CHEMICAL SUBSTANCES AND OTHER ISSUES UNDER STUDY

The TLV® Chemical Substances Committee solicits information, especially data, which may assist in its deliberations regarding the following substances and issues. Comments and suggestions, accompanied by substantiating evidence in the form of peer-reviewed literature, should be forwarded in electronic format to The Science Group, ACGIH® at science@acgih.org. In addition, the Committee solicits recommendations for additional substances and issues of concern to the industrial hygiene and occupational health communities. Please refer to the ACGIH® TLV®/BEI® Development Process found on the ACGIH® website for a detailed discussion covering this procedure and methods for input to ACGIH® (http://www.acgih.org/ TLV/DevProcess.htm).

The Under Study list is published each year by February 1 on the ACGIH® website (www.acgih.org/TLV/Studies.htm), in the ACGIH® Annual Reports, and later in the annual *TLVs® and BEIs®* book. In addition, the Under Study list is updated by July 31 into a two-tier list.

- Tier 1 entries indicate which chemical substances and physical agents **may** move forward as an NIC or NIE in the upcoming year, based on their status in the development process.
- Tier 2 consists of those chemical substances and physical agents that **will not** move forward, but will either remain on, or be removed from, the Under Study list for the next year.

This updated list will remain in two tiers for the balance of the year. ACGIH® will continue this practice of updating the Under Study list by February 1 and establishing the two-tier list by July 31 each year.

The substances and issues listed below are as of January 1, 2009. *After this date, please refer to the ACGIH® website (http://www.acgih.org/TLV/Studies.htm) for the up-to-date list.*

Chemical Substances

Acetaldehyde
Acetic anhydride
Allyl bromide
Allyl chloride
Atrazine (and related symmetrical triazines)
Barium sulfate
Benz[a]anthracene
Benzidine
Benzo[b]fluoranthene
Benzo[a]pyrene
Bisphenol A
Boron tribromide
Boron trifluoride
Bromodichloromethane
1-Bromopropane
sec-Butyl acetate
Butylated hydroxytoluene [BHT]
tert-Butyl hydroperoxide
Calcium silicate
Carbon black
Chlorine
Chrysene
Clopidol
Coal tar pitch volatiles
Creosote
2,4-D
Diacetyl
Dibutyl phthalate
3,3'-Dichlorobenzidine
1,3-Dichloro-5,5-dimethyl hydantoin

Dicyclopentadiene
Diethylene glycol monobutyl ether
Diethylhydroxylamine [DEHA]
Diisobutyl ketone
N,N-Dimethyl acetamide
Dimethylformamide
Dipropyl ketone
Ethyl cyanoacrylate
Ethylene oxide
Ethyl formate
Ethylidene norbornene
Gasoline, all formulations
Glycerin, mist
Hexamethylene diisocyanate
Iodoform
Isobutane
Isophorone diisocyanate
Lithium hydride
Methomyl
Methyl acetate
Methylacrylonitrile
Methylene bis (4-cyclohexyliso-cyanate)
Methylene bisphenyl isocyanate [MDI]
Methyl formate
Methyl isoamyl ketone
Methyl isopropyl ketone
Naphthalene
β-Naphthylamine
Nickel carbonyl
Nitrogen dioxide
Nonane
Paraquat
Pentachlorophenol
2,4-Pentanedione
Phthalic anhydride
o-Phthalodinitrile
p-Phthalodinitrile
Piperazine
Piperazine dihydrochloride
Polycyclic aromatic hydrocarbons [PAHs]
Polymeric MDI
Silica, Crystalline – α-Quartz and Cristobalite
Simazine
Soapstone
Stearates
Stoddard solvent
Talc
Thioglycolic acid
Titanium dioxide
Tributyl phosphate
Trichloroacetic acid
1,2,3-Trichloropropane
Triethanolamine
Triphenyl amine
Vinyl acetate
5-Vinyl-2-norbornene
Wood dusts

Other Issues

1. Definitions of various notations.

DEFINITIONS AND NOTATIONS

Definitions

Documentation

The source publication that provides the critical evaluation of the pertinent scientific information and data with reference to literature sources upon which each TLV® or BEI® is based. See the discussion under "TLV®/BEI® Development Process: An Overview" found at the beginning of this book. The general outline used when preparing the *Documentation* may be found in the Operations Manual of the Threshold Limit Values for Chemical Substances (TLV®-CS) Committee, accessible online at: www.acgih.org/TLV/OPSManual.pdf.

Minimal Oxygen Content

An oxygen (O_2)-deficient atmosphere is defined as one with an ambient ρO_2 less than 132 torr (NIOSH, 1980). The minimum requirement of 19.5% oxygen at sea level (148 torr O_2, dry air) provides an adequate amount of oxygen for most work assignments and includes a margin of safety (NIOSH, 1987; McManus, 1999). Studies of pulmonary physiology suggest that the above requirements provide an adequate level of oxygen pressure in the lungs (alveolar ρO_2 of 60 torr) (Silverthorn, 2001; Guyton, 1991; NIOSH, 1976).

Some gases and vapors, when present in high concentrations in air, act primarily as simple asphyxiants, without other significant physiologic effects. A simple asphyxiant may not be assigned a TLV® because the limiting factor is the available oxygen. Atmospheres deficient in O_2 do not provide adequate warning and most simple asphyxiants are odorless. Account should be taken of this factor in limiting the concentration of the asphyxiant particularly at elevations greater than 5000 feet where the ρO_2 of the atmosphere is less than 120 torr. Several simple asphyxiants present an explosion hazard. Consult the *Documentation* for further information on specific simple asphyxiants.

Note: See page 81 for Adopted Appendix F: Minimal Oxygen Content.

Notation

A notation is a designation that appears as a component of the TLV® in which specific information is listed in the column devoted to Notations.

Notice of Intended Change (NIC)

The NIC is a list of actions proposed by the TLV®-CS Committee for the coming year. This Notice provides an opportunity for public comment. Values remain on the NIC for approximately one year after they have been ratified by the ACGIH® Board of Directors. The proposals should be considered trial values during the period they are on the NIC. If the Committee neither finds nor receives any substantive data that change its scientific opinion regarding an NIC TLV®, the Committee may then approve its recommendation to the ACGIH® Board of Directors for adoption. If the Committee finds or receives substantive data that change its scientific opinion regarding an NIC TLV®, the Committee may change its recommendation to the ACGIH® Board of Directors for the matter to be either retained on or withdrawn from the NIC.

Values appearing in parentheses in the Adopted TLV® section are to be used during the period in which a proposed change for that value or notation appears on the NIC.

Particulate Matter/Particle Size

For solid and liquid particulate matter, TLVs® are expressed in terms of "total" particulate matter, except where the terms inhalable, thoracic, or respirable particulate mass are used. The intent of ACGIH® is to replace all "total" particulate TLVs® with inhalable, thoracic, or respirable particulate mass TLVs®. Side-by-side sampling using "total" and inhalable, thoracic, or respirable sampling techniques is encouraged to aid in the replacement of current "total" particulate TLVs®. *See Appendix C*: Particle Size-Selective Sampling Criteria for Airborne Particulate Matter, for the definitions of inhalable, thoracic, and respirable particulate mass.

Particles (insoluble or poorly soluble) Not Otherwise Specified (PNOS)

There are many insoluble particles of low toxicity for which no TLV® has been established. ACGIH® believes that even biologically inert, insoluble, or poorly soluble particles may have adverse effects and suggests that airborne concentrations should be kept below 3 mg/m^3, respirable particles, and 10 mg/m^3, inhalable particles, until such time as a TLV® is set for a particular substance. A description of the rationale for this recommendation and the criteria for substances to which it pertains are provided in Appendix B.

TLV® Basis

TLVs® are derived from publicly available information summarized in their respective *Documentation*. Although adherence to the TLV® may prevent several adverse health effects, it is not possible to list all of them in this book. The basis on which the values are established will differ from agent to agent (e.g., protection against impairment of health may be a guiding factor for some, whereas reasonable freedom from irritation, narcosis, nuisance, or other forms of stress may form the basis for others). Health impairments considered include those that shorten life expectancy, adversely affect reproductive function or developmental processes, compromise organ or tissue function, or impair the capability for resisting other toxic substances or disease processes.

The TLV® Basis represents the adverse effect(s) upon which the TLV® is based. The TLV® Basis column in this book is intended to provide a field reference for symptoms of overexposure and as a guide for determining whether components of a mixed exposure should be considered as acting independently or additively. Use of the TLV® Basis column is not a substitute for reading the *Documentation*. Each *Documentation* is a critical component for proper use of the TLV(s)® and to understand the TLV® basis. A complete list of the TLV® bases used by the Threshold Limit Values for Chemical Substances Committee may be found in their Operations Manual online at: (http://www.acgih.org/TLV/TLV-CS_Ops_Man_2006-2-9.pdf).

Abbreviations used:

Card – cardiac
CNS – central nervous system
COHb-emia – carboxyhemoglobinemia
convul – convulsion
dam – damage
eff – effects
form – formation
func – function
GI – gastrointestinal
Hb – hemoglobin
impair – impairment
inhib – inhibition
irr – irritation
LRT – lower respiratory tract
MeHb-emia – methemoglobinemia
PNS – peripheral nervous system
pulm – pulmonary
repro – reproductive
resp – respiratory
sens – sensitization
URT – upper respiratory tract

Notations/Endnotes

Biological Exposure Indices (BEIs®)

The notation "BEI" is listed in the "Notations" column when a BEI® (or BEIs®) is (are) also recommended for the substance. Three subcategories to the "BEI" notation have been added to help the user identify those substances that would use only the BEI® for Acetylcholinesterase Inhibiting Pesticides or Methemoglobin Inducers. They are as follows:

BEI_A = *See* the BEI® for Acetylcholinesterase Inhibiting Pesticide

BEI_M = *See* the BEI® for Methemoglobin Inducers

BEI_P = *See* the BEI® for Polycyclic Aromatic Hydrocarbons (PAHs)

Biological monitoring should be instituted for such substances to evaluate the total exposure from all sources, including dermal, ingestion, or non-occupational. See the BEI® section in this book and the *Documentation* of the TLVs® and BEIs® for these substances.

Carcinogenicity

A carcinogen is an agent capable of inducing benign or malignant neoplasms. Evidence of carcinogenicity comes from epidemiology, toxicology, and mechanistic studies. Specific notations (i.e., A1, A2, A3, A4, and A5) are used by ACGIH® to define the categories for carcinogenicity and are listed in the Notations column. See Appendix A for these categories and definitions and their relevance to humans in occupational settings.

Inhalable Fraction and Vapor (IFV)

The Inhalable Fraction and Vapor (IFV) endnote is used when a material exerts sufficient vapor pressure such that it may be present in both particle and vapor phases, with each contributing a significant portion of the dose at the TLV–TWA concentration. The ratio of the Saturated Vapor Concentration (SVC) to the TLV–TWA is considered when assigning the IFV endnote. The industrial hygienist should also consider both particle and vapor phases to assess exposures from spraying operations, from processes involving temperature changes that may affect the physical state of matter, when a significant fraction of the vapor is dissolved into or adsorbed onto particles of another

substance (such as water-soluble compounds in high humidity environments), and in selecting sampling techniques to collect both states of matter (Perez and Soderholm, 1991).

Sensitization

The designation "SEN" in the "Notations" column refers to the potential for an agent to produce sensitization, as confirmed by human or animal data. The SEN notation ***does not imply*** that sensitization is the critical effect on which the TLV® is based, nor does it imply that this effect is the sole basis for that agent's TLV®. If sensitization data exist, they are carefully considered when recommending the TLV® for the agent. For those TLVs® that are based upon sensitization, they are meant to protect workers from induction of this effect. These TLVs® are not intended to protect those workers who have already become sensitized.

In the workplace, respiratory, dermal, or conjunctival exposures to sensitizing agents may occur. Similarly, sensitizers may evoke respiratory, dermal, or conjunctival reactions. At this time, the notation does not distinguish between sensitization involving any of these organ systems. The absence of a SEN notation does not signify that the agent lacks the ability to produce sensitization but may reflect the paucity or inconclusiveness of scientific evidence.

Sensitization often occurs via an immunologic mechanism and is not to be confused with other conditions or terminology such as hyperreactivity, susceptibility, or sensitivity. Initially, there may be little or no response to a sensitizing agent. However, after a person is sensitized, subsequent exposure may cause intense responses, even at low exposure concentrations (well below the TLV®). These reactions may be life-threatening and may have an immediate or delayed onset. Workers who have become sensitized to a particular agent may also exhibit cross-reactivity to other agents that have similar chemical structures. A reduction in exposure to the sensitizer and its structural analogs generally reduces the incidence of allergic reactions among sensitized individuals. For some sensitized individuals, complete avoidance of exposure to the sensitizer and structural analogs provides the only means to prevent the specific immune response.

Agents that are potent sensitizers present special problems in the workplace. Respiratory, dermal, and conjunctival exposures should be significantly reduced or eliminated through process control measures and personal protective equipment. Education and training (e.g., review of potential health effects, safe handling procedures, emergency information) are also necessary for those who work with known sensitizing agents.

For additional information regarding the sensitization potential of a particular agent, refer to the TLV® *Documentation* for the specific agent.

Skin

The designation "Skin" in the "Notations" column refers to the potential significant contribution to the overall exposure by the cutaneous route, including mucous membranes and the eyes, by contact with vapors, liquids, and solids. Where dermal application studies have shown absorption that could cause systemic effects following exposure, a Skin notation would be considered. The

Skin notation also alerts the industrial hygienist that overexposure may occur following dermal contact with liquid and aerosols, even when airborne exposures are at or below the TLV®.

A Skin notation is not applied to chemicals that may cause dermal irritation. However, it may accompany a SEN notation for substances that cause respiratory sensitization following dermal exposure. Although not considered when assigning a Skin notation, the industrial hygienist should be aware that there are several factors that may significantly enhance potential skin absorption of a substance that otherwise has low potential for the cutaneous route of entry. Certain vehicles can act as carriers, and when pretreated on the skin or mixed with a substance can promote the transfer of the substance into the skin. In addition, the existence of some dermatologic conditions can also significantly affect the entry of substances through the skin or wound.

While relatively limited quantitative data currently exist with regard to skin absorption of gases, vapors, and liquids by workers, ACGIH® recommends that the integration of data from acute dermal studies and repeated-dose dermal studies in animals and humans, along with the ability of the chemical to be absorbed, be used in deciding on the appropriateness of the Skin notation. In general, available data which suggest that the potential for absorption via the hands and forearms during the workday could be significant, especially for chemicals with lower TLVs®, could justify a Skin notation. From acute animal toxicity data, materials having a relatively low dermal LD_{50} (i.e., 1000 mg/kg of body weight or less) would be given a Skin notation. When chemicals penetrate the skin easily (i.e., higher octanol–water partition coefficients) and where extrapolations of systemic effects from other routes of exposure suggest dermal absorption may be important in the expressed toxicity, a Skin notation would be considered. A Skin notation is not applied to chemicals that cause irritation or corrosive effects in the absence of systemic toxicity.

Substances having a Skin notation and a low TLV® may present special problems for operations involving high airborne concentrations of the material, particularly under conditions where significant areas of the skin are exposed for a long period. Under these conditions, special precautions to significantly reduce or preclude skin contact may be required.

Biological monitoring should be considered to determine the relative contribution to the total dose from exposure via the dermal route. ACGIH® recommends a number of adopted Biological Exposure Indices (BEIs®) which provide an additional tool when assessing the total worker exposure to selected materials. For additional information, refer to *Dermal Absorption* in the "Introduction to the Biological Exposure Indices," *Documentation of the Biological Exposure Indices* (2001), and to Leung and Paustenbach (1994). Other selected readings on skin absorption and the skin notation include Sartorelli (2000), Schneider et al. (2000), Wester and Maibach (2000), Kennedy et al. (1993), Fiserova-Bergerova et al. (1990), and Scansetti et al. (1988).

The use of a Skin notation is intended to alert the reader that air sampling alone is insufficient to quantify exposure accurately and that measures to prevent significant cutaneous absorption may be required.

References and Selected Reading

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All pertinent notes relating to the material in the Chemical Substances section of this book appear in the appendices for this section or on the inside back cover.