



Center for the
Polyurethanes Industry

**Guidance Document
for the
Purpose of Determining Occupancy Classifications
Involving the Storage, Use and Handling
of
MDI and PMDI**

August 2014

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Abbreviations Used in this Document:

- **MDI** - Monomeric methylene diphenyl diisocyanate (CAS # 101-68-8) - Monomeric MDI is a white to yellowish solid at room temperature with no odor. A spill involving a 55-gallon drum of monomeric MDI at room temperature will not vaporize.
- **PMDI** - Polymeric methylene diphenyl diisocyanate (CAS# 9016-87-9) - Polymeric MDI is a mixture of monomeric MDI with higher molecular weight oligomers of MDI. It is a dark brown liquid at room temperature and may have a slight musty odor. Polymeric MDI is more commonly used in the industry.
- **CAS Number** - Chemical Abstracts Service registry numbers assigned by the Chemical Abstracts Service of the American Chemical Society.
- **LC50** - Median (50%) lethal concentration (LC) when administered by continuous inhalation for one hour (or less if death occurs) to albino rats weighing between 200 and 300 grams each.
- **SDS - Safety Data Sheet** - Safety Data Sheets (SDSs) (formally known as MSDS) communicate the hazards of hazardous chemical products. The content and style is governed by 29CFR 1910.1200.
- **IFC - International Fire Code** - Contains regulations to safeguard life and property from fires and explosion hazards.

Purpose of this Document:

This document was developed for the purpose of assisting Building and Fire Code Officials in their assessment as to the appropriate occupancy classification in facilities storing and utilizing MDI and PMDI.

Occupancy Classification Situation:

In the Toxicological Information section on many of the Safety Data Sheets (SDSs) (formally known as Material Safety Data Sheets (MSDSs) for MDI and PMDI, the LC50 value meets the criteria in the International Building Code and International Fire Code (IFC) for a toxic or highly toxic hazardous material classification.

When classified as toxic or highly toxic hazardous materials, some code officials have required that the storage and use of MDI and PMDI in buildings, rooms, and areas be classified as a Group H-4 (high-hazard) occupancy when quantities exceed the Maximum Allowable Quantities per Control Area.

Statements in the Code Commentary Editions for both the International Building Code and IFC, however, imply that the classification of chemicals as toxic and highly toxic based solely on information provided on the SDSs are not definitive in determining whether those materials are considered as toxic or highly toxic by the codes. This is because the method of testing for the LC50 concentration level stated in the SDSs are not consistent with the form in which MDI and PMDI are used in industry and storage, airborne concentrations found in the LC50 study are not present in real world scenarios.

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Both the codes and the code commentary indicate that while the classification system is basically simple in application, any hazard evaluation that is required for the precise categorization of a material shall be performed by experienced person as deemed, technically competent by the code official.

The hazard evaluation and analysis for the toxicity classification of MDI and PMDI is explained in the remainder of this document. Further, the evaluation and analysis presented is based on considerable testing and analysis by experienced and technically competent research toxicologists. A review of the data critical to classification of both MDI and PMDI under the IFC is available in Appendix A of this document.

Background/Rationale:

Manufacturers of MDI and PMDI are obligated to identify and report relevant toxicity information, such as an LC50 value, on their SDSs. However, in order to conduct the required tests to determine the LC50 value for MDI and PMDI, it is necessary to create an artificially controlled atmosphere, as discussed below. Because of this artificially controlled atmosphere, the properties of the tested MDI and PMDI are no longer representative of the materials as stored and used in typical industrial and storage occupancies.

At room temperature, MDI is a solid and PMDI is a viscous liquid material with a low vapor pressure. For example, the vapor pressure of PMDI is 2.33×10^{-6} at 68°F (20°C).

The LC50 test protocol requires that samples of MDI and PMDI are generated into a respirable aerosol. This is accomplished by heating the substance to 176°F (80°C) and using a high-pressure nebulizer in order to create a stable atmosphere that contains a uniform distribution of particles that are <4 microns in diameter. The aerosol then either flows through a confined chamber containing 200 to 300-gram albino rats (whole body exposure), or passes over only the breathing zone of restrained rats (nose-only exposure). Exposures typically range between one and four hours, then the observation of potential lethal effects of exposure continues for 14 days. The test protocol cannot be conducted without these elaborate and technically difficult procedures because a sufficiently high aerosol concentration is not achievable via other methods. The aerosol size is important, as only small particles are not trapped by the nose and enter the lungs. Test protocols mandate the particle size, and non-compliance invalidates the study results.

Thus, the problem with developing a manipulated respirable aerosol that meets the testing criteria for the LC50 study to be valid is that it does not depict the typical storage and use conditions of MDI and PMDI in Group F (factory/industrial) or Group S (storage) type occupancies.

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Common Uses of MDI and PMDI:

The common uses of MDI and PMDI in Group F industrial and Group S storage type occupancies are:

Group F Occupancies:

- Pure MDI is used in the production of a variety of polyurethane products like elastomers, sealants, adhesives, and coatings.
- PMDI is a highly versatile product used to produce a wide variety of rigid, flexible, semi-rigid and polyisocyanurate thermoset foams.
- PMDI is also used to produce foam packaging systems.

Group S Occupancies:

- MDI may be stored as a solid in sealed drums at room temperature.
- MDI may also be stored as a liquid in heated sealed drums or bulk storage tanks at atmospheric pressure. The manufacturers' recommended storage temperatures typically range (for MDI as a liquid) between 104°F (40°C) and 113°F (45°C).
- PMDI is stored as a viscous liquid in sealed drums, intermediate bulk containers (tote tanks), and bulk storage tanks at room temperature and atmospheric pressure. The manufacturers' recommended storage temperatures typically range between 50°F (10°C) and 86°F (30°C).

Analysis:

The common uses of MDI and PMDI indicated in the previous section of this document represent forms of MDI and PMDI that are not heated and generated into a respirable aerosol, differentiating it from those conditions used to derive the LC50 values in laboratory experiments.

Conclusion:

The classification of MDI and PMDI, may not be based strictly on the LC50 value indicated in SDSs, is not applicable if MDI and PMDI is stored and used in a form that does not represent equivalent atmospheres to those utilized during LC50 test protocols.

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International Building Code (2000, 2003, 2006, 2009 & 2012 Editions)
Code Commentary Edition for the International Building Code (2003, 2006, 2009, & 2012 Editions)

International Fire Code (2000, 2003, 2006, 2009 & 2012 Editions)
Code Commentary Edition for the International Fire Code (2003, 2006, 2009, & 2012 Editions)

NFPA 704, *Standard System for the Identification of Hazards of Materials for Emergency Response* (2007 & 2012 Editions)

Guidance Documents on the Properties of MDI and PMDI by Anne H. Chappelle, Ph.D., DABT; October 30, 2013 & November 26, 2013

Letter to Building Plan Reviewer/Inspector; City of Rochester Hills, Michigan from Lee Salamone, Senior Director, Center for the Polyurethanes Industry; November 16, 2012

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Commentary on the Toxicity Classification of PMDI in the International Fire Code published in Alliance for the Polyurethanes Industry; October, 2002

Model for Predicting Environmental Exposure from an MDI Spill by W. P. Robert and G. T. Roginski (BASF Corporation) in 35th Annual Polyurethane Technical/Marketing Conference; October, 9-12, 1994

Guidance Document for the Purpose of Determining Occupancy Classifications Involving the Storage, Use and Handling of MDI and PMDI

ACC Legal Notice:

This guidance document was prepared by the American Chemistry Council's Center for the Polyurethanes Industry. It is intended to provide general information to Building and Fire Code Officials in their assessment as to the appropriate occupancy classification in facilities storing and utilizing MDI and PMDI under the International Fire Code. It is not intended to serve as a substitute for in-depth training or specific handling or storage requirements, nor is it designed or intended to define or create legal rights or obligations. It is not intended to be a "how-to" manual, nor is it a prescriptive guide. All persons involved in handling and storing MDI and PMDI materials have an independent obligation to ascertain that their actions are in compliance with current federal, state and local laws and regulations and should consult with legal counsel concerning such matters. The guidance is necessarily general in nature and individual companies may vary their approach with respect to particular practices based on specific factual circumstance, the practicality and effectiveness of particular actions and economic and technological feasibility. Neither the American Chemistry Council, nor the individual member companies of the Center for the Polyurethanes Industry of the American Chemistry Council, nor any of their respective directors, officers, employees, subcontractors, consultants, or other assigns, makes any warranty or representation, either express or implied, with respect to the accuracy or completeness of the information contained in this guidance document; nor do the American Chemistry Council or any member companies assume any liability or responsibility for any use or misuse, or the results of such use or misuse, of any information, procedure, conclusion, opinion, product, or process disclosed in this guidance document. NO WARRANTIES ARE GIVEN; ALL IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE ARE EXPRESSLY EXCLUDED.

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Appendix A: Review of data critical to classification of both MDI and PMDI under
the International Fire Code (IFC)

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Executive Summary:

Monomeric methylene diphenyl diisocyanate (MDI) and Polymeric MDI (PMDI) are chemicals found in commerce which are valued for their reactive isocyanate groups. These reactive groups are also responsible for adverse health effects observed in cases of overexposure. While lethal dose (*i.e.*, LC50/LD50) tests are generally intended to compare and rank the potency of substances, these values are often included as part of the data set used to derive storage and emergency response procedures. An experimentally derived, reliable and valid one-hour LC50 study is available for monomeric MDI and the data is applicable for PMDI. The one-hour LC50 (rat, dust/mist) is >2240 mg MDI/m³.

This document describes and reviews data critical to understanding the derivation of the LC50 for MDI and PMDI, as well as the use of this data to derive the recommended classification of both MDI and PMDI under the International Fire Code (IFC). Specific points include:

- Definition and description of MDI and PMDI.
 - The difference between pure MDI and PMDI is explained.
 - Why human health data for MDI or PMDI may be considered applicable to both chemicals.
- Explanation of Lethal Dose (LD) and Lethal Concentration (LC) testing methods.
 - Perspective on traditional use of the data to rank/compare toxicities.
 - Difficulties with directly extrapolating the data to human exposure scenarios.
- History of LC50 testing with MDI/PMDI, including the derivation of the 4-hour and 1-hour LC50 value. Methodological details are explained.
- Summary of relevant regulatory initiatives that use LC50 data for MDI and PMDI

We will demonstrate that, the acute inhalation toxicity of PMDI and MDI is considered to be low. In order to truly evaluate the risk of acute exposure to inhaled MDI/PMDI, it is important to determine whether a respirable atmosphere can be generated during regular use, including emergency situations. Based on the technical difficulties involved in generating respirable atmospheres in a well-controlled laboratory scenario, and the understanding of the physical characteristics of PMDI/MDI in normal workplace use and anticipated storage incidents, the risks to humans are expected to be low. The hazards of MDI/PMDI are fully characterized and are adequate to protect workers and Emergency Responders in the unlikely event of an incident

Definition and Description of MDI and Polymeric MDI:

In commerce, a majority of methylene diphenyl diisocyanate (MDI) is sold either as “pure” or “monomeric MDI” (typically containing greater than 95% of the 4,4'-MDI isomer) or as “polymeric MDI” (PMDI). PMDI is a complex mixture of monomeric MDI isomers and higher homologues (Figure 1). The letter ‘n’ in Figure 1 ranges from 0 upwards, meaning that in PMDI, polyisocyanates with 3 or more isocyanate groups (-NCO) per molecule are present. Table 1 lists the standard compositions of monomeric MDI and PMDI. Typically, PMDI consists of ~50% 4,4'-MDI, and ~50% higher homologues (30% triisocyanate, 10% tetra-isocyanate, 5% penta-isocyanate and 5% higher homologue). The pure MDI is produced only by distillation of PMDI.

Figure 1. Structure of monomeric MDI isomers and PMDI

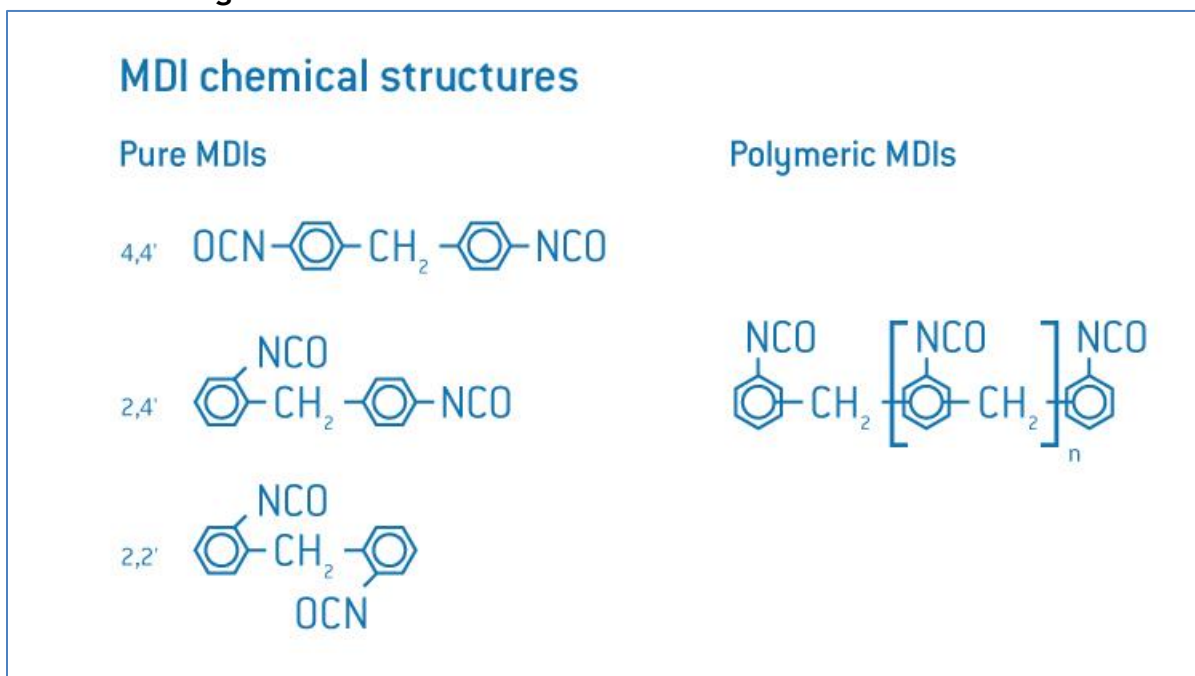


Table 1. Composition of MDI and PMDI

	Monomeric MDI CAS # 101-68-8	Polymeric MDI CAS # 9016-87-9
4,4'-MDI	>97%	40-50%
2,4'-MDI	1.5-2.5%	2.5-4%
2,2'-MDI	>0.5%	0.1-0.2%
Homologues	-	50-60%

Source: EC, 2006

To describe the relationship of monomeric MDI and PMDI through analogy, consider pure MDI to be sugar and PMDI to be molasses. At room temperature, both sugar and pure MDI are white solids, while PMDI and molasses are viscous, dark brown liquids. The primary component of molasses is sugar, but there are many other components in molasses. Just as both molasses and sugar are used as sweeteners; pure MDI and PMDI have the exact same isocyanate functional unit ($R-N=C=O$). The isocyanate portion of the molecule is responsible for the key functionality of this class of compounds. Isocyanates are electrophiles, and as such they are reactive toward a variety of nucleophiles including alcohols, amines, water and even themselves. When MDI reacts with a compound containing two or more alcohol (or “hydroxyl”) groups (a “polyol”), polymer chains are formed, making a polyurethane. The high reactivity of the isocyanate unit can also be responsible for the adverse health effects associated with overexposure.

Because PMDI contains at least 50% MDI monomer and the longer-chain homologues are very similar chemically, data gained on any mixture of MDI and PMDI, regardless of relative isomer proportions, as well as on any individual isomer, are considered representative for the purpose of hazard evaluation and risk assessment (EC, 2005). US agencies such as the EPA, OSHA, and NIOSH, and other global agencies such as the European Chemicals Bureau (ECB) and the World Health Organization (WHO) utilize this category approach for assessing MDI.

Lethal Dose / Lethal Concentration Testing:

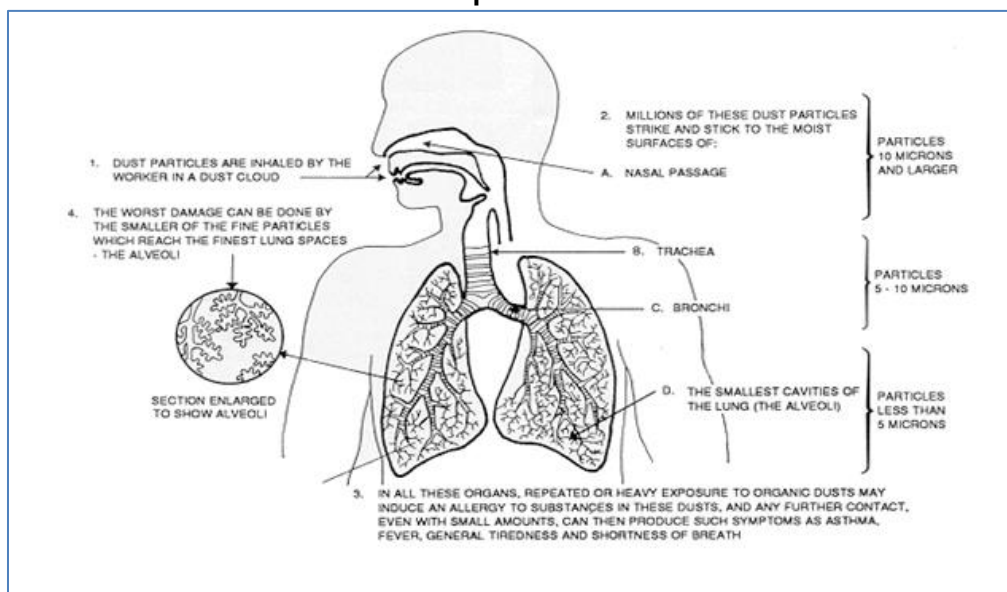
The Lethal Dose (LD) test is the amount of a material, given all at once (oral and dermal routes are most common), which causes the death of a certain percentage of a group of test animals. The LD50 is the death of 50% of the animals and is one way to measure the short-term poisoning potential (acute toxicity) of a material. Because different chemicals cause different toxic effects, comparing the toxicity of one to the toxicity of another is difficult. For example, one could measure the amount of a chemical that causes kidney damage, but not all chemicals will damage the kidney. One could say that nerve damage is observed when 10 grams of chemical A is administered, and kidney damage is observed when 10 grams of chemical B is administered. However, this information does not tell us if A or B is more toxic because we do not know which damage is more critical or harmful. Therefore, to compare the toxic potency or intensity of different chemicals, researchers must measure the same effect. LD50 tests use death as an “effect target,” which allows for comparisons between chemicals that impact the body in very different ways.

One of the primary technological hurdles in testing compounds via the inhalation route is in the generation of the test atmosphere. For gasses and vapors, generating an atmosphere is relatively straightforward - substances are volatilized, and then diluted to the appropriate concentration by adding a known concentration of air into a special chamber where the test animals will be exposed. In these experiments, the concentration that kills 50% of the animals is called an LC50. Results should include the test animal, form of the material (dust/mist, gas, vapor) and the duration of the exposure, e.g., LC50 (rat) - 1000 ppm/ 4hr (gas) or

LC50 (mouse) - $5\text{mg}/\text{m}^3$ / 2hr (dust/mist). However, for materials that are not volatile, generating the appropriate atmosphere is more difficult. Rodents can only breathe through their nose, and their nose is efficient at scrubbing (removing) large particles from inspired air. So, although there may be many techniques to create atmospheres (using different jets and nozzles, adjusting airflow, adding heat), the atmosphere has to be manipulated to the point where the average size of the particle is small enough to not be scrubbed out by the nose and hence are inhaled. This allows LC50 values to be compared between substances. Thus, the intrinsic hazard of an atmosphere tested in a LC50 test, does not necessarily represent an atmosphere that can be obtained without significant manipulation and effort and may not necessarily occur outside the laboratory.

Characterization of the particles in the atmosphere intended for inhalation aids in the understanding of the potential hazards. Particles greater than 10 microns (μm) in diameter are generally filtered out in the nose and upper respiratory tract (Figure 2), while smaller particles are able to penetrate deeper into the lung. Gasses and vapors, which are not limited by the physics of particle size, are more likely to penetrate the deep lung and alveoli.

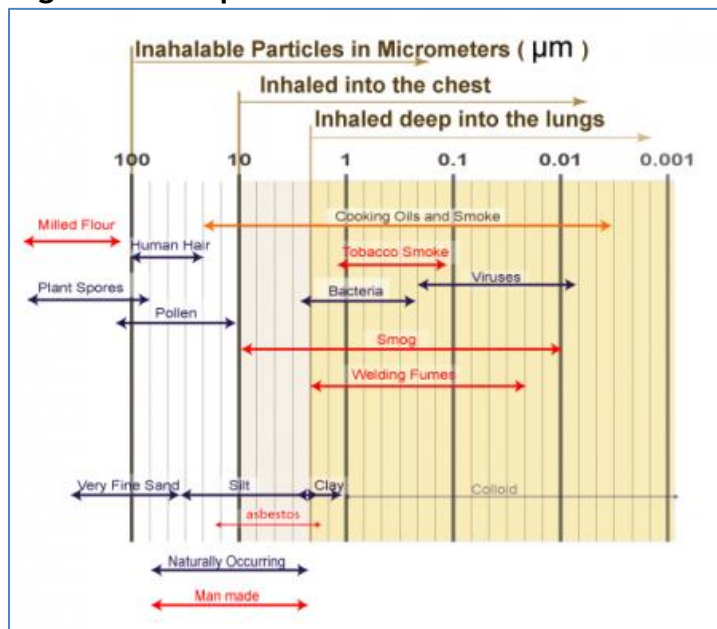
Figure 2. Schematic of the Human Lung indicating where particles of different sizes are deposited.



Source: Ontario Ministry of Agriculture, Food and Rural Affairs,
<http://www.omafra.gov.on.ca/english/livestock/swine/facts/93-003f1.gif>

A generalization of relative inhalable particle sizes in relation to deposition in the lung is presented as Figure 3. Typical 4-hour inhalation studies (OECD, 1981; OPPTS, 1988) require most of the particle sizes for dusts/mists/aerosols to be between 1-4 μm (SOT, 1992). Studies for one-hour LC50 determinations are slightly different and require that 90% of particles be less than 10 μm in diameter (DOT, 1994; NFPA 704, 1996).

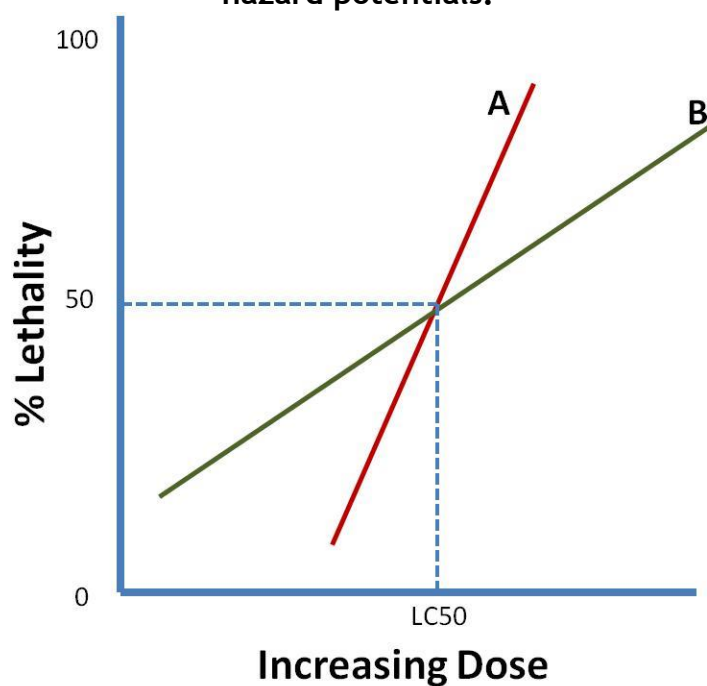
Figure 3. Comparison of Inhalable Particle Sizes



Source: Erin Rasmussen, <http://stoves.bioenergylists.org/content/particle-size-breathable-particles>

The LC test is used to Rank and Compare Toxicities: Substances are often compared, or ranked against each other based on their LC50, which can be a useful metric. However, when extrapolating the intrinsic chemical hazard to estimate risk to humans, more data is needed. Relying solely on LC50 values is an oversimplified approach because the LC50 is simply a single point on the dose-response curve that represents the potential of the compound to cause death. When assessing chemical safety, it is more important to consider the entire set of data available including the threshold dose and the slope of the dose-response curve. The dose response curve shows how fast the response increases as the dose increases. For example, in Figure 4, the LC50 is the same for both compounds A and B, but compound B is lethal to more animals at a lower dose, is therefore more potent and would be considered more toxic than compound A. However, due to the steeper slope of compound A, the range of the dose that results in lethality is much narrower than compound B. Theoretically, compound A may be a more significant hazard than compound B.

Figure 4. Graphical representation of two compounds with the same LC50, but different hazard potentials.



History of Lethal Concentration Testing with MDI and PMDI:

As PMDI is a liquid at room temperature, it tends to be the material that is used in toxicity tests. PMDI has a very low saturated vapor pressure concentration (SVC) (3 ppb [part per billion], or 0.00003 mg/L, at 20°C, Allport *et al.* 2003), and no toxicological effects were observed after inhalation exposure to animals at the SVC (Allport *et al.* 2003). There has been debate whether inhalation toxicity studies with MDI/PMDI should use vapors or an aerosol. For workers, exposures are in the low ppb range since the occupational exposure limit ceiling is 20ppb, or 0.0002 mg/L. Based on the SVC it can be presumed that pure MDI is present in the vapor phase (the SVC of 4,4'-MDI is about 6 ppb, or 0.00006 mg/L, at 20°C). However, to perform LC50 toxicity tests, exposure concentrations above the PMDI SVC are needed, and in addition the OECD guideline (OECD, 1981) which governs the testing protocol demands a highly respirable aerosol for inhalation testing. The only way to achieve such high concentrations would be to generate PMDI condensation aerosols, so both aerosol and vapor would have been present at the higher concentrations for the toxicity studies (Pauluhn, 2008).

PMDI four-hour LC50: In the United States, the Hazard Communication Standard (HCS) uses Appendix A to classify inhalation hazards (29 CFR 1910.1200). To comply with the HCS and classify hazards, a four-hour LC50 value is required (29CFR 1910.1200); however, a one-hour value is needed for evaluations related to storage and emergency responders. The four-hour LC50 value determined experimentally for PMDI was 0.49 mg/L with a 95 percent confidence interval of 0.38 to 0.64 mg/L (Appelman and de Jong, 1982; also reported in Reuzel *et al.*, 1994). This atmosphere was generated by exposing rats to a “mono-disperse,” respirable aerosol; that is, one with a specific, narrow range of particle sizes in order to make it completely respirable (“respirable” is the size range able to be inhaled and retained in the lungs) (Hussain *et al.*, 2011). These aerosol droplets were created using a high-pressure nebulizer, the sole purpose of which was to generate an atmosphere for the laboratory experiments. According to protocol, as described in the 1982 Appelman and de Jong study, the 95% of the mean diameter of the particles was <5µm. However, generating a vapor concentration of such an aerosol of PMDI that was sufficiently high and the correct particle size to produce a one-hour LC50 value was impossible at the time, as the temperature of the vapor would place the animals under heat-related stress. In lieu of having an experimentally derived value, “Haber’s Rule” (see description later) was applied to convert the four-hour value to the one-hour value. To do this, the four-hour value was simply multiplied by four, resulting in a one-hour value of 1.96 mg/L PMDI. Considering the 95 percent confidence limits, the range for the one-hour LC50 value would be 1.52 - 2.56 mg/L PMDI, which brings into question the validity of the “highly toxic” category for PMDI because the confidence intervals span two classification brackets. Only a single experiment was run to obtain the four-hour value, and no attempts have been made to create a concentration of 1.96 mg/L PMDI to verify the calculated value experimentally. Although it may be useful to compare these PMDI LC50 values in mg/L to MDI LC50 values in ppb, it is inappropriate because of the form of the material was different in each scenario (dust/mist vs. condensation aerosol), and the temperature of the material.

Haber's Rule should not be used to extrapolate a one-hour value: Haber's rule is a mathematical statement of the relationship between the concentration of a gas and how long the gas must be breathed to produce death or other toxic effects. Basically, for any gas, $Cxt = k$, where C is the concentration of the gas (mass per unit volume), t is the amount of time necessary to breathe the gas in order to produce a given toxic effect, and k is a constant, depending on both the gas and the effect. Thus, the simplified rule states that doubling the concentration will halve the time, for example. Work from ten Berge et al (1986) suggests Haber's rule should be modified to $C^nxt = k$. The value of the exponent (n) quantitatively defines the relationship between exposure concentration and exposure duration for a given chemical and for a specific health-effect endpoint; the empirically derived value of n ranges from 0.8 to 3.5. Without knowing the value of the exponent, it is inappropriate to arbitrarily assign a value of one. In conclusion, Haber's rule can only be valid if the work has been performed to identify the value of the exponent (n); since this has not been done for PMDI, it is not appropriate to extrapolate the four-hour LC50 to a one-hour LC50.

Why did it take until 2003 to generate a one-hour LC50? The 1982 Appelman and de Jong study that derived the four-hour LC50 for PMDI was intended to be a range finding study for a chronic study (Reuzel et al, 1994). Technical limitations in aerosol generation precluded the generation of a one-hour value until the work of Pauluhn in 2003. Thus, until 2003, the accepted LC50 value for PMDI was 490 mg/m³, 0.490 mg/L, PMDI (4 hour, rat, aerosol), and the extrapolated one-hour LC50 was 1.96 mg/L PMDI. This derivation was consistent with guidance from NFPA 704 (2012) and other standard hazard derivation methods. As the data for PMDI is applicable to pure MDI, if a LC50 value was needed for risk assessment or hazard classification purposes, the PMDI value was listed as a surrogate for a pure MDI value. Since that time, it has been demonstrated that Haber's Rule is not appropriate for extrapolating the PMDI four-hour value to a one-hour value.

Experimentally producing a One-Hour LC50: Due to the previously mentioned limitations in generating a stable atmosphere of PMDI at the levels required for a one-hour LC50, advances in aerosol generation technology allowed the use of pure MDI in a one-hour LC50. As previously stated, as pure MDI comprises approximately 50% of the commercially available PMDI mixture, and various regulatory bodies (eg EC, 2005) have states that data can reasonably be applied to either material. Pauluhn (2003) was able to generate a high and temporarily stable atmosphere of pure MDI using special aerosol generation equipment (a modified BGI 6-nozzle collision nebulizer that produced an average particle diameter of 4.9µm, meeting the aerosol size requirements of the OECD 403, EU Directive 92/69/EEC, OPPTS 870.1300 and NFPA 704 guidelines). The one-hour LC50 (rat, aerosol) was greater than 2240 mg/m³, (>2.2 mg/L) resulting in a No Observed Adverse Effect Level (NOAEL) of >2240 mg MDI/m³ air (>2.2 mg/L). As this was an experimentally derived value, this one-hour LC50, along with other relevant data on the toxicity of inhaled MDI should be used for IFC classification. For hazard classification purposes under 29 CFR §1910.1200, four-hour values should be used.

Applicability of the LC50 Value to Extrapolate Human Risk:

LC50 values are useful for comparing the rank order of potency of materials that are of near identical composition (e.g., which have the same particle size which contributes to delivered dose). One-hour LC50 values represent a guide by which acute toxicity can be evaluated in light of the potential risk of exposure to emergency response workers. Although death is the endpoint that is measured in LC50 studies, other clinical signs should also be considered. In the Pauluhn study (2003), a single hour exposure to extraordinarily high levels of respirable particles resulted in clinical signs associated with irritation (labored breathing pattern, breathing sounds, nasal discharge, etc.) and no injury was noted upon pathological examination of the surviving rats after the study. Only a single rat succumbed to the exposure. Clinical signs reported in the four-hour LD50 studies were similar to the one-hour studies, in that labored respiration was also observed. Animals that died after exposure died within two days after the termination of the exposure period. Exposures to a concentration of MDI or PMDI at the SVC would not be expected to cause toxicity. In summary, clinical signs in both the MDI and PMDI acute inhalation studies were similar, and were related to lung overload and irritation. The acute risk to humans is clearly understood, and is directly related to the amount of particles less than $<5\mu\text{m}$ that can reach the lower lung.

The low inhalation hazard of MDI/PMDI results in classification as “low toxicity” by various agencies:

Although MDI/PMDI is recognized as a respiratory sensitizer (ACGIH, 2013), the low volatility and physical properties contribute to it being generally recognized as a low hazard/risk. Examples of regulatory agency classifications are provided for comparison.

Transportation: Even though spills during transport of MDI/PMDI do occur on occasion, the DOT and UN TGD in 1994 declassified MDI/PMDI from transport regulation as UN Class 6.1; Packing Group III. As 4,4'-MDI is regulated under the Clean Air Act (CAA), the classification NA 3082; Class 9 in quantities greater than 5000lbs 4,4'-MDI applies. Thus, PMDI falls under NA 3082, Class 9 when the 4,4'-MDI concentration is greater than 5000lbs. To be clear, MDI/PMDI is classified for transport only because of the CAA, not because of the human health hazards. This is further reinforced in Robert and Roginski (1994) which discusses the model for predicting occupational exposure limits (similar to the ACGIH TLV[®] TWA) from a 5, 50 and 250 gallon spill. The paper presents conclusions derived from the modeling that demonstrated that the diffusion of the MDI from the spill is slow, and exposure limit concentrations stay close to the surface of the spill and do not expand far from the edge of the spill. The study determined that most spills reported are contained and remediated soon after discovery. Under these conditions, it appears unlikely that respiratory protection would be required to prevent excessive employee exposure to MDI vapors emitted from the spill. The article goes on to state, “We would not, therefore, recommend respiratory protection” (Robert and Roginski, 1994).

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MDI/PMDI are not included under the OSHA PSM Standard or EPCRA: The notion that MDI/PMDI should be not categorized as “Highly Toxic,” is further supported by OSHA’s Process Safety Management (PSM) Standard and EPA’s Emergency Planning and Community Right to Know (EPCRA) Standard. The OSHA PSM standard contains requirements for preventing or minimizing the consequences of catastrophic releases of toxic, reactive, flammable, or explosive chemicals. These releases may result in toxic, fire or explosion hazards. Under EPCRA, EPA is required to publish a list of extremely hazardous substances with threshold planning quantities which would trigger planning in states and local communities. MDI and PMDI are not listed in either regulation and not covered by these standards.

NFPA 704: Not classifying MDI/PMDI as “Highly Toxic” is consistent with guidance from the NFPA 704, Standard System for the Identification of the Hazards of Materials for Emergency Response (1996) and other standard hazard derivation methods. The NFPA 704 Health Rating for MDI/PMDI is listed as a Level “2” and is defined as materials that, under emergency conditions, can cause temporary incapacitation or residual injury. This material is not expected to be lethal or cause serious or permanent injury under emergency conditions.

Conclusions:

In order to truly evaluate the risk of acute exposure to inhaled MDI/PMDI, it is important to determine whether an atmosphere containing a sufficient concentration of respirable MDI/PMDI aerosol can be generated in an emergency situation. Other documents also fully describe the expected difficulty in generating MDI/PMDI atmospheres in these conditions (Grand and Lichtenberg, 2002). Based upon the technical difficulty in generating respirable atmospheres in a well-controlled laboratory scenario (Pauluhn 2003), and the understanding of the toxicity of PMDI/MDI in the workplace and upset conditions, the risk to humans is expected to be low. The hazards of MDI/PMDI are fully characterized and the controls are adequate to protect workers and Emergency Responders in the unlikely event of an incident.

Appendix A Prepared By:

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