TOXICOLOGY PROFILE
Glutaraldehyde IN THE HEALTH CARE INDUSTRY

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Summary

This report summarizes different aspects of glutaraldehyde in healthcare industry, including basic chemical and physical properties, exposure path in healthcare settings, toxicity, negative effects related to occupational over-exposure, regulations of glutaraldehyde as a chemical hazard and occupational hazard, as well as control measures.

Glutaraldehyde was introduced in cold sterilization and disinfection in healthcare as a substitute of formaldehyde, because of its broad biocidal spectrum and lower health risk compared with formaldehyde. Based on substantial animal and human studies, glutaraldehyde is a skin irritant and allergen. Also, it may induce peripheral sensory irritation and eye irritation. Animal studies indicate inconsistent results concerning glutaraldehyde as a respiratory sensitizer, but there are many case reports its potential to induce occupational asthma. Glutaraldehyde is not likely to be phototoxic based on controlled human study. *In vitro* and *in vivo* studies did not indicate clear genotoxic and mutagenic effects of glutaraldehyde. Animal studies concerning its carcinogenicity only indicated weak and obscure association between glutaraldehyde exposure and cancer or no association at all, and there is no elevated cancer rate in a human epidemiology study, which is the only one involving its potential as a human carcinogen. Animal studies did not find distinct reproductive and developmental effects of glutaraldehyde, and human studies did not reveal elevated risk of spontaneous abortion or malformation of glutaraldehyde exposure.

There are several commercially available substitutes for glutaraldehyde, either chemical alternates or instrumental alternatives. Local exhaust ventilation is one of the effective engineer control measures.
Part 1. General information

Substance Name
Glutaraldehyde

CAS Number
111-30-8

Synonyms and trade names
glutaral, glutaric aldehyde, glutardialdehyde, glutarolglutaric dialdehyde, 1,5-pentanedial, 1,5-pentanedione, Cidex®, Glutarex®, Sonacide®, Verucasep® and 1,3-diformylpropane.

Formula
C₅H₈O₂

Structure

Description of Chemical and Physical Property

Glutaraldehyde is a five-carbon aliphatic di-aldehyde. Oxidation of glutaraldehyde will form glutaric acid. Glutaraldehyde links with amino groups of collagen and other proteins to form intramolecular and intermolecular crosslinks (Wade et al, 1982). Commercial products containing glutaraldehyde are most frequently available as 2%, 10%, 25% and 50% aqueous solutions, which are not flammable and thus have no flash point. One the one side, glutaraldehyde will polymerize into stable hydrates under high-alkaline conditions; on the other side, its antimicrobial activity is maximum under alkaline conditions; so in order to keep its activity while avoid the polymerization, the pH range of its solution should be buffered within weak alkaline range (7.5 to 8.5). Within the mentioned pH range, glutaraldehyde is stable for at least 14 days. In order achieve the appropriate pH range, most glutaraldehyde used in hospitals for disinfection and sterilization purposes is a 2.0% concentration which has a two-components system that must be mixed together, or activated, prior to use. The two components are activated solution and alkalinizing agents, whose chemical components are 2.0% glutaraldehyde and 0.3% sodium bicarbonate respectively (Stonehill et al, 1963).

Glutaraldehyde has a wide spectrum of antimicrobial activity, because of its bactericidal, tuberculocidal, fungicidal and viricidal activity. Use of glutaraldehyde includes a fixative for electron microscopy, tanning of leather, crosslinking agent in microcapsules, preservative in cosmetics, and a crosslinking or immobilizing agent in food technology (Wade et al, 1982). Also, because of its antimicrobial activity, it is used widely in healthcare industry as sterilant and disinfectant.
Some other chemical and physical properties of glutaraldehyde are summarized in table 1.

Table 1. Chemical and physical properties of glutaraldehyde[^1]

<table>
<thead>
<tr>
<th>Physical Description</th>
<th>Colorless liquid with a pungent odor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conversion Factor</td>
<td>1ppm=4.09 mg/m³</td>
</tr>
<tr>
<td>Molecular Weight</td>
<td>100.01 g/mol</td>
</tr>
<tr>
<td>Boiling Point</td>
<td>100 °C</td>
</tr>
<tr>
<td>Freezing Point</td>
<td>-14 °C</td>
</tr>
<tr>
<td>Vapor Pressure</td>
<td>17 mmHg</td>
</tr>
<tr>
<td>Solubility</td>
<td>Miscible</td>
</tr>
<tr>
<td>Upper Explosive Limit/Lower Explosive Limit[^2]</td>
<td>N/A, non-combustible liquid</td>
</tr>
</tbody>
</table>

[^1]: All data retrieved from NIOSH Pocket Guide to Chemical Hazards (2007).
[^2]: % by volume
Part 2. Use of Glutaraldehyde in Healthcare Industry

Use as Cold Sterilant

A widespread use of glutaraldehyde is for the cold sterilization of dental, anesthetic and medical instruments and endoscopes, based on its broad spectrum of biocidal activity (Urbani et al, 1990). For this purpose of application, 2.0% glutaraldehyde is used. This is achieved by diluting stock solutions (acidic with pH 3.0~4.5) to alkalized solution (pH 7.8~8.0).

Use as Tissue Fixative

In some healthcare facilities, glutaraldehyde is used as a fixative in electron and light microscopy, or as a tissue preservative. Corresponding the function as intermediates and fixatives for tissues, a higher concentration of glutaraldehyde is necessary (25%~90%), so laboratory personnel may be exposed to solutions containing up to 50% glutaraldehyde during the preparation of fixative solutions for use in microscopy and histology, and to small quantities of working strength solutions (3~6%). Healthcare workers may be exposed to glutaraldehyde during the following tasks performed when glutaraldehyde is used as tissue fixative: 1) preparing glutaraldehyde solution from concentration to fill enclosed fixing basin, 2) removing and adding materials to the fixing basin, 3) handling materials fixed in the basin, 4) handling tissue samples for refrigeration, 5) rinsing tissue samples in a buffer, 6) slicing the tissue samples into slides. (NIOSH, 1986)

Use in X-rays Operations

Glutaraldehyde is used in developing solutions as a hardening agent to shorten the drying cycle in film processing. X-ray operators typically use 30~50% weight-to-weight ratio glutaraldehyde and dilute it to working strength solutions which contains less than 1~2% glutaraldehyde. The primary sources of formaldehyde exposure during e-ray processing are: 1) mixing glutaraldehyde developer solutions. 2) adding solutions to tanks and processors. 3) processing x-rays. 4) removing incompletely dried processed x-rays. 4) cleaning rollers and tanks on x-ray machines. 5) emptying tanks and processors. 6) fugitive emissions from open tanks, leaky hoses and equipment. 7) automatic processor exhaust. (NICNAS, 1994.)

The National Institute for Occupational Safety and Health (NIOSH) received a series of requests for health hazard evaluation in several hospitals, dental offices and other healthcare plants. Some investigation focused on glutaraldehyde or listed it as one health hazard. Results of these studies are summarized in table 2, with working area/department bolded. We can conclude that employees working in departments which involve the use of glutaraldehyde have a greater risk of exposure. By comparing the monitoring data and ACGIH exposure limit (15min-STEEL) of 0.05ppm, job
categories which may lead to glutaraldehyde over-exposure include: 1) hospital staff who work in areas with a cold sterilizing procedure that uses glutaraldehyde (for example, gastroenterology and cardiology department), 2) hospital staff who work in operating rooms, dialysis department, endoscopy units, and intensive care units where glutaraldehyde formulations are used in infection control procedures, 3) central service or supply workers who use glutaraldehyde as a sterilant, 4) research technicians or pharmacy personnel who either prepare the alkaline solutions or fix tissues in histology and pathology labs, 5) laboratory technicians who sterilize benchtops with glutaraldehyde solutions, 6) workers who operate X-rays. Some occupations, such as dental office receptionists, employees of medical waste disposal, on the other hand, have a lower risk of exposure. Another conclusion is that exposure level does not totally depend on concentration of glutaraldehyde solution used. For example, diluted solution (2%) is used in endoscopy unit, but employees could be exposed to higher airborne glutaraldehyde than tissue fixing technicians, who use concentrated solution.

### Table 2. Glutaraldehyde monitoring data in healthcare industry

<table>
<thead>
<tr>
<th>HHE Report No. (for NIOSH Report)</th>
<th>Author</th>
<th>Location</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>HETA-95-0239-2553[1]</td>
<td>Kiefer-M; Lushniak-BD</td>
<td>St. Vincent Medical Center, Staten Island, NY.</td>
<td>Personal samples for glutaraldehyde among employees who cleaned endoscopy tubes with Cidex (2.4% glutaraldehyde solution) showed an exposure level of 0.06ppm, well below exposure limit.</td>
</tr>
<tr>
<td>HETA-94-0017-2394[2]</td>
<td>Decker-JA</td>
<td>Dr. Gammuchia’s dental office, Apopka, FL.</td>
<td>The study investigated into employees of a dental office. Three samples were taken by personal pumps with silica gel sorbent. The two samples in the sterilization room showed an average concentration of 0.01ppm, while glutaraldehyde level in the reception area is not detectable.</td>
</tr>
<tr>
<td>HETA-90-296-2149[3]</td>
<td>Burkhart-JE</td>
<td>Monongalia General Hospital, Morgantown, WV.</td>
<td>Sample concentration ranged from below limit of detection to 0.08ppm among hospital employees who use Sporicidin (2% glutaraldehyde solution) to disinfect endoscope and bronchoscope.</td>
</tr>
<tr>
<td>HETA-87-176-1826[4]</td>
<td>Gunter-BJ</td>
<td>St. James Community Hospital, Butte, MT.</td>
<td>This study investigated glutaraldehyde exposure among technicians in the sigmoidoscopy and respiratory department. The average concentration for all nine samples was 0.22 mg/m³ (0.054ppm), individual level ranged from below LOD to 0.48mg/m³ (0.117ppm).</td>
</tr>
<tr>
<td>HETA-86-226-1769[5]</td>
<td>Crandall-MS</td>
<td>Montgomery Hospital, Norristown, PA.</td>
<td>The study investigated formaldehyde exposure among healthcare workers during disinfecting respiratory therapy equipment, bronchoscope, whirlpool tubs, surgical instruments, and anesthesia equipment parts, with the duration of 15 to 20 minutes. Environmental breathing zone sample results ranged from below LOD to 1.6mg/m³ (0.391ppm). Personal breathing zone sample results from below LOD to 1.5 mg/m³ (0.367ppm). Thus a health hazard of glutaraldehyde during disinfection and sterilization can be concluded.</td>
</tr>
</tbody>
</table>
Toxicological Profile of Glutaraldehyde in Healthcare Industry

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Author</th>
<th>Institution</th>
<th>Sample Source</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>HETA-85-257-1791</td>
<td>Pryor-P</td>
<td>Mercy Medical Center, Denver, CO.</td>
<td></td>
<td>The study evaluated the hazard of glutaraldehyde during disinfection procedure performed by nurses, who use glutaraldehyde to disinfect surgical equipment, bronchoscopes, x-ray table tops and other contaminated surfaces. Area air samples ranged up to 0.74mg/m³ (0.181ppm), and personal samples ranged up to 1.98mg/m³ (0.484ppm). All personal samples in the radiology and emergency departments exceeded the TLV. Thus it is concluded that workers in the radiology and emergency departments are more likely to be overexposed to glutaraldehyde.</td>
</tr>
<tr>
<td>HETA-84-535-1690</td>
<td>Pryor-P</td>
<td>National Jewish Hospital, Denver, CO.</td>
<td></td>
<td>The study evaluated the potential exposure to glutaraldehyde among research technologists in various stages of tissue fixing. Personal breathing zone samples showed no detectable glutaraldehyde. Samples taken of area air registered from not detectable to 0.21 mg/m³ (0.051ppm). Thus it is concluded that a health hazard did not exist from glutaraldehyde at this site.</td>
</tr>
<tr>
<td>HETA-2000-0041-2796</td>
<td>Gwin-K; Nemhause r-J.</td>
<td>OmniSource Corp., precious metal recycling facility, Ft. Wayne, IN.</td>
<td></td>
<td>All the ten area glutaraldehyde samples were below LOD, which indicated that glutaraldehyde was not one potential chemical hazard in the precious metal recycling (PMR) facility.</td>
</tr>
</tbody>
</table>

| N/A          | Axon, et al., 1981 | 37% of staffs in endoscopy units were reported to have had health problems associated with glutaraldehyde. |
| N/A          | Jachuck et al., 1989 | Among medical and nursing staff working in an endoscopy unit, eight out of nine staff were affected by glutaraldehyde exposure. Clinical manifestations included watering of eyes, rhinitis, dermatitis, respiratory difficulties, nausea and headache. Personal sampling result showed that maximum glutaraldehyde concentration is 12ppm. |

[3]: http://www2a.cdc.gov/hhe/select.asp?PjtName=12375&bFlag=0&ID=1
[4]: http://www2a.cdc.gov/hhe/select.asp?PjtName=7389&bFlag=0&ID=8
[6]: http://www2a.cdc.gov/hhe/select.asp?PjtName=12375&bFlag=0&ID=1
[7]: http://www2a.cdc.gov/hhe/select.asp?PjtName=12375&bFlag=0&ID=1

**Medication**

Glutaraldehyde can be used for medical purposes, including endodontic therapy, and the treatment of certain dermatological disorders including verruca, pitted keratolysis, hyperhidrosis, herpes zoster and herpes simplex, onychomycosis and epidermolysis bullosa (Ballantyne, 1984).
Part 3. Exposure Route and Metabolism

Inhalation
Like many other aqueous compounds, inhalation is the major route of exposure for humans (Ballantyne et al, 2001). For more information concerning inhalation of airborne glutaraldehyde, please refer to the previous part of the report.

Dermal
Skin absorption is another possible pathway, although only a small proportion of cutaneously applied glutaraldehyde has been shown to be available for systemic absorption (Derek et al, 2006).

One study focused on in vitro permeabilities of 0.75% and 7.5% [14C]-1,5-glutaraldehyde in skin for humans and various animals (Frantz et al, 1993). Recoveries were 0.05-1.55% in all species studies. For humans, recovery was approximately 0.2% at both glutaraldehyde 0.2% at glutaraldehyde concentrations, which was lower than those of other animals studied.

Technically, all workers who are accessible to glutaraldehyde may be dermally exposed to it, however, there are certain occupations in healthcare industry who are at higher risk of dermal exposure, due to contact frequency, contact duration, environmental glutaraldehyde level and so on. Case studies indicating dermal exposure of glutaraldehyde in healthcare are summarized in table 3.

Table 3. Job categories with potential dermal exposure to glutaraldehyde in healthcare

<table>
<thead>
<tr>
<th>Exposure route</th>
<th>Job category</th>
<th>Task performed</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin contact</td>
<td>Operating theater nurses</td>
<td>Cold disinfection or sterilization of equipment</td>
<td>Hemminki et al, 1985</td>
</tr>
<tr>
<td></td>
<td>Laboratory technicians</td>
<td>Fixing specimens for microscopy</td>
<td>Shaffer et al, 2000</td>
</tr>
<tr>
<td></td>
<td>X-ray technicians</td>
<td>Processing x-ray films</td>
<td>Fisher, 1981</td>
</tr>
<tr>
<td></td>
<td>Cleaners and Janitors</td>
<td>Cleaning and disinfecting</td>
<td>Nethercott et al, 1988</td>
</tr>
</tbody>
</table>

Metabolism
The major route of metabolism of glutaraldehyde is oxidization by the kidney and liver to glutaric-\(\alpha\)-semialdehyde, and then to glutaric acid, which is used to synthesize glutaryl-CoA, with further metabolism to glutaconyl-CoA, crotonyl-CoA, \(\beta\)-hydroxybutyryl-CoA, and acetyl CoA, and finally CO\(_2\) (Beauchamp et al, 1992).
Part 4. Health Effects

a) Irritation

I. Skin Irritation

Animal study indicated that glutaraldehyde is a moderate skin irritant with a skin irritation index of 2.125 (Milner et al, 1977). Primary irritant effects on rabbits are summarized in Table 4 (Ballantyne, 1995). From the table we can see that 45% and 50% aqueous glutaraldehyde produce severe local inflammation and corrosion, including erythema, edema and desquamation. 5~10% solution causes minor to moderate inflammation and 1% is a threshold for skin irritation. Other studies showed that 2.2% alkalized aqueous glutaraldehyde has no significant effect on the skin irritating potential (Myer et al, 1994).

Table 4. Irritation effects on rabbits with glutaraldehyde of different concentration gradients

<table>
<thead>
<tr>
<th>Glutaraldehyde concentration (%)</th>
<th>Contact time</th>
<th>Observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4 h</td>
<td>No effects</td>
</tr>
<tr>
<td>2</td>
<td>4 h</td>
<td>Minor erythema</td>
</tr>
<tr>
<td>5</td>
<td>4 h</td>
<td>Minor erythema and edema</td>
</tr>
<tr>
<td>10</td>
<td>4 h</td>
<td>Moderate erythema, minor edema and spotty necrosis</td>
</tr>
<tr>
<td>25</td>
<td>4 h</td>
<td>Moderate erythema, minor edema and punctuate necrosis</td>
</tr>
<tr>
<td>45</td>
<td>4 h</td>
<td>Moderate erythema, minor edema and punctuate necrosis</td>
</tr>
<tr>
<td>50</td>
<td>3 min</td>
<td>Minor transient erythema</td>
</tr>
<tr>
<td>50</td>
<td>1 h</td>
<td>Moderate erythema, desquamation, necrosis, scabs, alopecia, necrosis</td>
</tr>
<tr>
<td>50</td>
<td>4 h</td>
<td>Necrosis, moderate erythema, alopecia, edema</td>
</tr>
</tbody>
</table>

There are much fewer human studies on acute irritation effects of glutaraldehyde, because of ethical reasons. In one controlled study, it was determined that for short term, 0.5% aqueous glutaraldehyde was slightly irritant (erythema), 0.2% was marginally irritant, and 0.1% was non-irritant (Ballantyne et al, 1984).

II. Eye Irritation

Animal studies showed a clear dose-response relationship for conjunctivitis and corneal injury (Ballantyne, 1995). The lowest concentration causing corneal injury in rabbits is 1.0%. At the level of 5%, corneal injury could be severe. For conjunctival irritation the threshold level is 0.2%. Eye injury among humans caused by direct contact with glutaraldehyde is unusual, but there are a few case reports. In one case, use of Hoskin lens with 2% glutaraldehyde residue induced keratopathy. In another case, 2% glutaraldehyde used for anesthetic mask sterilization produced moderate conjunctivitis.
III. Peripheral sensory irritation

Glutaraldehyde is a peripheral sensory irritant material, as the molecule can interact with sensory nerve receptors in skin and exposed mucosal surfaces, thus resulting in sensations at the site of contact (Ballantyne et al, 2001). So with exposure airborne glutaraldehyde above threshold limit, symptoms such as eye discomfort, excess lacrimation, discomfort in the nose and possibly chest, rhinorrhea and cough or sneezing may develop. Two separate human studies showed sensory threshold for glutaraldehyde vapor at 0.24-0.26ppm (Whitmore, 1976) and 0.3ppm (Colwell, 1976) respectively.

b) Skin sensitization

I. Animal study

Several animal studies showed that glutaraldehyde could induce contact hypersensitivity-type of skin. One study showed that 1% glutaraldehyde could induce sensitization response based on mouse ear swelling test (MEST), and when challenged with 10% glutaraldehyde, 67% of mice had an average increase of 25% in ear thickness (Gad et al, 1986). Another study with local lymph node proliferation assay (LLNA) showed that after applying gradients of glutaraldehyde solutions to mouse ear, a clear concentration-related stimulation of lymph node activity was demonstrated, which indicated a skin sensitizing potential for glutaraldehyde (Hilton et al, 1998). Another animal study with guinea pig and mouse showed a clear dose-related hypersensitivity response that was statistically significant at the concentration of 0.3% in mice and 3% in both species (Stein et al, 1987). Also, the same study showed that unbuffered glutaraldehyde had a greater skin sensitizing potential than buffered glutaraldehyde.

II. Human study

Repeated exposure to glutaraldehyde may lead to the induction of sensitization, causing an allergic contact dermatitis, most often of the hands (Matthew, 2000). Case reports and group studies concerning skin sensitization effects of glutaraldehyde among healthcare workers are summarized in table 5.

<table>
<thead>
<tr>
<th>Author</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sanderson, 1968</td>
<td>Two nurses were contacted with glutaraldehyde from handling its solutions or disinfected instruments. Rashes and mild patchy eczema were developed. Patch tests showed that both of them were reactive to 1% aq. glutaraldehyde solution, and negative to 2% formalin.</td>
</tr>
<tr>
<td>Lyon, 1971</td>
<td>One female dental assistant was exposed to Cidex (2% aq. glutaraldehyde solution); she developed a rash on her fingers and hands that eventually spread to arms and legs; patch test results showed positive reaction to glutaraldehyde and negative reaction to formaldehyde, nickel sulfate and 12 other kinds of allergens.</td>
</tr>
<tr>
<td>Author(s), Year</td>
<td>Summary</td>
</tr>
<tr>
<td>------------------</td>
<td>---------</td>
</tr>
<tr>
<td>Goncalo et al, 1984</td>
<td>2 nursing aides developed a vesicular dermatitis of their hands and forearms after handling endoscopic disinfectants; both patients were positive to 1% glutaraldehyde and negative to 2% aq. formaldehyde; the dermatitis resolved following termination of the job for one case, but persisted after exposure for the other case.</td>
</tr>
<tr>
<td>Fowler, 1989</td>
<td>A respiratory therapy department worker developed an allergic contact dermatitis of her hands, arms, face and neck after using a 2% glutaraldehyde solution; patch testing to 1% aq. glutaraldehyde was positive at 48 hours, while all other allergens tested gave negative results.</td>
</tr>
<tr>
<td>Fisher, 1990</td>
<td>2 hospital workers were exposed to glutaraldehyde while disinfecting endoscopes; both cases showed positive patch test reactions to a 1% aq. solution of glutaraldehyde and negative reactions to formaldehyde.</td>
</tr>
<tr>
<td>Swierczynska, 1998</td>
<td>The incidence of allergy to glutaraldehyde in HCWs was 33/266 (12.4%) for glutaraldehyde and 37/266 (13.9%) for formaldehyde; dual positivity to glutaraldehyde and formaldehyde was seen in 6 patients; nurses, physicians and dental assistants were most frequently affected.</td>
</tr>
<tr>
<td>Swierczynska et al, 1999</td>
<td>The study examined 280 healthcare workers suffering from skin lesions. Allergy was diagnosed in 64 (22.8%) patients. The majority (85.9%) were sensitive to only one single aldehyde (formaldehyde, glutaraldehyde and glyoxal). Glutaraldehyde caused allergy slightly less frequently (12.4%) than formaldehyde (13.9%).</td>
</tr>
<tr>
<td>Matthew et al, 2000.</td>
<td>This is a 5-year study of 168 patients who were patch tested to glutaraldehyde, 55 of which were healthcare workers (HCWs). It showed that HCWs were more than 8 times more likely to be allergic to glutaraldehyde than non-HCWs. Also, they found that allergic contact dermatitis from glutaraldehyde often causes persistent dermatitis, which frequently forces patients to leave their jobs.</td>
</tr>
<tr>
<td>Nettis et al, 2002</td>
<td>The study examined 360 HCWs patients who were experiencing contact dermatitis at their hands, wrists and forearms. They found that glutaraldehyde (5 out of 72) is one of the major aetiological agents that induce occupational allergy.</td>
</tr>
</tbody>
</table>

In addition to these case reports and group studies, there are two definitive and controlled investigations into the dermal sensitizing potential of glutaraldehyde. One study (Marzulli et al, 1974) investigated the effect of inducing glutaraldehyde solutions of the concentration 0.1 and 5.0% to skin of male human aging from 21 to 50yr, using patch test. It turned that none of the 102 males receiving 0.1% glutaraldehyde were sensitized, and 7 out of 30 (23.3%) males receiving 5% glutaraldehyde showed positive patch response. The other study (Weaver et al, 1977) induced 0.022% and 0.0022% glutaraldehyde solutions on 340 and 366 subjects respectively, and none of the total 706 subjects developed dermal hypersensitivity. In addition, in the same study, they applied 0.055% glutaraldehyde to the arm of two subjects with confirmed dermal hypersensitivity to glutaraldehyde, and no inflammation developed at the site of application.

Different regions of the skin may have various hypersensitivities to glutaraldehyde. From reviewing case reports it is concluded that contact dermatitis occurred most often in the hands (Matthew, 2000). One study showed that 25% glutaraldehyde cannot induce skin hypersensitivity of feet; by comparison, 2.5% glutaraldehyde applied to regions around antecubital fossa region evoked a local hypersensitivity reaction (Maibach et al, 1977). The differences in response may be attributed to the differences in the thickness of the stratum corneumand keratin binding of glutaraldehyde at these sites, thus producing regional variations in the percutaneous penetration of glutaraldehyde (Ballantyne, 1984).
Since both formaldehyde and glutaraldehyde may be encountered among healthcare workers, it is important to know if cross reactivity will occur. From table 5, we can see that in most cases, HCWs who were hypersensitive to glutaraldehyde showed negative results for formaldehyde. In addition, by summarizing several reports investigating it is concluded that cross sensitization potential between glutaraldehyde and formaldehyde, it is concluded that such cross reactivity does not occur (Ballantyne, 1984).

c) Respiratory Sensitization

I. Animal studies

One study tested the respiratory sensitizing potential of glutaraldehyde vapor with male Hartley guinea pigs at the concentration of 13.9ppm and subsequent challenge concentration of 4.4ppm, and no evidence of respiratory sensitization was observed (Werley et al, 1995). However, in the same study, a concentration-related decrease in respiratory rate was observed, and the 50% decrease in respiratory rate (RD50) were measured to be 13.9ppm. Another similar study had same result, which induced 14ppm glutaraldehyde and a challenge concentration of 5ppm glutaraldehyde vapor to guinea pig, and there was no change in the respiratory waveform that would indicate a pulmonary hypersensitivity response (Desgroseillers et al, 1974). However, in one mouse IgE induction study, glutaraldehyde produced a concentration-related increase in serum IgE that was significant for the solutions of 25% and 10%, which were applied epicutaneously to the shaved flank skin (Ballantyne, 1995).

II. Human studies

There are many cases of occupational asthma induced by glutaraldehyde vapor exposure, and some of these are summarized in table 6.

<table>
<thead>
<tr>
<th>Author</th>
<th>Job Category</th>
<th>Detailed description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gannon et al, 1995</td>
<td>Endoscopy nurse</td>
<td>Glutaraldehyde can cause occupational asthma, based on exposure monitoring, peak expiratory flow (PEF) and specific bronchial provocation tests. The exposure levels measured in the workplace suggest that sensitization may occur at levels below the current occupational exposure standard.</td>
</tr>
<tr>
<td></td>
<td>X-ray secretary</td>
<td></td>
</tr>
<tr>
<td>Corrado et al, 1986</td>
<td>Endoscopy nurses</td>
<td>4 female endoscopy nurses who developed chest tightness, asthma and rhinitis. Provocation tests showed that syndrome of 2 among the 4 nurses was glutaraldehyde exposure related.</td>
</tr>
</tbody>
</table>
Toxicological Profile of Glutaraldehyde in Healthcare Industry

Quirce et al, 1999
Renal dialysis unit
The case was a 61-year-old nurse and ex-smoker, whose job task involved the use of 2% of glutaraldehyde. Ten years after working in the unit, bronchial challenge test specific for glutaraldehyde elicited an early asthmatic response. Her symptom included irritation of upper respiratory tract, chest tightness, shortness of breath, and dyspnea.

Ong et al, 2004
Laboratory technician
This is a female laboratory technician used 2.5% glutaraldehyde. Her symptom included episodic chest tightness and wheezing.

Cullinan et al, 1992
Radiographer
A 25-year-old female had worked as radiographer for 5 years, who developed breath difficulties. Serial peak flow test indicated her symptom was work-related, and further single blind inhalation tests showed exposure to glutaraldehyde at work provoked a late asthmatic response.

Chan-Yeung et al, 1993
Respiratory technologist
A workplace challenge test showed a progressive fall in FEV1 when the subject was exposed to glutaraldehyde in a sterilizing agent used to clean bronchoscopes at her workplace. After the diagnosis of occupational asthma was confirmed, the subject continued to assist with bronchoscopy but no longer cleaned the bronchoscopes.

d) Phototoxicity

In one study (Greim, 1997), 0.1~0.5% glutaraldehyde were applied six times during three weeks to the dorsal skin of 99 volunteers, and the application skin sites were exposed twice to erythematogenic doses of UV light (290-400nm). After 10~13 days, glutaraldehyde was applied to a remote skin site in the same fashion, and the site was irradiated with 6J/cm2 UVA (320-400nm). No photosensitivity was observed. Another study examined the phototoxic potential of a 2% solution of glutaraldehyde in a group of 12 healthy volunteer subjects of age range of 19~51 years (TKL Research, 1988). Then the experimental group was applied UV radiation, while the control group remains irradiated. By comparing the two groups, it was indicated that there are no Phototoxicity of glutaraldehyde.

Consequently, it is concluded that there are no signs of phototoxicity of glutaraldehyde.

e) Genotoxicity

There are many studies concerning genetic toxicity of glutaraldehyde, both in vivo and in vitro.

In vivo studies with standard methodology have generally shown no evidence for genotoxic activity (micronucleus, dominant lethal and Drosophila tests), with only one test in mice showing increased bone marrow chromosomal aberration following the intraperitoneal injection of glutaraldehyde (National Toxicology Program, 1999). The lack of genotoxic effects in vivo may be related to the rapid metabolism rate and protein-binding characteristic of glutaraldehyde. One study found that although [14C]-glutaraldehyde can be detected in cell cytoplasm, there are no significant fraction present in the nuclei (Ranly et al, 1990).
For *in vitro* studies, in most instances, geno-toxic activity of glutaraldehyde was weak and occurred in strains with enhanced sensitivity (Ballantyne et al, 2001). Most *in vitro* mammalian cell genetic toxicology assays and DNA damage and repair tests showed results from “no mutagenic activity” to “weak positive”. One study with Chinese Hamster ovary cells showed positive result (Galloway et al, 1985).

**f) Carcinogenicity**

**I. Animal study**

There are several animal studies concerning carcinogenicity of glutaraldehyde, and are summarized in table 7. From the table we can see that there are weak and obscure association between glutaraldehyde exposure and cancer in some studies, while others found no relationship at all.

<table>
<thead>
<tr>
<th>Author</th>
<th>Study design</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>van Birgelen et al, 2000</td>
<td>Rats and mice were exposed to glutaraldehyde vapor at the concentration gradients from 62.5 to 250 ppb, exposure duration was 6h/day, 5d/wk, and 104wks in total.</td>
<td>Only non-neoplastic nasal lesions, hyper-plasia, and inflammation of the squamous and respiratory epithelia were observed. So it was concluded that there was no evidence of carcinogenic activity under the conditions examined.</td>
</tr>
<tr>
<td>Zissu et al, 1998</td>
<td>Mice were exposed to glutaraldehyde vapor at 100 ppb for 6h/d, 5d/wk, and 52 or 78 wks in total.</td>
<td>Hyperplasia of the squamous epithelium lining the dorsal wall and lateral aspect of the atrioturbinate was observed in females. In addition, epidermal erosion and ulceration along with squamous and inflammatory exfoliation were noted in the nasal cavity. However, like the above study, it is difficult to relate the observed effect with cancer.</td>
</tr>
<tr>
<td>van Miller et al, 2002</td>
<td>Rats were given glutaraldehyde in drinking water at concentrations of 50, 250 and 1000 ppm for 52~104 weeks. Average glutaraldehyde consumption were 4, 17 and 64 mg/kg for males and 6, 25 and 86 mg/kg for females, respectively.</td>
<td>Bone marrow hyperplasia and renal tubular pigmentation were observed and were most like related to the low-grade hemolytic anemia that accompanies large granular lymphocytic leukemia (LGLL). And actually, the incidence of LGLL in the spleen was elevated at all exposure levels at 104 weeks. However, there are two obstacles relating LGLL occurrence with glutaraldehyde exposure: i) the incidence of LGLL was increased only in females. ii) LGLL occurs naturally in rats.</td>
</tr>
</tbody>
</table>
II. Human cancer study
Information on carcinogenicity of glutaraldehyde in humans is available from only one study. Among 186 factory employees between 1959 and 1978, monitoring data showed indoor glutaraldehyde concentration did not exceed 0.2ppm, and there was no increase in mortality or incidence of malignancy (Teta et al, 1995).

IARC does not list glutaraldehyde as “agents reviewed by the IARC monographs”. ACGIH categorized glutaraldehyde as “not classifiable as a human carcinogen”, due to lack of sufficient data.

g) Reproductive and developmental effects

I. Animal studies
Several toxicological studies have been conducted in different species to test the reproductive and developmental effects of glutaraldehyde. Mice given glutaraldehyde by gavage on gestational days 6~15 showed maternal toxicity at 50 and 100 mg/(kg-bodyweight*day), with some indication of fetotoxicity (Marks et al, 1980). At dosage below 50 mg/(kg*day) no maternally reproductive negativity was observed. A study with rats reduced body weighted gain and maternal mortality at the dose of 50 and 100 mg/(kg-bodyweight*day), but no effects on implantations, resorptions or number of live fetuses were observed (Emma et al, 1990) at all dosage range. Another rat study with pregnant female Wistar rats were given glutaraldehyde in water over gestational days 6~16 at concentrations of 50, 2.5 and 7.5ppm (which correspond dietary dosages of 5.2, 25.7 and 68.0 mg/kg) found to observable effects besides reduction in drinking consumption at the middle and high doses (Union Carbide Corporation, 1990). In a rabbit study in which glutaraldehyde was dosed by gavage at 5, 15 and 45 mg/(kg*day) over gestational days 7~19 observed that at highest dosage marked signs of maternal toxicity and embryo-fetotoxicity would occur, but no malformations, and neither maternal nor developmental effects was observed at lower doses (Ballantyne et al, 2001). For all the developmental studies conducted, none have shown any potential for teratogenic effects.

Regarding reproductive toxicity, one dominant lethal study in mice dosed at 30 or 60mg/kg by gavage and then mated with virgin females there was no evidence of reduced fertility and no effect on embryo-fetal viability (Tamada et al, 1978). In another study whose goal was to define reproductive effects of glutaraldehyde, rats were applied glutaraldehyde in drinking water over two generations at 50, 100 and 250 ppm, and only a dose-related decrease in parental water consumption and body weight without any reproductive activity were found (Neerper-Bradley et al, 2000).

Consequently, it is concluded that there are no significant reproductive and developmental effects of glutaraldehyde at the levels of those animal studies.
II. Human study

There are two studies on hospital workers concerning reproductive effects of glutaraldehyde, and are summarized in the table 8. Both studies found no elevated risk of spontaneous abortion or malformation of glutaraldehyde exposure.

Table 8. Human studies of reproductive effect of glutaraldehyde exposure among hospital workers

<table>
<thead>
<tr>
<th>Author</th>
<th>Methodology</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemminki et al, 1985.</td>
<td>Case control study of nurses working in different departments of Finland hospital. Case nurses were selected who had had a spontaneous abortion (N=217) or a malformed child (N=46), controls were nurses with normal birth.</td>
<td>Odds ratio for nurses with glutaraldehyde exposure was 1.1, which indicated no significant increase in risk of spontaneous abortion or malformation after glutaraldehyde exposure.</td>
</tr>
<tr>
<td>Hemminki et al, 1982</td>
<td>The study included all the sterilizing staff employed in Finnish hospitals in 1980; controls were nursing auxiliaries. Exposure assessment was based on questionnaire.</td>
<td>After adjusting factors such as age, parity, decade of pregnancy, smoking habits, and intake of coffee and alcohol, it was concluded that increased frequency of spontaneous abortion was not correlated with exposure to glutaraldehyde.</td>
</tr>
</tbody>
</table>
Part 5. Regulation

Hazard Classification

Table 9 summarized hazard classification of formaldehyde by different regulatory agencies.

<table>
<thead>
<tr>
<th>System</th>
<th>Substance</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canadian WHIMIS classification criteria</td>
<td>Glutaraldehyde aqueous solution (8~25%)</td>
<td>D1B “Poisonous and infectious material-Materials causing immediate and serious toxic effects-Toxic material”</td>
</tr>
<tr>
<td></td>
<td></td>
<td>D2A “Poisonous and Infectious Material-Materials causing other toxic effects-Very toxic material”</td>
</tr>
<tr>
<td></td>
<td></td>
<td>D2B “Poisonous and Infectious Material-Materials causing other toxic effects-Toxic material”</td>
</tr>
<tr>
<td></td>
<td></td>
<td>E “Corrosive material”</td>
</tr>
<tr>
<td>Canadian Ingredient Disclosure List</td>
<td>Glutaraldehyde</td>
<td>CAS# 111-30-8 is listed on the Canadian Ingredient Disclosure List[1].</td>
</tr>
<tr>
<td>Canadian Domestic Substance List (DSL)</td>
<td>Glutaraldehyde</td>
<td>CAS# 111-30-8 is listed on Canada’s DSL List[2].</td>
</tr>
<tr>
<td>NFPA</td>
<td>Glutaraldehyde aqueous solution (8~25%) [3]</td>
<td>Health: 3 (Short exposure could cause serious temporary or moderate residual injury)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Flammability: 0 (Will not burn)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Reactivity: 1 (Normally stable, but can become unstable at elevated temperatures and pressures)</td>
</tr>
<tr>
<td>European Labeling in Accordance with European Commission Directives</td>
<td>Glutaraldehyde aqueous solution (8~25%)</td>
<td><strong>Hazard Symbols:</strong> T (Toxic) [3]</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Risk Phrases:</strong> R22 Harmful if swallowed</td>
</tr>
<tr>
<td></td>
<td></td>
<td>R23 Toxic by inhalation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>R34 Causes burns</td>
</tr>
<tr>
<td></td>
<td></td>
<td>R42 May cause sensitization by inhalation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>R43 May cause sensitization by skin contact</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Safety Phrases:</strong> S26 In case of contact with eyes, rinse immediately with plenty of water and seek medical advice</td>
</tr>
<tr>
<td></td>
<td></td>
<td>S36 Wear suitable protective clothing</td>
</tr>
<tr>
<td></td>
<td></td>
<td>S37 Wear suitable gloves</td>
</tr>
<tr>
<td></td>
<td></td>
<td>S38 Wear eye/face protection</td>
</tr>
<tr>
<td></td>
<td></td>
<td>S45 In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>S61 Avoid release to the environment. Refer to special instructions/safety data sheets.</td>
</tr>
</tbody>
</table>

Table 9. Human studies of reproductive effect of glutaraldehyde exposure among hospital workers

stem Substance ClassificationSy
Canadian
Ingredie
nt Disclosure Glutaraldehyde CAS# 111-30-8 is listed
List on the Canadian Ingredient Disclosure List[1].
Canadian Domestic Glutaraldehyde CAS# 111-30-8 is listed on Canada’s DSL List[2]. Substance (DSL)
NFPA Glutaraldehyde aqueous solution (8~25%) [3] | Health: 3 (Short exposure could cause serious temporary or moderate residual injury) |
Reactivity: 1 (Normally stable, but can become unstable at elevated temperatures and pressures) |
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U.S. Toxic Substances Control Act (TSCA)

CAS# 111-30-8 is listed on the TSCA Inventory[4].

U.S. OSHA

Glutaraldehyde Not listed as “highly hazardous” by OSHA.

For ingredients in the Ingredient Disclosure List, their identity and concentration must be disclosed on a material safety data sheet if found in a controlled product.

Substances on the TSCA Inventory are considered “existing” chemicals in U.S. commerce, and substances not on the TSCA Inventory are “new” chemicals.

Exposure limit

Exposure limits of formaldehyde set up by four jurisdictions and agencies within or outside of Canada are summarized in table 10.

Table 10. Occupational exposure limits of glutaraldehyde

<table>
<thead>
<tr>
<th>Jurisdiction</th>
<th>WorkSafeBC</th>
<th>ACGIH</th>
<th>California’s division of OSHA[1]</th>
<th>NIOSH</th>
</tr>
</thead>
<tbody>
<tr>
<td>TWA</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>STEL</td>
<td>0.05 ppm</td>
<td>0.05 ppm</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Ceiling</td>
<td>0.05 ppm</td>
<td>N/A</td>
<td>0.2 ppm</td>
<td>0.2 ppm</td>
</tr>
<tr>
<td>Notation</td>
<td>S[2]</td>
<td>SEN[3]; A4[4]</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

[1] OSHA PEL not available
[2] “S” indicates that the substance is a sensitizer under section 5.57(1) of the OHS Regulation. For more information please refer to OHS Guideline G5.57 or follow the link http://www2.worksafebc.com/publications/OHSRegulation/Part5.asp#SectionNumber:5.57
[3] “SEN” refers to the potential for an agent to produce sensitization, as confirmed by human or animal data.
[4] “A4” refers to “Not Classifiable as a Human Carcinogen”, which indicates agents which cause concern that they could be carcinogenic for humans but cannot be assessed conclusively because of lack of data. In vitro or animal studies do not provide indications of carcinogenicity which are sufficient to classify the agent into one of the other categories.
Part 6. Control Measures

a) Substitution

OSHA suggests that when an alternative to glutaraldehyde is available which is at least as effective as an FDA-approved high level disinfectant, consideration should be given to whether the alternative is safer for employees (OSHA, 2006). In healthcare, the substitution can be achieved from two different paths: 1) Use a different drop-in liquid chemical disinfectant. 2) invest in new enclosed equipment technologies that do not utilize glutaraldehyde. Some of the substitutions are summarized in table 11 (Department of Health, Government of South Australia, 2004; Sustainable hospitals, 2009). From the table, we can see that certain glutaraldehyde alternatives, such as hydrogen peroxide, peracetic acid-hydrogen peroxide (PAHP) and ortho-phthalaldehyde, are suggested for the cold sterilization or disinfection of endoscopic equipment. The reason is that these substances may be safer than glutaraldehyde because of the less likelihood of causing allergic reactions (Rideout, 2005). However, it is also possible that the relative safety and carcinogenic potential of new disinfectants used to replace glutaraldehyde may not yet be known.

<table>
<thead>
<tr>
<th>Substitution Category</th>
<th>Name of Alternative</th>
<th>Chemical Ingredients</th>
<th>High-level-disinfection time[1]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drop-in Liquid Chemical Alternatives to Glutaraldehyde</td>
<td>Metrex Compliance TM</td>
<td>7.35% hydrogen peroxide and 0.23% peracetic acid.</td>
<td>15 min at 20°C</td>
</tr>
<tr>
<td></td>
<td>Sporox TM</td>
<td>7.5% hydrogen peroxide</td>
<td>30 min at 30°C</td>
</tr>
</tbody>
</table>
| | Cidex OPA | Active ingredient: 0.55% ortho-phthalaldehyde  
Inert ingredient: potassium phosphate dibasic (K2HPO4), potassium phosphate monobasic (KH2PO4), benzotriazole (C6H5N3), citric acid (C6H8O7), alizarin cyanine green (C28H20N2Na2O8S2), and trisodium HEDTA. | 12 min at 20°C |
| Enclosed Systems that perform High Level Disinfection | Steris 20™ Sterilant | 0.2% peracetic acid (diluted from 35%).  
Enclosed system generates hydrogen peroxide gas plasma.  
The Sterilox system generates chemically activated water with strong oxidizing properties. | Designed for sterilization[4]. Sterilizes in 12 min at 50° ~ 55°C. Designed for sterilization. Sterilization cycle is 45 min. The Sterilox system has FDA (510k) clearance for high level disinfection, which requires a contact time of 10 minutes at 25 degrees Centigrade. |

Table 11. Substitution of glutaraldehyde
U.S. EPA’s Case Study of Substitution

One case study investigated using Cidex OPA as an alternative of Cidex in the Gastroenterology Department of Kaiser Woodland Hills Medical Center, California (U.S. EPA, 2002). The department accounts for 50% of the hospital’s total glutaraldehyde consumption, and the major use of glutaraldehyde is for high-level disinfection of endoscopes. Active ingredient of Cidex OPA is ortho-phthalaldehyde at the concentration of 0.55% w/w, and the inert ingredients are potassium phosphate dibasic (K2HPO4), potassium phosphate monobasic (KH2PO4), benzotriazole (C6H5N3), citric acid (C6H8O7), alizarin cyanine green (C28H20N2Na2O8S2), and trisodium HEDTA (Department of Health, Government of South Australia, 2004).

The Environmental Health and Safety Director at Woodland Hills identified Cidex OPA as a possible glutaraldehyde alternative for the following reasons: 1) its lower inhalation exposure risk as a result of the low percentage of active ingredient and relatively lower vapor pressure, 2) reduced disinfecting time (12 minutes for Cidex OPA vs. FDA-approved 45 disinfecting time for glutaraldehyde solution), 3) the solution is approved for use in almost all of their equipment without negating the warranty. The price of Cidex OPA is approximately 25$ per gallon, which is three times more than glutaraldehyde. However, substituting glutaraldehyde with Cidex OPA costs significantly less than installing a more substantial ventilation system to minimize glutaraldehyde exposure. Due to the environmental impact of Cidex OPA, California legislation requires treating Cidex OPA with glycine (NH2-CH2-COOH) on site to render it a non-hazardous waste by the ratio of 25 grams of glycine per gallon Cidex OPA for 1 hour. The hospital complied with the regulation by purchasing the external treatment tank ($700), which includes a mobile cart, treatment tank, pump, and tubing, in additional to the costs of treatment device, they purchased glycine ($5 per gallon, including the cost of product and labor).

The substitution result in less frequent and significant less severe complaints among the hospital staff, though there are very mild symptoms, such as slight eye irritation and a “chalky” taste after prolonged use. Also, because Cidex OPA has a shorter disinfection time as mentioned above, the hospital saves approximately 8 minutes with each disinfection cycle, or a savings of 1 hour for each 8-hour automated endoscope reprocessor shift. This brings extra benefits, since the cost of endoscope is approximately $30,000 and the reprocessor around $15,000. In addition, the hospital found that Cidex OPA does not lose efficacy as fast as the glutaraldehyde-based product, so they are now able to disinfect 60% more endoscopes during the life of the solution.
b) Engineering Control

I. General room ventilation
American National Standard Institute (ANSI), in collaboration with the Association for the Advancement of Medical Instrumentation, recommended that rooms where glutaraldehyde disinfection or sterilization is performed should be large enough to ensure adequate dilution of vapor and have a minimum air exchange rate of 10 air exchanges per hour (ANSI/AAMI, 1996). One study showed that natural ventilation is not always reliable for reducing glutaraldehyde exposure, and may actually increase the dispersion of glutaraldehyde vapor to other workplaces (Naidu, 1995).

II. Local exhaust ventilation
ANSI/AAMI recommends that local exhaust ventilation also be installed at the point of release of glutaraldehyde vapors. California Department of Health Services also recommends local exhaust ventilation system as the “most effective” type of ventilation control, as it can capture contaminated air at the source before it spread.

In the case of using local exhaust ventilation, the healthcare facility must ensure that the ventilation system is operating properly and is not obstructed by drafts from sources such as fans, supply air diffusers, open widows and doors, and heavily traveled aisles. Local exhaust ventilation located at the level of vapor discharge is preferred, as it can capture and remove vapor at the source. Local exhaust ventilation system may include a “local exhaust hood” or “ductless fume hood”.

If local exhaust hood is applied as ventilation, minimum hood-induced air velocity necessary to capture and convey glutaraldehyde vapor into the hood and conduct it into the exhaust system is recommended to be at least 100 feet per minute (Pryor, 1984). In addition, the American Industrial Hygiene Association recommends an average “face velocity” (the average velocity of air drawn through the face of an open hood) of 80 to 120 feet per minute for laboratory exhaust hoods (AIHA, 1992 in ANSI/AAMI, 1996). Once the glutaraldehyde vapor is collected inside a suitable exhaust hood, it is transported through a duct system and then discharged to the outside via a fan.

If duct fume hoods were applied (duct fume hoods refer to ventilated enclosures that have their own exhaust fan that draws air out of the hood, passes it through an air cleaning filter and then discharges the cleaned exhaust air back into the workplace), then for glutaraldehyde, the filter material could be activated charcoal or other suitable sorbent material. Since the filter has limited absorbing capacity, a preventive maintenance program in accordance with the manufacture’s recommendations must be implemented to ensure optimum performance of the system.
III. Use of automated equipment

Automated transfer
OSHA recommends that reducing the release of glutaraldehyde vapor during transfer operations can be accomplished by the use of automated and enclosed equipment. For example, the transfer of glutaraldehyde from drums into process containers can be automated using pumps and closed transfer lines, which helps employees avoid glutaraldehyde exposure (OSHA, 2001). In addition, the use of “safety nozzle” for pouring reduces the potential for splashing during initial pouring of glutaraldehyde solutions. When using a “safety nozzle”, droplets of glutaraldehyde may remain inside the nozzle, so special attention should be paid to avoiding spraying droplets into the atmosphere when removing the nozzle from the container or screwing it onto another container (OSHA, 2006).

Automated disinfection
Automated disinfection equipment can significantly reduce glutaraldehyde exposures of employees performing disinfection procedure, as well as other employees and non-employees in the vicinity (OSHA, 2006). ANSI sets up standard for the purchase and installation of automated glutaraldehyde processing equipment (ANSI/AAMI ST58), and proper ventilation is still necessary for the automated equipment.

c) Administrative Control

Employee Information and Training

Employees who use, handle, or may have potential exposure to glutaraldehyde solutions must be provided information and training prior to their initial work assignment. According to OSHA regulation 29 CFR 1910.1200, the training should include the following elements: 1) methods and observations that may be used to detect the presence or release of glutaraldehyde in the workplace, 2) the physical and health hazards of glutaraldehyde, 3) measures that workers can take to protect themselves, 4) an explanation of MSDS, the employer’s labeling system, and how employees can obtain and use the appropriate hazard information.

Safety Work Practice—Spill Control and Cleanup Procedure

Glutaraldehyde spills have the potential to create vapor concentrations that exceed recommended exposure limits. Consequently, a suitable plan of action with procedures for handling glutaraldehyde spills should be developed and implemented by knowledgeable and responsible individuals at the facility. According to ANSI standard (ANSI/AAMI, 1996), spill control plan should incorporate the following key elements: 1) designation of individuals responsible for
managing spill cleanup, 2) evacuation procedures for nonessential personnel if necessary, 3) medical treatment procedures for exposed individuals, 4) site-specific reporting requirements, 5) cleanup procedures, the location of spill control supplies, and required personal protective equipment, 6) location and availability of material safety data sheets (MSDSs) for glutaraldehyde-based sterilants/disinfectants and manufacturer recommendations for emergency response.

d) Personal Protective Equipment

It should be noticed that PPE should not be used as an alternative for substitution, installing engineering and administrative control measures. The reasons for this are that PPE cannot eliminate hazard from the source, and the effectiveness of PPE in reality is much less than estimated. A study of Italian operating room staff showed that only 38% regularly wore appropriate PPE while handling glutaraldehyde solutions (Angelillo et al, 1999).

I. Skin protection

According to OSHA regulation 29 CFR 1910.138, employers must select and require employees to use appropriate hand protection when employee’s hands are exposed to potential skin absorption of substances such as glutaraldehyde. In addition, ANSI states that elbow-length gloves or protective sleeves made of glutaraldehyde impervious material should be worn to protect the hands and forearms (ANSI/AAMI, 1996). Among the chemical-protective materials, butyl rubber, nitrile and Viton are the most impervious to 50% glutaraldehyde solutions and have been shown to provide full shift protection against glutaraldehyde permeation (Jordan et al, 1996; Forsberg, 1999). For shorter exposures, gloves made of polyethylene and styrene-butadiene/styrene-isoprene copolymers (i.e., Allergard Synthetic Surgical Gloves) provide protection for several hours with dilute (2% to 3.4%) glutaraldehyde solutions (Jordan et al., 1996; Ansell Health Care, 2003). Latex gloves are not recommended for use with glutaraldehyde, as it provides far less margin of safety compared with the materials mentioned above. Polyvinyl chloride (PVC) and neoprene gloves cannot be used against glutaraldehyde exposure, as they may retain or absorb glutaraldehyde (Jordan et al., 1996).

II. Eye protection

According to OSHA regulation 29 CFR 1910.133, splash-proof goggles or safety glasses with full face shields must be worn wherever there is potential for glutaraldehyde solution to contact the eyes. In addition, suitable emergency eyewash equipment must be immediately available for quick drenching or flushing of the eyes for at least 15 minutes in all glutaraldehyde usage locations. It is recommended that emergency eyewash unit be accessible and located within 10 seconds travel time of the affected area.


III. Respiratory Protection

All personnel who may be required to wear a respirator for routine or emergency use must be included in a written respiratory protection program that meets the requirement of OSHA’s Respiratory Protection standard (29 CFR 1910.134).

Employers must select appropriate respirators based on an exposure assessment or a reasonable estimate of employee exposures to glutaraldehyde vapor during routine and/or emergency work procedures. For protection against exposures to glutaraldehyde vapor during routine procedures, employers may provide air-purifying respirators (i.e., a half-face or full-face air-purifying respirator with organic vapor cartridges), or air-supplying respirators (OSHA, 2006). Air-purifying respirators are preferred when exposures may be reasonably anticipated to be higher, especially emergency spill situations. OSHA also recommends that if air-purifying respirators are provided, employers must implement a change-out schedule for air-purifying canisters and cartridges to ensure that they are changed before the end of their service life. All respirators used must be certified by NIOSH and must be appropriate for use with glutaraldehyde (29 CFR 1910.134(d)(1)(i) and (ii)). The disposable air-purifying particulate respirators (filtering face pieces) are not effective against organic vapors, thus must not be used for glutaraldehyde protection.
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