INCIDENT REPORTS ASSOCIATED WITH

Formaldehyde

(methanal, oxomethane, oxymethylene, methylene oxide,
formic aldehyde, methyl aldehyde)

PC Codes: 043001

January 30, 2008

U.S. Environmental Protection Agency
Office of Pesticide Programs
Antimicrobials Division

TABLE OF CONTENTS

0.0 INTRODUCTION

The purpose of this chapter is to review the evidence of health effects in humans resulting from exposure to formaldehyde.

Two approaches are used in this section:

1. The potential health effects of formaldehyde in humans, reported as incident reports from different sources, are summarized.

2. A literature search of health effects associated with formaldehyde exposure, including results of epidemiological studies, is summarized.

1.0 INCIDENT REPORT DATA ASSOCIATED WITH HEALTH EFFECTS

The following databases have been consulted for incident data:

OPP Incident Data System (IDS) - The Incident Data System of The Office of Pesticide Programs (OPP) of the Environmental Protection Agency (EPA) contains reports of incidents from various sources, including registrants, other federal and state health and environmental agencies and individual consumers, submitted to OPP since 1992. Reports submitted to the Incident Data System represent anecdotal reports or allegations only, unless otherwise stated. Typically no conclusions can be drawn implicating the pesticide as a cause of any of the reported health effects. Nevertheless, sometimes with enough cases and/or enough documentation risk mitigation measures may be suggested.

Poison Control Centers - as the result of a data purchase by EPA, OPP received Poison Control Center data covering the years 1993 through 2003 for all pesticides. Most of the national Poison Control Centers (PCCs) participate in a national data collection system, the Toxic Exposure Surveillance System, which obtains data from about 65-70 centers at hospitals and universities. PCCs provide telephone consultation for individuals and health care providers on suspected poisonings involving drugs, household products, pesticides, etc.

California Department of Pesticide Regulation - California has collected uniform data on suspected pesticide poisonings since 1982. Physicians are required, by statute, to report to their local health officer all occurrences of illness suspected of being related to exposure to pesticides. The majority of the incidents involve workers. Information on exposure (worker activity), type of illness (systemic, eye, skin, eye/skin and respiratory), likelihood of a causal relationship, and number of days off work and in the hospital are provided.

Incidents and Epidemiological Studies Published in Scientific Literature - Some incident reports and/or epidemiological studies associated with formaldehyde related human health hazards are published in the scientific literature.

`

1.1 OPP's Incident Data System (IDS)

Seven incidents reported for human exposure to formaldehyde occurred in hospital workers (sterilization of instruments and spill clean-up) and in persons handling or being in close proximity to pesticide formulations containing this active ingredient (in combination with other chemicals). Five of the 7 incidents reported were solely due to inhalation of these chemical vapors. In one incident, where deliberate and intentional disposal of 9 gallons of formaldehyde (together with other variable quantities of chemicals) into the school drains exposed students to several mixtures of chemical vapors. One of the students affected was hospitalized due to severe respiratory problems. In a second incident, the person was exposed to a mixture of chemicals (formaldehyde, glacial acetic acid and sodium meta-bisulfite) in a holding tank, next to his work station; and suffered from insomnia, disorientation, bronchitis, sore throat and severe pain in hands and feet. Following a six month period, this person became totally non-functional. In the third incident, respiratory and gastro-intestinal tract problems were observed in 17 hospital workers who cleaned up spills of chemicals containing 4% glutaraldehyde and 3% formaldehyde. In the fourth incident, a technician working in proximity to glutaraldehyde and formaldehyde experienced asthma, arrhythmia, rhinitis, and was diagnosed as being sensitized to formaldehyde. Similar effects were observed in the fifth incident of human exposures to formaldehyde in combination with other chemicals.

The remaining 2 of 7 incidents occurred via combined routes (inhalation, dermal and ocular). A hospital worker exposed to formaldehyde and glutaraldehyde developed asthma, arrhythmia, airway disease, mucous in the throat, shortness of breath, rhinitis, dermatitis, eye irritation, focusing difficulties and symptoms of corneal burn. In another incident, a female worker selling industrial/laundry chemicals and pesticides (chlorinated organophosphorous pesticides, diazinon, malathion, formaldehyde, methyl ethyl ketone, perchloroethylene, sodium cyanide, benzene, toluene, vinyl chloride, DDT, chlordane, hepatochlor, trichloroethene, sodium sulfate, sodium chloride, sodium hypochlorite, chloroethene, herbicides, volatile organics, acid components, base neutral compounds and dissolved metals) experienced headaches, mental confusion, cutaneous T-cell lymphoma, syncopal spells, seizures, dizziness, loss of equilibrium, nausea, dermatitis, skin irritation and a rash, that continued for seven years.

The chemical formaldehyde is a known irritant when inhaled and can cause severe dermal, ocular and gastro-intestinal illnesses. However, the human incidents reported for formaldehyde do not reflect exposure to this chemical alone, but in combination with other chemicals.

1.2 Poison Control Center (1993 – 2003)

There is no one incidence reported in the Poison Control Center Data.

1.3 California Data - 1982 through 2004

There are 116 incidences that have been reported in the California Pesticide Surveillance Program Database (1982-2004) as definitely or probably related to formaldehyde alone or in combination. As summarized in Table 1, symptoms associated with eyes are the primary reported illness in all the associated incidences. Nausea, dizziness, headache, and sore throat are the primary systemic effects that have been reported. The primary dermal effects that have been reported are rash, burning sensation, itching, dry scaling irritation, cracking and thickened skin, itching, and blisters and rash on hands.

As summarized in Table 2, although there are some people who were unable to work after exposure for a certain period of time, no one was hospitalized.

Table 1. Cases Due to Formaldehyde Exposure in California Reported by Type of Illness and Year, 1982-2004

Year	Illness Type					
	Systemic [a]	Eye	Skin [b]	Respiratory	Combination [c]	Total
1982	1	3	-	-	-	4
1983	1	-	-	-	-	1
1984	-	1	1	-	-	2
1985	-	-	1	-	-	1
1986	-	1	-	-	-	1
1987	-	2	-	-	-	2
1988	4	2	-	-	-	6
1989	8	7	1	10	9	17
1990	-	3	-	2	1	4
1991	6	12	1	10	11	18
1992	5	7	2	3	4	13
1993	1	3	-	2	1	5
1994	1	2	-	1	1	3
1995	4	5	1	2	3	9
1996	-	3	2	1	1	5
1997	1	4	3	3	3	8
1998	1	5	2	3	2	9
1999	1	2	-	1	1	3
2001	-	3	-	-	-	3
2002	-	1	-	1	-	2
Total	34	66	14	39	37	116

[a] Category include cases where nausea, sore throat, dizziness, headache and other systemic effects occurred.
[b] Category includes burning sensation, dry scaling irritation, cracking and thickened skin, itching, and blisters and rash on hands.
[c] Category includes combined effects to eye, skin, respiratory and/or systemic effects.

Table 2. Number of days lost from work or Hospitalized for Indicated Number of Days after being Exposed to formaldehyde in California, 1982-2004.

	Number of Days lost from work	Number of Persons Hospitalized
One day	15	-
Two days	6	-
3-5 days	5	-
6-10 days	-	-
11-16 days	1	-
Indefinite [a]	1	-
Unknown[b]	11	-

Note:
(a) An entry of indefinite indicates the event occurred, but the time period is not known.
(b).An entry of unknown indicates no information was provided.

1.4 Incidents and Epidemiological Studies Published in Scientific Literature

There are many reported incidents and epidemiological studies been published in scientific literature.

Non-Carcinogenic - Dermal Exposure

Formaldehyde is a dermal irritant and a dermal sensitization agent. Engel and Calnan (1966) reviewed cases of dermatitis noted over three years (1962-1965) in a car factory among 150 employees who handled rubber weather strips coated with phenol-formaldehyde resins. A total of 50 cases of dermatitis were observed. The average duration of the eruption was 12 weeks, however, in three cases it persisted up to 2.5 years. The eruption was generally an erythematous vesicular rash of the fingers and hands. Exposure durations were for 1 day to two years before the onset of the eruption, with an average period of contact of 17 weeks. 29 dermatitis patients were patch-tested. Among the patch-tested patients, four (14%) gave a weak reaction to phenol alone, while 65% had a positive reaction to the adhesive resins.

Japanese Contact Dermatitis Research Group (1982) summarized patch tests with 2% formaldehyde (10 mg/cm^2) performed at 17 Japanese hospitals on more than 900 patients and healthy volunteer subjects. Irritation was noticed in 2.78% and a delayed reaction in 2.62% of the patients.

One hundred-sixty-seven doctors, 92 dentists, and 333 nurses were patch-tested with a standard

þanel of allergens plus allergens common to their work environment (Rudzki et al.1989). Among nurses, formaldehyde was the disinfectant that most frequently caused allergic reactions (9.6%).

Sneddon (1968) monitored 13 staff members for 3 weeks in a haemodialysis unit where formalin was used as a sterilant. Patch tests administered with 3% formalin, 6/13 developed dermatitis, 4 of the 6 were positive in patch test.

Dermal sensitization is induced only by direct skin contact with formaldehyde solutions in concentrations higher than 2% (WHO 1989). In sensitized patients, one of 5 volunteers reacted, under controlled conditions, to a challenge concentration of 0.01% formaldehyde (Marzulli and Maibach, 1973). Occluded patch test study of 20 sensitized subjects and 20 healthy volunteers (Flyvholm et al. 1977). No skin irritation occurred in the controls exposed to 1% formaldehyde. In sensitized subjects, the frequency of response decreased with decreasing formaldehyde concentrations as follows: 9/20 at 0.5%, 3/20 at 0.1%, 2/20 at 0.05%, and 1/20 at 0.025%. WHO (1989) concluded that the lowest patch test challenge concentration in an aqueous solution reported to produce a reaction in sensitized persons was 0.05%.

Non-Carcinogenic - Inhalation Exposure

Formaldehyde has a pungent odor detectable at low concentrations, and its vapor and solutions are known eye and upper respiratory irritants in human beings. The common effects of formaldehyde exposure are various symptoms caused by irritation of the mucosa in the eyes and upper airways.

As summarized by NRC (2007), no reports of deaths in humans resulting from inhaled formaldehyde were mentioned in the literature, and only a few case reports of accidental inhalation exposures resulting in human intoxication were found in the reviews consulted (IARC 1995; ATSDR 1999; ACGIH 2001; Health Canada 2001; WHO 2002; Liteplo and Meek 2003; NAC 2003). Effects of formaldehyde at high but unreported concentrations include tracheobronchitis and spasms and edema of the larynx (ACGIH 2001). Pulmonary edema, inflammation, and pneumonia occurred after exposure to airborne formaldehyde at concentrations of 50 to 100 ppm (ACGIH 2001).

Exposure to moderate levels of formaldehyde (1-3 ppm) can result in eye and upper respiratory tract irritation (Weber-Tschoppe et al., 1977; Kulle et al. 1987). Feinman (1988) states that most people cannot tolerate exposures to more than 5 ppm formaldehyde in air; above 10-20 ppm symptoms become severe and shortness of breath occurs. High concentrations of formaldehyde may result in nasal obstruction, pulmonary edema, choking, dyspnea, and chest tightness (Porter, 1975; Solomons and Cochrane 1984).

Health effects of low-level exposure to formaldehyde is also been monitored Main and Hogan (1983). Among 21 subjects exposed to formaldehyde (0.14 to 1.9 mg/m3) in a mobile home trailer were examined. 18 unexposed controls were included. No differences in lung function

were found between the two groups. However, there were significantly more complaints of eye and throat irritation, headache, and fatigue among the exposed.

Allergic reactions and asthma-like conditions also have been reported following occupational exposures. A medical intern exposure to formaldehyde over a period of 1 week developed dyspnea, chest tightness, and edema, following a final 2 hour exposure to high concentrations of formaldehyde (Porter 1975). Five workers exposed to high concentrations of formaldehyde from urea-formaldehyde foam insulation experienced intolerable eye and upper respiratory tract irritation, choking, marked dyspnea, and nasal obstruction (Solomons and Cochrane, 1984). However, the concentration of formaldehyde and the contribution of other airborne chemicals were unknown in both of the reports (OEEHA 1999).

Asthma has also been suggested in formaldehyde exposed occupational workers (Burge 1985). Bronchial provocation tests with a mean formaldehyde concentration of 4.8 mg/m3 (range not given) on 15 formaldehyde-exposed workers with symptoms suggesting occupation-related asthma. 3 subjects with delayed bronchio-spasm and 6 with an immediate reduction in forced expiratory volume in one second (FEV_1).

One hundred nine workers and 254 control subjects were studied to evaluate the effects of formaldehyde on the mucous membranes and lungs. A modified, respiratory symptom questionnaire and spirometry were admin to all study participants before and after their work shift, and formaldehyde levels were determined for each test subject. Over the course of the monitored work shift, test subjects demonstrated a dose-dependent excess of irritant symptoms and a statistically significant decline in certain lung function parameters. Baseline spirometry values were not significantly different between test and control groups, and formaldehyde-exposed workers did not report an excess of respiratory symptoms. Formaldehyde is a dose-dependent irritant of the eyes & mucous membranes at low-level exposures. It can exert a small, across-shift effect on airways but after a mean exposure of 10 yr does not appear to cause permanent respiratory impairment. (Horvath et. al. 1988)

The effect of formaldehyde exposure on medical students conducting dissections in the gross anatomy laboratory course was evaluated (Fleischer 1987). By using self-administered questionnaires designed to assess the frequency of occurrence of various symptoms associated with the acute effects of formaldehyde exposure. The questionnaires were given to a cohort of 1st-yr medical students on completion of the gross anatomy lab course. Air sampling of formaldehyde levels in the anatomy labs was carried out on one day during the time in which these students were conducting dissections. Although the results of the air sampling showed formaldehyde levels to be well below current occupational standards, significant numbers of students reported experiencing symptoms associated with formaldehyde exposure. In addition, it was found that female students were 3 times more likely to report formaldehyde-related symptoms than male students.

In a similar study, a group of 24 physical therapy students dissected cadavers for 3-hour periods per week over 10 weeks. Estimates of breathing zone formaldehyde concentrations ranged from

0.49 to 0.93 ppm (geometric mean 0.73±1.22 ppm). The peak expiratory flow rate (PEFR), the only pulmonary function variable measured in this study, was measured before and after each exposure period. Mean baseline PEFR declined by about 2%. Postexposure PEFR means were 1–3% lower than preexposure PEFR means during the first 4 weeks, but this difference was not apparent during the last 6 weeks. Fourteen weeks after the end of the 10-week period, the mean PEFR for the group returned to the preexposure baseline value (Kriebel et al. 1993).

A prospective evaluation of pulmonary function and respiratory symptoms among 103 medical students exposed at a TWA concentration that was generally less than 1 ppm with peak exposures less than 5 ppm was conducted over a 7-month period. Acute symptoms of eye and respiratory irritation were significantly associated with such exposure (Uba et al. 1989). Formaldehyde exposed workers (<1 mg/m3 with some higher peak values not stated) in a formaldehyde manufacturing factory . Nasal symptoms in 30 workers, about 40% of the workers had rhinitis with nasal obstruction and discharge (Wilhelmsson and Holmstrom, 1987).

38 employees exposed to formaldehyde when working with acid-hardening lacquers and 18 nonexposed control persons employed at the same company were examined to determine lung function (spirometry and nitrogen washout), total immunoglobulin blood concentration, and work-related symptoms. The mean exposure to formaldehyde during an 8-hr workday was 0.40 mg/m3 air, and the mean exposure to peak values was 0.70 mg/m3. Mean exposure to solvents was low, i.e., approximately 1/10 of the hygienic effect. The workers were employed for an average of 7.8 years; estimates of formaldehyde concentrations in workplace air ranged from 0.2 to 2.1 ppm with a TWA mean of 0.3 ppm. Eye, nose, and throat irritation was more common in exposed persons than in controls. Monday morning, after two exposure-free days, forced vital capacity (FVC) values were found to have declined by 0.24 L and forced expiratory volume in 1 sec (FEV_1) by 0.21 L, compared with normal values (Alexandersson. and Hedenstierna 1988).

Since January 1978 , the Wisconsin Division of Health has collected air samples and environmental data on mobile homes, conventional homes, and offices that have particleboard in their construction and foam insulation. The median formaldehyde concentration was 0.47 ppm (range < 0. 1-3.68 ppm) and a positive (inverse) association was present between age of the structure and formaldehyde concentration. The greatest prevalence of symptoms was for irritation of mucous membranes, but of the 256 subjects, 53% reported headaches and 38% reported difficulty in sleeping. Among infants and young children, vomiting, diarrhea, and respiratory problems were identified as particularly important conditions. The relationship between smoking and formaldehyde concentration in the dwelling was examined; smoking did not significantly increase formaldehyde concentration in the home at the time of concentration measurement (Dailly et al., 1981a and 1981b; Hanrahan et al. 1981 and 1984).

On December 1, 1978, a meeting was held in Washington, D.C. to exchange information dealing with the assessment of potential health problems associated with formaldehyde emissions following the installation of urea-formaldehyde foam insulation. Representatives of eleven states reported on complaints from residents of a total of 39 homes and apartments. At least two atmospheric samples were collected during each investigation. Shortly after the meeting, the

State of Colorado, Department of Law, Office of the Attorney General issued a warning. It stated that, " … urea-formaldehyde foam has characteristics which may adversely affect health…persons exposed to the substance may experience any one or all of the following symptoms: Difficulty in breathing, watery eyes, nasal congestion, ear, nose and throat irritation, upper respiratory stress, nausea, headache, difficulty in sleeping, disorientation, skin rashes, dizziness, vomiting, diarrhea, and asthmatic attacks." It was noted that 80 percent of the atmospheric sample results were less than 0.5 ppm formaldehyde (Wilson, 1987)

Respiratory health of plywood workers occupationally exposed to formaldehyde is been studied in several epidemiological studies. 93 plywood workers were compared with a group of 93 nonexposed subjects. The plywood workers were employed for a mean of 6.2±2.4 years in workplaces with estimated formaldehyde air concentrations ranging from 0.22 to 3.48 ppm. The mean product of employment duration times workplace air formaldehyde concentration was 6.2 ppm/year (sd 2.72 ppm/year) for the exposed group of workers; division of this value by the average duration of employment (6.2 years) arrives at an estimated average exposure concentration of 1 ppm formaldehyde. Reported average respirable and total wood-dust concentrations in workplace air were 0.60 and 1.35 mg/m3, respectively. The percentages of subjects with abnormal values for a number of pulmonary function variables (e.g., FEV_1 and FEF25–75) were significantly higher in the group of plywood workers compared with a group of nonexposed subjects. Mean values of baseline FEV1 and FEFR25–75, after adjustment for dust exposure, were reportedly statistically significantly lower in the exposed group of workers compared with the nonexposed group (FEV_1 2.78 L [sd 0.41] versus 2.82 L [sd 0.3]; and FEF25–75 3.14 L/second [sd 0.76] versus 3.44 L/second [sd 0.78]). Malaka and Kodama (1990) noted that although the small differences were statistically significant, their clinical significance was unclear.

Biopsy evaluation of the interior turbinate nasal mucosa of 20 men (average age, 36 years) who had been exposed at 0.1 to 1.1 ppm formaldehyde during particle board processing for an average of 7 years (Edling et al. 1985) The histopathological findings were compared to those from a reference group of 25 men, but who were without occupational exposure to “irritating agents.” Five of the formaldehyde-exposed men had swollen or dry changes, or both, of the nasal mucosa; microscopic evaluation revealed a loss of cilia and goblet cells, squamous metaplasia, and, in some individuals, mild dysplasia.

In a perspective study, Alexandersson, et al (1989) studied the pulmonary function in wood workers exposed to formaldehyde. Employees exposed to formaldehyde in the woodworking industry (N = 47) and nonexposed control subjects (N = 20) were examined in 1980 by spirometry and the nitrogen washout technique. A transient impairment of lung function was noted over a work shift. Five years later, 21 subjects were still experiencing exposure to formaldehyde. A transient decrease in lung function was again found over a work shift, as evidenced by a reduction in forced mid-expiratory (FEF25-75) of 0, 15 l/s and an increase in closing volume (CV%) of 3.0% in nonsmokers. Significant decreases in forced expired volume in 1 s as a percent of forced vital capacity (FEV 1.0/FVC) and FEF25-75 were also noted over the 5 y in nonsmokers (0.4% and 0, 2 l s/y, respectively, after correction for normal aging).

After 4 wk of no exposure (holidays), FEF25-75 and forced expired vital capacity (FVC, FEV1.0) returned to normal in the smoking group. Lung function in workers improved less during the holiday. A dose-response relationship was found between exposure to formaldehyde and decrease in lung function. Thus, industrial exposure to formaldehyde causes transient lung function impairment over a work shift, with a cumulative effect over the years. The impairment, however, can be reversed with 4 wk of no exposure.

Histological changes in nasal tissue specimens were examined from a group of 70 workers in a chemical plant that produced formaldehyde and formaldehyde resins for impregnation of paper, a group of 100 furniture factory workers working with particle board and glue components, and a nonexposed, control group of 36 office workers in the same village as the furniture factories (Holmstrom et al. 1989) . Mean durations of employment were 10.4 years for the chemical workers and 9.0 years for the furniture workers. Estimates of personal breathing zone air concentrations ranged from 0.04 to 0.4 ppm for the chemical workers, from 0.16 to 0.4 ppm for the furniture workers, and from 0.07 to 0.13 ppm in the late summer for the office workers with a year-round office worker median reported as 0.07 ppm with no standard deviation. The mean wood dust concentration in the furniture factory was reported to have been between 1 and 2 mg/m3. Nasal histology scores ranged from 0 to 4 for the chemical workers, from 0 to 6 for the furniture workers, and from 0 to 4 for the office workers. The mean histological score for the chemical workers, but not the furniture workers, was significantly different from the control score, thus supporting the hypothesis that the development of nasal lesions is formaldehyde-related and not obligatorily related to a possible interaction between formaldehyde and wood dust. The most severe epithelial change (light or moderate dysplasia) was found in two furniture workers. Among the control workers (not exposed to wood dust), loss of cilia, goblet cell hyperplasia, and cuboidal and squamous cell metaplasia replacing the columnar epithelium occurred more frequently than in the control group of office workers. Within both groups of formaldehyde-exposed workers, no evidence was found for associations between histological score and duration of exposure, index of accumulated dose, or smoking habit.

Horvath et al. (1988) studied the effects of formaldehyde on the mucous membranes and lungs in an industrial population. 109 workers and 254 control subjects were studied to evaluate the effects of formaldehyde on the mucous membranes and lungs. A modified, respiratory system questionnaire and spirometry were administered to all study participants before and after their work shift, and formaldehyde levels were determined for each test subject. Estimated TWA formaldehyde concentrations ranged from 0.17 to 2.93 ppm (mean 0.69 ppm). Median concentrations of airborne nuisance particulates (i.e., wood dust) in the particle board plant were 0.38 and 0.11 mg/m3 for total and respirable particulates, respectively. Over the course of the monitored work shift, test subjects demonstrated a dose-dependent excess of irritant symptoms and a statistically significant decline in certain lung function parameters. Formaldehyde is a dose-depended irritant of the eyes and mucous membranes at low-level exposures. It can exert a small, across-shift effect on airways but after a mean exposure of ten years does not appear to cause permanent respiratory impairment.

Non-Carcinogenic - Oral Exposure

Only limited acute cases with oral exposure to formaldehyde have been published in scientific literature. Burkhart et al (1990) reported a case of a 58-year-old man swallowed 4 ounces of formalin (517 mg formaldehyde/kg) in a suicide attempt. The man was found unconscious by a co-worker about 1 hour after his shift began. In the emergency room, the subject regained consciousness but was lethargic. Laboratory results indicated significant acidosis. Approximately 3 hours after ingesting the formalin, the patient complained of abdominal pain and began retching without emesis; he was admitted for observation and treated with ethanol. The patient's abdominal pains became more severe and he had difficulty breathing. At 5.5 hours after ingestion, the patient became obtund, and both his respiratory rate and blood pressure fell significantly; he was intubated and placed on 100% oxygen. Shortly thereafter, the patient began to experience seizures; treatment with diazepam and phenytoin was unproductive, but pancuronium was effective in treating the seizures. Intravenous bicarbonate and ethanol therapies were begun after the seizures started. The patient was transported for dialysis, but on arrival, had clinical signs of intravascular coagulopathy. He subsequently sustained a cardiac arrest from which he could not be revived. At autopsy, the patient's stomach was hard, white, and leathery; the esophagus and intestines appeared to be normal.

A 41-year-old woman swallowed 120 mL formalin (37% formaldehyde solution; 624 mg formaldehyde/kg). The woman was brought to the emergency room within 30 minutes. The patient complained of abdominal pain and subsequently lost consciousness. Upon admission, the patient was cyanotic, apneic, and hypotensive. Laboratory results indicated significant acidosis. The patient was intubated, ventilation was initiated, and gastric lavage was performed. Intravenous fluid therapy consisting of Ringers solution followed by 5% dextrose, epinephrine, and sodium bicarbonate was initiated and the patient was transferred to intensive care. The patient was maintained via endotracheal respiration and dopamine therapy. The patient became anuric approximately 7.5 hours after admission, and her health continued to deteriorate over the next day; she died 28 hours after admission (Eells et al. 1981)

Kochhar et al (1986) reported a case of a 26-year-old woman ingested 234 mg/kg formaldehyde. Extensive gastrointestinal damage was exhibited. Immediately after ingesting formaldehyde, the patient experienced repeated vomiting with occasional streaks of blood. Anti-emetics and antacids were prescribed but did not relieve symptoms. Examination of the oropharynx revealed ulceration and sloughing of the soft palate and posterior pharyngeal wall. Indirect laryngoscopy revealed ulceration of the epiglottis, pyriform fossae, and arytenoids. At 96 hours, an upper gastrointestinal endoscopy revealed that the esophageal mucosa was edematous and ulcerated with patches of black slough along the entire length. Areas of the stomach were hyperemic, and there was superficial ulceration in the distal body and antrum; the duodenal mucosa appeared normal. The patient underwent a feeding jejunostomy and made an uneventful recovery. At 4 weeks, a repeat endoscopy revealed a normal esophagus. The stomach appeared normal with the exception of slight hyperemia and limited distensibility of the antrum. Barium examination revealed scarring of the antrum and distal portion of the gastric body. At 6 weeks, the patient was asymptomatic.

`

Mutagenic and Carcinogenic Effects

Formaldehyde has been demonstrated to be genotoxic in a wide variety of experimental systems both in vitro in animal and human cells and in vivo in animals (IARC 1995). As summarized in Table 3, there are some epidemiological studies associated with potential formaldehyde exposure with the mutagenic concern of formaldehyde.

More than forty epidemiological studies have examined the carcinogenic potential of formaldehyde in animals and humans. The findings from those studies have been evaluated by a number of agencies and committees engaged in setting regulatory standards and guidelines (IARC 1995, 2004,, 2006 ; Paustenbach et al. 1997; ATSDR 1999; ACGIH 2001; WHO 2002; EPA 2003; NAC 2003).

Some epidemiologic studies (ATSDR 1999) have found an excess number of nasopharyngeal cancers. There are two meta-analyses (Blair et al. 1990; Partanen 1993) reported a relationship between exposure to formaldehyde and the occurrence of nasopharyngeal cancer was observed, However, those associations were relatively weak (relative risks [RR] = 2.1 [95% confidence interval (CI) = 1.1-3.5] and 2.7 [95% CI = 1.4-5.6] in Blair et al. [1990] and Partanen [1993], respectively).

In a more recently published meta-analysis (Collins et al. 1997), this correction for the underreporting was made. In addition, the exposure potential for the jobs included in the analysis was evaluated. The authors concluded that the epidemiological studies do not support a causal relationship between formaldehyde exposure and nasopharyngeal cancer.

The follow-up study by Hauptmann et al. (2003, 2004) of the National Cancer Institute (NCI) retrospective cohort mortality study of U.S. workers involved in the production or use of formaldehyde represents the best available data set for quantitative cancer risk assessments of lymphohematopoietic cancers and nasopharyngeal tumors based on human data. The NCI study is a large epidemiology study, and it provides individual quantitative exposure estimates for the workers.

The analyses conducted by the Agency are based on the lymphohematopoietic (Hauptmann et al., 2003) and nasopharyngeal (Hauptmann et al., 2004) cancer results from the NCI follow-up study. This is the largest study of the three independent studies, and it is the only one of the three with sufficient individual exposure data for exposure-response modeling. The NCI cohort consisted of 25,619 workers (88% male) employed in any of the 10 plants prior to 1966; the current follow-up analyzes 8,486 deaths (178 attributed to lymphohematopoietic malignancy and 9 to nasopharyngeal cancer). A detailed exposure assessment was conducted for each worker based on exposure estimates for different jobs held and tasks performed (Stewart et al., 1986). Exposure estimates were made using several different metrics - peak exposures, average intensity, cumulative exposure, and duration of exposure. Respirator use and exposures to formaldehyde particles and other chemicals were also considered. Significant increases in

relative risk for lymphohematopoietic cancer were observed primarily for myeloid leukemia and Hodgkin's disease and for the peak exposure and average intensity exposure metrics. For the nasopharyngeal cancers, significant trends were observed for the cumulative and peak exposure metrics.

With respect to the subtypes of lymphohematopoietic malignancy, the strongest exposure-response relationships were observed for Hodgkin's disease and myeloid leukemia for both the peak exposure and average intensity exposure metrics. The (all) lymphohematopoietic malignancies category also showed a highly significant trend for the peak exposure metric and a significant trend with the average intensity metric, and this was the category selected for the cancer risk analyses presented here. While other lymphohematopoietic cancer subtypes did not exhibit statistically significant increases, many did suggest increases in relative risk with formaldehyde exposure, and the subtype analyses were generally based on small numbers of cases (i.e., lower statistical power). Furthermore, as noted by the NCI investigators, "although the accuracy of death certificates for lymphohematopoietic malignancies is generally high, classification of subtypes of leukemia and lymphoma from death certificates is less accurate than from hospital records." Finally, the all lymphohematopoietic cancer category contains the most data, and the results are more stable.

Formaldehyde has been also been demonstrated to be associated with leukemia in workers. However, the evidence of causing leukemia or other nonrespiratory cancers in humans has been considered weaker than that for high-dose formaldehyde exposures to cause nasopharyngeal cancers on the basis of pharmacokinetic and toxicologic evidence (BEST, 2007)

The Agency's IRIS program grouped formaldehyde as a B1 (probable human carcinogen) based on limited evidence in humans, and sufficient evidence in animals. Human data include nine studies that show statistically significant associations between site-specific respiratory neoplasms and exposure to formaldehyde or formaldehyde-containing products. An increased incidence of nasal squamous cell carcinomas was observed in long-term inhalation studies in rats and in mice. The classification is supported by in vitro genotoxicity data and formaldehyde's structural relationships to other carcinogenic aldehydes such as acetaldehyde.

2.0 SUMMARY AND CONCLUSION

Although there are many reported incidences been reported associated with formaldehyde exposure, only limited incidences are associated with when formaldehyde is used as for antimicrobial agent (biocide). Formaldehyde is a dermal irritant and a dermal sensitizer. The primary dermal effects that have been reported are rash, burning sensation, itching, dry scaling irritation, cracking and thickened skin, itching, and blisters and rash on hands. Acute exposure, symptoms associated with eyes are the primary reported illness in all the associated incidences. Nausea, dizziness, headache, and sore throat are the primary systemic effects that have been reported. Allergic reactions and asthma-like conditions also have been reported following occupational exposures. Only limited acute cases with oral exposure to formaldehyde have been

þublished in scientific literature. Formaldehyde has been demonstrated to be genotoxic in many reported epidemiological studies. Formaldehyde exposure has been associated respiratory cancer (especially nasopharyngeal cancer), leukemia, and other nonrespiratory cancers in humans. The Agency's IRIS program grouped formaldehyde as a B1 carcinogen.

`

Table 3. Human Epidemiological Studies associated Potential Mutagenic Activity of Formaldehyde Exposure

Reference Information	Study Design	Results
Ballarin C, Sarto F, Giacomelli L, et al. 1992. Micronucleated cells in nasal mucosa of formaldehyde-exposed workers. Mutat Res 280:1-7.	15 nonsmoking workers (8 males, 7 females) who worked in a plywood factory for cytopathologic changes in nasal mucosal cells, were evaluated and the results were compared to matched controls. Mean levels of exposure to formaldehyde ranged from 0.07 to 0.08 ppm in the sawmill and shearing press departments to 0.32 ppm in the warehouse. The total range of exposure in all areas containing formaldehyde vapors was 0.06–0.49 ppm. Workers were also exposed to wood dust.	Nasal mucosal cells from exposed workers exhibited significantly increased incidence of micronuclei (0.9 versus 0.25 for controls), chronic inflammation, and a significantly higher frequency of squamous metaplasia cells (histological score: 2.3 versus 1.6) than cells from control workers. Micronuclei were found mainly in the ciliated cells.
Berke, J.H. (1987): Cytologic Examination of the Nasal Mucosa in Formaldehyde-Exposed Workers. J. Occup. Med. 29:681-684.	Cytologic study of the nasal mucosa of four groups of employees either engaged in phenol-formaldehyde impregnation or who were not known to have experienced regular occupational formaldehyde exposure. Berke used historical, environmental occupational hygiene data where formaldehyde excursions to 9 ppm were documented (with alleged excursions to 15 ppm). Smoking habits, measured as pack-years, were very similar for the exposed and control groups.	Among formaldehyde-exposed workers with personal monitoring data, exposures ranged from 0.02 to 2.0 ppm. A statistically significant ($p=0.04$) overall prevalence of nasal erythema, edema, and fissures among the nonsmokers was found which Berke concluded was consistent with localized tissue irritation as a consequence of formaldehyde exposure. Two people with nasal polyps were confirmed among the 42 formaldehyde workers, and none were found among the 38 controls. Berke concluded that there was, however, no significant association between formaldehyde exposure and "abnormal" nasal mucosal cytology after simultaneously controlling for age and smoking habits.

Table 3. Human Epidemiological Studies associated Potential Mutagenic Activity of Formaldehyde Exposure

Reference Information	Study Design	Results
Chebotarev AN, Titenko NV, Selezneva TG, et al. 1986. Comparison of the chromosome aberrations, sister chromatid exchanges, and unscheduled DNA synthesis when evaluating the mutagenicity of environmental factors. Cytol Genet 20:21-26.	The lymphocytes sister chromatic exchanges (SCEs) of 40 wood-working employees and 22 control workers were examined for chromosomal aberrations, SCEs, and unscheduled DNA repair or synthesis.	The level of chromosomal aberrations in formaldehyde-exposed workers was 2.76%, which was significantly elevated compared to spontaneous chromosomal aberrations in controls (1.64%, $p<0.05$). The incidence of chromosomal breakage in exposed workers (2.95%) was significantly greater than the frequency of spontaneous breakage (1.64%, $p<0.05$). No differences between exposed and control subjects were seen for SCEs either at baseline (8.01 versus 8.24 exchanges per cell) or after induction with the genotoxin thiotepa (23.32 versus 25.78 exchanges per cell). There were no differences between formaldehyde-exposed and control samples in unscheduled DNA repair rates at baseline (335.2 versus 341.9) or after treatment with hydroxyurea (179.8 versus 194.2). However, when treated with thiotepa, unscheduled DNA repair rates in lymphocytes from formaldehyde-exposed workers were lower than those from control workers (217.2 versus 270.4, $p<0.05$).

Table 3. Human Epidemiological Studies associated Potential Mutagenic Activity of Formaldehyde Exposure

Reference Information	Study Design	Results
Fleig I, Petri N, Stocker WG, et al. 1982. Cytogenetic analyses of blood lymphocytes of workers exposed to formaldehyde in formaldehyde manufacturing and processing. J Occup Med 24:1009-1012.	Chromosome analyses were performed on 15 exposed and 15 non-exposed employees from formaldehyde manufacturing facilities. Exposed workers had an average duration of exposure of 28 years (range 23–35 years). Average exposure concentrations did not exceed 5 ppm prior to 1971 and 1 ppm after 1971. The formaldehyde exposures of individual workers were classified into one of the three following categories: Category 1: exposure 25% of the maximum workplace concentration (MAK); Category 2: exposure up to a maximum of 60% MAK; and Category 3: exposure up to 100% of the MAK. Peripheral blood samples were collected from each worker and lymphocytes were separated and cultured for 70–72 hours at 37 °C. Cells were subsequently fixed and examined for chromatid- and chromosome-type aberrations.	There were no differences between exposed and control groups in the incidence of chromosomal aberrations. The mean frequency of aberrant metaphases among formaldehyde-exposed persons was 3.07 versus 3.33% in controls. No correlation was found between formaldehyde exposure levels and the number of aberrant metaphases.
Goh & Cestero (1979) Chromosomal abnormalities in maintenance hemodialysis patients. J. Med., 10: 167-174.	The chromosomal patterns of direct bone marrow preparations from 40 patients undergoing maintenance haemo-dialysis were studied. During the period of this study, each patient could have received up to 126 ± 50 mg of formaldehyde during each dialysis.	Aneuploidies, chromosomal structure abnormalities, and chromosomal breaks were seen in the metaphase.

Table 3. Human Epidemiological Studies associated Potential Mutagenic Activity of Formaldehyde Exposure

Reference Information	Study Design	Results
Shaham J, Bomstein Y, Meltzer A, et al. 1996a. DNA-protein crosslinks, a biomarker of exposure to formaldehyde - *in vitro* and *in vivo* studies. Carcinogenesis 17:121-125.	The formation of DNA-protein cross links in peripheral white blood cells of occupationally exposed workers (n=12) and unexposed controls (n=8) was measured. The average length of occupational exposure was 13 years. All subjects completed a questionnaire regarding demographics, occupational and medical background, and smoking and hygiene habits. Venous blood samples were collected from each worker and were processed to isolate DNA-protein cross links. Personal and room concentrations of formaldehyde were collected at various periods during the working day among the exposed subjects, with formaldehyde room concentrations ranging from 1.38 to 1.6 ppm. Personal monitoring devices indicated formaldehyde concentrations of 2.8–3.1 ppm during peak work and an average concentration of 1.46 ppm at times when work was usually completed.	Exposure to formaldehyde resulted in a significant increase in the incidence of DNA-protein cross links. Mean (±sd) incidences in exposed and nonexposed workers were 28±6 and 22±6%, respectively. Within the exposed workers group, technicians had significantly greater levels of DNA-protein cross links than physicians (32.3±4.3 and 26.3±4.4%, respectively). A linear relationship between years of exposure and DNA-protein cross links formation was also detected. When the data were analyzed considering worker smoking habits, DNA-protein cross links were consistently elevated among formaldehyde-exposed versus corresponding controls (p=0.03). The authors concluded that DNA-protein cross links can be used as a biomarker of exposure; however, the assay measures DNA-protein cross links in general, not those specific to formaldehyde cross link formation.

Table 3. Human Epidemiological Studies associated Potential Mutagenic Activity of Formaldehyde Exposure

Reference Information	Study Design	Results
Vasudeva N, Anand C. 1996. Cytogenetic evaluation of medical students exposed to formaldehyde vapor in the gross anatomy dissection level. J Am Coll Health 44:177-179.	The effects of formaldehyde exposure on the incidence of chromosomal aberrations in peripheral blood lymphocytes of 30 medical students exposed to formaldehyde vapors at concentrations of <1 ppm for 15 months were examined. Questionnaires established that the participants were healthy and had insignificant medical histories.	There was no difference in the incidences of chromosomal aberrations among the exposed and control groups. The mean frequencies of aberrant metaphases in the exposed and control groups were 1.2 and 0.9%, respectively. There was no correlation between reported irritant effects of formaldehyde and the number of aberrant metaphases, and the authors concluded that exposure to formaldehyde at concentrations seen in this study does not lead to chromosomal aberrations.
Yager JW, Cohn KL, Spear RC, et al. 1986. Sister-chromatid exchanges in lymphocytes of anatomy students exposed to formaldehyde-embalming solution. Mutat Res 174:135-139.	Peripheral lymphocytes from eight anatomy students exposed to formaldehyde-embalming solution over a 10-week course were examined for sister chromatid exchange (SCE). Results were compared with preexposure values for each student.	Breathing-zone monitoring revealed mean exposure of 1.2 ppm (range 0.73–1.95 ppm). A small average increase in the incidence of SCE was observed in the lymphocytes of the students after exposure (7.2/cell) when compared to values obtained before exposure (6.39/cell)

3.0 REFERENCES

ACGIH (American Conference of Governmental Industrial Hygienists). 2001. Formaldehyde in Documentation of the Threshold Limit Values and Biological Exposure Indices, 7th Ed. Cincinnati, OH: American Conference of Governmental Industrial Hygienists.

Alexandersson, R. and Hedenstierna, G. 1988. Respiratory Hazards Associated with Exposure to Formaldehyde and Solvents in Acid-Curing Paints. Arch. Env. Health. 43: 222-227.

Alexandersson, Rolf, M.D. and Hedenstierna, Goran, M.D. 1989 Pulmonary Function in Wood Workers Exposed to Formaldehyde: A Prospective Study. Arch. Env. Health. Vol. 44, No. 1. p. 5-11.

ATSDR (Agency for Toxic Substances and Disease Registry). 1999. Toxicological Profile for Formaldehyde. U.S. Department of Health and Human Services, Public Health Services, Agency for Toxic Substances and Disease Registry, Atlanta, GA. July 1999.

BEST (The Board on Environmental Studies and Toxicology) 2007. Formaldehyde. Emergency and Continuous Exposure Guidance Levels for Selected Submarine Contaminants Vol. 1. Page 103-138. The National Academies Press.

Blair, A., R. Saracci, P.A. Stewart, R.B. Hayes, and C. Shy. 1990. Epidemiologic evidence on the relationship between formaldehyde exposure and cancer. Scand. J. Work Environ. Health 16(6):381-393.

Burkhart KK, Kulig KW, McMartin KE. 1990. Formate levels following a formalin ingestion. Vet Hum Toxicol 32:135-137.

Collins, J.J., J.F. Acquavella, and N.A. Esmen. 1997. An updated meta-analysis of formaldehyde exposure and upper respiratory tract cancers. J. Occup. Envi- ron. Med. 39(7):639-651.

Dally, K. A., Eckamnn, A. D., Hanrahan, L. P, Anderson, H.A., and Kanarek, M. S. 1981. A follow-up study of indoor air quality in Wisconsin homes. International Symposium on Indoor Air Pollution, Health and Energy Conservation, October 13-16,

Dally, K. A., Hanrahan, L. P, Woodbury, M. A., and Kavarek, M. S. Formaldehyde exposure in non-occupational environments. Arch. Environ. Health 36: 277-284 (1981).

Edling, C.; Odkvist, L.; Hellquist, H. (1985): Formaldehyde and the Nasal Mucosa. Br. J. Ind. Med. 42: 570-571.

Eells JT, McMartin KE, Black K, et al. 1981. Formaldehyde poisoning: Rapid metabolism to formic acid. JAMA, J Am Med Assoc 246:1237-1238.

Engel, H.O. and Calnan, C.D. (1966) Resin dermatitis in a Car Factory. Brit. J. Ind. Med. 23: 62-66.

Feinman SE, editor. 1988. Formaldehyde sensitivity and toxicity. Boca Raton (FL): CRC Press Inc;.

Fleischer, J.M. 1987. Medical student's exposure to formaldehyde in gross anatomy laboratories, NY State J. Med., 87: 385–388.

Flyvholm, M.A.; Hall, B.M.; Agner, T.; Tiedemann, E.; Greenhill, P.; Vanderveken, W.; Freeberg, F.E.; and Menne, T. 1997. Threshold for occluded formaldehyde patch test in formaldehyde-sensitive patients: Relationship to repeated open application test with a product containing formaldehyde releaser. Contact Dermatitis 36:26-33.

Hanrahan, L. P, Anderson, H. A., Dally, K. A., Eckamnn, A. D., and Kanarek, M. S. 1981.An investigation of the off gassing decay function in aging mobile homes with climate corrected formaldehyde readings. International Symposium on Indoor Air Pollution, Health and Energy Conservation, October 13-16 1981.

Hanrahan, LP; Dally, KA.; Anderson, HA.; Kanarek, MS. And Rankin, J.1984. Formaldehyde vapor in mobile homes: a cross sectional survey of concentrations and irritant effects. Am J Public Health. 74: 1026–1027.

Hauptmann, M., J.H. Lubin, P.A. Stewart, R.B. Hayes, and A. Blair. 2003. Mortality from lymphohematopoietic malignancies among workers in formaldehyde industries. J. Natl. Cancer Inst. 95(21):1615-1623.

Hauptmann, M., J.H. Lubin, P.A. Stewart, R.B. Hayes, and A. Blair. 2004. Mortality from solid cancers among workers in formaldehyde industries. Am. J. Epidemiol. 159(12):1117-1130.

Holmstrom et al. (1989) Histological Changes in the Nasal Mucosa in Persons Occupationally Exposed to Formaldehyde Alone and in Combination with Wood Dust. Acta Otolaryngol (Stockh) 107:120-129.

Horvath EP, Anderson H, Pierce WE, Hanrahan L, Wendlick J. 1985. The effects of formaldehyde on the mucus membranes and lungs in an industrial population. Submitted to US Department of Labor for proposed rulemaking for exposure to formaldehyde (50 FR 50412, December 10, 1985).

Horvath Jr., E.P., H. Anderson Jr., W.E. Pierce, L. Hanrahan, and J.D. Wendlick. 1988. Effects of formaldehyde on the mucous membranes and lungs: A study of an industrial population. JAMA 259(5):701-707.

Horvath, E. P. Jr.et al. (1988) Effects of Formaldehyde on the Mucous Membranes and Lungs: A

` Study of an Industrial Population. JAMA, Vol. 259, No.5. p. 701-707.

IARC (International Agency for Research on Cancer). 1995. Formaldehyde. Pp. 217-362 in Wood Dust and Formaldehyde. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Vol. 62. Lyon, France: World Health Organization, International Agency for Research on Cancer.

IARC (International Agency for Research on Cancer). 2004. Formaldehyde (Group 1). IARC Monographs Programme on the Evaluation of Carcinogenic Risks to Humans, Vol. 88. International Agency for Research on Cancer, World Health Organization, Lyon

Japanese Contact Dermatitis Research Group (1982) [Standard patch test allergens for 1981 in Japan.] Skin Res. (Hifu), 24: 514-525 (in Japanese).

Kochhar R, Nanda V, Nagi B, et al. 1986. Formaldehyde-induced corrosive gastric cicatrization: Case report. Hum Toxicol 5:381-382.

Kriebel D, Sama SR, Cocanour B. 1993. Reversible pulmonary responses to formaldehyde: A study of clinical anatomy students. Am Rev Respir Dis 148:1509-1515.

Kulle JT, Sauder LR, Hebel JR, Green D, Chatham MD. 1987. Formaldehyde dose-response in healthy nonsmokers. J Air Pollution Control Assoc 37:919-924.

Liteplo, R.G., and M.E. Meek. 2003. Inhaled formaldehyde: Exposure estimation, hazard characterization, and exposure-response analysis. J. Toxicol. Env. Health. Part B. 6:85-114.

Main, DM and Hogan, TJ 1983. Health effects of low-level exposure to formaldehyde, J. Occup. Med. 25:896–900

Malaka T, Kodama AM. 1990. Respiratory health of plywood workers occupationally exposed to formaldehyde. Arch Environ Health 45:288-294

Marzulli F.N., Maibach H.J. 1973. Antimicrobials: experimental contact sensitization in man. J Soc Cosmet Chem 24:399-421.

NAC (National Advisory Committee). 2003. Acute Exposure Guideline Levels (AEGLs) for Formaldehyde. Draft1:02/2003. National Advisory Committee/AEGL, U.S. Environmental Protection Agency, Washington, DC.

NAC (National Advisory Committee). 2003. Acute Exposure Guideline Levels (AEGLs) for Formaldehyde. Draft1:02/2003. National Advisory Committee/AEGL, U.S. Environmental Protection Agency, Washington, DC.

OEHHA (Office of Environmental Health Hazard Assessment). 1999. Determination of Acute Reference Exposure Levels for Airborne Toxicants: Acute Toxicity Summary - Formaldehyde. CalEPA

Partanen, T. 1993. Formaldehyde exposure and respiratory cancer—A meta-analy- sis of the epidemiologic evidence. Scand. J. Work Environ. Health 19(1):8-15.

Paustenbach, D., Y. Alarie, T. Kulle, N. Schachter, R. Smith, J. Swenberg, H. Witschi, and S.B. Horowitz. 1997. A recommended occupational exposure limit for formaldehyde based on irritation. J. Toxicol. Environ. Health 50(3): 217-263.

Porter JAH. 1975. Acute respiratory distress following formalin inhalation. Lancet 1:603-604.

Rudzki E, Rebandel P, Grzywa Z. 1989. Patch tests with occupational contactants in nurses, doctors and dentists. Contact Dermatitis 20:247-259.

Sneddon, I.B. (1968) Dermatitis in an intermittent haemodialysis unit. Br. med. J., 1: 183-184.

Solomons K, Cochrane JWC. 1984. Formaldehyde toxicity: Part 1. Occupational exposure and a report of 5 cases. S Afr Med J 66:101-102.

Solomons K, Cochrane JWC. Formaldehyde toxicity: Part 1. Occupational exposure and a report of 5 cases. S Afr Med J 1984;66:101-102.

Uba, G., et al. (1989) Prospective Study of Respiratory Effects of Formaldehyde among Healthy and Asthmatic Medical Students. Am. J. Ind. Med. 15: 91-101.

Weber-Tschopp A, Fisher T, Granjean E. 1977. Irritating effects of formaldehyde on men. Int Occup Environ Health. 39:207-218.

WHO (World Health Organization) 1989. Formaldehyde WHO Environmental Health Criteria , 89 (1989) 219 p

WHO (World Health Organization). 2002. Formaldehyde, Concise International Chemical Assessment Document 40. Geneva: World Health Organization

Wilson, JT Jr., M.D. (1987) Formaldehyde Exposure Following Urea Formaldehyde Insulation. Environmental Health and Safety News, University of Washington, v.26.