitrogen dioxide, carbon monoxide, benzene and naphthalene.

Formaldehyde. The no-effect level (acute and chronic) is estimated to be at 30 $\mu\text{g}/\text{m}^3$ as 30-min average. Following the announcement of IARC, stating that there was sufficient evidence that formaldehyde causes nasopharyngeal cancer in humans, but there are limited evidence that formaldehyde exposure causes nasal cavity and paranasal cavity cancer and ‘strong but not sufficient’ evidence linking formaldehyde exposure to leukaemia, the expert group in the current study recommended a guideline value, which should be as low as reasonably achievable.

Management options:

- Restrict emissions of formaldehyde from building products, furnishings and household/office chemicals, and
- Discourage the use of formaldehyde-containing products.

Carbon Monoxide. The 1-h average guideline value of 30 mg/m^3 and the 8-h average guideline value of 10 mg/m^3 are recommended.

Management options:

- Apply the indoor air concentration guideline in the building design process,
- Develop building codes, ventilation standards and equipment/appliance standards (design, maintenance and use), so that all indoor combustion equipment will exhaust to chimneys/hoods/vents leading outdoors,
- Require regular mandatory inspections for indoor combustion equipment, and
- Recommend alarm systems responding to abnormally high concentrations (e.g., 50 mg/m^3).

Nitrogen dioxide. A long-term guideline value of 40 $\mu\text{g}/\text{m}^3$ (1-week average) and a short-term guideline value of 200 $\mu\text{g}/\text{m}^3$ are proposed.

Management options:

- Apply the indoor air concentration guideline in the building design process, and
- Develop building codes, ventilation standards and equipment/appliance standards (design, maintenance and use), so that all indoor combustion equipment will exhaust to chimneys/hoods/vents leading outdoors.

Benzene. As benzene is a human carcinogen, its concentration in the air should be as low as reasonably achievable. Indoor concentrations of benzene should not exceed outdoor concentrations.

Management options:

- Sources emitting benzene (tobacco smoking, etc.) should not be allowed in the indoor environment, and
- Lower the permissible benzene content in any building material and consumer product.

Naphthalene. A long-term guideline value of 10 $\mu\text{g}/\text{m}^3$ is recommended based on irritation/inflammation/hyperplasia. This level is at the lower extreme of the olfactory perception range.

Management option:

- Restrict the use of naphthalene-containing household products, particularly mothballs.

Conclusions

Indoor air pollutants were prioritized based on their health risks in Europe. In addition, recommendations to manage those risks were given, especially to policy

makers, and finally the need of a community strategy for indoor air pollution was identified in the INDEX project.

On the basis of knowledge available in this project, it is evident that some pollutants present at prevailing concentration levels in indoor air pose health risks to large populations in Europe. Therefore, it is clear that an indoor air strategy to manage health risks related to indoor air pollution at European level is needed. Within the framework of the Commission's Environment and Health Strategy and Action Plan, an action on IAQ is defined to evaluate the possible adverse health effects

associated with the presence of pollutants indoors and to stimulate research activities to improve the quality of air in confined spaces. The results of this project suggest that these actions should be supported and should lead to a launch of a community strategy on indoor air.

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