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July 13, 2009

*VIA ELECTRONIC MAIL*

Ms. Cynthia Oshita  
Office of Environmental Health Hazard Assessment  
1001 I Street, 19th Floor  
Sacramento, California 95812-4010

**RE: *Objections to Proposal to List DMAC as a Reproductive Toxin under Proposition 65***

Dear Ms. Oshita:

On behalf of our client E.I. du Pont de Nemours and Company (“DuPont”), we are submitting the comments below to object to OEHHA’s June 12, 2009 proposal to list the chemical N,N-dimethylacetamide (“DMAC”) as a chemical “known to the State” to cause reproductive toxicity for purposes of the Safe Drinking Water and Toxic Enforcement Act of 1986 (“Proposition 65”). DuPont also requests an opportunity to meet with the Director and OEHHA staff with responsibility for this proposal, to discuss the proposal and these comments.

**INTRODUCTION AND SUMMARY**

DuPont objects to OEHHA’s proposal to list DMAC as a reproductive toxin under Proposition 65. As a preliminary matter, we are obliged to note our belief that the “Labor Code Mechanism” referred to in the Request for Comments on the proposed listing is invalid.<sup>1</sup> We recognize that this issue will be resolved in the courts, however, and address the proposal on its own merits below.

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<sup>1</sup> “Request for Comments on Chemicals Proposed for Listing By The Labor Code Mechanism,” June 12, 2009 (referred to above and herein as “Request for Comments”).

In short, DMAC is not a “known reproductive toxin”<sup>2</sup> for purposes of the Labor Code Mechanism, and should not be designated pursuant to that mechanism as a chemical that is “known to the state to cause . . . reproductive toxicity” for purposes of Proposition 65.<sup>3</sup>

The Request for Comments indicates that OEHHA is considering whether DMAC should be listed because a Threshold Limit Value (“TLV”) was assigned for that chemical based “in part” on “a relevant reproductive or developmental effect.” That determination may serve as a productive starting point, but is not the standard that OEHHA must apply in determining whether a chemical should be listed. Rather, the agency must examine the TLVs assigned by the American Conference of Industrial Hygienists (“ACGIH”), and determine which of the chemicals for which TLVs have been assigned, if any, are “known reproductive toxins.”<sup>4</sup>

To assist in this endeavor, we have included with our comments the “Documentation”<sup>5</sup> for the DMAC TLV, extracted from the Documentation of the Threshold Limit Values and Biological Exposure Indices, 7<sup>th</sup> Edition (2001), which explains how the TLV for DMAC should be interpreted and applied.<sup>6</sup> We also have included the “ACGIH Operations Manual – ACGIH Threshold Limit Values for Chemical Substances Committee,”<sup>7</sup> which explains the process by which the TLV was derived.

These documents demonstrate that ACGIH did not designate DMAC as a reproductive toxin when it established the TLV. Nor did ACGIH make any comment in the Documentation from which it should be inferred that DMAC is a “known reproductive toxin.” In assigning a TLV for DMAC of 10 parts per million (“ppm”), the ACGIH TLV Committee included notations in its “Summary” that the “value is intended to minimize the potential for liver injury and jaundice and from reproductive or developmental effects reported in studies with rats.”<sup>8</sup> The Documentation carefully notes, however, that the only reproductive or developmental effects to

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<sup>2</sup> *Sierra Club v. Schwarzenegger*, No. RG07356881, Superior Court for Alameda, Minute Order, May 27, 2009.

<sup>3</sup> Cal. Health & Safety Code, § 25249.8(a), (b).

<sup>4</sup> The acronyms “ACGIH” and “TLV” are registered trademarks. For ease of reading, we have included the symbol ® only in quotations of materials from ACGIH publications.

<sup>5</sup> Attachment A.

<sup>6</sup> “The Documentation of the Threshold Limit Values and Biological Exposure Indices is the source publication for the TLV®s and BEI®s issued by ACGIH®. The Documentation gives the practitioner scientific information and data with reference to literature sources that were used to base each TLV® or BEI®. For better understanding of the TLV®s and BEI®s, it is essential that the Documentation be consulted when the TLV®s or BEI®s are being used.” Preface to Documentation of the Threshold Limit Values and Biological Exposure Indices, 7<sup>th</sup> Edition (2001).

<sup>7</sup> Attachment B.

<sup>8</sup> Attachment A.

which it was referring were observed at “dosages close to lethal” and at which “maternal toxicity” was recorded.

The brief notation above, indicating that the TLV for DMAC is “intended to minimize the potential” for reproductive or developmental effects is not a statement that DMAC is a known reproductive toxin, by any standard. By the standards that OEHHA and its Developmental and Reproductive Toxicant Identification Committee (“DART IC”) has promulgated in the implementation of Proposition 65, that is not even a close question.

For all of the reasons above, and those stated more fully herein, DMAC should not be listed as a chemical that is “known to the state to cause . . . reproductive toxicity.” On the record before the agency, the chemical does not meet the standard for listing under any listing “mechanism.”

## BACKGROUND

**DMAC AND ITS USES.** DMAC (CAS Reg. No. 127-19-5), is an industrial solvent. DuPont manufactures the chemical primarily for the company’s own use, principally in the production of DuPont™ Nomex® brand fiber and also to produce DuPont™ Tedlar® and Kapton® films.

DuPont™ Nomex® is a heat- and flame-resistant fiber used to produce heat- and flame-resistant fabrics and insulating materials that protect millions of people and processes worldwide. Nomex® fiber is inherently flame-resistant, will not melt, drip or support combustion in the air, is particularly strong and resistant to chemical attack, and offers outstanding resistance to a broad range of chemicals, acids and alkalis. Accordingly, the fiber is used to make protective apparel for use by first responders, military personnel, pilots and flight crews, racing drivers and pit crews, and industrial workers. It also is used to manufacture heat- and fire resistant components for automobiles and vehicles used in mass transportation; in transformers, motors, generators and other electrical equipment; and some consumer products.

DuPont™ Tedlar® products are used to make functional laminates as a critical element in photovoltaic modules used for alternative energy generation, in aircraft to enhance the safety performance of interior panels and in construction and automotive applications to extend component lifetime. DuPont™ Kapton® is widely used in electronic devices such as cell phones and lap top computers, for wire insulation, and in many medical and military applications. The product is being tested for use in next-generation photovoltaic materials (solar collectors), fuel cells and air bag sensors for cars. The value of these materials lies not only in their performance qualities, but also in their light weight and durability.

In all of these products, the use of DMAC presents enormous societal benefits. Protective apparel made with Nomex® fibers protect human beings from heat, fire and chemical injuries and save lives. Products made from Tedlar® and Kapton® present substantial

environmental benefits in the form of energy savings and disposal costs. Collectively, these products are at the leading edge of technology, and are extremely valuable to the national and California economies.

The only commercially viable substitute for DMAC in manufacturing Nomex® fibers is N-methyl pyrrolidone (CAS Reg. No. 872-50-4). This chemical is listed under Proposition 65 as a chemical “known to the state to cause developmental toxicity.” No substitute has been identified for use in the manufacture of Tedlar® or Kapton®.

**INELIGIBILITY FOR LISTING UNDER STATUTORY CRITERIA.** For the reasons below, it is self-evident that DMAC does not qualify for listing under the criteria set forth in the statute.

Section 25249.8(a) of Proposition 65 directs OEHHA, acting for the Governor, to publish a “list of those chemicals known to the state to cause cancer or reproductive toxicity within the meaning of this chapter.” In the next subsection of the same provision, Section 25249.8(b) provides that a “chemical is known to the state to cause cancer or reproductive toxicity” if: (1) “in the opinion of the state’s experts it has been clearly shown through scientifically valid testing according to generally accepted principles to cause cancer or reproductive toxicity,” or (2) “a body considered to be authoritative by such experts has formally identified it as causing cancer or reproductive toxicity,” or (3) an “agency of the state or federal government has formally required it to be labeled or identified as causing cancer or reproductive toxicity.

DMAC meets none of these criteria. Specifically, it has not been determined, “in the opinion of the state’s qualified experts [that DMAC] has been clearly shown through scientifically valid testing according to generally accepted principles to cause . . . reproductive toxicity.” Nor has any “authoritative body” ever “formally identified” DMAC as a reproductive toxin. Finally, no state or federal agency requires it to be labeled or identified as such.<sup>9</sup>

**ACGIH TLV FOR DMAC.** Although DMAC does not come within the statutory definition of a chemical “known to the state to cause . . . reproductive toxicity,” the chemical is proposed for listing now under the asserted “Labor Code listing mechanism,” because a Threshold Limit Value (“TLV”) was established for the chemical by the American Conference of Governmental and Industrial Hygienists (“ACGIH”), “based solely or in part on a relevant reproductive or developmental effect.”<sup>10</sup>

For reasons discussed in the Objections to Listing below, it would be improper for OEHHA to characterize DMAC as a known reproductive toxin merely because the ACGIH assigned a TLV that was “based on” a reproductive or developmental effect, and even more so if the TLV was based on such an effect only “in part.” Rather, assuming that the Labor Code

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<sup>9</sup> Cal. Health & Safety Code § 25249.8(b).

<sup>10</sup> Request for Comments, June 12, 2009.

listing mechanism is valid, it is OEHHA's responsibility to examine the TLV and the reasons for which ACGIH assigned the TLV, and determine from that information whether DMAC is a "known reproductive toxin." In order to do that, it is necessary to understand the purpose of TLVs and the process by which ACGIH goes about assigning them.

As background, it is important to note that ACGIH is not a governmental agency or a standard-setting body. Rather, it is a private non-profit corporation whose members are industrial hygienists or other occupational health and safety professionals dedicated to promoting health and safety within the workplace. In that capacity, ACGIH committees review scientific literature for certain nominated chemicals, and the ACGIH assigns TLVs and Biological Exposure Indices ("BEIs") for them, *for use by industrial hygienists* in making decisions regarding safe levels of exposure in the workplace. These recommendations or guidelines are intended for use in the practice of industrial hygiene, "to be interpreted and applied only by a person trained in this discipline." *TLVs "are not developed for use as legal standards and ACGIH does not advocate their use as such."*<sup>11</sup>

For this reason, the ACGIH cautions that "[i]t is not appropriate for individuals or organizations to impose on the TLVs® . . . their concepts of what the TLVs® . . . should be or how they should be applied or to transfer regulatory standards or requirements to the TLVs® . . ." <sup>12</sup> That warning is especially appropriate here, because the ACGIH very clearly does not "classify" chemicals as reproductive toxins, even when it may assign a TLV that relates "in part" to a reproductive or developmental effect.

In that context, ACGIH established a TLV for DMAC of 10 parts per million ("ppm") in 1961. The TLV has been reviewed and its Documentation revised many times since then, but the TLV itself has remained unchanged. The intent of the TLV was, and remains, to protect humans from adverse effects in the liver that were associated with exposure to DMAC by the inhalation route. In reviewing the scientific literature on DMAC, the TLV Committee to which the chemical was assigned reviewed human data demonstrating this effect in humans at exposure concentrations of 20 ppm and greater, and animal data showing adverse effects in livers of dogs and rats at far greater concentrations. Some of the animal data demonstrated developmental effects in rats at exposures high enough to be "close to lethal" and to cause "maternal toxicity." Thus, the Committee included a phrase to its comments describing the TLV, indicating that the TLV also would protect against those "effects observed in studies in rats." Neither in assigning nor describing the TLV did ACGIH conclude that DMAC is a known developmental toxin, by any standard.

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<sup>11</sup> ACGIH, Documentation of the Threshold Limit Values and Biological Exposure Indices, 7<sup>th</sup> Edition (2001) (Policy Statement on the Uses of TLVs and BEIs.)

<sup>12</sup> *Id.*

This is clear from the “Documentation” for the TLV. “Documentation” is a term of art in the ACGIH TLV-setting process. Each TLV is established and described by a “Documentation,” which appears in a book published by the ACGIH, entitled *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 7<sup>th</sup> Edition (2001). In a “Special Note to User,” the preface explains that the TLVs listed in this book are “intended for use . . . as guideline or recommendations to assist in the control of potential workplace health hazards and for no other use. . . . *It is imperative that the user of this publication read the Introduction to each section and be familiar with the Documentation of the TLVs® . . . before applying the recommendations . . .*”<sup>13</sup>

In keeping with that admonition, we have summarized below the Documentation for the TLV for DMAC<sup>14</sup> and pertinent provisions of the ACGIH Operations Manual<sup>15</sup> that establish the procedure by which the ACGIH TLV Committee goes about establishing TLVs for chemical substances.<sup>16</sup>

According to the Operations Manual, “the primary purpose of the TLV® Documentation is to describe and analyze the scientific literature that specifically supports the derivation of a TLV® . . . .” The Documentation is to “describe the key literature studies that define the range of exposure information and animal and human health effects associated with a substance.”<sup>17</sup> “The text of each section should present the studies regarded as most relevant and reliable to derivation of the TLV® . . . .”<sup>18</sup>

The Operations Manual includes a template for preparing the Documentation which, among other things, lists the sections that should appear in the Documentation, under a series of enumerated headings. Those sections, headings and instructions for completing them that are pertinent to the issue of whether DMAC should be listed under Proposition 65 appear in the table below, which is extracted and quoted verbatim from a longer table in the Operations Manual.

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<sup>13</sup> Documentation of the Threshold Limit Values and Biological Exposure Indices, 7<sup>th</sup> Edition (2001).

<sup>14</sup> Attachment A.

<sup>15</sup> Attachment B.

<sup>16</sup> To be clear, we believe that the “Documentation” is incorporated by reference and must be included as part of the ACGIH materials that OEHHA must review in evaluating the TLV for DMAC, especially in light of the “Special Note to User” above, which makes it clear that the TLV has little meaning in the absence of the Documentation. *See also* ACGIH, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 7<sup>th</sup> Edition (2001) (Introduction to the Chemical Substances, Definition of the TLVs®) (“those who use the TLVs® **MUST** consult the latest Documentation to ensure that the understood the basis for the TLV® and the information used in its development.) Emphasis in original.

<sup>17</sup> Operations Manual at 29.

<sup>18</sup> *Id.* at 30.

“Section”	“Comments/Boilerplate”
<p><b>“TLV® Recommendation</b>            * * *</p> <p>This section should have a clear explanation about each of the following items: a description of the key health effects . . . and <i>the reasoning for the selection of a value.</i>”<sup>19</sup></p> <p>* * *</p>	
<p><b>“TLV® Basis</b>  <i>This section should briefly list the critical health effects that support the derivation of the TLV®. This description will be used to complete the “TLV® Basis-Critical Effects” column in the TLV®s and BEIs® book”</i><sup>20</sup></p>	
<p><b>“Human Studies</b>            Studies among occupationally exposed populations should be given priority for detailed description.”            * * *</p>	
<p><b>“Animal Studies:</b>  <b>Reproductive/Developmental Toxicity</b>            “This section should briefly describe adverse changes, presenting reproductive studies first, followed by developmental toxicity studies. The studies should also be organized by route of exposure with relevant routes of exposure, such as inhalation and skin, described first.”</p>	<p>“For most substances, this section does not drive the TLV® Basis, but may be used as modifier of the TLV® Recommendation.”</p>

<sup>19</sup> Emphasis added.

<sup>20</sup> Emphasis added.

“Section”	“Comments/Boilerplate”
<p><b>“TLV® Chronology</b>            The purpose of this section is to describe only the historical and/or pending/actionable activities (dates) associated with the TLV® Documentation.”</p>	

The Documentation for DMAC, consistent with these instructions, includes a description of all of the data and findings on which the TLV was based:

- Under the Section heading “**Summary**,” the document states that *the TLV is* “intended to minimize the *potential* for liver injury and jaundice and from reproductive or developmental effects reported in studies with rats.”
- There is no Section heading for “**Basis**.” Instead, the reader must consider the commentary in other Sections.
- Under the Section heading, “**Animal Studies**,” the Documentation indicates that ACGIH considered animal data in the following categories: acute toxicity, subchronic toxicity, and reproductive/developmental toxicity.
- Under the Section subheading “**Reproductive/Developmental Toxicity**” the “Comments” explain that “studies for embryotoxicity have shown fetal deaths in pregnant rats by intraperitoneal injection” *at “dosages close to lethal.”* Teratogenic effect were observed only at *levels where “[m]aternal toxicity* and increased post implantation loss *were also recorded.”*
- Under the Section heading “**Human Studies**,” the Documentation indicates that “*Jaundice has been observed to result in workers exposed repeatedly at from 20 ppm to 25 ppm,*” and that *workers exposed to DMAC “for 2-10 years show abnormal liver function.”*<sup>21</sup>

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<sup>21</sup> Jaundice, as OEHHA is aware, is a condition resulting from malfunctioning of the liver.

- Under the Section Heading “TLV Recommendation,” the Documentation states that a TLV of 10 ppm, “is recommended to reduce the *potential for injury to liver and fetus . . .*”

In other words, a TLV was set to limit exposure to workers to 10 ppm, because that would protect workers from harmful effects on the liver, which have been shown to arise when exposure reaches 20 ppm. While the document indicates that such a TLV would “reduce the potential for injury to the . . . fetus,” it is plain that *the only “injury” to the fetus that is contemplated would occur at “dosages close to lethal” or where “maternal toxicity [was] also recorded.”*

In summary, the ACGIH assigned a TLV for DMAC at 10 ppm. The Documentation is the authoritative reference for understanding why and how the TLV was set, and how it is to be applied. The Documentation was revised as recently as 1991, and republished more recently with a “Summary” in Seventh Edition. The Documentation does not show a “Basis” for the TLV. The comments under the heading “Summary” indicate that the TLV is *“intended to minimize the potential for liver injury and jaundice and from reproductive or developmental effects reported in studies with rats.”* Instructions associated with the sub-heading “Reproductive/Developmental Toxicity” in the documentation template in the Operations Manual indicate that the “driver” for the TLV was to protect humans from adverse effects on the liver, which were shown to occur at exposure in concentrations of 20 ppm or greater, and that concerns regarding “developmental effects reported in studies with rats” were not the driver. Rather, a TLV at this level also would protect against any adverse effects observed at exposures greater than 10 ppm, including “developmental effects reported in rats” which had been shown to occur at exposure levels that were “lethal” and resulted in “maternal toxicity.”<sup>22</sup> Comments under the heading “Recommendation,” explaining the reasoning for the selection of the value, confirm this. Therefore, while the Documentation notes the maternal and fetal effects that were observed in rats at “close to lethal” doses, the documentation is not a finding that DMAC is known to be a reproductive toxin, or that the chemical is “known” to cause reproductive or developmental effects.

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<sup>22</sup> Other comments in the Documentation, not quoted above, confirm this. Other effects in animal studies included acute toxicity (lethality) in pregnant rats at rabbits at 7.5 and 5.0 g/kg body weight, respectively; fatty infiltration of livers in dogs at 4 mg/kg body weight, and liver hypertrophy and nasal irritation in rats at 288 ppm, necrosis of the liver in rats at 195 ppm; effect observed in humans and animals, and on industrial experience. Because all of these effects occur at concentrations above those which cause liver toxicity, and since the TLV<sup>®</sup> value was established to prevent liver toxicity in exposed workers, this value is also protective of all the other effects that occur at the higher levels of exposure. See Documentation (Attachment A).

## OBJECTIONS TO LISTING

*The “Labor Code” Listing Mechanism Is Invalid.* OEHHA has requested comments whether DMAC should be listed as a chemical “known to the state to cause . . . reproductive toxicity” under Proposition 65, pursuant to the so-called “Labor Code listing mechanism.” This asserted mechanism for listing chemicals under the Act is the subject of substantial ongoing controversy. Without belaboring the point, the background for that controversy is critical to determining whether the law requires or allows DMAC to be listed, and thus is summarized below.

OEHHA asserts that Health & Safety Code section 25249.8(a) imposes a “ministerial” duty on the agency to add substances to the Proposition 65 list of those chemicals “identified by reference in Labor Code section 6382(b)(1) and those substances identified additionally by reference in Labor Code Section 6382(d).” Numerous parties, including the California Chamber of Commerce (“Chamber”) in litigation described below, contend that Section 25249.8(a) established the requirement to publish the list (and re-publish it annually), and that the inclusion of chemicals identified by reference to the Labor Code was merely a shortcut to be used for populating the “initial list” of chemicals quickly and efficiently by March 1, 1987, the deadline for its first publication.

In the Chamber’s view, the methods for adding chemicals to the list are established implicitly by the three statutory criteria for determining when a chemical is “known to the state to cause cancer or reproductive toxicity,” recited above, which appear at Section 25249.8(b). That provision, again, defines a chemical as “known to the state to cause cancer or reproductive toxicity” only where: (1) “in the opinion of the state’s experts it has been clearly shown through scientifically valid testing according to generally accepted principles to cause cancer or reproductive toxicity,” or (2) “a body considered to be authoritative by such experts has formally identified it as causing cancer or reproductive toxicity,” or (3) an “agency of the state or federal government has formally required it to be labeled or identified as causing cancer or reproductive toxicity.”

The disputed interpretation of Section 25249.8 is the subject of litigation in *Sierra Club v. Schwarzenegger* (Alameda County Superior Court, Case No. RG07356881), consolidated with *California Chamber of Commerce v. Schwarzenegger* (San Diego County Superior Ct. Case No. 37-2008-00096549-CU-WM-CTL) (the “Labor Code Action”). On April 24, 2009, the Alameda County Superior Court entered an order finding that Health & Safety Code section 25249.8(a) imposed on OEHHA a ministerial duty to include, in the Proposition 65 chemical list, those substances identified by Labor Code sections 6382(b)(1) and (d). The court entered judgment in favor of the State on June 11, 2009, after acknowledging many times in open court that the issue would be resolved on appeal. The California Chamber of Commerce filed a Notice of Appeal on June 12, 2009, and is actively pursuing that appeal at this time.

Because the Superior Court's order remains the subject of a pending appeal, DuPont does not concede that the Labor Code listing mechanism is lawful, or that a chemical may be listed as "known to the State to cause cancer or reproductive toxicity" if it does not meet one of the criteria by which that term is defined in Section 25249.8(b). DuPont thus incorporates by reference herein all of the arguments made in the Chamber's submissions in the Labor Code Action, and reserves its rights to pursue these and other arguments opposing the legal basis of the asserted Labor Code listing mechanism.

***DMAC Does Not Meet the Standard for Listing Under the Labor Code Mechanism.***  
We understand that OEHHA is taking this action to list DMAC in the belief that it must do so to comply with the ruling of the Alameda Superior Court referred to above. In granting OEHHA's Motion for Judgment on the Pleadings and denying a similar motion by the Chamber of Commerce, the Court ruled that

"[Section 25249.8 requires that the substances identified by reference in Labor Code sections 6382(b)(1) and 6382(d) be included on the list of chemicals known to the state to cause cancer or reproductive toxicity . . . . Thus, the statute imposes a clear ministerial duty on Respondents to list the carcinogens and reproductive toxins identified by reference in the above Labor Code sections without further review."<sup>23</sup>

Addressing the issue of whether chemicals for which the ACGIH had assigned TLVs were included within the scope of Section 25249.8, the Court ruled that the

"[Chamber's] argument that the ACGIH chemicals are not "substances identified . . . by reference in Labor Code section 6382(d) . . . is not well taken. Labor Code section 6382(d) clearly identifies "any substance within the scope of the federal Hazard Communications Standard, 29 C.F.R. § 1910.1200(d)(3)." Any ambiguity created by the fact that the [federal Hazard Communication Standard] lists substances other than carcinogens and reproductive toxins was addressed by the court in *AFL-CIO v. Deukmajian* [citation omitted] [. . . the initial list, and subsequent lists published thereafter, need not include all substances listed under the [federal Hazard Communication Standard] but ***only known carcinogens and reproductive toxins*** listed there]."<sup>24</sup>

This is the Order with which OEHHA is attempting to comply.

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<sup>23</sup> *Sierra Club v. Schwarzenegger*, No. RG07356881, Superior Court for Alameda, Minute Order, May 27, 2009.

<sup>24</sup> *Id.* (emphasis added).

The action at issue here was initiated in the Request for Comments, posted on the OEHHA website on June 12, 2009, and appears to flow from the Court's ruling. Thus, the Request for Comment recites that Section 25249.8(a) of Proposition 65

“requires that *certain* substances identified as causing reproductive toxicity in 29 CFR part 1910, Subpart Z, Toxic and Hazardous Substances, Occupational Safety and Health Administration or in the Threshold Limit Values for Chemical Agents in the Work Environment, American Conference of Governmental Industrial Hygienists [ACGIH] (latest edition be listed as known to cause reproductive toxicity under Proposition 65. *As the lead agency for the implementation of Proposition 65, the OEHHA evaluates whether listing under Proposition 65 is required.*” (emphasis added).

In the following paragraph, under the heading “OEHHA’s determination,” the Request for Comments states that

“In the case of [all of the chemicals identified on the notice (except one chemical not pertinent here)] the ACGIH Threshold Limit Value was established solely or in part on a relevant reproductive or developmental effect.”

Finally, under the heading “Request for comments,” OEHHA solicits

“comments as to whether the chemicals identified [in the Request for Comments (including DMAC)] meet the requirements for listing as causing reproductive toxicity, as specified in Section 25249.8(a). *Because these are ministerial listings, comments should be limited to the question whether the ACGIH has established a TLV for the chemical . . . that is based in whole or in part on a reproductive or developmental effect . . . .*”

(emphasis in original).<sup>25</sup>

Because this is the agency’s only public statement of any basis for proposal to list DMAC, we assume that this is the extent of OEHHA’s rationale. If so, then this misstates the requirements imposed under Section 25249.8(a) and the cross-referenced provisions of the Labor Code, including the federal Hazard Communication Standard, even as the Superior Court interprets them.

Under the Superior Court’s ruling, OEHHA’s duty is to identify “known carcinogens and reproductive toxins listed” under the federal Hazard Communication Standard. This is not the same as determining whether a TLV is “based in whole or in part on a reproductive or toxic effect,” and limiting the inquiry to that determination would not satisfy OEHHA’s duty. As

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<sup>25</sup> Request for Comments (Attachment B).

discussed above, notations in the TLV Handbook and the Documentation for the TLV for DMAC do not indicate that this chemical is a “known reproductive toxin.” Rather, they identify, by their own terms, a series of potential effects that the TLV is intended to protect against, including developmental effects that were observed in rats at exposure levels “close to lethal” and that cause “maternal toxicity,” regardless of whether DMAC is a known reproductive toxin.

Thus, and for reasons discussed below, the ultimate question that must be answered before DMAC could be listed under this mechanism is whether the ACGIH record shows the chemical to be a “known reproductive toxin.” The starting point is Section 25249.8(a) itself. In describing the list of chemicals “known to the state to cause cancer or reproductive toxicity,” that provision states that

“[s]uch list shall include at a minimum those substance identified by reference in Labor Code Section 6382(b)(1) and those substances identified additionally by reference in Labor Code Section 6382(d).”

Cal. Health & Safety Code § 25249.8(a).

Putting aside the pending dispute (whether this provision refers to a process for populating the “initial list” or a means for adding chemicals to the initial list, as discussed above) the pertinent inquiry is to determine what chemicals are “identified by reference” in those provisions of the Labor Code. Because the scope of Section 6382(b)(1) is limited to carcinogenicity, and DMAC is proposed for listing as a reproductive toxicant, the analysis is limited to the meaning of Section 6382(d). That provision, in pertinent part, refers to:

“any substance within the scope of the federal Hazard Communication Standard (29 C.F.R. Sec. 1910(1200) . . . .”

Cal. Labor Code § 6382(d).

As OEHHA would agree, there is no readily identifiable list of substances that are “within the scope” of the Hazard Communication Standard. Rather, it is necessary to refer to certain provisions and definitions in the Standard that describe its scope and the chemicals to which the Standard applies.

Section 1910.1200(b) of the Standard, entitled “Scope and application” indicates in general terms that the Standard applies to chemicals that are used in the workplace, and excludes various chemicals on the basis of certain uses, *e.g.*, as pesticides that are subject to regulation under the Federal Insecticide, Fungicide and Rodenticide Act, food additives, drugs or cosmetics that are regulated under the Federal Food, Drug and Cosmetic Act, etc. The provision further makes clear that the various requirements under the Standard apply to chemicals that are “hazardous.”

This leads to the provision that is the asserted basis of listing DMAC, and is reproduced in full below:

“The chemical manufacturer, importer or employer evaluating chemicals shall ***treat the following sources as establishing that the chemicals listed in them are hazardous:***

(i) 29 CFR Part 1910, subpart Z, Toxic and Hazardous Substances, Occupational Safety and Health Administration (OSHA): or,

(ii) ***Threshold Limit Values for Chemical Substances*** and Physical Agents in the Work Environment, American Conference of Governmental Industrial Hygienists (ACGIH) (latest edition) . . .”

29 C.F.R. § 1910.1200(c)(3).

This provision of the Standard thus indicates that any chemical for which the ACGIH has assigned a TLV is to be considered “hazardous” and, returning to Section 6383(d) of the California Labor Code, thus comes “within the scope of the federal Hazard Communication Standard.”

This analysis takes us back to Section 25249.8(a) of Proposition 65. If that provision were to be interpreted literally, then any chemical for which ACGIH has assigned a TLV is “identified by reference in Labor Code Section 6382(d)” and must be included in the “list” of “chemicals known to the state to cause cancer or reproductive toxicity.”

OEHHA does not interpret Section 25249.8(a) literally, however. Nor should it, because the definition of “hazardous chemical” under the federal Hazard Communication Standard includes hazards whose scope is more broad than just cancer or reproductive toxicity. Rather the definition includes chemicals that pose “physical hazards” such as explosivity, flammability, and combustibility, and “health hazards,” which embrace, *e.g.*, chemicals that are acutely toxic, irritants, corrosives, and which damage the lungs, skin, eyes and other organs. *See* 29 C.F.R. § 1910.1200(c)(3). Similarly, ACGIH assigns TLVs to address hazards such as acute toxicity, organ damage, and sensitization, in addition to cancer and reproductive toxicity, as well as ***potential*** hazards of the same varieties.

Therefore, it would be clearly inappropriate to include every chemical that comes “within the scope of the federal Hazard Communication Standard” (including every chemical for which ACGIH has assigned a TLV) on the Proposition 65 list of “chemicals known to the State to cause cancer or reproductive toxicity.” Rather, it is incumbent upon OEHHA to parse these secondary sources, and choose from among these collateral groups any chemicals that are known to “cause cancer or reproductive toxicity” within the meaning of Proposition 65.

This duty results from, in the words of the Superior Court, the “ambiguity created by the fact that the [federal Hazard Communication Standard] lists substances other than carcinogens and reproductive toxins,” which was resolved previously by the Court of Appeal in *AFL-CIO v. Deukmajian*, 212 Cal. App. 3d 425 (1989). Because the resolution of that issue is critical in defining OEHHA’s mandate here, it is appropriate to recite in full the question that was raised in that case, and the Court’s full response.

In *AFL-CIO v. Deukmajian*, the Health & Welfare Agency (OEHHA’s predecessor agency) was defending its judgment that animal carcinogens were not included among the chemicals “known to cause cancer” that the Governor was required to place on the “initial list.” The State argued that

“a literal construction of Section [25249.8(a)] would] lead to absurd results, requiring the listing of substances not known to cause cancer [because *the Hazard Communication Standard*] referred to in Labor Code Section 6382 includes *thousands of substances that are not carcinogens or reproductive toxins*. A literal construction of the statute, [the State argued], would require the initial list to include these substances . . . .”

The Court of Appeal responded:

“It is true that ‘any substance within the scope of the federal [Hazard Communication Standard] includes chemicals other than known carcinogens. Section [25249.8(a)] and the Act itself, however, are concerned only with those substances that authoritative bodies have concluded are known to cause cancer or reproductive toxicity. *Thus, the initial list, and subsequent lists published thereafter, need not include all substances listed under [the federal Hazard Communication Standard] but only known carcinogens and reproductive toxins* listed there.”

212 Cal. App. 3d at 437, 438 (emphasis added).

Obviously, the same logic applies here. If the Labor Code listing mechanism is valid, it is OEHHA’s duty to list not all substances for which ACGIH has assigned a TLV, but only those chemicals “*but only known . . . reproductive toxins*” for which TLVs have been issued.

With this background, it is appropriate to re-examine the Request for Comments. In the first paragraph recited above, and now repeated here, OEHHA recites that Section 25249.8(a):

“requires that *certain* substances identified as causing reproductive toxicity in 29 CFR part 1910, Subpart Z, Toxic and Hazardous Substances, Occupational Safety and Health Administration or in the Threshold Limit Values for Chemical Agents in the Work Environment, American Conference of Governmental Industrial Hygienists [ACGIH] (latest edition be listed as known to cause reproductive

toxicity under Proposition 65. *As the lead agency for the implementation of Proposition 65, the OEHHA evaluates whether listing under Proposition 65 is required.*"

We agree with this observation that "certain" substances for which ACGIH has issued TLVs must be listed, and that it is the responsibility of OEHHA to "evaluate" whether listing is required. In the next paragraph, however, OEHHA states that

"In the case of [all of the chemicals identified on the notice (except one chemical not pertinent here)] *the ACGIH Threshold Limit Value was established solely or in part on a relevant reproductive or developmental effect.*"

We disagree that OEHHA's duty in evaluating whether listing is required is limited to identifying whether a TLV "*was established solely or in part on a relevant reproductive or developmental effect.*" Rather, in the words of Proposition 65, it is OEHHA's duty to select from among the chemicals for which ACGIH has assigned TLVs those that are "known to the state to cause . . . reproductive toxicity." Or, in the words of the Court, it is OEHHA's duty to review the TLV chemicals and identify "*known . . . reproductive toxins listed there.*" If OEHHA identifies any such chemicals, then it has a "ministerial" duty to list them, without further procedures or delay.<sup>26</sup>

*The TLV for DMAC Does Not Establish that the Chemical is "Known" to Cause Reproductive Toxicity.* As discussed above, the TLV for DMAC does not represent a finding that DMAC is a known reproductive toxicant. That is clear on the face of the Documentation. First, the Documentation does not include such a statement by ACGIH. Nor does the Documentation refer to any findings by other bodies that DMAC is a reproductive or developmental toxicant. Finally, the Documentation does not make any statement that would support such a finding. Rather, the text under the heading "Reproductive/Developmental" toxicity, summarizing the studies that explain how the TLV was "derived," supports the opposite conclusion, *i.e.*, that DMAC is not "known to cause reproductive toxicity," as OEHHA employs that term.

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<sup>26</sup> In narrowing the scope of its Request for Comments, OEHHA characterized its proposed listings as "ministerial." The Superior Court also used that term, holding that Section 25249.8(a) imposes "a clear ministerial duty on Respondents to list the carcinogens and reproductive toxins identified by reference in the above Labor Code sections without further review." Given the brevity of the Request for Comments, it is not clear what duties OEHHA believes to be ministerial, but we assume that the agency interprets the duty consistently with the Superior Court. If so, then the "ministerial" portion of this listing process is to place "known carcinogens and reproductive toxins" on the list, after they have been identified, without further processes to inquire as to the quality of the underlying scientific data as other listing mechanisms, *e.g.*, "the authoritative bodies" mechanism would allow. This would not imply that OEHHA is prohibited from exercising sound scientific judgment in reviewing TLVs, including the Documentations that explain their meaning and, in this case, from evaluating whether ACGIH concluded that DMAC is a "known reproductive toxin."

It is not necessary to examine the underlying scientific data, or the “weight and quality of the evidence,” to reach this conclusion. Although we do not accept OEHHA’s position that it “cannot consider scientific arguments concerning” the data that would or would not support listing, we note that we are not questioning the data to support listing here. Indeed, ***no party is contending that the data support listing.*** Rather, the proposal to list DMAC implies that the TLV alone supports listing. In response, we insist that neither the TLV nor the rationale explaining how the TLV was derived would support a conclusion that DMAC is “known to cause reproductive toxicity.” To the contrary, the concern that ACGIH intended to address in assigning the TLV, in its own words, were developmental effects that were observed at “***dosages close to lethal***” and where “***maternal toxicity*** and increased post implantation loss were also recorded.”

By its own standards, set forth in the Proposition 65 regulations and the Criteria set by the State’s Scientific Advisory Board, this would not amount to a conclusion that a chemical is “known to the state to cause reproductive toxicity.” In reviewing findings by “authoritative bodies” under Section 25249.8(b), OEHHA would have to conclude that ***studies showing developmental effects at “dosages close to lethal” are not sufficient*** to designate a chemical “as causing reproductive toxicity.” The same regulations require the state’s Developmental and Reproductive Toxicant Identification Committee (“DART IC”) to consider “***maternal toxicity***” in evaluating data.<sup>27</sup> And the DART IC’s articulation of these criteria require the Committee to take into account “***maternal and systemic toxicity.***”<sup>28</sup>

## CONCLUSION

For all of the reasons above, DMAC should not be listed. In short, DMAC does not satisfy any of the three statutory criteria that would render the chemical “clearly shown to cause . . . reproductive toxicity” established at Section 25249.8(b), which define that term. The asserted “Labor Code listing mechanism” recited as the basis for listing DMAC under Section 25249.8(a) is not valid, because that “mechanism” for listing chemicals was restricted to populating the “initial list.”

OEHHA’s notice indicates that chemicals should be listed under this mechanism when substances have been “*identified as causing reproductive toxicity in . . . in the Threshold Limit Values for Chemical Agents in the Work Environment, American Conference of Governmental Industrial Hygienists.*” This is incorrect. Even assuming that this listing mechanism is valid, there is no basis for interpreting the statutory phrase “hazardous,” as it appears in the federal Hazard Communication Standard, to include on the Proposition 65 list every chemical for which

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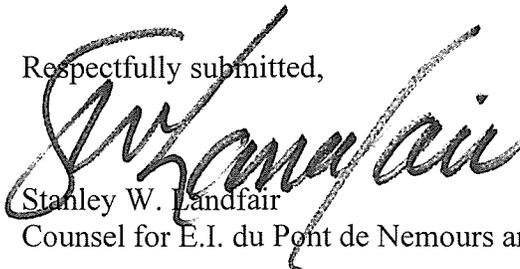
<sup>27</sup> See Cal. Code Regs., *tit.* 27, § 25306(g),(h).

<sup>28</sup> Criteria for Recommending Chemicals for Listing as “Known to the State to Cause Reproductive Toxicity,” DART IC (1993) at 4.

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Office of Environmental Health Hazard Assessment  
July 13, 2009  
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a TLV has been set. Rather, a chemical should not be included on the Proposition 65 list unless its TLV is consistent with a finding by the ACGIH that the chemical is a known reproductive toxin. Thus, although the ACGIH assigned a TLV for DMAC, a plain reading of the Documentation does not support the conclusion that the chemical is a reproductive toxin, and certainly does not indicate that the ACGIH identified the chemical as a known reproductive toxin. Rather it shows that ACGIH observed reproductive and developmental effects in experimental animals at levels that were “lethal” or caused “maternal toxicity.” By any standard, but most importantly OEHHA’s standards in implementing Proposition 65, that is not a statement that DMAC is “known to the state to cause . . . reproductive toxicity.”

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'Stanley W. Landfair', is written over the typed name and title.

Stanley W. Landfair

Counsel for E.I. du Pont de Nemours and Company

cc: Joan Denton, Ph.D., Director, OEHHA  
George Alexeeff, Ph.D., Deputy Director, OEHHA  
Carol Monahan-Cummings, Chief Counsel, OEHHA

# **ATTACHMENT A**

# N,N-DIMETHYL ACETAMIDE

CAS number: 127-19-5

*Synonyms:* Acetic acid dimethylamide; Acetyl dimethylamide; Dimethyl acetamide; DMA; DMAC

Molecular formula: C<sub>4</sub>H<sub>9</sub>NO

Structural formula: CH<sub>3</sub>CON(CH<sub>3</sub>)<sub>2</sub>

## Skin

**TLV–TWA, 10 ppm (36 mg/m<sup>3</sup>)**

**A4 — Not Classifiable as a Human Carcinogen**

## Summary

A TLV–TWA of 10 ppm (36 mg/m<sup>3</sup>) is recommended for occupational exposure to N,N-dimethyl acetamide (DMA) via the airborne route. This value is intended to minimize the potential for liver injury and jaundice and from reproductive or developmental effects reported in studies with rats. Because dermal exposure contributes significantly to the overall toxicity of this compound, the airborne TLV–TWA is dependent on the prevention of skin contact with liquid DMA. A Skin notation is assigned, based on the significance of the dermal route of exposure and the reported systemic effects in animals and workers so exposed. In view of the lack of published data among workers exposed to DMA, an A4, Not Classifiable as a Human Carcinogen, notation is recommended.

Sufficient data were not available to recommend a SEN notation or a TLV–STEL. DMA is a substance for which Biological Exposure Indices (BEIs) have been recommended (see *BEI Documentation for N,N-Dimethyl Acetamide*).

## Chemical and Physical Properties

DMA is a colorless liquid with a faint ammonia-like odor. An odor threshold of 47 ppm has been reported.<sup>(1)</sup> Chemical and physical properties include:<sup>(2)</sup>

- Molecular weight: 87.12
- Specific gravity: 0.94 at 20°C
- Melting point: –20°C
- Boiling point: 166°C at 760 torr
- Vapor pressure: 1.5 torr at 20°C
- Flash point: 70°C, open cup
- Explosive limits: lower, 1.8%; upper, 11.5% by volume in air
- Solubility: miscible with water, aromatic compounds, esters, ketones, and ethers

Conversion factors at 25°C and 760 torr:

1 ppm = 3.56 mg/m<sup>3</sup>; 1 mg/m<sup>3</sup> = 0.281 ppm

## Major Uses

DMA is used as a solvent for many organic reactions, resins, polymers, crystallization, and purification.

## Animal Studies

### Acute

Undiluted DMA applied to the rabbit eye was given a score of three, according to the Smyth et al. rating scheme<sup>(3)</sup> which connotes a small area of corneal necrosis. Skin irritation was rated a two, connoting the least visible capillary injection of the epidermis. The lethal dose for skin absorption of DMA by pregnant rats and rabbits was approximately 7.5 and 5.0 g/kg body weight, respectively.<sup>(4)</sup>

### Subchronic

Repeated, dermal applications to dogs of DMA at 4 mg/kg body weight for 6 weeks produced extensive fatty infiltration of liver tissue.<sup>(5)</sup>

Rats exposed 6 hours/day for 2 weeks at 288 ppm DMA had nasal irritation and liver hypertrophy.<sup>(5)</sup>

Daily exposure of rats at 195 ppm DMA for 6 months produced focal necrosis of the liver.<sup>(6)</sup> No liver damage resulted in dogs and rats exposed to DMA 6 hours/day, 5 days/week for 6 months at 40 ppm.<sup>(6)</sup>

### Reproductive/Developmental

Studies for embryotoxicity have shown fetal deaths in pregnant rats by intraperitoneal injection of DMA at dosages close to lethal (2 g/kg body weight)<sup>(7)</sup> or when applied to the skin.

Teratogenic effects from dermal application of DMA were reported in rats when DMA was applied on gestation days 10 and 11 at a total dose of 2400 mg/kg body weight.<sup>(4)</sup> When DMA was administered to rats by gavage at a dosage of 400 mg/kg/day on days 6 through 19 of gestation, malformations of the heart, major blood vessels, and oral cavity were reported. Maternal toxicity and increased postimplantation loss were also recorded at this dosage.<sup>(8)</sup>

### Human Studies

In practice, the dermal factor is so significant that no air concentration, however low, will provide protection if skin contact with DMA (liquid) is permitted. Jaundice was observed in workers as a result of repeated exposures at 20 to 25 ppm DMA, but appreciable skin penetration undoubtedly contributed to this effect.<sup>(9)</sup>

Workers exposed to DMA for 2 to 10 years showed abnormal liver function; exposure concentrations were not reported in the study.<sup>(10)</sup> DMA concentrations between 0 and 2 ppm, with occasional excursions between 11 and 34 ppm, in a polymer manufacturing operation caused dizziness, lethargy, and weakness.<sup>(11)</sup> Concentrations between 0 and 3 ppm in metal finishing caused the same symptoms.<sup>(11)</sup>

### TLV Recommendation

Based on the animal studies, coupled with industrial experience, a TLV-TWA of 10 ppm DMA, with a Skin notation, is recommended to reduce the potential for injury to the liver and fetus, provided skin contact is prevented.<sup>(5-10)</sup> In view of the lack of published data among workers exposed to DMA, an A4, Not Classifiable as a Human Carcinogen, notation is recommended.

Sufficient data were not available to recommend a SEN notation or a TLV-STEL. The reader is expected to be familiar with the section on *Excursion Limits* in the "Introduction to the Chemical Substance TLVs" found in the current edition of the *Documentation of the TLVs and BEIs* for the guidance and control of excursions above the

TLV-TWA, even when the 8-hour TWA is within the recommended limit.

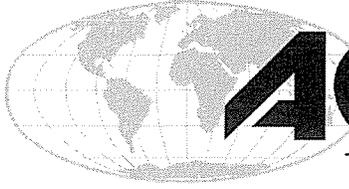
DMA is a substance for which Biological Exposure Indices (BEIs) have been recommended (see *BEI Documentation* for N,N-Dimethyl Acetamide).

### Historical TLVs

1961: *Proposed*: TLV-TWA, 10 ppm  
1962: *Proposed*: Skin  
1963-present: TLV-TWA, 10 ppm; Skin  
1976-1985: TLV-STEL, 15 ppm  
1984: *Proposed*: Withdraw TLV-STEL  
1986: TLV-STEL withdrawn

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*Defining the Science of Occupational and Environmental Health*<sup>®</sup>

**OPERATIONS MANUAL**

**THRESHOLD LIMIT VALUES FOR CHEMICAL  
SUBSTANCES COMMITTEE**

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## COMMITTEE MISSION

The Threshold Limit Value Chemical Substances (TLV<sup>®</sup>-CS) Committee is appointed by the Board of Directors of ACGIH<sup>®</sup> to develop occupational exposure guidelines for chemical substances. The issuance of Threshold Limit Values (TLVs<sup>®</sup>) and their supporting *Documentation* is the principal mechanism for the dissemination of these guidelines, although the Committee may also develop more general positions, instructional materials, educational media, or topical symposia to focus on issues of concern. This Committee's vision is to be a respected, worldwide leader in the development and dissemination of health-based occupational exposure guidelines.

Specifically, the mission of the TLV<sup>®</sup>-CS Committee is to recommend airborne concentrations of agents and exposure conditions for use in the practice of industrial hygiene and by other qualified professionals to protect worker health. The charge of the TLV<sup>®</sup>-CS Committee is to develop and disseminate occupational exposure guidelines (i.e., TLVs<sup>®</sup>). TLVs<sup>®</sup> are based on the best available data and, whenever possible, peer-reviewed literature on human health effects resulting from industrial, occupational or other exposure situations; from experimental human and animal studies; human epidemiological studies; and when possible, from a combination of all these sources. The goal of the Committee is to develop occupational exposure guidelines for chemical substances that are:

- Scientifically credible
- Leading edge
- Well-supported (i.e., TLVs<sup>®</sup> are based on ACGIH<sup>®</sup>'s review of "peer-reviewed scientific literature")
- Scientifically valid
- Reliable
- Understandable and clear
- Produced with a balanced, unbiased and clearly-defined process

The TLV<sup>®</sup>-CS Committee operates under the Bylaws of ACGIH<sup>®</sup> and the administrative policies and procedures approved by the ACGIH<sup>®</sup> Board of Directors.

## **MEMBERSHIP**

### ***Eligibility***

Members of the TLV<sup>®</sup>-CS Committee must be members of ACGIH<sup>®</sup> or must join ACGIH<sup>®</sup> upon appointment as a Full Committee member. The Committee may have up to 30 members who should represent the four disciplines necessary to establishing TLVs<sup>®</sup> (industrial hygiene, occupational medicine, occupational epidemiology, and toxicology). The Committee will function within the guidelines and policies of the Board of Directors regarding the percentage of membership categories. Under current ACGIH<sup>®</sup> policy, a committee must maintain a simple majority of Regular members. The Committee may utilize consultants, as necessary, for additional specialized or temporary expertise. Consultants do not have voting privileges and attend meetings at the invitation of the Chair.

### ***Member Selection***

Individuals interested in joining the TLV<sup>®</sup>-CS Committee will be asked to complete a basic Application Form and provide a resumé or curriculum vitae. The Membership Subcommittee will review the application and determine whether the applicant is eligible and has qualifications that fit the needs of the Committee. This process is described in detail in the Membership Subcommittee section.

The following criteria will be used to evaluate an applicant for membership:

- Disciplinary training and education
- Professional background
- Past relevant experience
- Personal characteristics

The following criteria will be used to assess the overall membership of the Committee and whether a particular applicant fits with the Committee's activities:

- The Committee should have a mix and balance of persons who have expertise in one or more of the following: industrial hygiene, occupational medicine, epidemiology, toxicology or other related specialties (e.g., statistics, chemistry, etc.)
- Preference will be given to individuals with 10 or more years of professional experience and with advanced degrees in their field of expertise
- Individuals should demonstrate competence in writing and communication through publications, presentations or other activities
- The Membership should reflect the diversity of the industrial hygiene and occupational health field
- Preference will be given to individuals with multi-disciplinary backgrounds and experience or strength in a particular field

## ***Member Responsibilities and Expectations***

Each Member of the TLV<sup>®</sup>-CS Committee, with the exception of the Chair, will be affiliated with one of the TLV<sup>®</sup>-CS Subcommittees. TLV<sup>®</sup>-CS Committee Members are expected to prepare and review *Documentation* for TLV<sup>®</sup>-CS substances. The expected number of TLV<sup>®</sup> *Documentation* prepared and reviewed annually may vary for individual members, depending on other activities they undertake that serve the TLV<sup>®</sup>-CS Committee's priorities. In addition to TLV<sup>®</sup>-CS Subcommittee activities, each member of the Committee is encouraged to participate on at least one TLV<sup>®</sup>-CS Administrative Subcommittee, excluding the Steering Subcommittee. Individual members will arrange their activities with their respective Subcommittee Chairs, with review by the TLV<sup>®</sup>-CS Committee Chair.

TLV<sup>®</sup>-CS Committee Members are expected to contribute to the work of the Committee. This includes time spent attending up to three face-to-face meetings each year, preparing and reviewing TLV<sup>®</sup> *Documentation*, and participating in Administrative Subcommittee activities. More senior members are expected to provide guidance and to mentor new members.

Members are expected to comply with all Policies and Procedures of ACGIH<sup>®</sup>. Members are expected to interact at all times in a collegial fashion with other members of the TLV<sup>®</sup>-CS Committee and Staff.

Participation on the Committee is a privilege that must be continually earned, through on-going productivity, participation and collegial behavior. When considering re-appointment, the Chair will review a member's participation in light of membership expectations and length of tenure on the Committee. As members serve additional terms they are expected to take on a greater role in the Committee, which may include preparing additional *Documentation*, chairing a TLV<sup>®</sup>-CS or Administrative Subcommittee, and other activities as needed.

It is essential that Committee Members regularly attend Committee meetings, participate in all scheduled conference calls, and prepare and review *Documentation*.

## ***Member Candidates***

The TLV<sup>®</sup>-CS Committee may choose to invite potential members to participate in Committee activities as "Member Candidates" before recommending them for formal appointment to the Committee. This practice allows the potential member to understand the role of Committee members, and allows the Committee to evaluate the potential member. The Board of Directors must approve Committee Member Candidates. Member Candidates must follow all ACGIH<sup>®</sup> policies and procedures.

## ***Consultants***

When the TLV<sup>®</sup>-CS Committee needs specific technical expertise that is not available within the Committee, the Committee may request appointment of a Consultant.

Consultants should only be used when specific technical expertise is needed for a limited period of time. Consultants must be appointed by the Board of Directors. Consultants are not required to be members of ACGIH<sup>®</sup>, but must follow all ACGIH<sup>®</sup> policies and procedures.

### ***Emeritus Members***

Emeritus members are former, long-serving (20 years or more) members who are retired, but continue to contribute to the TLV<sup>®</sup>-CS Committee, although not as voting members. To remain as an Emeritus member, the former member must have contributed in some substantial manner, such as a written contribution or review of a draft TLV<sup>®</sup> *Documentation*, during the year. Emeritus Members are not required to be members of ACGIH<sup>®</sup>, but must follow all ACGIH<sup>®</sup> policies and procedures.

### ***Conflict of Interest***

The TLV<sup>®</sup>-CS Committee Members, Emeritus Members, Member Candidates and Consultants, hereafter referred to in this section as “Members”, are required to follow the ACGIH<sup>®</sup> Policy and Process on Bias and Potential Conflicts of Interest (COI), published on the website at [www.acgih.org](http://www.acgih.org). Any “Member” with a potential, real, or perceived conflict of interest with respect to a chemical substance or issue under consideration by the TLV<sup>®</sup>-CS Committee must orally disclose the conflict of interest to the full TLV<sup>®</sup>-CS Committee. In addition, a written declaration must be completed at the same time. It is essential that potential, real, or perceived conflicts of interest be identified before the TLV<sup>®</sup> process begins. Likewise, it is important that “Members” recognize and identify their particular technical or scientific biases, so that these differing perspectives can be balanced during Committee deliberations. Selected information of particular relevance to the TLV<sup>®</sup>-CS Committee and its conflict of interest process are described below.

All “Members” must complete an annual oral and written COI declaration at a full TLV<sup>®</sup>-CS Committee meeting that includes information about their sources of funding, including professional services and consultancies, professional affiliations, service on boards or committees, legal testimonies, and other activities that may represent a potential conflict of interest for participation in the affairs of the Committee. In addition, the individual should disclose their publications history and identify any technical biases. As part of this annual declaration process, the TLV<sup>®</sup>-CS Committee Chair will conduct a presentation and discussion of conflict of interest. This presentation will include a variety of scenarios and possible methods for resolving conflicts while maintaining participation. This declaration is required annually and when material changes in their status occur. Typically at the beginning of a TLV<sup>®</sup>-CS Subcommittee meeting the Subcommittee Chair will inquire about material changes in each member’s COI and bias status.

- Bias is defined as “views stated or positions taken that are largely intellectually motivated or that arise from close identification or association of an individual with a particular point of view or the position or perspectives of a particular group.” Conflict of interest means “any financial or other interest which conflicts with the service of an individual because it (1) could impair the individual’s

objectivity or (2) could create an unfair competitive advantage for any person or organization.”

- In the case of bias, the TLV<sup>®</sup>-CS Committee attempts to create a balance of opinions and views by maintaining a diversity of professional affiliations, disciplines and activities among its membership.
- In the case of conflict of interest, the TLV<sup>®</sup>-CS Committee has created a number of avenues for minimizing or eliminating the potential effects of conflict of interest while allowing a “Member” to participate as fully as possible in Committee activities. The Committee believes that it is the primary responsibility of the individual to identify his/her potential conflicts and to consider carefully the level of participation that is appropriate.
- Within a Subcommittee meeting, each TLV<sup>®</sup>-CS Subcommittee Chair will begin the review of new substances with a request for notification of conflict of interest from the “Members” present. In addition, any “Member” who develops a new conflict of interest for an ongoing chemical *Documentation* is required to notify the other members of the Subcommittee.

It may not always be in the best interests of the TLV<sup>®</sup>-CS Committee for a “Member” who has significant conflicts of interest to remove himself/herself entirely from the development of a TLV<sup>®</sup> because they may be very knowledgeable about that particular substance. In these cases, the TLV<sup>®</sup>-CS Subcommittee Chairs should work directly with the “Member” to assure these conflicts are minimized while allowing for as full participation as possible.

Open and free discussion of conflict of interest is key to this process. The classification of conflict and the selection of the appropriate action should not be left to the individual but is based on a consensus of the whole Subcommittee. If there is no consensus with the Subcommittee, the appropriate action is at the discretion of the Subcommittee Chair. The Committee Chair should be informed of all high levels of conflict and proposed action.

To assist in identifying levels of conflict and possible actions for mitigating conflict, the following definitions are offered as guidance.

#### High Degree of Conflict

A “high” level of conflict exists if a “Member” has been or currently is directly involved with the substance.

Examples of situations with a high level of conflict are:

- a. A “Member” working with a regulatory agency who plays a role in developing regulations for the chemical substance.
- b. A “Member” affiliated with an academic institution and who performs research central to the TLV<sup>®</sup>.
- c. A “Member” who works for a company that is a major producer of a chemical substance under review by the TLV<sup>®</sup>-CS Committee.

- d. A “Member” who performs consultation services for an associated trade organization or a producer of a chemical substance under review by the TLV<sup>®</sup>-CS Committee and plays a direct role in the development of internal exposure levels.

Where a high degree of conflict exists, the “Member” is not permitted to author or co-author *Documentation*, and must recuse themselves from discussions about the recommended TLV<sup>®</sup> value and notations. Full members with a high degree of conflict must also abstain from voting on the recommended TLV<sup>®</sup> and *Documentation*; although, the “Member” may discuss matters of science.

#### Medium Degree of Conflict

A “medium” level of conflict exists if a “Member” has been or is indirectly involved with the chemical substance.

Examples of situations with a medium level of conflict include:

- a. A “Member” who works for a regulatory agency that regulates the chemical substance, does not have a direct role in developing regulations but may be concerned with enforcing regulations.
- b. A “Member” who is an academic and whose present, past, or anticipated research may be concerned with the chemical substance but is not central to the determination of a TLV<sup>®</sup>.
- c. A “Member” employed by a company that is a major producer of a chemical substance that is competing with a chemical substance under review by the TLV<sup>®</sup>-CS Committee.
- d. A “Member” who performs consultation services for an associated trade organization or a producer of a chemical substance under review by the TLV<sup>®</sup>-CS Committee but who plays a minor role in the internal development of exposure levels.

When an intermediate level of conflict has been identified, the matter should be carefully discussed with the Subcommittee Chair and members, and appropriate steps taken to mitigate the conflict. Typically, this will mean assigning a co-author or a reviewer for the *Documentation*. In some cases, abstention from voting on the TLV<sup>®</sup> is also appropriate.

#### Low Degree of Conflict

A “low” level of conflict exists if the “Member” is affiliated with an organization that has a financial or other interest in the substance but has a very minor or nonexistent role with respect to the substance.

Examples of situations with a low level of conflict include:

- a. A “Member” affiliated with an academic institution who does not conduct research relevant to the chemical substance but whose immediate colleagues have research that is directly concerned with the substance.
- b. A “Member” working for a regulatory agency that regulates the substance but whose role is non-regulatory.
- c. A “Member” working for a company that is a minor producer and has no role in the development of internal occupational exposure levels.

- d. A “Member” who performs consultation services for an associated trade organization or a producer of a chemical substance under review by the TLV<sup>®</sup>-CS Committee but who has no role in the development of internal occupational exposure levels.

In most cases, simply informing the Subcommittee and Committee members about low-level conflicts is all that is needed.

All “Members” who have participated fully in the TLV<sup>®</sup>-CS Subcommittee and Committee discussions about conflict of interest and who have made their best effort to eliminate or minimize personal conflicts will be eligible to participate in all votes. In cases where there are high levels of conflict, “Members” must recuse themselves from any discussions, reviews, and votes related to that substance.

Failure by any “Member” to report a conflict of interest is grounds for immediate termination of that member’s service on the Committee. The Chair will conduct a review with the Steering Subcommittee and make a recommendation to the Board. Depending on the status of the TLV<sup>®</sup> (under study, proposed, or adopted), it may be necessary to carry out a complete review of the decision-making process for the substance to determine appropriate action.

### **Terms**

Members, who are annually appointed by the Board of Directors generally begin their term on January 1. The TLV<sup>®</sup>-CS Committee Chair will consult with the appropriate TLV<sup>®</sup>-CS Subcommittee Chair/Vice Chairs and other members of the Committee prior to recommending re-appointment.

Expectations for continuing membership include, at a minimum:

- Attending all meetings,
- Participating in all scheduled conference calls, and
- Preparing and reviewing *Documentation* each year.

### **Awards**

The ACGIH<sup>®</sup> TLV<sup>®</sup>-CS Committee is a voluntary activity of extremely busy and competent professionals with expertise in a range of scientific areas who contribute to international worker health and safety and the development of OEVs.

The contributions over time of these TLV<sup>®</sup>-CS Committee members will be recognized by Membership Service Awards based on years of service to the TLV<sup>®</sup>-CS Committee. In particular, TLV<sup>®</sup>-CS Committee members will be recognized for 5, 10, and 20 years of service. This recognition will occur at a TLV<sup>®</sup>-CS Committee meeting. Awards will be presented by the TLV<sup>®</sup>-CS Committee Chair in consultation with the Membership Subcommittee. The funds to support the Membership Service Award will be included in the budget for the TLV<sup>®</sup>-CS Committee.

Every third year (starting with 2002) the TLV<sup>®</sup>-CS Committee will submit a recommendation to the Board of Directors for the William D. Wagner Award. The award

will be given to someone (not necessarily a member of the Committee) who has been an outstanding example of commitment and dedication to the creation and dissemination of OEVs. Funds to support the travel expenses for the recipient will be determined by the Board of Directors and managed through the ACGIH® awards program.

## TLV<sup>®</sup> PRODUCTION GUIDE

### *TLV<sup>®</sup> Development Process*

The TLV<sup>®</sup>-CS Committee follows the TLV<sup>®</sup>/BEI<sup>®</sup> Development Process: An Overview, posted on the ACGIH<sup>®</sup> website (<http://www.acgih.org/TLV/DevProcess.htm>). Specific details relating to TLV<sup>®</sup> Development in the TLV<sup>®</sup>-CS Committee are listed below. Note: Important dates are listed at the end of this section.

#### Under Study

List of substances/issues under study are published by February 1 in the Annual Reports of the Committees on TLVs<sup>®</sup> and BEIs<sup>®</sup> and on the ACGIH<sup>®</sup> website ([www.acgih.org](http://www.acgih.org)) to allow public review and to solicit comments and data. This list is current as of January 1.

Substances are initially assigned to the Under Study list by a consensus of the respective Subcommittee, and can be added to or removed from the list throughout the year as needed, by the TLV<sup>®</sup>-CS Subcommittee Chair(s) or Committee Chair. Changes are posted on the ACGIH<sup>®</sup> website.

In addition, the Under Study list is updated by July 31 into a two-tier list. Tier 1 indicates which substances/issues may move forward as an NIC in the upcoming year, based on their status in the development process. Tier 2 consists of those substances/issues that will not move forward, but will either remain on, or be removed from, the Under Study list for the next year. Once the tiered list has been released to the public, any substances/issues added to the Under Study list must be placed on Tier 2. This updated list will remain in two-tiers for the balance of the year.

#### Draft Documentation on Under Study

An author is assigned by the TLV<sup>®</sup>-CS Subcommittee Chair(s) to prepare the draft *Documentation*. (Note: Draft *Documentation* is not available to the public through this stage of the development process and is not released until it is at the Notice of Intended Changes (NIC) stage.)

The draft *Documentation* is reviewed by the TLV<sup>®</sup>-CS Subcommittee. Subsequently, a decision is made by consensus of the Subcommittee to bring the TLV<sup>®</sup> value(s), any notations, and draft *Documentation* to the Full Committee for review.

The Subcommittee Chair(s) or Subcommittee member summarizes the draft *Documentation* and proposes a motion to place it on NIC. If the motion is seconded, the Full Committee will discuss and then vote on the proposed action. Approval requires a majority of the voting members present at the Full Committee meeting. Recommendation to place a draft *Documentation* on the NIC can be done at the Spring or Fall TLV<sup>®</sup>-CS Committee meeting.

The Committee’s recommendation is sent to the Board of Directors for review and ratification. If ratified by the Board of Directors, the TLV<sup>®</sup> value(s) and any notations are listed on the NIC and the *Documentation* is published and available as a “draft”.

Draft *Documentation* on the Notice of Intended Change (NIC)

A substance must be held on the NIC for at least one year for public review and comment before adoption. The comment period is defined in the TLV<sup>®</sup>/BEI<sup>®</sup> Development Process. Comments are forwarded by Staff to the TLV-CS Committee Chair, Vice Chair, Subcommittee Chair(s), the author, and the reviewer. At a minimum, the author and co-author or reviewer of the *Documentation* must review all of the comments in detail to ensure that the discussion at the subcommittee level includes a full consideration of the points raised therein. During the Subcommittee meetings, comments are reviewed by the Subcommittee and the draft *Documentation* is amended if necessary.

After Subcommittee review and approval (by consensus) of the draft *Documentation*, the TLV<sup>®</sup> value(s), any notations, and draft *Documentation* are brought to the Full Committee for review.

The Subcommittee Chair(s) or Subcommittee member will summarize the draft *Documentation* and propose one of the following actions:

- 1) Retain the TLV<sup>®</sup> value(s)/notations and draft *Documentation* on the NIC for an additional year,
- 2) Change the TLV<sup>®</sup> value(s)/notations and draft *Documentation* and retain on the NIC for an additional year,
- 3) Adopt the NIC TLV<sup>®</sup> value(s)/notations and draft *Documentation*, or
- 4) Withdraw the NIC TLV<sup>®</sup> value(s)/notations and draft *Documentation*.

If the motion is seconded, the Committee will discuss and subsequently vote on the proposed action. Approval requires a majority of the voting members present at a Full Committee meeting. Recommendation to adopt, withdraw, or retain NIC *Documentation* are typically done at the Fall TLV<sup>®</sup>-CS Committee meeting.

The Committee’s recommendation is sent to the Board of Directors for review and ratification. If ratified by the Board of Directors, the TLV<sup>®</sup> value(s), any notations and the *Documentation* are published.

Under Study Important Dates

Fall Meeting	Subcommittee establishes Under Study list (for upcoming year).
February 1	Under Study list is published in the Annual Report and posted on the web site.
Spring Meeting	Subcommittee updates Under Study list into two-tier list.
By July 31	Tier 1 and 2 lists released to the public.
Year Round	Under Study list can be updated, however, once the tiered list has been released to the public those substances/issues must be placed on Tier 2.

### Notice of Intended Change (NIC) Important Dates

Spring Meeting	Committee votes to place a draft <i>Documentation</i> for an Under Study substance on the NIC.
	Committee votes to adopt, withdraw or retain NIC <i>Documentation</i> . (Note: Typically this will be done at the Fall meeting.)
Fall Meeting	Committee votes to place a draft <i>Documentation</i> for an Under Study substance on the NIC. (Note: Where practical, this will be done at the Spring meeting.)
	Committee votes to adopt, withdraw or retain NIC <i>Documentation</i> .

### ***Voting Procedures***

The Committee follows the TLV<sup>®</sup>/BEI<sup>®</sup> Committee Voting Procedure.

### ***TLV<sup>®</sup> Documentation Guidelines***

An outline of a TLV<sup>®</sup> *Documentation* is included in Appendix A.

The purpose of the TLV<sup>®</sup> *Documentation* is to clearly describe, present and interpret the appropriate scientific information supporting the derivation of the TLV<sup>®</sup> and its associated notations for a given chemical. In general, the entire *Documentation* should be no longer than 10 pages in length; however, exceptions will be made where circumstances warrant it. *Documentation* should be formatted as designated by the Documentation Template (included in Appendix A). It should be kept in mind that TLV<sup>®</sup> *Documentation* is not a complete review of all the literature available on a particular substance. It has as its purpose the derivation of a number and the identification of notations, for the purpose of protecting employees in occupational settings. The primary user of the TLV<sup>®</sup> *Documentation* is intended to be the industrial hygiene professional.

### ***Literature Search***

For new TLVs<sup>®</sup>, the author of the *Documentation* or Assistant to the Chair shall conduct a full literature search using the appropriate online databases. ACGIH<sup>®</sup> Staff, Assistant to the Chair or other Committee members may provide assistance with those references to which a member does not have access. Basic toxicology and other references should also be consulted (see Appendix B).

For TLVs<sup>®</sup> requiring revision, the Committee member should request an electronic copy of the current TLV<sup>®</sup> *Documentation* from ACGIH<sup>®</sup>. Staff should provide copies of any references currently on file. A full literature search should then be conducted using on-line databases and references listed in Appendix B.

The TLV<sup>®</sup> *Documentation* is to rely on published, peer-reviewed information from scientific journals and books. Other types of information may be used, if necessary, to

provide a more complete picture of the substance and its health effects. However, care must be taken in the use of such information.

When unpublished information is used, it must meet the following criteria:

1. The information should have undergone some form of peer review. The importance of the information to the *Documentation* determines the degree of peer review necessary. For example, if the information is one of several reports in agreement about a particular aspect of the substance, then peer review by the Subcommittee may be adequate. If the information plays a larger or more important role (e.g., it is in disagreement with other information or it is the only information of its type), then a broader peer review may be necessary by the Full Committee. It will be up to the Subcommittee to determine the nature of peer review that is appropriate. When conducting such peer review, the Subcommittee should ensure that accepted scientific methods were used to obtain and analyze the data.
2. If unpublished data is used, a signed copy of permission to use, cite and release to a third party upon request must be filed with ACGIH® Staff before it can be used or referenced in a NIC or final *Documentation*.
3. Robust summaries can be used with some limitation for TLV® Development, keeping the following limitations in mind:
  - a. Can be used as further information in the *Documentation*, if not deriving the TLV® or notation
  - b. Can be used to support another source reference
  - c. Can be used to support a TLV® or notation if they are the only data available upon which to base a TLV® or notation. Use of a robust summary in this manner is contingent upon review and approval of the Committee, and limited on a case by case basis.

If the information is contained in a “government” document it should not be assumed that it has undergone peer review.

Secondary sources may be used for an overview of the data. However, primary sources should be relied upon for discussion of specific studies. In particular, conflicting results require review of the original data (e.g., research paper).

In the case of translated information, care must be taken to ensure the information has been properly interpreted. Translation of non-English sources may be possible, if the study is critical to the TLV® recommendation. The need for such translation should be discussed with the Subcommittee Chair; such requests should then be sent by the Subcommittee Chair to the TLV®-CS Committee Chair for review and recommendation to the ACGIH® Staff for approval.

## COMMITTEE STRUCTURE

### *Organization Chart*

The Committee organization chart is shown in Appendix C.

### *Position Descriptions*

#### TLV<sup>®</sup>-CS Committee Chair

**Method of Selection and Appointment.** Candidate(s) for the Chair of the Committee is/are recommended through an internal Committee nomination and vote process, the results of which are sent to the Board of Directors for final selection and approval. Prior to the expiration of the current Chair's appointment, the Membership Subcommittee will seek nominations from Committee members for candidates. Candidates may be drawn from current members of the Committee or may be people from outside the Committee. The latter must meet the criteria for Regular membership within ACGIH<sup>®</sup>, as well as the membership criteria of the TLV<sup>®</sup>-CS Committee. The Membership Subcommittee will screen nominees and present names to the Committee, accompanied by background information and a statement from each nominee. All Committee members will be asked to vote for one of the nominees. The Membership Subcommittee will tally votes (with assistance from Staff). The slate of nominees and number of votes received by each nominee will be sent to the Board of Directors for final selection and approval. The Chair of the TLV<sup>®</sup>-CS Committee will hold the position, contingent upon annual re-appointment by the Board of Directors.

**Duties.** The Chair leads the TLV<sup>®</sup>-CS Committee and works closely with the Vice Chair and Steering Subcommittee to ensure the Committee's progress toward fulfilling its mission and goals. The Chair:

- Assists and oversees TLV<sup>®</sup>-CS Subcommittee activities
- Monitors the annual selection of substances
- Oversees budget management, spending, meeting plans (with assistance from Staff)
- Monitors overall workload and makeup of the Committee
- Monitors and assists the activities of the Administrative Subcommittees
- Assures regular, clear communications with Staff and Board of Directors by interacting with the Board Liaison, Committee's Staff Persons, and other staff or Board members, as necessary
- Assures regular, clear communications with external parties by such processes as reviewing comments received, providing input to replies prepared by Staff, etc.
- Assures communication between all members of the Committee by consulting regularly with the Steering Subcommittee (Chair, Vice Chair and TLV<sup>®</sup>-CS Subcommittee Chairs)
- Consults regularly with the Vice Chair to assure proper functioning of internal Committee activities
- Works closely with the Chairs of the Administrative Subcommittees to assure their groups are functioning according to their guidelines and policies.

- Represents the TLV<sup>®</sup>-CS Committee to the public in accordance with ACGIH<sup>®</sup> Public Affairs and Communication Policy
- Represents the TLV<sup>®</sup>-CS Committee to the ACGIH<sup>®</sup> Board of Directors and communicates and consults regularly with the Committee's Board Liaison

**Reporting.** The Chair reports directly to the Board of Directors of ACGIH<sup>®</sup> and the Committee's Board Liaison.

### Assistant to the Chair

**Method of Selection and Compensation.** The Assistant to the Chair will be selected by the Chair of the Committee after consultation with Staff. Compensation for the Assistant to the Chair must be approved by the Board of Directors.

**Duties.** The Assistant to the Chair will work directly with the Chair in providing support and assistance in assuring that the Chair's responsibilities and various activities are adequately addressed and managed. The job description of this Assistant may vary with the individual in the Chair position and will be defined and negotiated with the ACGIH<sup>®</sup> Executive Director.

**Reporting.** The Assistant to the Chair will report directly to the Chair. The Chair will report on activities and progress of the Assistant to the Board of Directors and Staff as requested.

### Vice Chair

**Method of Selection and Appointment.** The Committee Chair recommends the Vice Chair to the Board of Directors, which approves the recommendation and appoints the Vice Chair for a one-year term. The Vice Chair may be re-nominated by the Chair and annually re-appointed by the Board.

**Duties.** The Vice Chair is responsible for assisting the Chair in assuring that internal Committee functions are adequately cared for. The Vice Chair will undertake the responsibilities of the Chair when s/he is unable or unavailable to do so. The Vice Chair may be a candidate for future appointment as Committee Chair.

The Vice Chair assists the Chair as necessary. In particular, the Vice Chair participates in the Steering Subcommittee and oversees internal Committee activities that support *Documentation* preparation and membership.

Specifically, the Vice Chair will:

- Assure the internal functioning of the Committee. As such, the Vice Chair is specifically responsible for overseeing the Administrative Subcommittees.
- Determine the make-up of all the Administrative Subcommittees, in consultation with the Chair. Members will be asked for their preferences and assigned to an Administrative Subcommittee. Every effort will be made to meet a member's preference, if possible. However, the Vice Chair will also ensure an appropriate

mix of members on the Administrative Subcommittees (by TLV<sup>®</sup>-CS Subcommittee affiliation, professional background and skills, etc.).

- Participate in decisions on Member Candidates recommended to the Board of Directors by consulting regularly with the Membership Subcommittee.

**Reporting.** The Vice Chair will report to the Chair of the Committee on his/her individual activities and the activities and make-up of the Administrative Subcommittees.

### **TLV<sup>®</sup>-CS Subcommittee Chairs**

**Method of Selection.** The Committee consists of three TLV<sup>®</sup>-CS Subcommittees:

- Hydrogen, Oxygen and Carbon Compounds (HOC)
- Dusts and Inorganic Compounds (D&I), and
- Miscellaneous Compounds (MISCO).

Each of these Subcommittees is headed by a Chair, who is nominated by the Committee Chair in consultation with the Vice Chair. There is no established term for a TLV<sup>®</sup>-CS Subcommittee Chair. The TLV<sup>®</sup>-CS Committee Chair will review the activities of each TLV<sup>®</sup>-CS Subcommittee Chair on a regular basis, seeking input from members of the Subcommittee. While continuity is important in ensuring the on-going productivity of these Subcommittees, it is also important to build leadership skills among all Committee members who demonstrate skill and interest. Subcommittee Chairs shall select, in consultation with the Committee Chair, another individual within their Subcommittee to serve as a Vice Chair. This person should become versed in the management of the Subcommittee and should be given opportunities to play a leadership role within the Subcommittee. In case of the Subcommittee Chair's absence, this person should be prepared to chair meetings and ensure progress toward completion of the Subcommittee's activities.

**Duties.** TLV<sup>®</sup>-CS Subcommittee Chairs are members of the Steering Subcommittee. (Vice Chairs, as described above, should be included in Steering Subcommittee meetings, as well.) The TLV<sup>®</sup>-CS Subcommittees have the most important function within the TLV<sup>®</sup>-CS Committee. Thus, the Chair of a TLV<sup>®</sup>-CS Subcommittee carries the largest degree of responsibility for assuring that the Committee's products are of high quality and fulfill the goals of the Committee. It is very important that the TLV<sup>®</sup>-CS Subcommittee Chair communicates and consults regularly with the Chair, Steering Subcommittee, Staff, and with members of their Subcommittee.

TLV<sup>®</sup>-CS Subcommittee Chairs are responsible for the *Documentation* preparation activities of their Subcommittee. In this capacity, TLV<sup>®</sup>-CS Subcommittee Chairs:

- Assign substances to individual members, following the definitions offered as guidance in the Conflict of Interest section of this manual
- Assure that each member meets the expectations for *Documentation* preparation
- Assist members, when necessary, with aspects of *Documentation* development
- Assign a mentor to all new members and Member Candidates
- Keep members informed of relevant decisions of the Steering Subcommittee
- Track the progress of *Documentation* preparation and keep members informed of this progress

- Provide feedback to members about their activities with respect to membership expectations.

TLV<sup>®</sup>-CS Subcommittee Chairs are responsible for their Subcommittee's productivity, both in quality and quantity of *Documentation*. In this capacity, they will arrange regular Subcommittee meetings throughout the year, establish meeting agendas in consultation with members, and run well-organized and productive meetings. They will also ensure formal minutes are taken for all meetings and will provide copies of these minutes to all Subcommittee members and the Committee Chair. Minutes may consist of decisions and a simple "to do" list, rather than a formal description of the discussion.

Generally, no voting takes place in the TLV<sup>®</sup>-CS Subcommittees. Decisions are made by consensus, if possible. However, the TLV<sup>®</sup>-CS Subcommittee Chair may ask for a vote of the Subcommittee members if consensus is not reached. In this case, a quorum of the Subcommittee must be present and a simple majority vote will be required to bring TLV<sup>®</sup> *Documentation* to the Full Committee. The TLV<sup>®</sup>-CS Subcommittee Chair must seek Subcommittee consensus for all substances currently on the NIC and on the Under Study list. In a case where the Subcommittee could not reach consensus or majority vote, the TLV<sup>®</sup>-CS Subcommittee Chair may not bring a TLV<sup>®</sup> to all members of the Committee without receiving approval from the Committee Chair and Vice Chair.

TLV<sup>®</sup>-CS Subcommittee Chairs are responsible for ensuring that full communication takes place within the Committee, particularly among the Steering Subcommittee members and with the Staff. As such they should:

- Review communications received from external parties and ensure that members of their Subcommittee have an opportunity to review and discuss comments.
- Respond to questions from the Staff in a timely manner.
- Direct all questions and comments (written and oral) received from external parties directly to the Staff. TLV<sup>®</sup>-CS Subcommittee Chairs are not to contact external parties. TLV<sup>®</sup>-CS Subcommittee Chairs are expected to respond to all external parties by directing them to the Staff.
- Work with the relevant Administrative Subcommittees on activities not directly related to the preparation of TLV<sup>®</sup> *Documentation*. For example, internal education events should be planned in consultation with the TLV<sup>®</sup>-CS Education Development Coordinator; external education events should follow the guidelines of the ACGIH<sup>®</sup> Events Development Planner worksheet; and changes to the TLV<sup>®</sup> notations, appendices, etc. should be discussed and coordinated with the Notations Subcommittee.

**Terms.** There is no established term for a TLV<sup>®</sup>-CS Subcommittee Chair.

**Reporting.** The TLV<sup>®</sup>-CS Subcommittee Chairs report to the TLV<sup>®</sup>-CS Committee Chair.

### **TLV<sup>®</sup>-CS Subcommittee Vice Chairs**

**Method of Selection and Appointment.** Each TLV<sup>®</sup>-CS Subcommittee Chair shall select a Vice Chair, in consultation with the Committee Chair.

The TLV<sup>®</sup>-CS Subcommittee Vice Chair will work closely with the TLV<sup>®</sup>-CS Subcommittee Chair to assist in leadership and decision-making responsibilities. The Subcommittee Vice Chair may take on the duties of the Subcommittee Chair, in case of the latter's absence. The Subcommittee Vice Chair participates fully in all Committee leadership activities (Steering Subcommittee, etc.).

**Reporting.** The TLV<sup>®</sup>-CS Subcommittee Vice Chair reports directly to the TLV<sup>®</sup>-CS Subcommittee Chair.

**Term.** There is no established term for a TLV<sup>®</sup>-CS Subcommittee Vice Chair.

### **Administrative Subcommittee Chairs**

**Method of Selection.** The Administrative Subcommittee members are responsible for identifying a Chair.

**Reporting.** The Administrative Subcommittee Chair is responsible for ensuring that the duties of the Subcommittee are adequately fulfilled, as described in the Operations Manual. The Administrative Subcommittee Chair is responsible for reporting the Subcommittee's activities to the Chair, Vice Chair and Steering Subcommittee. The Chair of the Membership Subcommittee is expected to work most closely with the Vice Chair, who holds primary responsibility for their activities. The Chair of the Notations Subcommittee will work most closely with the Chair, who holds primary responsibility for their activities.

### ***Description of Administrative Subcommittees***

#### **Steering Subcommittee**

**Method of Selection and Appointment.** The Steering Subcommittee consists of the TLV<sup>®</sup>-CS Committee Chair and Vice Chair, as well as the TLV<sup>®</sup>-CS Subcommittee Chairs and Vice Chairs (HOC, D&I, MISCO). The Committee Chair also chairs the Steering Subcommittee.

**Duties.** The Steering Subcommittee:

- Advises the Committee Chair on issues.
- Reviews Committee productivity, progress toward goals and mission, and spending and budget.
- Recommends specific annual goals and annual Committee work plan to the Committee Chair to be submitted to the Board of Directors for approval.
- Reviews, changes, and updates Committee policies, for Full Committee approval.
- Assures Committee resources are reviewed and properly allocated.
- Identifies and uses external resources, as necessary.
- Reviews special projects and requests from Subcommittees, as necessary.
- Reviews the progress of the TLV<sup>®</sup>-CS Subcommittees and Administrative Subcommittees.

## **Membership Subcommittee**

**Method of Selection.** The Membership Subcommittee will consist of at least one member from each of the TLV<sup>®</sup>-CS Subcommittees. Membership Subcommittee members are appointed annually by the TLV<sup>®</sup>-CS Committee Vice Chair. The Subcommittee members, in consultation with the TLV<sup>®</sup>-CS Committee Vice Chair, will identify the Subcommittee Chair.

### **Duties.**

New Members. The Membership Subcommittee is responsible for recruiting, reviewing, and recommending Member Candidates or new members for consideration by the Committee Chair and Vice Chair, and for monitoring the probationary progress of Member Candidates. Recruitment may be accomplished by various methods, including advertisements and personal communications.

Any person indicating interest in participating on the TLV<sup>®</sup>-CS Committee will be sent an application form by Staff. Applicants will be asked to submit a completed membership application and their resumé/curriculum vitae. Applicants will be informed of the expectations and responsibilities of members of the TLV<sup>®</sup>-CS Committee, and will be asked to review and accept these responsibilities as part of their application. Staff will review the completeness of applications received and issue a letter confirming receipt of the application. Completed applications with resúmes/curriculum vitae will be sent to the members of the Membership Subcommittee and the TLV<sup>®</sup>-CS Committee Chair and Vice Chair. The Membership Subcommittee will meet and consider all new applications at least once per year, or more frequently if necessary.

The Membership Subcommittee Chair will advise the TLV<sup>®</sup>-CS Committee Chair and Vice Chair of the applicants and of their backgrounds. The TLV<sup>®</sup>-CS Committee Chair and Vice Chair may consult with other members of the TLV<sup>®</sup>-CS Committee as to their opinions about the prospective member(s).

Once this process is completed, the TLV<sup>®</sup>-CS Committee Chair will assess each application and forward to the ACGIH<sup>®</sup> Board of Directors the name(s) of those whom he/she recommends for approval to appoint as a Member Candidate of the TLV<sup>®</sup>-CS Committee. A copy of the applicant's resumé/curriculum vitae will be provided to the Board, as part of the Chair's recommendation. After Board approval, the Committee Chair can extend an invitation to the Member Candidate to attend and participate in a Full Committee meeting. The Member Candidate will be given the opportunity during a Committee meeting to attend a portion of each of the three TLV<sup>®</sup>-CS Subcommittee meetings and the Full TLV<sup>®</sup>-CS Committee meeting, as well as a meeting of the Notations Subcommittee, if possible.

The TLV<sup>®</sup>-CS Committee Chair will assign the applicant to a TLV<sup>®</sup>-CS Subcommittee for a probationary period. Applicants will be referred to as "Member Candidates" during this period. As such, they will be expected to attend all meetings of their TLV<sup>®</sup>-CS Subcommittee and of the Full TLV<sup>®</sup>-CS Committee. The respective TLV<sup>®</sup>-CS Subcommittee Chair and Vice Chair will identify and assign responsibilities to the

Member Candidate during the probationary period. These responsibilities will include assignment of a *Documentation* to be developed as a draft to the TLV<sup>®</sup>-CS Subcommittee during the probationary period, administrative activities, and other duties. The Member Candidate may not vote in Full Committee meetings, but will be expected otherwise to participate fully in TLV<sup>®</sup>-CS Subcommittee and Committee discussions.

During the probationary period, the TLV<sup>®</sup>-CS Subcommittee Chair will make a recommendation to the Membership and Steering Subcommittees for full membership. The Membership Subcommittee will then submit the names of all applicants who have completed their probationary period satisfactorily to the TLV<sup>®</sup>-CS Committee Chair. If needed, the Chair will solicit input from all Committee members concerning membership for Member Candidates completing their probationary period. The TLV<sup>®</sup>-CS Committee Chair will evaluate each Member Candidate and make the final decision concerning a recommendation for membership. Names of recommended Member Candidates will then be forwarded by the TLV<sup>®</sup>-CS Committee Chair to the ACGIH<sup>®</sup> Board of Directors for a decision regarding approval and formal appointment as a TLV<sup>®</sup>-CS Committee member.

The ACGIH<sup>®</sup> Staff will handle all communication with applicants and candidates regarding the status of their application or membership.

Nominating the Committee Chair. The Membership Subcommittee will serve as the nominating group for the TLV<sup>®</sup>-CS Committee Chair. [See the section on Method of Selection and Appointment for the Committee Chair for more details on this process.]

**Reporting.** The Chair of the Membership Subcommittee will be asked to report the activities and progress of the Membership Subcommittee to the TLV<sup>®</sup>-CS Committee Chair, Vice Chair and the Steering Subcommittee on a regular basis.

### **Notations Subcommittee**

**Method of Selection.** The Notations Subcommittee will consist of at least one member from each of the three TLV<sup>®</sup>-CS Subcommittees, designated by the Vice Chair. The Subcommittee will select its own Chair, in consultation with the Vice Chair. Other ACGIH<sup>®</sup> Committees or task groups (e.g., BEI<sup>®</sup>, Physical Agents, Air Sampling Instruments) may also be identified and asked to participate in the Subcommittee's activities, as the need arises.

**Duties.** The Notations Subcommittee has as its mission to:

- Determine the appropriate types of notations for TLVs<sup>®</sup>.
- Facilitate consistent use of all notations.
- Respond to emerging issues as they arise.

Specific responsibilities of the Subcommittee include:

- Review current notations and recommend changes and modifications as necessary in their definitions.
- Develop criteria that guide authors in determining which notations are appropriate and how they should be applied.

- Identify experts (internal and external to the Committee) that can be consulted for specific notations.
- Recommend workshops, seminars, webinars or tutorials for the purpose of providing input to the Committee on emerging issues.
- Establish ad hoc groups, where necessary, to consider special issues.
- Develop “standard” language for the *Documentation* Guidelines that can be used in *Documentation* development and in the TLVs<sup>®</sup> and BEIs<sup>®</sup> book to describe notations and special issues.
- Provide attention to the consistent application of notations across the three TLV<sup>®</sup>-CS Subcommittees.
- Create and revise appendices and other related documents.

It is the responsibility of the TLV<sup>®</sup>-CS Subcommittees and individual authors to ensure that notations are both considered and applied for specific substances. The Notations Subcommittee will serve as a consultant concerning the applicability of a notation to a specific substance. The *Documentation* author is responsible for the initial decisions about notations.

At this time, the types of notations that should be addressed by an author and on which they might consult with the Notations Subcommittee include:

- Carcinogen
- Skin
- BEI<sup>®</sup>
- Sensitizer (SEN)
- TLV<sup>®</sup> Basis
- Mixtures
- Atypical work schedules
- STEL
- TWA
- Ceiling

In the case of the adoption of a new notation, the Notations Subcommittee will be responsible for developing a written definition and assuring adequate review within the Committee.

**Reporting.** The Chair of the Notations Subcommittee will report activities and progress to the Chair and Steering Subcommittee on a regular basis.

### Other

**TLV<sup>®</sup>-CS Education Development Coordinator.** This individual is responsible for coordinating and overseeing educational event development internal and external to the Committee.

## COMMUNICATIONS

### *External to the Committee*

The Committee recognizes that there are many different groups with an interest in the TLV<sup>®</sup> process and its outcomes. The Committee's goal is to assure that all such parties are given timely and complete information about its process and decisions. At the same time, it is important that these external parties not compromise the Committee's decision process, which is based primarily on peer-reviewed scientific information. Thus, the Committee has established a written process that allows input from external groups to the Committee concerning substances currently under review. Also, comments are welcome for any other substances as well. The TLV<sup>®</sup>/BEI<sup>®</sup> Development Process is available on the ACGIH<sup>®</sup> website at [www.acgih.org](http://www.acgih.org). There are several important points to consider throughout this process:

- The appropriate method for an interested party to contribute to the TLV<sup>®</sup> and BEI<sup>®</sup> process is through the submission of literature that is peer-reviewed and public. ACGIH<sup>®</sup> strongly encourages interested parties to publish their studies, and not to rely on unpublished studies as their input to the TLV<sup>®</sup> and BEI<sup>®</sup> process. Also, the best time to submit comments to ACGIH<sup>®</sup> is in the early stages of the TLV<sup>®</sup> and BEI<sup>®</sup> development process, preferably while the substance or agent is on the Under Study list.
- An additional venue for presentation of new data is an ACGIH<sup>®</sup>-sponsored symposium or workshop that provides a platform for public discussion and scientific interpretation. ACGIH<sup>®</sup> encourages input from external parties for suggestions on symposium topics, including suggestions about sponsors, speakers and format. See the Symposium section within this Operations Manual for further information.
- ACGIH<sup>®</sup> periodically receives requests from external parties to make a presentation to a committee about specific substances or issues. It is *by exception* that such requests are granted. While there are various reasons for this position, the underlying fact is that the Committee focuses on data that have been peer-reviewed and published and not on data presented in a private forum. A committee may grant a request when the data are significantly new, has received peer review, are the best vehicle for receipt of the information, and are essential to the Committee's deliberations. The presentation is not a forum to voice opinions about existing data. In order for a committee to evaluate such a request, the external party must submit a request in writing that, at a minimum, addresses the following elements: (a) a detailed description of the presentation; (b) a clear demonstration of why the information is important to the Committee's deliberations; and (c) a clear demonstration of why a meeting is the necessary method of delivery. This request must be sent to the ACGIH<sup>®</sup> Science Group ([science@acgih.org](mailto:science@acgih.org)).

The TLV<sup>®</sup>-CS Committee may invite subject experts to present/speak at Committee education sessions.

## **Confidentiality**

The TLV<sup>®</sup>-CS Committee communicates with its users and interested parties by publishing its decisions as *Documentation*, following a clearly delineated process. Authorship of *Documentation* is a confidential matter. Such authorship may not be discussed with any person external to the Committee. Methods for seeking information from external parties while ensuring anonymity should be discussed with the Subcommittee Chair or Committee Chair and performed through ACGIH<sup>®</sup> Staff. Information, materials, *Documentation*, etc. may not be shared with anyone external to the Committee. Draft Chemical Substance *Documentation* can be shared with other TLV<sup>®</sup>/BEI<sup>®</sup> Committees once approved by the applicable Subcommittee or approved by the Subcommittee Chair/Vice Chair. Committee members are to follow the ACGIH<sup>®</sup> Public Affairs and Communication Policy and ACGIH<sup>®</sup> Information Release Policy.

## ***Internal Communications***

### **Communications Within the Committee**

The TLV<sup>®</sup>-CS Committee relies on meeting minutes for documenting its activities and tracking its progress.

Formal minutes will be taken at Full Committee meetings, generally by ACGIH<sup>®</sup> Staff or Assistant to the Chair. These minutes are used to record the activities and formal votes of the Full Committee (typically without identification of individual names). Copies will be sent to members of the Committee and the Board Liaison.

Formal minutes are required at TLV<sup>®</sup>-CS and Notations Subcommittee meetings. At a minimum, Subcommittee notes should indicate the date, members present and absent, important points of discussion, major decisions taken and future activities planned. Copies of these minutes will be made available to the Committee Chair (or the Assistant to the Chair).

### **Communications Between the Committee and ACGIH<sup>®</sup> Staff and Board of Directors**

The Committee assures timely and consistent communication with the ACGIH<sup>®</sup> organization through its Board Liaison and ACGIH<sup>®</sup> Staff. ACGIH<sup>®</sup> Staff attends Full Committee meetings and many of the TLV<sup>®</sup>-CS and Administrative Subcommittee meetings. The Staff communicates regularly with the Committee Chair about Committee activities. ACGIH<sup>®</sup> Staff works closely with the Committee Chair on issues, including budgeting and spending, meeting arrangements, publications, communications with external parties, etc.

The Board Liaison also attends Full Committee meetings, providing input to the Committee from the Board of Directors and relaying Committee concerns and thoughts to the Board. The Board Liaison also works with the Chair during budgeting, policy-making and other issues that bear directly on the organization.

## SYMPOSIA AND WORKSHOPS

### *Procedure for Developing a Symposium or Workshop*

The education of TLV<sup>®</sup> Committee members is an important aspect of the development of TLVs<sup>®</sup> and TLV<sup>®</sup> *Documentation*. Suggestions for educational symposium topics should be forwarded to the Science Department of ACGIH<sup>®</sup> or TLV<sup>®</sup>-CS Education Development Coordinator in writing. Symposium topics can come from Committee members, ACGIH<sup>®</sup> Staff, and external parties. The proposal should include a justification for the necessity of the symposium, the topic's relevance to the TLV<sup>®</sup>-CS Committee, a suggested list of participants, and if possible, a list of potential academic, governmental, or industrial sponsors.

The Events Development Planner (EDP) will serve as the formal planning document during symposium development. The ACGIH<sup>®</sup> Staff will work with the Committee through all aspects of planning and executing a workshop or symposium.

Several criteria will be used by the Committee to determine the appropriateness of the symposium as being of interest to the TLV<sup>®</sup>-CS Committee. A symposium must be the most efficient format in which to present TLV<sup>®</sup>-CS Committee members with new information that will assist in the scientific judgment used in the setting of TLVs<sup>®</sup> and in the writing of supporting *Documentation*.

Because of the timing of TLV<sup>®</sup> setting and *Documentation*, it is important that a symposium be suggested as early in the process as possible. Symposia require considerable time, commitment, and resources to develop and, thus, proposals should preferably be submitted while a substance is on the Under Study list. Symposium suggestions submitted while a substance is on the NIC will be considered, but usually this will be too late in the decision-setting process. A symposium will not be favorably reviewed if its purpose is solely to provide a forum for voicing opinions about existing data. Rather, there must be on-going research, scientific uncertainty about currently available data, or another scientific reason for the symposium.

Representatives of external organizations may have expressed a desire to meet with the TLV<sup>®</sup>-CS Committee because the Committee might benefit from discussions of the scientific data or because the many issues to be discussed on a given chemical are likely to be important and of interest to a wide range of interested parties. Yet symposia require commitment of substantial resources and presentations and discussions are often scheduled for a period as long as two days, far more time than the TLV<sup>®</sup>-CS Committee could commit to a single topic. Thus, it is important that care be taken in the review and selection of topics for symposia.

The Steering Subcommittee will review the original proposal. It may choose to seek further input from individual groups or members of the Committee in its review. The Steering Subcommittee will make a final recommendation to the Committee Board Liaison, indicating whether the TLV<sup>®</sup>-CS Committee has an interest in and wishes to participate in the development of a particular symposium. It will communicate its

recommendation to the individual(s) and/or Subcommittee that proposed the symposium topic, as well.

If a symposium proposal recommended by the TLV<sup>®</sup>-CS Committee is approved by the Board of Directors, the Steering Subcommittee will identify a small "task force" to work with ACGIH<sup>®</sup> Staff during the development phase. It is recommended that a member of the Steering Subcommittee serve as a member. In addition, a Board member will act as liaison to the task force. The task force will work closely with the Staff and, in addition to regular reporting to the Steering Subcommittee, will seek input and ideas from TLV<sup>®</sup>-CS Committee members about sponsors, speakers, format, etc. The task force will be responsible for ensuring that the TLV<sup>®</sup>-CS Committee's scientific decision-making needs are met and that all relevant external parties have an opportunity to give input to the planning of a symposium. To ensure that there is appropriate balance of scientific viewpoints and to maximize the available research to choose from, each symposium will utilize a call for papers to initiate and announce the planned symposium. The task force will be responsible for selecting speakers from responses as well as those identified from any other internal and external sources.

The symposium will typically be held immediately preceding or immediately following a scheduled meeting of the TLV<sup>®</sup>-CS Committee to facilitate the attendance of Committee members. Since the attendance of Committee members is in the interest of both the symposium and the TLV<sup>®</sup> development process, members will be encouraged to attend in their capacity as representatives of the TLV<sup>®</sup>-CS Committee.

If a symposium proposal is rejected, the Staff will be informed of the proposal and the Steering Subcommittee's review. The individual who submitted the proposal will also be notified. The organization may decide to proceed without the TLV<sup>®</sup>-CS Committee's formal sponsorship or involvement. In this latter case, potential symposium sponsors and attendees must be made aware that the TLV<sup>®</sup>-CS Committee has expressed no interest in formal sponsorship or participation. In addition, it must be made clear that TLV<sup>®</sup>-CS Committee members will not attend the meeting in their capacity as members or representatives of the TLV<sup>®</sup>-CS Committee, although they may, of course, attend as interested scientists.

## **APPENDICES**

## APPENDIX A

### TLV<sup>®</sup> Documentation Guidelines

#### **Background**

This guideline provides general instructions for preparing the main body of the TLV<sup>®</sup> *Documentation*. It provides the TLV<sup>®</sup> *Documentation* authors with a compendium of tools to efficiently and effectively update or create a new TLV<sup>®</sup> *Documentation*. It includes procedures and conventions for not only completing, gathering information, and reviewing the literature but also for incorporating a balance of information to support the TLV<sup>®</sup> recommendation. Among the many resources found in this guideline is a TLV<sup>®</sup> *Documentation* Template, which is designed to aid the author in drafting TLV<sup>®</sup> *Documentation*. It contains all required headings and some boilerplate language for assistance in writing *Documentation*. This guideline is updated periodically and should be considered a work in progress.

The primary purpose of the TLV<sup>®</sup> *Documentation* is to describe and analyze the scientific literature that specifically supports the derivation of a TLV<sup>®</sup> and any associated notations. Although the *Documentation* is not intended to be a comprehensive review of the literature for a substance, it should describe the key literature studies that define the range of exposure information and animal and human health effects associated with a substance. To facilitate an organized description of this literature, the TLV<sup>®</sup> *Documentation* Guidelines are divided into appropriate sections for description and analysis of the relevant studies. The review of the literature should not be just a recitation of the findings and conclusions of individual reports, but also must provide appropriate integrated analyses as to which study(s) are most appropriate for consideration in derivations of the TLV<sup>®</sup>. When a study seems to suggest the TLV<sup>®</sup> or any of its notations should be different from that selected, the reason for discounting this study should be provided.

#### **Definitions**

In order to write or update a TLV<sup>®</sup> *Documentation*, the most current definitions cited in the *TLVs<sup>®</sup> and BEIs<sup>®</sup>* book must be used (i.e., TLV<sup>®</sup>-TWA, TLV<sup>®</sup>-STEL, TLV<sup>®</sup>-Ceiling, Skin, SEN, etc.). The ACGIH<sup>®</sup> TLV<sup>®</sup>-CS Committee periodically reviews, clarifies, updates, and/or adds new definitions that must be considered in the development of the TLV<sup>®</sup> *Documentation*.

#### **Responsibilities**

Specific responsibilities for authors are described in the TLV<sup>®</sup>-CS Operations Manual.

#### **Procedures**

#### **Getting Started**

## APPENDIX A

- A TLV<sup>®</sup> *Documentation* is assigned to an author by the specific TLV<sup>®</sup>-CS Committee (D&I, MISCO, HOC).
- Conduct a literature search yourself or with the assistance of ACGIH<sup>®</sup> Staff or the Assistant to the Chair. See Appendix B, the Literature Search Process Guidelines, of this document for recommended websites and procedures.

### General Procedures

- For each major heading and subheading, it is not necessary to describe all studies, but only those regarded as reliable and relevant to the TLV<sup>®</sup> recommendation (adequate description of methodology, reported in peer-reviewed literature, and evidence or reproducibility).
- The text of each section should present the studies regarded as most relevant and reliable to derivation of the TLV<sup>®</sup> first, followed by descriptions of studies deemed of lesser, but corroborative value. For studies that describe differential or contradictory findings, a brief rationale should be presented for weighting the information of greatest value to the TLV<sup>®</sup> evaluation (e.g., appropriateness of route of exposure; full characterization of dose-response, adequacy of elements of study design, adequacy of description of study methodologies and results, etc.).
- Keep summaries of papers cited concise.
- If no studies are available for a major heading (e.g., Animal Studies, Human Studies, etc.) indicate this with the standard statement “No studies available.”
- If no data are available for a subheading (e.g., Oral, Dermal, Chronic, etc.), do not include the subheading in the outline.
- Any comprehensive literature reviews relevant to a major heading should be discussed first, before any subheadings. Information in reviews relevant to subheading topics should be summarized there.
- Bibliographic references in the body of the *Documentation* should be presented as follows: ...text. [Smith et al., 1999]. Do not use italics or bolding. Note, when the document is published, the references within the body of the document will be alphabetized by ACGIH<sup>®</sup> Staff.
- Use of unpublished information requires that the entire study or communication be on file at ACGIH<sup>®</sup> headquarters, and be available for public release if requested.

## APPENDIX A

### TLV<sup>®</sup> Documentation Outline

Section	Comments / Common Boilerplate
<b>Title</b> Provide formal chemical name in all capitals.	Subcommittee may decide on most common name for document title.
<b>CAS Number(s)</b> Provide CAS number(s) describing the substance.	
<b>Synonyms</b> Provide listing of other chemical synonym(s) for this substance.	Merck is a good reference for this. Also include common trade names.
<b>Chemical Formula</b> <ul style="list-style-type: none"> <li>• Provide chemical equation.</li> <li>• Provide chemical structure on separate line, if appropriate.</li> </ul>	Provided by ACGIH <sup>®</sup> Staff.
<b>TLV<sup>®</sup>-TWA</b> <ul style="list-style-type: none"> <li>• List current TLV<sup>®</sup>-TWA expressed in appropriate units.</li> <li>• If particulate, describe appropriate form.</li> </ul>	
<b>TLV<sup>®</sup>-STEL</b> <ul style="list-style-type: none"> <li>• List value in appropriate units.</li> <li>• If no value assigned, do not list.</li> </ul>	
<b>TLV<sup>®</sup>-C</b> <ul style="list-style-type: none"> <li>• List value in appropriate units.</li> <li>• If no value assigned, do not list.</li> </ul>	
<b>Skin</b> If no "Skin" notation assigned, do not list.	
<b>Sensitizer (SEN)</b> If no "Sensitizer" notation assigned, do not list.	
<b>Carcinogenicity</b> List notation as A1, A2, A3, A4, or A5, with summary definition. <ul style="list-style-type: none"> <li>• If no information, do not list cancer designation.</li> </ul>	

## APPENDIX A

Section	Comments / Common Boilerplate
<p><b>TLV<sup>®</sup> Recommendation</b></p> <ul style="list-style-type: none"> <li>Focus only on study(s) providing the rationale for deriving the TLV<sup>®</sup> recommendation, including notations. For example: <ul style="list-style-type: none"> <li>human study(s).</li> <li>animal study(s) expressing most relevant route of exposure, doses, and appropriate responses.</li> </ul> </li> <li>Include the relevant bibliographic references (e.g., Smith, 1999). The results of these studies should not be repeated in detail; provide only the key conclusion(s) as they support the rationale for the TLV<sup>®</sup> recommendation.</li> <li>This section should have a clear explanation about each of the following items: a description of the key health effects, a discussion of why particle size fraction was selected for the TLV<sup>®</sup> (for aerosols), and the reasoning for the selection of a value. Adjustments do not need to be quantified, but rather explained. Notations and other relevant information should also be described and explained.</li> <li>Identify appropriate notations and explain reasoning for their selection. <ul style="list-style-type: none"> <li>Carcinogenicity designation (see Appendix A in the <i>TLVs<sup>®</sup> and BEIs<sup>®</sup></i> book).</li> <li>SEN (see Annex D).</li> <li>Skin (see Definition in the <i>TLVs<sup>®</sup> and BEIs<sup>®</sup></i> book).</li> </ul> </li> <li>Refer to BEI<sup>®</sup>, if available for substance.</li> </ul>	<p>Look at the critical study for the basis. Has enough been said about it? Is it clear to the reader? Look for contradictions.</p> <ul style="list-style-type: none"> <li>How do you select the appropriate TLV<sup>®</sup>? – see the description below this outline.</li> <li>Do not restate definition of a notation used.</li> <li>When assigning a cancer designation, revisit the definition in the <i>TLVs<sup>®</sup> and BEIs<sup>®</sup></i> book and make sure that back up evidence supports the rationale.</li> </ul> <p>Some useful boilerplate language:</p> <ul style="list-style-type: none"> <li>A TLV<sup>®</sup>-TWA of __ mg/m<sup>3</sup>, measured as <b>inhalable particulate matter (or IFV, or R, T)</b>, is recommended for occupational exposure to _____.</li> <li>Sufficient data were not available to recommend a TLV<sup>®</sup>-<b>STEL</b>.</li> <li>A TLV<sup>®</sup>-<b>Ceiling</b> of _____ is recommended to minimize the <i>acute irritation</i> associated with occupational exposure to _____.</li> <li>Sufficient data were not available to recommend a <b>Skin</b> notation.</li> <li>Sufficient data were not available to recommend a <b>SEN</b> notation.</li> <li>Available data on sensitization from exposure to _____ warrants the addition of the <b>SEN</b> (sensitizer) notation.</li> <li>_____ is a substance for which <b>Biological Exposure Indices</b> (BEIs<sup>®</sup>) have been recommended (see BEI<sup>®</sup> <i>Documentation</i> for _____).</li> </ul>
<p><b>TLV<sup>®</sup> Basis</b></p> <p>This section should briefly list the critical health effects <u>that support derivation of the TLV<sup>®</sup></u>. This description will be used to complete the “TLV<sup>®</sup> Basis – Critical Effect(s)” column in the <i>TLVs<sup>®</sup> and BEIs<sup>®</sup></i> book.</p>	<p>See TLV<sup>®</sup> Basis Table – Annex B.</p> <p>Each TLV<sup>®</sup>-CS Subcommittee will ensure that the TLV<sup>®</sup> Basis is appropriate for each new or revised TLV<sup>®</sup> <i>Documentation</i>. Consider the following rules of thumb in selecting the appropriate TLV<sup>®</sup> Basis:</p> <ul style="list-style-type: none"> <li>If there is no TLV<sup>®</sup> Basis, leave it blank. Do not use “other”.</li> <li>If a TLV<sup>®</sup> Basis is not on the current list of TLV<sup>®</sup> Basis, contact ACGIH<sup>®</sup> Staff.</li> <li>Use Cancer as a TLV<sup>®</sup> Basis only if it drives the TLV<sup>®</sup> Basis. In this case, specify the type of cancer. Use “cancer” without a type in rare instances.</li> <li>The first TLV<sup>®</sup> Basis listing should be the primary effect.</li> <li>If there is already a Skin or SEN notation, use care in using as a TLV<sup>®</sup> basis, unless it’s the primary basis.</li> </ul>
<p><b>Chemical and Physical Properties</b></p> <ul style="list-style-type: none"> <li>Provide a brief text description of the chemical and physical forms of the substance (e.g., solid, liquid,</li> </ul>	<p>Log octanol/water partition coefficients (sometimes called log K o/w) should be included, if available. When there is more than one partition coefficient use</p>

## APPENDIX A

Section	Comments / Common Boilerplate
<p>color, composition, contaminants, decomposition products, and known odor or taste properties).</p> <ul style="list-style-type: none"> <li>• The text section is followed by a specific listing of properties, some examples of which are provided below. If some of the specific data are not available, do not list the subheading.               <ul style="list-style-type: none"> <li>• Molecular weight: XXX.XX</li> <li>• Specific gravity: X.XXX at XX°C</li> <li>• Melting point: (Centigrade)</li> <li>• Boiling point: (Centigrade)</li> <li>• Vapor pressure: Use torr and specify temperature (Centigrade)</li> <li>• Saturated Vapor concentration: (especially for compounds which will have an IFV endnote)</li> <li>• Flash point: (Centigrade)</li> <li>• Flammable limits: lower and upper</li> <li>• Autoignition temperature: (Centigrade)</li> <li>• Solubility:</li> <li>• Conversion factors at 25°C and 760 torr: X ppm = XX.X mg/m<sup>3</sup>, 1 mg/m<sup>3</sup> = X ppm</li> </ul> </li> </ul>	<p>the middle of the range. The best reference is: Leo A; Hansch C; Elkins D: Partition Coefficients and Their Uses. Chem Rev 71(6):525-616 (1971).</p> <p>A combination of the log K o/w and molecular weight of the chemical can be used to (very roughly) estimate skin permeability from an AQUEOUS solution. The best reference is: Potts RO; Guy RH: Predicting Skin Permeability. Pharm Res 9(5):663-669 (1992).</p> <p>List odor threshold, if available. Useful references include:</p> <p>AIHA: Odor Thresholds for Chemicals with Established Occupational Health Standards (1989).</p> <p>Amoore JE; Hautala E: Odor as an Aid to Chemical Safety: Odor Thresholds. J Appl Toxicol 3(6):272-90 (1983).</p> <p>Ruth JH: Odor Thresholds and Irritation Levels of Several Chemical Substances: A Review. Am Ind Hyg Assoc J 47:3, A-142 (1986).</p> <p>U.S. EPA: Reference Guide to Odor Thresholds for Hazardous Air Pollutants Listed in the Clean Air Act Amendments of 1990. U.S. Environmental Protection Agency, Washington, D.C., EPA/600/R-92/047.</p>

## APPENDIX A

Section	Comments / Common Boilerplate
<p><b>Major Sources of Exposure</b> Describe in text format where available-</p> <ul style="list-style-type: none"> <li>• How the substance is produced (e.g., methods of manufacture, by-product of...).</li> <li>• Uses.</li> <li>• Production volumes and estimated numbers of workers exposed.</li> <li>• Major routes of exposure associated with manufacture and use (what forms are encountered during use, e.g., vapor, dusts, aerosol, liquid, etc.).</li> <li>• Particle size issues and characterizations, if relevant.</li> </ul>	<p>Resources</p> <ul style="list-style-type: none"> <li>• Use EPA Section Interagency Testing Committee for estimated number of employees exposed. Include the date.</li> <li>• TSCA database – check for production volumes.</li> <li>• U.S. Geological Survey/Dept of Interior: <a href="http://minerals.usgs.gov/minerals/pubs/commodity/">http://minerals.usgs.gov/minerals/pubs/commodity/</a></li> </ul> <p>List tonnage and year, e.g., date from Department of Commerce via internet.</p>
<p><b>Animal Studies</b> This major heading and its subheadings describe the relevant <i>in vivo</i> and <i>in vitro</i> studies supporting assessment and derivation of the TLV®-TWA.</p>	<p>Detailed descriptions of animal toxicology studies are generally not required. However, if known, the minimum information for each study should include:</p> <ul style="list-style-type: none"> <li>• Species, sex, route and mode of administration (inhalation, oral gavage, oral diet, dermal, etc.), duration of dosing, specific doses tested, relevant toxic effects, No-Observed-Effect Levels (NOELs/NOAELs), Lowest-Observed-Effect Levels (LOELs/LO), and toxic responses at higher dose levels.</li> <li>• Mechanistic studies (e.g., animal model and pharmacokinetic relevance) that provide perspective for appropriate extrapolation of animal findings to humans.</li> <li>• Published expert reviews (IARC, WHO, U.S. EPA, U.S. NIOSH, etc.) that offer analysis of human relevance of animal studies.</li> </ul>
<p><b>Animal Studies:</b> <b>Acute (less than 2 weeks duration)</b> <b>INHALATION</b></p> <ul style="list-style-type: none"> <li>• As available, incorporate minimum information noted above in the animal studies comments column.</li> <li>• Describe LC<sub>50</sub> value(s) or equivalent indicator(s) of toxicity.</li> <li>• Describe minimum lethal concentrations / doses (LC<sub>Lo</sub>, LC<sub>50</sub>) and any reported clinical signs.</li> <li>• If no lethality found, indicate full range of concentrations, clinical observations, and NOEL and effect-level concentrations.</li> <li>• If relevant, include particle size characterization or lack thereof.</li> </ul> <p><b>DERMAL</b> Same as inhalation above. Include description of nature of applied substance (neat, concentration of solutions and vehicles, formulations, etc.)</p> <ul style="list-style-type: none"> <li>• Describe systemic toxicity resulting from skin absorption.</li> <li>• Describe specific toxicity to skin (irritation, burns, etc.);</li> </ul>	<p>For LD<sub>50</sub> and LC<sub>50</sub> studies, the results can usually be summarized in a single sentence such as:</p> <ul style="list-style-type: none"> <li>• The LC<sub>50</sub> for substance XXX ranged from 588 to 1004 mg/m<sup>3</sup> in mice and rats with signs of wheezing and coughing.</li> </ul>

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<p>include assessment (classification) of toxic response (non-irritant, type of irritant — corrosive).</p> <ul style="list-style-type: none"> <li>As available, incorporate minimum information noted above.</li> <li>Describe LD<sub>50</sub> value(s) or equivalent indicator(s) of toxicity.</li> <li>Describe minimum lethal doses (LD<sub>Lo</sub>, LC<sub>50</sub>) and any reported clinical signs.</li> <li>If no lethality found, indicate full range of doses, clinical observations, and NOEL and effect-level doses.</li> </ul> <p><b>SENSITIZATION</b> Include species, doses, routes of administration, protocol used, ancillary information (adjuvant used, etc.), end results (dose-response; NOEL, ancillary skin irritation, skin and/or respiratory sensitization).</p> <p><b>OTHER STUDIES</b> As available, include minimum information noted above for each of the relevant “other studies” described. Examples of potentially relevant “other studies” include:</p> <ul style="list-style-type: none"> <li>Eye irritation.</li> <li>Respiratory irritation RD<sub>50</sub> studies (measures sensory irritation).</li> </ul>	<p>Schaper M (1993): Development of a database for sensory irritants and its use in establishing occupational exposure limits. Am Ind Hyg Assoc J 54(9):488–544.</p>
<p><b>Animal Studies:</b></p> <p><b>Subchronic (&gt;2 weeks ≤ 3 months)</b></p> <ul style="list-style-type: none"> <li>Same information as acute studies.</li> <li>Organized by route of exposure.</li> </ul>	<ul style="list-style-type: none"> <li>Subchronic studies are often the driver of the TLV<sup>®</sup> Basis.</li> <li>Give the strain and #s of animals if more than one similar study.</li> <li>Report studies low to high dose.</li> <li>Give LOEL/LOAEL, NOEL/NOAEL, if can.</li> <li>Summarize by kind of study, species, route, dose, # applications, and results.</li> </ul>
<p><b>Animal Studies:</b></p> <p><b>Chronic/Carcinogenicity (&gt; 3 months ≤ animal lifetime)</b></p> <ul style="list-style-type: none"> <li>Same information as above, organized by route of exposure.</li> <li>If you include any carcinogenicity classification determinations published by internationally recognized review bodies, make sure that the date is cited (IARC, U.S. NTP, U.S. EPA, MAK, etc.).</li> </ul>	<p>The 2-year bioassay is considered the “gold standard.”</p>

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<b>Section</b>	<b>Comments / Common Boilerplate</b>
<p><b>Animal Studies:</b></p> <p><b>Genotoxicity</b>                      The results should be described briefly and may be useful in the selection of the carcinogenicity category. Therefore, the results of <i>in vitro</i> and <i>in vivo</i> studies should be described very briefly.</p>	<p>Example:                      Several genotoxicity studies have been reported but were generally negative. Positive findings were noted only in <i>in vitro</i> studies using the Ames test, forward mutation assays, and xx only with metabolic activation. Negative findings were found in other <i>in vitro</i> studies and <i>in vivo</i> studies using the micronuclei test in mice and chromosomal aberrations in rats.</p>
<p><b>Animal Studies:</b></p> <p><b>Reproductive/Developmental Toxicity</b>                      This section should briefly describe adverse changes, presenting reproductive studies first, followed by developmental toxicity studies. The studies should also be organized by route of exposure with relevant routes of exposure, such as inhalation and skin, described first.</p>	<p>For most substances, this section does not drive the TLV<sup>®</sup> Basis, but may be used as a modifier of the TLV<sup>®</sup> Recommendation.</p>

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Section	Comments / Common Boilerplate
<p><b>Absorption, Distribution, Metabolism, and Excretion (Toxicokinetics)</b> Describe the animal studies first followed by human studies within each section.</p> <ul style="list-style-type: none"> <li>• Absorption information may be available for oral, inhalation, and/or dermal exposures.</li> <li>• Distribution of the chemical or metabolites into blood fluids and various tissues should be described.</li> <li>• Metabolism of the chemical in the liver or at the route of entry should be described. Important metabolites and their relative toxicity should be described, if known.</li> <li>• Elimination of the chemical or metabolites via exhalation, urine, or feces should be described (half-lives or clearance values).</li> <li>• If a PB-PK or classical compartmental model is available for the chemical it should be referenced.</li> <li>• Dose-response evaluations with relevance to the TLV<sup>®</sup> should be included.</li> </ul>	<ul style="list-style-type: none"> <li>• Studies may address the amount of chemical absorbed when the chemical is given orally and an absorption fraction for inhalation. For dermal absorption studies, the order of preference for absorption information is 1) permeability coefficient (kp), 2) flux, and 3) percentage of applied dose absorbed.</li> <li>• Distribution of the chemical should be described if known, the octanol/water partition is important information that helps understand distribution. Any tissues that act as a "sink" for the chemical (such as fat) could be identified.</li> <li>• It may be important to identify types of metabolism the chemical undergoes, i.e., P<sub>450</sub> (with specific isozyme if known) or glutathione conjugation. If metabolism is significant, a diagram could be useful. Relative toxicities of the parent and metabolite may be important.</li> <li>• Primary route of elimination should be identified, e.g., exhalation, urine, or feces. Relative amounts eliminated through each route may be important, if known. Elimination half-lives may be useful.</li> <li>• References to published compartmental or physiologically based pharmacokinetic models (PB-PK) should be cited if known. Details are not necessary but number of compartments for classical and general type of model for PB-PK (stochastic, flow or diffusion limited) could be described). The exposure route(s) that the models have been validated for should also be described.</li> <li>• Dose-response evaluations such as slope factors (for cancer) or model-based extrapolations of NOELs may be available.</li> </ul>
<p><b>Human Studies</b> Studies among occupationally exposed populations should be given priority for detailed description.</p> <ul style="list-style-type: none"> <li>• The organization of the human studies and the order in which they are presented will vary greatly between substances based on the critical effects and the amount of human data available.</li> <li>• If there are relatively few human studies it may be appropriate to describe all in detail. However, if there are many studies only the key studies for deciding the TLV<sup>®</sup> or the notations should be described in detail.</li> <li>• Where there are many epidemiological studies, use the boilerplate which states that many studies exist, but only discuss those used in the derivation of the TLV<sup>®</sup>.</li> <li>• Cite available process-related occupational exposure findings, even if dose-response is not available.</li> </ul>	<ul style="list-style-type: none"> <li>• Key studies are generally those which: <ol style="list-style-type: none"> <li>1. Evaluate health effects in relation to level of exposure (i.e., assess dose-response)</li> <li>2. In the absence of #1, provide some information on the level of exposure</li> <li>3. Cohort and case-control studies that contribute to assigning the cancer notation</li> <li>4. Studies of groups of people that evaluated respiratory and skin sensitization</li> <li>5. Studies that demonstrate systemic toxicity following dermal exposure</li> </ol> </li> <li>• For key studies, include the following information: <ol style="list-style-type: none"> <li>1. Type of study (e.g., cross sectional, case control, cohort, experimental, or other);</li> <li>2. Study population (include location of study, number of participants, and pertinent demographic information);</li> <li>3. Measurements of disease or death (e.g., death certificates, physical examination, laboratory analyses, questionnaires, etc);</li> <li>4. Measurements of exposure (e.g., laboratory</li> </ol> </li> </ul>

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	<p>analyses, air measurements, questionnaires, etc);</p> <ol style="list-style-type: none"> <li>5. The analysis, if not obvious based on the description of results</li> <li>6. The results relevant to setting the TLV<sup>®</sup> or assigning notations. Include the measure of health effect (i.e., odds ratio, relative risk, standardized mortality/morbidity ratio [SMR], cross- shift change in physiologic measurement, etc...) and the confidence intervals or p values. Present the results for critical health effects regardless of the statistical significance</li> <li>7. Other potential causes of the health effect considered (e.g., age, sex, smoking, and other exposures present) and whether the results were adjusted for these factors.</li> </ol> <ul style="list-style-type: none"> <li>• Non-key studies are those that describe health effects without any indication of level of exposure, those that describe health effects that occur at levels well above the proposed TLV<sup>®</sup>, those that indirectly contribute to our understanding of the critical effects. For non-key studies it is acceptable to summarize the results of studies and to cite reviews from the peer-reviewed literature or those conducted by public agencies that are widely available (i.e., ATSDR, IARC).</li> <li>• If there are many human studies with similar designs, make tables of the data where possible to summarize the key information listed above.</li> </ul>
<p><b>TLV<sup>®</sup> Chronology</b></p> <ul style="list-style-type: none"> <li>• The purpose of this section is to describe only the historical and/or pending/actionable activities (dates) associated with the TLV<sup>®</sup> <i>Documentation</i>. It is not intended to describe the detailed history of actions completed on the <i>Documentation</i>. ACGIH<sup>®</sup> Staff completes this section. See example below:</li> <li>• Because the author knows exactly where inserts have been made, Staff would appreciate guidance in identifying the new section(s) and reference(s) when a <i>Documentation</i> is updated, but the TLV<sup>®</sup> remains the same. This precludes a word-for-word proofing of an updated <i>Documentation</i> against its original. The “Comments/Common Boilerplate” column at right provides examples.</li> </ul> <p>19XX: <i>Proposed</i>: TLV<sup>®</sup>–TWA, XX ppm            19XX–present: TLV<sup>®</sup>–TWA, XX ppm            20XX: <i>Documentation</i> revised. Describes current <i>Documentation</i> revision efforts; use only when <i>Documentation</i> is revised but TLV<sup>®</sup> is not changed.            20XX: <i>Proposed</i>: TLV<sup>®</sup>–TWA, XX ppm, notation(s). If necessary, describe published (NIC) <i>Proposed</i></p>	<p>Example statements to insert in historical section of TLV<sup>®</sup> <i>Documentation</i> when there are no changes to the TLV<sup>®</sup> or Notations:</p> <ul style="list-style-type: none"> <li>• _____ (cite year of change): TLV Basis update to <i>Documentation</i> _____ (cite year), retaining adopted TLV(s)<sup>®</sup> and notation(s)...see section (cite section), paragraph _____ (cite paragraph number)...cite additional sections/paragraphs as appropriate).               <ul style="list-style-type: none"> <li>▪ Example: 2004: TLV<sup>®</sup> Basis update to <i>Documentation</i> 2001, retaining adopted TLV(s)<sup>®</sup> and notation(s) – see Summary; Animal Studies; and TLV<sup>®</sup> Recommendation.</li> </ul> </li> <li>• _____ (cite year of change): Editorial clarification made to <i>Documentation</i> _____ (cite year), retaining adopted TLV(s)<sup>®</sup> and notations see section (cite section), paragraph _____ (cite paragraph number)...cite additional sections/paragraphs as appropriate).</li> <li>• _____ (cite year of change): New information and reference(s) added to <i>Documentation</i> _____ (cite year), retaining adopted TLV(s)<sup>®</sup> and notations; see section (cite section) and new reference # _____ (cite reference numbers). Cite additional</li> </ul>

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Section	Comments / Common Boilerplate
<p>TLV<sup>®</sup> values and associated notations that have not been adopted by ACGIH<sup>®</sup>.</p>	<p>sections/paragraphs/new references as appropriate).</p> <ul style="list-style-type: none"> <li>▪ Example: 2004: New information and references added to <i>Documentation</i> 1996, retaining adopted TLV(s)<sup>®</sup> and notation(s) – see Animal Studies <i>Acute</i>, paragraphs two and four; Animal Studies Chronic/Carcinogenicity, paragraph one; Human Studies <i>Cancer</i>, paragraphs one, two, and six; new Human Studies <i>Reproduction</i> section; and new references 14,23, and 31.</li> <li>• _____ (cite year of change): New section(s) and reference(s) added to <i>Documentation</i> _____ (cite year), retaining adopted TLV(s)<sup>®</sup> and notations; see section (cite section) and new reference # _____ (cite reference numbers), cite additional sections/paragraphs/new references as appropriate.</li> <li>• _____ (cite year of change): Comprehensive revision of <i>Documentation</i> _____ (cite year), retaining adopted TLV(s)<sup>®</sup> and notations or</li> <li>• The TLV<sup>®</sup> <i>Documentation</i> has been updated and revised to reflect new scientific data, but the TLV<sup>®</sup> recommendation has not been changed.</li> </ul>

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<p><b>References</b> List in alphabetical order.</p> <p>Unlike the reference style of the past, use a modified MedLine style, e.g., all extraneous punctuation and capitalization are eliminated in journal citations (e.g., article titles are treated as a sentence).</p>	<p><b>Journal Articles:</b> List all authors when there are four or less. If five or more, list the first three, followed by "et al."</p> <p>Davies CN: Dust sampling and lung disease. <i>Br J Ind Med</i> 9:120 (1952).</p> <p>Deskin R; Bursain SJ; Edens FW: The effect of chronic manganese administration on some neurochemical and physiological variables in neonatal rats. <i>Gen Pharmacol</i> 12:279–280 (1981).</p> <p>Wagner WD; Fraser DA; Wright PG; et al.: Experimental evaluation of the threshold limit of cristobalite — calcined diatomaceous earth. <i>Am Ind Hyg Assoc J</i> 29:211–221 (1968).</p> <p><b>Online Citations:</b> U.S. National Library of Medicine: Substance name. In: Hazardous Substances Data Bank. Toxicology Data Network (TOXNET). Online at: <a href="http://toxnet.nlm.nih.gov/">http://toxnet.nlm.nih.gov/</a> Accessed: xx/xx/xx</p> <p>U.S. Environmental Protection Agency: Integrated Risk Information System (IRIS) Substance File: Substance name. U.S. EPA, Washington, DC (1996). Online at: <a href="http://www.epa.gov/iris/subst/0373.htm">http://www.epa.gov/iris/subst/0373.htm</a> Accessed: xx/xx/xx</p> <p>U.S. National Toxicology Program: Substance name. In: Testing Information and Study Results, Results and Status. Online at: <a href="http://ntp-server.niehs.nih.gov/main_pages/NTP_ALL_STDY_PG.html">http://ntp-server.niehs.nih.gov/main_pages/NTP_ALL_STDY_PG.html</a> Accessed: xx/xx/xx</p> <p><b>Federal Agency Publications:</b> U.S. National Toxicology Program: Toxicology and Carcinogenesis Studies of Manganese (II) Sulfate Monohydrate (CAS No. 10034-96-5) in F344/N Rats and B6C3F1 Mice (Feed Studies) Technical Report No. 428. DHHS (NIH) Pub. No. 94-3159. NTP, Research Triangle Park, NC (1993).</p> <p>U.S. Agency for Toxic Substances and Disease Registry, Toxicological Profile for Manganese (Update). U.S. Department of Health and Human Services, ATSDR, Atlanta, GA (September 2000).</p> <p><i>With Author(s)</i> Anderson HA; Dally KA; Hanrahan LP; et al.: The Epidemiology of Mobile Home Formaldehyde Vapor Concentration and Residents' Health Status. Pub. No. EPA-905/1-83-001. U.S. Environmental Protection Agency, Washington, DC (1983).</p>

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Section	Comments / Common Boilerplate
	<p><b>Books:</b> <i>Sections/Chapters with Specific Author(s)</i></p> <p>Beliles RP: The metals. In: Patty's Industrial Hygiene and Toxicology, 4th ed., Vol. 2C, Toxicology, pp. 2106–124. Clayton GD; Clayton FE (Eds.). John Wiley &amp; Sons, New York (1994).</p> <p>Matanoski GM: Risk of cancer associated with occupational exposure in radiologists and other radiation workers. In: Cancer Achievements, Challenges, and Prospectives for the 1980s, Vol. 1, pp. 241–254. J.H. Burchenal JH (Ed.). Grune and Stratton, New York (1981).</p> <p><i>With Editor(s) Only</i></p> <p>Hathaway GJ; Proctor NH; Hughes JP (Eds.): Substance name. In: Proctor and Hughes' Chemical Hazards of the Workplace, 4th ed. Van Nostrand Reinhold, New York (1996).</p> <p>Lide DR; Frederikse HPR (Eds.): Substance name. In: Handbook of Chemistry and Physics, 77th ed. CRC Press, Boca Raton, FL (1996).</p> <p><b>Proceedings:</b></p> <p>Andersen I: Formaldehyde in the indoor environment — health implications and the setting of standards; and discussion. In: Indoor Climate: Effects on Human Comfort, Performance and Health in Residential, Commercial, and Light Industry Buildings, pp. 65–87. Fanger PO; Volbjorn O (Eds.). Proceedings of the First International Indoor Climate Symposium, Copenhagen, August 30–September 1, 1978. Danish Building Research Institute, Copenhagen (1979).</p> <p>Failing A; Knecht U; Woitowitz HJ: Biological monitoring of a standardized tetrahydrofuran exposure (in German). In: Proceedings of the 34th Meeting of the German Society of Occupational and Environmental Medicine in Wiesbaden, pp. 375-376. Kessel R (Ed.). Gentner Verlag, Stuttgart (1994).</p> <p>Boyle MJ: Tropic of Capricorn — assessing hot process conditions in northern Australia. In: Proceedings of 14th Annual Conference, pp. 54–57. Australian Institute of Occupational Hygienists, Adelaide (1995).</p> <p>Budd GM: Stress, strain and productivity in Australian wildfire suppression crews. In: Proceedings of the Society of American Foresters National Convention, San Francisco, pp. 119–123. SAF, Bethesda, MD</p>

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	<p>(1991).</p> <p>Industrial Health Foundation: Proceedings of a Symposium on an Industry Approach to Chemical Risk Assessment: Caprolactam and Related Compounds as a Case Study. IHF, Arlington, VA (1984).</p> <p><b>CD-ROMs:</b>            U.S. National Institute for Occupational Safety and Health: Criteria for a Recommended Standard: Occupational Exposure to Substance name. DHEW (NIOSH) Pub. No. Fill in the number from original reference; 19???. In: NIOSH Criteria Documents Plus CD-ROM. DHHS (NIOSH) Pub. No. 97-106; NTIS Pub. No. PB-502-082. National Technical Information Service, Springfield, VA (1997).</p> <p>Merck &amp; Co., Inc.: Substance name. In: The Merck Index, 12th edition on CD-ROM, Version 12:1. S Budavari, M O'Neil, A Smith, et al., Eds. Chapman &amp; Hall, New York (1996).</p> <p>Lewis Sr, RJ (Ed.): Hawley's Condensed Chemical Dictionary, 13th ed. In: Comprehensive Chemical Contaminants Series CD-ROM. Van Nostrand Reinhold, New York (1997).</p>

### Selecting an Appropriate TLV®

1. Decide critical health effects – those that occur at the lowest exposure levels and will drive the TLV® number.
2. Decide which type of TLV® (TWA, STEL, C) is warranted.
  - a. Review definitions to select the appropriate form of a TLV®.
  - b. Although the type of available data may affect this, in general:
    - **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 without 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

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necessarily protect against these effects if the daily TLV<sup>®</sup>-TWA is exceeded. The TLV<sup>®</sup>-STEL usually supplements the TLV<sup>®</sup>-TWA where there are recognized acute effects from a substance whose toxic effects are primarily of a chronic nature; however, the TLV<sup>®</sup>-STEL may be a separate, independent exposure guideline.

- **Threshold Limit Value-Ceiling (TLV<sup>®</sup>-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.
  - c. Some substances may fit into more than one category.
  - d. In exceptional cases, other schemes may be chosen, if clearly described and supported in the *Documentation*.
3. Decide the value of the TLVs<sup>®</sup>
    - a. Develop a summary table of key studies and findings as they relate to the TLV<sup>®</sup>. From this information, select a point at which it appears no adverse health effects are likely to occur in nearly all workers.
    - b. Describe the relationship of recommended TLV<sup>®</sup> to known human or animal toxicity responses.
    - c. Describe how the TLV<sup>®</sup> reflects uncertainties in the available data. If the uncertainty in the available data is high, so state. Using professional judgment, adjust the TLV<sup>®</sup> to reflect an appropriate degree of conservatism.
    - d. When animal data are the primary source, uncertainty considerations include:
      - The quality of the studies
      - Available exposure information
      - Use language that avoids referring to these adjustments as “factors”.
      - The TLV<sup>®</sup> number should have only one significant figure, unless your data are very precise.
      - If route-to-route conversion factors are used, be explicit/transparent.
      - See Annex C for conversion guides.
  4. Consider whether the substance may occur or be generated in the form of an aerosol.
    - a. If so, it may be necessary to develop a TLV<sup>®</sup> for an aerosol form in addition to the vapor form.
      - It may be necessary to determine separate TLVs<sup>®</sup> for these two forms.
      - If the TLV<sup>®</sup> number is the same for both forms, then a designation of both vapor and aerosol must be made.
    - b. If the TLV<sup>®</sup> may refer to an aerosol, one of the three PSS-TLV<sup>®</sup> designations must be selected. In general, the following relationship will determine which one:

In which part of the respiratory system can deposition or absorption lead to health effects?	PSS
Throughout respiratory system	Inhalable
Lung airways and gas exchange	Thoracic
Gas exchange areas	Respirable

- c. Exposure data that include particle size distributions may be useful in helping identify the PSS.
5. Identify appropriate notations and explain reasoning for their selection

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- a. Carcinogenicity designation (see Appendix A in the *TLVs<sup>®</sup> and BEIs<sup>®</sup>* book)
  - b. SEN (see Definition in *TLVs<sup>®</sup> and BEIs<sup>®</sup>* book)
  - c. Skin (see Definition in *TLVs<sup>®</sup> and BEIs<sup>®</sup>* book)
6. Author should insert the boilerplate language if and when particular TLV<sup>®</sup> forms are not recommended or certain notations are not assigned. ACGIH<sup>®</sup> Staff will insert, if missing. See TLV<sup>®</sup> *Documentation Outline* above for recommended boilerplate.

## APPENDIX A:

### Annex A

## TLV<sup>®</sup> Documentation Template

This *Documentation* is in DRAFT format, and its content is subject to change. We are providing it as such because we believe it is important to provide access as early as practical to the data and technical information cited herein which are the basis for the proposed TLV(s)<sup>®</sup>, BEI(s)<sup>®</sup>, and related notations.

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Chemical name – page 1

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(Note: Header should be on every page.)

## CHEMICAL NAME

CAS number:

*Synonyms:*

Molecular formula:

Chemical structure:

TLV<sup>®</sup>-TWA,

TLV<sup>®</sup>-STEL,

TLV<sup>®</sup>-Ceiling,

Skin

Sensitizer (SEN)

Carcinogenicity Classification

### TLV<sup>®</sup> Recommendation

A TLV<sup>®</sup>-TWA<sup>®</sup> of XX mg/m<sup>3</sup>, measured as inhalable particulate matter (or IFV, or R, T), is recommended for occupational exposure to XXXX.

If there is a BEI<sup>®</sup> state: XXXX is a substance for which *Biological Exposure Indices* (BEIs<sup>®</sup>) have been recommended (see BEI<sup>®</sup> *Documentation* for XXXX).

If there are no other notations recommended state: Sufficient data were not available to recommend a TLV<sup>®</sup>-STEL. Sufficient data were not available to recommend a Skin or SEN notation.

TLV<sup>®</sup> Basis

## **APPENDIX A:**

### **Annex A**

#### **Chemical and Physical Properties**

Molecular weight:  
Specific gravity:  
Melting point: °C  
Boiling point: °C  
Vapor pressure: °C  
Saturated vapor concentration:  
Flash point: °C  
Flammable limits:  
Autoignition temperature: °C  
Solubility:  
Octanol/water partition coefficients:  
Conversion factors at 25°C and 760 torr:

#### **Major Sources of Occupational Exposure**

##### **Animal Studies**

##### *Acute/Subacute*

**ORAL**

**DERMAL**

**INHALATION**

**SENSITIZATION**

**OTHER STUDIES**

##### *Subchronic*

##### *Chronic/Carcinogenicity*

##### *Genotoxicity*

##### *Reproductive/Developmental Toxicity*

**APPENDIX A:  
Annex A**

**Absorption, Distribution, Metabolism, and Excretion**

**Human Studies**

**TLV<sup>®</sup> Chronology**

**References**

**APPENDIX A:**

**Annex B**

**TLV® Basis Table**

Terms used as the TLV® Basis with abbreviations (last updated October, 2006).

<b>Group</b>	<b>Effect Name</b>	<b>Abbreviation (if necessary)</b>
<b>Cancer</b>	Bladder cancer Cancer Kidney cancer Larynx cancer Leukemia Liver cancer Lung cancer Mesothelioma Nasal cancer Prostate cancer Sino-nasal cancer Skin cancer Testicular cancer Upper respiratory tract cancer	Bladder cancer Cancer Kidney cancer Larynx cancer Leukemia Liver cancer Lung cancer Mesothelioma Nasal cancer Prostate cancer Sino-nasal cancer Skin cancer Testicular cancer URT cancer
<b>Entire Human Body</b>	Body weight effects Cytochrome oxidase inhibition Fatigue Malaise Metabolic acidosis Muscular stimulation Nausea Simple asphyxia Stimulation of basal metabolism	Body weight Cyto oxid inhib Fatigue Malaise Metabolic acid Muscular stim Nausea Asphyxia Basal metab
<b>Upper Respiratory Tract</b>	Anosmia Halitosis Larynx metaplasia Upper respiratory tract inflammation Upper respiratory tract irritation	Anosmia Halitosis Larynx metaplasia URT inflam URT irr
<b>Lower Respiratory Tract</b>	Asthma Berylliosis Beryllium sensitization Bronchitis Bronchopneumonia Lower respiratory tract irritation Lung damage Metal fume fever Pneumoconiosis Pulmonary edema Pulmonary emphysema Pulmonary fibrosis Respiratory sensitization Pulmonary function Pneumonitis	Asthma Berylliosis Beryllium sens Bronchitis Bronchopneumonia LRT irr Lung dam Metal fume fever Pneumoconiosis Pulm edema Pulm emphysema Pulm fibrosis Resp sens Pulm func Pneumonitis
<b>Autonomic Nervous System</b>	Autonomic nervous system impairment Cholinesterase inhibition	ANS impair Cholinesterase inhib
<b>Central Nervous System</b>	Auditory nerve impairment	Audit nerve impair

**APPENDIX A:**

**Annex B**

<b>Group</b>	<b>Effect Name</b>	<b>Abbreviation (if necessary)</b>
	Central nervous system convulsion Central nervous system impairment Cochlear impairment Cognitive decrements Dizziness Headache Neurotoxicity Ocular nerve damage Vestibular impairment Visual impairment	CNS convul CNS impair Cochlear impair Cognitive decrement Dizziness Headache Neurotoxicity Ocular nerve dam Vestibular impair Visual impair
<b>Peripheral Nervous System</b>	Peripheral nervous system impairment Peripheral neuropathy	PNS impair Periph neuropathy
<b>Gastrointestinal System</b>	Gastrointestinal damage Gastrointestinal irritation	GI dam GI irr
<b>Cardiac System</b>	Cardiac sensitization Cardiac system impairment Myocardial effect	Card sens Card impair Myocard
<b>Vascular System</b>	Vascular system impairment Vasoconstriction Vasodilation	Vasc sys impair Vasoconstriction Vasodilation
<b>Hematopoietic System</b>	Anemia Carboxyhemoglobinemia Coagulation problems Hematologic effects Hemolysis Hemosiderosis Hypoxia/Cyanosis Increased platelet count Inhibition of heme synthesis Leucopenia Methemoglobinemia Nitrosylhemoglobin formation Porphyrin effects	Anemia COHb-emia Coagulation Hematologic Hemolysis Hemosiderosis Hypoxia/Cyanosis Incr platelets Inhib heme synth Leucopenia MeHb-emia Nitrosyl-Hb form Porphyrin
<b>Immune System</b>	Immune system impairment	Immun impair
<b>Reproductive System</b>	Female reproductive system damage (excluding teratogenic effects and embryonic and fetal damage) Male reproductive system damage Pregnancy loss Reproductive effects Testicular damage	Female repro  Male repro Pregnancy loss Repro Testicular dam
<b>Eye</b>	Cataract Corneal necrosis Eye damage Eye irritation Eye photosensitization	Cataract Corneal necrosis Eye dam Eye irr Eye photosen
<b>Skin</b>	Alopecia Argyria Chloracne Dermatitis Skin damage Skin irritation	Alopecia Argyria Chloracne Dermatitis Skin dam Skin irr

**APPENDIX A:**

**Annex B**

<b>Group</b>	<b>Effect Name</b>	<b>Abbreviation (if necessary)</b>
	Skin photosensitization Skin sensitization	Skin photosen Skin sens
<b>Teeth</b>	Dental erosion Dental fluorosis	Dental erosion Dental fluorosis
<b>Bones</b>	Bone damage Fluorosis	Bone dam Fluorosis
<b>Thyroid</b>	Thyroid effect	Thyroid
<b>Liver</b>	Hepatic necrosis Liver damage	Hepatic necrosis Liver dam
<b>Spleen</b>	Spleen damage	Spleen dam
<b>Kidney/Urinary tract</b>	Bladder irritation Glomerular damage Kidney damage Kidney irritation Tubular damage	Bladder irr Glomerular dam Kidney dam Kidney irr Tubular dam
<b>Embryo or fetus</b>	Embryo/fetal damage Teratogenic effect	Embryo/fetal dam Teratogenic
<b>Genetic effects</b>	Mutagenic effect	Mutagenic

***Alphabetical Listing***

Alopecia
Anemia
Anosmia
Argyria
Asthma
Auditory nerve impairment
Autonomic nervous system impairment
Berylliosis
Beryllium sensitization
Bladder cancer
Bladder irritation
Body weight effects
Bone damage
Bronchitis
Bronchopneumonia
Cancer
Carboxyhemoglobinemia
Cardiac sensitization
Cardiac system impairment
Cataract
Central nervous system convulsion
Central nervous system impairment
Chloracne
Cholinesterase inhibition
Coagulation problems
Cochlear impairment
Cognitive decrements
Corneal necrosis
Cytochrome oxidase inhibition

## APPENDIX A:

### Annex B

Dental erosion
Dental fluorosis
Dermatitis
Dizziness
Embryo/fetal damage
Eye damage
Eye irritation
Eye photosensitization
Fatigue
Female reproductive system damage (excluding teratogenic effects and embryonic and fetal damage)
Fluorosis
Gastrointestinal damage
Gastrointestinal irritation
Glomerular damage
Halitosis
Headache
Hematologic effects
Hemolysis
Hemosiderosis
Hepatic necrosis
Hypoxia/Cyanosis
Immune system impairment
Increased platelet count
Inflammation
Inhibition of heme synthesis
Kidney cancer
Kidney damage
Kidney irritation
Larynx cancer
Larynx metaplasia
Leucopenia
Leukemia
Liver cancer
Liver damage
Lower respiratory tract irritation
Lung cancer
Lung damage
Malaise
Male reproductive system damage
Mesothelioma
Metabolic acidosis
Metal fume fever
Methemoglobinemia
Muscular stimulation
Mutagenic effect
Myocardial effect
Nasal cancer
Nausea
Neurotoxicity
Nitrosylhemoglobin formation
Ocular nerve damage

## APPENDIX A:

### Annex B

Peripheral neuropathy
Peripheral nervous system impairment
Pneumoconiosis
Pneumonitis
Porphyrin effects
Pregnancy loss
Prostate cancer
Pulmonary edema
Pulmonary emphysema
Pulmonary fibrosis
Pulmonary function
Reproductive effects
Respiratory sensitization
Simple asphyxia
Sino-nasal cancer
Skin cancer
Skin damage
Skin irritation
Skin photosensitization
Skin sensitization
Spleen damage
Stimulation of basal metabolism
Teratogenic effect
Testicular cancer
Testicular damage
Thyroid effect
Tubular damage
Upper respiratory tract cancer
Upper respiratory tract inflammation
Upper respiratory tract irritation
Vascular system impairment
Vasoconstriction
Vasodilation
Vestibular impairment
Visual impairment