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Proposed residential indoor air quality guidelines for formaldehyde

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Inside front cover

PROPOSED RESIDENTIAL INDOOR AIR QUALITY GUIDELINES FOR FORMALDEHYDE

Author:

Nicolas Gilbert — Health Canada

Reviewers:

Barry Jessiman — Health Canada
Serge Lamy — Health Canada
Benoît Lévesque — Institut national de santé publique du Québec
Robert Liteplo — Health Canada
Ron Newhook — Health Canada
Sharon Wilbur — Agency for Toxic Substances and Disease Registry (ATSDR), USA

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ABSTRACT

In the 1980s, Health Canada and the Federal-Provincial Advisory Committee on Occupational and Environmental Health (CEOH) developed a series of indoor air quality guidelines that were published in 1987 in a report entitled Exposure Guidelines for Residential Indoor Air Quality (CEOH 1989). For formaldehyde, target and action levels were set at 60 µg/m^3 (50 ppb) and 120 µg/m^3 (100 ppb), respectively. However, since then, a significant amount of research has been carried out and published on the health effects of some of these substances, warranting a reassessment of the scientific basis of the guidelines and potentially a revision of the guidelines themselves. The purpose of this document is to revisit the guidelines developed for formaldehyde in view of epidemiological and toxicological studies published since 1987.

Based on human clinical studies and on animal experiments, the primary effects of acute exposure to formaldehyde are the irritation of the mucosa of the upper respiratory tract and the eyes. The no observable adverse effects level (NOAEL) and lowest observable adverse effects level (LOAEL) for this outcome are 615 and 1,230 µg/m^3, respectively.

Epidemiological studies on the effects of chronic formaldehyde exposure consistently found respiratory and allergic effects at levels below 123 µg/m^3. In one study, formaldehyde levels in homes were associated with increased risk of atopy, after ruling out confounding from other indoor air pollutants. In another study, formaldehyde levels were significantly associated with hospitalization for asthma in children aged six months to three years, again after ruling out confounding from other indoor air pollutants. No effects were found in children exposed to 10 to 29 µg/m^3 and 30 to 49 µg/m^3 formaldehyde, a non-significant increase of risk was observed at 50 to 59 µg/m^3 and a significantly increased risk was observed at 60≥µg/m^3. An association between low-level exposure to formaldehyde and the development of allergic sensitization and/or asthma is biologically plausible as it is consistent with observations in animals.

There is evidence from toxicological and epidemiological studies that inhaled formaldehyde is carcinogenic. However, formaldehyde-induced carcinogenicity appears to be a consequence of proliferative regeneration following cytotoxicity, and the risk of cancer associated with formaldehyde levels sufficiently low to prevent irritation and inflammatory responses appears therefore to be negligible.

The following guidelines are therefore proposed for formaldehyde:

- a guideline for short-term (1-hour averaged) exposure at 123 µg/m^3 (100 ppb); and
- a guideline for long-term (8-hours averaged) at 50 µg/m^3 (40 ppb).

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1. PREAMBLE

In the 1980s, Health Canada and the Federal-Provincial Advisory Committee on Occupational and Environmental Health (CEOH) developed a series of indoor air quality guidelines that were published in 1987 in a report entitled Exposure Guidelines for Residential Indoor Air Quality (CEOH 1989). Limit values for formaldehyde, carbon monoxide, carbon dioxide, nitrogen dioxide, sulfur dioxide, ozone, and particulate matter provided in this document were based on the scientific evidence available at the time the document was prepared. For formaldehyde, target and action levels were set at 60 µg/m^3 (50 ppb) and 120 µg/m^3 (100 ppb), respectively. The 120 µg/m^3 value was one tenth of the lowest value concentration found to cause irritation symptoms following controlled exposure (1,200 µg/m^3). However, since then, a significant amount of research has been carried out and published on the health effects of some of these substances, warranting a reassessment of the scientific basis of the guidelines and potentially a revision of the guidelines themselves.

In the late 1990s, formaldehyde was assessed under the *Canadian Environmental Protection Act (1999)* (CEPA 1999). Formaldehyde was found to be a sensory irritant and a potential carcinogen; however, the risk of cancer associated with the exposure of the Canadian population to formaldehyde was estimated to be "extremely low," and the major health concern was that "in some indoor locations, concentrations may approach those associated with eye and respiratory tract sensory irritation in humans" (Environment Canada, Health Canada 2001). Formaldehyde was therefore declared "toxic," as it is "entering the Canadian environment in a quantity or concentration that constitutes or may constitute a danger for the environment on which life depends and a danger in Canada to human life or health" (Environment Canada, Health Canada 2001).

The purpose of this document is to revisit the guidelines developed for formaldehyde in view of epidemiological and toxicological studies published since 1987. Epidemiological studies relevant for setting indoor air quality (IAQ) guidelines (i.e. in which the only route of exposure to formaldehyde was inhalation) were reviewed. Studies of workers handling formaldehyde or formaldehyde-containing products (e.g. pathologists, embalmers, painters) were excluded from the review as immunologic sensitization from dermal contact may modify or confound the effect of formaldehyde inhalation. Toxicological studies have been extensively reviewed as part of the CEPA assessment mentioned above and in the Toxicological Profile prepared by the U.S. Agency for Toxic Substances and Diseases Registry (ATSDR 1999); only the key inhalation studies cited in these documents were reviewed.

2. PHYSICAL AND CHEMICAL PROPERTIES

TABLE 1. PHYSICAL AND CHEMICAL PROPERTIES OF FORMALDEHYDE

Molecular formula	
Molecular weight	30.03 g\mol
Melting point	-118 to -92 °C
Boiling point	-21 to -19 °C
Vapour pressure	516 kPa
Conversion ppb ➜ µg/m^3	x 1.23

Sources: Environment Canada, Health Canada 2001; WHO 1989.

Low-molecular weight aldehydes, such as formaldehyde, are reactive, highly flammable compounds. The reactivity of formaldehyde results from the presence of a polarized carbon-oxygen double bond. At room temperature, formaldehyde is a reactive gas (Table 1).

3. INDOOR SOURCES

Extensive reviews of formaldehyde emissions sources have been published by the World Health Organization (WHO 1989), and Environment Canada and Health Canada (2001). Sources that influence indoor levels of formaldehyde can be divided into two broad categories: combustion and off-gassing. Combustion sources include cigarettes and other tobacco products, and open fireplaces. Off-gassing sources include wood products such as particle board and other building materials made with adhesives containing formaldehyde, varnishes, paints, carpeting, drapes and curtains.

3.1 Combustion

Formaldehyde is released into the air by incomplete combustion of organic matter, especially wood. Formaldehyde emissions from residential stoves were assessed with birch wood and spruce wood, under normal and air-starved conditions. Under normal conditions, combustion of birch and spruce emitted 0.058 g and 0.041 g formaldehyde per kg wood, respectively. Air-starved conditions (i.e. with air supply almost completely shut) strongly increased formaldehyde production: birch and spruce combustion emitted 1.722 g and 0.255 g formaldehyde per kg wood, respectively (Ramdahl et al. 1982). In another study, aldehyde emissions from wood stoves were assessed with four types of wood: jack pine, cedar, red oak and green ash. Formaldehyde emissions ranged from 0.089 to 0.708 g per kg wood, and accounted for 8% to 42% of total aldehyde emissions (Lipari et al. 1984).

When a residential wood stove and a residential charcoal-fueled heater were tested under similar controlled conditions, charcoal combustion produced less formaldehyde than wood combustion. Under normal conditions (i.e. without air starvation), it emitted 0.0012 g formaldehyde per kg charcoal (Ramdahl et al. 1982).

Health Canada's Tobacco Control Programme (unpublished data) determined total formaldehyde emitted in mainstream smoke (smoke inhaled and exhaled by the smoker) and in sidestream smoke (released directly by the burning end of a cigarette) from cigarette brands marketed in Canada.
Under standard testing conditions, the formaldehyde content of mainstream smoke of 20 cigarette brands tested ranged from 11 to 128 µg per cigarette with a mean of 53 µg per cigarette, and that of sidestream smoke of 5 brands tested ranged from 327 to 440 µg per cigarette, with a mean of 367 µg per cigarette (Table 2).

TABLE 2. FORMALDEHYDE CONTENT IN SMOKE FROM CIGARETTEBRANDS MARKETED IN CANADA

Smoke	Mainstream		Sidestream	
Test conditions	ISO	intense	ISO	intense
Number of brands tested	20	20	5	5
Formaldehyde (µg/cigarette)				
Minimum	10.7	46.8	327	275
Maximum	128	248.3	440	334
Mean	53.4	139.7	367	302
Standard deviation	32.8	47.8	44	22

Smoke generated by smoke machines.
ISO conditions: 35 ml/puff, 2-second puffs each 60 seconds, ventilation holes unobstructed.
Intense conditions: 55 ml/puffs, 2-second puffs each 30 seconds, ventilation holes obstructed.

Source: Final Report: Cigarette Tobacco and Cigarette Smoke, Toxic Emission Information: Assessment, Characterization and Verification. 2002. Health Canada Contract Number H4097-015017/001/SS, work performed by Labstat International Inc. for Health Canada.

3.2 Gaseous Emissions

3.2.1 Wood products

Formaldehyde is released from pressed wood products made with urea-formaldehyde resins (e.g. particle board, hardwood plywood, medium-density fibreboard), and at lower levels from wood products with phenol-formaldehyde resins (e.g. softwood plywood, oriented strand board). Concerns about potential health impacts from these emissions led the wood products industry to adopt voluntary standards on formaldehyde emissions from particle board (ANSI 208.1) and medium-density fibre (MDF) board (ANSI 208.2) in the 1990s (Composite Panel Association 1999; 2002).

Kelly et al. (1999) assessed formaldehyde emissions from several wood products in a chamber over 24 hours. Emissions from coated urea-formaldehyde wood products (e.g. melamine, laminate) ranged from <2.7 to 55 μg/m^{2}h with the exception of one product emitting 460 μg/m^{2}h, and emissions from bare phenol-formaldehyde wood products ranged from 4.1 to 9.2 μg/m^{2}h. Among bare urea-formaldehyde wood products, emissions from plywood products ranged from 8.6 to 103 μg/m^{2}h, emissions from particle board products ranged from 104 to 1,580 μg/m^{2}h, and emissions from MDF products ranged from 210 to 364 μg/m^{2}h.

Brown (1999) assessed formaldehyde emissions from particle board panels and MDF panels in different small chambers and room chambers for several months, starting 7 days after manufacturing. Emissions factors from all the products tested were approximately 300 to 400 μg/m^{2}h in the first few weeks and 80 to 240 μg/m^{2}h after 6 to 10 months.

3.2.2 Varnishes, floor finishes, and paints

Varnishes are also known to emit formaldehyde. Three conversion varnishes tested by the U.S. Environmental Protection Agency still emitted detectable levels of formaldehyde more than 720 hours (one month) after application; and one of the three varnishes emitted 170 μg/m^{2}h formaldehyde 2,762 hours (about 115 days) after application (Howard et al. 1998). Formaldehyde was still emitted 3,300 hours (about 138 days) after varnish application and the cumulative formaldehyde emission to then was about 700% to 800% of the free formaldehyde amount present in the varnish at the time of application, indicating that formadehyde was formed during the curing process (McCrillis et al. 1999).

Two commercially applied floor finishes were tested by Kelly et al. (1999). In typical conditions, a base coat emitted 1,050,000 μg/m^{2}h formaldehyde immediately after application, and 10,800 μg/m^{2}h 24 hours later; a top coat emitted 421,000 μg/m^{2}h immediately after application and 4,660 μg/m^{2}h 24 hours later.

Water-based paints also emit formaldehyde. In a chamber study by Chang et al. (1999) of four interior water-based paints (water content 40.7%–55.4%) advertised as "low-VOC," two of the paints tested emitted significant amounts of formaldehyde after application; formaldehyde emissions from one paint were still detectable 50 hours after application. Actual emission rates were not shown in the paper. Additional studies were conducted with the paint that had the highest formaldehyde emission (Chang et al. 2002). It was shown that formaldehyde emissions can be characterized by three stages: an initial "puff" of instant decay, a fast decay phase, and a slow decay phase lasting more than 300 hours post-application (emission levels and duration not specified in the paper). Elimination and replacement of the biocide (not specified) from the paint resulted in a 55% decrease in formaldehyde emissions.

3.2.3 Other consumer products

Some carpets emit formaldehyde into the air. The Canadian Carpet Institute (CCI) has established a voluntary emission standard of 50 μg/m^{2}h. In a chamber experiment, the time-course of VOC emissions from four different carpets wasdetermined, but only one was found to release aldehydes: formaldehyde emission rates were 57.2 μg/m^{2}h after 24 hours and 18.2 μg/m^{2}h after 168 hours (Hodgson et al. 1993).

Some textile fabric finishes such as dimethylol-dihydroxyethyleneurea (DMDHEU), melamine resin, and wax water repellent have been found to emit formaldehyde; emissions were decreased but not eliminated by curing (Martin et al. 1998). In another study, formaldehyde emissions from cottons treated by DMDHEU-based finishes were measured in a dynamic chamber; emissions reached a peak after about 2 hours, and decreased to a non-detectable level within 4 days (Kottes Andrews and Trask-Morrell 1997).

3.3 Secondary Production from Ozone

Formaldehyde may also be formed by the chemical reaction of ozone with some building and surface materials. A chamber study showed that the presence of ozone increased the release of formaldehyde from plaster, plywood and fitted carpet (Moriske et al. 1998). Formaldehyde is also formed through the oxidation of R-(+)-limonene, a VOC that is common in indoor environments, by ozone (Clausen et al. 2001). Indoor ozone-releasing devices such as photocopiers and laser printers have been found to release formaldehyde, and this is thought to result from the reaction of ozone with aliphatic hydrocarbons. When a single dry-process photocopier was sent to four different laboratories for chamber experiments, formaldehyde emissions rates ranging from 1.3 to 4.7 g/h of operation were measured (Leovic et al. 1998). Emission from laser printers were also assessed, and were found to range from non-detectable to 0.3 g/h of operation (Tuomi et al. 2000).

4. INDOOR CONCENTRATIONS

4.1 Indoor Formaldehyde Concentrations in Canada

Some surveys of indoor formaldehyde were carried out in Canada in the 1980s following complaints and/or to assess the exposure arising from urea formaldehyde foam insulation (UFFI) and formaldehyde-containing

TABLE 3. INDOOR FORMALDEHYDE CONCENTRATIONS IN CANADA

Place and time	Houses	Sampling time and flow	Range (µg/m^3)	Mean or median (µg/m^3)	Reference
Quebec Feb.-Apr. 1995	73 apartments within 10 mid-rise residential buildings	5 to 7 days	25 to 86	37	Consortium Dessau-Siricon 1996
Vancouver, Ottawa and Toronto	24 apartments from 8 mid-rise buildings	7 days	12 to 74		Scanada Consultants Limited 1997
Windsor (Ontario) 1991-92	22 homes where all inhabitants were non-smokers, 12 homes in which there was at least one smoker, and 18 offices/hotels where smoking was prohibited	24-hour samples	smoke-free homes: 2.5–59.5 smoker homes: 6.6–107.2 Smoke-free offices: 5.9–87.0	*Medians:* smoke-free homes: 22.8 smoker homes: 31.4 smoke-free offices: 14.1 *Means* smoke-free homes: 27.1 smoker homes: 39.4 smoke-free offices: 17.6	Bell et al. 1994
Québec City and surrounding towns	34 homes with a fireplace or a wood stove and 6 homes with no wood- burning appliance. No other combustion source (smoker, furnace, or attached garage) present.	24-hour active sampling at 0.4 L/min on the ground floor (in houses with a wood-burning appliance, samples collected while appliance in use)	Houses with wood- burning appliance: 23.4 houses without wood-burning appliance: 19.5	Houses with wood- burning appliance: 8.2 (SD 4.6) Houses without wood- burning appliance: 9.9 (SD 5.5)	Lévesque et al. 2001
Prince Edward Island Jan.-Apr. 2002	55 homes where no smoker lived, and 4 homes inhabited by at least one smoker (total 59)	19.5 to 57.2 hours (median 23.8 hours) at 0.1 L/min	smoke-free homes: 5.5–87.5 smoker homes: 22.7–70.8	*Medians* no smokers 29.6 smokers: 38.2	Gilbert et al. 2005

wood products (Williams et al. 1981; Broder et al. 1988a; 1988b; 1988c). However, little Canadian data were collected after the UFFI ban in 1980 and the adoption of voluntary formaldehyde emission standards by particle board and MDF producers in the early 1990s (Table 3). These studies were all carried out for specific purposes (e.g. descriptive indoor air quality surveys) and covariate data were collected accordingly. None of these studies, therefore, presents a comprehensive picture of factors associated with indoor levels of formaldehyde.

In the 1990s, the Canadian Mortgage and Housing Corporation (CMHC) funded some surveys of air quality in residential buildings. In 73 apartments within 10 mid-rise residential buildings in the province of Quebec tested from February to April 1995, formaldehyde concentrations (sampling time 5 to 7 days) ranged from 25 to 86 $\mu g/m^3$, with a mean level of 37 $\mu g/m^3$ (Consortium Dessau-Siricon 1996). In 24 apartments from 8 mid-rise buildings in Vancouver, Ottawa and Toronto, 7-day formaldehyde concentrations ranged from 12 to 74 $\mu g/m^3$ (Scanada Consultants Limited 1997).

In Windsor in 1991-92, the Ontario Ministry of Environment and Energy measured indoor formaldehyde concentrations in 22 homes where all inhabitants were non-smokers and in 12 homes in which there was at least one smoker. Formaldehyde levels ranged from 2.5 to 59.5 $\mu g/m^3$ (median 22.8 $\mu g/m^3$) in smoke-free homes, and from 6.6 to 107.2 $\mu g/m^3$ (median 31.4 $\mu g/m^3$) in smoker homes. Formaldehyde levels were also measured in 18 offices and hotels where smoking was prohibited, and ranged from 5.9 to 87.0 $\mu g/m^3$ (median 14.1 $\mu g/m^3$) (Bell et al. 1994).

In Québec City, the Direction de la santé publique (DSP) measured 24-hour formaldehyde concentrations in 40 homes, of which 34 had a fireplace or a wood stove, and 6 had no wood- burning appliance. No other combustion source (smoker, furnace, attached garage) was present in any of these homes. In the houses with a wood stove, samples were collected while the appliance was in use. The highest formaldehyde concentration measured in that study was 23.4 $\mu g/m^3$. Average formaldehyde concentrations on the ground floor of houses with and without wood-burning appliances were 8.2 $\mu g/m^3$ (SD 4.6 $\mu g/m^3$) and 9.9 $\mu g/m^3$ (SD 5.5 $\mu g/m^3$), respectively (Lévesque et al. 2001).

In Prince Edward Island in winter 2002, Health Canada sampled 59 homes for 19.5 to 57.2 hours (median 23.8 hours). Samples were collected in the main living room of the homes. Formaldehyde concentrations ranged from 5.5 to 87.5 $\mu g/m^3$ with a median of 29.6 $\mu g/m^3$ in homes where no smoker lived (n=55), and from 22.7 to 70.8 $\mu g/m^3$ with a median of 38.2 $\mu g/m^3$ in the 4 homes inhabited by at least one smoker (Gilbert et al. 2005).

With the exception of the study of Lévesque et al. (2001) in Québec, results from the 1990s and early 2000s consistently indicate that formaldehyde concentrations in Canadian homes range between 2.5 and 88 $\mu g/m^3$ with an average between 30 and 40 $\mu g/m^3$. The lower levels found in the Québec study may be explained in part by the absence of a combustion source other than wood-burning appliances.

4.2 Determinants of Indoor Formaldehyde Levels

4.2.1 Building characteristics

A Swedish research group studied determinants of indoor formaldehyde levels in Uppsala, Sweden. Two-hour formaldehyde levels were measured in 62 dwellings in 1991-92, and 88 people inhabiting these dwellings completed questionnaires on factors likely to affect exposure, such as building materials, indoor painting in the last 12 months, mechanical ventilation, presence of carpets, and presence of smokers. Formaldehyde concentrations ranged between <5 and 110 $\mu g/m^3$, and were higher in houses with wall-to-wall carpets (Norbäck et al. 1995). A logistic regression was performed to assess the association between individual building characteristics and indoor formaldehyde, adjusting for all other significant factors. Wooden house, wall-to-wall carpets and

painted wood were independently associated with formaldehyde concentration increments of 7 μg/m^3 (95% CI 1–13), 13 μg/m^3 (95% CI 4–22) and 16 μg/m^3 (95% CI 7–25), respectively. No significant influence of building age, mechanical ventilation or environmental tobacco smoke was found (Wieslander et al. 1997). Also, the association between formaldehyde concentration and classroom furnishing was investigated in 181 classrooms randomly selected in 48 schools. Formaldehyde concentrations were measured over 4 hours, and ranged from <3 to 72 μg/m^3 (geometric mean 3 μg/m^3). Also, in each classroom, a "shelf factor" was calculated as the length of open shelves in relation to room volume and a "fleece factor" as m^2 of fabrics in relation to room volume. After adjustment for season and air exchange rate, formaldehyde concentrations were positively correlated with the "fleece factor" ($p=0.013$) and the "shelf factor" ($p<0.001$). The authors hypothesized that formaldehyde might be adsorbed onto indoor surfaces and re-emitted in the indoor environment (Smedje and Norbäck 2001).

In France, 72-h formaldehyde samples were collected in 61 dwellings located in the Paris region (Clarisse et al. 2003). Geometric mean formaldehyde levels were 21.7 μg/m^3 (SD 1.9 μg/m3) in kitchens, 24.3 μg/m^3 (SD 1.9 μg/m^3) in living rooms and 24.5 μg/m^3 (SD 2.0 μg/m^3) in bedrooms. A multiple linear regression analysis showed that temperature ($p=0.01$) and the age of floor coverings ($p=0.02$) were significantly associated with formaldehyde levels, while CO_2 ($p=0.36$), the type of floor covering ($p=0.32$), the presence of pressed wood products ($p=0.90$), the age of wall coverings ($p=0.55$) and smoking ($p=0.30$) were not.

4.2.2 Season

In the United Kingdom, indoor formaldehyde levels were measured every 4 to 6 weeks during 3 years in five homes. Mean formaldehyde concentrations in years 1, 2 and 3 were 17, 19 and 17 μg/m^3, respectively; no long-term trend was observed. However, there was a clear seasonal pattern: concentrations measured from April to September were significantly higher ($p<0.05$) than those measured from October to March (Brown et al. 1995).

4.2.3 Outdoor air supply

In Montréal, the impact of outdoor air supply on levels of indoor air contaminants was determined by manipulating experimentally the mechanical ventilation system of two major office buildings. Among the contaminants monitored, formaldehyde was the most tightly associated with air exchange: 96% of the variance of formaldehyde concentrations was explained by outdoor air supply, compared to 87% of CO_2 variance and less than 30% for all other chemicals monitored (Menzies et al. 1996). A German study of 252 houses sampled from 1986 to 1993 found a significant negative correlation between formaldehyde levels (ranging from 12–649 μg/m^3) and air exchange rate expressed in hours^{-1} ($r=-0.2105$, $p<0.01$). No significant association was found between formaldehyde and temperature, or between formaldehyde and relative humidity (Salthammer et al. 1995).

5. HEALTH EFFECTS

5.1 Epidemiological Studies: Effects Other Than Cancer

5.1.1 Irritation

Three cross-sectional studies (summarized in Table 4) have investigated the association between indoor concentrations of formaldehyde and the prevalence of irritation symptoms in occupants.

Olsen and Døssing (1982) administered a health questionnaire to 70 employees from seven "mobile" daycare centres where urea-formaldehyde-glued particle board was used for indoor paneling, and to 34 employees from three "permanent" daycare centres where no particle board was used as building material. The two groups

TABLE 4. IRRITATING EFFECTS OF INDOOR FORMALDEHYDE – OBSERVATIONAL STUDIES

Country/years	Subjects	Design	HCHO Levels	Results	Reference
Denmark	70 employees from 7 "mobile" daycare centres with urea-formaldehyde-glued particle board indoor paneling, and 34 employees from 3 "permanent" daycare centres with no particle board	Cross-sectional study E: not specified D: self-administered symptom questionnaire	"Permanent" daycare centres: 50–110 µg/m^3 (median 80 µg/m^3) "mobile" daycare centres: 240–550 µg/m^3 (median 430 µg/m^3) NOTE: lower air- exchange rates in mobile daycare centres	Higher prevalence of nose and throat irritation, unusual tiredness and headache in employees from the "mobile" centres ($p<0.01$ for each symptoms).	Olsen and Døssing 1982
Wisconsin, USA	61 adults and teenagers inhabiting mobile homes	Cross-sectional study E: active sampling at 1 L/min for 1 hour D: self-administered health questionnaire	Range: <123–984 µg/m^3 Geometric mean: 197 µg/m^3	Burning eyes and eye irritation showed "a statistically-significant, positive dose–response relationship to indoor formaldehyde exposure concentration" (no RR shown) after controlling for age, gender and smoking status.	Hanrahan et al. 1984
Minnesota, USA, 1979–1981	"nearly 2000" residents from 397 mobile homes and 494 conventional homes concerned about possible HCHO exposure	Cross-sectional study E: 30-minute active sampling at 1 L/min D: symptom questionnaires administered by an interviewer	Not specified	Positive, statistically significant dose–response relationships were found for eye irritations, nose and throat irritations, headaches and skin rash.	Ritchie and Lehnen 1987

E: Exposure assessment D: Outcome assessment

were not different with respect to smoking and age distribution. The prevalences of nose and throat irritation, unusual tiredness and headache were higher in employees from the "mobile" centres than in those from "permanent" centres ($p<0.01$ for each symptom). Formaldehyde concentrations ranged from 50 to 110 μg/m^3, with a median of 80 μg/m^3, in "permanent" centres, and from 240 to 550 μg/m^3, with a median of 430 μg/m^3, in "mobile" centres; "mobile" centres also had lower air exchange rates (range 0.3–0.5 changes/h) than "permanent" centres (range 0.6–1.1 changes/h). The two categories of buildings were different not only with respect to formaldehyde, but also with ventilation. Lower air exchange rates have been associated with increased prevalence of respiratory symptoms (Seppänen et al. 1999), and therefore confounding cannot be ruled out.

A total of 61 adults and teenagers inhabiting mobile homes responded to a self- administered health questionnaire after having 1-hour formaldehyde concentrations measured in their homes (Hanrahan et al. 1984). The geometric mean concentration of formaldehyde was 197 μg/m^3 (160 ppb). After controlling for age, gender and smoking status, burning eyes and eye irritation showed "a statistically-significant, positive dose–response relationship to indoor formaldehyde exposure concentration." The prevalence rates by exposure category are not shown, and the statistical analysis is not described in this paper.

In Minnesota, between 1979 and 1981, the Department of Health offered free-of-charge formaldehyde testing to residents concerned about possible exposure to that contaminant (Ritchie and Lehnen 1987). Under the program, 30-minute formaldehyde concentrations were determined in 397 mobile homes and 494 conventional homes, and symptom questionnaires were administered to "nearly 2000" residents of these homes. Prevalences of eye irritations, nose and throat irritations, headaches and skin rash were calculated in residents of houses with formaldehyde levels of <123 μg/m^3, 123 to 369 μg/m^3, and 369 μg/m^3 and above. Positive, statistically significant dose–response relationships were found for each of these symptoms. These findings, however, should be considered with caution in view of participants' self- selection based on concern about formaldehyde (a design prone to bias). The sampling time was also very short, increasing the likelihood of exposure misclassification.

In summary, significant associations were found in all these studies, but methodological limitations preclude the use of these studies as a basis for health risk assessment.

5.1.2 Lung function, respiratory symptoms, and asthma

Exposure to gaseous formaldehyde is a suspected cause of occupational asthma (Burge et al. 1985; Malo and Bernstein 1993) but the effects of chronic exposure to formaldehyde levels occurring in dwellings are less well characterized. There is, however, an increasing body of epidemiological evidence from cross-sectional and case–control studies, and from one cohort study suggesting that chronic low-level exposure to formaldehyde is associated with an increased risk of developing allergic sensitization and/or asthma (Table 5) .

Formaldehyde concentrations were measured in the main room, kitchen and bedrooms of 202 dwellings for two 1-week periods using passive diffusion samplers. Individual characteristics and chronic respiratory symptoms of 298 children 15 years of age or less, and 613 adults living in these houses were documented through a self-administered questionnaire. Peak expiratory flow (PEF) was also self-assessed by subjects (208 children and 526 adults) using portable peak flow meters in morning, near noon, in the evening and before bed. The mean concentration of formaldehyde was 32 μg/m^3 (26 ppb), and the maximum was 172 μg/m^3 (140 ppb). In children, prevalences of physician-diagnosed chronic bronchitis and asthma were significantly higher in children exposed to environmental tobacco smoke (ETS) and >74 μg/m^3 formaldehyde than in those exposed to ETS only. No association between formaldehyde and asthma or chronic bronchitis was found in children not exposed to ETS. Also, in children, PEF decreased significantly with increasing formaldehyde; each 1.23 μg/m^3 (1 ppb)-increment in formaldehyde was associated with a 1.28 L/min decrease (standard error 0.46 L/min, $p<0.05$) in PEF. Exposure to ETS had no effect on PEF or its relation to formaldehyde (Krzyzanowski et al. 1990). One major strength of this study is that the length of the sampling time allowed the investigators to average out daily variations of formaldehyde levels in this study. Conversely, the only other indoor air pollutant determined was ETS. There is, therefore, some potential for confounding by unmeasured indoor contaminants.

TABLE 5. RESPIRATORY AND ALLERGIC EFFECTS OF INDOOR FORMALDEHYDE – OBSERVATIONAL STUDIES

Country/years	Subjects	Design	HCHO Levels	Results	Reference
Arizona, USA	298 children 15 years of age or less, and 613 adults living in 202 dwellings	Cross-sectional study E: two 1-week periods using passive diffusion samplers D: self-administered questionnaire. Peak expiratory flow (PEF) self-assessed in a sub-sample (208 children and 526 adults) using portable peak flow meters	Mean 32 µg/m^3 Max 172 µg/m^3	Prevalence of chronic bronchitis and asthma significantly higher in children exposed to ETS and >74 µg/m^3 HCHO than in those exposed to ETS only. Among all children, PEF decreased with increasing HCHO; each 1.23 µg/m^3-increment in HCHO associated with a 1.28 L/min decrease (SE 0.46 L/min, p<0.05) in PEF. Exposure to ETS had no effect on PEF or its relation to HCHO.	Krzyzanowski et al. 1990
Uppsala, Sweden 1991-92	88 people 20–45 years of age living in 62 dwellings	Cross-sectional study E: 2-hour active sampling at 0.25 L/min D: respiratory symptom questionnaire	Range: <5–100 µg/m^3	A 10-fold increase in HCHO associated with nocturnal breathlessness (OR 12.5, 95% CI 2.0–77.9, adjusted for age, sex, current smoking, wall-to-wall carpets and house dust mites).	Norbäck et al. 1995
Uppsala, Sweden 1993	627 pupils 13–14 years of age attending 11 randomly selected secondary schools	Cross-sectional study E: 4-hour active sampling at 0.2 L/min in schools D: questionnaires to parents	Range: <5–72 µg/m^3	HCHO in schools associated with current physician-diagnosed asthma (OR 1.1, 95% CI 1.01–1.2, adjusted for atopy, food allergy and daycare centre >3 years).	Smedje et al. 1997
Uppsala, Sweden 1993–97	1,347 children (mean age in 1993; 10.3 years) attending 39 different schools in 1993	Cohort study: E: 4-hour active sampling at 0.2 L/min 1993 and 1995 in classrooms D: Questionnaires to parents in 1993 and 1997	Range: <5–72 µg/m^3 Arithmetic mean 8 µg/m^3	Among children not atopic in 1993, incident asthma (i.e. diagnosed during follow-up) associated with HCHO in classroom: OR 1.7 (95% CI 1.1–2.6) per 10 µg/m3 increase adjusted for sex, age and smoking.	Smedje and Norbäck 2001

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TABLE 5. RESPIRATORY AND ALLERGIC EFFECTS OF INDOOR FORMALDEHYDE – OBSERVATIONAL STUDIES

Country/years	Subjects	Design	HCHO Levels	Results	Reference
Uppsala, Sweden	234 school workers from 12 schools	Cross-sectional study E: 4-hour active sampling at 0.2 L/min D: measurement of the nasal cavity by acoustic rhinometry; nasal lavage		A 10 µg/m^3 increase in HCHO in school associated with a 2.7-µg/L (95% CI 1.7–3.5), increase of eosinophil cationic protein (ECP), a protein released by eosinophils, with a 3.0 µg/L (95% CI 1.7–4.3) increase in lysozyme, in the nasal lavage fluid, and with decreased nasal patency after adjustment for age, sex, atopy, current smoking and room temperature in schools.	Norbäck et al. 2000
Australia, March 1994–February 1995	88 people 20–45 years of age living in 62 dwellings	Cross-sectional study E: 96-hour passive measurements in homes, four times over 1 year D: skin prick tests on 145 children with 12 common environmental allergens (mite, fungi, pets, and pollens); questionnaire to parents of all children	HCHO in bedrooms (geometric mean): Atopic children 19.0 µg/m^3, 95% CI 16.7–21.7 µg/m^3 Non-atopic children 16.4 µg/m^3, 95% CI 14.3–18.8 µg/m^3 (p=0.06) Highest HCHO level in home (geometric mean): Atopic children 38.3 µg/m^3, 95% CI 33.8–43.3 µg/m^3 Non-atopic children 28.6 µg/m^3, 95% CI 24.6–33.3 µg/m^3 (p=0.002)	OR for atopy with a 10-µg/m^3 increase in HCHO in bedroom: 1.40 (95% CI 0.98–2.00), adjusted for gender and parental asthma. No significant association between HCHO and asthma or respiratory symptoms.	Garrett et al. 1999
Australia	224 healthy children aged 6 to 13	Cross-sectional study E: 24-hour passive measurements in homes D: Spirometry (FEV_1 and FVC), skin prick tests for 7 common allergens, and exhaled NO (marker for inflammation)	Not specified	Exhaled NO significantly higher in children living with homes with HCHO 61.5 µg/m^3 (p=0.02). Difference remained significant after adjustment for age and atopy (p=0.002). No association between HCHO and lung function.	Franklin et al. 2000

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TABLE 5. RESPIRATORY AND ALLERGIC EFFECTS OF INDOOR FORMALDEHYDE – OBSERVATIONAL STUDIES

Country/years	Subjects	Design	HCHO Levels	Results	Reference
Australia	Children aged between 6 months and 3 years	Case-Control Cases: children discharged from a hospital emergency department with an asthma diagnosis (n=88) Controls: community controls without physician-diagnosed asthma (n=104) E: 8-hour passive sampling in winter and summer D: Questionnaire	Living room: mean 27.5 µg/m^3, max 189.7 µg/m^3 Child's bedroom: mean 30.2 µg/m^3, max 224 µg/m^3	Non-significantly increased risk of asthma (OR 1.2) at 50–59 µg/m^3. Significantly increased risk of asthma (OR 1.39, p<0.05) with HCHO60 µg/m^3, compared to <10 µg/m^3. ORs adjusted for house dust mite allergens, relative humidity, indoor temperature, atopy, family history of asthma, socio-economic status, ETS, pets, air conditioning, humidifier and gas appliances.	Rumchev et al. 2002
Austria 1992–93	62 children (mean age 8 years) moved in January 1993 from a school paneled with particle board to a brick building, and 19 control children (mean age 8.5 years) not attending this school	Intervention Study E: "acetyl-acetone method" D: IgE antibodies specific to HCHO measured by radioallergosorbent test (RAST) in all children in December 1992, and re-assessed in March 1993 in 20 out of 24 children (all from the particle board-paneled school) who had elevated results at the first test	Particle board-paneled school (December 1992): 53-92 µg/m^3 Brick school (March 1993): 29-36 µg/m^3	December 1992: Elevated results found in 24/62 children from the particle board-paneled school, and in none of the 19 control children. March 1993: 10/20 children (initially elevated) with normal results.	Wantke et al. 1996

Norbäck et al. (1995) measured 2-hour indoor formaldehyde, VOC and allergen concentrations in 62 dwellings, and results were linked to the responses that 88 inhabitants of these dwellings, aged 20 to 45 years, had given to a previous survey of respiratory symptoms. Formaldehyde concentrations ranged from <5 to 100 µg/m^3. After adjusting for age, sex, current smoking, presence of wall-to-wall carpets and presence of house dust mites, a 10-fold increase in formaldehyde concentrations was associated with an increased risk of nocturnal breathlessness (OR 12.5, 95% CI 2.0–77.9). Formaldehyde was not associated with bronchial hyperresponsiveness, PEF or forced expiratory volume in 1 second (FEV1). The relationship between formaldehyde with one asthma-related symptom, but not the others, is difficult to interpret.

Wantke et al. (1996) measured formaldehyde-specific IgE antibodies in 62 children (mean age 8 years) attending a school paneled with particle board, using a radioallergosorbent test (RAST). Positive tests were

found in 24 children. Formaldehyde levels in their classrooms ranged from 53 to 92 μg/m^3 (43–75 ppb). Because of these findings, children were moved to a brick school building, where formaldehyde concentration in classrooms ranged from 29 to 36 μg/m^3, and 2 months later 20 out of the 24 IgE-positive children were re-assessed; 10 of them were negative. These findings are hard to interpret in terms of health risk because the biological significance of the outcome investigated is unclear, and because of the design which is prone to clustering effect as children attending one school may tend to be similar with respect to more than one risk factor.

Smedje et al. (1997) carried out a cross-sectional study in 11 randomly selected secondary schools. Trained occupational hygienists inspected the schools and measured several indoor air contaminants, including formaldehyde (4-hour samples); questionnaires were also sent to 762 pupils 13 and 14 years of age, 627 of whom responded. A multiple logistic regression analysis indicated that formaldehyde exposure was associated with current physician-diagnosed asthma (increment unspecified: OR 1.1, 95% CI 1.01–1.2). There is no indication in this paper that the authors took into account clustering effect, and this is certainly an issue for a barely significant (p=0.042) statistical association.

A total of 234 school workers from 12 schools in Uppsala county underwent measurement of the nasal cavity by acoustic rhinometry and nasal lavage (Norbäck et al. 2000). Four-hour formaldehyde samples were collected. After adjustment for age, sex, atopy, current smoking and room temperature in schools, a 10 μg/m^3 increase in formaldehyde concentration in schools was associated with a 2.7 μg/L (95% CI 1.7–3.5) increase of eosinophil cationic protein (ECP), a protein released by eosinophils, and with a 3.0 μg/L (95% CI 1.7–4.3) increase in lysozyme, in the nasal lavage fluid. The same formaldehyde increment was also associated with a decreased nasal patency. The small number of schools may have led to clustering, and therefore underestimation of the standard error of the risk estimates. No adjustment was made for other indoor air contaminants. Also, the biological significance of the health outcomes investigated is not discussed in the paper.

Smedje and Norbäck (2001) carried out a prospective study of 1,347 children who were surveyed twice 4 years apart. The mean age of children at enrolment was 10.3 years. Participants were attending 39 different schools at the time of the first survey. Concentrations of VOCs, formaldehyde, particles, bacteria and moulds in the air of classrooms were determined at the start of the study and at the middle of follow-up. Formaldehyde concentrations ranged from <5 to 72 μg/m^3 (arithmetic mean 8 μg/m^3). After adjustment for sex, age, atopy at enrolment and smoking, the odds ratios for incident asthma (i.e. diagnosed during the follow-up period) per 10 μg/m^3 increase in formaldehyde levels in classrooms was 1.2 (95% CI 0.8–1.7). Among children who were not atopic at enrolment, the odds ratio for incident asthma per 10 μg/m^3 increase in formaldehyde levels, adjusted for sex, age and smoking, was 1.7 (95% CI 1.1–2.6). The cohort design is usually a strong one as it allows investigators to ensure that the exposure precedes the occurrence of disease. However, analyses were not adjusted for other indoor pollutants, although airborne fungi were also associated with a higher risk of incident asthma. Confounding cannot therefore be ruled out.

Garrett et al. (1999) measured 96-hour formaldehyde concentrations in indoor air on four occasions over 1 year in 80 households, and a respiratory health questionnaire was completed for 148 children 7 to 14 years of age inhabiting these houses. Also, skin prick tests were performed on 145 participating children with 12 common environmental allergens (mite, fungi, pets and pollens). The geometric mean concentrations of formaldehyde in the bedrooms of atopic and non-atopic children were 19.0 μg/m^3 (95% CI 16.7–21.7 μg/m^3) and 16.4 μg/m^3 (95% CI 14.3–18.8 μg/m^3), respectively. The difference between these two groups was not significant (p=0.06). The highest formaldehyde level measured in atopic children's homes (geometric mean: 38.3 μg/m^3, 95% CI 33.8–43.3) was significantly higher than that of non- atopic children's homes (28.6, 95% CI 24.6–33.3; p=0.002). The odds ratio for atopy with a 10-μg/m^3 increase in the mean formaldehyde level in the bedroom, adjusted for gender and parental asthma, was 1.40 (95% CI 0.98–2.00). No significant association was found between formaldehyde levels and asthma or respiratory symptoms after adjusting for gender and parental asthma. House dust mites, airborne fungal spores and indoor nitrogen dioxide were also measured in this study, but no association was found between these contaminants and formaldehyde. This study provides evidence of an

association between formaldehyde levels and atopy: potential confounders were considered, and analyses were adjusted when necessary. Another strength of the study is the relatively long sampling time (96 hours) and the use of repeated measurements (four occasions over 1 year), providing exposure estimates likely to be representative. One weakness is the enrolment of more than one child per dwelling, leading to a clustering effect and, therefore, underestimation of the standard error of the risk estimates.

Lung function and exhaled nitric oxide (a marker of airway inflammation) were measured in 224 healthy children 6 to 13 years of age, and formaldehyde concentrations were measured in their home (bedroom and living room) (Franklin et al. 2000). Indoor formaldehyde was not associated with children's FEV_1 and forced vital capacity (FVC). Geometric mean (95% CI) exhaled nitrous oxide levels were 8.7 ppb (7.9–9.6 ppb) in children from homes with formaldehyde concentrations below 61.5 µg/m^3 (50 ppb), and 15.5 ppb (10.5–22.9 ppb) in those from homes with formaldehyde levels of 61.5 µg/m^3 or more. The difference was significant in univariate analysis (p=0.02) and remained significant after controlling for all other variables in a multiple linear regression model including children's age and atopic status (p=0.002). This study provides some evidence that formaldehyde exposure is associated with inflammatory responses. However, no measurement of other contaminants was made in this study; confounding cannot therefore be ruled out. Also, the dichotomous categorization of formaldehyde exposure makes this study not very useful for quantitative risk assessment.

A case-control study was conducted in children 6 months to 3 years of age (Rumchev 2001; Rumchev et al. 2002; K. Rumchev, personal communication). Cases (n=88) were children who attended the emergency department of a hospital and were discharged with an asthma diagnosis, while controls (n=104) were recruited in the community serviced by that hospital among children never diagnosed with asthma. Eight-hour formaldehyde concentrations (sampling from 9:00 to 17:00) were measured using passive samplers in winter and summer in the living room and children's bedroom (Table 6). Formaldehyde concentrations were significantly higher in summer than in winter (p<0.001), both in the child's bedroom and the living room. A significant association was found between indoor formaldehyde and asthma, after adjustment for house dust mite allergens, relative humidity, indoor temperature, atopy, family history of asthma, socio-economic status, ETS, pets, air conditioning, humidifier, and gas appliances (Table 7). This study is a strong one because of:

TABLE 6. INDOOR FORMALDEHYDE CONCENTRATIONS (µg/m^3) IN THE AUSTRALIAN CASE-CONTROL STUDY OF CHILDHOOD ASTHMA (RUMCHEV 2001; RUMCHEV ET AL. 2002)

Season	Room	Min	Max
Winter	Child's bedroom	0.24	62.91
	Living room	0.61	80.05
Summer	Child's bedroom	0.49	224
	Living room	0.73	189.72

TABLE 7. ASSOCIATION BETWEEN INDOOR FORMALDEHYDE AND CHILDHOOD ASTHMA (RUMCHEV 2001; RUMCHEV ET AL. 2002)

Formaldehyde (µg/m^3)	Cases	Control	OR	95% CI
<10	17	33	1	Reference
10–29	44	45	0.98	0.82–1.1
30–49	14	15	0.99	0.78–1.21
50–59	2	0	1.22	0.89–1.62
≥60	6	3	1.39	1.09–1.69

Odds ratios adjusted for house dust mite allergens, relative humidity, indoor temperature, atopy, family history of asthma, socio-economic status, ETS, pets, air conditioning, humidifier and gas appliances

1) the relatively long air sampling duration (8 hours); 2) the use of measurements in two different seasons; 3) the adjustments for other potential confounders, including other indoor air contaminants (ensuring that the association observed between formaldehyde and asthma does not reflect an effect of other indoor contaminants associated with formaldehyde); and 4) the use of exposure categories that allowed the investigators to verify the existence of a dose–response pattern. One limitation is the retrospective design: formaldehyde levels were measured after the onset of respiratory symptoms in cases and, moreover, after the assessment of the health status of cases and controls. Another problem in this study is that asthma diagnosis in the age group (<3 years) is uncertain, and 45% of controls did wheeze compared to 85% of cases. It is therefore possible that a proportion of controls has an undiagnosed asthma, and the outcome actually assessed in this study may be "hospitalization for asthma" rather than "having asthma." Nevertheless, the study provides evidence that formaldehyde exposure is associated with increased risk of asthma-related hospitalization in children.

In summary, exposure to indoor formaldehyde levels below the current guideline of 123 μg/m^3 (100 ppb) appears to be associated with an increased risk of atopy, airway inflammation measured by exhaled nitric oxide, reduction in peak expiratory flow and physician-diagnosed asthma. While most studies did not adequately control for potential confounders such as mould, two well-designed studies (Garrett et al. 1999; Rumchev et al. 2002) which adequately controlled for confounding did find significant associations between formaldehyde and atopy or asthma.

5.2 Epidemiological Studies: Cancer

Case-control and cohort studies of formaldehyde exposure and cancer have been extensively reviewed by the International Agency for Research on Cancer (IARC 1995) and CIIT (1999) (Table 8). The cancer sites most suspected of being linked to formaldehyde are nasopharyngeal cancer (NPC) and sinonasal cancer (SNC). The fact that these are very rare cancer limits the power of epidemiological studies, especially those with a cohort design. All but one of the reviewed studies considered only occupational exposure to formaldehyde; the exception is Vaughan et al. (1986b) who did not measure formaldehyde concentrations in homes, but considered "living in mobile home" as a proxy for residential formaldehyde exposure: living in a mobile home for more than 10 years was associated with an increased risk of nasopharyngeal cancer (OR adjusted for cigarette smoking and ethnic origin: 5.5; 95% CI 1.6–19.4). However, as noted by the authors themselves and by IARC reviewers, formaldehyde may not be the only exposure associated with this type of residence. Two case-control studies found significant associations between occupational exposure to formaldehyde and NPC (Roush et al. 1987; West et al. 1993) while another found no such association (Vaughan et al. 1986a). As well, two case- control studies found associations between occupational exposure to formaldehyde and SNC (Hayes et al. 1986; Luce et al. 1993), while another found no association (Olsen and Asnaes 1986). Three major studies published since the 1995 IARC review provided additional evidence of an association between formaldehyde and NPC. First, in the United States, a multi-centre study compared 231 men and women aged 18 to 74 years, diagnosed with any type of NPC, with 244 controls "frequency-matched" by age, gender and cancer registry, and identified by random-digit dialing. Cases and controls were classified with respect to their exposure to formaldehyde and wood dust by occupational hygienists on the basis of their occupational history. The probability of exposure was classified as "definitively not or unlikely," "possible," "probable" or "definite," and exposure levels were classified as low (8-hour time-weighed average <123 μg/m^3), moderate (123 to <615 μg/m^3) and high (615 μg/m^3 or higher). Odds ratios were adjusted for age, gender, race, smoking, education and self vs. proxy surveys. "Probable" or "definite" exposure (ever exposed vs. never) was associated with an increased risk of epithelial "not otherwise specified" (NOS) cancer (OR 3.1, 95% CI 1.0–9.6), but not other histological types of NPC. There was no dose–response relationship, as the highest risk was found in the low exposure category, but risk increased with duration of exposure (p for trend=0.036). "Definite" exposure to formaldehyde increased the risk of squamous cell carcinoma and epithelial NOS (OR 13.3, 95% CI 2.5–7.0). No such association was found between wood dust and NPC: the odds ratio for wood dust exposure ("possible" or higher probability) with squamous cell carcinoma or epithelial NOS cancer was 1.5 (95% CI 0.7–3.3) with no trend for level, duration or cumulative exposure. The authors concluded that formaldehyde exposure increases the risk of NPC, and that there is no evidence that this association is confounded by wood dust (Vaughan et al. 2000).

TABLE 8. EPIDEMIOLOGICAL STUDIES OF FORMALDEHYDE EXPOSURE AND CANCER

Country	Design	HCHO exposure	Results	Reference
United States	Case-Control Cases: 205 cases of oro- or hypopharyngeal cancer (OHPC), 27 cases with nasopharyngeal cancer (NPC) and 53 cases with sinonasal cancer Controls: 552, identified by random-digit dialing. "Frequency-matched" for age and sex.	Based on occupational histories. Probability classified as unlikely, possible or probable, and level (for exposures of probable or higher probability) classified as low, medium and high.	No association between occupational exposure to formaldehyde and any cancer site. Living in a mobile home for >10 years associated with increased risk of NPC (OR 5.5; 95% CI 1.6–19.4, adjusted for cigarette smoking and ethnic origin).	Vaughan et al. 1986a; 1986b
Netherlands	Case-control Cases: 91 males with newly diagnosed epithelial cancer of the nasal cavity or the nasal sinuses Controls: 195 unmatched males	Assessed independently, on the basis of job descriptions, by two industrial hygienists (assessment A and B). Since wood dust is strongly associated with nasal cancer, the analysis was then restricted to subjects with no or low exposure to wood dust.	Moderate/high exposure associated with increased risk of cancer (assessment A: OR 3.0, 90% CI 1.0–8.7; assessment B: OR 2.1, 95% CI 1.1–4.1).	Hayes et al. 1986
United States	Historical cohort 26,561 workers employed after January 1, 1966 in 10 plants where formaldehyde exposure was documented and followed until January 1, 1980	Individual exposure estimates based on job title, job tasks and monitoring data.	Overall cancer mortality not related to HCHO exposure. Small, non-significant excesses of Hodgkin's disease (SMR 142, 95% CI 78–238), larynx cancer (SMR 142, 95% CI 73–248) and lung cancer (SMR 111, 95% CI 96–127) found in exposed workers, but not related with duration or level of HCHO exposure.	Blair et al. 1986
Denmark	Case-control Cases: 287 with cancer of the nasal cavity, 179 with cancer of the paranasal sinuses, and 293 with NPC, diagnosed between 1970 and 1982 Controls: 2,465 with cancer of the colon, rectum, prostate or breast, unmatched	Based on occupational histories; classified as unexposed, probably or certainly exposed, or unknown	Non-significant association between formaldehyde and cancer of the nasal cavity or paranasal sinuses after adjustment for wood dust exposure (OR for HCHO exposure 2.3, 95% CI 0.9–5.8; OR for HCHO exposure with a 10-year latency: 2.4, 95% CI 0.8–7.4). No association between HCHO and NPC.	Olsen and Asnaes 1986

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TABLE 8. EPIDEMIOLOGICAL STUDIES OF FORMALDEHYDE EXPOSURE AND CANCER

Country	Design	HCHO exposure	Results	Reference
United States	Case-Control Cases: 198 with sinonasal cancer (SNC) and 173 with nasopharyngeal cancer (NPC) Controls: 605 controls. All subjects deceased at the time of study; information was retrieved from death certificate and city directories.	Based on occupational history. Probability of exposure classified as none, possible probable, or definite, and levels of formaldehyde exposure as 0, <1,230, or >=1,230 µg/m^3.	Non-significant increased risk of NPC associated with probability of definite exposure >1,230 µg/m^3. 20 years or more prior to death (OR 2.3, 95% CI 0.9–2.3, adjusted for age at death, year of death and availability of occupational information).	Roush et al. 1987
Philippines	Case-control Cases: 104 histologically confirmed NPC cases Controls: 104 hospital controls matched for age, sex and hospital ward type, and 101 community controls matched for sex, age and neighbourhood	Based on occupational histories	Exposure to HCHO 25+ years before diagnosis associated with NPC (OR 2.7, 95% CI 1.1–6.6).	West et al. 1993
France	Case-control Cases: 207 with cancer of the nasal cavity or paranasal sinuses Controls: 323 diagnosed with a non-respiratory cancer and 86 individuals identified by the cases themselves (excluding their colleagues) and matched for gender and age ±10 years (total 409)	Based on occupational histories. Probability of exposure classified as none, possible, probable or definite, and levels of exposures with “possible” or higher probability classified as low, medium and high	No association between HCHO exposure and squamous cell carcinomas. In men, both HCHO and wood dust associated with nasal adenocarcinoma, but an independent effect of HCHO could not be isolated since most cases exposed to HCHO were also exposed to wood dust.	Luce et al. 1993
France	Case-control Cases: 296 with a cancer of the larynx and 201 with a cancer of the hypopharynx Controls: 296 diagnosed with non- respiratory cancers in the same hospitals or in similar hospitals nearby	Based on occupational histories. Probability of exposure classified as low (10%–50%), medium (50%–90%) or high (>90%), and level of exposure classified as low, medium or high (<308, 308–1,230, and >1,230 µg/m^3, respectively)	No association between HCHO exposure and cancer of the larynx. Medium or higher probability of HCHO exposure associated with an increased risk of cancer of the hypopharynx (OR 3.78, 95% CI 1.50–9.49 adjusted for age, smoking, alcohol consumption, coal dust exposure and asbestos exposure). Longer duration of exposure and higher cumulative exposure level also associated with increased risk.	Laforest et al. 2000

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TABLE 8. EPIDEMIOLOGICAL STUDIES OF FORMALDEHYDE EXPOSURE AND CANCER

Country	Design	HCHO exposure	Results	Reference
United States	Multi-centre case-control study Cases: 231 men and women aged 18 to 74 years with any type of nasopharyngeal cancer (NPC) Controls: 244, "frequency-matched" by age, gender and cancer registry, and identified by random-digit dialing Cases and controls were classified with respect to their exposure to formaldehyde and wood.	Based on occupational history. Probability of exposure classified as "definitively not or unlikely," "possible," "probable" or "definite," and exposure levels classified as low (8-hour time-weighed average <123 µg/m3), moderate (123 to <615 µg/m^3) and high (615 µg/m3 or higher)	"Probable" or "definite" exposure associated with increased risk of epithelial "not otherwise specified" (NOS) cancer (OR 3.1, 95% CI 1.0–9.6), but not other histological types of NPC. No dose–response relationship, but risk increased with duration of exposure (p for trend=0.036). "Definite" exposure increased the risk of squamous cell carcinoma and epithelial NOS (OR 13.3, 95% CI 2.5–7.0). No association between wood dust and NPC. (All ORs adjusted for age, gender, race, smoking, education and self vs. proxy surveys)	Vaughan et al. 2000

In France, 296 cases with a cancer of the larynx and 201 cases with a cancer of the hypopharynx were compared with 296 controls diagnosed in the same period with non- respiratory cancers in the same hospitals or in similar hospitals nearby. Exposure to several agents, including formaldehyde and wood dust, was assessed by occupational hygienists on the basis of occupational histories. Subjects' probability of exposure to each agent was classified as low (10%–50%), medium (50%–90%) or high (>90%), and level of each exposure identified was classified as low, medium or high (for formaldehyde: <308, 308–1,230 and >1,230 µg/m^3, respectively). No association was found between formaldehyde exposure and cancer of the larynx, while a probability of exposure to formaldehyde >50% was associated with an increased risk of cancer of the hypopharynx after adjusting for age, smoking, alcohol consumption, coal dust exposure and asbestos exposure (OR 3.78, 95% CI 1.50–9.49). After excluding subjects with probabilities of exposure <10%, longer duration of formaldehyde exposure and higher cumulative exposure level were also associated with an increased risk (Laforest et al. 2000).

A meta-analysis of formaldehyde exposure and sinonasal cancer has been published recently (Luce et al. 2002). Twelve case-control studies have been pooled, yielding a total of 195 cases with sinonasal adenocarcinoma, 432 cases with squamous cell carcinoma, and 3,136 controls. No significant association was found between formaldehyde exposure and squamous cell carcinoma, while an increased risk of nasal adenocarcinoma was found in men exposed to 0.31 to 1.23 mg/m^3 (OR 2.4, 95% CI 1.3–4.5) or >1.23 mg/m^3 (OR 3.0, 95% CI 1.5–5.7), and in women exposed to >1.23 mg/m^3 formaldehyde (OR 6.2, 95% CI 2.0–19.7), after controlling for age, study and cumulative exposure to wood dust and leather dust.

In 2004, IARC re-assessed formaldehyde and concluded that there was "sufficient evidence" that formaldehyde causes NPC in humans. Formaldehyde was therefore re-classified as "carcinogenic to humans."[1]

[1] *The full IARC Monograph was not published or available at the time this assessment report was written.*

5.3 Exposure Chamber Studies

Short-term effects of formaldehyde inhalation were investigated through controlled exposure in experimental chambers (Table 9).

Odor thresholds of 116 and 68 μg/m^3 were found respectively in 22 heavy-smoking women and 22 non-smoking women (age-matched) exposed to formaldehyde concentrations ranging from 9 to 1,230 μg/m^3; the difference between the two groups was statistically significant (Berglund and Nordlin 1992).

Nine healthy non-smokers were exposed to 3,690 μg/m^3 formaldehyde for 3 hours, during which they were engaged in intermittent physical exercise. Exposure to formaldehyde caused a significant increase of nose or throat irritation and eye irritation ($p<0.01$). Lung function was measured at 30-minute intervals; slight but significant decreases of FEV_1 and $PEF_{25\%–75\%}$ (2% and 7% respectively, $p<0.05$ compared to a control exposure with clean air) were observed after 30 minutes of exposure, but these differences were no longer apparent in later assessments. No change in bronchial responsiveness to methacholine was observed (Sauder et al. 1986). Nine non-smoking asthmatic volunteers were exposed to formaldehyde under a similar protocol; as in healthy volunteers, significant increases in nose and throat irritation symptoms ($p<0.05$) and eye irritation ($p<0.05$) were observed, but there was no significant change in lung function or bronchial responsiveness to methacholine (Sauder et al. 1987).

Twenty-two healthy subjects and 16 asthmatic subjects, all non-smoking, were exposed to both clean air and 3,690 μg/m^3 formaldehyde for 1 hour, in random order and separated by 1 week; subjects were not told of the exposure being performed. During exposure, healthy subjects were engaged in intermittent heavy exercise and asthmatic subjects were engaged in intermittent moderate exercise. Irritation symptoms and lung function were assessed at several time points during exposure. Mean symptoms scores for nose/throat irritation and eye irritation was significantly increased by formaldehyde exposure ($p<0.01$) in both healthy and asthmatic subjects. In healthy subjects, mean FVC and FEV_1 slightly but significantly decreased ($p<0.05$) at t=55 min during formaldehyde exposure, compared to the same time point in clean air exposure. No significant lung function change was observed in asthmatics (Green et al. 1987).

Fifteen healthy non-smokers were exposed to 0 and 2,460 μg/m^3 formaldehyde in a double-blind, random manner. The experience was repeated on a separate day with the subjects performing moderate physical exercise. Subjects exposed to formaldehyde experienced sore throat, nasal irritation and eye irritation. At rest, 8/15 subjects reported eye irritation during formaldehyde exposure, compared to 0/15 subjects during control exposure. No statistically significant change in lung function or in bronchial responsiveness to methacholine was observed either at rest or with exercise (Schachter et al. 1986). Fifteen asthmatics completed a similar protocol and experienced similar irritation symptoms; again, no significant decrease in lung function or increase in responsiveness to methacholine was observed (Witek et al. 1987).

Nineteen healthy non-smoking subjects were exposed to 0, 625, 1,230, 2,460 and 3,690 μg/m^3 formaldehyde, for 3 hours at each concentration, in a random order. Self-perceived irritation was reported as none, mild (present, but not annoying), moderate (annoying) and severe (debilitating). At 0, 615, 1,230, 2,460 and 3,690 μg/m^3, the proportions of subjects reporting mild eye irritation were 1/19, 0/10, 4/19, 6/19 and 5/9, and the proportions of subjects reporting moderate eye irritation were 0/19, 0/10, 1/19, 4/19 and 4/9; no subject reported severe irritation. Only mild nose and throat irritation was reported, with no dose–response relationship (Kulle 1993). Although the increase of eye irritation symptoms frequency was not statistically significant at formaldehyde concentrations below 2,460 μg/m^3, the fact that 5/19 subjects experienced symptoms at 1,230 μg/m^3, compared to 1/19 at 0 μg/m^3, indicate that a similar experience with a larger population size may find a significant effect at that level, and possibly below.

Eleven healthy subjects and nine patients occupationally exposed to formaldehyde and suffering from skin hypersensitivity to formaldehyde were exposed to 615 μg/m^3 formaldehyde for 2 hours in an inhalatio

TABLE 9. HEALTH EFFECTS OF FORMALDEHYDE–CONTROLLED INHALATION STUDIES

Subjects	Exposure	Outcome assessment	Results	Reference
9 healthy non-smokers	0 and 3,690 µg/m^3 for 3 hours, with intermittent physical exercise	Lung function measured at 30-minute intervals Bronchial challenge with methacholine Symptom questionnaires	Significant increase of nose or throat irritation and eye irritation ($p<0.01$). Slight but significant decreases of FEV_1 and $PEF_{25\%–75\%}$ (2% and 7% respectively, $p<0.05$) at t=30 min (differences were no longer apparent in later assessments) No change in bronchial responsiveness.	Sauder et al. 1986
9 non-smoking asthmatics	0 and 3,690 µg/m^3 for three hours, with intermittent physical exercise	Lung function measured at 30-minute intervals Bronchial challenge with methacholine Symptom questionnaires	Significant increases in nose and throat irritation symptoms ($p<0.05$) and eye irritation ($p<0.05$). No significant change in lung function or bronchial responsiveness.	Sauder et al. 1987
22 healthy subjects and 16 asthmatics, all non-smoking	0 and 3,690 µg/m^3 for 1 hour in a random order and separated by 1 week; subjects blind Healthy subjects engaged in intermittent heavy exercise and asthmatics engaged in intermittent moderate exercise.	Lung function measured and symptom questionnaires completed at 1=0, 17, 25, 47 and 55 minutes	Mean symptoms scores for nose/throat irritation and eye irritation increased ($p<0.01$) in both healthy and asthmatic subjects. In healthy subjects, mean FVC and FEV_1 slightly but significantly decreased ($p<0.05$) at t=55.	Green et al. 1987
15 healthy non-smokers	0 and 2,460 µg/m^3 double-blind, random manner. Experience repeated a separate day with the subjects performing moderate physical exercise.	Respiratory symptom questionnaire upon entry in the chamber, at 30 minutes of exposure, and 4, 18 and 24 hours later. Pulmonary function tests (FEV_1, FVC, PEF) before exposure, at t=5, 15, 25 and 40 minutes of exposure, and 10 and 30 minutes after the end of exposure Methacholine inhalation challenge before and after exposure	Increased number of subjects reporting eye irritation, both at rest (8/15 vs. 0/15) and during exercise (8/15 vs. 1/15). No statistically significant change in lung function or in bronchial responsiveness to methacholine.	Schachter et al. 1986

CONTINUED ON PAGE 20

TABLE 9. HEALTH EFFECTS OF FORMALDEHYDE–CONTROLLED INHALATION STUDIES

Subjects	Exposure	Outcome assessment	Results	Reference
15 asthmatics	0 and 2,460 µg/m^3 double-blind, random manner Experience repeated a separate day with the subjects performing moderate physical exercise.	Respiratory symptom questionnaire upon entry in the chamber, at 30 minutes of exposure, and 4, 18 and 24 hours later Pulmonary function tests (FEV_1, FVC, PEF) before exposure, at t=5, 15, 25 and 40 minutes of exposure, and 10 and 30 minutes after the end of exposure. Methacholine inhalation challenge before and after exposure	Increased number of subjects reporting eye irritation. No statistically significant change in lung function or in bronchial responsiveness to methacholine.	Witek et al. 1987
19 healthy non- smokers	0, 625, 1,230, 2,460 and 3,690 µg/m^3 for 3 hours in a random order	Questionnaires: self-perceived irritation was reported as none, mild (present, but not annoying), moderate (annoying) and severe (debilitating)	EYE IRRITATION HCHO Mild Moder. Severe 0 1/19 0/19 0 615 0/10 0/10 0 1,230 4/19 1/19 0 2,460 6/19 4/19 0 3,690 5/9 4/9 0 Only mild nose and throat irritation reported with no dose–response relationship.	Kulle 1993 Green et al. 1987
11 healthy subjects with normal IgE and negative skin prick tests to common allergens, and nine patients occupationally exposed to formaldehyde and suffering from skin hypersensitivity to formaldehyde	0 or 615 µg/m^3 for 2 hours in an inhalation chamber, separated by a 1- week interval Single-blind	Nasal lavages performed immediately before, immediately after, and 3 and 18 hours after exposure	Significantly increased number of eosinophils, and concentrations of albumin and total protein in nasal washing of both healthy and HCHO-sensitized subjects.	Pazdrak et al. 1993

chamber. Subjects were also exposed to clean air under a similar protocol, as a placebo, 1 week after or before exposure to formaldehyde. Nasal lavage was performed immediately before, immediately after, and 3 and 18 hours after exposure. Both healthy and sensitized subjects presented a significantly increased number of eosinophils, albumin and total protein in their nasal washing following formaldehyde exposure (Pazdrak et al. 1993). This is the only chamber study reporting subclinical inflammatory responses in the respiratory mucosa. Such changes appear to occur following short-term moderate exposure (615 µg/m^3) in healthy subjects.

All the irritation studies reviewed above included a control exposure and were theoretically "blind," since participants were not told what they were exposed to. However, the blinding may not have been complete, since the formaldehyde levels tested were far above the odor threshold of this compound. These studies showed some consistent patterns in that exposures between 2,460 and 3,690 μg/m^3 caused eye, nose and throat irritation, and that exposure to 3,690 μg/m^3 caused transient lung function changes in healthy subjects, but not in asthmatics. Inflammatory responses were observed at exposure levels lower than those causing subjective irritation symptoms. Only one study (Kulle 1993) included several exposure levels and was therefore suitable for the assessment of dose–response relationships. Based on this study, the NOAEL and LOAEL for eye irritation in humans are 615 and 1,230 μg/m^3, respectively.

5.4 Toxicological Studies

5.4.1 Short-term, sub-chronic and chronic toxicity

Inhalation studies of formaldehyde with animal models were reviewed recently under CEPA (Environment Canada, Health Canada 2001). Most short-term and subchronic studies in rodents have shown histopathological effects such as hyperplasia, squamous metaplasia, inflammation, erosion, ulceration, and disarrangements in the nasal cavity at concentrations of 3.7 mg/m^3 and above (NOAEL 1.2 mg/m^3). These histopathological effects appear to be a function of the formaldehyde concentration in inhaled air rather than of the cumulative dose.

Several chronic inhalation studies investigated the carcinogenic effects of chronic exposure to formaldehyde (6 hours/day, 5 days/week, for 2 years) in rats and mice. Two of these studies were particularly strong in design (Kerns et al. 1983; Monticello et al. 1996), having used several exposure levels and a large number of animals (90 to 150) per exposure level. Carcinogenicity studies consistently found an increased incidence of carcinomas of the nasal cavity at levels of 6.7 mg/m^3 or over; no such tumours were found at lower concentrations (up to 2.4 mg/m^3). The mechanisms of formaldehyde carcinogenicity have not been entirely elucidated, but regenerative proliferation following cytotoxicity appears to be "an obligatory intermediate step in the induction of cancer by formaldehyde" (Environment Canada, Health Canada 2001). The dose–response relationship between formaldehyde inhalation and cancer risk in humans was modelled by CIIT on the basis of the Monticello et al. (1996) study and morphological and physiological differences between animal models and humans. Based on this model, the predicted additional risks of upper respiratory tract cancer associated with an 80-year continuous exposure to levels of formaldehyde between 1.23 and 123 μg/m^3 ranged from 2.3×10^{-10} to 2.7×10^{-8} in non-smokers (CIIT 1999). More recently, a biologically based quantitative modelling of the relationship between formaldehyde inhalation and the development of nasal squamous cell carcinoma was carried out by Conolly et al. (2003) on the basis of the Kerns et al. (1983) and Monticello et al. (1996) data. The modelled amount of formaldehyde reaching target tissue was related with two carcinogenic mechanisms, namely direct mutagenesis and cytolethality-regenerative cellular proliferation (CRCP). The analysis suggested evidence of : 1) a CRCP mechanism with little or no involvement of direct mutagenesis; and 2) a J-shaped dose–response relationship between formaldehyde and squamous cell carcinoma.

5.4.2 Immunologic sensitization

Because of the allergic and respiratory effects associated with formaldehyde exposure in epidemiological studies, studies investigating allergic responses in animal models are of particular interest for the assessment of risks associated with indoor airborne exposure to formaldehyde. Two such studies were reviewed in the CEPA assessment:

Groups of mice were either not exposed to formaldehyde (controls), or exposed to 2 mg/m^3 formaldehyde, either 6 hours/day for 10 days, or to 6 hours/day once a week for 7 weeks. Then, all mice were sensitized

intranasally with ovalbumin. Following sensitization, titer of serum anti-ovalbumin IgE antibodies were significantly higher in mice exposed to formaldehyde 6 hours/day for 10 days, compared to mice exposed 6 hours/week for 7 weeks or untreated. The authors concluded that formaldehyde facilitates animal sensitization to ovalbumin through histological changes occurring in the upper respiratory tract (Tarkowski and Gorski 1995).

Guinea pigs were exposed to formaldehyde concentrations of 0 (controls), 160 or 310 $\mu g/m^3$ for 5 days, followed by sensitization to inhaled ovalbumin at days 5 and 19. On day 26, a bronchial provocation test with ovalbumin was performed, followed by repeated lung function measurements to monitor bronchial obstruction. Also, blood samples were taken on day 0 (before formaldehyde exposure) and day 25 (before bronchial provocation test), and tested for anti- ovalbumin IgG1 antibodies. Following ovalbumin challenge, 10/12 animals exposed to 310 $\mu g/m^3$ showed bronchial obstruction, compared with 3/12 control animals ($p<0.01$); animals exposed to 160 $\mu g/m^3$ were not significantly different from controls. Anti-ovalbumin IgG antibodies were not detectable (<10 ELISA units or EU) in any animal at day 0, but were detectable in 0/12 controls, 3/12 animals exposed to 160 $\mu g/m^3$, and 6/12 animals exposed to 310 $\mu g/m^3$ at day 25 (Riedel et al. 1996).

These findings indicate that the association observed in epidemiological studies between formaldehyde exposure and allergic responses and asthma is biologically plausible.

6. SUMMARY OF CRITICAL EFFECTS AND DERIVATION OF GUIDELINES

6.1 Short-term Effects

Based on human clinical studies and on animal experiments, the primary effects of acute exposure to formaldehyde are the irritation of the mucosa of the upper respiratory tract and the eyes.

Several studies assessed effects of short-term exposure to formaldehyde in healthy and asthmatic adults but only one of them (Kulle et al. 1993) included a range of exposure levels enabling the assessment of exposure–response relationship. In this study, the most sensitive effect was eye irritation: the LOAEL for this outcome was 1,230 $\mu g/m^3$ and the NOAEL was 615 $\mu g/m^3$. Another study (Pazdrak et al. 1993) found a subclinical inflammatory response at 615 $\mu g/m^3$, the only exposure level tested.

6.2 Chronic Effects Other Than Cancer

Epidemiological studies on the effects of chronic formaldehyde exposure consistently found respiratory and allergic effects at levels below 123 $\mu g/m^3$ (Krzyzanowski et al. 1990; Smedje et al. 1997; Garrett et al. 1999; Franklin et al. 2000; Smedje and Norback 2001; Rumchev et al. 2002).

In one of these studies (Garrett et al. 1999), formaldehyde levels in homes (96-hour samples collected four times over 1 year) were associated with increased risk of atopy, after ruling out confounding from other indoor air pollutants. In another study (Rumchev et al. 2002), formaldehyde levels (8-hour samples taken in summer and winter) were significantly associated with hospitalization for asthma in children aged 6 months to 3 years, again after ruling out confounding from other indoor air pollutants. No effects were found in children exposed to 10 to 29 $\mu g/m^3$ and 30 to 49 $\mu g/m^3$ formaldehyde, a non-significant increase of risk was observed at 50 to 59 $\mu g/m^3$ (OR 1.2) and a significantly increased risk was observed at 60 $\mu g/m^3$ (OR 1.39, $p<0.05$).
An association between low-level exposure to formaldehyde and the development of allergic sensitization and/or asthma is biologically plausible as it is consistent with observations in animals: formaldehyde-enhanced allergic sensitization to ovalbumin in mice and guinea pigs (Tarkowski and Gorski 1995; Riedel et al. 1996).
The observed dose–response relationship, the strong design of this study (especially the control of confounding variables) and the strong biological plausibility of the association observed make this study appear to be the most suitable for risk assessment because of extensive controlling for potential confounders. Based on its findings, long-term exposure to formaldehyde levels below 50 $\mu g/m^3$ appear not to be associated with adverse effects.

6.3 Cancer

There is evidence from toxicological and epidemiological studies that inhaled formaldehyde is carcinogenic; this effect appears to be limited to the nasal cavity (Environment Canada, Health Canada 2001). The IARC has classified formaldehyde as carcinogenic to humans (Group 1), based on sufficient evidence both in humans and in animals.

However, formaldehyde-induced carcinogenicity appears to be a consequence of proliferative regeneration following cytotoxicity (CIIT 1999; Environment Canada, Health Canada 2001). Based on a dose–response model developed by CIIT, the additional risk of respiratory cancer associated with a lifelong formaldehyde exposure ranging from 1.23 and 123 $\mu g/m^3$ in non-smokers ranged from 2.3×10^{-10} to 2.7×10^{-8} (Environment Canada, Health Canada 2001). The risk of cancer associated with formaldehyde levels sufficiently low to prevent irritation and inflammatory responses appears therefore to be negligible.

6.4 Proposed Guidelines

It is recommended that a guideline be established for short-term (1-hour averaged) exposures to formaldehyde at 123 μg/m^3 (100 ppb) (i.e. one tenth of the lowest concentration at which eye irritation was reported in the 1993 Kulle et al. controlled exposure study).

It is recommended that the guideline for long-term (8-hour averaged) exposure to formaldehyde be based on the NOAEL derived from the Rumchev (2002) case-control study of childhood asthma. Based on this study, the guideline would be 50 μg/m^3 (40 ppb). Although formaldehyde is probably carcinogenic to humans, the cancer risk associated with a lifelong exposure to that concentration of formaldehyde is estimated to be negligible.

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