INTRODUCTION
TO THE CHEMICAL SUBSTANCES

General Information

The TLVs® are guidelines to be used by professsional industrial hygienists. The values presented in this book are intended for use only as guidelines or recommendations to assist in the evaluation and control of potential workplace health hazards and for no other use (e.g., neither for evaluating or controlling community air pollution; nor for estimating the toxic potential of continuous, uninterrupted exposures or other extended work periods; nor for proving or disproving an existing disease or physical condition in an individual). Further, these values are not fine lines between the safe and dangerous conditions and should not be used by anyone who is not trained in the discipline of industrial hygiene. TLVs® are not regulatory or consensus standards.

Editor's note: The approximate year that the current *Documentation* was last substantially reviewed and, where necessary, updated may be found following the CAS number for each of the adopted entries in the alphabetical listing, e.g., Aldrin [309-00-2] (2006). The reader is advised to refer to the "TLV Chronology" section in each *Documentation* for a brief history of the TLV® recommendations and notations.

Definition of the TLVs®

Threshold limit values (TLVs®) refer to airborne concentrations of chemical substances and represent conditions under which it is believed that *nearly all* workers may be repeatedly exposed, day after day, over a working lifetime, without adverse health effects.

Those who use the TLVs® **MUST** consult the latest *Documentation* to ensure that they understand the basis for the TLV® and the information used in its development. The amount and quality of the information that is available for each chemical substance varies over time.

Chemical substances with equivalent TLVs® (i.e., same numerical values) cannot be assumed to have similar toxicologic effects or similar biologic potency. In this book, there are columns listing the TLVs® for each chemical substance (that is, airborne concentrations in parts per million [ppm] or milligrams per cubic meter [mg/m^3]) and critical effects produced by the chemical substance. These critical effects form the basis of the TLV®.

ACGIH® recognizes that there will be considerable variation in the level of biological response to a particular chemical substance, regardless of the airborne concentration. Indeed, TLVs® do not represent a fine line between a healthy versus an unhealthy work environment or the point at which material impairment of health will occur. TLVs® will not adequately protect all workers. Some individuals may experience discomfort or even more serious adverse health effects when exposed to a chemical substance at the TLV® or even at concentrations below the TLV®. There are numerous possible reasons for increased susceptibility to a chemical substance, including age, gender, ethnicity, genetic factors (predisposition), lifestyle choices (e.g., diet, smoking, abuse of alcohol and other drugs), medications, and pre-existing medical conditions (e.g., aggravation of asthma or cardiovascular disease). Some individuals may become more responsive to one or more chemical substances following previous exposures (e.g., sensitized workers). Susceptibility to the effects of chemical substances may be altered during different periods of fetal development and throughout an individual's reproductive lifetime. Some changes in susceptibility may also occur at different work levels (e.g., light versus heavy work) or at exercise — situations in which there is increased cardiopulmonary demand. Additionally, variations in temperature (e.g., extreme heat or cold) and relative humidity may alter an individual's response to a toxicant. The *Documentation* for any given TLV® must be reviewed, keeping in mind that other factors may modify biological responses.

Although TLVs® refer to airborne levels of chemical exposure, dermal exposures may possibly occur in the workplace (see "Skin" in the ***Definitions and Notations*** section starting on page v).

Three categories of TLVs® are specified: time-weighted average (TWA); short-term exposure limit (STEL); and a Ceiling (C). For most substances, a TWA alone or with a STEL is relevant. For some substances (e.g., irritant gases), only the TLV–Ceiling is applicable. If any of these TLV® types are exceeded, a potential hazard from that substance is presumed to exist.

Threshold Limit Value–Time-Weighted Average (TLV–TWA): The TWA concentration for a conventional 8-hour workday and a 40-hour workweek, to which it is believed that nearly all workers may be repeatedly exposed, day after day, for a working lifetime without adverse effect. Although calculating the average concentration for a workweek, rather than a workday, may be appropriate in some instances, ACGIH® does not offer guidance regarding such exposures.

Threshold Limit Value–Short-Term Exposure Limit (TLV–STEL): A 15-minute TWA exposure that should not be exceeded at any time during a workday, even if the 8-hour TWA is within the TLV–TWA. The TLV–STEL is the concentration to which it is believed that workers can be exposed continuously for a short period of time with-out suffering from 1) irritation, 2) chronic or irreversible tissue damage, 3)

dose-rate-dependent toxic effects, or 4) narcosis of sufficient degree to increase the likelihood of accidental injury, impaired self-rescue, or materially reduced work efficiency. The TLV–STEL will not necessarily protect against these effects if the daily TLV–TWA is exceeded. The TLV–STEL is not a separate, in-dependent exposure guideline; rather, it supplements the TLV–TWA where there are recognized acute effects from a substance whose toxic effects are primarily of a chronic nature. Exposures above the TLV–TWA up to the TLV–STEL should be less than 15 minutes, should occur no more than four times per day, and there should be at least 60 minutes between successive exposures in this range. An averaging period other than 15 minutes may be recommended when this is warranted by observed biological effects.

Threshold Limit Value–Ceiling (TLV–C): The concentration that should not be exceeded during any part of the working exposure. If instantaneous measurements are not available, sampling should be conducted for the minimum period of time sufficient to detect exposures at or above the ceiling value.

ACGIH® believes that TLVs® based on physical irritation should be considered no less binding than those based on physical impairment. There is increasing evidence that physical irritation may initiate, promote, or accelerate adverse health effects through interaction with other chemical or biologic agents or through other mechanisms.

Excursion Limits

For many substances with a TLV–TWA, there is no TLV–STEL. Nevertheless, excursions above the TLV–TWA should be controlled, even where the 8-hour TLV–TWA is within recommended limits. Excursion limits apply to those TLV–TWAs that do not have TLV–STELs.

> *Excursions in worker exposure levels may exceed 3 times the TLV–TWA for no more than a total of 30 minutes during a workday, and under no circumstances should they exceed 5 times the TLV–TWA, provided that the TLV–TWA is not exceeded.*

The approach here is that the maximum recommended excursion should be related to the variability generally observed in actual industrial processes. In reviewing large numbers of industrial hygiene surveys conducted by the U.S. National Institute for Occupational Safety and Health, Leidel et al. (1975) found that short-term exposure measurements were generally lognormally distributed.

While a complete discussion of the theory and properties of the lognormal distribution is beyond the scope of this section, a brief description of some important terms is presented. The measure of central tendency in a lognormal distribution is the antilog of the mean logarithm of the sample values. The distribution is skewed, and the geometric mean (m_g) is always smaller than the arithmetic mean by an amount that depends on the geometric standard deviation. In the lognormal distribution, the geometric standard deviation (sd_g) is the antilog of the standard deviation of the sample value logarithms, and 68.26% of all values lie between m_g/sd_g and $m_g \times sd_g$.

If the short-term exposure values in a given situation have a geometric standard deviation of 2.0, 5% of all values will exceed 3.13 times the geometric mean. If a process displays variability greater than this, it is not under good control, and efforts should be made to restore control.

The approach is a considerable simplification of the lognormal concentration distribution concept but is considered more convenient. If exposure excursions are maintained within the recommended limits, the geometric standard deviation of the concentration measurements will be near 2.0, and the goal of the recommendations will be accomplished. It is recognized that the geometric standard deviations of some common workplace exposures may exceed 2.0 (Buringh and Lanting, 1991). If such distributions are known and workers are not at increased risk of adverse health effects, recommended excursion limits should be modified, based upon workplace-specific data. When the toxicologic data for a specific substance are available to establish a TLV–STEL or a TLV–C, these values take precedence over the excursion limit.

TWA and STEL versus Ceiling (C)

A substance may have certain toxicological properties that require the use of a TLV–C rather than a TLV–TWA excursion limit or a TLV-STEL. The amount by which the TLVs® may be exceeded for short periods without injury to health depends upon a number of factors such as the nature of the contaminant, whether very high concentrations — even for short periods — produce acute poisoning, whether the effects are cumulative, the frequency with which high concentrations occur, and the duration of such periods. All factors must be taken into consideration in arriving at a decision as to whether a hazardous condition exists.

Although the TWA concentration provides the most satisfactory, practical way of monitoring airborne agents for compliance with the TLVs®, there are certain substances for which it is inappropriate. In the latter group are substances that are predominantly fast-acting and whose TLV® is more appropriately based on this particular response. Substances with this type of response are best controlled by a TLV–C that should not be exceeded. It is implicit in these definitions that the manner of sampling to determine noncompliance with the TLVs® for each group must differ. Consequently, a single, brief sample that is applicable to a TLV–C is not appropriate to the TLV–TWA; here, a sufficient number of samples are needed to permit determination of a TWA concentration through-out a complete cycle of operation or throughout the workshift.

Whereas, the TLV–C places a definite boundary

that exposure concentrations should not be permitted to exceed, the TLV–TWA requires an explicit limit to the excursions, which are acceptable above the recommended TLV–TWAs.

Mixtures

Special consideration should also be given to the application of the TLVs® in assessing the health hazards that may be associated with exposure to a mixture of two or more substances. A brief discusion of basic considerations involved in developing TLVs® for mixtures and methods for their development, amplified by specific examples, is given in Appendix E.

Deviations in Work Conditions and Work Schedules

Application of TLVs® to Unusual Ambient Conditions

When workers are exposed to air contaminants at temperatures and pressures substantially different than those at normal temperature and pressure (NTP) conditions (25°C and 760 torr), care should be taken in comparing sampling results to the applicable TLVs®. For aerosols, the TWA exposure concentration (calculated using sample volumes not adjusted to NTP conditions) should be compared directly to the applicable TLVs® published in the TLVs® and BEIs® book. For gases and vapors, there are a number of options for comparing air-sampling results to the TLV®, and these are discussed in detail by Stephenson and Lillquist (2001). One method that is simple in its conceptual approach is 1) to determine the exposure concentration, expressed in terms of mass per volume, at the sampling site using the sample volume not adjusted to NTP conditions, 2) if required, to convert the TLV® to mg/m^3 (or other mass per volume measure) using a molar volume of 24.45 L/mole, and 3) to compare the exposure concentration to the TLV®, both in units of mass per volume.

A number of assumptions are made when comparing sampling results obtained under unusual atmospheric conditions to the TLVs®. One such assumption is that the volume of air inspired by the worker per workday is not appreciably different under moderate conditions of temperature and pressure as compared to NTP (Stephenson and Lillquist, 2001). An additional assumption for gases and vapors is that absorbed dose is correlated to the partial pressure of the inhaled compound. Sampling results obtained under unusual conditions cannot easily be compared to the published TLVs®, and extreme care should be exercised if workers are exposed to very high or low ambient pressures.

Unusual Work Schedules

Application of TLVs® to work schedules markedly different from the conventional 8-hour day, 40-hour workweek requires particular judgment to provide protection for these workers equal to that provided to workers on conventional work shifts. Short workweeks can allow workers to have more than one job, perhaps with similar exposures, and may result in overexposure, even if neither job by itself entails overexposure.

Numerous mathematical models to adjust for unusual work schedules have been described. In terms of toxicologic principles, their general objective is to identify a dose that ensures that the daily peak body burden or weekly peak body burden does not exceed that which occurs during a normal 8-hour/day, 5-day/week shift. A comprehensive review of the approaches to adjusting occupational exposure limits for unusual work schedules is provided in *Patty's Industrial Hygiene* (Paustenbach, 2000). Other selected readings on this topic include Lapare et al. (2003), Brodeur et al. (2001), Caldwell et al. (2001), Eide (2000), Verma (2000), Roach (1978), and Hickey and Reist (1977).

Another model that addresses unusual work schedules is the Brief and Scala model (1986), which is explained in detail in *Patty's Industrial Hygiene* (Paustenbach, 2000). This model reduces the TLV® proportionately for both increased exposure time and reduced recovery (i.e., non-exposure) time, and is generally intended to apply to work schedules longer than 8 hours/day or 40 hours/week. The model should not be used to justify very high exposures as "allowable" where the exposure periods are short (e.g., exposure to 8 times the TLV–TWA for 1 hour and zero exposure during the remainder of the shift). In this respect, the general limitations on TLV–TWA excursions and TLV–STELs should be applied to avoid inappropriate use of the model with very short exposure periods or shifts.

The Brief and Scala model is easier to use than some of the more complex models based on pharmacokinetic actions. The application of such models usually requires knowledge of the biological half-life of each substance, and some models require additional data. Another model developed by the University of Montreal and the Institute de Recherche en Sante et en Securite du Travail (IRSST) uses the Haber method to calculate adjusted exposure limits (Brodeur et al., 2001). This method generates values close to those obtained from physiologically based pharmacokinetic (PBPK) models.

Because adjusted TLVs® do not have the benefit of historical use and long-time observation, medical supervision during initial use of adjusted TLVs® is advised. Unnecessary exposure of workers should be avoided, even if a model shows such exposures to be "allowable." Mathematical models should not be used to justify higher-than-necessary exposures.

TLV® Units

TLVs® are are expressed in ppm or mg/m^3. An inhaled chemical substance may exist as a gas, vapor, or aerosol.

1. A gas is a chemical substance whose molecules are moving freely within a space in which they are confined (e.g., cylinder/tank) at normal temperature and pressure (NTP). Gases assume no shape or volume.
2. A vapor is the gaseous phase of a chemical substance that exists as a liquid or a solid at NTP. The amount of vapor given off by a chemical substance is expressed as the vapor pressure and is a function of temperature and pressure.
3. An aerosol is a suspension of solid particles or liquid droplets in a gaseous medium. Other terms used to describe an aerosol include dust, mist, fume, fog, fiber, smoke, and smog. Aerosols may be characterized by their aerodynamic behavior and the site(s) of deposition in the human respiratory tract.

TLVs® for aerosols are usually established in terms of mass of the chemical substance in air by volume. These TLVs® are expressed in mg/m^3.

TLVs® for gases and vapors are established in terms of parts of vapor or gas per million parts of contaminated air by volume (ppm), but may also be expressed in mg/m^3. For convenience to the user, these TLVs® also reference molecular weights. Where 24.45 = molar volume of air in liters at NTP conditions (25°C and 760 torr), the conversion equations for gases and vapors [ppm↔mg/m^3] are as follows:

$$\text{TLV in ppm} = \frac{(\text{TLV in mg/m}^3)\,(24.45)}{(\text{gram molecular weight of substance})}$$

OR

$$\text{TLV in mg/m}^3 = \frac{(\text{TLV in ppm})(\text{gram molecular weight of substance})}{24.45}$$

When converting values expressed as an element (e.g., as Fe, as Ni), the molecular weight of the element should be used, not that of the entire compound.

In making conversions for substances with variable molecular weights, appropriate molecular weights should be estimated or assumed (see the TLV® Documentation).

User Information

Each TLV® is supported by a comprehensive *Documentation*. It is imperative to consult the latest *Documentation* when applying the TLV®.

Additional copies of the *TLVs® and BEIs®* book and the multi-volume *Documentation of the Threshold Limit Values and Biological Exposure Indices,* upon which this book is based, are available from ACGIH®. *Documentation* of individual TLVs® is also available. Consult the ACGIH® website (www.acgih.org/store) for additional information and availability concerning these publications.

References and Selected Readings

Brief RS; Scala RA: Occupational health aspects of unusual work schedules: a review of Exxon's experiences. Am Ind Hyg Assoc J 47(4):199–202 (1986).

Brodeur J; Vyskocil A; Tardif R; et al.: Adjustment of permissible exposure values to unusual work schedules. Am Ind Hyg Assoc J 62:584–594 (2001).

Buringh E; Lanting R: Exposure variability in the workplace: its implications for the assessment of compliance. Am Ind Hyg Assoc J 52:6–13 (1991).

Caldwell DJ; Armstrong TW; Barone NJ; et al.: Lessons learned while compiling a quantitative exposure database from the published literature. Appl Occup Environ Hyg 16(2):174–177 (2001).

Eide I: The application of 8-hour occupational exposure limits to non-standard work schedules offshore. Ann Occup Hyg 34(1):13–17 (1990).

Hickey JL; Reist PC: Application of occupational exposure limits to unusual work schedules. Am Ind Hyg Assoc J 38(11):613–621 (1977).

Lapare S; Brodeur J; Tardif R: Contribution of toxicokinetic modeling to the adjustment of exposure limits to unusual work schedules. Am Ind Hyg Assoc J 64(1):17–23 (2003).

Leidel NA; Busch KA; Crouse WE: Exposure measurement action level and occupational environmental variability. DHEW (NIOSH) Pub. No. 76-131; NTIS Pub. No. PB- 267-509. U.S. National Technical Information Service, Springfield, VA (December 1975).

Paustenbach DJ: Pharmacokinetics and Unusual Work Schedules. In: Patty's Industrial Hygiene, 5th ed., Vol. 3, Part VI, Law, Regulation, and Management, Chap. 40, pp. 1787–1901. RL Harris, Ed. John Wiley & Sons, Inc., New York (2000).

Roach SA: Threshold limit values for extraordinary work schedules. Am Ind Hyg Assoc J 39(4):345–348 (1978).

Stephenson DJ; Lillquist DR: The effects of temperature and pressure on airborne exposure concentrations when performing compliance evaluations using ACGIH TLVs and OSHA PELs. Appl Occup Environ Hyg 16(4):482–486 (2001).

Verma DK: Adjustment of occupational exposure limits for unusual work schedules. Am Ind Hyg Assoc J 61(3):367–374 (2000).

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 pO_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 pres-sure in the lungs (alveolar pO_2 of 60 torr) (Silver-thorn, 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 pro-vide 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 pO_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. *See* the newly Adopted Appendix F: Minimum 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 and solicits suggestions of substances to be added to the list. 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 during the year, the Committee neither finds nor receives any substantive data that changes its scientific opinion regarding the 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 changes 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 *Documentations*. Although adherence to the TLV® may pre-vent several adverse health effects, it is not pos-sible 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, where-as 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 sub-stances 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 under-stand the TLV® basis. A complete list of the TLV® Basis used by the Threshold Limit Values for Chemical Substances Committee may be found in their Operations Manual online at: (www.acgih.org/TLV/OpsManual.pdf).

ABBREVIATIONS USED

CNS — central nervous system
GI — gastrointestinal
LRT — lower respiratory tract
PNS — peripheral nervous system
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. Two 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* 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) end-note 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 Indus-trial 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 com-pounds 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, even when exposures are at or below the TLV®.

Vehicles present in solutions or mixtures can also significantly enhance potential skin absorption. While some materials are capable of causing irritation, dermatitis, and sensitization in workers, these properties are not considered relevant when assigning a Skin notation. However, the development of a dermatologic condition could significantly affect the potential for dermal absorption.

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

ACGIH American Conference of Governmental Industrial Hygienists: Dermal absorption. In: Documentation of the Biological Exposure Indices, 7th ed., pp. 21–26. ACGIH®, Cincinnati, OH (2001).

Fiserova-Bergerova V; Pierce JT; Droz PO: Dermal absorption potential of industrial chemicals: criteria for skin notation. Am J Ind Med 17(5):617–635 (1990).

Guyton AC: Textbook of Medical Physiology, 8th ed. W.B. Sanders Co., Philadelphia (1991).

Kennedy Jr GL; Brock WJ; Banerjee AK: Assignment of skin notation for threshold limit values chemicals based on acute dermal toxicity. Appl Occup Environ Hyg 8(1):26–30 (1993).

Leung H; Paustenbach DJ: Techniques for estimating the percutaneous absorption of chemicals due to occupational and environmental exposure. Appl Occup Environ Hyg 9(3):187–197 (1994).

McManus N: Safety and Health in Confined Spaces. Lewis Publishers, Boca Raton, FL (1999).

NIOSH U.S. National Institute for Occupational Safety and Health: A Guide to Industrial Respiratory Protection, DHEW (NIOSH) Pub. No. 76-198. NIOSH, Cincinnati, OH (1976).

NIOSH U.S. National Institute for Occupational Safety and Health: Working in Confined Spaces. DHHS (NIOSH) Pub. No. 80-106. NIOSH, Cincinnati, OH (1980).

NIOSH U.S. National Institute for Occupational Safety and Health: NIOSH Respirator Decision Logic. DHHS (NIOSH) Pub. No. 87-108. NIOSH, Cincinnati, OH (1987).

Perez C; Soderholm SC: Some chemicals requiring special consideration when deciding whether to

sample the particle, vapor, or both phases of an atmosphere. Appl Occup Environ Hyg 6:859–864 (1991).
Sartorelli P: Dermal risk assessment in occupational medicine. Med Lav 91(3):183–191 (2000).
Scansetti G; Piolatto G; Rubino GF: Skin notation in the context of workplace exposure standards. Am J Ind Med 14(6):725–732 (1988).
Schneider T; Cherrie JW; Vermeulen R; Kromhout H: Dermal exposure assessment. Ann Occup Hyg 44(7):493–499 (2000).
Silverthorn DE: Human Physiology: An Integrated Approach, 2nd ed. Prentice-Hall, New Jersey (2001).
Wester RC; Maibach HI: Understanding percutaneous absorption for occupational health and safety. Int J Occup Environ Health 6(2):86–92 (2000).