U.S. Department of Labor

Assistant Secretary for
Occupational Safety and Health
Washington, D.C. 20210

JUL 0 5 2011

MEMORANDUM FOR: SCOTT A. MASTEN, PhD, DABT
Director, Office of Nomination and Selection
National Toxicology Program
[Redacted]

07-11-11P03:47 RCVD

FROM: DAVID MICHAELS, PhD, MPH

SUBJECT: Request for Nomination to the National Toxicology Testing Program

The Occupational Safety and Health Administration (OSHA) nominates trimethylsilyldiazomethane (TMSD) to the National Toxicology Program for formal inhalational toxicologic testing. TMSD is a commercially available, synthetic methylating reagent used in organic synthesis. It is also used with gas chromatography to analyze various compounds, e.g. pesticides. TMSD was developed as a safer substitute for diazomethane, a highly explosive, toxic methylating reagent that causes severe pulmonary injury in humans.[1] TMSD is commonly described as "safe" in the scientific literature and widely regarded as nontoxic by professional chemists.[2] Of note, there are 57,980 chemists in the United States who work in either the manufacturing sector or professional, scientific and technical services.[3]

In 2008, OSHA investigated the death of a chemist who developed delayed pulmonary edema after he synthesized TMSD in ether, spilled 200-300 ml cc of the compound, and then cleaned the spill. His fatality was attributed to the inhalation of a "diazomethane compound" and his employer received an OSHA citation for lapses in Hazard Communication. The employer appeared to have followed industry standards in handling this substance. Therefore, OSHA did not issue a citation related to lapses in workplace safety.[4] In 2009, an abstract in Clinical Toxicology reported the death of another chemist in Canada. The second fatality was attributed to the inhalation of TMSD in hexane while working in a non-functioning fume hood.[5]

These cases have been reviewed by occupational medicine physicians from OSHA and the National Institute of Occupational Safety and Health (NIOSH) and by toxicologists from NIOSH, the Environmental Protection Agency (EPA), Public Health Service Commissioned Corps (USPHS) and the National Institute of Environmental Health Sciences (NIEHS). Although TMSD has been manufactured and used for decades, little is known about its toxicological effects. OSHA is aware of a study that evaluated the dermal toxicity of TMSD in rabbits and found it to be non-toxic at 1,010 mg/kg.[6] This study was commissioned following the 2008 fatality described above. No inhalational toxicology studies have been performed to date.

The material safety data sheet (MSDS) from Sigma-Aldrich for (Trimethylsilyl) diazomethane solution (revised 4-8-2011)[7] has the following toxicologic information:

**Oral LD50 -** no data available
**Inhalation LC50 -** no data available
**Dermal LD50 -** LD50 Dermal - rat - > 2,000 mg/kg
**Other information on acute toxicity -** no data available
**Skin corrosion/irritation -** no data available
**Serious eye damage/eye irritation -** Eyes: no data available
**Respiratory or skin sensitization -** no data available
**Germ cell mutagenicity -** no data available

According to Dr. Gregory Fritz, EPA, "It is the artifacts and potential byproducts from the methylation reaction mechanisms that may make acute inhalation exposure to TMSD equally problematic to diazomethane. The desired methylation reaction using TMSD requires the presence of methanol to optimize yield and produces a trimethylsilyl blocked methanol byproduct. One might envision this same mechanism in the lungs of a person exposed to TMSD via inhalation - not only will the chemical methylate reactive sites like diazomethane but the TMSD has the potential to coat the aviolae surfaces with trimethylsilyl groups as well."

**Nomination Elements**

i. **Chemical Identification**
   - **a. Chemical Abstracts Service (CAS) preferred name:** (Trimethylsilyl)diazomethane
   - **b. Synonym:** (Diazomethyl)trimethylsilane
   - **c. CAS Registry Number:** 18107-18-1
   - **d. Chemical Family:** Organosilane **Related compound:** diazomethane (see attachment D)
   - **e. Physical and chemical properties**
     - i. **Physical Description:** Trimethylsilyldiazomethane, 2M in diethyl ether: a straw to pale yellow-green liquid with mild odor.
     - ii. **Molecular Formula:** $C_4H_{10}N_2Si$ **Molecular Weight:** 114.22
     - iii. **Boiling Point:** 96º C **Freezing Point:** < 0º C
     - iv. **Solubility in water:** insoluble, reacts slowly
     - v. **Stability and Reactivity:** Stable in sealed containers stored under a dry inert atmosphere. Flammable; avoid contact with heat, sparks or open flame.
       Incompatibility: Avoid contact with alcohols, acids, oxidizers.
       Decomposes on exposure to light. Hazardous decomposition products: Organic acid vapors, NOx
     - vi. **Other Relevant Information:**
       **Vapor Density (air=1):** >1
       **Evaporation rate:** not determined
       **Flammability Limits:** not determined
       **Unusual Fire and Explosion Hazards:** Irritating fumes of organic acid

vapors may develop when material is exposed to water or open flame
**TLV:** not established
**OSHA PEL:** not established

**f. Commercial Product(s) composition:** Trimethylsilyldiazomethane, 2M in diethyl ether; Trimethylsilyldiazomethane, 2M in hexane

ii. **Production, Use, Occurrence, and Analysis**

**a. Production**

i. Source and synthesis:
ii. Current production and pathway

**b. Uses:** safe substitute for hazardous diazomethane, is useful both as a reagent for introducing a $C_1$ unit and as a C-N-N synthon for the preparation of azoles. (Shioiri, T.; Aoyama, T. Yuki Gosei Kagaku Kyokaishi 1986, 44, 149; Chem. Abstr. 1986, 104, 168525q.)

**c. Occurrence in the Environment:**

**i. Naturally occurring:** N/A –synthetic compound
ii. **Air, water, and soil:** Unknown

**d. Analysis**

iii. **Toxicology**

**a. Human case reports:** see attached OSHA case report; Canadian report

**b. Experimental animal studies:** Kuhn J, Acute Dermal Toxicity Study in Rabbits, report by Stillmeadow Incorporated submitted to Gelest, Inc., Morrisville, PA, March, 2008. Concluded that dermal exposure to compound is not toxic to humans.

**c. *In vitro* and other short-term tests:** N/A

**d. Other relevant information:** none known

iv. **Disposition and Structure-activity relationships**

**a. Absorption, distribution, metabolism and excretion:** Unknown

**b. Structure-activity correlations and considerations:** The MSDS from Sigma-Aldrich for (Trimethylsilyl) diazomethane solution (revised 4-8-2011) has the following warning "TMSD in alcoholic solvents under acidic or basic conditions can lead to the formation of diazomethane." This hazard was predicted by a software model, based on the molecular formula of TMSD.

v. **Ongoing Toxicological Studies in the Government, Industry, and Academia:** None known

vi. **Rationale for Recommendation and Suggested Studies**

The questions that remain regarding this chemical are:

1) Is TMSD significantly more hazardous than previously thought? Animal skin toxicologic studies show it to be relatively benign, but no inhalational toxicology has been done. This is a critically important first step, and we are petitioning the National Toxicology Program to conduct acute inhalational toxicity testing to determine the LD 50 for this material in animal models.

2) Alternatively, is the real issue that TMSD is unstable and forms diazomethane (known to cause inhalational deaths) much more readily than anticipated? This question only becomes relevant in the event adequate inhalational toxicity testing is conducted for TMSD and

determines it to be non-toxic by this route. If this is the case, what are the circumstances in which occupational usage of TMSD can be anticipated to generate diazomethane, and what workplace protections and warnings would be required?

In either case, additional data is necessary to perform risk assessment for exposed workers. Major revisions in laboratory protocols, worker training and hazard communication may be needed. Inhalational toxicology data from inhalational animal studies will be critical to the performance of this risk assessment.

**References**

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[1] Aoyama T, Shiori T. New Methods & Reagents in Organic Synthesis. TMSCHN2 as a Stable and Safe Substitute for Hazardous Diazomethane. Its Application to the Arndt-Eistert Synthesis. Chem Pharm Bull 1981; 29 (11): 3249-55.

[2] Bray P, interview with Barry Arkles, PhD, June 16, 2008.

[3] Bureau of Labor Statistics, http://data.bls.gov/oes/ using search for 'one occupation, multiple industries', May 18, 2011.

[4] Bray P, Internal OSHA Report to Investigation Case File on Fatality in Chemist, June, 2008.

[5] Murphy, et al, Fatal Occupational Exposure to Trimethylsilyldiazomethane, abstract in Clinical Toxicology, Vol 47, No. 7, 2009.

[6] Kuhn J**,** Acute Dermal Toxicity Study in Rabbits, report by Stillmeadow Incorporated submitted to Gelest, Inc., Morrisville, PA, March, 2008.

[7] Sigma-Aldrich, Material Safety Data Sheet for (Trimethylsilyl) diazomethane solution, Version 3.14, Revision Date 04/08/2011, product number 527254, accessed via sigma-aldrich.com, March 23, 2011.

**Attachments**

A. Description of fatality of U.S. chemist, 2008
B. Clinical Toxicology abstract concerning fatal occupational exposure in Canadian chemist, 2008.
C. Chemical and Engineering News article describing Canadian OSH penalty for workplace fatality, May 5, 2011
D. Information on Related Chemical, Diazomethane

**APPENDIX A**
**CASE REPORT**
**Office of Occupational Medicine:**
**Patricia Bray MD, MPH**
**Medical Officer**

**Background**
The decedent was a 24 year-old male chemist employed at Gelest, Inc, in Morrisville, PA. Gelest is a supplier of commercial and research quantities of organosilicon, tin, and germanium compounds as well as metal alkoxides, metal diketonates and silicones. He died on January 4, 2008 approximately 15 hours following his exposure to a chemical spill of trimethylsilyldiazomethane ($TMSCHN_2$) at Gelest, Inc. The Burlington County Medical Examiner reported the cause of death as "complications of a diazomethane compound exposure" following this spill. The fatality was deemed accidental by the medical examiner.

**Case Information Sources**
The field investigation, including laboratory reports, autopsy reports, procedure information and extensive interviews, is located in the formal case files and provided the basis for this report.

**Chemical Spill Incident**
On 1/04/2008 at approximately 7:00 AM the decedent started his shift. At approximately 7:30 AM he is engaged in the preparation of trimethylsilyldiazomethane. At this step, he was filtering a crude product of the compound in solution with diethyl ether. Because he was having difficulty with the transfer, he began working outside of the fume hood, a practice considered acceptable by the employer. The employer estimates the solution contained between 20% and 30% trimethylsilyldiazomethane. The decedent dropped the flask containing the solution, spilling approximately 300 ml to 400 ml on the workbench, floor, and himself. There was no known heat source, e.g. a hot plate, nearby. The decedent cleaned up the spill, using gloves and safety glasses as PPE. During the cleanup process, a supervisor observed that a spill had occurred. The decedent changed his pants, which had been contaminated by an unknown amount of the material, after between 5 and 20 minutes. He returned to work and finished his shift. His employer reported he was asked during the day if he was feeling well. The decedent is reported to have denied any symptoms.

The decedent returned home after work and complained to his girlfriend of "asthma-like" symptoms. He then went to bed for a nap. His mother later checked on him and noted that he looked and felt "awful". She summoned an ambulance. He was intubated on scene and transported to a local hospital, where his condition steadily declined, and he was pronounced dead at 10:52 pm the same evening.

Three co-workers who shared a common workspace of ~200 square feet, but who did not work in the immediate vicinity of the decedent's workbench, were referred by the employer for pulmonary evaluations, which were reportedly normal.

An autopsy report by the New Jersey Medical Examiner, Dr. Blanchard, reported the cause of death as "complications of a diazomethane compound exposure." Dr. Blanchard later reported that her findings were consistent with inhalational toxicity from a diazomethane compound. Dr.

Blanchard stated that she has "no doubt" that the cause of death was an occupational inhalation of a diazomethane compound. She stated that it is not possible, based on the autopsy findings, to identify exactly what the inciting chemical was, particularly given the multiple biochemical reactions that would have taken place internally. Specific autopsy findings included: mucosal erythema (redness) extending from the epiglottis and larynx to the bilateral bronchial system, marked congestion and edema in the lungs, heavy pleural and pericardial effusion, myocardial discolorization with subendocardial hemorrhage, and congestion of the spleen, liver, and kidneys. The autopsy findings were also significant for a 2 inch diameter circular zone of partly-adherent pink-tan serous fluid with underlying faint pink-tan, slightly shiny, discoloration of the skin at the lateral lower left leg. The overlying fluid washed off with water. Toxicology evaluation showed acetaminophen in blood and ethanol in the stomach, consistent with the history of using Nyquil for a "cold".

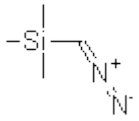
**Past Medical History**

The available medical records do not reveal a contributory past medical history. The decedent had experienced a recent upper respiratory infection. There is no description of asthma or use of inhaled medications. It should be noted that he was an athletically fit, semi-professional baseball player.

**Chemical Exposures and Health Effects**

Trimethylsilyldiazomethane ($TMSCHN_2$) is a methylating reagent used in organic chemical synthesis[1]. Trimethylsilyldiazomethane is considered to have significant advantages over its predecessor, diazomethane, because it is less thermally labile and less explosive[2]. Several of its chemical properties are summarized as follows[3]:

| | |
|---|---|
| **Molecular Formula:** | $C_4H_{10}N_2Si$ |
| **Formula Weight:** | 114.22 |



| | |
|---|---|
| **Registry number:** | 18107-18-1 |
| **MDL number:** | MFCD00053946 |
| **Density:** | 0.675 |
| **Boiling point:** | 96 °C |
| **Flash point:** | -23 °C |

[1] http://www.nlm.nih.gov/cgi/mesh/2008/MB_cgi?mode=&term=trimethylsilyldiazomethane

[2] Aoyama T, Shiori T. New Methods & Reagents in Organic Synthesis. TMSCHN2 as a Stable and Safe Substitute for Hazardous Diazomethane. Its Application to the Arndt-Eistert Synthesis. Chem Pharm Bull 1981; 29 (11): 3249-55

[3]http://www.acros.com/DesktopModules/Acros_Search_Results/Acros_Search_Results.aspx?search_type=CatalogSearch&searchstring=Trimethylsilyldiazomethane

Though trimethylsilyldiazomethane is considered less toxic than diazomethane, there is very little scientific information available about its toxicological properties. A search of the National Library of Medicine's (NLM) TOXNET yielded several publications regarding trimethylsilyldiazomethane uses, but none on its toxicity. Information about toxicity was not found in several standard reference textbooks[4,5,6] or upon the MEDLINE database using the keyword "trimethylsilyldiazomethane." The material safety data sheet (MSDS) from Sigma-Aldrich indicates that $TMSCHN_2$ toxicological properties have not been thoroughly studied, but that mucous membrane and upper airway irritation are possible. Additionally, Sigma-Aldrich's MSDS notes that $TMSCHN_2$ contact with water may liberate toxic gas[7].

According to Dr. Gregory Fritz, USEPA, "It is the artifacts and potential byproducts from the methylation reaction mechanisms that may make acute inhalation exposure to trimethylsilyldiazomethane equally problematic to diazomethane [the cancer concern from chronic exposure to TMSD was considered the same as exposure to diazomethane during the PMN review]. The desired methylation reaction using trimethylsilyldiazomethane requires the presence of methanol to optimize yield and produces a trimethylsilyl blocked methanol byproduct. One might envision this same mechanism in the lungs of a person exposed to trimethylsilyldiazomethane via inhalation - not only will the chemical methylate reactive sites like diazomethane but the trimethylsilyldiazomethane has the potential to coat the alveolar surfaces with trimethylsilyl groups as well. This type of reaction has been observed in the trimethylsilyldiazomethane bottles that were contaminated with phenol [from the Aldrich Co. manufacturing process], when trimethylsilyl- and methyl- ethers of the phenol impurity were found in significant quantities."

**Diazomethane (not on-site at Gelest)**
Although diazomethane was not used at Gelest, discussion of diazomethane is included here because it is chemically related to trimethylsilyldiazomethane and because of the similarity between known health effects of diazomethane and the pathologic findings noted on autopsy.

Diazomethane was discovered in 1894 by Pechman[8] and is a powerful methylating agent used in pesticide and pharmaceutical manufacture[9]. Diazomethane is an explosive gas that is heavier than air and may travel along the ground, causing a distant ignition. Occupational exposure limits are noted below.[10]

| | |
|---|---|
| ACGIH TLV | TWA 0.2 ppm |
| OSHA PEL | TWA 0.2 ppm |
| NIOSH REL | TWA 0.2 ppm |

[4] Lewis R. Sax's dangerous properties of industrial chemicals. 11th ed 2004.
[5] Bretherick L. Bretherick's handbook of reactive chemical hazards. 4th ed 1990.
[6] Ed. Sittig, M. "Diazomethane." Handbook of toxic and hazardous chemicals and carcinogens. Noyes: Park Ridge 1991. 539-42.
[7] http://www.sigmaaldrich.com/
[8] Cited from Lewis CE. Diazomethane Poisoning: Report of a Case Suggesting Sensitization Reaction. J Occ Med 1968; 10: 91-2
[9] Ed. Sittig, M. "Diazomethane." Handbook of toxic and hazardous chemicals and carcinogens. Noyes: Park Ridge 1991. 539-42.
[10] http://www.cdc.gov/niosh/ipcsneng/neng1256.html

Cases of diazomethane pneumonia have been reported[11], though other symptoms such as severe headache, muscle aches and fatigue have also been documented[12]. The TLV is selected as 0.2 ppm due to a mechanism of toxicity similar to that of phosgene[13],[14]. Diazomethane is felt to be extremely toxic and may result in severe lung damage, including pulmonary edema or pneumonitis that may not onset until hours or days after exposure[15].

**Diethyl Ether**

Diethyl ether is a multi-purpose solvent that can be used as a chemical reagent for various organic reactions[16]. Diethyl ether also has many other general uses, including general anesthesia.

Occupational exposure limits for diethyl ether are noted below[17]

| | |
|---|---|
| ACGIH TLV | 400 ppm, 1210 mg/m$^3$ TWA |
| OSHA PEL | 400 ppm, 1200 mg/m$^3$ TWA |
| NIOSH REL | No Established REL |
| NIOSH IDLH | 1900 ppm |

Diethyl ether is noted to have low acute toxicity to animals and humans[18]. Local toxicity consists of irritation to the eyes, nose and throat, whereas systemic toxicity is predominantly of narcosis[19]. Therefore, health effects occurring following a toxic exposure would be noted by observers without a significant delay. A literature search did relate the case of a 49 year-old Greek merchant who committed suicide by means of diethyl ether[20]. Another report described a 36 year-old woman who suffered acute respiratory distress syndrome after intravenous injection of ether into her intravenous access port.[21]

**Summary:**

The death of a 24 year-old chemist was an occupational fatality, related to the inhalation of a diazomethane substance, incurred during the course of a chemical synthesis. It is unknown whether the toxic inhalation was solely related to trimethylsilyldiazomethane exposure outside

[11] Ely T. Diazomethane Pneumonia. J Occ Med 1968; 10: 326

[12] Lewis CE. Diazomethane Poisoning: Report of a Case Suggesting Sensitization Reaction. J Occ Med 1968; 10: 91-2

[13] ACGIH. Diazomethane. In: Documentation of the threshold limit values for substances in workroom air. 3rd ed. Cincinnati, OH: American Conference of Governmental Industrial Hygienists, pp. 71-72.

[14] Potts AM, Simon FP, Gerard PW. Arch Biochem 1949; 24: 329. Cited from reference 13.

[15] Ed. Sittig, M. "Diazomethane." Handbook of toxic and hazardous chemicals and carcinogens. Noyes: Park Ridge 1991. 539-42.

[16] Ed. Sittig, M. "Ethyl Ether." Handbook of toxic and hazardous chemicals and carcinogens. Noyes: Park Ridge 1991. 775-77.

[17] http://www.osha.gov/dts/chemicalsampling/data/CH_240480.html

[18] Elvestad K, Engel Hansen L, Jelnes JE. Criteria Document for Diethyl Ether. CEC Occupational Exposure Limits 1993. Abstract accessed at http://toxnet.nlm.nih.gov/cgi-bin/sis/search/f?./temp/~Ng5hhP:4

[19] Ed. Sittig, M. "Ethyl Ether." Handbook of toxic and hazardous chemicals and carcinogens. Noyes: Park Ridge 1991. 775-77.

[20] Athanaselis S, Stefanidou M, Karakoukis N, Koutselinis A. Asphyxial Death by Ether Inhalation and Plastic-bag Suffocation Instructed by the Press and the Internet. J Med Internet Res 2002; 4 (3): e18

[21] Lambermont B, Dubois C, Fraipont V, et al. Near fatal respiratory distress following massive ether intravenous injection. Intensive Care Med 1998; 24: 624-5.

of the fume hood. It is possible that an unintended toxic byproduct evolved or that a synergistic effect occurred with another, unknown chemical. The clinical case reports and pathology reports are most consistent with delayed pulmonary edema following exposure to a diazomethane-like compound.

Abstracts of the 2009 North American Congress of Clinical Toxicology Annual Meeting, September 21–26, 2009, San Antonio, Texas, USA
Clinical Toxicology Aug 2009, Vol. 47, No. 7: 702–765.
http://informahealthcare.com/doi/full/10.1080/15563650903076924#h48

**48. Fatal Occupational Exposure to Trimethylsilyl-Diazomethane**

Murphy NG,[1] Varney SM,[2] Tallon JM,[1] Thompson JR,[1] Blanc PD.[3]
*[1]IWK Regional Poison Centre, Halifax, NS, Canada; [2]Rocky Mountain Poison & Drug Center-Denver Health, Denver, CO, USA; [3]Division of Occupational and Environmental Medicine, UCSF, San Francisco, CA, USA*.

*Background:* Diazomethane (DM) is a highly explosive, toxic methylating reagent causing severe pulmonary injury. Trimethylsilyl-diazomethane (TSDM) is a less explosive analogue that may not be less toxic. We describe the first documented case of a fatality following TSDM exposure. *Case report:* A 46 year-old male pharmaceutical chemist presented to the ED with progressive dyspnea. At noon on the prior day, as part of a chemical analysis, he had mixed 2 mL of acetone with 25 mL of L-Malic acid to which was added TSDM dissolved in n-hexane. After 1 hour this mix was combined with an inert gas and a small amount of methylene chloride under a fume hood that was later reported to be nonfunctioning. Although he experienced no immediate mucous membrane irritation, 8 hours post-exposure he developed cough, pleuritic chest pain, hemoptysis, and progressive shortness of breath; by 15 hours, he presented to the ED in respiratory distress, hypoxic (PaO2 67), hypercarbic (PaCO2 46), and acidemic (pH 7.26). A chest radiograph showed an acute lung injury pattern. By 23 hours he required intubation. At 26 hours post-exposure he developed profound bradycardia, refractory hypotension, and asystole. *Case discussion:* DM inhalation is known to cause fatal pulmonary edema without an immediate irritant prodrome and with a similar time course to this case. Structural modification of DM with an added trimethylsilyl group makes TSDM less explosive, but its propensity for lung injury is unclear. The chemical admixture as described in this case may have liberated nitrogen gas, but this should not have led to pulmonary injury; nitrogen dioxide should not have evolved. The toxicity may stem from residual DM present in the reagent or a direct effect of TSDM, its metabolites or breakdown products, or potential intracellular formaldehyde formation. *Conclusion:* The temporal relationship to exposure with inadequate ventilation and clinical effects similar to the analogue toxicant DM support a causal relationship between TSDM and acute lung injury. Additional safety data for this chemical is warranted, including experimental inhalation testing in animals.

http://pubs.acs.org/cen/news/89/i19/8919notw8.html
May 5, 2011

# Firm Fined For Chemist's Death

Safety: Sepracor Canada admits lack of lab ventilation in worker fatality case

**Jyllian N. Kemsley**

Michel Daigle

Drugmaker Sepracor Canada pleaded guilty in a Canadian court on May 2 to one charge of failing to provide proper workplace ventilation and will pay a US$47,000 fine for the death of chemist Roland Daigle.

Daigle died on Oct. 8, 2008, from lung failure after exposure to trimethylsilyldiazomethane (TMSD) in a quality control laboratory at the company's Windsor, Nova Scotia, facility.

The plea and fine were part of a deal in which the prosecutor dropped four other charges against the company, a subsidiary of Sunovion Pharmaceuticals. The other charges involved hazardous material training, use of personal protective equipment, and maintaining the security of the accident scene.

The day before he died, Daigle, 46, worked with TMSD, $(CH_3)_3SiCHN_2$, when lab fume hoods were not operating because of roof work. TMSD can be used as a methylating reagent in place of diazomethane, which is explosive. When inhaled, diazomethane can also cause fatal lung damage akin to that experienced by Daigle. It is unclear whether TMSD has the same toxic properties as diazomethane, or whether Daigle's lung damage was caused by breakdown products or residual diazomethane (*Clin. Toxicol.,* DOI: 10.1080/15563650903076924).

Daigle's family is disappointed that court proceedings did not explain why Daigle and coworkers worked in the lab without adequate ventilation, says a statement prepared by the family and obtained by C&EN from Lynda MacDonald, Daigle's sister. The statement adds that $47,000 "is but a slap on the hand of a giant pharmaceutical company."

"Sepracor Canada continues to mourn Roland Daigle's loss as well as to extend its sympathies to Roland's family and many friends," Sunovion spokeswoman Susan Adler says. Adler adds that the Nova Scotia Department of Labour & Advanced Education did not recommend any changes to work practices at the Windsor facility after department officials investigated Daigle's death.

At least one other chemist has also died in recent years from TMSD exposure. On Jan. 4, 2008, 24-year-old chemist Jason Siddell died after spilling TMSD at chemical company Gelest in Morrisville, Pa. The U.S. Occupational Safety & Health Administration cited Gelest for violating hazard communication standards, and the company paid a $1,500 fine.

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## Chemical Information on Related Compound, Diazomethane

(http://www.cdc.gov/niosh/idlh/334883.html)

**CAS number:** 334–88–3
**NIOSH REL:** 0.2 ppm (0.4 mg/m3) TWA
**OSHA PEL:** 0.2 ppm (0.4 mg/m3) TWA
**1993-1994 ACGIH TLV:** 0.2 ppm (0.34 mg/m3) TWA
**Description of Substance:** Yellow gas with a musty odor.
**LEL:** Unknown
**Original (SCP) IDLH:** 2 ppm
**Basis for original (SCP) IDLH:** The only available acute inhalation toxicity data concerning diazomethane is the statement by Patty [1963] that a 10-minute exposure to 175 ppm was lethal for cats [Flury and Zernik 1931]. This concentration is obviously too high for an IDLH. ACGIH [1971] reported that the toxicity of diazomethane seems comparable to that of phosgene. Therefore, the chosen IDLH is based on an analogy with phosgene, which has an IDLH of 2 ppm.
**References:**

1. ACGIH [1971]. Diazomethane. In: Documentation of the threshold limit values for substances in workroom air. 3rd ed. Cincinnati, OH: American Conference of Governmental Industrial Hygienists, pp. 71-72.
2. Flury F, Zernik F [1931]. Schädliche gase dämpfe, nebel, rauch- und staubarten. Berlin, Germany: Verlag von Julius Springer, p. 420 (in German).
3. Patty FA, ed. [1963]. Industrial hygiene and toxicology. 2nd rev. ed. Vol. II. Toxicology. New York, NY: Interscience Publishers, Inc., pp. 940, 2214.

## Human Case Reports

Stain JP, Nouvet G, Morere P. [Poisoning by diazomethane inhalation]. [Article in French]. Toxicol Eur Res. 1983 Sep;5(5):217-9.
A case of Diazomethane intoxication has been reported. Diazomethane is gaz commonly used by pharmacological and industrial chemist. This case of intoxication is rare, since only 15 other cases have been published up to now. A review of the literature leads leads describe the clinical feature of such an intoxication by gaz inhalation. When Diazomethane is inhaled it induces respiratory and general disorders. In some cases, it be fatal, and, in some other cases, when a second exposure happens, bronchial asthma may appear. Post mortem studies show pulmonary oedema lesions with important inflammatory reaction localized in the peribronchia. It must be emphasized that direct aggression is probably responsive of toxical discorders, but increase of the symptoms consecutive to a second exposure are related to allergical mechanisms. PMID: 6675207

LeWinn EB. Diazomethane poisoning; report of a fatal case with autopsy. Am J Med Sci. 1949 Nov;218(5):556-62. PMID: 15392072.