Mining the Chemical Literature to Support Lab Risk Assessments

Ralph Stuart, CIH, CCHO
Chemical Hygiene Officer
Environmental Safety Manager
Keene State College
Abstract and Agenda

• Laboratory risk assessment is a challenge because work conducted there is often novel. Moreover, the risks associated with laboratory work are poorly described in the literature chemists use to develop their procedures.

• This presentation will discuss how EHS professionals can help lab workers improve their risk assessments by mining the relevant literature to identify and assess the hazards associated with laboratory work. The presentation will also discuss how chemists can share their safety discoveries with the chemistry community at large.

• Learning Objectives (maximum 2,000 words)
  • Recognize which chemical safety data sources are most likely to answer questions about specific laboratory processes
  • Identify keywords appropriate to the data source you are searching to find the information you are interested in
  • Know how to support chemistry researchers in including important safety information in new research publications

Three Big Topics:

1. The challenge of searching for chemical safety information on the Internet

2. Our ACS work with undergrad IT students and graduate chemists to 1) develop a chemical safety search strategy and 2) improve the crowd-sourced Chemical Safety Library

3. Does emerging AI help Chemical Safety research?
Part 1: A Chemical Safety Question Arises

• In 1997, an animal sciences lab at UVM was cleaning out a storeroom and found a rusted 5 gallon can of DMSO. The professional lab techs open the bunghole and noticed solids floating in the liquid. They don’t know what the solids are so, they called EHS.

• My first thought as a hazmat chemist is "Could the solids be an explosive peroxide have formed in the can?"

• The lab has no idea if this is a possibility.

• In many situations, the next step would be a call to the bomb squad.

• Can you figure out what is going on?
1. Define the question before you start searching

- Are the solids organic peroxides?
- If they aren’t peroxides, what are they?

**Contextual Questions**
1. Are you familiar with DMSO as a solvent?
2. What is the quantity of the chemical we are dealing with?
3. Is DMSO a reactive chemical, a health concern, or both?

---

**Google**

*What are the hazards of DMSO?*

- Inhalation: Causes respiratory tract irritation. Symptoms from exposure to high vapor concentrations may include coughing, shortness of breath, headache, dizziness and sedation. Ingestion: Causes gastrointestinal tract irritation, and an unusual garlic-onion-oyster may develop on breath, and body skin.

---

**PubChem reactivity section**

**PubChem** Dimethyl Sulfoxide (Compound LC85)

9. Stability and Reactivity

9.1 Reactivity Profile

- DMF, sulfoxide decomposes violently or react with many acryl halides and related compounds such as acryl chloride, acryl dichloride, acryl dichloride, acryl dichloride, acryl dichloride, acryl dichloride, acryl dichloride, and tryptophan.

9.2 Reactivity Alerts

---

**ACS Pubs**

*Potential Explosion Hazards Associated with the Autocatalytic Thermal Decomposition of Dimethyl Sulfoxide and Its Mixture*

Sang Yoon Yin, Il-Ho Cho, Seokjun L Song, and Craig T. Cooler. Systems Engineering and Science Laboratory, NASA, 2101 N. Magnolia Ave., Suite 320, Huntsville, AL 35801, USA.

*Oprand Chemicals*
My 1997 Answer and 2023 Observations

After about an hour of searching paper references, it turns out that:

1. DMSO isn't considered a peroxide former
   (Prudent Practices was the most authoritative source available at the time)
2. DMSO freezes around room temperature; the solids were frozen DMSO
3. In 2023, it's pretty easy to find that solids in containers are a common observation in commercial uses of DMSO
4. This is a good example of the gap between academic chemistry and hazmat chemistry

How to reliquefy DMSO

Dimethyl sulfoxide

From Wikipedia, the free encyclopedia

"DMSO* redirects here. For other uses, see DMSO (disambiguation)

Dimethyl sulfoxide (DMSO) is an organosulfur compound with the formula (CH₃)₂SO. This colorless liquid is the sulfoxide most widely used commercially. It is an important polar aprotic solvent that dissolves both polar and nonpolar compounds and is miscible in a wide range of organic solvents as well as water. It has a relatively high boiling point. DMSO has the unusual property that many individuals perceive a garlic-like taste in the mouth after DMSO makes contact with their skin.[5]

In terms of chemical structure, the molecule has idealized C₃ symmetry. It has a trigonal pyramidal molecular geometry consistent with other three-coordinate S(IV) compounds,[8] with a nonbonded electron pair on the approximately tetrahedral sulfur atom.

Explosion hazard [edit]

Dimethyl sulfoxide can produce an explosive reaction when exposed to acyl chlorides; at a low temperature, this reaction produces the oxidant for Swern oxidation.

DMSO can decompose at the boiling temperature of 189 °C at normal pressure, possibly leading to an explosion. The decomposition is catalyzed by acids and bases and therefore can be relevant at even lower temperatures. A strong to explosive reaction also takes place in combination with halogen compounds, metal nitrides, metal perchlorates, sodium hydride, periodic acid and fluorinating agents.[53]
What is the current state of Lab Risk Assessment?  
2022 UMN RAMP Workshop

Year in Graduate Program
- 18.4% 1
- 13.2% 2
- 10.5% 3
- 15.8% 4
- 31.6% 5
- 10.5% 6

Department
- 71.1% CHEM
- 26.3% CEMS
- 2.6% Both

RAMP Session(s) Attended
- 52.6% Morning session
- 44.7% Afternoon session
- 2.6% Both

Number of respondents = 38
Take Away: Risk Assessment Education is New to Some & Crucial to All

- Nearly $\frac{2}{3}$ of respondents work in labs that do not document risk assessments while all plan to or might document in the future

- Over 80% of respondents report that the workshop increased the value in documentation of risk assessments

- More than 50% of respondents have discovered new questions about their work

- Workshop resulted in inspiration to:
  - reread SOPs and/or existing risk assessments
  - discuss lab safety with peers, PI, and/or EHS
  - use different safety literature sources

“It is a good reminder to take it seriously and put time into it. Also, a strong reminder that foresight is flawed, and time need be dedicated to consider potential hazards in the lab. Like I mentioned, I need to strongly encourage myself and others to slow down and assess risks more than we do.”
The group compared three risk assessment approaches: 1) 5 questions, 2) RAMP rubric and 3) "What If"

Of the three approaches, nearly ½ of respondents are most likely to use the “5 Questions”. This approach made sense and over 80% of respondents think it is adequate to support a safe laboratory community.

The “What If” approach generated new safety questions for over 80% of respondents.

There is a desire for:
- **Wider applicability** to encompass more hazards (e.g., physical hazards)
- **Again, step-by-step frameworks or simplified rubrics/templates**
- **More concrete examples of their effective usage**
2022 Lesson: The RAMP Rubric is "functional but impractical"

- RAMP rubric successfully enables users to think deeply about risks and to ask the right questions
  - About ½ of respondents find the RAMP rubric adds value when reviewing risk assessments
  - Practical for widely-used, complicated, and/or high-risk procedures
- Barriers to wide implementation by lab mates and for all protocols were identified
  - Drawbacks: time-consuming (main), overly-comprehensive, and redundant
- Respondents are eager for a “user friendly” RAMP rubric
  - Simplified verbiage, condensed categories, and defined limits for an “acceptable” assessment
  - “How to” documents explaining its use to enable adoptability
Part 2: The Chemical Safety Library: Building a Bridge Between Bench Chemists and the EHS Community
The CSL is a crowd sourced collection of hazardous reactions

• The original synthesis was done in the UK and is described in United States Patent 4,835,278, *Preparation of Piperidinylcyclopentyleheptenoic Acid Derivatives*

• The exothermic reaction creates hydrogen gas as a byproduct. If the NaBH₄ is powdered, it dissolves rapidly and there is an uncontrolled reaction that consistently catches fire. To control this, the chemist must use pelletized NaBH₄; the dissolved pellet reduces the reaction rate and thus the amount of H₂ generated; this is not mentioned in the patent

• Fires happened at BMS two times in a year.

• Based on these events in the company, **process chemists at BMS** suggested sharing safety information within Pharma "pre-competitively" via the Pistoia Alliance
CSL Incident Submission

Chemical Safety Library
Hazardous Reaction Incident Submission Form

Thank you so much for contributing to the Pistoia Alliance Chemical Safety Library (CSL), a community crowd-sourced collection of hazardous reaction incidents, those "reactions gone wrong in the lab." This important new source allows all of us to learn from the wider community's experiences.

Your entry (excluding your contact information) will be published to the CSL database, and will be deposited in PubChem (section 12.8.3.1). You can request a copy of the entire database (as a .csv file) from the Chemical Safety Library administrator.

Enter your reaction incident information in the form below. Be as complete as possible. Our curators will enter the data you provide into the CSL database. If they have any questions about your entry, they will be in touch via email.

Key points

• We are interested in hazardous reactions between two or more chemicals
• They can be experienced either first hand or found in the literature
• The catalog is expected to be a one stop shop for searching for and recording events in the chemistry lab
Data Sources for the Data Mining CSL Project at Purdue

**Cameo Chemicals**
- Open Hazardous Chemical Database
- Hazards, Properties, & Response Recommendations
- "Predict Reactivity" function

**PubChem**
- Open Substance, Compound, and BioAssay Database
- Properties & Laboratory Chemical Safety Summary Datasheet

**CAS Common Chemistry**
- Open community resource for common/frequently regulated chemicals from CAS Registry®
- Properties & Identifiers
Exploring PubChem Reactivity Data from CAMEO

• PubChem Home
  • Browse Data
    • PubChem Classification Browser
    • PubChem Compound ToC Tree
  • Safety and Hazards
    • Stability and Reactivity
      • Reactivity Profile
• Existence of the Reactivity Profile indicates of a documented hazardous reaction with another chemical species
• Structured subsection that contains necessary information in the incidence report

Reactivity Profile for Acetaldehyde from CAMEO

• ACETALDEHYDE undergoes a vigorously exothermic condensation reaction in contact with strong acids, bases or traces of metals. Can react vigorously with oxidizing reagents such as *dinitrogen pentaoxide*, *hydrogen peroxide*, *oxygen*, *silver nitrate*, etc.

• Contamination often leads either to reaction with the contaminant or polymerization, both with the evolution of heat.


• An oxygenation reaction of acetaldehyde in the presence of *cobalt acetate* at -20 °C exploded violently when stirred. The event was ascribed to peroxyacetate formation [Phillips B. et al., J. Am. Chem. Soc., 1957, 79, p. 5982].
Frequency of Keywords

Keywords are identified based on the chemical safety related documents and list of the frequent words from the reactivity profile.

Keywords are generated by a hazmat reading of the chemistry literature, primarily from Bretherick’s, although the provenance is inconsistently sourced.

In that context, the Top 15 words make sense.
Our Chemical Safety Search Strategy at UMN

We identify 13 databases appropriate for 4 groups:

1. Foundational databases all lab people should be familiar with (4 free databases: PubChem, CAS Common Chemistry, CAMEO chemicals, Pistoia CSL)
2. Databases that undergraduate chemistry student researchers should be familiar with (5 additional sources)
3. Databases that research and specialty laboratory staff should be familiar with (3 additional)
4. Databases that EHS professionals should be familiar with (1 more)

Each database has different emphases and access privilege systems. These databases are cumulative; it is best to be aware of the databases that describe your role in the lab as well as those listed above you.

Not Voodoo X and the Chemical Safety Library is designed for crowd sourced contributions.
2023 Workshop: PubChem Practice with the CSL

Just under one half of the attendees are chemistry researchers. The other half are in related lab fields.

Most are current LSOs.

About 1/3 attended the 2022 RAMP workshop about lab risk assessment.
LST Leadership Feelings after the workshop

On a scale of 1 to 5, how much of the information presented in the workshop was new to you?
19 responses

<table>
<thead>
<tr>
<th>Score</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>0%</td>
</tr>
<tr>
<td>1</td>
<td>5</td>
<td>26.3%</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>21.1%</td>
</tr>
<tr>
<td>3</td>
<td>9</td>
<td>47.4%</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>5.3%</td>
</tr>
</tbody>
</table>

Overall, was the workshop a good use of your time?
19 responses

<table>
<thead>
<tr>
<th>Score</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4</td>
<td>21.1%</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>15.8%</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>21.1%</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>21.1%</td>
</tr>
<tr>
<td>5</td>
<td>4</td>
<td>21.1%</td>
</tr>
</tbody>
</table>

How likely are you to enter reaction information (either from the literature or real life experiences) into the Chemical Safety Level in the future?
19 responses

<table>
<thead>
<tr>
<th>Likelihood</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Likely</td>
<td>5</td>
<td>26.3%</td>
</tr>
<tr>
<td>Likely</td>
<td>5</td>
<td>26.3%</td>
</tr>
<tr>
<td>Likely</td>
<td>6</td>
<td>31.6%</td>
</tr>
<tr>
<td>Unlikely</td>
<td>3</td>
<td>15.8%</td>
</tr>
<tr>
<td>Unlikely</td>
<td>0</td>
<td>0%</td>
</tr>
</tbody>
</table>

Which of these incentives do you think will most motivate bench chemists into adding entries to CSL?
19 responses

- Chemical Safety Library away: -7 (36.8%)
- Public recognition of contributions: -11 (57.9%)
- DOi References that you could point to in your scholarly work: -11 (57.9%)
- Financial compensation: -12 (63.2%)
- Just making it worth their time: 0 (0%)
- Emphasis on how CSL will be used to help others: 0 (0%)

None
It was all new to me

Unlikely
Habitually
Lessons Learned from the 2023 workshops:

• PubChem and Scifinder are currently the leading sources for this information in the chemistry community.

• The CSL is a voluntary, crowd sourced database of unexpected lab scale chemistry reactions, either from the literature or personal experience. The CSL provides the opportunity to share notes on these events. Grad students see the value of this as a resource.

• The time required to enter an event into the CSL is less than 10 minutes per reaction.

• There is an institutional role in supporting chemists' participation in the CSL.
Other Crowd Sourced Incident Reporting Efforts

Teaching Labs: Not Voodoo X.4

Informal reporting of organic teaching and research lab learning events. Upvoting of events gives some idea of frequency.

Government Labs:

OPEXSHARE provides tools to enable DOE agencies to connect with others to share operating experiences. Requires several layers of internal review to provide professional reports on safety events.

Also:

• 30 year European data base of industrial incidents
• IHAC process in China

Industrial Chemistry Settings:

Part 3: The Role of AI

• In 1984, I was a full-time lab tech in an IH lab at UVM. I collected airborne dust in the Vermont granite industry to assess worker exposure to silica dust.

• We used dimethyl formamide (DMF) with ultrasound to dissolve the filters and then measured silica levels using X-ray diffraction.

• One day, when I went to dissolve about 50 dust-laden filters, I found the hood crowded with someone's asbestos samples. That person was not in the lab that day.

• I decided to set up the sonicator at the front of the hood. This meant that I couldn't close the sash. I was wearing latex gloves.

• After about 20 minutes, I got dizzy, so I put on a respirator; I completed the work with no further symptoms.

• However, when I went to play softball that evening and started exercising, I suddenly got dizzy, felt faint and had to lie down for about 20 minutes to recover. I didn't seek medical attention.
My Investigation into How I was Exposed

• I was worried and suspected that DMF was the source of the problem. The next day I did some research.

• I used a chemical dictionary and the Merck Index to do a "literature review" of DMF hazards. This convinced me that DMF caused my symptoms.

• However, the data indicated that it could be either inhalation or skin exposure or both. So, I wasn’t sure how to prevent a recurrence of the exposure.

• My CIH-educated guess is that the primary exposure was inhalation, although it could have been both skin and respiratory
My 2023 question

*Why were we using DMF instead of, say acetone, to dissolve the filters?*

- or, more generally -
*Is the state of the art of lab risk assessment different in 2023 than it was in 1984?*

Spoiler alert:
I suspect it was to avoid the fire hazard.

**Acetone Flashpoint** = -4 degrees F

**DMF Flashpoint** = 136 degrees F
What are the risks associated with using DMF as a laboratory solvent?

DMF (N,N-Dimethylformamide) is a widely used solvent in the laboratory due to its ability to dissolve a wide range of organic and inorganic compounds. However, DMF poses several risks to human health and the environment, including:

1. Health Risks: DMF is classified as a hazardous substance and can cause a range of health problems, including skin and eye irritation, respiratory problems, and even cancer. Long-term exposure to DMF may also cause liver and kidney damage.
2. Environmental Risks: DMF is toxic to aquatic life and can cause serious harm to the environment if not handled properly. It is also a volatile organic compound (VOC) and can contribute to air pollution.
3. Flammability: DMF is highly flammable and can ignite if exposed to heat or open flame.
4. Reactivity: DMF can react with some chemicals, such as strong acids or bases, and may release toxic gases or heat.
5. Absorption: DMF can be absorbed through the skin, and inhalation of its vapors can result in significant exposure.

Therefore, it is important to handle DMF with care, and use it in a well-ventilated area with proper personal protective equipment (PPE), including gloves, goggles, and a lab coat. Additionally, proper storage, handling, and disposal of DMF are critical to reduce the risk of environmental contamination and harm to human health.
5 questions later: Have you read the SDS?

Please specify a SDS that describes DMF as highly flammable, given that its GHS hazard designation does not include flammability.

I apologize for the error in my previous responses. Upon reviewing the available safety data sheets (SDSs) for DMF, I found that the GHS hazard classification for DMF does not include flammability. Instead, the primary hazards listed in most SDSs for DMF are related to health effects, such as skin and eye irritation, respiratory effects, and potential for liver and kidney damage with long-term exposure.

I did not find any SDSs that specifically describe DMF as "highly flammable". While some SDSs mention the flashpoint of DMF, they do not use the term "highly flammable" to describe it. Rather, they generally indicate that DMF is combustible and can present a fire hazard under certain conditions, and provide information on appropriate fire-fighting measures and precautions to prevent fires.

It is important to note that while DMF may not be classified as a flammable liquid under GHS, it can still pose a fire hazard if exposed to heat, sparks, or flames, and proper handling and storage procedures should be followed to prevent accidents.
"When I was pursuing my PhD in chemistry at Northwestern University, I regularly received emails from the Office for Research Safety reporting laboratory accidents. They almost always included the statement, “Fortunately, no one was hurt.” It never occurred to me that conducting reactions in the lab rather than on the page carried an added risk — not until an older graduate student made an offhand remark while we were chatting in the office one day. “I’m definitely closer to cancer and less fertile than I was before,” she said.

“She had … worked with harsh chemicals such as dimethylformamide (DMF), which has been linked to liver damage, according to the CDC. … we used fume hoods to prevent inhalation and wore gloves to protect against skin contact, but was this personal protective equipment enough?”

- Sarah Anderson, PhD
The DMF reference cited in the editorial

Preventing Adverse Health Effects from Exposure to: Dimethylformamide (DMF)

DHHS (NIOSH) PUBLICATION NUMBER 90-105

View all Alerts

Warning! Avoid skin contact with dimethylformamide (DMF)! This chemical is easily absorbed through the skin and can cause liver damage and other adverse health effects.

The National Institute for Occupational Safety and Health (NIOSH) requests assistance in reducing the health risks to workers exposed to the solvent dimethylformamide (DMF). This substance is readily absorbed through the skin and is known to be toxic to the liver; recent evidence shows that liver damage may occur in exposed workers who appear to be healthy. DMF is also known to cause skin problems and alcohol intolerance. Some reports also suggest an increase in cancer among workers exposed to DMF, but the evidence is not conclusive at this time. NIOSH and other organizations are working to determine whether exposure to DMF increases the risk of developing cancer.

This Alert describes engineering controls, good work practices, and personal protective equipment (PPE) recommended for controlling exposures to DMF by inhalation and skin contact. NIOSH requests editors of appropriate trade journals, safety and health officials, and employers to bring these recommendations to the attention of workers, supervisors, and managers.

The Current TLV documentation

TLV® Chronology

1964: proposed: TLV–TWA, 10 ppm; Skin
1966–present: TLV–TWA, 10 ppm; Skin
1986: TLV–STEL deleted
1995: proposed: A4, Not Classifiable as a Human Carcinogen
1996–present: TLV–TWA, 10 ppm; Skin, A4, Not Classifiable as a Human Carcinogen
2017: proposed: TLV–TWA, 5 ppm; Skin, A3, Confirmed Animal Carcinogen with Unknown Relevance to Humans
2018: Adopted: TLV–TWA, 5 ppm; Skin, A3, Confirmed Animal Carcinogen with Unknown Relevance to Humans

In 1990, the TLV was 10 ppm
How many papers about the toxicity of DMF were published before and after 2000?

ChatGPT responds:
As an AI language model, I don't have real-time access to specific data sources or the ability to browse the internet. However, I can provide some general information about the literature on the toxicity of dimethylformamide (DMF).

DMF has been a subject of scientific research due to its potential health hazards. Before and after 2000, numerous studies have examined the toxicity of DMF, including its effects on human health, animal models, and environmental impact. These studies have investigated various aspects such as acute toxicity, chronic effects, target organs, carcinogenicity, reproductive and developmental toxicity, and more.

To determine the exact number of literature pieces published on DMF toxicity before and after 2000, it would be best to consult scientific databases or research platforms such as PubMed, Scopus, or Web of Science. … By using relevant search terms like "dimethylformamide toxicity" or "DMF toxicity," you can filter the results based on publication dates to obtain the number of literature pieces published before and after 2000 specifically related to the toxicity of DMF.
Building a Good Lab Safety Question

Whether we are talking to a person or a ChatBot, the three key elements of a lab safety question are:

• Completeness
• Clarity
• Specificity

It's usually up to the EHS professional to ask questions until these three things are defined enough to develop an answer.
Three Take Home Messages

• The chemistry literature is not built for risk assessment purposes
  o "Recognition" data is generically available, but “Assessment” information is scarce.
  o The chemist needs to lead the literature review, but EHS should be able to ask leading questions
  o Chemists need help with the "Management” and Emergency “Planning” Steps of RAMP

• Systematic risk assessment is not a skill chemists develop as part of their education
  o Today's chemistry grad students are aware of lab safety concerns, but need more guidance in working more safely

• The Human Element
  o Critical communication skills are needed whether working with humans or with ChatBots

Can you tell me one thing you learned from this presentation?

Questions?
References

• Data Sources
  • Cameo Chemicals: https://cameochemicals.noaa.gov/
  • CAS Common Chemistry: https://commonchemistry.cas.org/
  • Pistoia Alliance Chemical Safety Library: https://safescience.cas.org/

• Tools
  • Gensim: https://radimrehurek.com/gensim/
Thank You To Our
2023 Conference Sponsors

Platinum
- Campus Optics
- Safety Stratus

Gold
- Adam Melder
- ACS Publications
- Cintas
- SciShield
- ORS

Silver
- Chemical Insights
- Chimera
- Veolia

Bronze