



# TMAH Safety in Academic Cleanrooms: Clinical, Industrial, and Toxicological Evidence

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# Re-evaluating TMAH Risk in Academic Cleanrooms

- *TMAH: Managing Hazards of Tetramethylammonium Hydroxide Solutions*  
**UGIM 2022 Symposium (Madison, WI)**  
**Speaker: Mary Tang**, Stanford University (Nanofabrication Facility).

Stanford's internal reevaluation of TMAH hazards, moving it from a standard corrosive category to a **high-hazard toxicant**



## Tetramethylammonium Hydroxide (TMAH) Fact Sheet

- TMAH can cause severe skin burns and has severe toxicity; these effects occur within minutes
  - *Any exposure must be washed in a safety shower immediately for 15 minutes, after which personnel should immediately seek medical attention*
- TMAH is a chemical commonly used in device fabrication
- Exposures to concentrations of TMAH as low as 2.38% have resulted in potentially fatal symptoms within one hour; concentrations of 25% have resulted in several deaths
- TMAH can be used safely with proper precautions, many of which are already standard in labs

<https://ehs.stanford.edu/reference/tetramethylammonium-hydroxide-tmah-fact-sheet>

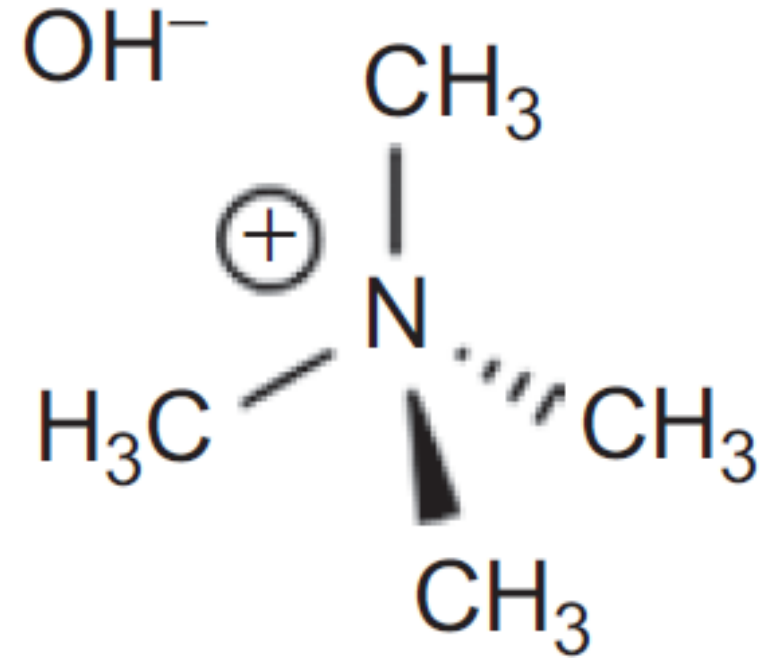
# Why TMAH Became Essential in Semiconductor Manufacturing ?

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TMAH provides:

- High pH without metal contamination
- Highly precise photoresist development
- Anisotropic silicon etching
- Effective photoresist stripping

By the 1980s, TMAH had become a major chemical in photolithography processes



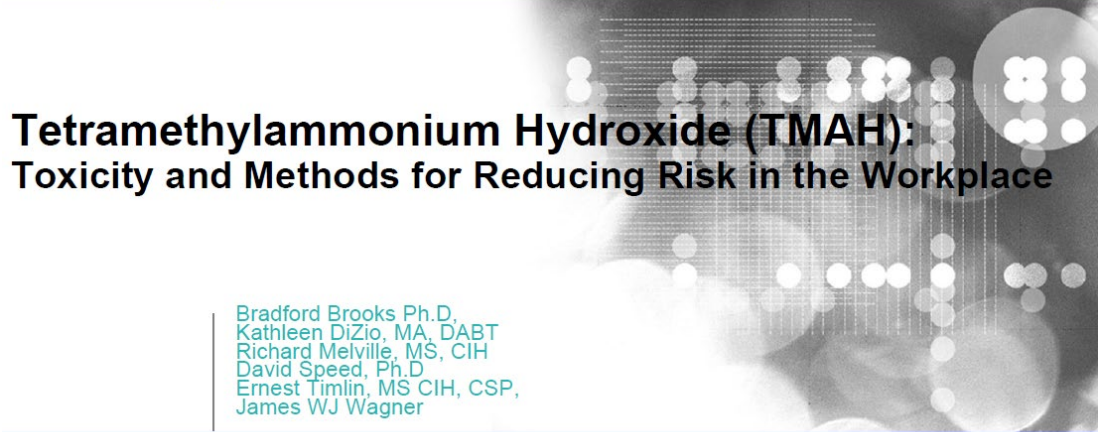

Structural formula of tetramethylammonium hydroxide (TMAH)

# Early Industrial Toxicology Research (IBM – 1990s)

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1950s– 1970s	<p>Tetramethylammonium neurotoxicity known in academic literature</p> <ul style="list-style-type: none"><li>• <b>Lyons et al, 1948</b> (J. Am. Med. Ass.)</li><li>• <b>Quilliam and Shad, 1964</b> (Brit. J. Pharmacology)</li><li>• <b>Parsons, 1969</b> (American Journal of Physiology)</li><li>• <b>Chiou, 1970</b> (European Journal of Pharmacology)</li></ul>
1980s	<p>Semiconductor industry begins using TMAH widely</p>
1990s	<p>IBM performs toxicology studies</p>

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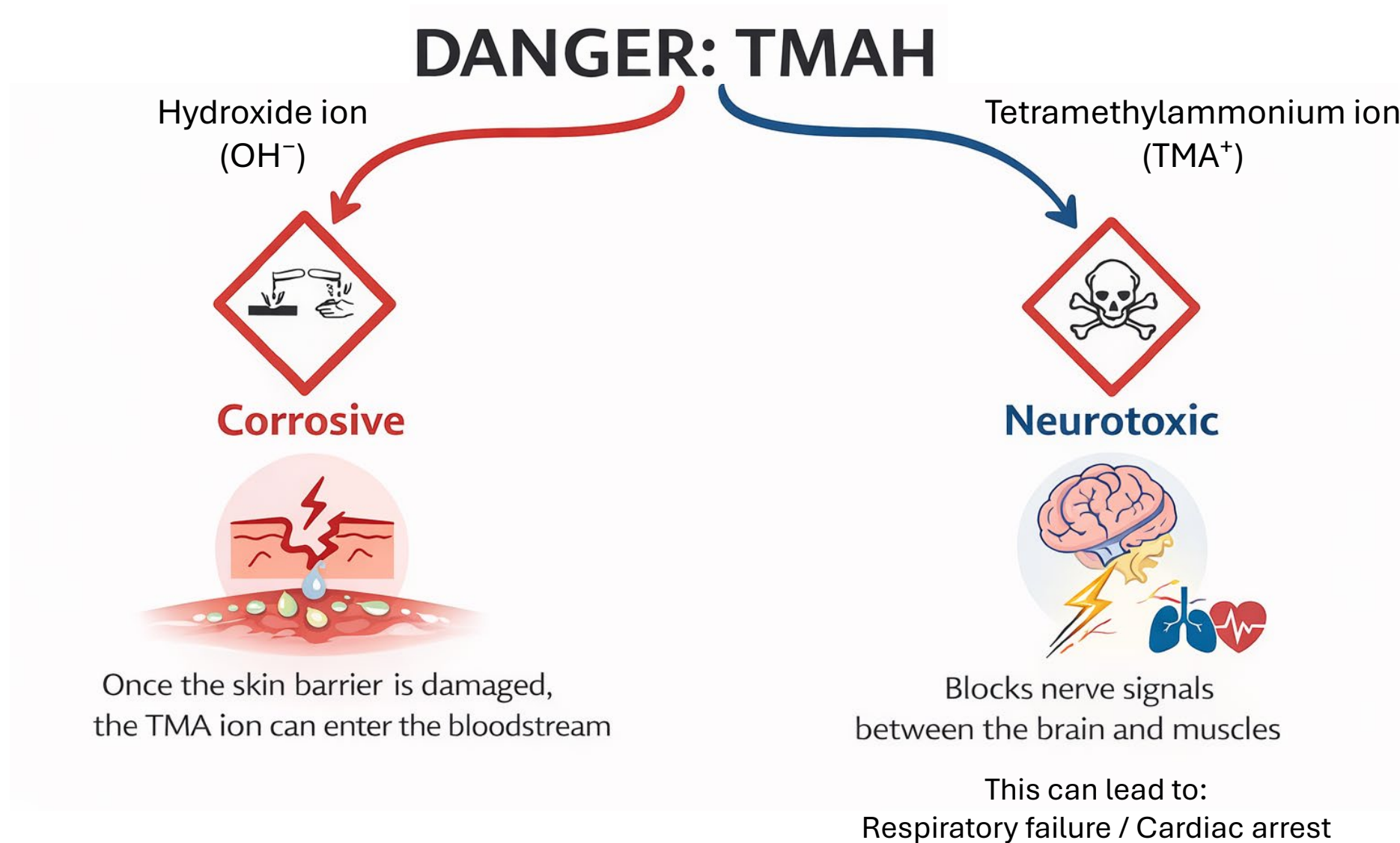
**Tetramethylammonium Hydroxide (TMAH): Toxicity and Methods for Reducing Risk in the Workplace**

Bradford Brooks Ph.D.  
Kathleen Dizio, MA, DABT  
Richard Melville, MS, CIH  
David Speed, Ph.D.  
Ernest Timlin, MS CIH, CSP,  
James WJ Wagner

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1 5/11/2011 © 2005 IBM Corporation

1999-2001 IBM submits TSCA risk notice to EPA that TMAH poses a 'substantial risk'.



# How IBM Findings Reached Industry

IBM's findings spread primarily through:

- industry safety networks  
(Semiconductor Environmental Safety and Health Association)
- conference presentations
- supplier safety documentation

The information was not widely published in peer-reviewed medical or toxicology journals and **awareness in the broader scientific and academic laboratory community developed more slowly.**

# Major Safety Improvements in Semiconductor Facilities

## Permeation Testing Data Against 25% TMAH<sup>1</sup>

Material	Breakthrough time (min)
Ansell Sol-Vex® 37-165 gloves (22 mil)	>480
MAPA® Professional E-194 TRIonic® gloves (20 mil)	>480
Tychem® SL coveralls	>480

1. Testing performed in accordance with ASTM F739.

Reduced manual handling by implementing closed chemical delivery systems and automated chemical distribution

Improved splash protection by enhanced personal protective equipment

Updated emergency response procedures for TMAH exposure

- emergency shower access within 10 seconds travel distance
- contacting emergency personnel immediately in the event of exposure to or a spill or leak
- removal of contaminated clothing within seconds
- immediate decontamination with large amounts of water until the arrival of emergency personnel
- respiratory support is a central element of emergency treatment

Worker training programs

- hazard awareness
- safe work practices
- process/ maintenance procedures

Tetramethylammonium Hydroxide Safety

## Examples of IBM exposure controls (Continued)

Representative TMAH Task	Minimum Required PPE			
	Eye and face	Hand	Body	Foot
Pouring	Goggles and Face shield (Face shield not required when working behind a hood sash)	Sol-Vex or Trionic gloves	Chemical resistant apron coat	N/A
Maintenance where accidental contact could occur	Goggles and face shield or full face respirator (if contact with mist could occur)	Sol-Vex or Trionic gloves	Chemical resistant apron coat	N/A

# Changes in Safety Documentation

- Older MSDS-style document treated TMAH primarily as a strong alkaline corrosive.
- It did not show dermal toxicity

## Material Safety Data Sheet (MSDS)

Date of Issue: 07/16/2004 25% TMAH Page 1 of 4  
(supercedes 03/01/04)

### 1 IDENTIFICATION OF THE SUBSTANCE/PREPARATION AND OF THE COMPANY/UNDERTAKING

#### Identification of the Preparation:

25% TMAH

#### Product use:

Developer and cleaner in the electronics industry.

#### Company/Undertaking:

Manufacturer:

Moses Lake Industries, Inc.

8248 Randolph Rd NE

Moses Lake, WA 98837

USA

(509) 762-5336 FAX (509) 762-5981

### 3 HAZARDS IDENTIFICATION

#### Emergency Overview

**Danger!** **Corrosive** Causes eye and skin burns. May cause severe respiratory tract irritation with possible burns in mist or aerosol form. May cause severe digestive system tract irritation with possible burns if ingested. May be harmful or fatal if inhaled or swallowed.

- SDS descriptions AFTER the toxicology findings (2000s–present)
- Include much stronger hazard language.
- Shows that TMAH is **both corrosive and toxic**.

## SAFETY DATA SHEET



### AZ 300 MIF Developer

Version  
5.3

Revision Date:  
01.07.2024

SDS Number:  
70MDGM184411

## SECTION 2. HAZARDS IDENTIFICATION

### GHS Classification

Corrosive to Metals : Category 1

Acute toxicity (Oral) : Category 4

Acute toxicity (Dermal) : Category 3

Skin corrosion : Category 1C

Serious eye damage : Category 1

Specific target organ toxicity - single exposure : Category 1 (Central nervous system)

Specific target organ toxicity - repeated exposure : Category 1 (Liver, thymus gland)

# Regulatory Changes in Transport Classification for TMAH

Material	Old Classification	New Classification
TMAH Solid (UN 3423)	Corrosive (PG II)	Toxic + Corrosive (PG I)
TMAH Solution $\geq 25\%$ (UN 3560)	Corrosive (PG II)	Toxic + Corrosive (PG I)
TMAH Solution 2.5–25% (UN 1835)	Corrosive (PG II)	Corrosive + Toxic subsidiary
TMAH Solution $\leq 2.5\%$	Corrosive (PG III)	unchanged

- $< 2.5\%$  TMAH + surfactant could become UN 2927 – Toxic liquid, corrosive, organic, n.o.s. (depends on mixture toxicity calculation).
- Transport classification relies on specific, acute toxicity limits.

# Early Clinical Evidence of TMAH Toxicity

## Chih-Hao Lin et al. 2010 (Clinical Toxicology)

- 13 exposures reported to the Taiwan Poison Control Center (1986–2009).
- Four patients were exposed to 25% TMAH; three of them died despite burns classified as relatively minor.
- One worker exposed to 2.38 % TMAH developed severe systemic toxicity, and required mechanical ventilation but survived.
- Nine patients were exposed to 2.38% TMAH survived.

### Factors that may have contributed to the severity of early incidents:

- Captured mainly severe incidents, because:
  - reporting systems were still developing
  - milder exposures were often not reported
- Awareness of systemic dermal toxicity was limited, and safety controls were not developed

**Table 1.** Summary of 13 patients with dermal tetramethylammonium hydroxide (TMAH) exposure in Taiwan

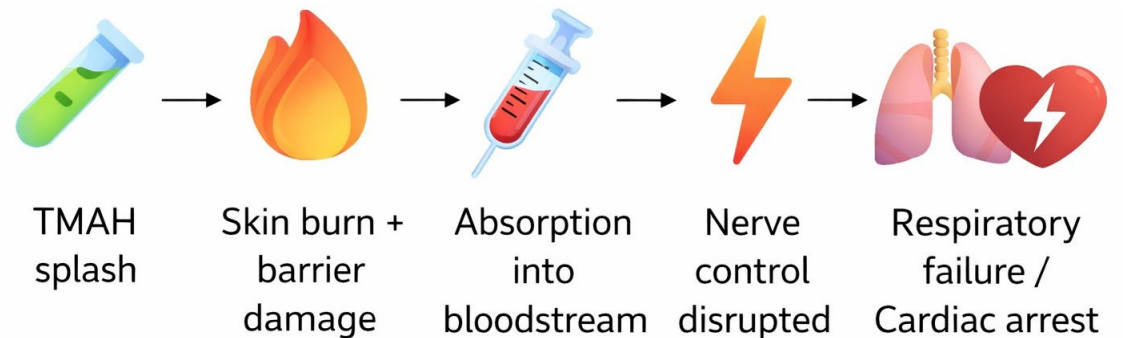
Case no. <sup>a</sup>	Age/sex	Concentration of TMAH (%)	Exposed BSA	Elapsed time to decontamination	Clinical manifestations	Laboratory abnormalities	Treatment/outcome <sup>b</sup>
1	33/M	2.38	28% BSA	10 min	Second to third degree chemical burn, dyspnea, salivation, respiratory failure, weakness	Leukocytosis, hyperglycemia	Supportive, endotracheal intubation, intensive care/survived
2	36/M	2.38	5% BSA	<10 min	First to third degree chemical burn, dermal pain, skin rashes	None	Supportive/survived
3	?/M	2.38	<1% BSA	<10 min	None	None	Supportive/survived
4	?/M	2.38	<1% BSA	<10 min	None	None	Supportive/survived
5	34/M	2.38	18% BSA	Unknown	First to second degree chemical burn	None	Supportive/survived
6	36/M	2.38	5% BSA (face)	<1 min	Limb weakness, skin rashes	None	Supportive/survived
7	29/M	2.38	1% BSA (finger)	2 h	Dermal pain and swelling, skin rashes	None	Supportive/survived
8	61/M	2.38	Eye	<1 min	Conjunctivitis	None	Supportive/survived
9	33/M	2.38	2% BSA	<1 min	First to second degree chemical burn, dermal pain, skin rashes	None	Supportive/survived
10	31/M	25	3% BSA	<30 min	Second to third degree chemical burn, dermal pain, skin rashes	None	Supportive/survived
11	28/M	25	7% BSA	<1 min	Second to third degree chemical burn, coma, dyspnea, shock, ventricular tachycardia	Hyperglycemia, leukocytosis, metabolic acidosis	ACLS, intensive care/died due to OHCA
12	35/M	25	7% BSA	<1 min	Second to third degree chemical burn, coma, dyspnea, shock Bradycardia, second to third degree chemical burn, coma, miosis, shock, salivation, weakness	Hyperglycemia, leukocytosis	ACLS, intensive care/died due to OHCA
13	22/M	25	29% BSA	>30 min		Hyperglycemia, leukocytosis, metabolic acidosis	ACLS, intensive care/died due to OHCA

# Mechanistic Confirmation of Toxicity

Controlled experimental studies:

- **Lee et al. 2011 (Toxicology and Industrial Health)** — developed animal models  
Dermal LD50 values:
  - 25% Concentration: was fatal at 28.7 mg/kg
  - 2.38% Concentration: was fatal at 85.9 mg/kg
- **Wu et al. 2012 (Burns)** — evaluated role of hydroxide burns
- **Wu et al. 2012 (Resuscitation)** — demonstrated ganglionic toxicity causing respiratory failure.

These experiments provided peer-reviewed mechanistic confirmation of what earlier toxicology (including IBM work) had suggested. TMAH toxicity involves both corrosive injury and systemic neurotoxicity. The tetramethylammonium ion can be absorbed through the skin and disrupt autonomic nerve signaling, potentially leading to rapid respiratory failure or cardiac arrest.



# Later Exposure Cases and Changing Safety Context

## Huang et al. 2020 (BMC Pharmacology and Toxicology):

- Captures a more modern semiconductor safety environment:
  - 29 dermal exposure cases (2010–2017)
  - Many exposures involved 2.38 % TMAH developer
  - Most cases involved small splashes
  - Mostly localized burns
  - Few systemic toxicity symptoms
  - No fatalities reported

The absence of fatalities in later datasets likely reflects improved safety controls — not reduced inherent toxicity. These safety controls reduced large splash exposures, which caused many earlier fatalities.

Authors emphasized that even dilute TMAH solutions can cause systemic toxicity through dermal absorption, and exposures should still be treated as potentially life-threatening. The risk depends on: absorbed dose, exposed skin area, contact time — not only concentration.

Case No	Age/sex	Concentration of TMAH (%)	Exposed BSA	Elapsed time to decontamination	Decontamination time	Diphtherine	Clinical manifestations	Laboratory abnormalities	Treatment/outcome
1	34/M	25%	5% BSA	5 min	> 15 min	Used	First to second degree chemical burn, dyspnea, drowsiness, bradycardia	Leukocytosis, hypokalemia	Supportive, intensive care /survived
2	29/M	25%	2% BSA	N/A	15 min	None	Second-degree chemical burn	All normal	Supportive, intensive care /survived
3	22/M	25%	1% BSA	< 1 min	N/A	Used	First-degree chemical burn	All normal	Supportive/survived
4	27/M	25%	< 1% BSA	< 1 min	N/A	Used	First-degree chemical burn	All normal	Supportive/survived
5	46/M	25%	< 1% BSA	N/A	N/A	None	First-degree chemical burn	N/A	Supportive/survived
6	48/M	25%	1% BSA	N/A	N/A	None	First-degree chemical burn	N/A	Supportive/survived
7	23/M	20% diluted	1% BSA	< 1 min	N/A	Used	First-degree chemical burn	All normal	Supportive/survived
8	25/M	2.38%	< 1% BSA	N/A	N/A	None	First-degree chemical burn	N/A	Supportive/survived
9	25/F	2.38%	< 1% BSA	N/A	N/A	Used	First-degree chemical burn	N/A	Supportive/survived
10	36/M	2.38%	< 1% BSA	N/A	N/A	None	First-degree chemical burn	N/A	Supportive/survived
11	28/M	2.38%	< 1% BSA	N/A	N/A	None	First-degree chemical burn	N/A	Supportive/survived
12	23/F	2.38%	< 1% BSA	N/A	N/A	None	None	None	Supportive/survived
13	35/M	2.38%	1% BSA	N/A	N/A	None	First-degree chemical burn	None	Supportive/survived
14	29/M	2.38%	< 1% BSA	< 5 min	30 min	None	None	None	Supportive/survived
15	37/M	2.38%	< 1% BSA	< 5 min	30 min	None	None	None	Supportive/survived
16	33/M	2.38%	< 1% BSA	N/A	N/A	None	First-degree chemical burn	None	Supportive/survived
17	34/M	2.38%	2% BSA	N/A	N/A	None	First-degree chemical burn	None	Supportive/survived
18	36/M	2.36%	< 2% BSA	N/A	N/A	None	None	All normal	Supportive/survived
19	43/M	2.38%	N/A (Right arm)	N/A	N/A	None	First-degree chemical burn	N/A	Supportive/survived
20	23/M	0.50%	Nearly entire body	30 min	20 min	None	None	All normal	Supportive/survived
21	26/M	0.50%	Nearly entire body	30 min	20 min	None	None	Leukocytosis	Supportive/survived
22	27/M	N/A	< 1% BSA	N/A	N/A	None	First-degree chemical burn	N/A	Supportive/survived
23	22/M	N/A	1% BSA	N/A	N/A	None	First-degree chemical burn	N/A	Supportive/survived
24	34/M	N/A	< 1% BSA	N/A	20 min	None	None	All normal	Supportive/survived
25	39/M	N/A	< 1% BSA	N/A	15 min	None	First-degree chemical burn	All normal	Supportive/survived
26	30/M	3%	N/A (Bil. forearm)	N/A	N/A	None	None	All normal	Supportive/survived
27	27/F	N/A	< 1% BSA	40 min	30 min	None	First-degree chemical burn	None	Supportive/survived
28	25/F	N/A	< 1% BSA	N/A	N/A	None	First-degree chemical burn	All normal	Supportive/survived
29	22/F	1–3%	< 1% BSA	None	None	None	First-degree chemical burn	N/A	Supportive/survived

# Severe Poisoning from Dilute TMAH Solutions

Korean case reports:

- **Park J.-S. et al., 2013 (J Occup Health) — 8.75% fatal exposure**
- 39-year-old man exposed to 8.75 % TMAH cleaner
- ~12 % body surface area burns
- Severe respiratory failure and death within several hours after exposure
  
- **Park J.-H. et al., 2022 (Toxicology) — 2.38% cardiac arrest and brain damage**
- 34-year-old man exposed to 2.38 % TMAH developer
- ~10 % body surface area burns
- Cardiac arrest occurred shortly after dermal exposure
- Brain MRI showed severe anoxic-ischemic encephalopathy
- TMAH detected in blood and urine
- Patient was resuscitated and survived

**Even dilute solutions can cause life-threatening systemic toxicity.**

# Diphoterine™ Skin Wash



Developed by Prevor in the 1990s as an active decontamination solution  
Mechanisms:

- Amphoteric (reacts and neutralizes both acids and bases)
- Chelating (can bind certain harmful ions)
- Hypertonic (has higher osmotic pressure than tissue, which may help draw chemicals out of skin/eye tissue).

Registered as a medical device in Europe, Canada, Brazil, Mexico, and Australia.

**Fosse M. 2010** (Cutaneous and Ocular Toxicology):

- In-vitro model skin after exposure to 25% TMAH, washing with Diphoterine restored normal skin pH using 17 times less volume than tap water.
- 66.5% of cells remained viable after Diphoterine washing following a 30-second TMAH exposure, compared to 33.8% after water washing.

# Diphoterine – Key Reasons for Lower U.S. Adoption

## Regulatory classification dispute

- U.S. FDA classified Diphoterine as a drug / combination product
- Prevor argued it should be a medical device / decontamination product
- Court case: Prevor v. FDA Court twice ruled FDA classification was not adequately justified FDA asked to reconsider classification

## U.S. safety standards emphasize water flushing

- OSHA and ANSI require:
  - safety showers, eyewash stations, 15-minute water flushing
- Water remains the primary legally required decontamination method.

## Evidence expectations

- Most research consists of:
  - laboratory models, and observational workplace reports
- Large randomized clinical trials are ethically difficult

In the U.S., water-based emergency flushing remains the regulatory requirement, while Diphoterine may be used as a supplementary decontamination product.



**Tetramethylammonium Hydroxide (TMAH) Fact Sheet**

- TMAH can cause severe skin burns and has severe toxicity; these effects occur within minutes
  - Any exposure must be washed in a safety shower immediately for 15 minutes, after which personnel should immediately seek medical attention
- TMAH is a chemical commonly used in device fabrication
- Exposures to concentrations of TMAH as low as 2.38% have resulted in potentially fatal symptoms within one hour; concentrations of 25% have resulted in several deaths
- TMAH can be used safely with proper precautions, many of which are already standard in labs

**Tetramethyl ammonium hydroxide**

**Any solution >1% TMAH over a few percent of the body is a "life-threatening event"**

Tetramethylammonium hydroxide (TMAH) post-exposure guidance

Created: 3/22/2024  
Revised: / /

**Tetramethylammonium Hydroxide (TMAH) Operating Procedure**

Updated on 08/04/2025 by IC

**Warnings and Notes**

- TMAH is a **toxic** liquid. The tetramethylammonium ion affects nerves



DOC #:	EHS-0225	Revision #:	0.0
DOC Type:	Fact Sheet	Implementation Date:	04/05/2024
Page #:	1 of 4	Last Reviewed/Update Date:	04/05/2024
Owner:	Ben Erjavac	Approval:	Jim Doughty

**Chemical Fact Sheet:**

**Tetramethylammonium hydroxide (TMAH)**



Exposure to as little as 2% of the body as a life-threatening event requiring immediate hospitalization, regardless of concentration.

# The Shift in TMAH Safety Standards

University cleanrooms and research facilities are reevaluating and tightening safety policies regarding the use of Tetramethylammonium hydroxide (TMAH) and TMAH-based developers (e.g., apply HF-level safety controls) due to their severe toxicity and history of fatal exposure cases.



**TETRAMETHYLAMMONIUM HYDROXIDE**

All users of tetramethylammonium hydroxide (TMAH) must review this document prior to its use.

TMAH is a quaternary ammonium salt which is commonly encountered as concentrated solutions in water or methanol. It is used in micro- or nanofabrication as an etchant and developer. TMAH is typically one of several ingredients in commercial etching/stripping mixtures, although it may also be used pure. It presents significant health hazards, must be handled with extreme caution and should only be used if there is no safer alternative. There have been several recorded fatalities from skin exposure to TMAH solutions since 2007. Three of these fatalities occurred due to heart attacks despite immediate decontamination and prompt medical care. **There is no known antidote for TMAH poisoning through either ingestion, skin, or eye contact. Immediate removal of the material using a safety shower/eyewash for at least 15 minutes is critical.**

Hi Mario,

For most photolithography spin-coating and **development processes, we don't request extra PPE**. Generally users are wearing cleanroom coveralls, nitrile gloves and safety goggles. Most positive MIF developers are TMAH (2.1~2.3% weight concentration) solutions.

But we will always bring up the high concentration TMAH, 25% TMAH (Aqueous solution) to attention. Some users use 25% TMAH as a HSQ ebeam resist developer. **25% TMAH is a strong base which could cause severe caustic burns.** Users **must** wear a secondary PPE to use 25% TMAH including Tychem 4000 Apron, double/triple long sleeve nitrile gloves (disposable), safety goggles plus face shield and silver shield chemical resistant boot covers. **Photolitho users should never touch TMAH 25% bottles even they are also stored in the general base cabinets.**

We set up secondary PPE stations beside our benches. HF bench has its own. Users can always protect themselves when necessary.

Best,

Jing

-----  
Jing Guo Ph.D.  
Cleanroom Manager/Research Scientist  
SEA Cleanroom (SST 017)  
Rice University

Mario,

There are two parts to this. Isolating the chemistries from each other and protecting the user. We have installed spin coaters in independent, flow controlled benches. Likewise with developers (AZ 400K 1:4, AZ300-MIF). Our users handle resists and **developers with standard cleanroom attire** (Nitrile gloves, bunny suit, wrap around goggles).

(Although this isn't part of your question, some additional information)

- RCA/Piranha PPE - Tychem Apron, +2 pairs of Microflex 93-260 (3 pairs of gloves total), full coverage face shield.
- HF PPE - PVC Apron, same PPE as above.

My users are inexperienced students enrolled in our cleanroom classes, hence the maximalist approach with single use gloves. Other labs I know use one pair of trionic gloves for corrosives, which they reuse.

Prashant

Prashant Srinivasan,  
Teaching Cleanroom Engineer  
Electrical & Computer Engineering  
University of California, Santa Barbara  
Santa Barbara, California 93106

Mario,

We require safety glasses, face shield, and nitrile gloves while using photoresist spinners, and at the wet bench for **handling and developing**. **No aprons, and no special protection provided** that there is adequate ventilation. For spills, heavier gloves and possibly a respirator would be needed.

Garry J. Bordonaro  
Microlithographic Engineer  
Cornell NanoScale Facility  
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(607) 254-4936  
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<http://www.cnf.cornell.edu/>

Dear Network,

**In our cleanrooms, we handle photoresists and developers with common cleanroom apparel (coveralls, hoods, nitrile gloves and eye protection).** Do any of you require extra special aprons, full visors and 4H gloves? I've worked in many cleanrooms and never encountered such requirements.

Mario

Mario Beaudoin, Ph.D.  
Research Associate & Sr. Scientist  
Nanofabrication Facility  
Stewart Blusson Quantum Matter Institute  
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# 4/21/2026: [labnetwork] Cleanroom gowning to handle resists and developers

# Discussion questions:

1. Should 2.38% TMAH developer be managed under the same safety framework as 25% TMAH, or is a tiered (“lower risk”) approach justified?
2. Are the highest-risk tasks (automatic station maintenance, bottle changes, waste handling) adequately controlled?
3. How quickly can a user realistically reach a safety shower in your cleanroom layout?
4. Do users understand that TMAH splashes can be life-threatening?
5. If a serious incident occurred tomorrow, would we feel that our current controls were sufficient?