Human health risks of formaldehyde indoor levels: An issue of concern

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Abstract

Formaldehyde is a carcinogenic substance for humans. Exposure to formaldehyde may also cause eye and respiratory tract irritation, as well as skin sensitization. The main indoor sources of formaldehyde are wood-pressed products, insulation materials, paints, varnishes, household cleaning products and cigarettes, among others. Although this chemical is a well-known indoor pollutant, data on indoor concentrations of formaldehyde are still scarce in some countries. In February 2014, 10 homes in Catalonia, Spain, were randomly selected to collect indoor (bedroom and living room) and outdoor air samples. Ten additional samples were also collected at different workplaces (e.g., offices, shops, classrooms, etc.). Formaldehyde air levels found in homes ranged from 10.7 to 47.7 $\mu g/m^3$, from 9.65 to 37.2 $\mu g/m^3$, and from 0.96 to 3.37 $\mu g/m^3$ in bedroom, living room, and outdoors, respectively. Meanwhile, at workplaces indoor air levels ranged from 5.86 to 40.4 $\mu g/m^3$. These levels are in agreement with data found in the scientific literature. Non-carcinogenic risks were above the threshold limit (HQ>1), and carcinogenic risks were not acceptable as well ($>10^{-4}$). Despite the current study limitations, the results confirm that formaldehyde indoor levels are a matter of health concern, which must be taken into account by policy makers and regulatory bodies.

Keywords: Indoor air, workplace, inhalation, formaldehyde, human exposure, health risks

Introduction

Formaldehyde is a natural compound formed in vegetal residues decomposition and combustion processes. It is also a normal component of blood, being essential in human metabolism for the biosynthesis of purines, thymidine, and some amino acids. [1-4] At room temperature, formaldehyde is a colorless gas with an acrid and irritating odor, highly reactive and flammable. Due to its properties and reactivity, formaldehyde is used as precursor for more complex compounds. [5] Urea-formaldehyde resins, representing about 46% of formaldehyde world consumption, are used as adhesive in particle board and plywood production and color preservative in clothes. The other formaldehyde-derived resins are used for products applications in automobile components, fiber glass insulation, laminates, and surface coatings. [6] Finally, other applications for formaldehyde derived products compounds are paints, varnishes, textiles, fungicide, fertilizers, preservers, and cosmetics, among others. [7-11] Formaldehyde does not accumulate in the environment due to its low half-life. However, it is continuously released or formed, leading to a long-term exposure for populations living near emission sources or production activities. [12] Furthermore, formaldehyde can also be formed in a reaction of ozone with unsaturated volatile organic compounds (VOCs). [13,14]

Despite its widespread use, formaldehyde is classified as a carcinogen (Group 1) by the International Agency for Research on Cancer (IARC), and as a known human carcinogen by the US National Toxicology Program. [3,4] Formaldehyde causes cancer of the nasopharynx and leukaemia and a positive correlation between formaldehyde exposure and sinonasal cancer has been showed. [4] Short-term exposure symptoms include eyes and respiratory airways irritation, with a concentration-dependent increase of tearing, sneezing, coughing, nausea, dyspnoea and finally death. [15] Long-term exposure to elevated formaldehyde levels results in airway and eye irritation, as well as in degenerative, inflammatory and hyperplastic changes of the nasal mucosa. [15] Formaldehyde can be found in the air of most, if not all, homes and buildings. [1,4,7,8,11,16-20] However, there is a lack of data in the scientific literature regarding formaldehyde and other (e.g., xylene, toluene, benzene) indoor pollutant levels in a number of countries, including Spain. [18] For that reason, the present study was aimed at determining air formaldehyde levels in homes and workplaces in Catalonia, Spain, as well as assessing the associated human health risks.

Materials and methods

Sampling

In January/February 2014, forty air samples were collected in Tarragona County, Catalonia, Spain. Ten homes were randomly selected and three samples, one in bedroom, one in living room and another one outside the building (terrace or balcony) were collected in each house. Ten more samples were collected at different workplaces including kindergarten, shops, classrooms, and offices. The researchers requested to the residents (homes) and workers (workplaces) to continue with their normal activities during the sampling. Details about sampling points are given in Table 1.
An Airchek 2000 sampling pump (SKC Inc., Eighty Four, PA, USA) was used for air collection. Samples were collected by passing air through sorbent tubes containing 2,4-dinitrophenylhydrazine-coated silica gel. Flow rates were set at 1 L/min, with a sampling duration of 8 h. Total air volumes were approximately 480 L. After collection, samples were frozen and kept at −20°C until analysis. The temperature during the

sampling ranged between 19 and 23ºC, and between 9 and 17ºC, in indoor and outdoor environments, respectively. The indoor and outdoor ranges of relative humidity were 32-58% and 32-63%, respectively.

Analytical method

Formaldehyde was desorbed from tubes with 2 mL of acetonitrile in an ultrasonic bath for 30 min. The analysis was performed by high pressure liquid chromatography with ultraviolet detection (HPLC-UV), using a C-18 column. [21] The initial mobile phase was acetonitrile:water (50:50). The gradient program for acetonitrile, given as time-concentration percentage, was the following: min. 0.1 – 50%, min. 5 – 50%, min. 20 – 80%, min. 25 – 100%, min. 48 – 50%, min. 52 – stop. Calibration was done by using standard solutions of DNPH derivatives of aliphatic aldehydes in acetonitrile. Blank and replicates were analysed every batch of samples for QC/QA. The detection limit was 0.2 μg/m^3.

Human health risk assessment

The formaldehyde concentrations were used to assess the inhalation risk for human health through inhalation. The numeric expressions were taken from the United States Environmental Protection Agency (US EPA) RAGS methodology. [22] Inhalation exposure levels (Exp_{inh}) (in μg/(kg·day)) were calculated according to the equation 1.

$$Exp_{inh} = \frac{\Sigma_i (C_i \times IR_i \times F_i) \times EF}{BW \times 365} \quad (1)$$

where C_i was the concentration of formaldehyde in air (in μg/m^3) in each location, IR_i was the inhalation rate (in m^3/day), F_i was the day time fraction spent (unitless), EF was the exposure frequency (in day/year), BW was the body weight (in kg), and 365 was a conversion unit factor (in day/year).

After exposure evaluation, the associated non-carcinogenic and carcinogenic risks were assessed. Inhalation risks were calculated based on the inhalation dosimetry methodology. [20] In contrast with the old intake methodology, in which inhalation rate and body weight were key parameters, the new method suggests that the amount of chemical reaching the target site through inhalation, is directly related to the exposure concentration (EC), being not a simple function of inhalation rate and body weight. [20] Exposure concentrations (EC) were used for the assessment of non-carcinogenic and carcinogenic risk, meanwhile Exp_{inh} informs regarding exposure levels of the population to formaldehyde. Once the EC was assessed, the characterization of non-carcinogenic risks consisted of the calculation of the Hazard Quotient (HQ), which is defined as the relation between the predicted exposure concentration and the inhalation reference dose (RfD_{inh}). Cancer risks were assessed by multiplying the predicted exposure concentration by the inhalation unit risk (IUR). The RfD_{inh} and the IUR were obtained from the risk assessment information system. [23] The equations to determine the risks were the following (equations 2 to 4):

$$EC = \frac{\Sigma_i (C_i \times Fi) \times EF \times ED}{AT \times 365} \quad (2)$$

$$HQ = \frac{EC}{RfD_{inh}} \quad (3)$$

$$Cancer\ risk = \mathrm{EC} \times \mathrm{IUR} \quad (4)$$

where C_i was the concentration of formaldehyde in air (in µg/m^3) in each location, F_i was the day time fraction spent (unitless), EF was the exposure frequency (day/y), ED was the exposure duration (in years), AT was the averaging time (in years), BW was the body weight (in kg), 365 was a conversion unit factor (in day/y), RfD_{inh} was the inhalation reference dose of formaldehyde (in µg/m^3), and IUR was the inhalation unit risk (in m^3/µg).

The uncertainties associated to the human exposure and health risks were also assessed by means of Monte-Carlo simulations, which were done by applying the Crystal Ball 4.0 software (Decisioneering, Inc.), and considering 100,000 iterations. Each modelling parameter was expressed as a probability distribution function so that a probabilistic distribution was obtained as a result. Detailed information of the probabilistic parameters is shown in Table 2.

Statistics

Data analysis was carried out by means of the statistical software package SPSS 20.0. The level of significance was set at a probability level lower than 0.05 ($p<0.05$). To evaluate significant differences between formaldehyde levels groups in the different locations, the Levene test was applied to verify the equality of variances. ANOVA or Kruskal Wallis tests were subsequently applied depending on whether the data followed a normal distribution or not, respectively.

Results and discussion

Formaldehyde levels

The concentrations of formaldehyde in sampled air are depicted in Figure 1, with the correspondent median, maximum, and minimum values, as well as the 25th and 75th percentiles. Formaldehyde mean levels in samples of indoor air were 27.3 µg/m^3 (range from 10.7 to 47.7 µg/m^3) and 22.5 µg/m^3 (range from 9.6 to 37.2 µg/m^3) in bedrooms and living rooms, respectively. Similar levels were found in indoor air at workplaces, with a mean concentration of 21.8 µg/m^3, ranging from 5.9 to 40.4 µg/m^3. Outdoor level in houses (terrace or balcony) was significantly ($p<0.05$) lower than indoor levels, being the average outdoors 1.6 µg/m^3 (range: 1.0-3.4 µg/m^3). No significant differences ($p<0.05$) were obtained between indoor formaldehyde levels (bedroom, living room and workplaces). A positive significant correlation of indoor formaldehyde concentrations ($p<0.01$) was found between bedrooms and living rooms (Pearson's correlation coefficient: 0.855). This could be due to the common sources of emission or/and diffusion of formaldehyde indoor levels through house rooms. No correlation between formaldehyde indoor and outdoor levels was found. Generally, outdoor formaldehyde does not contribute to indoor pollution (or the contribution is minor) since ambient levels are usually rather low. [24]

Indoor and outdoor formaldehyde levels are consistent with those reported in other countries. In a recent review, Sarigiannis et al. [18] found that typical indoor concentrations ranged from 10 to 50 µg/m^3, being 46 and 37 µg/m^3 in bedrooms and living rooms, respectively. In the same review, Sarigiannis et al. [18] also pointed out that indoor formaldehyde levels in residential buildings of North and Central European countries were higher (29.8 µg/m^3 (range from 4.8 to 115 µg/m^3)) than in Southern European countries (12.7 µg/m^3 (range from 5.2 to 32.9 µg/m^3)). In turn, Nielsen et al. [19] reported that usual indoor levels in US and Europe homes are within 20-40 µg/m^3, while ranges of outdoor levels are between 1 and 4 µg/m^3. According to Salthammer [11], formaldehyde concentrations in urban areas may usually reach 40 ppb (49.2 µg/m^3) and 15 ppb (18.5 µg/m^3) in indoor and outdoor environments, respectively. However, these "normal" concentrations should not be considered as safe.

Recent data, not included in the abovementioned reviews, are summarized in Table 3. Excepting some point cases, such as remodelled dwellings in China, or mobile homes in USA, the results (Table 3) are in agreement with the levels found in the current study. In Spain, Alves et al. [25] found concentrations around 4-6 µg/m^3 in two sport facilities, and below 2 µg/m^3 in outdoor air. Similarly, when evaluating the performance of two different passive samplers, Villanueva et al. [26] reported a mean indoor air level of 6.7 µg/m^3. According to our results, indoor air concentrations of formaldehyde in Catalan homes and workplaces seem to be higher than those found in other locations of Spain.

Levels of formaldehyde in outdoor air have been generally reported to be <0.001 and <0.02 mg/m^3 in remote and urban environments, respectively. [24] In Spain, outdoor formaldehyde levels analyzed in a national park were below 2.6 µg/m^3, [27] and from 2.0 to 7.9 µg/m^3 around a municipal solid waste treatment plant in the metropolitan area of Barcelona. [21] The fact that in both studies higher levels were found in summer than in winter, could be explained by a major biogenesis of the vegetation and a higher photochemical oxidation of hydrocarbons. [3,24]

Human health risks

In the present study, the exposure scenario for risk assessment only considered the adult exposure through air inhalation in the following sites: i) bedroom, while subjects are sleeping, ii) living room, for other home activities, iii) workplace, during labour time, and iv) outdoors, during outdoor activities. Other activities such as cooking or travelling (by car, bus, train or subway) were not considered due to the short time spent by the Catalan general population on them. [28]

For the general population, inhalation exposure levels (Exp_{inh}), using mean values, was 3.94 µg/(kg·day). From the total, 53% of the contribution to total inhalation exposure came from the indoor activities at home (excluding sleeping), 26% during sleeping and 19% at workplace. Only 2% of the total exposure corresponded to outdoor activities, partly because of the low levels detected and short time spent outdoors. After applying a Monte Carlo simulation, inhalation exposure levels (Exp_{inh}) ranged from 0.77 to 21.3 µg/(kg·day), being the mean value 4.16 ± 1.61 µg/(kg·day).

According to the scientific literature, the main route of formaldehyde exposure is air inhalation. [24] However, other exposure pathways, such as dermal contact with textiles and personal care products, could be also important. [29-31] Claeys et al. [32] estimated the dietary formaldehyde ingestion by the Belgian population as 0.10 mg/(kg day). However, it must be taken into account that not all formaldehyde is bioavailable, and that it is not carcinogenic via oral route.

Regarding non-carcinogenic risks, two different RfD_{inh} were used to calculate HQ, one from the US EPA (9.83 µg/m^3) and another from the Office of Environmental Health Hazard Assessment (OEHHA) (9 µg/m^3). [23,33] HQ are twice times higher than the safety limit (HQ=1) independently on the RfD_{inh} used. Using a Monte Carlo simulation, HQ mean value was 2.17 ± 0.62 (ranging from 0.57 to 8.15). More than 97.5% of the trials performed in the Monte Carlo simulation were above the safety limit (HQ=1) (Fig. 2).

For carcinogenic risks, two different IUR were again proposed, $1.3\cdot10^{-5}$ by the US EPA and $6\cdot10^{-6}$ by the OEHHA. [23,33] The results, applying a deterministic methodology with the mean values, were $2.66\cdot10^{-4}$ for US EPA's IUR, and $1.23\cdot10^{-4}$ for OEHHA's IUR. Both values were above the threshold considered as acceptable (10^{-6}), and above the range considered as assumable (10^{-6}-10^{-4}). [34] Applying the probabilistic methodology, the mean cancer risk was $1.94\cdot10^{-4}$ (range: $4.72\cdot10^{-5}$-$9.45\cdot10^{-4}$). More than 95% of the simulations were above the 10^{-4} threshold, which indicates an unacceptable carcinogenic level (Fig. 2). Similar findings were also reported for employees who worked in the laboratories of an adhesive manufacturer producing formaldehyde and urea-formaldehyde resin in Thailand. [35]

According to the guidelines from different countries, most of them focused on occupational protection regulations (Table 4), the exposure levels of formaldehyde range from 0.02 mg/m^3 (8-h exposure in the US), to 2.5 mg/m^3 (8-h exposure in the UK). Regarding short-term exposure, the recommendations range from 0.123 mg/m^3 (1 h-exposure) in Canada to 2.5 mg/m^3 (15 min-exposure) in the US and the UK. The results on human health risks obtained in the present study clearly show that the daily inhalation of formaldehyde for the Catalan population, predominantly resulting from the indoor environments, is higher than threshold levels. For similar reasons, Koistinen et al. [36] considered formaldehyde as a chemical of concern when levels exceed 1 µg/m^3. The number and ubiquity of formaldehyde emission sources, as well as the high time ratios spent indoors, must lead public authorities to consider formaldehyde a pollutant of concern.

Conclusions

Formaldehyde air levels found in Catalan homes ranged from 9.65 to 47.7 µg/m^3, and from 0.96 to 3.37 µg/m^3, in indoor and outdoor air, respectively. At workplaces, indoor air levels ranged from 5.86 to 40.4 µg/m^3. These levels are in agreement with those found in the scientific literature. However, the human health risk assessment clearly show that the current daily exposure to formaldehyde is too high. For most of the trials, non-carcinogenic risks were above the threshold limit (HQ>1), and that carcinogenic risks were also not acceptable (>10^{-4}). Despite the current study limitations (i.e., number of samples, not all daily activities or potential formaldehyde sources included), the results confirm that formaldehyde indoor levels should be regarded an issue of concern that must be taken into account by policy makers and regulatory agencies.

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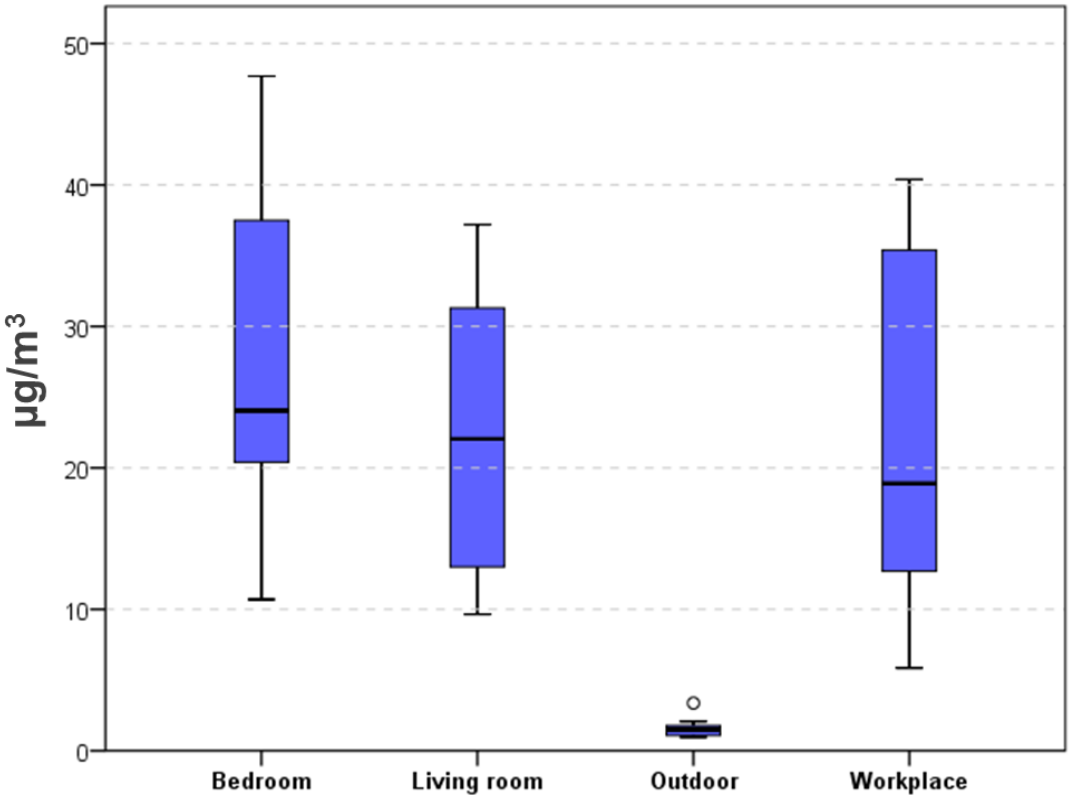
FIGURE CAPTIONS

Figure 1. Formaldehyde levels in µg/m^3 (median, percentile 25^{th} and 75^{th}, maximum and minimum).

Figure 2. Frequency charts for the Hazard Quotient (HQ) and the cancer risk.



473 **Fig 1.**

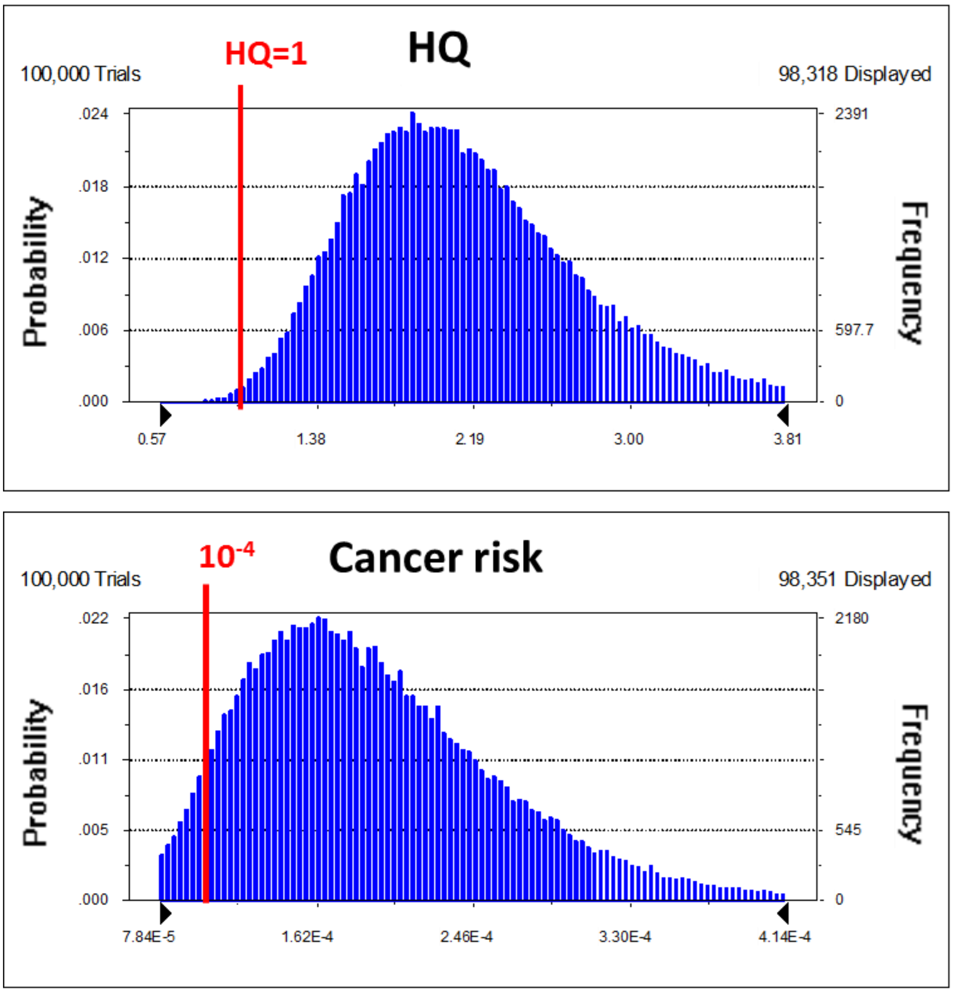

HQ=1
HQ
100,000 Trials
98,318 Displayed
Probability
Frequency
.024
.018
.012
.006
.000
2391
597.7
0
0.57
1.38
2.19
3.00
3.81
10^{-4}
Cancer risk
100,000 Trials
98,351 Displayed
Probability
Frequency
.022
.016
.011
.005
.000
2180
545
0
7.84E-5
1.62E-4
2.46E-4
3.30E-4
4.14E-4

Fig 2.

Table 1. Sampling sites description.

Homes	**Background**	**Year of construction**	**Inhabitants (Age)**	**Smokers**	**Heating**	**Area m^2 (Bedroom/ living room)**
1	Rural	1975	2 (59/61)	No	Fireplace	18/22
2	Urban	2000	1 (27)	No	-	11/18
3	Urban	1975	2 (41)	No	Radiator	10/16
4	Urban	1960	1 (28)	No	Electrical	14/17
5	Urban	1993	1 (35)	No	Heat pump	12/12
6	Rural	2005	2 (32/36)	No	Heat pump	20/35
7	Urban	1990	2 (67/65)	No	Radiator	12/64
8	Rural	1980	2 (30/31)	No	Fireplace	8/25
9	Urban	2005	2 (29/32)	No	Radiator	20/25
10	Urban	1970	1 (35)	Yes	Radiator	20/50
Workplace	**Background**	**Year of construction**	**Occupancy**	**Kind**	**Heating**	**Area m^2**
1	Urban	2000	10	Office	Heat pump	24
2	Urban	2000	4	Office	Heat pump	15
3	Urban	1970	5	Pharmacy	Heat pump	150
4	Rural	2008	8	Kindergarten	Heat pump	18
5	Urban	2005	4	Office	Heat pump	28
6	Urban	1970	2	Tobacconist	Heat pump	30
7	Rural	1990	1	Office	Heat pump	19
8	Urban	1950	1	Office	Heat pump	16
9	Urban	1950	0	Classroom	Heat pump	35
10	Urban	1970	3	Shop	Heat pump	50

Table 2. Monte Carlo human health risk assessment parameters.

Symbol	Parameter	Distribution	Type	Units	References
C_i	Air concentration	(mean±SD)	Log-normal	µg/m^3	This study
	Bedroom	27.3±11.3			
	Living room	22.5±10.6			
	Outdoor	1.62± 0.71			
	Work	21.8±12.9			
IR_i	Inhalation rate	(mean; 95th)	Log-normal	m^3/day	[33]
	Sedentary/passive activities	7.58; 10.0			
	Light intensity activities	18.1; 23.4			
	Moderate intensity activities	38.8; 54.2			
F_i	Time fraction	(mean±SD)	Log-normal*	unitless	[28]
	Bedroom	0.36±0.04			
	Indoor (excl. bedroom)	0.37±0.04			
	Outdoor	0.10±0.01			
	At work	0.14±0.01			
EF	Exposure frequency	350	Point	day/year	[22]
BW	Body weight	(mean±SD) 69.4±14.3	Log-normal	kg	[28]
AT	Averaging time		Point	year	[22]
	Non-cancer	30			
	Cancer	70			
ED	Exposure duration		Point	years	[22]
	Non-cancer	30			
	Cancer	70			
RfD_{inh}	Inhalation reference dose	9.00-9.83	Uniform	µg/m^3	[23,33]
IUR	Inhalation unit risk	$1.3 \cdot 10^{-5}$-$6 \cdot 10^{-6}$	Uniform	m^3/µg	[23,33]

* Since distribution is unknown, authors assume a standard deviation equal to 10% of the mean.
SD: Standard deviation.

Table 3. Indoor air levels of formaldehyde (in µg/m^3) in other recently published studies.

Value	Type	Location	Source	Reference
131±90	Mean±SD	Beijing (China)	Remodelled dwellings	[37]
85±56	Mean±SD	Beijing (China)	Remodelled offices	
4.62; 21.7	Median; Max	Perth (Australia)	Bedroom	[38]
3.77; 23.9	Median; Max	Perth (Australia)	Lounge-room	
15.5 (ND-46.0)	Mean (Range)	Perth (Australia)	Domestic indoor	[39]
ND	Mean (Range)	Perth (Australia)	Outdoor	
9.7	Mean (Range)	Perth (Australia)	Schools	
29.8 (6.5-136.5)	Mean (Range)	Austria	Schools	[40]
20.5±15.6	Mean±SD	(Sweden)	Housing stock	[41]
51.4±2.6	GeoMean±GeoSD	Seul (Republic of Korea)	Libraries and reading room	[42]
42-350	Range	France	Schools	[43]
1.2-7.1	Range	France	Outdoor	
50 (20-100)	Mean (Range)	Harbin (China)	Bedroom	[44]
100 (80-130)	Mean (Range)	Harbin (China)	Living room	
30 (20-40)	Mean (Range)	Harbin (China)	Kitchen	
110 (60-160)	Mean (Range)	Harbin (China)	Study room	
29 (13-272)	Median (Range)	Dailan (China)	Bedroom	[45]
30.6 (13-167)	Median (Range)	Dailan (China)	Kitchen	
14 (ND-40)	Median (Range)	Dailan (China)	Outdoor	
100 (89-113)*	GeoMean (95% CI)	USA	Travel trailers	[46]
70 (60-80)*	GeoMean (95% CI)	USA	Mobile homes	
54 (47-65)*	GeoMean (95% CI)	USA	Park models	
29.2±28.0	Mean±SD	Minamisoma (Japan)	Temporary houses	[47]
1.84±1.12	Mean±SD	Minamisoma (Japan)	Outdoor	
43.1±2.4*	GeoMean±GeoSD	Boston (USA)	Indoor	[48]
1.3–85.6	Range	Beijing (China)	Indoor	[49]
5.6-82*	Range	USA	Retail stores	[50]
63.7±22.8	Mean±SD	Zajecar (Serbia)	Primarily school	[51]

*Converted: 1 ppb = 1.23 µg/m^3 (at 293ºK and 1013 mbar);
ND: Not detected; 95% CI: 95% confidence interval

Table 4. A summary of worldwide guidelines for formaldehyde, considering the exposure via inhalation.

	Guideline	Time	Additional information
Canada [52]	0.123 mg/m³	1 hour	Eye irritation. Residential indoor air
	0.050 mg/m³	8 hour	Respiratory symptoms in children. Residential indoor air
US [53]	0.75 ppm (0.92 mg/m^3)	8 hour	Permissible exposure limits. Occupational standards
	2 ppm (2.5 mg/m^3)	15 min	Permissible exposure limits. Occupational standards
US [54]	0.02 mg/m^3	8 hour	Recommendable exposure limit
	0.15 mg/m^3	15 min	Recommendable exposure limit
UK [55]	2.5 mg/m^3	8 hour	Occupational standards
	2.5 mg/m^3	15 min	Occupational standards
Europe [24]	0.1 mg/m^3	30 min	Air Quality Guidelines. Sensory irritation.
Europe [56]	0.2 ppm (0.3 mg/ m^3)	8 hour	Occupational exposure
	0.4 ppm (0.5 mg/ m^3)	15 min	Occupational exposure
Spain [57]	0.37 mg/m^3	Short Term Exposure	Occupational exposure