

DISCUSSION PAPER

1. TITLE

Changes to the Occupational Exposure Limits for Formaldehyde

2. ISSUE

WorkSafeBC is considering whether to adopt the American Conference of Governmental Industrial Hygienists (“ACGIH”) Threshold Limit Value (“TLV”) for formaldehyde

3. BACKGROUND

In general, while occupational exposure limits (“OELs”) are established according to the TLVs adopted by the ACGIH, WorkSafeBC has the authority, in accordance with the provisions of section 5.48 of *Occupational Health & Safety Regulation (“OHSR”)*, to develop OELs for specific chemical substances that differ from the ACGIH TLVs. The excluded substances were listed in Prevention Policy R5.48-1 for the following reasons:

- The OEL for the excluded substance was more protective than the ACGIH TLV;
- The ACGIH had no TLV for the substance; or
- Industry was unable to meet the TLV.

Following a period of extensive consultation with stakeholders and research by WorkSafeBC staff, formaldehyde was deemed an excluded substance and placed in policy. It was established that industry could not meet the TLV. Accordingly, the OEL assigned to formaldehyde is less protective than the current ACGIH TLV.

4. DISCUSSION

In the summer of 2005, the Policy and Research (“PRD”) advised stakeholders that the Board of Directors (“BOD”) was considering adopting the ACGIH TLV for formaldehyde and requested feedback on what steps would need to be taken to achieve the proposed limit.

The table below shows the current OELs that are in effect in BC (both an 8-hour TWA and a Ceiling Limit) and the TLV (Ceiling Limit only) established by the ACGIH.

Table of Current WorkSafeBC OELs and ACGIH TLVs for Formaldehyde

Current WCB OELs (ppm)		ACGIH TLV (ppm)	
TWA	Ceiling Limit	TWA	Ceiling Limit
0.3	1.0	---	0.3

Formaldehyde is listed as a Group 1 carcinogen (“carcinogenic to humans”) by the International Agency for Research on Cancer (“IARC”) and a Group A2 carcinogen (“suspect human carcinogen”) by the ACGIH.

The PRD undertook a detailed assessment to determine if the current TLV recommended by the ACGIH for formaldehyde should be applied in BC workplaces, which included:

- a) Meetings with industry and labour representatives;
- b) Review of written submissions;
- c) Review of the literature on the health effects of formaldehyde;
- d) Comparison of occupational exposure limits, both nationally and internationally;
- e) Analysis of workplace exposure data collected by WorkSafeBC and other sources;
- f) Tour of a large plant which uses formaldehyde; and
- g) Analysis of WorkSafeBC claims data.

a) Meetings with Industry and Labour Representatives:

At the request of industry representatives, two meetings were held with staff from WorkSafeBC. The first occurred on September 30, 2005 with industry representatives and the second was held on February 5, 2006 with both industry and labour representatives (Appendix A).

b) Written Submissions

Industry and Employers:

Responses to the proposal to adopt the ACGIH Ceiling Limit for formaldehyde were received from 29 employer stakeholders, with the majority voicing strong opposition to the adoption of the ACGIH Ceiling Limit. Opposition was received primarily from the large-scale industrial users of formaldehyde (panel board industry, including plywood, particle / fibre board, oriented strand board and laminated wood producers), as well as from the chemical industry and industry associations. Other users, such as a university laboratory manager and a funeral home representative, were also opposed. Support for the adoption of the ACGIH Ceiling Limit received a smaller response and a number of these respondents either did not use, or were no longer using the substance, or used the substance on a small scale.

The primary reasons expressed by the employer group for opposing the adoption the ACGIH Ceiling Limit can be summarized as follows:

- Both the ACGIH and IARC have not kept current with recent toxicological and epidemiological evidence;
- There is a lack of substantive evidence that formaldehyde is a cancer-causing agent in humans and that it has been misclassified as a “human carcinogen” by IARC;
- BC already has some of the most stringent exposure limits for formaldehyde, both nationally and internationally;
- Implementation of the ACGIH Ceiling exposure limit in BC workplaces is not feasible;
- A competitive disadvantage would result for BC industries in favour of their counterparts in adjacent jurisdictions;
- At least one forest products (panel board) facility in the BC Interior would face closure. There may be other facilities facing closure that WorkSafeBC has not been apprised of.

A great deal of information was provided by the industry and employer representatives (Appendix A).

Labour:

Based on their single written submission, labour was in strong support of adopting the ACGIH TLV Ceiling Limit value. The submission is reviewed in Appendix A.

The primary reasons expressed by labour in support of their position include:

- WorkSafeBC should consider adopting the ACGIH 0.3 ppm Ceiling Limit, along with the sensitization and human carcinogen designation, in order to adequately protect workers since the current limits are too high;
- It is important for workers not to be exposed to short duration peak exposures above 0.3 ppm;
- A Ceiling Limit value of 0.3 ppm will protect workers from the adverse health effects of formaldehyde, including the cancer-causing effects;
- Wherever best practices are adopted, a Ceiling Limit is or can be met in BC industries.

c) Health Effects of Formaldehyde:

An extensive body of literature exists on both the acute and chronic health effects of this chemical. Much new information has become available since the late 1990s including a revised model for carcinogenesis, using formaldehyde as a focus. Several expert panels have recently re-evaluated the health effects of formaldehyde, including large cohort epidemiological studies. Details of these reports are discussed in Appendix B. A summary of the acute and chronic health effects is provided below.

Acute Health Effects:

The primary route of exposure of formaldehyde is through inhalation. There is no indication that the substance is absorbed to any extent through the skin.

Formaldehyde's adverse health effects are primarily related to its irritative or inflammatory properties. It is a highly reactive chemical that readily reacts with biological tissues, particularly the mucous tissues lining the respiratory tract and the eyes. Mucous tissues by nature are moist and characterized by a thin-walled cellular (epithelial) layer that is highly susceptible to chemical irritation. As a result of its reactivity, inhaled formaldehyde is rapidly and almost entirely absorbed by the mucous tissues lining the upper respiratory tract, penetrating no farther than the major bronchi of the respiratory tract at low or medium concentrations. The mucous tissues of the eyes are also a susceptible target. Neither formaldehyde nor its metabolic by-products accumulate to any significant extent in the body even at elevated ambient formaldehyde concentrations.¹

Localized irritation of mucous epithelial tissues by formaldehyde, if prolonged, can lead to localized tissue damage; basically the cytotoxic effects of formaldehyde may result in histopathological changes.² Evidence indicates that tissue damage in experimental

¹ NOTE: Formaldehyde exists naturally at very low levels in cells and tissues in plants, animals and humans, a result of normal metabolic processes.

² Cytotoxic = toxic to cells; histopathological = damage to the epithelial tissues, including reddening, sloughing of cells, leakage of plasma, bleeding, an increase in the number of cells (hyperplasia),

animals occurs at airborne formaldehyde concentrations above 4 – 6 ppm. Severe effects have been reported following exposure to very high concentrations (in excess of 50 ppm). These effects include pulmonary edema, pneumonia, and death as a result of the complete breakdown of the tissues lining the respiratory tract and the lungs.

Recent studies, involving testing of human response to airborne formaldehyde, indicate that due to the pungent and unpleasant odour of formaldehyde, it has been difficult to distinguish:

- a) mucous tissue irritation (localized changes to the cells and tissue) from
- b) chemosensory stimulation which involves stimulation of local nerve endings.

Chemosensory stimulation will not necessarily lead to cellular irritation and any histopathological changes. Earlier studies conducted on establishing levels of irritation experienced by test subjects failed to distinguish actual mucous tissue irritation from chemosensory irritation. Several expert panels have recently reviewed and researched this apparent dichotomy, and have concluded that cytotoxic effects of formaldehyde do not appear to occur at levels below 0.75 to 1.0 ppm formaldehyde. A level of 1.0 ppm is considered the no-observed-adverse-effect-level (NOAEL) for nasal injury in humans. This is further supported by the fact that at concentrations below 1.0 ppm, symptoms disappear very quickly, underlying the non-adversity of the irritating effects at low concentrations.

Appendix C provides further details on the chemical characteristics of formaldehyde, routes of entry, biochemical pathways, and adverse health effects associated with exposure to the substance.

Chronic Health Effects:

Evidence on the adverse effects in humans based on long term (chronic) exposures to formaldehyde is minimal. Information on chronic health effects is based almost entirely on animal studies. Repeat dose inhalation studies have been conducted on mice, rats and monkeys. Cellular (histopathological) changes are observed in all species with slight damage to the tissues of the nose and upper respiratory tract at concentrations at 2 – 3 ppm, with more pronounced damage at levels up to approximately 6 ppm. Severe cellular damage to respiratory tract tissue – severe rhinitis, tissue death and extensive hyperplasia³ – occurs at concentrations 6 ppm and above. The no-observed-adverse-effect-level (NOAEL) for respiratory tract irritation in experimental animals is claimed to be in the 1 – 2 ppm range. A level of 1.0 ppm is considered the NOAEL for injury to the nasal passages in humans.

Mutagenicity & Carcinogenicity:

IARC has evaluated formaldehyde and determined that there is sufficient evidence that formaldehyde be classified as a human carcinogen. On the other hand, the ACGIH has determined that formaldehyde is not a proven human carcinogen but a suspect human carcinogen. This is also the conclusion of a number of other jurisdictions and reference organizations, as detailed in Appendix B.

change in cellular composition (metaplasia), and a breakdown of cellular components, leading to cellular death.

³ A general term for an increase in the number of the cells of an organ or tissue due to a number of causative factors including, increased demand, chronic inflammatory response, and other triggers.

According to current information, formaldehyde is shown to be genotoxic agent⁴ at concentrations that cause severe tissue damage. This is primarily due its activity as a reactive alkylating agent⁵ and like other alkylating agents, a likely candidate for being a mutagen or a carcinogen. Accordingly, formaldehyde is classified as a mutagen and also a potential carcinogen.

More specifically, it has been shown that while formaldehyde is clearly an experimental animal carcinogen of the upper respiratory tract, it is not of any other tissues or organs; that is, tissues must be in direct contact with formaldehyde in order to induce tumorous growth. Hence, its systemic effects (e.g., liver, kidneys and other organs and tissues at distance from the site of contact) are negligible when the route of entry is via the respiratory tract. Nasal tumours most probably arise as a consequence of pronounced localized chronic tissue irritation of the nasal passages in association with genotoxic effects at the cellular level – a “site-of-contact” effect. Genotoxic effects include the formation of DNA-protein cross-links and other indicators of genetic damage.

As detailed in Appendix B, several expert panels recently re-evaluated the epidemiological studies conducted in the 1980s and early 1990s – including the cohort studies on which IARC has based its conclusions. The expert panels conclude that the evidence falls short in providing conclusive proof that formaldehyde exposure results in nasopharyngeal cancer in humans. Accordingly, jurisdictions, such the United Kingdom and German occupational health and safety authorities and the European Scientific Committee on Occupational Exposure Limits (“SCOEL”), have classified formaldehyde as a suspect human carcinogen similar to the ACGIH due to the insufficiency of the evidence for cancer induction in humans but that it is capable of inducing cancers in experimental animals.

Reproductive Toxicity:

There is no evidence that formaldehyde is a reproductive toxicant.

Sensitization:

In humans, formaldehyde is classified as a skin sensitizer due to its direct irritative effects on tissues and its ability to induce an immune response at the site of contact.

Formaldehyde is not considered a significant cause of occupational asthma. Experimental evidence shows that exposure of asthmatic individuals to formaldehyde does not change the nature or status of the asthmatic condition.

Summary of the adverse health effects of formaldehyde:

Figure 1 summarizes current knowledge on the adverse health effects and carcinogenic potential of formaldehyde in experimental rats and humans relative to airborne exposure levels. An “effect level” – as shown in the figure 1 – is a response elicited by an experimental rat or human relative to the concentration in air, and includes eye irritation, nasal irritation, level of tolerance (human), and cytotoxic and carcinogenic responses. The term “subjective” in the figure is a verbal or similar communicative response by the human subject to the tester (“I can smell / detect formaldehyde”); an “objective” response is one that can be measured and quantified such as a record of the rate and

⁴ Toxic to the genetic material of the cell including DNA.

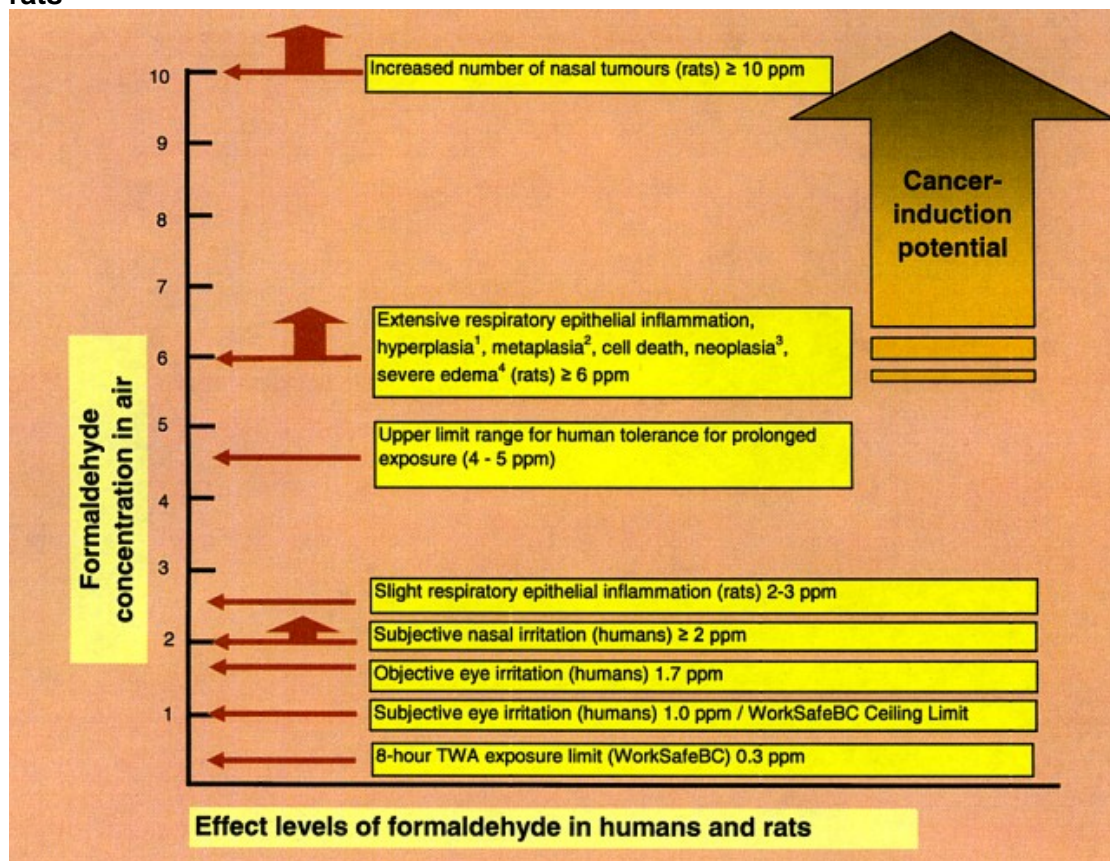
⁵ A chemical that acts on the genetic material in the nucleus of the cell – deoxyribonucleic acid (DNA), causing mutagenic or carcinogenic effects.

frequency of blinking. An objective response is far superior, scientifically, to a subjective response.

Of note is that formaldehyde levels in air must be above 6 ppm in order to initiate the growth of tumours – both benign and cancerous. At concentrations at 10 ppm and greater, cancerous tumours are well established. Humans are not able to tolerate levels of exposure to airborne formaldehyde above 4 – 5 ppm.

WorkSafeBC’s current Ceiling Limit of 1.0 ppm is at the subjective eye irritation level and below the objective eye irritation level of 1.7 ppm for humans. The current TWA of 0.3 ppm is significantly lower than both subjective and objective eye irritation levels and below nasal irritation levels based on the most current experimental information.

Figure 1: Summary of effects levels of formaldehyde in humans and experimental rats



- ¹ Means an increase in the number of cells of an organ or tissue.
- ² Means the replacement of one cell type with a differentiated cell type – usually due to chronic irritation and inflammation; it is reversible and a natural protective response allowing the substitution of cells that are better able to survive where a more fragile cell type is likely to succumb.
- ³ Means abnormal disorganized growth in a tissue or organ; also known as a tumour which may be either benign or malignant.
- ⁴ Edema = severe rhinitis (“a very runny nose”).

d) OELs for Formaldehyde in BC and Other Jurisdictions

Regulated occupational exposure limits for formaldehyde from all Canadian as well as American and international jurisdictions are portrayed in Table 1.

Table 1: Current and Scheduled Regulated OELs for Formaldehyde: Canadian and Other Jurisdictions

<i>Jurisdiction</i>	<i>8-Hour TWA (ppm) or equivalent</i>	<i>Short-Term Exposure Limit – STEL (ppm) or equivalent</i>	<i>Ceiling Exposure Limit – “C” (ppm) or equivalent</i>
<u>Canadian Jurisdictions</u>			
<i>ACGIH⁶</i> <ul style="list-style-type: none"> • <i>Manitoba</i> • <i>Nova Scotia</i> • <i>PEI</i> • <i>Newfoundland and Labrador</i> 			0.3
<i>Alberta</i>	0.75		2
<u>British Columbia</u>	0.3		1
<i>New Brunswick</i>	0.5		1.5
<i>Northwest Territories⁷</i>			0.3
<i>Ontario</i>	1	2	
<i>Effective December 31, 2007</i>		1	1.5
<i>Québec</i>			2
<i>Saskatchewan</i>			0.3
<i>Yukon</i>	1	2	
<i>Canada Labour Code (Federally regulated workers)</i>			0.3
<u>American Jurisdictions</u>			
<i>California</i>	0.75	2	
<i>Oregon</i>	0.75	2	
<i>Washington State</i>	0.75	2	
<u>International Jurisdictions</u>			
<i>Germany⁸</i>	0.3	0.6	1

⁶ These four jurisdictions automatically adopt the annual ACGIH TLV updates.

⁷ Based on the 2001 TLVs issued by the ACGIH.

⁸ The Deutsche Forschungsgemeinschaft (DFG) endorses this MAK Commission value. Note: the STEL and Ceiling Limit values indicated are based on DFG's protocol for establishing these values (multipliers).

Jurisdiction	8-Hour TWA (ppm) or equivalent	Short-Term Exposure Limit – STEL (ppm) or equivalent	Ceiling Exposure Limit – “C” (ppm) or equivalent
United Kingdom	2	2	
Netherlands⁹	1	1.5	
France	0.5	1	
Switzerland	0.5	1	
Norway	0.5	1.5	1
Sweden	0.5		1
Finland	0.3		1
Denmark			0.3
Australia	1	2	
New Zealand			1

TWA: the time weighted average (TWA) concentration of a substance in air which may not be exceeded over a normal 8 hour work period.

STEL: the time weighted average (TWA) concentration of a substance in air which may not be exceeded over any 15 minute period, limited to no more than 4 such periods in an 8 hour work shift with at least one hour between any 2 successive 15 minute excursion periods.

Ceiling: the concentration of a substance in air which may not be exceeded at any time during the work period.

With respect to establishing an OEL, much new information has come forth over the last 6 to 8 years as a number of jurisdictions have completed their reviews on formaldehyde, or are currently in the process of considering appropriate exposure limits for formaldehyde – be it an 8-hour TWA, a Short Term Exposure Limited (“STEL”), or Ceiling Limit, or a combination of the three. Quebec and Germany have completed their reviews as have Australia, the United Kingdom, Holland and the Nordic nations.

As Table 1 indicates, a Ceiling Limit of 0.3 ppm with no 8-hour TWA limit has been adopted in Denmark, and in several Canadian jurisdictions, including Manitoba, Saskatchewan, Nova Scotia, Newfoundland, PEI and the Northwest Territories, as well as for federally regulated workers. Quebec has a Ceiling Limit of 2 ppm with no 8-hour TWA limit. All other provinces and other jurisdictions shown have a combination of 8-hour TWAs, STELs and Ceiling Limits.

BC, along with Finland and Germany have the lowest 8-hour TWAs at 0.3 ppm. Germany and the Nordic countries along with BC enforce a Ceiling Limit of 1.0 ppm. Ontario is currently has a TWA of 1.0 ppm and STEL of 2.0 ppm which came into effect

⁹ Not legally binding at this time; under review; an 8-h TWA of 0.5 ppm and STEL of 1 ppm is being considered.

March 31, 2006. Effective December 31, 2007, Ontario will forego the TWA limit and adopt a more protective STEL (dropping from 2.0 to 1.0 ppm). They will also adopt a Ceiling Limit of 1.5 ppm.

US jurisdictions neighbouring BC prescribe less protective OELs. Washington State and Oregon enforce an 8-hour TWA of 0.75 ppm and a STEL of 2.0 ppm; no Ceiling Limit is prescribed.

Overall, BC has one of the lowest 8-hour TWA OELs among the major jurisdictions along with a Ceiling Limit OEL that is also among the lowest. A Ceiling Limit of 1.0 ppm is more protective than a STEL of 1.0 ppm. Hence, notwithstanding the jurisdictions that have adopted the ACGIH Ceiling Limit TLV, the current OELs in BC are some of the most protective in all jurisdictions.

The German occupational health and safety authority takes the position that formaldehyde does not significantly contribute to human cancer provided the MAK value (8-hour TWA) of 0.3 ppm is observed and the Ceiling Limit of 1.0 ppm is not exceeded.

Several reference agencies, including the German MAK Commission and the Working Group on Action to Control Chemicals (“WATCH”) Committee of the UK Health & Safety Executive, make the following observations:

- IARC’s classification of formaldehyde as a human carcinogen is not supported;
- IARC has been selective in their review; a number of epidemiological studies not supportive of IARC’s position were not included in their 2004 report;
- The avoidance of cellular damage and sustained regenerative proliferation are decisive factors for establishing an appropriate exposure limit;
- In the low dose range – less than 1.0 ppm – the toxic effects of formaldehyde on the genetic material (“genotoxic effect”) play only a minimal role in its carcinogenic potential so that no significant contribution to human cancer risk is expected in the low dose range;
- Cancer risk factors become of concern only when formaldehyde levels exceed 2 – 3 ppm on a chronic or long term basis;
- With respect to the strong and pungent odour of formaldehyde, the ACGIH did not distinguish sensory stimulation from cellular irritation in their recommendation of a 0.3 ppm TLV Ceiling Limit; and
- Eye irritation – which can be measured and quantified experimentally – unlike nasal irritation, is considered the most appropriate indicator of the irritative nature of formaldehyde and a more objective determinant of an appropriately assigned exposure limit.

The reference agencies, based on recent re-evaluations of the scientific literature on controlled nasal and eye irritation studies, conclude that a level of 1 ppm avoids eye irritation in a majority of test subjects and that nasal irritation is avoided if formaldehyde concentrations are kept below 2 ppm. As a result, airborne levels of formaldehyde below 1 ppm are considered low enough to protect workers against nasal tissue damage, and consequently, also against a potential risk of nasal cancer. In consideration of these factors, an 8-hour TWA of 0.3 ppm was adopted in Germany. Furthermore, Paustenbach *et al.* 1997 concluded that a level of 1 ppm formaldehyde would avoid eye irritation in at least 75% and up to 95% of exposed workers. In another very recently published report, Arts *et al.* 2006 re-evaluated eye and nasal irritation data and concluded that when minimal/mild/slight irritation is taken as a cut off level, eye and

nasal irritation were found at formaldehyde levels of greater than or equal to (\geq) 1 ppm and \geq 2 ppm, respectively.

Additional information pertaining to the findings of the reference agencies can be found in Appendix B.

e) Worker Exposures to Formaldehyde in British Columbia and other Locations:

Sampling data collected by WorkSafeBC over a period of 15 years (1990 to 2005 inclusively) indicate that worker exposure to formaldehyde is likely to occur primarily in the forest panel board manufacturing sector (plywood, particle / fibre board, oriented strand board, laminated wood products manufacturing), resin manufacture, acute care hospitals, university and other laboratories, and funeral homes. A compilation of compliance sampling data collected by WorkSafeBC over this time frame is included in Appendix D along with exposure data from other sources, including Ontario, Quebec, and the Netherlands.

The exposure data indicates that overall, exposure levels have decreased over time as improved control and procedural measures have been implemented. This is particularly evident when one compares readings taken in the early 1980s are compared with those in the late 1990s.

The results indicate that industries in which exposure levels were predominantly below the current 0.3 ppm 8-hour TWA exposure limit include:

- Foundries;
- Resin manufacturing; and
- Plywood manufacturing.

Industries in which the current 0.3 ppm 8-hour TWA exposure limit was exceeded at times include (range of exposures shown):

- Paperboard & cardboard manufacturing (0.04 – 0.38 ppm);
- Laminated wood products manufacturing (0.24 – 0.38 ppm);
- Pressed / panel particle / fibre board manufacturing (0.07 – 5.00 ppm);
- Oriented strand board manufacturing (0.03 – 0.32 ppm);
- Funeral homes (none detected to 0.74 ppm);
- University laboratories (0.52 – 1.15 ppm);
- Hospitals & medical clinics and laboratories (0.02 – 1.35 ppm); and
- Poultry hatcheries (0.1 – 0.35 ppm).

In 2004, Quebec's Institute de Reserche Robert Sauvé en Santé et en Sécurité du Travail (IRSST) published a report on the health impact of formaldehyde in the workplace, at a cost of approximately \$1 million, with specific focus on the panel board industry, namely oriented strand board, medium density fibre board, particle board plants. This study demonstrates a similar worker exposure pattern to formaldehyde as seen in BC panel board plants. Proximity to the press (a key component of the panel board process and found in all plants) resulted in exposures in excess of 0.3 ppm, at times exceeding 1.0 ppm or more. In general, exposures were highest in particle board and medium density fibre board plants – generally in excess of the 8-hour TWA exposure limit of 0.3 ppm.

In order to determine if the Ceiling Limit for formaldehyde is being exceeded an electronic instrument capable of instantaneous read-out must be used. The historical data presented in this report is based on sampling equipment that is limited to providing only time-weighted-average (TWA) readings. Datalogging electronic equipment was not available for use as personal exposure monitors for formaldehyde until very recently.¹⁰

As such, all of the 500+ data points of WorkSafeBC's exposure data are TWAs of varying duration – from 10 to approximately 480 minutes (8-hour). In essence, a STEL is a 15 minute TWA. TWA readings are an integrated average of all the readings within the defined sampling period. TWA readings just below the Ceiling Limit value (1 ppm) will typically include spikes or excursions above 1 ppm; these spikes will not be recorded, however.

f) Plant Tour:

WorkSafeBC staff (occupational hygienists from the Policy and Research Division and the Worker and Employer Services Division) conducted a walk-through survey of a medium density fibre board plant. Details of the survey are provided in Appendix B.

g) WorkSafeBC Compensation Claims Data – Formaldehyde Exposure:

A review of WorkSafeBC's data on occupational disease claims over the period of 1990 to 2005, inclusively, indicates that about 26 claims were classified as being formaldehyde-related. Most of the claims appear to be associated with exposures sustained during spills of formaldehyde solutions (formalin), and exposures to formaldehyde-based resins and adhesives, resulting in localized skin irritation, possible allergic contact dermatitis, and upper respiratory tract irritation, as a result of skin contact or inhalation of formaldehyde vapours, respectively. None of the claims appear to be the result of chronic (long term) exposure to airborne formaldehyde. The Quebec Commission on Health and Occupational Safety report similar findings on formaldehyde-related claims for Quebec workers.

There are no recorded incidences of upper respiratory tract cancers recorded for workers in BC that can be causally linked to formaldehyde exposure.

5. OPTIONS AND IMPLICATIONS

Based on the analysis of findings, two options for exposure limits for formaldehyde in BC workplaces have been developed:

Option 1 – Status Quo

Under this option the 8-hour TWA limit and Ceiling Limit would remain the same at 0.3 and 1.0 ppm, respectively.

¹⁰ More recently, personal monitoring equipment capable of datalogging real-time exposure data including peak transient exposures has become commercially available (cost estimate: US\$4000+ ea).

Implications:

- Under this option BC's current exposure limits for formaldehyde would remain among the lowest of the currently regulated exposure limits in the western industrialized world;
- The current exposure limits would remain lower than the exposure limits in place at proximate jurisdictions including Alberta, Washington State, Oregon and California;
- The current exposure limits would remain lower than those imposed by other Canadian jurisdictions with a significant panel board industry, including Ontario and Quebec;
- BC has a similar 8-hour TWA limit and Ceiling Limit to that adopted in Germany where the OELs for formaldehyde were recently reviewed;
- A substantial body of scientific evidence indicates that BC's current exposure limits will protect workers from the adverse health effects of formaldehyde;
- According to a majority of expert panels, BC's current Ceiling Limit of 1.0 ppm is protective from the irritative properties of formaldehyde, providing an acceptable margin of safety;
- WorkSafeBC's current Ceiling Limit of 1.0 ppm is at the subjective eye irritation level and below the objective eye irritation level of 1.7 ppm for humans. The current 8-hour TWA of 0.3 ppm is significantly lower than both subjective and objective eye irritation levels and below nasal irritation levels based on the most current experimental information;
- This option will simplify exposure monitoring of workers allowing the use of standard occupational hygiene sampling methods that measure time-weighted-average (TWA);
- Employer representatives – particularly from the forest products / panel board sector – would likely support this option; and
- Organized labour would likely not support this option.

Option 2 – Adopt the Ceiling Limit recommended by the ACGIH

Under this option, the current 8-hour TWA limit would be withdrawn, and the Ceiling Limit reduced from 1.0 to 0.3 ppm.

Implications:

- Adoption of a Ceiling-only exposure limit would place BC, along with Manitoba, Nova Scotia, Prince Edward Island, Northwest Territories, Newfoundland / Labrador and Denmark, among those jurisdictions with the lowest exposure limit among all western industrialized nations;
- The ACGIH is the only organization that has recommended an exposure limit based solely on a Ceiling-based exposure limit; the other four reference organizations, namely the Dutch Expert Committee (DECOS), the German MAK Commission, the European Union Scientific Committee for the Occupational Exposure Limits to Chemical Agents (SCOEL), and the Australian National Industrial Chemicals Notification and Assessment Scheme (NICNAS) Committee have recommended both 8-hour TWA OELs and STELs for formaldehyde;
- Fibre and particle board plants will not be able to comply with this option due to the limitations placed on the operations by a Ceiling-only exposure limit. Currently, full shift exposures can approach the current 8-hour TWA exposure limit of 0.3 ppm; the most transient of exposures, including spikes of several seconds or less above 0.3 ppm, would place the plant in non-compliance;

- The Funeral home industry and medical facilities will find it difficult to comply with this option. Exposures typically are of short duration; opening a container of formalin is likely to result in an exposure exceeding a momentary spike of 0.3 ppm;
- Employer representatives – particularly from the forest products / panel board sector – will likely not support this option; and
- Organized labour will likely support this option.

6. RECOMMENDATION

The PRD recommends Option 1 which is to retain the 8-hour TWA limit of 0.3 ppm and a Ceiling Limit of 1.0 ppm.

Formaldehyde is an important industrial chemical used worldwide in the manufacture of resins, particle, fibre and oriented strand boards, plywood, leather goods, paper, pharmaceuticals and a myriad of other products. Formaldehyde has been exceptionally well studied, particularly over the last decade, and health effects have been well defined in terms of specifying a safe level of exposure for both workers and the public. The current 8-hour TWA and Ceiling Limits provide an adequate level of protection for workers exposed to the substance as long as effective control measures are in place.

7. CONSULTATION

Stakeholders are invited to provide feedback on this discussion paper.

Stakeholder comments will be accepted until 4:30 pm on Friday, June 29, 2007. When responding, please provide:

- your name;
- your e-mail address;
- whether your feedback is on your own behalf, or on behalf of an organization (please provide the name of the organization);
- whether you are responding from a worker's perspective or an employer's perspective; and
- whether you generally agree, are neutral, or disagree with the recommendation.

Comments may be sent via the online survey, mail, fax, or email to:

By [online survey](#)

By mail: Formaldehyde OEL
Policy and Research Division
WorkSafeBC
P.O. Box 5350, Stn. Terminal
Vancouver, BC V6B 5L5

By fax: 604 279-7599

By email: regquery@worksafebc.com

WorkSafeBC's governing body, the Board of Directors, will consider the comments submitted by stakeholders before making a decision.

Please note that all comments become part of the Policy and Research Division's database and are releasable under the *Freedom of Information and Protection of Privacy Act*.

Appendix A – Stakeholder Consultation and Feedback

Following the notification letter sent to stakeholders in August 2005 the PRD received numerous responses from both labour and employer representatives. All responses, except one, were received from the employer group. Table A1 summarizes the responses by the representatives from various industries and organizations as well as from small or independent employers such as photography processing labs, funeral homes. Responses were received by email as well as by mail. The industry association along with the chemical / resin & coatings manufacturers and panel board industry collectively provided a very comprehensive package of information on the health effects of formaldehyde, including critical reviews of the scientific literature. One written submission was received from labour.

The majority of the submissions were not in support of adopting the ACGIH Ceiling Limit of 0.3 ppm with no prescribed 8-hour TWA limit.

Table A1: Consultation Submissions – by Industry, Associations and Independent Employers. Responses: those that Approve, Oppose, or have a Neutral Response to the Adoption the ACGIH TLV

<i>Industry, Organizations, Small / Independent Employers</i>	<i>Opposed</i>	<i>Approve</i>	<i>Neutral</i>
<i>Panel board including: plywood, particle board, oriented strand board; laminated wood</i>	5	1	
<i>Resin & Coatings Manufacture</i>	2	1	2
<i>Chemical Manufacturing</i>	1	1	
<i>Industry / Employer Association</i>	7		
<i>Miscellaneous¹¹</i>	2	2	5
<i>Labour Organization</i>		1	
<i>Total</i>	17	6	7

Meetings with Stakeholders

Meetings with Industry Representatives:

At the request of industry representatives, two meetings were held with staff from the PRD. The first occurred on September 30, 2005 and the second was held on February 5, 2006.

¹¹ Includes photo labs, funeral homes, mortuaries, veterinary clinics, poultry hatcheries, universities, foundries.

Appendix A – Stakeholder Consultation and Feedback

September 30, 2005 Meeting:

Representatives of the following forest products sector, chemical manufacturers and industry associations attended:

Composite Panel Association
Hexion Specialty Chemicals, Inc.
Western Fraser Timber Co. Ltd.
Northern Engineered Wood Products Inc.
Engineered Wood Association (APA)
CanPar Industries
Canadian Plywood Association
Dynea Inc.
Methanex Corp.
Formaldehyde Council Inc.

Representatives came from BC, Quebec, Ontario, Washington State and Ohio. The delegation provided an overview of the industry's position on the health effects of formaldehyde with a critique of ACGIH's rationale for establishing the Ceiling Limit TLV for formaldehyde. An extensive number of supportive studies were distributed. These are reviewed in Appendix B.

February 5, 2006 Meeting

The second meeting provided an opportunity for the industry representatives to discuss details of the earlier meeting with worker representatives.

Employer representatives:

Composite Panel Association
Hexion Specialty Chemicals
Western Fraser Timber Co. Ltd.
Northern Engineered Wood Products Inc.
Engineered Wood Association (APA)
CanPar Industries
Canadian Plywood Association
Dynea Inc.

Worker representatives:

BC Federation of Labour
IWA / Steelworkers Union
BC Nurses Union
Construction Industry Training Institute, Building Trades

The industry representatives maintained that the basis for carcinogenicity of formaldehyde to humans is not well founded, and that the epidemiology is inconsistent in demonstrating causality as to the types and patterns of cancers associated with formaldehyde. They mentioned that the National Cancer Institute ("NCI") – in response to recent criticism from the scientific community – is planning to re-evaluate earlier cohort studies on the association of nasopharyngeal cancer and formaldehyde in workers.

Both labour and industry representatives discussed the feasibility of achieving compliance if the ACGIH Ceiling Limit is adopted. Industry representatives maintained

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that the panel board and plywood industry would likely not be able to achieve compliance with an exposure limit based solely on a ceiling limit value. Labour offered the comment that users such as hospitals would likely be able to comply.

A Review of the Submissions

Generally, employers would like to retain the current status as an excluded substance with an 8-hour TWA of 0.3 ppm and Ceiling Limit of 1.0 ppm. Worker representatives would like to see the ACGIH Ceiling Limit of 0.3 ppm adopted with no specified 8-hour TWA limit. Salient points of submissions from both parties are outlined below.

Worker Submissions

In a written submission by the BC Federation of Labour, labour's position remains in support of the ACGIH Ceiling Limit of 0.3 ppm for formaldehyde. The submission, dated March 23, 2006 entitled: *Formaldehyde OEL*, reports the following:

- It is important to avoid short duration peak exposures above 0.3 ppm;
- The rationale for limiting exposure to below 0.3 ppm is due to the increased risk of both acute and chronic respiratory effects as well as the need to minimize the risk of a carcinogenic effect;
- The health effects of exposure to formaldehyde above 0.1 ppm TWA and peak exposures (ceiling limits) over 0.3 ppm are well documented in the literature;
- Levels of exposure above 0.1 ppm cause irritant effects and short duration exposures above 0.3 ppm induce pathological effects that increase risk of cancer;
- In a study at a plywood plant it has been shown that where workers were exposed to levels above 0.8 ppm asthma symptoms increased;
- Peak exposures below 0.3 ppm are identified as necessary to prevent histological damage which will increase the risk of nasopharyngeal cancer, the target area of this known human carcinogen; and
- WorkSafeBC must adopt the ACGIH 0.3 ppm Ceiling Limit, along with the sensitization and human carcinogen designation, as well as the as-low-as-reasonably-achievable ("ALARA") requirement.

Labour's concern about the health effects of formaldehyde is not limited to the forest products industry. Concern is also expressed about protecting the health of workers who may also be exposed to high formaldehyde levels in the health care industry. Labour's submission offers the following comments regarding the achievability of a 0.3 ppm Ceiling Limit by industry:

- Formaldehyde exposure in various industries has been steadily reduced over the years;
- Data from major users – including plywood manufacturers in the US, indicates that 25 years ago levels were in the 0.35 to 0.38 ppm range; these levels are now lower;
- A study on Quebec particleboard plants indicate levels are below or near 0.1 ppm and below the 0.3 ppm ceiling in many locations, and that levels measured in New Zealand plants had a geometric mean of 0.06 ppm, well below the proposed exposure limits.

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They conclude that whenever best practices are adopted the proposed limits are or can be met in BC industries. The report states that “determining achievability must be based on best practices, not on the worst ones”.

With respect to achieving compliance, labour would have no concerns:

- With employers applying for a variance from WorkSafeBC if individual plants have difficulty achieving the proposed Ceiling Limit and can demonstrate that they cannot comply;
- With the use of respiratory protection, as opposed to engineering controls, to protect the most highly-exposed workers assigned to areas where compliance with the Ceiling Limit may not be achievable (e.g. press operators, maintenance workers) and where a variance from WorkSafeBC has been obtained.

Employer Submissions

In several written submissions, including a PowerPoint presentation at the September 2005 meeting with PRD staff, spokespersons for the associations and a number of individual companies representing the forest products industry acknowledged that there is a need to ensure that the exposure limit defined for formaldehyde provides an appropriate level of short- and long-term health protection for workers in BC, but that there is also a need to ensure that the cost of complying with a regulation does not threaten the industry's competitive position, either with respect to its Canadian counterparts or its significant export markets, particularly the US.

The concerns raised by the employers fall into three distinct categories: health issues, economic issues, and technical issues, as follows:

a) *Overriding perspective*

- The weight of scientific evidence does not indicate that lowering the standard from the current OELs would provide any further measure of worker protection;
- BC's OELs are among the lowest in any jurisdiction;
- A Ceiling Limit of 0.3 ppm is unnecessarily low, economically and technically impossible to meet;
- Adoption of the 0.3 ppm Ceiling Limit may result in major plant closures and job losses in BC.

b) *Health Issues*

- Formaldehyde is produced by the human body as part of normal metabolic processes;
- It is a natural by-product of all life forms, including plants;
- ACGIH seeks to eliminate virtually all sensory/discomfort effects with the 0.3 ppm Ceiling Limit;
- Concerns with sensory irritation are addressed by WorkSafeBC's existing 8-hour TWA and Ceiling Limit;
- Quebec's IRSST 2004 study on formaldehyde, commissioned by the Quebec Commission of Health & Safety – CSST, is a significant contributor in understanding the irritation threshold and sheds new light on earlier studies conducted in the 1980s and which formed the basis for ACGIH's current TLV. This study examined more than 2,000 workers in the wood products

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- manufacturing industry in Quebec and concluded that an exposure level below 0.75 ppm would not provide improved health protection to workers;
- The stakeholders note that the ACGIH recommendation of a Ceiling Limit of 0.3 ppm was based on even the mildest irritation, and that the ACGIH did not consider the quality of the studies;
 - They point out that other researchers have concluded that sensory irritation at levels below 1.0 ppm is often difficult to distinguish from responses experienced in controls;
 - Reports of irritation below 0.3 to 0.5 ppm were too unreliable to attribute to formaldehyde alone;
 - Eye irritation does not become significant until at least 1.0 ppm is reached;
 - They pointed out that the IRSST concluded that a ceiling value of 1 ppm for 15 minutes was appropriate to prevent moderate, although transitory, eye irritation;
 - The stakeholders referred to a very recent study by researchers (Arts *et al*, 2006) from the Netherlands Organization for Applied Scientific Research (TNO) published March 2006 which evaluated sensory irritation relative to carcinogenicity regarding inhaled formaldehyde and pointed out the following factors;
 - The subjectively measured sensory irritation threshold levels in humans were assessed relative to findings obtained in animal studies;
 - Using Benchmark Dose Analysis it was estimated that at 1 ppm, 9.5% of healthy volunteers experienced moderate (i.e., annoying) eye irritation;
 - Subjective testing does not exclude the perception factor or trigeminal nerve stimulation (this is distinguished from actual irritation – it is merely that the subject detects the presence of formaldehyde); this is an important consideration in that formaldehyde has a very strong odour;
 - Furthermore, respiratory tract irritation can be either a localized pathophysiological response to a chemical (direct localized effect) or a chemosensory effect – interaction with local nerve endings (*nervus trigeminus*) – the trigeminal effect;
 - Trigeminal stimulation will not necessarily lead to cellular or tissue damage;
 - In several of the studies assessed, the control or “0” ppm test condition was missing;
 - Based on long-term inhalation studies in animals, a level of 1 ppm is considered the no-observed-adverse-effect-level (NOAEL) for nasal injury;
 - They conclude that at levels less than 1 ppm where the prevalence of sensory irritation is minimal both in incidence and degree, risks of respiratory tract cancer are considered to be negligibly low.
 - The employer group pointed out that the evidence supporting an association between formaldehyde exposure and nasopharyngeal cancer is highly questionable;
 - Formaldehyde is not likely to cause cancer in the upper respiratory tract when there is no cytotoxic effects;
 - Tumours development in experimental animal studies occurs at concentrations that cause severe local irritation of the upper respiratory tract (5 – 6+ ppm), including cell death followed by an increase in cell proliferation and damage to the genetic material;

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- It was pointed out that IARC based its classification on a large cohort study by the NCI involving 25,000+ workers followed over time;
- Recent re-evaluations of the epidemiological data by non-NCI researchers of NCI data indicates that:
 - Nasopharyngeal cancer is rare – 10 cases were found in the 25,000 worker cohort (representing 10 plants);
 - Most of these cancers came from one specific plant (six out of 10 cases) with high exposures (average exposures above 1 or 2 ppm with frequent peak exposures at 4+ ppm);
 - Three of the cancer cases were workers employed for less than one year at the plant;
 - The authors referenced by the employer representatives (i.e., Marsh *et al* – several papers) could not support NCI’s suggestion of a causal association between formaldehyde exposure and mortality from nasopharyngeal cancer; they found no such association;
 - Furthermore, there was a less than expected mortality rate for nasopharyngeal cancer at the other nine plants;
- In response to these critiques of its earlier studies, NCI is planning a re-evaluation of its earlier studies and a report is expected due for release later in 2006 [not available as of end January, 2007];
- Stakeholders urge WorkSafeBC not to proceed until this study becomes available;
- There is no biologically plausible link between formaldehyde exposure and leukemia;
 - Formaldehyde does not act as a systemic carcinogen;
 - It is rapidly metabolized within the body and is highly unlikely to be transported to the bone marrow, nor has it been demonstrated to be “marrow-toxic” – a precursor for leukemia induction.

Stakeholders asked WorkSafeBC to consider the findings of the 2004 IRSST formaldehyde report. It is a critical review of the literature of sensory irritation effects of formaldehyde – the basis of the ACGIH 0.3 ppm Ceiling Limit. The findings of the IRSST report are summarized in Appendix B. The employer submission indicates that, according to the IRSST, the threshold for sensory irritation (eye) is in the range of 0.75 to 1.0 ppm, which is far greater than the 0.3 ppm ceiling proposed by WorkSafeBC. The evidence indicates that the difference in the prevalence of significant health effects would not be expected by reducing the current WorkSafeBC levels to those recommended by the ACGIH.

The employer submission also requested WorkSafeBC consider the 1997 Paustenbach *et al* study. Details germane to this paper are summarized in Appendix B.

The employer submission requests that WorkSafeBC consider the Chemical Industry Institute of Toxicology (“CIIT”) model for carcinogenicity which has been adopted by several national and international standard-setting bodies including Health Canada / Environment Canada, the German MAK Commission, Environmental Protection Agency, Australia’s Department of Health and Aging (NICNAS), the OECD, the WHO (CICAD) and the Dutch Expert Committee (DECOS). The employer submission pointed out that IARC did not reference the CIIT model in their recommendations for carcinogenicity for

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formaldehyde. The employers also point to the fact that the MAK Commission, NICNAS, WHO-CICAD, DECOS and others conclude that formaldehyde exposure poses a carcinogenic effect under conditions that both induce toxicity and cause sustained regenerative proliferation (i.e., damage in the DNA replication process following severe tissue damage). The 1999 CIIT study is reviewed in Appendix B.

c) Economic Issues

Employer representatives maintain that in order for this industry to remain competitive both in and outside of Canada, the exposure limit for formaldehyde should reflect that of other jurisdictions. In particular, since Canada's primary trading partner is the US, the exposure limit should not be lower than that of the Occupational Safety and Health Agency ("OSHA"). Their primary concerns with respect to economic impacts are that if the exposure limit is lowered too much, there is the potential for marked disparity in compliance and manufacturing costs between BC and its competitors, and the industry in BC will, as a result, become less competitive.

Their submission states that 14,884 employees are directly employed in formaldehyde monomer, polymer and downstream facilities (primarily the wood products industry) in BC, equivalent to over \$540 million in wages. When direct, indirect and induced economic contribution of formaldehyde in BC is tallied, this rises to 80,164 jobs and C\$2.9 billion in wages with purchases of C\$1.7 billion and sales in excess of C\$3.9 billion.

The employer submission claims that consumers in the US and Canada would have to spend an additional \$17 billion per year if formaldehyde-based products were replaced by substitute materials. Substitution is, in many cases, not practical due to increased energy requirements, manufacturing safety issues, poor performance, and costs of alternate materials.

In another report provided by the employers – a report prepared by the Composite Panel Association – it is shown that the wood paneling industry in BC employs 4,419 employees directly (as of November 2005). They state that the panel board plants which are at risk are located in rural BC, in communities such as Grand Forks, Quesnel, and Smithers. These plants provide the base for economic activities in these areas and provide a much needed outlet for sawmill residues that were previously directed to beehive burners creating an environmental concern and wasting a valuable resource.

In a report received in the 1990's by WorkSafeBC from the Canadian Particle Board Association, it was estimated that the capital cost of complying in 1993 with an proposed Ceiling Limit of 0.3 ppm would be in the order of C\$676,000 per plant, with additional operating costs of C\$335,000 per year (per plant) in BC. It was stated at the time that the additional annual operating costs would largely be the result of higher energy costs associated with heating the additional air exhausted by the enhanced ventilation systems.

The employers suggest that achievability may be possible in plywood plants but is unlikely in particleboard plants and, correspondingly, anticipate that the cost of compliance would be higher for the particleboard industry than for the oriented strand board and plywood industries. They also suggest (based on OSHA estimates) that the

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greatest impact may be felt by the furniture industry because it uses particleboard as a raw material.

d) Technical Issues

Concerns have also been raised regarding the technical feasibility of monitoring exposure to and demonstrating compliance with such low levels of formaldehyde. It was suggested that uncertainty about the accuracy and precision of monitoring data would pose problems from the standpoint of both compliance monitoring and enforcement.

Workplace Site Visit

Occupational hygienists from WorkSafeBC visited a panel / fibre board plant in order to assess the feasibility of implementing a lower TLV for formaldehyde. As noted by the employer group at the September 30th, 2005 meeting with WorkSafeBC staff, a particle or fibre board plant is likely to be the most challenged in meeting the proposed Ceiling Limit of 0.3 ppm.

Issues identified During the Site Visit:

- Urea-formaldehyde resin is used in large quantities in making medium density fibre board;
- The resin component is 10% by weight of a typical board or panel; the balance is wood fiber obtained from waste wood supplies (sawdust) from sawmills;
- Formaldehyde is released to the air in the plant at a number of locations along the process line; the initial mixing area, the panel press section, fabrication section (panels are cut into various sizes and sanded), and packaging / shipping areas;
- Engineering controls are used throughout the plant primarily through the use of ventilation, including wet scrubbing systems;
- Ventilated air exhausted from the building exhaust is matched with an equal amount of heated make-up air provided to the plant; heat is supplied via natural gas;
- Other engineering controls include enclosed control rooms and laboratory; these are positively pressurized via dedicated HVAC systems;
- Staff spend most of their shift in these enclosed environments but enter the plant to take samples, oversee the process, carry out routine maintenance and similar job duties;
- Worker exposures are routinely measured by onsite environmental / occupational hygiene staff using a calibrated electronic “formaldemeter” and other sampling devices;
- Periodically, consultants will conduct worker exposure surveys;
- Exposure results are posted on staff bulletin boards and discussed at joint OH&S committee meetings;
- Sampling results indicate the following levels for the period January to June 2006 (based on 7 to 14 readings per month at each location; range indicated over the 6 month period):
 - Laboratory: ranged from 0.06 – 0.27 ppm;
 - Control room: 0.07 – 0.16 ppm;
 - Press infeed area: 0.23 – 0.30 ppm;

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- Press outfeed area: 0.32 – 1.19 ppm;
 - Mezzanine: 0.23 – 0.35 ppm;
 - Catwalk over press: 0.39 – 0.63 ppm;
 - Sander station: 0.05 – 0.12 ppm;
 - Packaging station: 0.04 – 0.11 ppm; and
 - Maintenance shops: 0.03 – 0.06 ppm.
- Few workers work for a full shift in the open plant; hence their time spent in the open plant are conservatively estimated to be about $\frac{1}{4}$ of a full shift or less, depending on the job tasks;
 - Practically, this means an 8-hour exposure well under 0.3 ppm on a time weighted basis;
 - The Ceiling Limit values of 1.0 ppm can be exceeded when a worker is located in a potentially high level area such as the press outfeed;
 - Workers who are required to work for longer periods in the plant are provided with the appropriate respiratory protection which is assigned based on the protocols established by the plant's respiratory protection program;
 - This plant would consistently be in non-compliance if a Ceiling Limit of 0.3 ppm with no 8-hour TWA is enforced.

Appendix B – Formaldehyde OELs and Carcinogen Status According to Various Regulatory Jurisdictions and Reference Organizations

This appendix details information on the proposed OELs by reference organizations such as the ACGIH, the German MAK Commission, and the UK WATCH¹² Committee among others.

Cancer Classification of Formaldehyde by Various Jurisdictions

Part 5 of the *Occupational and Safety Regulation (OHSR)* recognized the classification system for carcinogens based on the classification systems of the ACGIH and the IARC, both reference organizations. Other jurisdictions have adopted classification systems based on the recommendations by reference organizations other than the ACGIH or IARC. One of the most noteworthy is the classification system of the Scientific Committee on Occupational Exposure Limits (“SCOEL”). SCOEL’s recommendations on the carcinogen classification have been adopted by the regulatory agencies of the EU countries. Germany based its classification system on that of the MAK Commission and other national research organizations such as the German Federal Institute for Risk Assessment (Bundesinstitut für Risikobewertung – “BfR”).¹³ Table B1 provides an overview of the carcinogen classification for formaldehyde by these reference organizations.

Table B1. Current Classifications of the Carcinogenic Status for Formaldehyde

<i>Reference Organization</i>	<i>Classification for Formaldehyde</i>	<i>Description</i>
ACGIH	A2	Suspected human carcinogen – limited evidence of carcinogenicity in humans and sufficient evidence of carcinogenicity in experimental animals with relevance to humans in quality but are conflicting or insufficient to classify the substance as a confirmed human carcinogen.
IARC	1	Carcinogenic to man based on sufficient evidence in humans and in experimental animals. Sufficient evidence that formaldehyde causes nasopharyngeal cancer, strong but not sufficient evidence of leukemia, and limited evidence of sinonasal cancer.
European Union – SCOEL	3	Concern for man owing to possible carcinogenic effects but the available information is not adequate for making a satisfactory assessment. There is some evidence from appropriate animal studies but this is insufficient to place the substance in Category 2 (suspected human

¹² Working Group on Action to Control Chemicals Committee, a subcommittee of the Advisory Committee on Toxic Substances of the UK Health & Safety Executive.

¹³ Federal Institute for Risk Assessment (Bundesinstitut für Risikobewertung) – Germany.

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<i>Reference Organization</i>	<i>Classification for Formaldehyde</i>	<i>Description</i>
		carcinogen).
Dutch - DECOS¹⁴	3	As per SCOEL
German MAK Commission¹⁵	4	Genotoxicity plays no or at most a minor part. No significant contribution to human cancer is expected provided the MAK value is observed.
United Kingdom Health & Safety Executive	R40 (SCOEL “3”)	Limited evidence of a carcinogenic effect in humans. Similar to SCOEL.
Australia NICNAS¹⁶	2	Produces tumours in animals – specifically nasal tumours at high concentrations.

OEL Reference Organizations – Exposure Limits for Formaldehyde

ACGIH

ACGIH proposed a Ceiling Limit of 0.3 ppm for formaldehyde as far back as 1989 (a “Notice of Intended Change” substance). The posted limits at the time were a TLV TWA of 1.0 ppm and a TLV STEL of 2.0 ppm. In 1992, ACGIH adopted the 0.3 ppm TLV Ceiling Limit. ACGIH has listed formaldehyde as a “suspected human carcinogen” (A2) since 1982. The basis for recommending a ceiling limit is outlined in the 2001 TLV Documentation©, and can be summarized, in part, as follows:

“There is a substantial population, comprising up to 20% of the population, for whom airborne formaldehyde at concentrations on the order of 0.25 to 0.5 ppm is troublesome. Despite the intent of the TLV recommendations to protect most workers, it is believed that the recommended formaldehyde 0.3 ppm ceiling TLV will not protect that portion of the workforce reported to be responsive to low ambient concentrations of this chemical.

While the epidemiologic studies and case reports do not confirm that occupational exposure to formaldehyde is carcinogenic for human beings, several groups have reported that occupational formaldehyde exposure may be a factor in the potentiation or predisposition of upper respiratory tract cancer when a worker is also exposed to other known or suspected occupational carcinogens. Nevertheless, interpretation of the biologically based animal cancer risk assessment data¹⁷ indicates that the oncogenic potential of formaldehyde is a threshold phenomenon and that prevention of upper respiratory tract irritation and the associated

¹⁴ Dutch Expert Committee on Occupational Standards.

¹⁵ Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, a reference organization of the German Research Foundation (FDR), Germany.

¹⁶ National Industrial Chemicals Notification and Assessment Scheme.

¹⁷ CIIT study.

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regenerative hyperplasia should eliminate, for all practical purposes, any excess cancer risk posed by occupational formaldehyde exposure alone.

ACGIH holds to the opinion that TLVs based on physical irritation should be considered no less binding than those based on physical impairment. There is increasing evidence that physical irritation may initiate, promote, or accelerate physical impairment through interaction with other chemical or biological agents. Inasmuch as formaldehyde is associated with rapid onset of irritation, a ceiling designation is deemed appropriate for this chemical.

The recommended TLV–Ceiling of 0.3 ppm for workplace air formaldehyde is based on evidence of irritation from reports of occupational exposure to formaldehyde as well as human formaldehyde exposures in other settings. This recommended TLV may not eliminate all worker complaints of sensory irritation associated with exposure to this chemical. However, ACGIH believes that the 0.3 ppm ceiling value should result in a significant reduction of complaints currently associated with exposure to formaldehyde. The A2, Suspected Human Carcinogen, notation, based on cancer in experimental animals and where the epidemiologic studies are conflicting or insufficient to confirm an increased risk of cancer in workers, is considered appropriate for this chemical.

In light of the numerous reports of allergic reaction or sensitization associated with exposure to formaldehyde and products containing formaldehyde, the sensitizer notation (SEN) is recommended. Individuals who may already be sensitized or otherwise unusually responsive to formaldehyde may not be adequately protected from adverse health effects caused by formaldehyde exposures at or below the recommended TLV”.

As noted, the ACGIH based its decision on adopting its current TLV recommendation on experimental and epidemiological evidence up to and included data published no later than the mid-90s. Many of the studies – including studies by the National Cancer Institute and those contemporary at the time (i.e., published prior to the mid-90s) on which the current ACGIH Ceiling Limit of 0.3 ppm adopted TLV is based – have since received critical re-evaluations. Much new information has come to light since the mid-90s. The MAK Commission, responsible for recommending exposure limits in Germany, has completed recent reviews (published 2002, 2006), as discussed in Appendix B. Other evaluations have been completed including a 2004 review by the IRSST¹⁸ in Quebec, DECOS¹⁹ in 2003, DECOS/NEG²⁰ in 2003, WHO-IPCS²¹ in 2002, Environment Canada / Health Canada in 2001, Australia’s NICNAS²² in 2005, UK’s WATCH²³ Committee in 2005, Australia’s EPHC²⁴ in 2003, WHO / CICAD²⁵ and Germany’s BfR²⁶ in 2006. OSHA issued a “final Rule” on an OEL for formaldehyde in June 1992. However, no further re-evaluation has been conducted by this US regulatory agency.

¹⁸ Institute de Reserche Robert Sauvé en Santé et en Sécurité du Travail – Quebec.

¹⁹ Dutch Expert Committee on Occupational Standards.

²⁰ Nordic Expert Group – Norway, Sweden and Finland.

²¹ International Programme on Chemical Safety – World Health Organization.

²² National Industrial Chemicals Notification and Assessment Scheme. Australia.

²³ Advisory Committee on Toxic Substances – Working Group on Action to Control Chemicals, UK Health & Safety Commission, England.

²⁴ Environmental Protection & Heritage Council, National Environmental Protection Measures – Australia.

²⁵ Concise International Chemical Assessment Document – World Health Organization / International Labour Organization..

²⁶ Federal Institute for Risk Assessment (Bundesinstitut für Risikobewertung) – Germany.

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With the exception of OSHA, most regulatory as well as reference agencies have utilized the new information, particularly the evidence provided by a pivotal study on the carcinogenic process involving formaldehyde published by the CIIT²⁷ in 1999. This study is described in this Appendix.

MAK Commission

The MAK Commission recently reviewed the OEL and carcinogenic status of formaldehyde. In its 2002 publication it declared formaldehyde a category 4 carcinogen and prescribed an 8-hour TWA of 0.3 ppm with a Ceiling Limit of 1.0 ppm. The MAK Commission considered “that the genotoxicity of formaldehyde plays no or at most a minor part in its carcinogenic potential so that no significant contribution to human cancer risk is expected”. Formaldehyde is classified as a carcinogen category 4 of Section III of the *List of MAK and BAT Values*. These OELs and carcinogen classification has been adopted in Germany as regulatory values.

The 2006 MAK Commission report makes the following observations:

“Evaluations of the data now available for the carcinogenic effects confirm that the occurrence of tumours in the nasal mucosa of rats and mice are the result of chronic proliferative processes caused by the cytotoxic effects of formaldehyde. The dose-response relationship for all the parameters investigated, such as damage to the nasal epithelium, cell proliferation, and tumour incidence and also the formation of DNA cross-links is very flat for low level exposures and become much steeper at higher levels of exposure. As long as the cellular proliferation rate is not increased – which requires exposure to concentrations in excess of 2 ppm – the probability that DNA-protein crosslinks are transformed into mutations is considered low”.

In the low dose range, the MAK Commission states formaldehyde plays no or least a minor part in its carcinogenic potential so that no significant contribution to human cancer risk is expected. This conclusion is supported by the results of a risk assessment by CIIT (1999) which, for persons exposed to concentrations of 0.1 ppm at the workplace for 40 years, yielded a very low additional risk of cancer for non-smokers of 1.3×10^{-8} . The Commission therefore classified formaldehyde in category 4.

In establishing a MAK for formaldehyde – which also takes the carcinogenic risk into account, the avoidance of cellular proliferation is therefore decisive. The cause of cell proliferation is the irritative effect of the substance on the upper respiratory tract. The report states that for this parameter the data base is insufficient for the establishment of a MAK value. However, the database for the irritative effects of formaldehyde on the eye – a more sensitive parameter – is sufficient. Based on the Paustenbach's *et al* study (1997) in which practically all workers were protected against eye irritation when exposed on a daily basis to a maximum concentrations of 0.3 ppm, the Commission established a MAK value of 0.3 ppm (8-hour TWA). Concurrently, the STEL is set at 0.6 ppm and the Ceiling Limit at 1 ppm. At concentrations greater than 1 ppm, irritative effects are to be expected.

Due to the sensitizing effects on the skin, the MAK Commission designated formaldehyde as a sensitizer – “Sh”.

²⁷ Chemical Industry Institute of Toxicology – USA.

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The Commission also classified formaldehyde as a germ cell category 5 mutagen, and reported that in experimental exposures – even at high exposure levels – the equilibrium concentration maintained in the blood by endogenous formaldehyde (i.e., metabolically produced by the body) was not found to be increased. Due to the rapid metabolism it is also unlikely that even moderate exposure levels can increase the systemically available concentration noticeably. The Commission concluded that given observance to a MAK value of 0.3 ppm, exposure to airborne formaldehyde is not expected to make a noticeable contribution to the genetic risk for man.

WATCH Committee – a Health & Safety Executive (HSE) Working Group, United Kingdom

The WATCH Committee's overall interpretation of the data from the post-2000 studies (which includes review by Hauptmann *et al* (2004), Marsh *et al* (2002)) is that they justify increased concern for the carcinogenic potential of formaldehyde in humans – especially in relation to nasopharyngeal cancer – but that it falls short of providing conclusive evidence that formaldehyde exposure has caused nasopharyngeal cancer. There are inconsistencies in the findings of the studies which lack a clear explanation. Similarly, the Committee reports that the study by Coggon *et al* (2003) – in a British cohort study of chemical industry workers – provided no convincing evidence for an association between formaldehyde exposure and cancer in humans. The Committee also found the US garment worker cohort study by Pinkerton *et al* (2004) unconvincing. They found it essentially uninformative about the possible association between the substance and nasopharyngeal cancer.

In relation to the apparent association seen in some studies between formaldehyde exposure and leukemia, based on recent reviews of the evidence,²⁸ and also considered biological plausibility, the WATCH Committee considers that there is no basis for any concern for leukemia associated with formaldehyde exposure.

The Committee considers formaldehyde a genotoxic carcinogen for which a threshold can be determined. No OELs appear to have been recommended for formaldehyde by this Committee at this time.

The Committee recognizes that some authorities advocate approaches for deriving exposure standards for “non-threshold” genotoxic carcinogens based on mathematical modelling of animal carcinogenicity data to predict exposure levels associated with a predetermined level of risk in humans (e.g. excess lifetime risk of developing cancer of 10^{-5} or 10^{-6}). These are the traditional linear extrapolation methods in deriving thresholds for carcinogens – methods used by the US Environmental Protection Agency (“US-EPA”) and other agencies until the late 1990s at which time other methodologies became apparent such as those developed by the CIIT (1999). There are also “model-free” linear extrapolation approaches, but both methods involve extensive extrapolation below the observed range of data and both methods rest on the assumption of low dose linearity. Low dose linearity does not appear to apply to formaldehyde. The Committee identified a number of concerns related to these methods that are elaborated below:

²⁸ Including: Collins and Lineker (2004); Heck and Casanova (2004), Cole and Axten (2004); Marsh and Youk (2004).

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- These methods all rely on an assumption of low-dose linearity but at low exposures this assumption may not be correct. DNA repair mechanisms may lead to a sub-linear dose response at lower doses leading to overestimates of risk.
- The risk estimates derived by mathematical modelling or linear extrapolation lie far below the observed experimental range of data and can never be validated by empirical observation (to validate a lifetime increased risk of 10^{-5} or 10^{-6} would require far more than the 50 animals per sex per dose group used in standard carcinogenicity bioassays).
- These approaches do not adequately convey the uncertainties involved and so imply a level of precision that cannot be justified. A spurious impression of scientific accuracy is thereby conveyed.
- The usual design of rodent carcinogenicity studies (low, medium and high dose groups of 50 per sex) cannot distinguish between the various mathematical models available in terms of identifying a model that provides the best fit to the data.
- Although the various models can be shown to fit the observed data equally well, these models can lead to risk estimates at low doses that vary over several orders of magnitude, and there is no way of knowing which model, if any, leads to a true approximation of risk.

The PRD is not aware of any OELs that have been recommended for formaldehyde by the WATCH Committee at this time.

NOTE: The US-EPA, Health Canada and other authorities either have adopted or are considering adopting the multi-model biological model developed by the CIIT in lieu of the no-threshold model which assumes that cancer risk is linear to zero. There is no indication that IARC has considering the biological model.

German Federal Institute for Risk Assessment (BfR) / European Union Scientific Committee for the Occupational Exposure Limits to Chemical Agents (SCOEL)

Both SCOEL and the BfR each issued review reports on formaldehyde in 2006 – SCOEL issued provisional OELs for formaldehyde. The proposed draft is currently out for consultation within Europe. The BfR report focuses more on public health and safety. Both organizations had similar findings and will therefore be discussed jointly here. As noted by both, in general, epidemiological data cannot be used to support the existence of a threshold for genotoxic carcinogenicity. It is not possible to “prove” the existence of a threshold due to the statistical limitations. Hence, evidence concerning the existence of thresholds will need to be based on mechanistic and experimental rather than epidemiological data.

Both organizations conclude that the carcinogenic mechanism of formaldehyde is based on a combination of repeated exposures of cell proliferation due to local tissue irritation (cytotoxic effects) of inhaled formaldehyde and also to the formation of DPX (DNA-protein cross-links). Hence the mechanism is a combination of non-genotoxic and genotoxic events. Experimental animal evidence indicates a no observed adverse effect level (“NOAEL”) for cytotoxicity (non-genotoxic effect) of 2 ppm. However, a clear threshold for the induction of DPX (genotoxic effect) could not be identified but the dose-

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response data showed a steep increase in DPX formation only occurred at concentrations above 2 ppm. Increases in cell proliferation only occurred at concentrations above 2.7 ppm. Taking other observations into account it was considered that there would be no increase in genotoxic changes at exposures below the NOAEL for cytotoxicity.

A clear threshold for respiratory tract cytotoxicity could not be identified in humans, and both authorities considered that the NOAEL for sensory irritation in humans could be used as a surrogate. A weight of evidence approach to the analysis of human data from a number of volunteer studies (Paustenbach *et al*, 1997) indicated a NOAEL for sensory irritation of 0.1 ppm. In the BfR assessment it was noted that the NOAEL for sensory irritation was not contraindicated by animal data indicating a threshold for cytotoxicity at 2 ppm. Overall, 0.1 ppm was proposed by BfR as a “safe-level” for exposure to formaldehyde in the general public. This, according to BfR, is in good agreement with the MAK value of 0.3 ppm for worker protection in the workplace. This is the regulated OEL for Germany.

In their 2006 review, SCOEL stated that a NOAEL of 0.3 ppm for local irritancy is the departing point for setting an OEL. At the same time, SCOEL considers that the onset of eye irritation is a very sensitive parameter that provides a safety margin to the onset of irritation-induced cellular proliferation. Considering the “preferred value approach” in setting OELs, an OEL of 0.2 ppm is therefore proposed. Short-term irritation may be prevented by an STEL of 0.4 ppm. At these levels, they state that no systemic effect of formaldehyde is to be expected. No European regulatory agency has yet adopted these values.

WHO / CICAD²⁹ Assessment on Formaldehyde

The 2003 WHO report is based on the research conducted by Health Canada and Environment Canada scientists in conjunction with US-EPA, the CIIT among others. It is an omnibus review and considers the toxicological and other harmful properties of formaldehyde from both an environmental and human perspective.

They report that based on inhalation studies in laboratory animals, formaldehyde causes degenerative non-neoplastic effects in mice and monkeys and nasal tumours in rats. *In vitro*, formaldehyde induced DNA–protein crosslinks, DNA single-strand breaks, chromosomal aberrations, sister chromatid exchange, and gene mutations in both human and rodent cells. Formaldehyde administered by inhalation or gavage to rats *in vivo* induced chromosomal anomalies in lung cells and micronuclei in the gastrointestinal mucosa.

The results of epidemiological studies in occupationally exposed populations are consistent with a pattern of weak positive responses for genotoxicity, with good evidence of an effect at site of contact (e.g., micronucleated buccal or nasal mucosal cells). Evidence for distal (i.e., systemic) effects is ambiguous. Overall, based on studies in both animals and humans, formaldehyde is weakly genotoxic, with good evidence of an effect at site of contact (i.e., within upper the respiratory tract), but less convincing evidence at distal sites (i.e. other body organs and tissues).

²⁹ Concise International Chemical Assessment Document – WHO / ILO.

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Epidemiological studies taken as a whole do not provide strong evidence for a causal association between formaldehyde exposure and human cancer, although the possibility of increased risk of respiratory cancers, particularly those of the upper respiratory tract, cannot be excluded on the basis of available data. Therefore, based primarily upon data derived from laboratory studies, the inhalation of formaldehyde under conditions that induce cytotoxicity (generally levels above 2 to 3 ppm) and sustained regenerative proliferation is considered to present a carcinogenic hazard to humans.

The concentration response relationships for DNA–protein crosslinking, cytotoxicity, proliferative response, and tumours are highly non-linear, with significant increases in all end-points being observed at concentrations of 4 ppm and above. This correlates well with the concentration at which mucociliary clearance is inhibited and glutathione-mediated metabolism saturated (i.e., 4 ppm). Histological changes, increased epithelial cell proliferation, and DNA–protein crosslinking are all more closely related to the exposure concentration than to the total cumulative intake or dose of formaldehyde. While the respective roles of DNA–protein crosslinking, mutation, and cellular proliferation in the induction of tumours in the rat nose are not fully delineated, the hypothesized mode of carcinogenesis is in keeping with the growing body of evidence supporting the biological plausibility that prolonged regenerative cell proliferation can be a causal mechanism in chemical carcinogenesis.

Regenerative cell proliferation following formaldehyde-induced cytotoxicity increases the number of DNA replications and thus increases the probability of a DNA–protein crosslink initiating a DNA replication error, resulting in a mutation. This proposed mode of action is consistent with the observed inhibition of DNA replication in the rat nose at elevated concentrations and point mutations in the p53 tumour suppressor gene in tumours from the noses of rats exposed to formaldehyde as well as increased p53 expression in pre-neoplastic lesions.

The hypothesized mode of induction of formaldehyde-induced tumours that satisfies several criteria for weight of evidence, including consistency, concordance of exposure–response relationships across intermediate end-points, and biological plausibility and coherence of the database, is likely relevant to humans, at least qualitatively. Increased cell proliferation and DNA–protein crosslink formation within epithelia of the upper respiratory tract have been observed in monkeys exposed to formaldehyde vapour. Although not sufficient in itself as a basis for inferring causality, direct evidence on histopathological lesions in the nose of humans exposed primarily to formaldehyde in the occupational environment is consistent with a qualitatively similar response of the upper respiratory tract in humans and experimental animals to formaldehyde. Increased human epithelial cell proliferation following *in situ* exposure to formaldehyde has also been observed in a model system in which rat trachea populated with human tracheobronchial epithelial cells were xenotransplanted into athymic (thymus gland removed) mice.

Because formaldehyde is highly reactive at the site of contact, dosimetry is of critical importance when extrapolating across species that have significantly different anatomical features of the nasal and respiratory passages and patterns of flow of

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inhaled air. Since humans as well as other primates are oro-nasal breathers, compared with rats, which are obligate nose breathers, effects associated with the inhalation of formaldehyde are likely to be observed in a larger area, including deeper parts of the respiratory tract. Indeed, in rats exposed to moderate levels of formaldehyde, histopathological changes, increased epithelial cell proliferation, and DNA–protein crosslink formation are restricted to the nasal cavity; in formaldehyde-exposed monkeys (as surrogates for humans), on the other hand, these effects have been observed further along within the upper respiratory tract. While the epidemiological studies taken as a whole do not provide strong evidence for a causal association between formaldehyde exposure and human cancer, the possibility of increased risk of respiratory cancers, particularly those of the upper respiratory tract, cannot be excluded on the basis of available data.

The CICAD report concludes:

Based primarily upon data derived from laboratory studies, therefore, the inhalation of formaldehyde under conditions that induce cytotoxicity and sustained regenerative proliferation is considered to present a carcinogenic hazard to humans. CICAD did not recommend OEL values for formaldehyde.

Dutch Expert Committee on Occupational Standards (DECOS) and the Nordic Expert Group in Conjunction with DECOS

DECOS completed a comprehensive review on formaldehyde published in 2003. Concurrently NEG issued a similar review report on the substance with similar findings and conclusions. Both DECOS and NEG are research organization charged with the review of OELs and recommending OELs for regulatory consideration by the authorities in their perspective countries.

DECOS and NEG make similar conclusions to those of WHO / CICAD and CIIT on the health effects of formaldehyde.

In view of the evidence in experimental animals and humans, and a thorough and critical appraisal of the available data, DECOS posed a question:

- Does an exposure limit of 0.12 ppm protect workers against cytotoxicity-induced hyper-proliferation of the nasal respiratory epithelium, and consequently also against the potential risk of nasal cancer?

Their answer is in the positive, and DECOS considers a health based 8-hour TWA occupational exposure level (HBR-OEL) of 0.12 ppm formaldehyde low enough to protect workers against nasal tissue damage, and as a consequence, also against the potential risk of nasal cancer. DECOS states that this conclusion is strongly supported by the results of a recently published quantitative cancer risk assessment of airborne formaldehyde, using a very sophisticated biologically-based model that predicts for occupational exposure (40 years beginning at the age of 18, 8 hours/day, 5 days/week) to 0.1 ppm formaldehyde an increased lifetime risk for cancer of 10^{-7} for smokers and 4.1×10^{-9} for non-smokers (CIIT, 1999), which are regarded as negligibly small risks.

To avoid peak exposures possibly entailing cytotoxicity-induced hyper-proliferation and metaplasia of the nasal respiratory epithelium, DECOS recommends for formaldehyde a

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STEL, using data from the review of Paustenbach *et al* 1997, and others. The review of Paustenbach suggested that at a concentration of 1.0 ppm sensory effects might occur. The committee concluded that the total body of evidence indicates that 0.42 ppm is an exposure level which is low enough to avoid significant sensory irritation from short term exposures and thus, more importantly, also will be low enough to avoid nasal cytotoxicity from such short exposures. In conclusion, the committee considers a factor of 2 sufficient for the extrapolation from lowest observed adverse effect level (“LOAEL”) to the no-adverse-effect-level (“NAEL”). Therefore, DECOS recommends a STEL of 0.42 ppm.

Conclusion: DECOS recommends a health-based occupational exposure limit of 0.12 ppm formaldehyde, as an 8 hour time-weighted average, and a short term exposure limit, 15 minutes TWA, of 0.42 ppm. Neither Holland nor the Nordic countries, including Sweden, Norway or Finland have adopted these OELs for regulatory purposes.

National Industrial Chemical Notification Assessment Scheme (NICNAS) of the Australian Department of Health and Aging

NICNAS, a reference agency for the Australian government, released its draft Formaldehyde Priority Existing Chemical Assessment Report in 2005 for stakeholder and public consultation. It released a response report in November of that year. While their consultation period is still active, NICNAS has made the following statements that are germane to this review:

- In order to classify a chemical as a category 1 carcinogen, there must be sufficient human evidence to establish a causal association between exposure to the chemical and cancer.
- NICNAS concluded that the strength of the epidemiology data was not sufficient to establish a casual relationship between formaldehyde exposure and cancer in humans. For nasopharyngeal cancers there are several epidemiological studies that show an increased risk, whereas other studies do not.
- Of the three recently published cohorts, only the NCI study (Hauptmann *et al*, 2004) showed an increased risk of nasopharyngeal cancers and this was associated with increased average exposure intensity and highest peak exposures.
- Marsh and Youk (2005) reevaluated the data of the NCI study and concluded that there was little support for NCI’s suggestion of a causal relationship between formaldehyde exposure and mortality from nasopharyngeal cancer.
- Coggon *et al* (2003) and Pinkerton *et al* (2004) did not observe an increased risk for nasopharyngeal cancers.
- There are also concerns for an increased risk for formaldehyde-induced myeloid leukemia. However, the available data are not considered sufficient to establish an association and there is currently no postulated mode of action to support such an effect.
- Therefore, it is considered that there is currently insufficient evidence to establish a causal association between human exposure and the development of cancer on the basis of epidemiological data.
- While they acknowledge the fact that it is difficult to identify a definitive no observed effect level (“NOEL”) for sensory irritation, they have taken a cautionary approach and selected 0.5 ppm as the lowest observed effect level (“LOEL”) and

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added appropriate uncertainty factors to establish the recommended occupational exposure standard (8-hour TWA) as 0.3 ppm. This value provides a level that will not only manage the risk of sensory irritation, but also manage the cancer risk.

- NICNAS considers the clonal growth model developed by CIIT and further developed by Conolly *et al*, 2004 the best estimate of cancer risk for formaldehyde.
- The clonal growth model predicts that for 40-year occupational exposure to 0.3 ppm formaldehyde (the NICNAS recommended occupational exposure standard) the estimated additional risk for respiratory tract cancers is approximately 2 in 10 million.
- While at 1 ppm (the current Australian occupational exposure standard) the estimated additional risk is approximately 50 in a million. Similarly for public exposure, at the recommended indoor air guidance value (80 ppb or 0.08 ppm), the estimated additional risk is approximately 3 in 10 million.
- Although NICNAS considers the risk of cancer to be low, they do not consider that the strength of data nor the degree of certainty is sufficient to conclude that the cancer risk is negligible.
- Based on the information, NICNAS is showing support for an 8-hour TWA of 0.3 ppm and a 0.6 ppm STEL and that formaldehyde be classified as a category 2 carcinogen (producing tumours in animals – specifically nasal tumours at high concentrations).
- In the draft, NICNAS makes the following statement:
 - “In order to protect the majority of workers from sensory irritation, the recommended exposure standard should be a concentration that is a lower than the LOEL identified. As this is a reversible effect and effects are generally mild at 0.5 ppm, the standard should be slightly lower than the LOEL. For these reasons the recommended exposure standard is 0.3 ppm TWA and 0.6 ppm STEL. At this level, the nasal cancer risk can be also managed. Furthermore the recommended exposure standards are consistent with best practice overseas and from industry information submitted for this report appear technically achievable in most Australian workplaces.”

This statement is similar to that of the MAK Commission. They conclude by stating that there is an ongoing follow-up for the NCI study, which is likely to be published in 2007. NICNAS believes it is important to review the NCI data and any other significant epidemiological data, when they become available. They propose that the following text be added to section 19, Secondary Notification:

“NICNAS should re-evaluate the cancer hazard classification if and when any new significant epidemiology data becomes available.”

Conclusion: NICNAS recommends an 8-hour TWA OEL of 0.3 ppm and a STEL of 0.6 ppm and classify formaldehyde as a category 2 carcinogen. This is a similar conclusion to that of the MAK Commission.

IRSST – Quebec

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This study, commissioned by the IRSST, was completed by research scientists at the Université de Montréal. It was initially published in 2004 in French with an English version issued January 2006.

Overall, the project aimed to evaluate the impact of lowering the current Quebec Commission of Health and Safety permissible exposure value – Ceiling Limit for formaldehyde, which is currently set at 2 ppm; they are considering setting it to 1.0, 0.75 or 0.3 ppm. The objective of this study was to estimate as precisely as possible the dose-response relationship between exposure to formaldehyde and the appearance of health-related effects in workers.

A series of criteria was established in order to select and classify the parameters based on their scientific qualities; statistical analyses were conducted in order to establish this exposure-response relationship for the earliest effects after an acute exposure, i.e., the irritating effects. The determination of the risk of cancer after a long-term exposure was obtained by considering dose-response relationships provided by different agencies and by applying them to the Quebec data.

The IRSST notes the following:

- The study data systematically defines the dose-response relationship, allowing calculation of responses attributable to formaldehyde according to the site of the irritative effect (eye, nose, throat);
- They conclude that for concentrations less than 0.75 ppm, the frequency of irritation in workers exposed to formaldehyde was about the same one observed in individuals without occupational exposure, indicating that appearance of irritation at such concentrations can hardly be associated with occupational exposure to the substance;
- Among the workers exposed to a formaldehyde concentration between 0.75 and <1.0 ppm, 6.3% are likely to experience moderate eye irritations;
- None would be likely to experience severe eye irritations and 1.6% would have moderate nose and throat irritations;
- As shown in Figure B2,
 - Between 0 to less than 0.75 ppm no irritating effects are noted;
 - Between 1 ppm and less than 2.0 ppm, 10.1% experienced moderate eye irritation, 0.8% severe eye irritation, 4.5% moderate nose irritation and 4.6% moderate throat irritation;
 - Above 2 ppm a corresponding increase in responses are noted.

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Figure B2: Average theoretical percentage of the exposed population that is likely to experience irritating eye, nose or throat effects attributable exclusively to formaldehyde according to the severity of the effect for a given class of exposure (adapted from IRSST 2006).

Effect considered	Fraction of the population exposed (in %) experiencing irritating effects				
	0 - <0.3 ppm	0.3 - <0.75 ppm	0.75 - <1.0 ppm*	1 - <2.0 ppm*	≥2.0 ppm*
Eye irritation Moderate effect	0%	0%	6.3%	10.1%	14.9%
Eye irritation Severe effect	0%	0%	0%	0.8%	1.9%
Nose irritation Moderate effect	0%	0%	1.6%	4.5%	12.4%
Throat irritation Moderate effect	0%	0%	1.6%	4.6%	12.6%

* The values of these classes were calculated for the middle of the classes of exposure, based on quadratic regression models from which the background noise had been subtracted.

Note: The ≥2.0 ppm class represents the individuals exposed between 2.0 and <3.0 ppm

- From a compensation claims perspective, IRSST notes that complaints due to formaldehyde exposure reported to the CSST (Quebec Commission of Health and Occupational Safety) are rather rare. As for cases of protective reassignment, 11 cases were reported in four years among six CAEQ (Quebec Economic Activities Classification) codes, four business sectors and nine different occupations. No cases of occupational illness that were attributable to formaldehyde were reported in the same period.
- On the basis of the epidemiological data in literature and the position of several agencies of toxicological risk evaluation, there is limited evidence of formaldehyde's carcinogenic effects on humans.
- If one refers to the exposure data of the IRSST, the probability of frequent exposure to the ceiling values indicated in the matrices is low. The duration of the ceiling values in these matrices is about one minute each. In other words, a worker exposed to an average value for eight hours that was low, cannot have been exposed to ceiling values of a relatively high frequency and intensity. Otherwise, the average would be higher.
- ACGIH also evaluated the health impact of formaldehyde exposure. The majority of the studies selected and analyzed for this evaluation were the same as the ones the IRSST selected. The conclusions of these studies are therefore the same between the ACGIH analysis and this analysis. However, ACGIH went one step further than scientific evaluation. They proposed a recommendation of an acceptable Ceiling Limit of 0.3 ppm based on their own interpretation of the data. This recommendation is based on the desire to avoid a maximum of irritations in workers. This includes even the mildest irritation, given that some studies showed that the most sensitive people complained of irritation at concentrations as low as 0.3 ppm, without taking into account the degree of severity of effects (only the presence or absence of effect is taken into account,

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without giving more weight to more severe effects), or the population response at background level (in controlled studies, an equal or a higher incidence was observed at 0 ppm than at 0.3 ppm.). In addition, the quality difference between the controlled studies and the studies involving workers was not taken into account in the process of risk evaluation. The ACGIH therefore recommends a ceiling value of 0.3 ppm and specifies “concentrations should be reduced to the lowest levels detectable by the measuring equipment.”

- IRSST’s analysis of the selected epidemiological studies demonstrates that some studies showed an association between formaldehyde exposure and cancer, while other studies did not show such a relationship. Nevertheless, all these epidemiological studies have methodological limitations that reduce the confidence level of the results. These limitations are mainly lack of power, the presence of confounding factors, the fact that an effect is observed in the least exposed groups and but no effect in the most exposed groups, the lack of measurement of exposure level in numerous cases, or sporadic measurements. Consequently, there is limited proof of the carcinogenic potential of formaldehyde in epidemiological studies but it is not possible, based on epidemiological studies, to establish a dose-response relationship between formaldehyde exposure and the onset of cancer.
- Because of the inconsistencies among the results of the epidemiology studies regarding the association and strength of association, frequent methodological limitations such as lack of power and a limited determination of actual exposure, the inability of cohort studies to observe an increased risk because the studied types of cancer are rare, and the lack of a dose-response relationship that increases with increasing doses, the evidence for a causal association is very limited, although it cannot be entirely excluded. In animals, the proof of a causal relationship appeared sufficient to us, but the increase in cancer was observed only at high concentrations. The cellular alterations in the tissues of the respiratory tract make this relationship plausible. It must be remembered, however, that the concentrations at which an excess of cancer was observed in animals also induce severe irritation. These factors can contribute to a significant increase in cancer risk through an epigenetic or promoter mechanism.
- These observations suggest that at concentrations at which irritation is low or non-existent, the cancer risk, if any, increases more slowly with the increase in dose than when irritation is severe and chronically present. At the concentrations at which cancer was observed in animals (5.6 ppm and higher), no worker could remain in his work environment, because irritation to the respiratory tract and eyes would be completely intolerable.
- As far as the estimations of excess risk are concerned, based on high-to-low dose mathematical extrapolation models, the CIIT model appears more appropriate than the US EPA model in estimating the workers’ risk. This is especially true since the estimates of this model for low doses approach the levels of excess risk observed in the epidemiological studies where a positive statistical association was observed.

Conclusion: The IRSST concludes that for concentrations less than 0.75 ppm, the frequency of irritation in workers exposed to formaldehyde was about the same one

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observed in individuals without occupational exposure. There is no indication that the IRSST has made recommendations regarding OELs.

Summary of Recommendations of OELs for Formaldehyde by Reference Organizations.

Table B3 summarizes recommendations for occupational exposure limits from the ACGIH and other reference agencies from Europe, the United Kingdom, Quebec and Australia. The MAK Commission recommendations (adopted as regulated OELs in Germany) are identical with the recommendations by NICNAS with the exception that the Australian organization did not recommend a Ceiling Limit value. The MAK recommendation is identical to the currently prescribed OELs in British Columbia - in place since 1998. The WATCH Committee has not recommended OELs at this point; nor has the IRSST.

Table B3: OELs recommended by reference organizations

<i>Reference Organization</i>	<i>8-h TWA OEL ppm</i>	<i>STEL OEL ppm</i>	<i>Ceiling Limit OEL ppm</i>
<i>ACGIH - USA</i>	-	-	0.3
<i>DECOS - Holland</i>	0.12	0.42	-
<i>MAK Commission³⁰ - Germany</i>	0.3	0.6	1
<i>SCOEL- EU</i>	0.2	0.4	-
<i>NICNAS - Australia</i>	0.3	0.6	-
<i>WATCH - UK</i>	-	-	-
<i>IRSST- Quebec</i>	-	-	-

Non-Reference Organizations

For the purposes of reviewing the health effects of formaldehyde and considerations for setting an appropriately protective occupational exposure limits for the substance, two critical studies referenced by WATCH, DECOS, NEG, and others reviewed above, are brought into this discussion.

Chemical Institute of Toxicology 1997 report:

Derivation of the dose–response model and selection of various parameters as it relates to formaldehyde are presented in this 336 page omnibus study undertaken by the CIIT in conjunction with scientists from the US EPA, Health Canada, University of Pittsburgh

³⁰ Adopted by the German regulatory agency - Deutsche Forschungsgemeinschaft (DFG).

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and others. Only a brief summary is provided here. Basically, the CIIT model (which incorporates various toxicological, mechanistic and dosimetric parameters) has superseded earlier models such as the “no threshold” model that assumes that cancer risk is linear to zero as used by the US EPA, the NCI and most regulatory agencies since the 1970s. This is despite the fact that it has been recognized that tumour dose–response relationship is highly non-linear. Since then, a great deal of research has focused on better characterizing the factors that play a role in the etiology of nasal tumours so that a better understanding of the likely shape of the dose response curve in the low dose region can be determined. This includes additional research on the induction, persistence, and repair of DNA-protein crosslinks (“DPX”) at low and high concentrations and for acute and longer-term exposures. It also includes research on the induction of cell proliferation, which is considered to be an essential precursor event to the development of cancer in rats and other species, including humans.

The CIIT multi-modal model is considered by many to be a far more powerful and precise predictor of cancer risks and greatly minimizes the need for unfounded assumptions and uncertainties as in currently used regulatory approaches to carcinogens – the “no threshold” model. The CIIT model for formaldehyde predicts a risk for cancer a 1,000-fold less than the EPA prediction.

CIIT’s clonal growth model is similar to other biologically based, two-stage clonal growth models (also known as Moolgavkar – Knudsen – Venzon (MVK) models), incorporating information on normal growth, cell cycle time, and cells at risk (in various regions of the respiratory tract). In modelling, formaldehyde is assumed to act as a direct mutagen, with the effect considered proportional to the estimated tissue concentration of DPX. The concentration-response curve for DPX formation is linear at low exposure concentrations and increases in a greater than linear manner at high concentrations, similar to those concentrations administered in the rodent carcinogenicity bioassays. For cytotoxicity and subsequent regenerative cellular proliferation associated with exposure to formaldehyde, the non-linear, disproportionate increase in response at higher concentrations is incorporated. Values for parameters related to the effects of formaldehyde exposure upon the mutagenic (i.e., DPX formation) and proliferative response (i.e., regenerative cell proliferation resulting from formaldehyde-induced cytotoxicity) were derived from a two-stage clonal growth model developed for rats, which describes the formation of nasal tumours in animals exposed to formaldehyde.

Species-specific dosimetry within various regions of the respiratory tract in laboratory animals and humans was also incorporated. Regional dose is a function of the amount of formaldehyde delivered by inhaled air and the absorption characteristics of the lining within various regions of the respiratory tract. The amount of formaldehyde delivered by inhaled air depends upon major airflow patterns, air-phase diffusion, and absorption at the air–lining interface. The “dose” (flux) of formaldehyde to cells depends upon the amount absorbed at the air-lining interface, mucus/tissue-phase diffusion, chemical interactions such as reactions and solubility, and clearance rates. Species differences in these factors influence the site-specific distribution of lesions.

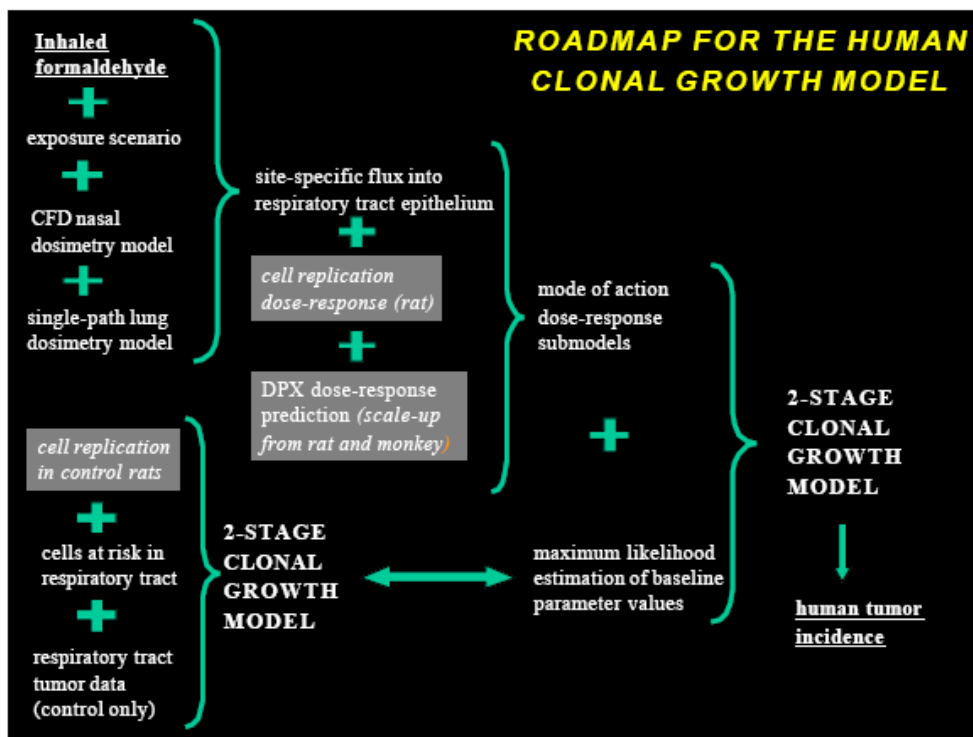
The F344 rat and rhesus monkey nasal surface for one side of the nose and the nasal surface for both sides of the human nose were mapped at high resolution to develop

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three-dimensional, anatomically accurate computational fluid dynamics (“CFD”) models of rat, primate, and human nasal airflow and inhaled gas uptake. The approximate locations of squamous epithelium and the portion of squamous epithelium coated with mucus were mapped onto the reconstructed nasal geometry of the CFD models. These CFD models provide a means for estimating the amount of inhaled gas reaching any site along the nasal passage walls and allow the direct extrapolation of exposures associated with tissue damage from animals to humans via regional nasal uptake. Although development of the two-stage clonal growth modelling for rats required analysis of only the nasal cavity (rats being obligate nose breathers), for humans carcinogenic risks were based on estimates of formaldehyde dose to regions (i.e., regional flux) along the entire respiratory tract.

The human clonal growth modelling (Figure B4) predicts the additional risk of formaldehyde-induced cancer within the respiratory tract under various exposure scenarios. Two of the parameters in the human clonal growth model – the probability of mutation per cell division and the growth advantage for pre-neoplastic cells, both in the absence of formaldehyde exposure – were estimated statistically by fitting the model to human 5-year age group lung cancer incidence data for non-smokers. The parameter representing the time for a malignant cell to expand clonally into a clinically detectable tumour was set at 3.5 years.

Figure B4: Roadmap (conceptual framework) for the human clonal growth model.



The figure shows interrelationships of the major components of the dosimetry and clonal growth models used to model tumor incidence in humans. The gray boxes indicate components of the human program that use data from rats or monkeys for cases where

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the equivalent human data were not available. CFD = computational fluid dynamics; DPX = DNA-protein cross-linking (from CIIT, 1999 and CICAD, 2002).

Estimates of carcinogenic risks using the human clonal growth model were developed for typical environmental exposures (i.e., continuous exposure throughout an 80-year lifetime to concentrations of formaldehyde ranging from 0.001 to 0.1 ppm). The human clonal growth model describes a low-dose, linear carcinogenic response for humans exposed to levels of formaldehyde of 0.1 ppm, where cytotoxicity and sustained cellular regenerative proliferation do not appear to play a role in tumour induction. Indeed, the effect of formaldehyde upon regenerative cellular proliferation did not have a significant impact upon the predicted carcinogenic risks at exposures between 0.001 and 0.1 ppm.

Conclusion: Based on the multi-modal model, CIIT considers that formaldehyde exposure poses a carcinogenic effect only under conditions that both induce toxicity and cause sustained regenerative proliferation (damage in the DNA replication process).

NOTE: The CIIT model for carcinogenicity has been widely used by other agencies and organizations (e.g., Environment Canada / Health Canada 2002, CICAD 2002, NICNAS 2005) as a more reliable estimate of cancer risk for formaldehyde exposures than the standard default assumptions used by the EPA and others in the past.

Paustenbach *et al* 1997 study:

This study presents the findings of a panel of scientists to identify an occupational exposure limit for formaldehyde that would prevent irritation. Upon review of 150 papers published on irritant effects of formaldehyde, the panel felt that 18 were pertinent in developing an exposure limit based on irritation. They concluded that, for most persons, the eye is the most sensitive indicator of irritation. They report that moderate to severe eye, nose, and throat irritation does not occur until airborne concentrations exceed 2 to 3 ppm. They also opined that at levels up to 0.3 ppm there is no increase in eye irritation above background. Nevertheless, studies of exposures ranging from 0.3 ppm to 0.5 ppm showed tremendous variability with reported irritation responses ranging from 0 to 90%.

The weight of evidence concentration-response curve considered by the panel showed that 5 to 25% of workers could report eye irritation in the 0.5 to 1.0 ppm range following ¼ to 6 hours of exposure and that eye irritation does not become significant until levels of formaldehyde reach at least 1 ppm. The panel concluded that at a level of 1 ppm would avoid eye irritation in at least 75% and up to 95% of exposed workers.

The panel subsequently put forth a position that they felt that the ACGIH TLV of 0.3 ppm (ceiling) was unnecessarily restrictive and they recommended an exposure limit of 0.3 ppm (8-hour time-weighted average) with a ceiling limit of 1 ppm. They also put forward the position that any occupational or environmental guideline for formaldehyde should be based primarily on controlled experimental studies in humans since nearly all other studies are compromised by the presence of other contaminants.

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Conclusion: A level of 1 ppm avoids eye irritation in at least 75% and up to 95% of exposed workers. The panel recommended an 8-hour TWA OEL of 0.3 ppm with a ceiling limit of 1 ppm.

Arts *et al*, 2006 study:

Following the Paustenbach *et al* 1997 study, this peer-reviewed article by scientists at the Netherlands Organization for Applied Scientific Research (“TNO”) evaluated the adverse health effects of formaldehyde exposure including sensory irritation and the potential for tumour development in the upper respiratory tract, comparing animal data with subjectively measured sensory irritation thresholds in humans. They also looked at benchmark dose analysis (“BMD”) of sensory irritation – a mathematical model approach to fitting experimental data, plotting response against dosage.

Findings of the study are as follows:

- The absolute odour threshold for formaldehyde, defined as the concentration at which a group of observers can detect the odour in 50% of the presentations, has been shown to be between 0.05 and 0.18 ppm.
- Formaldehyde is irritating to the eyes and respiratory tract. Respiratory tract irritation on the one hand is a localized patho-physiological response to a chemical involving local redness, swelling, pruritis, or pain.
- On the other hand, respiratory tract irritation and eye irritation can also involve a chemosensory effect, i.e. interaction with local nerve endings (*nervus trigeminus*) which is called trigeminal stimulation or sensory irritation.
- Over a broad range of concentrations, the trigeminal nerve stimulation will not necessarily lead to cell or tissue damage. In contrast, it will lead to a reduction in the breathing frequency aimed to reduce the total amount of inhaled material in order to protect the individual.
- For several odorous irritating chemicals, such as formaldehyde, substantial differences in the lowest concentration found to be irritating to eyes, nose and/or throat in humans exist.
- These observations can generally not be explained by differences in method sensitivity, inherent variability in biological response, or fluctuations in the exposure concentrations. These chemicals usually have a strong odour, and at least part of the wide variation in the findings may be ascribed to insufficient distinction between olfactory and trigeminal stimulation in several of the studies.
- The response at low formaldehyde levels should therefore be translated into perception or awareness rather than an annoying eye or nasal irritating reaction.
- It can, therefore, be concluded that when minimal/mild/slight irritation, which is still not annoying, is taken as a cut off level, eye and nasal irritation were found at formaldehyde levels of equal to / greater than (\geq) 1 and equal to / greater (\geq) 2 ppm, respectively, with the annotation that the threshold level of 1 ppm for eye irritation was based on the study by Bender *et al.* (1983) using pre-selected volunteers. Using the same reasoning, the minimal/mild/slight irritation level would be equal to / greater than (\geq) 3 ppm formaldehyde for throat irritation, whereas levels of up to 3 ppm did not result in dyspnea (chest tightness / discomfort) or cough (Sauder *et al.*, 1986; Kulle *et al.*, 1987; Kulle, 1993).
- A similar conclusion was reached by Paustenbach.

Appendix B – Formaldehyde OELs and Carcinogen Status According to Various Regulatory Jurisdictions and Reference Organizations

- At concentrations below 1 ppm, symptoms disappeared very quickly, underlining the non-adversity of the effects at low concentrations.
- Sensory irritation, as perceived by human subjects, can be strongly influenced by subjective feelings and interpretations when subjected to substances with strong, distinctive odours such as formaldehyde, it is a difficult job to set occupational exposure limits for odorous substances.
- Asthmatics do not seem to be more sensitive to formaldehyde than non-asthmatics exposed to concentrations up to 3 ppm.
- The NOEL for respiratory epithelial hyper/metaplasia found in long-term inhalation toxicity studies in rats suggests that formaldehyde is carcinogenic only at cytotoxic levels, i.e. at levels at which sustained regenerative epithelial proliferation is observed (≥ 6 ppm).
- Therefore, based primarily upon data derived from animal studies, inhalation of formaldehyde under conditions that induce cytotoxicity and sustained regenerative epithelial proliferation within the respiratory tract is considered to represent a carcinogenic hazard to humans. Airborne levels of formaldehyde below 1 ppm, therefore, seem low enough to protect workers against nasal tissue damage, and consequently, also against the potential risk of nasal cancer.

Table B4: Summary of effect levels of formaldehyde in humans and rats (from Arts *et al*, 2006)

Symptom	Formaldehyde concentration
Subjective eye irritation (humans)	≥ 1 ppm
Objective eye irritation (humans)	1.7 ppm
Subjective nasal irritation (humans)	≥ 2 ppm
Slight respiratory epithelial hyper/metaplasia (rats)	2-3 ppm
Extensive respiratory epithelial hyper/metaplasia, necrosis, and severe rhinitis (rats)	≥ 6 ppm
Increased number of nasal tumours (rats)	≥ 10 ppm
Objective sensory irritation (RD50 rats)	14 and 32 ppm

Conclusion: The report by Arts *et al* indicates that airborne levels of formaldehyde below 1 ppm appear are low enough to protect workers against nasal tissue damage, and consequently, also against the potential risk of nasal cancer

Appendix C – Chemical Characteristics, Routes of Entry, Biochemical Pathways, Chronic and Adverse Health Effects Associated with Exposure to Formaldehyde

Sections C1 and C2 summarize information from a number of sources including ASTDR 1999, ACGIH 2001, IARC 1995, DECOS 2003, NEG / DECOS 2003, ECOTEC 1995, CITT 1999, MAK Commission 2002 / 2006, WHO 2003, Health Canada / Environment Canada 1999, and SCOEL 2006. Since many of these organizations provide very similar information germane to the topics outlined in this appendix, no effort has been made to identify and distinguish specific references.

C1: Chemical Characteristics of Formaldehyde:

- Formaldehyde (CAS No. 50-0-0) is a colourless, highly flammable gas;
- Formaldehyde enters the environment from natural sources (including forest fires) and from direct human sources, such as automotive and other fuel combustion and industrial uses;
- Secondary formation also occurs by the oxidation of natural and anthropogenic organic compounds present in air. The highest concentrations measured in the environment occur near anthropogenic sources; these are of prime concern for the exposure of humans and other biota;
- Formaldehyde does not persist in the environment.

C2: Routes of Entry, Biochemical Pathways, Elimination of Formaldehyde:

Exogenous Formaldehyde (sources external to the body)

- External sources of formaldehyde enter either the body via inhalation of gaseous or vaporous formaldehyde or via ingestion of formaldehyde-containing substances;
- There is some potential for dermal absorption, but this has not been well characterized;
- The substance is rapidly and almost entirely absorbed following exposure by both the oral and inhalation routes.

Endogenous Formaldehyde (sources internal to the body)

- Formaldehyde is produced endogenous within the body, a product of normal metabolism;
- It is an essential metabolic intermediate present in all cells and is readily incorporated into macromolecules via normal metabolic pathways. Endogenous sources of formaldehyde include the metabolism of serine, glycine, methionine, and choline; it is also produced by the demethylation of N-, O-, and S-methyl compounds;
- Formaldehyde is an essential intermediate in the biosynthesis of purines, thymidine, and some amino acids;
- Because formaldehyde is a normal metabolic intermediate, it is not stored in any tissue to an appreciable extent;
- Hence, the substance is always present in the body and exists in all organs and tissues at quantifiable levels (2 – 3 µg/g range in humans; similar levels in the rat and monkey).

Appendix C – Chemical Characteristics, Routes of Entry, Biochemical Pathways, Chronic and Adverse Health Effects Associated with Exposure to Formaldehyde

Absorption

- Due to its highly hydrophilic (“water loving”) nature, inhaled formaldehyde is rapidly and almost entirely absorbed in the respiratory tract. In obligate nasal breathers (“nose breathing only”) such as rats, formaldehyde is almost completely absorbed in the nasal passages; in monkeys (“oronasal breathers”), absorption occurs primarily in the nasal passages but also to a lesser extent in the trachea and proximal regions of the major bronchi;
- The species-specific differences in the actual sites of formaldehyde uptake, and hence sites of nasal lesions, are determined by complex interactions among nasal anatomy, ventilation, and breathing patterns (e.g., nasal versus oronasal);
- Humans are oronasal breathers, such that there is a greater potential for formaldehyde to impact the oropharynx and portions of the lower respiratory tract, specifically the tracheobronchial region. The degree to which humans use oral versus nasal breathing is generally affected by activity patterns, with a greater ventilatory drive requiring increased mouth breathing;
- Following oral administration, absorption of formaldehyde is also rapid. Only 1% of the radioactivity from an administered oral dose (7 mg/kg) of C¹⁴ labelled formaldehyde was excreted in the feces, indicating almost complete absorption.

Distribution within the Body

- Formaldehyde reacts very quickly at the site of contact and is rapidly metabolized by enzymes in the target tissue;
- It can also be metabolized by enzymes in erythrocytes (blood cells), so that exposure to even high concentrations of atmospheric formaldehyde does not result in an increase in blood concentrations;
- In a study with human volunteers who were exposed to 1.9 ppm formaldehyde for 40 min, the level of formaldehyde in blood was not increased above pre-exposure levels. Neither were blood levels elevated in rats exposed to 14.4 ppm formaldehyde in another study for 2h duration or monkeys exposed to 6 ppm formaldehyde for 6 h/day, 5 days/wk for 4 wk.

Metabolism

- Formaldehyde is efficiently metabolized to formate by all tissues of the body as a normal metabolic process. Endogenous and exogenous formaldehyde are handled metabolically by the same processes;
- Following inhalation, formaldehyde is rapidly metabolized in the respiratory tissues with which it first comes into contact;
- Formaldehyde dehydrogenase is the primary enzyme involved in the metabolism of formaldehyde and is widely distributed in all tissues;
- Other enzymes (e.g., nonspecific aldehyde dehydrogenase and catalase) can also catalyze the oxidation of formaldehyde but are not specific for formaldehyde;
- The specific pathway for the metabolism of absorbed formaldehyde involves reaction with glutathione to form S-hydroxymethyl-glutathione. This hemithioacetal is then oxidized by formaldehyde dehydrogenase to form S-formylglutathione, which is subsequently hydrolyzed to release glutathione and formate;

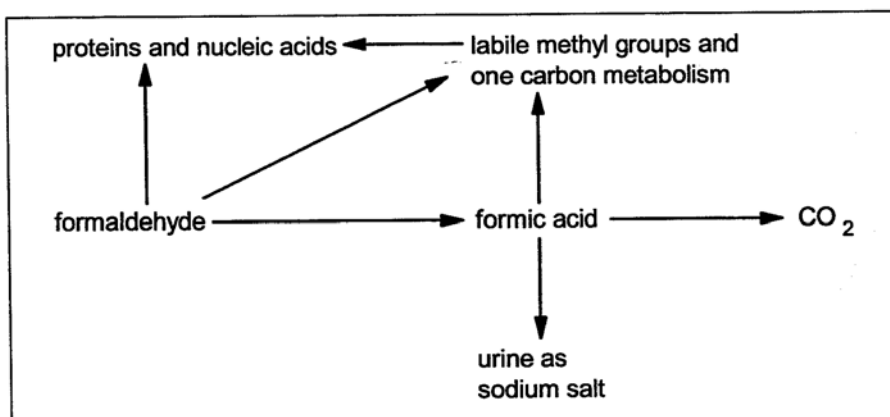
Appendix C – Chemical Characteristics, Routes of Entry, Biochemical Pathways, Chronic and Adverse Health Effects Associated with Exposure to Formaldehyde

- Formate can then enter the one-carbon pool to be utilized in purine synthesis, excreted in the urine, or further metabolized to $\text{CO}_2 + \text{H}_2\text{O}$ to be expelled via the respiratory tract.

Excretion

- Formaldehyde is eliminated via two pathways – exhalation via the respiratory tract or via renal elimination, as noted above;
- Although there appears to be no human data available, studies on rats exposed to C^{14} labelled formaldehyde indicated that about 62% of the inhaled radioactivity was excreted renally (as formic acid) and about 40% exhaled as C^{14} labelled- CO_2 ;
- Neither formaldehyde nor its metabolic derivatives (formate, formic acid) accumulate to any significant extent in the body.

The overall metabolism of formaldehyde can be summarized diagrammatically as follows (source: DECOS 2003).



C3: Health Effects:

Numerous studies have been conducted to evaluate the health effects associated with exposure to formaldehyde. Documented effects include: irritation of the eyes, respiratory tract, and skin; allergenic skin sensitization; carcinogenicity and mutagenicity.

Irritation

Formaldehyde's irritant effects have been documented over a wide range of concentrations. Irritation of the eyes and upper respiratory tract, specifically the nose and throat, and increased upper airway resistance have been observed in some studies at concentrations between 0.05 and 25 ppm. In other studies, effects on the lower airways and chronic pulmonary obstruction have been reported in the range of 5 to 30 ppm. More severe effects — including pulmonary edema, inflammation, pneumonia, and death — have been reported following exposure to higher concentrations (50 to more than 100 ppm).

Appendix C – Chemical Characteristics, Routes of Entry, Biochemical Pathways, Chronic and Adverse Health Effects Associated with Exposure to Formaldehyde

Sensitization

Both skin and respiratory sensitization due to exposure to formaldehyde have been reported in the literature. Skin effects may be either acute or chronic, depending on the physical form of formaldehyde to which individuals are exposed. Acute effects seem to be related to gaseous exposure, resulting in an acute dermatitis which affects the eyelids, face, neck, scrotum and flexor surfaces of the arms. The more chronic effects have been associated with direct handling of formaldehyde-containing substances (e.g. resins), leading to eczema of the hands and arms. The ACGIH documentation states that "the skin sensitivity apparently stems from both the direct irritant effect of formaldehyde and the development of a true skin/immunological phenomenon".

Whether formaldehyde is a respiratory sensitizer at low concentrations is less clear, and according to the ACGIH, there is not enough information available to establish a threshold for respiratory sensitization. In some studies, exposure to formaldehyde via inhalation challenge resulted in broncho-constriction and asthma-like symptoms; in others, no such responses were observed.

HSE has previously looked at the evidence for the potential for formaldehyde to induce occupational asthma (HSE, 1997). The available evidence indicates that although formaldehyde has induced asthma in some individuals, the numbers of such cases are extremely low in relation to the overall numbers of people exposed. Consequently, formaldehyde should not be regarded as a significant cause of occupational asthma.

Repeat Dose Toxicity

In humans, repeated exposure to formaldehyde under occupational or residential conditions has led to symptoms associated with irritation of the upper respiratory tract and eye at concentrations between 0.1 - 3 ppm. Studies investigating the effect of repeated formaldehyde exposure on pulmonary function in humans show little or no convincing evidence of any adverse effects, certainly when exposures are less than about 1 ppm. In studies reporting changes in pulmonary function, the changes have been small (e.g. less than 5 - 10% compared with reference values); exposures in these studies range from less than 1 ppm to about 3.5 ppm.

A few studies have undertaken histopathological examination of the nasal epithelium (biopsy specimens) in workers exposed to formaldehyde. These studies have consistently reported increases in the occurrence of mild nasal epithelial lesions (loss of ciliated cells, goblet cell hyperplasia, mild dysplasia) in exposed workers compared with unexposed controls. Mean formaldehyde exposures were in the region 0.2 - 2 ppm.

A large number of repeat dose inhalation studies have been conducted in rats, mice and monkeys. In studies in which exposure duration varied between 3 days to 13 weeks, damage to and increased cell proliferation in the nasal epithelium is reported. The histopathological changes, seen in all species, range from slight hyperplasia and squamous cell metaplasia of the ciliated and non-ciliated respiratory epithelium at concentrations of 2 - 3 ppm, to severe rhinitis, necrosis and extensive hyperplasia and metaplasia of the nasal epithelium at concentrations of 6 ppm and above. The NOAELs

Appendix C – Chemical Characteristics, Routes of Entry, Biochemical Pathways, Chronic and Adverse Health Effects Associated with Exposure to Formaldehyde

for these studies are in the range of 1 - 2 ppm. In the one study involving monkeys, exposure to 6 ppm (the only dose level used) for 6 hours/day, 5 days/week for 1 or 6 weeks, produced histopathological changes and increased epithelial cell proliferation in the upper respiratory tract. The effects were more severe after 6 weeks compared with 1 week.

Longer-term inhalation studies (up to 28 months) have also been performed in rodents. Non-neoplastic effects observed in these studies range from a minimal degree of hyperplasia and squamous cell metaplasia of the nasal respiratory epithelium (reported at concentrations between 0.3 - 2 ppm) to rhinitis, necrosis and extensive restorative hyperplasia and metaplasia of the nasal respiratory epithelium at concentrations of 6 - 15 ppm. The NOAELs in these studies are generally in the range 1 - 2 ppm.

Mutagenicity

Formaldehyde is genotoxic *in vitro* at high concentrations. It induces mutations and DNA damage in bacteria. DNA-protein cross-links, DNA single-strand breaks, chromosomal aberrations, sister chromatid exchanges and gene mutations are induced in human and rodent cells.

The mutagenic potential of formaldehyde has been well-studied *in vivo*, with data available from both humans and animals. The profile that emerges is consistent with formaldehyde acting as a site-of-contact mutagen. Overall, the animal studies show negative results in studies of systemic tissues (bone marrow, spleen, leucocytes, spermatocytes) but positive results in studies investigating mutagenicity at the site of contact (increased incidences of chromosomal aberrations in cells from the lung and GI tract). Inhalation of formaldehyde leads to the formation of DNA-protein cross-links in the nasal respiratory mucosa of rats and monkeys.

In humans, increased incidences of micronuclei are reported in the cells of the buccal cavity and respiratory epithelium, but no increases in chromosome aberrations in lymphocytes and no changes in sperm morphology are reported.

Overall, the available data indicate that formaldehyde should be considered as a site-of-contact mutagen *in vivo*. This is consistent with its toxicokinetic profile described by IARC, 1995, DECOS, 2003 and NEG / DECOS 2003, among others.

Carcinogenicity

Formaldehyde is a reactive alkylating agent and like other alkylating agents which are known or suspected carcinogens, it is biologically plausible that formaldehyde may also be carcinogenic. Other evidence supporting biological plausibility includes: formaldehyde's severe irritancy effects (irritation has been shown to be a potential precursor of cancer) and mutagenicity in short-term lab studies.

Formaldehyde is clearly an experimental animal carcinogen, at least in rats, producing nasal tumours. In 2-year inhalation studies in rats, no nasal tumours were seen with exposure to 2 ppm but clearly increased incidences of tumours were seen at 10 ppm and above. Signs of nasal epithelium inflammation were apparent soon after exposure

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began. The incidence and severity were exposure duration- and concentration-dependent, with such effects seen at concentrations down to 0.3 ppm for 24 months. Any carcinogenic potential of formaldehyde is less evident in mice and hamsters. In mice, 2/120 males showed nasal tumours following 2-year exposure to 14 ppm formaldehyde (103/240 tumours detected in male and female rats under the same exposure conditions) whilst no such tumours were seen in 88 male hamsters exposed to 10 ppm for a lifetime.

No toxicologically significant increases in tumour incidence are reported in reliable oral studies in rats or in a dermal study in mice.

Overall, the animal carcinogenicity data on formaldehyde and the available background knowledge of other substances that have one or both of the properties of site-of-contact genotoxicity and chronic inflammatory potential suggest that the nasal tumours in rats most probably arise as a consequence of pronounced chronic irritation of the respiratory tract in association with genotoxicity at this site. By extrapolation, a combination of these circumstances in humans would be of concern in relation to cancer.

Data in humans are available in the form of a large number of epidemiology studies and meta-analyses of groups of studies, some of which are reviewed in this paper. In 2004, IARC concluded that there was 'sufficient evidence' that formaldehyde has caused nasopharyngeal cancer in humans (a class 1 carcinogen), 'strong but not sufficient evidence' for a causal association between formaldehyde exposure and leukemia, and 'limited evidence' that formaldehyde has caused sinonasal cancer in humans. The available evidence did not support a causal role for formaldehyde having caused cancer at any other sites, including the lung. The ACGIH did not come to same conclusion and subsequently classified formaldehyde as a class A2 carcinogen – a suspect carcinogen.

A study-by-study appraisal by HSE's WATCH (2005) of the studies considered by IARC (and as well, studies not referenced by IARC, including papers by Marsh, CIIT), in relation to nasopharyngeal cancer was conducted by HSE's WATCH (2005), details of which are discussed in Appendix B, concludes that although an increased concern for the carcinogenic potential of formaldehyde in humans (specifically in relation to nasopharyngeal cancer), but that this falls short of providing conclusive evidence that formaldehyde exposure has caused nasopharyngeal cancer in humans; there is an inconsistent pattern to the findings of the most prominent new studies which lacks a clear explanation. Other reviews, including those conducted by DECOS, NEG, NICNAS, each have reached a similar conclusion: namely that although some individual studies are suggestive of formaldehyde possibly having caused nasopharyngeal or nasal cancer in exposed populations, the overall strength of evidence has fallen short of showing a clear and causal association.

A number of reviews that specifically address the apparent association seen in some studies between formaldehyde exposure and leukemia were published in 2004. All reach the conclusion that formaldehyde is not a causative agent for leukemia (Collins and Lineker, 2004; Heck and Casanova, 2004; Cole and Axten, 2004; Marsh and Youk,

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2004); based on an assessment of the evidence and also on biological plausibility, HSE agrees with this position.

Conclusion: Formaldehyde is an experimental animal carcinogen of the upper respiratory tract but no other organs or tissues. Although there is an increased concern for the carcinogenic potential of formaldehyde in humans the evidence falls short of providing conclusive evidence that formaldehyde exposure has caused nasopharyngeal cancer in humans.

NOTE: Regulatory authorities responsible for establishing OELs such as the HSE and the Deutsche Forschungsgemeinschaft, consider formaldehyde a genotoxic carcinogen for which a threshold can be determined. For more detail refer to Appendix B.

Reproductive toxicity

Although no fertility studies on formaldehyde have been conducted, repeat dose studies have revealed no adverse effects to the reproductive organs. There is no evidence that formaldehyde adversely affects fetal development when administered by inhalation, or by oral or dermal means. Most recently, no developmental toxicity has been reported in two inhalation studies in which rats were exposed to formaldehyde up to 40 ppm 6 hours/day on days 6 – 20 of gestation or up to 10 ppm 6 hours/day on days 6 - 15 of gestation.

Conclusion: Formaldehyde is not considered to be a reproductive toxin.

Appendix D – Workplace Exposure to Formaldehyde

Workplaces where workers could be exposed to formaldehyde

This appendix covers the types of industries where workers may be exposed to formaldehyde, and the levels to which workers have been exposed based on an extensive review of WorkSafeBC exposure data as well as that of other jurisdictions, including DECOS, Ontario, and other sources.

In BC, formaldehyde is used in the industries as shown in Table D1. Some industries use it in small quantities; for others it is a major component in production. WorkSafeBC classification unit identifiers are also shown.

Table D1: Types of Industries in which workers may be exposed to formaldehyde

<i>Classification Unit (CU)</i>	<i>Industry Type</i>
701021	Poultry hatchery
712013	Foundry
713001	Acid, base, salt, chemical, or dye mfg (NES)
713015	Glue or adhesive mfg
713020	Paint, putty, stain, sealant, or varnish mfg
713033	Synthetic resin compound mfg
714001	Cardboard or paper container mfg
714009	Laminated wood structural support product mfg
714012	Oriented strand board mfg
714019	Pressed board manufacture (NES)
714027	Veneer or plywood mfg
714034	Wooden furniture mfg
714042	Woodworking or carpentry shop
714040	Wooden truss mfg
763026	Photo film processing or microfilming
763032	Veterinary hospital, services
764027	Funeral undertaking
765007	University
766001	Acute care

Appendix D – Workplace Exposure to Formaldehyde

Formaldehyde is a widely-used product, finding use in numerous industrial applications. Its largest volume use is in the following products:

- Urea-formaldehyde resin/adhesive;
- Phenol-formaldehyde resin/adhesive;
- Plastics manufacturing; and
- Chemical intermediary.

Other uses:

- Preservative for grains and seeds;
- Preservative and drying agent in cosmetics;
- Preservative – biocide in well-drilling fluids;
- Fumigant in egg hatchery room;
- Stabilizer in gasoline;
- Corrosion inhibitor in metal fabrication;
- Photographic film hardener;
- Starch modifier;
- Chemical intermediary for dye manufacturing;
- Embalming preservative;
- Histopathology tissue preservative;
- Antiseptic and fumigant in veterinary medicine; and
- Textile fibre modifier and anti-wrinkle agent.

A review of occupational exposure to formaldehyde in British Columbia, Ontario, Quebec and other countries

To determine the extent to which workers were exposed to formaldehyde, the WorkSafeBC laboratory database (Laboratory Information Management System – LIMS) was reviewed and analyzed for the period of January 1, 1990 to December 31, 2005, inclusive. To provide a broader perspective, exposure data from Ontario, Quebec and DECOS are also included.

WorkSafeBC occupational hygiene sampling data for British Columbia workplaces

In total, over 100 WorkSafeBC laboratory analysis summary documents covering in excess of 500 individual samples, were analyzed for this evaluation of exposures to formaldehyde, covering the period of January 1, 1990 to December 31, 2005. This data is based primarily on workplace samples taken during the course of inspection by WorkSafeBC occupational hygiene officers. This database covers identifiable exposures by workers to the substance in facilities where formaldehyde is used directly (e.g., as a solution such as used in histology lab in a hospital) or exposure is to formaldehyde as a by-product (e.g., off-gassing of the substance during the curing process of urea-formaldehyde glue in a plywood plant). Data related to exploratory type sampling, such as when an occupational hygiene officer is requested to conduct an air quality assessment in a facility that does not routinely use formaldehyde, was not included. Efforts were made to obtain detail on actual exposure conditions (job type, specific task, or area).

Appendix D – Workplace Exposure to Formaldehyde

Results are presented as ranges of exposures; that is, the range from lowest to highest exposure levels in parts per million is shown. Formaldehyde levels below the laboratory quantification limit are indicated as “ND” – none detected. Data was grouped on the basis of the type of industry based on WorkSafeBC’s CU classification system. The type of sampling – area and personal – is also indicated. A personal sample is where a worker is wearing a collection device for the duration of the sampling period. An area sample is where the collection device is positioned in a fixed location usually in close proximity to the worker, usually a stationary work location such as a specific piece of equipment (e.g., a MDF press operator station). The point of sampling is to ascertain what the worker is exposed to while at the work location – to profile the amount of formaldehyde in the worker’s breathing zone. At times, the intent was to assess formaldehyde levels at the point of emission – a location where a worker would not be expected to be close proximity to. This is termed “worst-case sampling”. There is the obvious preference for personal samples since this records the actual real-time exposure experienced by the worker during the work shift, or portion thereof. Despite some of the inherent limitations of the data, the results do provide insight into the levels of formaldehyde to which workers in BC were historically been exposed to. In addition, the data are useful as they give a sense of how exposure levels changed over time in some of these industries.

The duration of sampling with the range samples is shown in minutes. 480 minutes constitutes full-shift sampling. Due to the fact that the OEL for formaldehyde has been primarily based on an 8-hour TWA, very few short term exposure samples have been collected. Of the over 500 data points analyzed over the study period only a few samples show sample duration of less than 15 minutes. Therefore, this data cannot provide a perspective on STEL or Ceiling Limit exposures.

Due to the limited number of samples taken and other factors, the data does not allow statistical analysis.

Concentrations shown in the following tables are TWA exposures. A TWA reflects all the exposures experienced over the duration of the sampling period. The TWA is basically an integrated value. As a result, any peaks and valleys the collecting device sampled over the duration of the sampling period are “hidden” since a TWA is the average concentration for the time period in which the measurement was taken. Thus, when comparing these concentrations with the proposed limit, one should keep in mind that it is possible that excursions above the limit may have occurred during the sample collection period. With TWA readings, it is not possible to determine if Ceiling Limits did indeed occur or what the magnitude or duration of those peaks may have been. To do this, one must use a direct reading, continuous monitoring device capable of measuring and recording data-logged concentrations.

Table D2 provides a summary of the occupational hygiene sampling surveys conducted for formaldehyde for the period of January 1990 to end of December 2005 in a variety of industries in British Columbia. Exposures are shown in terms of the TWA since no Ceiling Limit determinations were recorded in the LIMS system as a result of the type of sampling devices used by the Occupational Health Officers during their exposure surveys. The data is shown in two time periods where feasible – a) 1990 to 2000, and b) 2001 to 2005, allowing one to compare earlier exposure with more recent exposures. TWA exposure levels are shown as a range – from the lowest level to the highest level

Appendix D – Workplace Exposure to Formaldehyde

recorded. Data allowed Short Term Exposure Limit – STEL determinations for three entries. STELs, as defined by regulation, are time-weighted averages for 15 minute durations. For the purposes of this report, this includes exposure durations of 4 to 15 minutes.

Table D2. Formaldehyde Concentrations for the Period January 1990 to December 2005 in BC Workplaces, based on WorkSafeBC database

<i>Industry Type</i>	<i>Time frame</i>	<i>Type of Sample: (P)ersonal (A)rea</i>	<i>Exposure Time – Duration (min)</i>	<i>Exposure Levels – Range (ppm)</i>
<i>Hatchery – poultry (701021)</i>	1995	P	11 – 148	0.1 – 0.35
<i>Sausage mfg (711020)</i>	2003	A	455 – 462	0.055 – 0.18
<i>Foundry (712013)</i>	1995	P	84 – 107	0.20 – 0.24
<i>Foundry (712013)</i>	2001	P	114 – 150	0.010 – 0.012
<i>Foundry (712013)</i>	1995 – 1996	A	80 – 120	0.1 – 0.3
<i>Resin mfg (713015)</i>	1997	P	110 – 308	0.04 – 0.20
<i>Resin mfg (713015)</i>	2005	P	409 – 431	ND – 0.049
<i>Resin mfg (713015)</i>	1997	A	110 – 308	0.05 – 1.10
<i>Paperboard & cardboard mfg (714001)</i>	1992 – 1996	A	20 - 153	0.04 – 4.70
<i>Laminated wood products mfg – included under 714009, 714032, 714037</i>	1992 – 1998	A	10 – 522	ND – 1.20
<i>Laminated wood products mfg – included under 714009, 714032, 714037</i>	2001	A	117 – 133	ND
<i>Laminated wood products mfg – included under 714009, 714032, 714037</i>	1996 – 1998	P	90 - 499	0.01 – 1.20
<i>Laminated wood products mfg – included under 714009, 714032, 714037</i>	2005	P	437 – 455	0.239 – 0.381
<i>Oriented strand board (714012)</i>	2002	A	19 -132	0.099 – 1.420
<i>Oriented strand board (714012)</i>	1996 – 1997	P	102 – 182	0.10 – 0.30
<i>Oriented strand board (714012)</i>	1997 – 1999	P	15 – 455	0.03 – 0.32

Appendix D – Workplace Exposure to Formaldehyde

Industry Type	Time frame	Type of Sample: (P)ersonal (A)rea	Exposure Time – Duration (min)	Exposure Levels – Range (ppm)
<i>Pressed fibre board, MDF (714019)</i>	1996 – 2000	A	15 – 455	0.07 – 5.00
<i>Plywood (714027)</i>	1992 – 1997	A	15 – 500	ND – 0.99
<i>Plywood (714027)</i>	2002 – 2003	A	30 – 490	ND – 0.069
<i>Plywood (714027)</i>	1997 – 1999	P	88 – 129	ND – 0.249
<i>Plywood (714027)</i>	2002	P	112 – 129	0.086 – 0.220
<i>Funeral undertaking (764027)</i>	1990 – 1991	A	105 – 150	0.30 – 1.60
<i>Funeral undertaking (764027)</i>	1991	P	135 – 166	0.110 – 0.166
<i>Funeral undertaking (764027)</i>	2003 – 2004	A	84 – 86	0.485 – 0.600
<i>Funeral undertaking (764027)</i>	2003 – 2004	P	84 – 350	ND – 0.737
<i>University (765007)</i>	1998	P	26 – 84	0.520 – 0.702
<i>University (765007)</i>	1998	P	10 – 15 (STEL)	0.52 – 1.15
<i>Hospital & medical clinic (766001, 766015)</i>	1990 – 2000	A	14 – 445	ND – 0.96
<i>Hospital & medical clinic (766001, 766015)</i>	2001 – 2003	A	92 – 445	ND – 0.96
<i>Hospital & medical clinic (766001, 766015)</i>	1994 – 1998	A	5 (STEL)	3.0 – 5.2
<i>Hospital & medical clinic (766001, 766015)</i>	1990 – 2000	P	23 – 450	ND – 0.48
<i>Hospital & medical clinic (766001, 766015)</i>	2001 – 2003	P	90 – 435	0.03 – 0.35
<i>Hospital & medical clinic (766001, 766015)</i>	2000 – 2001	P	4 – 15 (STEL)	0.02 – 1.35

ND = none detected – below the detection limit of the analytical instrument or laboratory method

The results indicate that industries in which exposure levels were predominantly below the current 0.3 ppm 8-hour TWA OEL include:

- Foundries
- Resin manufacturing
- Plywood manufacturing.

Industries in which the current 0.3 ppm 8-hour TWA OEL was exceeded at times include:

- Poultry hatcheries

Appendix D – Workplace Exposure to Formaldehyde

- Paperboard & cardboard manufacturing
- Laminated wood products manufacturing
- Pressed (particle / fibre) board manufacturing
- Oriented strand board manufacturing
- Funeral homes
- Universities
- Hospitals & medical clinics.

The data also allows comparison of changes over time for some of the industries. Foundries, resin-, laminated wood-, plywood-manufacturing, and hospitals demonstrate an improvement over the earlier time period. In terms of the three STELs shown, workers would be over-exposed if the STEL OEL was established at 1.0 ppm or 2.0 ppm, particularly for hospitals. Levels up to 5.0 ppm can be expected during clean-up of spills of formaldehyde solution (histology) in a laboratory or surgical suite.

Other BC-based occupational hygiene survey

BC resin manufacturing plant survey with an electronic direct reading monitor, November 1996 – May 1997

Levels of formaldehyde at a formaldehyde-based resin manufacturing, taken by WorkSafeBC, were measured with a “formaldemeter” – a direct reading rapid response electronic instrument capable of providing near instantaneous measurements of formaldehyde. It can thus be used to determine if the Ceiling Limit is exceeded. Table D3 shows formaldehyde readings – spot readings – for the period covering November 1996 to May 1997.

Table D3: Spot readings - Formaldehyde levels at a BC resin manufacturing plant during 1996 and 1997

<i>Date</i>	<i>No. of Samples</i>	<i>Range of Results (ppm) for Formaldehyde</i>
Nov 96	7	0.13 – 0.35
Dec 96	7	0.10 – 0.38
Feb 97	7	0.02 – 0.36
Mar 97	7	0.02 – 0.36
April 97	7	0.04 – 0.38
May 97	7	0.03 – 0.40

As shown in the table, a Ceiling Limit of 0.3 ppm would be exceeded at least once on every sampling occasion over the time period shown. Of the 42 instantaneous area measurements taken by the formaldemeter, 6 exceeded 0.3 ppm. These excursions consistently occurred in the same area of the plant — specifically, in or around the dry products building. Of the 30 personal samples taken, only one yielded a concentration greater than 0.3 ppm; this measurement was taken on the shipper/receiver. It is evident

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that for most areas of the plant and for most jobs compliance with a time-weighted average or ceiling exposure limit of 0.3 ppm is achievable for this plant.

Occupational exposure data on formaldehyde – Ontario

Table D4. Formaldehyde exposure levels in plywood and pressed board products manufacturing, September 2002 (Ontario Ministry of Labour)

<i>Location</i>	<i>Date</i>	<i>8-hour TWA reading (ppm)</i> <i>Range</i> <i>MVUE¹ (LCL², UCL³)</i>	<i>15-minute STEL reading (ppm)</i> <i>Range</i> <i>MVUE¹ (LCL², UCL³)</i>	<i>Formaldehyde Instantaneous Ceiling Limit reading (ppm)</i> <i>Range</i> <i>MVUE¹ (LCL², UCL³)</i>
<i>Company A</i> <i>Particle board plant</i>	Sept. 9, 2002	0.07 – 0.20 0.146 (0.110, 0.228)	0.15 – 0.54 -----	0.18 – 7.47 1.435 (0.941, 3.110)
<i>Company B</i> <i>Plywood plant</i>	Sept. 11, 2002	0.16 – 0.17 0.164 (0.159, 0.169)	0.14 – 0.29 0.205 (0.153, 0.348)	0.33 – 0.44 0.357 (0.332, 0.387)
<i>Company C</i> <i>Particle board plant</i>	Sept. 11, 2002	0.08 – 0.11 0.090 (0.077, 0.110)	0.14 – 0.29 -----	0.17 – 0.50 0.309 (0.268, 0.369)
<i>Company D</i> <i>Oriented strand board (OSB) plant</i>	Sept. 12, 2002	0.03 – 0.08 0.054 (0.042, 0.082)	0.24 – 0.26 -----	0.09 – 0.97 0.391 (0.315, 0.542)

Calculations completed by PRD.

¹ MVUE = estimated arithmetic means, lognormal parametric. Blanks indicate too few data points to allow statistical calculations.

² LCL = 95% lower confidence limit (LCL_{1,95%})

³ UCL = 95% upper confidence limit (UCL_{1,95%})

The Ontario exposure data indicated that the current 8-hour TWA of 0.3 ppm for formaldehyde was not exceeded in either of the two particle board plants, plywood mill, or oriented strand board plant. On the other hand, instantaneous readings show that the ACGIH-TLV Ceiling Limit of 0.3 ppm would be exceeded on most occasions; certainly the arithmetic means are exceeded for all plants, with particle board plant “A” showing the highest arithmetic mean, based on 19 samples. Spot readings were recorded as high as 7.47 ppm at this plant. This reading was taken at the press outfeed and flying cut-off saw location. The exhaust fan servicing the press outfeed (used to control formaldehyde levels at the point of emission) was not functioning at the time of the survey. This is an important observation to consider – if exhaust air extraction systems are not operating, the potential for worker over-exposure is greatly increased.

Based on the arithmetic means for instantaneous readings, the current Ceiling of 1.0 ppm was not exceeded in all plants with the exception of Plant A – the particle board

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plant. As noted in the source document, during the survey conducted at the oriented strand board plant, several roof fans were noted running in reverse and the press area was not receiving enough make-up air (an adequate supply needs to be delivered to compensate for the quantities of air pulled through the exhaust system(s) servicing the press).

Quebec exposure data on formaldehyde collected at pressed (particle / oriented strand / medium density fibre) board manufacturing plants - 2001 & 2002

As part of an extensive health study on the impact of changing occupational exposure limits for formaldehyde, the IRSST funded several occupational hygiene surveys of workplace in that province. Past and present formaldehyde measurements made in various pressed wood manufacturing plants in Quebec were studied as part of an evaluation of the health effects undertaken in Quebec in order to determine worker exposure levels. This study, as summarized in Table D5, is part of a larger report (Lavoue, *et al*, 2003).

Table D5. Formaldehyde exposure levels at Quebec oriented-strand board (OSB), medium density fibre board (MDF) and particle board (PB) plants – 2001 to 2002.

<i>Type of Plant</i>	<i>Job Title, Location</i>	<i>(P)ersonal or (A)rea Sample</i>	<i>Exposure Level¹ Geometric Mean</i>
<i>Oriented Strand Board Plant</i>	Asst. press operator	P	0.04 / 0.07
	Shipper	P	0.06 / 0.10
	Finisher	P	0.05 / 0.07
	Press operator	P	0.03 / 0.08
	Maintenance worker	P	0.06 / 0.08
	Chip preparer	P	0.04 / 0.11
	Storage / shipping	A	0.04 / 0.06
	Finishing	A	0.09 / 0.09
	Main Production area	A	0.05 / 0.15
	Resin production storage	A	0.05 / 0.09
<i>Medium Density Fibre Board Plant</i>	Raw material – chip preparation	A	0.08 / 0.10
	Asst. press operator	P	0.09 / 0.27
	Shipper	P	----- 0.19

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Type of Plant	Job Title, Location	(P)ersonal or (A)rea Sample	Exposure Level ¹ Geometric Mean
	Finisher	P	0.16 / 0.24
	Maintenance worker	P	0.12 / 0.11
	Resin operator	P	0.22 / 0.34
	Storage / shipping	A	0.17 / 0.37
	Finishing	A	0.22 / 0.33
	Main Production area	A	0.26 / 0.75
	Resin production storage	A	----- 0.35
	Raw material – chip preparation	A	0.16 -----
<i>Particle Board Plant</i>	Asst. press operator	P	0.20 / 0.28
	Shipper	P	0.16 / 0.20
	Finisher	P	0.19 / 0.26
	Maintenance worker	P	0.10 / 0.22
	Resin operator	P	0.16 / 0.41
	Flat mill operator	P	0.12 / 0.17
	Storage / shipping	A	0.09 / 0.17
	Finishing	A	0.20 / 0.29
	Main production	A	0.75 / 0.56
	Resin production storage	A	0.08 / 2.00
	Raw material – chip preparation	A	0.42 / 0.03

¹The values shown are based on samples collected by both the Quebec government occupational hygiene inspectors (CSST) (column 1) and research scientists IRSST) data (Lavoue, *et al*, 2003).

The Quebec research team collected 275 samples during 2001 – 2002 while 590 measurements dating back to 1984 were obtained from government records (Commission of Health & Occupational Safety – CSST). The area measurements had a global geometric mean of 0.28 ppm while that for personal samples was 0.17 ppm. Higher levels were found in the government data as compared to research data. This sampling bias is most likely due to the fact that government occupational hygienists tend to sample “worst-case” exposures. This observation can also be applied to the WorkSafeBC data – there is a “worst-case” sampling bias. Proximity to the press and processes resulted in the highest exposures. Overall, exposure levels are below BC’s current 0.3 ppm TWA OEL for the Quebec oriented strand board industrial plants

Appendix D – Workplace Exposure to Formaldehyde

studied. There are some exposures in excess of BC's 8-hour TWA OEL recorded for the medium density fibre board and particle board plants, but most are below the BC-based 8-hour TWA OEL of 0.3 ppm. However, these exposure levels are based on time-weighted averaged measurements. The data does not provide any information on instantaneous peaks that may have occurred during the time the sample was being taken.

DECOS 2003 Formaldehyde Exposure Data

DECOS completed an extensive health study on formaldehyde in 2003. The report includes an extensive summary of exposure data – much of it dates back over 20 years ago. Some of this data is shown Table D6 for a number of different industries of interest to the situation in BC.

Table D6. Formaldehyde exposure data in various industries (DECOS, 2003)

<i>Industry</i>	<i>Date</i>	<i>Job / task or work area</i>	<i>(P)ersonal or (A)rea sample</i>	<i>Exposures to Formadehyde Range – ppm</i>
Formaldehyde resin mfg	1980	Plant work areas - various	A	0.05 – 0.37
	1980		P	0.06 – 5.40
	1983		A	0.12 – 0.89
Plywood & particle board	1979	Plant work areas - various	A	1.0 – 2.5
Wood furniture mfg	1983	particle board veneering	A	0.008 – 6.40
Paper & paperboard mfg	1976	Paper treatment – resin impregnation	P	0.01 – 0.23
			A	0.04 – 0.08
Foundry	1976	Core machine operators	P	0.07 – 18.30
		Moulding	P	0.03 – 0.78
Fiberglass insulation	1980	Installers	P	0.007 – 0.33
Funeral home	1975	Embalmers	A	0.09 – 5.26
	1980		P	0.20 – 3.99
Hospital	1975	Autopsy	P	0.57 – 1.58
	1975		A	0.13 – 13.57
	1979		A	2.20 – 7.90
University	1983	Animal dissection	P	<0.38 – 1.04
			A	0.05 – 0.40

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DECOS provided no recent exposure data. Very high levels were recorded, particularly during autopsy work in hospitals and for core machine operators in foundries. For the latter, exposure is via the urea or phenol formaldehyde thermosetting resin binder used in forming the sand-based moulds for that industry. Currently, low-emission urea-formaldehyde / phenol-formaldehyde thermosetting resin binders are being used in the foundry industry and exposure levels are correspondingly lower. This data indicates how much lower the exposure levels have become over the years.

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