

A PROPOSAL FOR GUIDELINE FOR PREVENTION OF ALLERGIC OCCUPATIONAL ASTHMA –IN CONFORMITY WITH THE GLOBALLY HARMONIZED SYSTEM OF CLASSIFICATION AND LABELLING OF CHEMICALS (GHS)

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The use of chemical products to enhance and improve life is a widespread worldwide practice. Alongside the benefits of these products, there is also the potential of chemicals for adverse effects to people or the environment. As a result, a number of countries or organizations have developed laws or regulations over the years that require information to be prepared and transmitted to those using chemicals, through labels or Safety Data Sheets (SDS). Their differences are significant enough to result in different labels or SDS for the same product in different countries. In July 2003, United Nations (UN) recommended the globally harmonized system of classification and labelling of chemicals (GHS). We, special committee of Japanese Society of Occupational and Environmental Allergy proposed a guideline for prevention of allergic occupational asthma and sensitizers (n=60) causing occupational asthma or contact dermatitis in conformity with respiratory and skin sensitization criteria of GHS. We should propose these 60 sensitizers to the chemical industry association and governments to control, regulate and label them in each country.

There are over 20 million chemicals in the world. Many countries address classification and labelling for at least some chemicals in their countries. In the area of trade, the need to comply with multiple regulations regarding hazard classification and labelling is costly and time-consuming. Small to medium enterprises are effectively precluded from international trade in chemicals due to the regulatory burden of compliance. In 1992, the United Nations Conference on the Environmental and Development (UNCED) took place in Brazil. Agreements endorsed by the United Nations General Assembly established 6 program areas to strengthen national and international efforts related to the environmentally sound management of chemicals. (Chapter 19, Agenda 21) 'Harmonization of classification and labelling of chemicals' is GHS (Globally Harmonized System of classification and labelling of chemicals).

In July 2003, United Nations (UN) recommended and published 'Globally harmonized system of classification and labelling of chemicals (GHS)' (The purple book) (1). Web site is also available (<http://www.unece.org/trans/danger/publi/ghs/officialtext.html>). GHS would be available all over the world in 2008. For example, New Zealand has adopted the GHS system as the basis for the Hazardous Substances and New Organisms Act (1996) and Associated Regulations (2000). Pictograms of the GHS are also used in New Zealand. New Zealand is an advanced country as to GHS. On the other hand,

GHS pilot implementation previous countries are South Africa and Zambia. In 2005, 3 ASEAN countries, and 3 other African countries will join. Most of these countries are developing countries. These countries need the support of UN. GHS has 10 Health and Environmental Hazards criteria. We pay attention to respiratory or skin sensitization criteria of GHS. Human positive evidences or appropriate animal positive results are important for both criteria. Figure 1 shows the pictogram of respiratory sensitizer. Signal word is 'Danger'. Hazard statement is 'may cause allergy or asthma symptoms or breathing difficulties if inhaled'. Figure 2 indicates the label of skin sensitizer. Signal word is 'Warning'. Hazard statement is 'may cause an allergic skin reaction' (1).

MATERIALS AND METHODS

However, GHS document does not list sensitizers in conformity with GHS respiratory and skin sensitization criteria. The American Conference of Governmental Industrial Hygienists (ACGIH) lists about 30 sensitizers (2). Commission for the Investigation of Health Hazards of Chemical Compounds in the Working Area (MAK) in Germany lists over 200 sensitizers (3). European Chemical Bureau (ECB) in Italy lists 26 skin sensitizers, 51 skin and respiratory sensitizers and 643 skin sensitizers (4). A group of dermatologists in Germany listed 244 skin sensitizers (5). Japanese Society of Contact Dermatitis lists about 150 skin sensitizers (6). On the other hand, the committee of occupational exposure limits in Japan Society for Occupational Health lists 18 airway sensitizers and 30 skin sensitizers (7). Thus, we reviewed several papers (8-

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**Danger****Fig. 1.** Pictogram of respiratory sensitizers.

14) and selected sensitizers in conformity with the criteria of GHS. The criteria for respiratory or skin sensitizer in GHS is as follows (1); A respiratory sensitizer is a substance that will induce hypersensitivity of the airway following inhalation of the substance. If there is evidence in human that the substance can induce specific respiratory hypersensitivity and/or, if there are positive results from an appropriate animal test. A skin sensitization is a substance that will induce an allergic response following skin contact. If there is evidence in humans that the substance can induce sensitization by skin contact in a substantial number of persons, or If there are positive results from an appropriate animal test.

RESULTS

We selected 60 respiratory and/or skin sensitizers (Table I). The uses and workplaces of the substances are also indicated. Substances with asterisk (*) had been reported as only skin sensitizers. Substances with sharp(#) had been reported as only respiratory sensitizer. Substances with no mark had been reported as sensitizers to both respiratory and skin.

DISCUSSION

The guideline of occupational asthma is critical. We summarized it as follows;

1. Primary Prevention: Exposure concentration is defined as the concentration of a sensitizer in the air which will be inhaled by a worker without the use of protective respiratory equipment. OEL (Occupational Exposure Limits) recommended by the Japan Society for Occupational Health (7), TLV (Threshold Limit Values) recommended by ACGIH(USA) (2) and TLV by MAK(Germany) (3). Exposure concentration should be limited below these values. If OEL or TLV are not recommended yet, the exposure should be limited to as low as possible by prevention of volatilization and improvement of ventilation. Protective respiratory equipment (mask, gauze and so on) should always be used. Exposure duration should be shortened.
2. Secondary prevention: Taking a history to determine if a person has a past history or family history of allergic diseases, or if he is sensitive to an occupational asthmagen. Taking an occupational

**Warning****Fig. 2.** Pictogram of skin sensitizers.**Table I.** Sensitizers (n=60) of occupational allergy and their uses.

Sensitizers	Uses, workplace
α -amylase#	bread (baker's asthma)
Benzofuran*	pesticide, insecticide
Beryllium	alloy, nuclear reactor
Bisphenol type A, F*	epoxy resin
Butyl acrylate*	acryl fiber, adhesives
Casein	tanner, food industry
Cephalosporine#	pharmacy, medical staff
Chlorhexidine	disinfectant
Chromium (Cr)	alloy, gilding
Cobalt (Co)	alloy, catalyst
Colophony (Rosin)	adhesives, tire industry
Copper*	alloy
4,4'-diaminodiphenylmethane*	adhesives, paint
Diazomethane#	organic chemical industry
Diazonium	plastic, rubber
Dibenzoyl peroxide*	wheat flour, bleach
Dibutylphthalate*	lacquer, adhesives
Dichloropropane*	solvent, synthetic intermediate
Dinitrochlorobenzene(DNCB)*	dyes, synthetic intermediate
Diphenylmethane-4,4'-diisocyanate (MDI)#	adhesives, paint
Ethylenediamine	dyes, resin
Ethylene oxide*	organic synthesizer
Formaldehyde	antiseptic, synthetic resin
Glutaraldehyde	disinfectant
Hevein (latex antigen)	medical gloves
Hexamethylene diisocyanate(HDI)#	adhesives, paint
Hydrazine*	jet fuel, foaming agent
Hexachlorophene	chemical and cosmetic industry
2-hydroxyethyl methacrylate*	construction materials, paint, adhesives
Hydroquinone*	photographic development
Iodine (I)*	disinfectant, medicine
Isophoron diisocyanate#	polyurethane
Maleic anhydride	resin, plastic, stabilizer
Mercury*	electrode, amalgam, extraction of gold
4-methoxyphenol*	stabilizer, chemical stabilizer
Methyl acrylate*	acryl fiber, adhesives, paint
Methyl 2-cyanoacrylate	petroleum industry
Methyl methacrylate	construction material, Paint, adhesives
Methyltetrahydrophthalic anhydride(MTHPA)	polyester resin
1,5-naphthylene diisocyanate (NDI)#	adhesives, paint
Nickel (Ni)	coin, alloy, gilding
Penicilline#	pharmacy, medical staff
m-phenylenediamine*	azo dyes, hair dye
o-phenylenediamine*	dye intermediate, fungicide
p-phenylenediamine*	dye intermediate, hardener
Phthalic anhydride#	phthalic plastic, paint
Piperazine	detection reagent, catalyst, pesticide
Platinum (Pt)	catalyst, jewelry, platinum refinery
Picatic acid#	carpenter, woodman
Polyvinylchloride (PVC)*	clothes, interior for industry
Pyrazolone derivatives	photographic processing, Chemical laboratory staff
Resorcinol*	explosive, dye
Rhodium (Rh)	gilding
Styrene#	polystyrene resin, Synthetic gum
Tetracycline#	pharmacy, medical staff
Tetramethylthiuram disulfide(TMTD)	rubber accelerator, anti-fungus
Toluene diisocyanate (TDI)#	polyurethane
Trimellitic anhydride (TMA)	plasticizer
Turpentine oil*	solvent, medicine
Vanilline#	perfumery

#respiratory sensitization

*skin sensitization

history is essential. The time association between exposure and symptoms should be taken. Inhalation challenge test to identify a suspicious agent allows a correct diagnosis of occupational asthma. Treatment is in conformity with routine asthma treatment.

3. Tertiary prevention: The symptoms last for several years if a person take an occupational asthma. Therefore its recognition and compensation are important.

Of these three preventions, we pay attention to first

prevention. To attain 'first prevention', control, regulate and label sensitizers in our country, we should expand sensitizers to hundreds of chemicals as Germany (3) or ECB (4). In Japan, the committee of occupational exposure limits (OEL committee) in Japan Society for Occupational Health lists 18 airway sensitizers (Group 1: 11, Group 2: 7) and 30 skin sensitizers (Group 1: 12, Group 2: 18) (7). The criteria of OEL committee are as follows;

This list of occupational sensitizers is recommended for the airway and skin. The sensitizers are classified into Group 1 substances which induce allergic reactions in humans and Group 2 substances which probably induce allergic reactions in humans. Recommendation of occupational exposure limits (OEL) for the occupational sensitizers does not necessarily consider either prevention of sensitization or allergic reaction.

We hold the special committee of listing sensitizers within OEL committee in Japan Society for Occupational Health at this symposium (ISOEAID'05). We reviewed the process how the sensitizers were determined at previous time and discussed the criteria for sensitizer and the extent of investigating chemicals. We would hold the next special committee in 2006.

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