ACS GUIDE TO SCHOLARLY COMMUNICATION

1.3 Communicating Safety Information

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1.3.1 Introduction

In 2011, the U.S. Chemical Safety Board (CSB) issued its first investigation of a chemical accident at an academic research institution. The incident involved the sudden detonation of a nickel hydrazine perchlorate (NHP) derivative that resulted in severe and permanent injury to a fifth-year chemistry graduate student at Texas Tech University (TTU). Student researchers were involved in a multi-institutional research project to characterize new potentially energetic materials. They decided to scale up their synthesis by two orders of magnitude to provide enough sample so that all testing could be performed on one batch but neglected to assess safety ramifications. The final CSB report for the TTU incident found in both this case and prior incidents in the same research area that (1):

- No formal hazard evaluation and risk assessment had been completed to char-acterize the potential danger of the research activity and to plan for the worst-case scenario.
- The student sought peer advice.
- No policy was in place at the laboratory, department, or university level to prompt a student to seek PI advice or evaluation of experimental activities.

The investigation clearly indicates that the students did not have the information they needed to prepare themselves for the increased risk posed by their decision to scale up.

The CSB primarily investigates and reports on large scale incidents in the chemical and related industries where hazard evaluation and risk assessment are well established to facilitate improved safety management across the industry. Chemistry research is fundamentally a study of transforming materials though chemical reactivity and in the academic sector also presents a diversity of often unrecognized hazards associated with novel research. It is imperative for the safety of researchers and the scientific community to be aware of the potential risks and to communicate these to others who may be conducting similar work. Safety summaries in research articles are an excellent opportunity to report observations of significant health and safety concerns that arise during the course of experimentation to help others prepare for unusual or special risks.

In 2016, Grabowski and Goode examined author guidelines of 726 chemistry journals from 28 different publishers to determine the nature of chemical safety precautions that authors were asked to include in manuscripts as well as how often safety guidance appeared in select synthesis articles (2). They found that only 8% of the journals surveyed included any one of four keywords in the author guidelines: caution, hazard, safety, or danger. Since the publication of the Grabowski and Goode article, communicating safety information in manuscripts has been recognized by the American Chemical Society (ACS) as one way to improve safety practices in experimental research and education (3).

[1] *Texas Tech University Laboratory Explosion*; Report No. 2010-05-I-TX; U.S. Chemical Safety and Hazard Investigation Board, Office of Congressional, Public, and Board Affairs: Washington, DC, 2011. https://www.csb.gov/texas-tech-university-chemistry-lab-explosion (accessed 2019-09-25).

[2] Goode, S. R.; Grabowski, L. E. Review and analysis of safety policies of chemical journals. *J. Chem. Health Saf.* **2016**, *23*, 30–35. DOI: 10.1016/j.jchas.2015.10.001

[3] Kemsley, J. ACS journals enact new safety policy. *Chem. Eng. News* **2016**, *94* (48), 7. https://cen.acs.org/content/cen/articles/94/i48/ACS-journals-enact-new-safety.html (accessed 2019-01-31).

As outlined by the ACS on Chemical Safety in the Chemical Enterprise (4),

> Chemistry professionals have ethical and legal responsibility to work with chemicals safely.
>
> - They protect themselves, their communities, and the wider environment from the risks associated with the hazards of chemicals.
> - They address safety and health issues when contributing to the scientific literature.
>
> Chemistry professionals need to develop competency in evaluating hazards, conducting assessments, and mitigating the risks of those hazards.

Readers may also want to consider international guidance on safety and ethics in the The Hague Ethical Guidelines, of which ACS is a co-signer (5).

Utilizing risk assessment during laboratory procedures will streamline the documentation process when preparing the safety summary. Additionally, when risk assessment is included in the experimental design and planning phases, hazards are identified early and controls can be incorporated more efficiently to prevent undesired results. As with any area of work, better planning makes for better research. Appreciating and preparing for the dangers involved in conducting a specific experiment involves recognizing hazards, assessing risks, minimizing risks, and preparing for emergencies. These principles are often referred to by the acronym RAMP (6) and inform a general process for assessing and communicating both potential risk and relevant safety precautions. The RAMP process will be discussed in greater detail later.

It is also worth noting the pedagogical value of safety summaries in publications. Risk assessment has been recognized as a learning objective for undergraduate students by the ACS as outlined in the Guidelines for Chemical Laboratory Safety in Academic Institutions (7). Learning is enhanced when topics are integrated throughout the curriculum and used in research and teaching labs to familiarize students with the ideas. Applying a "spiral" learning approach to concepts of risk assessment throughout the educational process will gradually prepare professional chemists with strong safety competencies (8).

Including safety statements in manuscripts will introduce students to the paradigm of safety that is often minimal in their course of study (9). To instill best practices in the chemical education process, educators are encouraged to have students include relevant safety

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[4] *Chemical Laboratory & Safety, Chemical Enterprise*; American Chemical Society, Washington, DC. https://www.acs.org/content/acs/en/chemical-safety/workplace-and-industry.html (accessed 2019-01-31).

[5] *The Hague Ethical Guidelines*; Organisation for the Prohibition of Chemical Weapons. https://www.opcw.org/hague-ethical-guidelines (accessed 2019-01-31).

[6] Hill, R. H., Jr.; Finster, D. C. *Laboratory Safety for Chemistry Students*, 2nd ed.; John Wiley & Sons, Inc.: Hoboken, NJ, 2016.

[7] Committee on Chemical Safety (CCS) Task Force for Safety Education Guidelines.*Guidelines for Chemical Laboratory Safety in Academic Institutions*; American Chemical Society: Washington, DC, 2016. https://www.acs.org/content/dam/acsorg/about/governance/committees/chemicalsafety/publications/acs-safety-guidelines-academic.pdf (accessed 2019-09-25).

[8] Sigmann, S. Chemical safety education for the 21st century—Fostering safety information competency in chemists. *J. Chem. Health Saf.* **2018**, *25*, 17–29. DOI: 10.1016/j.jchas.2017.11.002

[9] Sigmann, S. B.; McEwen, L. R.; Stuart, R. A Community approach to academic research safety. *Trends Chem.* **2019**, *1*, 275–278. DOI: 10.1016/j.trechm.2019.03.015

information as a part of the experimental section in oral presentations and posters as well as in their laboratory notebooks. As safety information is included in non-published and published material, the practice will become more integral to the overall research process. Prudent Practices in the Laboratory: Handling and Management of Chemical Hazards (prepared by the National Research Council) provides guidance on managing chemical hazards at laboratory scale. Prudent Practices in the Laboratory notes that "the ability to accurately identify and address hazards in the laboratory is not a skill that comes naturally, and it must be taught and encouraged through training and ongoing organizational support." ((10)).

1.3.2 Safety Guidelines in Scientific Publications

This chapter aims to augment or otherwise provide guidance that may be lacking to assist authors in documenting appropriate safety information when preparing research and educational articles for chemistry and allied discipline journals. The goal is to alert readers to unusual hazards or procedures which present significant risk or require special control measures beyond those reasonably anticipated to be commonly present in a chemistry teaching or research laboratory setting. It is expected that scientists schooled in the art and following published procedures will appropriately prepare for commonly known hazards in their field of study.

TIP: Including properly prepared safety information in your research publications alerts other scientists to unusual hazards that present significant risks or require special control measures.

Safety information in scientific publications is subject to the professional judgment of authors, editors, and reviewers and will vary depending on the scope of the ***journal***, the ***chemistry***, and the ***audience***. Of the journals surveyed by Grabowski and Goode, most that do call out safety in the author guidelines provide only very broad requirements, often as a general statement in the ethics guidelines (11). Other journals may cite more specific requirements based on the chemistry and procedures involved. See examples in Table 1.3.1.

[10] National Research Council. *Prudent Practices in the Laboratory: Handling and Management of Chemical Hazard*, updated ver.; National Academies Press: Washington, DC, 2011; p 7. DOI: 10.17226/12654 (accessed 2019-01-31).

[11] Goode, S. R.; Grabowski, L. E. Review and analysis of safety policies of chemical journals. *J. Chem. Health Saf.* **2016**, *23*, 30–35. DOI: 10.1016/j.jchas.2015.10.001

TABLE 1.3.1

Author Guidelines on Safety Information Requirements from Select Chemistry Journals and Publishers

Journal or publisher	Safety information requirements
Journal of Organic Chemistry	"Authors must emphasize any unexpected, new, and/or significant hazards or risks associated with the reported work. This information should be in the Experimental Section of the full article and in the main text of a letter." (last updated December 15, 2018) (12)
European Journal of Organic Chemistry	"Authors should highlight significant hazards (whether new or known) associated with their experimental work, when applicable. This information should be contained within the Experimental Section in the text of the article and/or the Supporting Information." (accessed October 23, 2019) (13)
Organic Process Research & Development	"Given the scope of the journal, particular attention has to be given to the relevance of the described chemistry to be performed reliably on scale. In this context, attention to safety, including choice of acceptable solvents, workup, and isolation procedures is critically important to give the reader the trust that the chemistry is reliable and likely to be scalable. The scientific rationale for the choice of the optimal reaction conditions must be explained." (last updated December 13, 2018) (14)
Royal Society of Chemistry	"Authors must highlight very clearly, in the experimental details, any hazards or risks associated with the reported work and include appropriate warnings. Authors must call attention to any hazardous materials or operations and it is vital that any relevant safety precautions or standard codes of practice are explicitly cited, or included as supplementary information, as appropriate." (accessed October 23, 2019) (15)

[12] *Journal of Organic Chemistry Author Guidelines*; American Chemical Society: Washington, DC, 2018. https://pubs.acs.org/paragonplus/submission/joceah/joceah_authguide.pdf (accessed 2019-09-17).

[13] *European Journal of Organic Chemistry Notice to Authors*; John Wiley & Sons, Inc.: New York. https://onlinelibrary.wiley.com/page/journal/10990690/homepage/notice-to-authors (accessed 2019-09-23).

[14] *Organic Process Research & Development Author Guidelines*; American Chemical Society: Washington, DC, 2018. https://pubs.acs.org/paragonplus/submission/oprdfk/oprdfk_authguide.pdf (accessed 2019-09-17).

[15] *Author responsibilities*; Royal Society of Chemistry: Cambridge, UK. https://www.rsc.org/journals-books-databases/journal-authors-reviewers/author-responsibilities/#Safety-and-hazards (accessed 2019-09-23).

The *Journal of Chemical Education* (JCE) is targeted specifically at the chemistry teaching profession and has required safety information in articles for many years, particularly in activities involving chemicals of known hazard (16). As a result, JCE safety statements tend to be well developed and must include detailed information useful for those working with students in teaching labs, specific to the type of manuscript being submitted. From the JCE Author Guidelines (last updated December 14, 2018):

> Any manuscript type should contain a Hazards section if it describes the use of or exposure to hazardous chemicals or the use of equipment or procedures that present health or safety risks. A Hazards section is required in Demonstration and Laboratory Experiment manuscript types and in Communication manuscripts if they pertain to these manuscript types. Hazards and safety precautions relating to the handling or use of chemicals or the manipulation of materials or equipment must be completely and clearly described in this section.
>
> Authors describing laboratory procedures, activities, and demonstrations are urged to consult the following resources to determine the appropriate-ate and accepted standards for chemical laboratory safety practice:
>
> - *Prudent Practices in the Laboratory: Handling and Management of Chemical Hazards, Updated Version*, from the National Research Council details standards for chemical laboratory safety practice.
> - *The Guidelines for Chemical Laboratory Safety* publications from the ACS include a laboratory safety resource specifically written for secondary schools and one written specifically for academic institutions from two-year colleges through graduate school.
> - *Safety Guidelines for Chemical Demonstrations* from the ACS Division of Chemical Education outlines current best practices with a checklist of key issues for demonstrators.
>
> The Journal does not publish manuscripts that involve the use of domes-tic (i.e., kitchen) microwave ovens because such use is potentially hazardous and poses safety concerns. The Journal also does not publish manuscripts in which authors describe the use of or exposure to chemicals known to be toxic, such as n-hexane, benzene, and others, unless the author presents a convincing case that such use or exposure does not pose a risk to health and safety.

In manuscripts that discuss procedures in which products are formed, the author must provide hazard and safety information about these compounds, inasmuch as in some cases they may be more hazardous than the reactants. If the hazards of the products of a reaction are not known, the author should state the hazards or safety concerns that might be assumed (16).

It is important to check in multiple places in journal author guidelines to note if safety information is called out in different sections of the article for different manuscript types. Authors working with hazards of significant concern should further consult with editors for additional guidance if needed as they prepare their manuscripts. The goal is to provide safety precautions for managing hazards specific to the procedures as they were conducted. Readers will need to further assess the risks in their own contexts, depending on the local laboratory environment, current state of the art, level of training, and many other factors. For example, the

[16] *Journal of Chemical Education Author Guidelines*; American Chemical Society: Washington, DC, 2018. https://pubs.acs.org/paragonplus/submission/jceda8/jceda8_authguide.pdf (accessed 2019-09-17).

cautionary notice provided in the *Science of Synthesis* emphasizes the range of possible hazards that can arise even in carefully reviewed and documented methods and the responsibility of the user to prepare for these (17):

> Warning! Read carefully the following: Although this reference work has been written by experts, the user must be advised that the handling of chemicals, microorganisms, and chemical apparatus carries potentially life-threatening risks. For example, serious dangers could occur through quantities being incorrectly given. The authors took the utmost care that the quantities and experimental details described herein reflected the current state of the art of science when the work was published. However, the authors, editors, and publishers take no responsibility as to the correctness of the content. Further, scientific knowledge is constantly changing. As new information becomes available, the user must consult it. Although the authors, publishers, and editors took great care in publishing this work, it is possible that typographical errors exist, including errors in the formulas given herein. Therefore, it is imperative that and the responsibility of every user to carefully check whether quantities, experimental details, or other information given herein are correct based on the user's own understanding as a scientist. Scale up of experimental procedures published in *Science of Synthesis* carries additional risks. In cases of doubt, the user is strongly advised to seek the opinion of an expert in the field, the publishers, the editors, or the authors. When using the information described herein, the user is ultimately responsible for his or her own actions, as well as the actions of subordinates and assistants, and the consequences arising therefrom.

1.3.3 Safety Summaries – Overview

Safety summaries in publications serve multiple purposes. They:

- help organize and communicate safety information specific to an experimental method in a consistent manner appropriate to scientific journal articles
- inform readers about hazards requiring caution beyond common laboratory safety measures (e.g., basic personal protective equipment or PPE, basic laboratory emergency response equipment, and safety rules)
- help those reproducing experiments to understand, mitigate, and prepare for unusual or special risks in reported methods for research or teaching

This section provides a general overview of what types of hazards present significant risk and should be highlighted in a safety summary. Further detail on formulating a safety summary, what information to include, and some specific examples are provided later.

For research applications, safety summary statements should highlight unusual hazards and procedures that present significant risk based on risk assessment or require special control measures beyond those reasonably anticipated to be commonly present or known to those schooled in the art. For example, an exothermic reaction revealed by differential scanning calorimetry (DSC) or a reactive decomposition observed while determining a melting point

[17] *Safety Statement in Science of Synthesis*; Thieme: Stuttgart, New York; 2019. https://www.thieme.de/statics/dokumente/thieme/final/en/dokumente/tw_chemistry/SOS-safety-statement.pdf (accessed 2019-12-18).

should be included. In contrast, the strong oxidation properties of nitric acid or potassium permanganate need not be mentioned unless they introduce a non-obvious risk to the chemistry process. In research literature, the specifics of PPE need only be noted only when the risks from the agents, conditions, and activities are very high, such as the risks presented by dimethylmercury, hydrofluoric acid, *tert*-butyllithium, trimethylsilyldiazomethane, radiation, and reaction scale up.

In education-related articles, safety summaries should include any relevant information needed to protect and guide instructors, teachers, and/or students in developing safety practices. In this way, safety summaries in manuscripts for teaching laboratory activities can support the integration of safety concepts into student learning as well as communicating hazards and controls to end users. See the *Guidelines for Chemical Laboratory Safety in Academic Institutions* for more detailed learning objectives related to safety terminology and concepts (18).

The safety summary statement describing significant hazards of concern should be a precise communication of hazard management from the author regarding the specific experimental scenario and directed to researchers and others downstream who will reproduce the science. The information in a statement should be based on the assessed risks of the experimental processes based on RAMP methodology.

Several methods for applying RAMP are presented in the ACS resource, *Identifying and Evaluating Hazards in Research Laboratories*, including templates for checklists, standard operating procedures (SOPs), and job hazard analyses (19). Conducting risk assessments for your specific experiments and documenting these in your laboratory notebook (as suggested by the CSB report on the TTU incident) (20) can be augmented and refined over time and become a resource for planning future runs of the procedure, both in your own work as well as by others who may wish to repeat it. The information that you capture in your risk assessment can form the basis of the safety summary when the results of a research project are prepared for publication.

[18] Committee on Chemical Safety (CCS) Task Force for Safety Education Guidelines. *Guidelines for Chemical Laboratory Safety in Academic Institutions*; American Chemical Society: Washington, DC, 2016. https://www.acs.org/content/dam/acsorg/about/governance/committees/chemicalsafety/publications/acs-safety-guidelines-academic.pdf (accessed 2019-09-25).

[19] American Chemical Society Committee on Chemical Safety. *Identifying and Evaluating Hazards in Research Laboratories*; American Chemical Society: Washington, DC, 2015. https://www.acs.org/content/dam/acsorg/about/governance/committees/chemicalsafety/publications/identifying-and-evaluating-hazards-in-research-laboratories.pdf (accessed 2019-09-19).

[20] *Texas Tech University Laboratory Explosion*; Report No. 2010-05-I-TX; U.S. Chemical Safety and Hazard Investigation Board, Office of Congressional, Public, and Board Affairs: Washington, DC, 2011. https://www.csb.gov/texas-tech-university-chemistry-lab-explosion (accessed 2019-09-25).

1.3.4 Recognizing Hazards of Significant Concern

Experimental hazards can result from a variety of agents, conditions, and/or activities. The information in a safety summary should address any type of hazard presenting significant risk, be it due to the chemicals involved, the science involved, the equipment involved, or the environment where the work is being performed. For chemical hazards, authors should refer to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) (21). Figure 1.3.1 illustrates the nine GHS pictograms and their hazard classes. The chemical label on the source container will depict the associated GHS symbol and can indicate at a glance the overall seriousness of the potential hazard of individual chemicals (22). The original safety data sheet (SDS) from the manufacturer can provide additional information on general handling, controlling exposure and stability, among other information (23). For general information on GHS and SDS, refer to OSHA's Hazard Communication Guidance Documents on these topics.

[21] United Nations Economic Commission for Europe. *Globally Harmonized System of Classification and Labelling of Chemicals (GHS)*, 8th ed.; United Nations: Geneva, Switzerland, 2019. http://www.unece.org/trans/danger/publi/ghs/ghs_rev08/08files_e.html (accessed 2019-11-22).

[22] *Hazard Communication Standard: Labels and Pictograms*; OSHA Brief DSG BR-3636; Occupational Safety and Health: Washington, DC, 2013. https://www.osha.gov/Publications/OSHA3636.pdf (accessed 2019-01-31).

[23] *Hazard Communication Standard: Safety Data Sheets*; OSHA Brief DSG BR-3514; Occupational Safety and Health: Washington, DC, 2012. https://www.osha.gov/Publications/OSHA3514.pdf (accessed 2019-01-31).

FIGURE 1.3.1

GHS hazard communication element: pictograms and associated hazards.

GHS classification (summarized at PubChem) places chemical hazards into three broad categories: physical (H200−H290), health (H300−H373), and environmental (H400−H420) (24). Selected hazard classes of particular concern that are likely to arise in research are listed

[24] *GHS Classification*; PubChem; National Center for Biotechnology Information; U.S. National Library of Medicine; National Institutes of Health; Department of Health and Human Services: Bethesda, MD. https://pubchem.ncbi.nlm.nih.gov/ghs/ (accessed 2019-07-09).

in Table 1.3.2. Chemicals in these classes should be considered for inclusion in safety summaries because their use brings an expectation of significant risk in each situation.

TABLE 1.3.2

Hazard Classes of Significant Concern to Highlight in Safety Summaries

GHS Symbol	Hazard Class	Category	Code(s)	Hazard Description
	Explosive	Div. 1.1 Div. 1.2 Div. 1.3	H201 H202 H203	Substances that have an explosion hazard, whether mass or projection.
	Flammable	1	H220 H222 H224 H228	Substances (gases, aerosols, liquids, or solids) which are readily ignitable under the reaction conditions.
	Self-Reactive	Type A Type B Type C	H240 H241 H242	Substances which can detonate, deflagrate, or self-heat under storage or handling conditions.
	Pyrophoric	1	H250	Substances (liquids or solids) which ignite upon contact with air.
	Self-Heating	1	H251	Substances which self-heat sufficiently to ignite.
	Organic Peroxide	Type A	H240	Any organic peroxide which, as stored or handled, can detonate or deflagrate rapidly

	Acute Toxicity	1	H310 H330	Concentration varies in this category based on the route of entry. $LD_{50} \leq 50$ mg/kg bodyweight (dermal) or $LC_{50} \leq 100$ ppmV; ≤ 0.5 mg/L; ≤ 0.05 mg/L (inhalation of gases, vapors, dusts & mists - respectively).
	Respiratory Sensitizer	1A	H334	Substance shows a high frequency of occurrence for respiratory sensitization in humans based on testing and/or severity.
	Germ Cell Mutagenicity	1A	H340	Positive evidence from human epidemiological studies.
	Carcinogenicity	1A, 1B	H350	Known to, or presumed to have carcinogenic potential for humans based on human (1A) or animal evidence (1B).
	Reproductive Toxicity	1A, 1B	H360	Known to, or presumed to be a human reproductive toxicant based on human (1A) or animal evidence (1B).
	Specific Target Organ Toxicity (STOT), Single Exposure	1	H370	Substances that have produced significant toxicity in humans based on reliable human or animal evidence.

GHS and SDS information should be readily available in or near the laboratory and can provide a starting point for considering the hazards of individual chemicals. However, neither of these sources provides enough information to inform decisions about the significance of these hazards in your specific experiment or laboratory scenario. Neither labels nor SDSs consider the individual user's situation, such as scale of the reaction, laboratory environment, or other circumstances.

TIP: GHS and SDS information is a starting point to consider when researching the hazards of individual chemicals. Often additional information sources will be needed.

Manufacturers supply the same SDS for each product regardless of use, from industrial scale handling to an academic research laboratory. Each scenario presents much different concerns about hazardous release or concentration. A 2017 survey of safety information practices in academic research institutions found that SDSs for individual chemicals are the most commonly used source of safety information, but these hazard profiles can vary between suppliers and most researchers do not compare or validate safety information across sources (25). RAMP provides the methodology to apply this general information along with more specific criteria about your experiment, such as quantity or rate of heating (see Figure 1.3.2).

Hazards from nonchemical sources should also be specifically considered. For example, when heating a solvent on a hotplate, the solvent flammability is an intrinsic physical hazard of the chemical. The electrical hazard associated with hotplates is often overlooked, but the additional potential for a spark adds to the risk inherent in the procedure. Other hazards, chemical conditions, or activities of significant potential risk to consider in a safety summary might include:

- Elevated pressure or temperature where apparatus or conditions could reasonably lead to a fire, explosion, or loss of containment;
- Oxygen at greater than 25% or oxygen/fuel mixtures that are ignitable;
- Compounds with a ratio of less than 6 carbons per energetic functional group (such as azide, diazo, nitro) (see Information on Azide Compounds) (26);
- Oxidations of organic molecules, particularly at elevated temperature and/or gram scale or greater;
- Processes with high exothermicity that could lead to a runaway reaction;
- Processes in which the energetics of scalability are insufficiently defined or require special cooling;
- Additional factors that can introduce complexity into the procedure (e.g., biological pathogens, radiation, nanoparticles).

The fishbone diagram is a tool used to organize possible causes for a problem or action and place them in relevant categories. These categories can be used to inform a process of assessment and decision to manage the concern. In Figure 1.3.2, agents and conditions or "triggers" are arranged to illustrate the types of hazards that should lead a more thorough risk assessment process.

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[25] McEwen, L.; Stuart, R.; Sweet, E.; Izzo, R. Baseline survey of academic chemical safety information practices. *J. Chem. Health Saf.* **2018**, *25*, 6–10. DOI: 10.1016/j.jchas.2017.10.009

[26] Stanford University, Department of Environmental Health and Safety. *Information on Azide Compounds*; Stanford University: Stanford, CA. https://ehs.stanford.edu/reference/information-azide-compounds (accessed 2019-09-25).

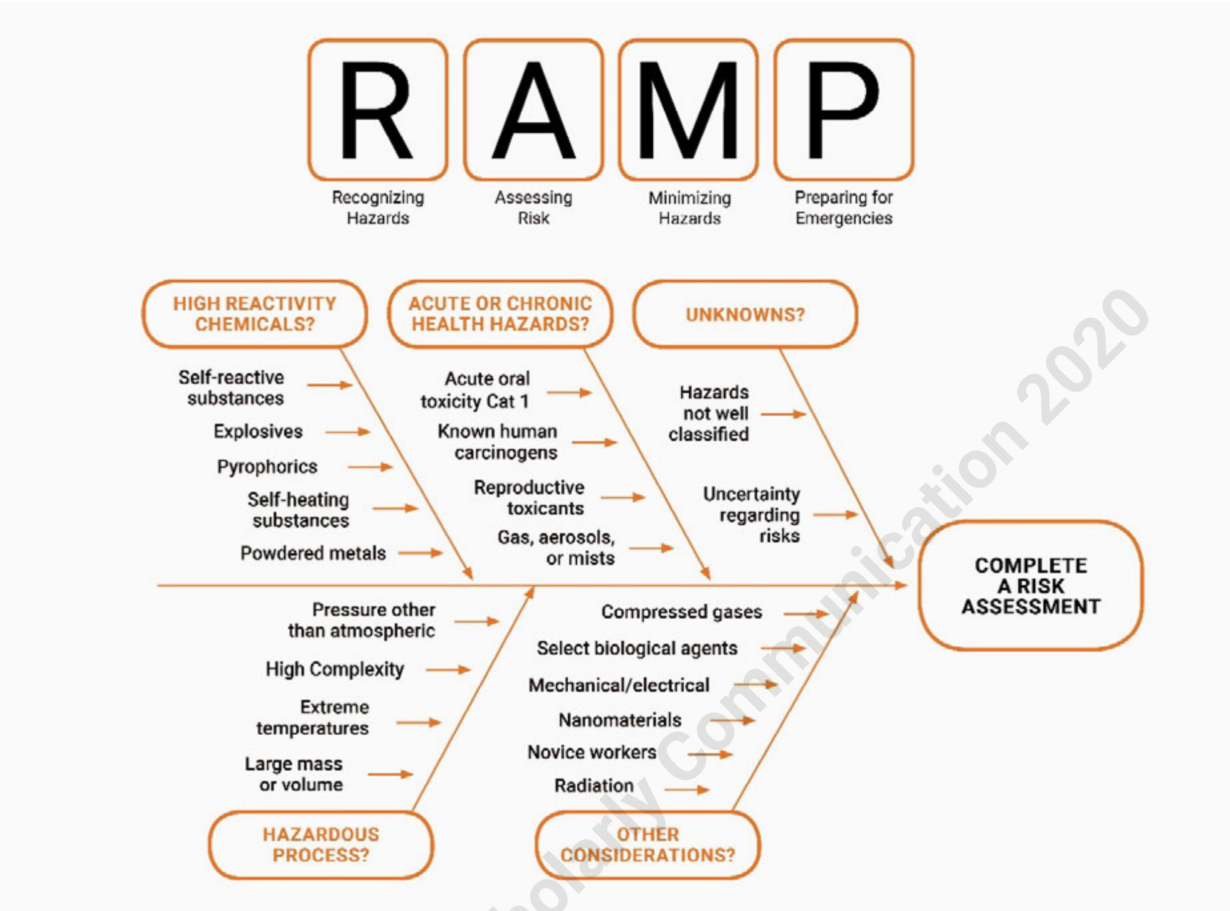

FIGURE 1.3.2

Fishbone diagram of hazard indicators that should trigger further risk assessment.
Adapted from ref (27). Copyright 2015 American Chemical Society.

As previously noted, the CSB report on the TTU incident pointed out that failure to perform a formal risk assessment process on a previous incident in the same lab was a missed opportunity that could have prevented the event in 2010. Referring to Figure 1.3.2, it can be seen that the synthesis of a derivative of NHP (nickel hydrazine perchlorate), a novel and highly reactive compound, and uncertainty regarding risks should have triggered an evaluation using risk assessment. Scaling up the reaction and concerns about friction were also factors that should have been considered in assessing risk (28).

[27] American Chemical Society Committee on Chemical Safety. *Identifying and Evaluating Hazards in Research Laboratories*; American Chemical Society: Washington, DC, 2015. https://www.acs.org/content/dam/acsorg/about/governance/committees/chemicalsafety/publications/identifying-and-evaluating-hazards-in-research-laboratories.pdf (accessed 2019-09-19).

[28] *Texas Tech University Laboratory Explosion*; Report No. 2010-05-I-TX; U.S. Chemical Safety and Hazard Investigation Board, Office of Congressional, Public, and Board Affairs: Washington, DC, 2011. https://www.csb.gov/texas-tech-university-chemistry-lab-explosion (accessed 2019-09-25).

Assessing Risks

Assessment of risk involves the application of additional physical, chemical, and toxicological data to evaluate the hazards present at the start and over the course of conducting your experiment. It is critical to have accurate information when considering the potential consequences of high hazard chemicals and procedures because, just as it is understood that scientific knowledge and methodology are constantly evolving, the same is true for information about hazards and safety management.

A variety of safety information resources are listed in Table 1.3.3, including authoritative, publicly available sources from a number of federal and international agencies. These sources may not be targeted at all scales or sectors of use, and it is important to follow original citations to determine if the data are reported under similar conditions. Safety sources can be updated frequently as information changes; make every effort to use the latest editions available and provide the full citation for any sources you use in preparing your risk assessment and safety summary. These resources are openly available, unless otherwise noted.

TABLE 1.3.3

Safety Information Resources

TYPE: Safety Documentation

Source	Title
National Research Council, Committee on Prudent Practices in the Laboratory	Prudent Practices in the Laboratory: Handling and Management of Chemical Hazards
ACS Committee on Chemical Safety (CCS)	ACS Chemical and Laboratory Safety—Safety Resources Safety in Academic Chemistry Laboratories: Best Practices for First- and Second-Year University Students Guidelines for Chemical Laboratory Safety in Secondary Schools Guidelines for Chemical Laboratory Safety in Academic Institutions Identifying and Evaluating Hazards in Research Laboratories
ACS Publications	ACS Chemical Health and Safety *by subscription or via membership*

Millipore Sigma (formerly Sigma-Aldrich)	Chemistry Technical Bulletins *(for handling specialty equipment and hazardous chemicals)*
Safety Emporium	Internet Resources for MSDS
International Safety Equipment Association (ISEA)	Eye and Face Protection Selection Tool *(eye protection)*
VWR International	Chemical Penetration Guides Ansell North Safety (ASTM standard product safety testing for laboratory gloves)

TYPE: Reported incidents & known reactivities

Source	Title
Elsevier	Bretherick's Handbook of Reactive Chemical Hazards *By subscription* (some information available through HSDB, PubChem LCSS)
Chemical & Engineering News (ACS)	C&EN Safety Letters—Compiled from C&EN Letters to the Editor
Alison Frontier, University of Rochester	Not Voodoo X *(supported by a grant from the National Science Foundation)*

TYPE: Safety related data sources

Source	Title
The National Institute for Occupational Safety and Health (NIOSH)	Fact sheets and hazard reports from the National Institute for Occupational Safety and Health
National Library of Medicine (NLM), National Institutes of Health (NIH)	ChemIDplus Advanced—National Library of Medicine search system PubChem Laboratory Chemical Safety Summary (LCSS)
Environmental Protection Agency (EPA)	CompTox Chemicals Dashboard

National Oceanic and Atmospheric Administration (NOAA)	Computer-Aided Management of Emergency Operations (CAMEO Chemicals)

Data in these sources include a variety of indicators to help evaluate the relative degree of the hazard in the context of the experiment, including types of toxicity (e.g., lethal dose, LD_{50}), exposure limits (e.g., permissible exposure limits, PEL), and routes of exposure that could arise during handling. Also consider potential sensitivity to changes in pressure or temperature in experimental conditions which may increase risk of use, as indicated by vapor density, flammability limits, and other factors. In addition to hazards from starting materials, consider any significant hazards that may be presented by products, intermediates (particularly ones that are isolated), solvents, other reagents, and how these might react together. Not all chemicals are well studied and many lack reactivity, toxicological, and regulatory data; in these cases, it is useful to look at hazards associated with chemicals containing similar functional groups (see reactivity functionality in CAMEO Chemicals).

The PubChem Laboratory Chemical Safety Summary (LCSS) aggregates data from multiple resources, which can assist the user in determining which chemical hazards are most relevant to their scenario. Extracting pertinent information requires developing a competency in reading SDSs and other safety documents (29). Prudent Practices in the Laboratory provides further guidance on using chemical information and data to help assess risk; see Box 4.1 and Tables 4.1 and 4.2 for toxicity risk assessment information, Box 4.2 for physical and reactive hazard assessment information, and Box 4.3 for biological hazard assessment information (30).

Risk determination is complex because it consists of subjective and objective components. Several useful scales and matrices have been developed to help assess objective risk [(31); see Identifying and Evaluating Hazards in Research Laboratories], including factors such as:

- Likelihood: How likely is it that exposure to a hazard will result from a complete sequence of events leading to an adverse consequence. This component is often associated with descriptors such as rare, unlikely, possible, likely, and almost certain.
- Exposure: For chemicals, exposure encompasses the nature of the chemical and how it is being used. Here chemical toxicity, route of entry, chemical form, length of exposure, etc. are the considerations. The nonchemical hazards [see Table D1: Common Hazards and Descriptions in Identifying and Evaluating Hazards in Research Laboratories ((31), pp 100–104)] must be factored as well.
- Consequence: This component of risk considers what the damages will be should the hazard result in an adverse event. Severity is typically assessed as harm to humans (range is first aid to death) and magnitude of monetary damages. Institutionally, reputation and loss of work time can also considered.

[29] Sigmann, S. Chemical safety education for the 21st century—Fostering safety information competency in chemists. *J. Chem. Health Saf.* **2018**, *25*, 17–29. DOI: 10.1016/j.jchas.2017.11.002

[30] National Research Council. *Prudent Practices in the Laboratory: Handling and Management of Chemical Hazard*, updated ver.; National Academies Press: Washington, DC, 2011 DOI: 10.17226/12654 (accessed 2019-01-31).

[31] American Chemical Society Committee on Chemical Safety. *Identifying and Evaluating Hazards in Research Laboratories*; American Chemical Society: Washington, DC, 2015. https://www.acs.org/content/dam/acsorg/about/governance/committees/chemicalsafety/publications/identifying-and-evaluating-hazards-in-research-laboratories.pdf (accessed 2019-09-19).

Factoring subjective risk is more difficult as it is based on life experiences, individual perceptions, and information that is known and available. Balancing objective information with different individuals' perceptions can introduce additional risk. Making adjustments to experimental design can also introduce new hazards. If such changes are not assessed, they can lead to an unwanted event, emphasizing the importance of revisiting risk assessments for every new situation. Always reevaluate when there is a change of conditions, new chemicals, modified equipment used, scale up of the experiment, glassware preparation, and many other process factors which can be altered. Refer back to Figure 1.3.2 for a summary view of trigger factors to consider when assessing the safety of a given laboratory scenario and specific known change factors (31).

Minimizing Risks

Evaluating the scope and degree of risk relative to a specific experiment can inform more appropriate strategies for minimizing exposure to unusual or particularly significant hazards. Various approaches to controlling hazards are organized as a hierarchy to prioritize their order of effectiveness in minimizing risk. If the risk is high enough, it may be more prudent to consider if it is possible to eliminate the use of specific chemicals, for instance, those that are particularly toxic or air-sensitive, or to substitute a different method, such as ball-milling rather than a solution-based reaction. Where possible, specific controls used should be mentioned in safety summaries.

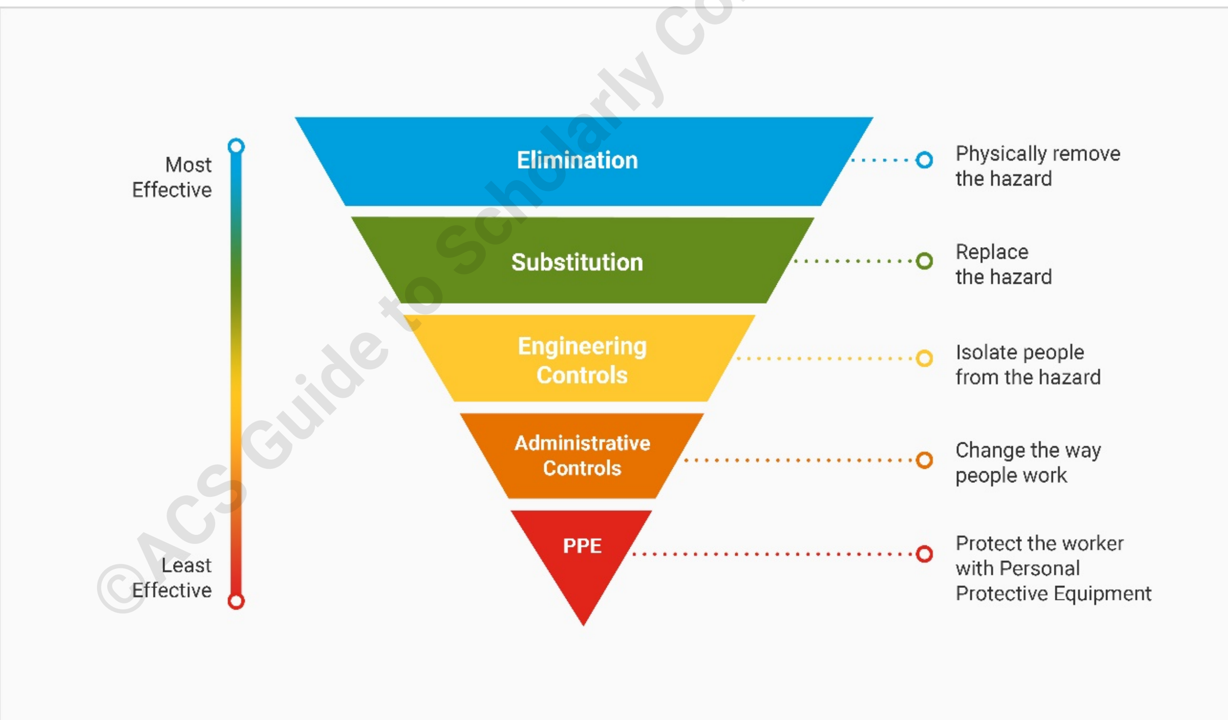

FIGURE 1.3.3

Hierarchy of controls from The National Institute for Occupational Safety and Health (NIOSH). Reprinted with permission from ref (32). Copyright 2015 U.S. Department of Health & Human Services.

Using appropriate equipment for handling sensitive materials, for separating waste streams, and for specific procedures for washing and sterilizing glassware to ensure that no organic residues remain are all examples of preventive practices for minimizing exposure and potential for risk when working with highly reactive chemicals and should be noted in the safety summary. Administrative controls such as SOPs with specific operation limits or written permissions can help manage communication, particularly if changes to procedures are being considered.

PPE is a good baseline safety practice offering one level of protection in case any material should spill, flame up, or behave unexpectedly, but as shown in Figure 1.3.3, it is the researcher's last line of defense. If PPE fails and that is the only control in place, there will be exposure. Choice of eye protection should consider the level of potential for chemical splash (see Table 2 in the eye protection guide from ISEA). Choice of glove material from different manufacturers should be carefully considered for chemical penetration rates to match the level of hazard presented in the laboratory work (see VWR International, chemical penetration guides in Table 1.3.3). Without matching PPE to your specific work using risk assessment, you may be working with a false sense of security—you don't know what you don't know.

Consider a fatal incident in 1997 when a senior researcher at Dartmouth University accidentally dripped a couple of small drops of dimethylmercury from a pipet onto her latex gloves; this exposure to a highly toxic material resulted in her death within a year (33). In planning her research, she had tried to eliminate the hazardous chemical, but her experiments had not worked as planned without dimethylmercury. She was taking all precautions known at the time, but it would later be shown that the penetration time of latex gloves is 15 seconds or less for this mercury compound and special plastic laminate gloves are required for adequate protection (34). Both this incident and those at TTU are examples of the importance of communicating lessons learned from working with hazards of significant concern.

Preparing for Emergencies

Laboratory work always introduces the potential for unwanted events. Planning for contingencies is critical for mitigating the effects of any exposure or damage that could occur. Unexpected situations can range from minor spillage, with the potential need for special gloves and a spill kit; to larger scale spillage or spontaneous combustion, requiring immediate wash or shower; and further emergencies that necessitate immediate egress from the laboratory building. Any of these scenarios could arise at any time, particularly if larger pieces of electrical equipment or pressurized gas cylinders are present in the laboratory. Preparing for potential

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[32] *Hierarchy of Controls*; The National Institute for Occupational Safety and Health (NIOSH); Centers for Disease Control and Prevention; U.S. Department of Health & Human Services: Washington, D.C., 2015. https://www.cdc.gov/niosh/topics/hierarchy/default.html (accessed 2019-07-09).

[33] Endicott, K. The Trembling edge of science: Losing world-class chemist Karen Wetterhahn to mercury poisoning redrew the boundaries of safety and risk. *Dartmouth Alumni Magazine* **1998**, *90* (7), 22–31. http://archive.dartmouthalumnimagazine.com/issue/19980401 (accessed 2019-09-23).

[34] Blayney, M. B.; Winn, J. S.; Nierenberg, D. W. Handling dimethylmercury. *Chem. Eng. News.* **1997**, *75* (19), 7. DOI: 10.1021/cen-v075n019.p007

emergencies ahead can provide direction and focus for appropriate response, should unanticipated circumstances arise.

The risk assessment process will help zero in on points in the procedure where loss of control could result in critical danger, and highlight the most effective mitigation options for reducing chance of harm. It can be helpful to map preventive and mitigative strategies from a risk assessment onto “bowtie diagrams” for the most significant hazards in an experiment. The visual layout is easily communicated: emphasizing a sequence of checkpoints to address the potential triggers identified up front, such as setting an automated pressure monitor and shutoff, as well as specific procedures for minimizing the highest risks of exposure in case of need, such as ensuring a decontamination kit is on hand. Figure 1.3.4, illustrating a bowtie of the TTU scenario from an organizational-level perspective, was created during a workshop at an ACS National Meeting in 2016 (35). The specific categories and information included in a bowtie diagram may vary depending on the needs of the user; for example, for use in the laboratory, you may want to emphasize the specific risks and controls about the experimental setup that you determine through RAMP.

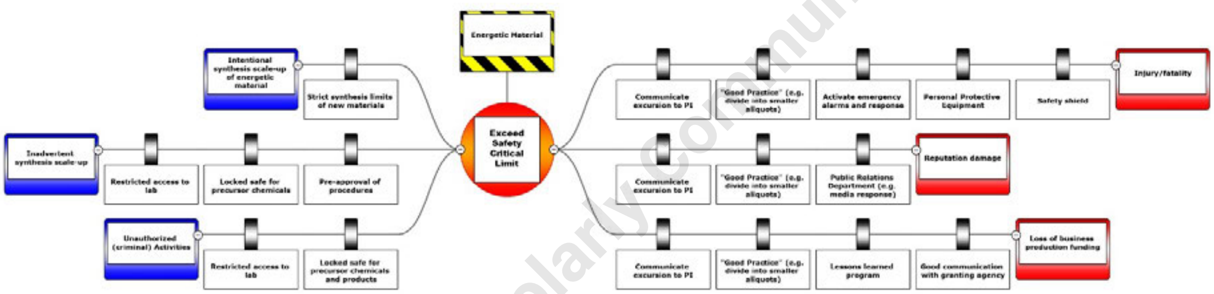

FIGURE 1.3.4

Bowtie diagram for the detonation of energetic material in a laboratory setting.

Reprinted with permission from ref (35). Copyright 2017 Elsevier.

[35] Mulcahy, M. B.; Boylan, C.; Sigmann, S.; Stuart, R. Using bowtie methodology to support laboratory hazard identification, risk management, and incident analysis. *J. Chem. Health Saf.* **2017**, *24*, 14–20. DOI: 10.1016/j.jchas.2016.10.003

1.3.5 Formulating Safety Summary Statements

The safety summary that authors prepare should not restate the general SDS from the manufacturer for the starting chemicals used in the experiment, but instead consider each aspect of RAMP described above relative to significant hazards presented by the procedures. In most cases, the safety summary statement would be included in proximity to the experimental procedures or methodology sections, though in some cases hazards noted in observation may be indicated by footnotes.

The information should be based on the author's experience with, and knowledge of, the chemistry being reported. Note and emphasize GHS statements for particularly hazardous chemicals involved (see Table 1.3.1) and keywords such as "Caution", "Hazards", "Safety", "Danger", or as required in the journal's author guidelines. Include precautionary handling procedures, special waste disposal procedures, and any other safety considerations in adequate detail so workers repeating the experiments can take appropriate safety measures. Full risk assessments can also be documented as supporting information files for particularly complex procedures involving specific safety precautions.

The following checklist contains potential information to include in a well-crafted summary statement (as applicable to the journal, chemistry, and intended audience). Numbering or bulleting the key risks and mitigations may make them easier for the reader to review.

Information to Include in a Safety Summary Statement (as Applicable): Checklist

- ✓ Names and CAS Registry Numbers of substances of notable hazard.
    - o Include products, intermediates, solvents, catalysts, etc.
    - o See categories listed in Table 1.3.2.
- ✓ GHS hazard communication elements for hazardous compounds noted.
    - o Include symbol, signal word, hazard statement, code, and category.
- ✓ Note hazards of novel compounds.
    - o Anticipate hazards based on those of closely related known analogues.
    - o Assume highest precaution based on active functional groups.
- ✓ For the specific procedure used.
    - o Note concentration of reagents.
    - o Note scale of the experiment.
- ✓ Note specific laboratory apparatus used to safely handle particularly hazardous compounds.
- ✓ Note appropriate mitigation strategies required beyond basic PPE.
- ✓ Note appropriate emergency equipment needed beyond standard laboratory equipment.
- ✓ Note any modifications to laboratory equipment.
- ✓ Note additional laboratory or facility requirements required for specific hazards.
    - o Note, for example, work with biohazardous or radioactive materials.

Including the GHS hazard classifications for notable hazardous chemicals will help to more effectively index safety information about using these compounds in research. External sources of reported toxicology or other safety information used to assess and manage risk for significant hazards should also be cited in the safety summary statement and included in the bibliography of the article with other references in accordance with the journal requirements. A safety summary statement might also reference a specific procedure for handling highly reactive compounds, such as one of the methods described in "Sigma-Aldrich Technical Bulletin AL-134: Handling Air-Sensitive Reagents" (36). SDSs, technical bulletins, and regulations and other government sources often have specific reference styles; see the References chapter in this ACS Guide for further information.

Table 1.3.4 provides a simple example of how a RAMP assessment can be used to develop a safety summary directed at a teaching audience. This is followed by the corresponding safety summary for publication.

TABLE 1.3.4

General Solvent Risk Assessment for Teaching Audience

Recognized hazard	Assessed risk	Minimization controls	Emergency preparation
Flammable	Flash fire when ignition source is present	▪ Maintain laboratory or higher ventilation levels to reduce fugitive vapors ▪ Minimal amounts of solvent in work area ▪ Maintain safe distance between fuel and ignition source OR ▪ Use hot plate to boil water	▪ Prelab discussion to raise awareness and inform students about appropriate actions for small vapor trail fire (e.g., turn off gas, smother with watch glass) ▪ Ensure proper emergency response equipment is present and functioning (e.g., fire blanket, fire extinguisher).
Acute Toxicity	Most organic solvents have some level of dermal and/or inhalation toxicity with the level of risk very dependent on the solvent and duration of contact	▪ Work in fume hood or work using table top hoods ▪ Students should wear solvent appropriate gloves for splash contact ▪ Assign prelab reading on solvent toxicity	▪ Prelab discussion to raise awareness and inform students about signs and symptoms of exposure (e.g., dizziness, confusion, redness or drying of skin)

[36] *Technical Bulletin AL-134: Handling Air-Sensitive Reagents*; Sigma Aldrich: Saint Louis, MO, 2012. https://www.sigmaaldrich.com/content/dam/sigma-aldrich/docs/Aldrich/Bulletin/al_techbull_al134.pdf (accessed 2019-01-31).

Corresponding safety summary

Flammability and inhalation hazards are controlled by using minimal amounts of solvents (<10 mL) which are distributed to students in individual containers for use in the work area. Local ventilation efficiently exhausts the escaping vapor. Stock bottles of solvents and ignition sources should not be present in the lab. There is de minimis solvent waste (<0.5 g) from this procedure which can be collected if required by local regulations. Hotplates should be used to prepare water baths. Nitrile gloves will protect students from splash contact.

1.3.6 Example Safety Statements

To assist authors in developing useful safety statements for significant hazards, below are some samples of wording that could be used to note key findings from your risk assessment and safety precautions. These are followed by some quoted examples from the literature.

The wording might be that a specific hazard is not present, as was done by Pollack et al. [(37), p. 9445]

Example 1

- Compound 1 shows a sharp melting point at 125 °C. No obvious thermal anomaly was detected by differential scanning calorimetry (DSC).

Alternatively, the wording could reflect a different situation.

Example 2

- Compound 2 decomposed with gas release at 125 °C. A 40 kJ/mol exotherm at 108 °C was detected by differential scanning calorimetry (DSC).

Unexpected events during the research should be noted.

Example 3

- A sudden 25°C temperature increase occurred when the reaction was run in THF. No such thermal event occurred in hexane or octane.

The quantity or scale of the reported experiment should be considered in evaluating the risks.

Example 4

- This reaction has not been evaluated at a scale greater than 100 mg per batch.

Example 5

[37] Pollak, D.; Goddard, R.; Pörschke, K. R. Cs[$H_2NB_2(C_6F_5)_6$] Featuring an Unequivocal 16-Coordinate Cation. *J. Am. Chem. Soc.* **2016**, *138*, 9444–9451. DOI: 10.1021/jacs.6b02590

- The exothermic nature of this reaction increases the fire risk during scale-up, and appropriate mitigation should be considered.

Statements may combine the hazard and risk mitigation.

Example 6

- Reaction 1 may undergo a thermal runaway. Synthesis apparatus should be placed behind a blast shield and temperature should be carefully monitored. A dry ice/propylene glycol slurry should be available for rapid, external quenching.

Special control equipment or maintenance requirements should be noted.

Example 7

- An acrylic shield was installed in front of the vacuum line.

Example 8

- Serious fouling of the over-pressure relief valve necessitated cleaning the valve after every reaction.

When appropriate, specialized emergency control equipment may be mentioned.

Example 9

- When using metal alkyls, have dry sand or powdered sodium bicarbonate immediately available for fire suppression.

Research Audience

Example 1

- $TMSN_3$ was transferred from the commercial container to a pressure bomb excluding air and moisture. In laboratory scale, $TMSN_3$ was always handled in a ventilated enclosure (fume hood) to prevent exposure to HN_3 vapors. On kilogram scale, handling of $TMSN_3$ was done using double gloves (inner-nitrile surgical style, outer-silvershield), a silvershield apron, and a supplied air respirator [(38), p. 2055].

Example 2

- **DO NOT store the resulting solution in a closed system, as pressure may build up** as a result of cyanate decomposition. Always check the compatibility of all constituents of the aqueous cyanide solution with H_2O_2.
- **Stability of *N*-Acetyl Hydrazine.***N*-acetylhydrazine was found to be very hygroscopic and prone to decomposition giving *N*,*N*'-di-acetylhydrazine along with hydrazine. The

[38] González-Bobes, F.; Kopp, N.; Li, L.; Deerberg, J.; Sharma, P.; Leung, S.; Davies, M.; Bush, J.; Hammand, J.; Hrytsak, M. Scale-up of Azide Chemistry: A Case Study. *Org. Process Res. Dev.* **2012**, *16*, 2051–2057. DOI: 10.1021/op3002646

decomposition is relatively fast at room temperature. After a few months already, the solid material has turned into a semi-liquid mass, with product concentrations going <80%. At 4 °C, however, in a triple polyethylene bag with a desiccant present, the product is reasonably stable (no decomposition after 3 months). *N*-acetylhydrazine HCl was found to be stable at room temperature (no change after 4 months) [(39), p. 166].

Example 3

- Caution: Sodium azide and $TMSN_3$ release hydrazoic acid (HN_3) in acidic media. Hydrazoic acid is a volatile, highly toxic and explosive compound. Fuming sulfuric acid is capable of causing very severe burns and reacts violently with water. Reactions with these reagents should not be undertaken without proper safety precautions put in place [(40), p. 1066].

Example 4

- CAUTION: Although 2-azido-1,3-dimethylimidazolinium hexafluorophosphate (ADMP) was found to be safe and stable in the safety tests (impact sensitivity test, friction sensitivity test, DSC), it is potentially explosive. It must be handled with care. This preparation should be carried out in a well-ventilated hood and should be conducted behind a safety shield (41).

Example 5

- Caution! *tert*-Butylithium is extremely pyrophoric and must not be allowed to come into contact with the atmosphere. This reagent should only be handled by individuals trained in its proper and safe use. It is recommended that transfers be carried out by using a 20-mL or smaller glass syringe filled to no more than 2/3 capacity, or by cannula. For a discussion of procedures for handling air-sensitive reagents, see Aldrich Technical Bulletin AL-134. [Note added August 2009] (42).

Example 6

- Caution! Nickel carbonyl is a flammable, volatile (b.p. 43°), highly toxic reagent. Safety glasses, gloves, and an apron should be worn when handling this reagent and the first step of this preparation should be conducted in an efficient hood (Note 1) (43).

[39] De Knaep, A. G. M.; Vandendriessche, A. M. J.; Daemen, D. J. E.; Dingenen, J. J.; Laenen, K. D.; Nijs, R. L.; Pauwels, F. L J.; Van den Heuvel, D. F.; Van der Eycken, F. J.; Vanierschot, R. W. E.; van Laar, G. M. L. W.; Verstappen, W. L. A.; Willemsens, B. L. A. Development Summary towards a Manufacturable Process for R 83842 [(*S*)-6-[(4-chlorophenyl) (1*H*-1,2,4-triazol-1-yl)methyl]-1-methyl-1*H*-benzotriazole]. *Org. Process Res. Dev.* **2000**, *4*, 162–166. DOI: 10.1021/op990081n

[40] Gutmann, B.; Elsner, P.; O'Kearney-McMullan, A.; Goundry, W.; Robergeand, D. M.; Kappe, C. O. Development of a Continuous Flow Sulfoxide Imidation Protocol Using Azide Sources under Superacidic Conditions. *Org. Process Res. Dev.* **2015**, *19*, 1062–1067. DOI: 10.1021/acs.oprd.5b00217

[41] Kitamura, M.; Murakami, K. Synthesis of 2-Azido-1,3-dimethylimidazolinium Hexafluorophosphate (ADMP). *Org. Synth.* **2015**, *92*, 171–181. DOI: 10.15227/orgsyn.092.0171

[42] Busacca, C. A.; Eriksson, M. C.; Haddad, N.; Han, S. H.; Lorenz, J. C.; Qu, B.; Zeng, X.; Senanayake, C. H. Practical Synthesis of Di-*tert*-Butyl-Phosphinoferrocene. *Org. Synth.* **2013**, *90*, 316–326. DOI: 10.15227/orgsyn.090.0316

[43] Semmelhack, M. F.; Helquist, P. M. Reaction of Aryl Halides with π-Allynickel Halides: Methallylbenzene. *Org. Synth.* **1972**, *52*, 115. DOI: 10.15227/orgsyn.052.0115

Note 1: The treatment for nickel carbonyl poisoning involves intramuscular injection of BAL (2,3-dimercapto-1-propanol).[1]

[1]Stecher, P. G. The Merck Index, 8th ed., Merck and Co.: Rahway, N.J., 1968; p. 372.

Teaching Audience

In research, solvent use is common and hazards such as flammability and toxicity would not usually need further explanation. However, in manuscripts for the teaching audience, more detail may be prudent. A safety summary such as "Hexane is flammable—use caution" is not necessarily useful. Additional precautionary information may also be important for other types of hazards, such as unknown products. See JCE Author Guidelines, for further suggestions (44). Please note that any superscript citations shown in the examples are those from the original article.

Example 1

- *p*-Xylene has known reproductive effects, but there is inadequate evidence for human carcinogenicity.[1] This solvent has GHS warnings for skin and eye irritation. Nitrile gloves offer sufficient protection for splash hazard.[2]*p*-Xylene is a respiratory tract and aspiration hazard and so the solvent should be poured in a fume hood.[1] The solvent is flammable. Tabletop hoods or some local ventilation option at work stations add an additional control for these hazards. *p*-Xylene solutions must be collected as hazardous waste.

  [1]*p-Xylene*; National Center for Biotechnology Information; PubChem Database; P-Xylene, CID=7809. https://pubchem.ncbi.nlm.nih.gov/compound/P-Xylene#datasheet=LCSS (accessed Jun. 27, 2019).

  [2]*p*-Xylene; SDS Product No. 95680, ver. 3.11; Sigma Aldrich: Saint Louis, MO, November 10, 2018. https://www.sigmaaldrich.com/catalog/product/sial/95680?lang=en&region=US (accessed Jan. 31, 2019).

Example 2

HAZARDS

- Before the commencement of any chemical demonstration, it is advisable to review the American Chemical Society Safety Guidelines for Chemical Demonstrations.[18] Standard safety procedures should be followed, but the most significant hazard of this demonstration was eliminated by removing flammable solvents as the matrix for introducing salts into the flame. When handling the salts and preparing the saturated salt solutions, chemical splash goggles, nitrile gloves, and proper lab attire should be worn. Cutting the soft insulating firebrick generates dust, and wearing a dust mask is recommended. Dust can be minimized by having the brick slightly damp.

[44] *Journal of Chemical Education Author Guidelines*; American Chemical Society: Washington, DC, 2018. https://pubs.acs.org/paragonplus/submission/jceda8/jceda8_authguide.pdf (accessed 2019-09-17).

- The demonstration should be performed a minimum of 3 m from the audience. A safety shield is recommended. The demonstrator should wear a flame retardant/resistant lab coat, safety goggles, and possibly heat resistant gloves. The demonstration should be performed only with adequate ventilation (laboratory air changes recommended) as fumes from some of the salts can cause respiratory irritation.[19–24] The demonstration setup should be kept away from flammable and/or combustible materials, and an appropriate fire extinguisher should be available. Allow the burner, firebrick, and tweezers to cool before handling and storing.
- Care should be taken when refilling the micro burners with butane. The burners should never be refilled when hot, in the presence of an audience, or from a large butane container. Additionally, burners should always be refilled away from any heat or ignition sources as jetting of the butane can occur. An appropriate fire extinguisher should be available and proper safety glasses and gloves should be worn[25–27](45).

[18]ACS Safety Guidelines for Chemical Demonstrations. https://www.acs.org/content/dam/acsorg/education/policies/safety/divched_2018_safetyflyer2pager_proof1.pdf (accessed 2019-06-18).

[19]LiCl MSDS. https://www.fishersci.co.uk/store/msds?partNumber=10578430&productDescription=250GR+Lithium+chloride+anhydrous%2C+Certified+AR+for+analysis&countryCode=GB&language=en (accessed 2019-06-18).

[20]NaCl MSDS. https://fscimage.fishersci.com/msds/21105.htm (accessed 2019-06-18).

[21]KCl SDS. https://www.fishersci.com/shop/msdsproxy?productName=P21710 (accessed 2019-06-18).

[22]$CaCl_2$ MSDS. https://fscimage.fishersci.com/msds/03901.htm (accessed 2019-06-18).

[23]$CuCl_2$ MSDS. https://fscimage.fishersci.com/msds/05625.htm (accessed 2019-06-18).

[24]$SrCl_2$ MSDS. https://fscimage.fishersci.com/msds/21980.htm (accessed 2019-06-18).

[25]Butane Refill MSDS. http://eurotool.com/ftp_files/MSDS_Sheets/Micro_Therm_Torch_Butane_Refill.pdf (accessed June 18, 2019).

[26]How to use your portable butane micro burner video. https://www.carolina.com/teacher-resources/Interactive/how-to-use-your-portable-butane-micro-burner-video/tr39543.tr (accessed 2019-06-18).

[27]RK4203-Micro Burner & Stove. https://www.youtube.com/watch?v=fX_n7lPWfB0 (accessed 2019-06-18).

[45] Canal, J. P.; Sharma, R. D.; Tailor, H. N. A Convenient, Effective, and Safer Flame Demonstration. *J. Chem. Educ.* **2019**, *96*, 2261–2265. DOI: 10.1021/acs.jchemed.8b01010

1.3.7 Glossary of Safety Organizations & Concepts

CAMEO—Computer-Aided Management of Emergency Operations

CHAS—ACS Division of Chemical Health & Safety

CCS—ACS Committee on Chemical Safety

EPA—Environmental Protection Agency

GHS—Globally Harmonized System of Classification and Labelling of Chemicals

HSDB—Hazardous Substances Data Bank

ISEA—International Safety Equipment Association

JCHAS—Journal of Chemical Health and Safety, now ACS Chemical Health & Safety

JHA—Job hazard analysis

LCSS—Laboratory Chemical Safety Summary

LD50—The lethal dose for 50% of the test population

NIOSH—The National Institute for Occupational Safety and Health

OSHA—Occupational Safety and Health Administration

PEL—Permissible exposure limit

PPE—Personal protective equipment

RAMP—Recognize, assess, minimize, prepare

SDS—Safety data sheet

SOP—Standard operating procedure

TLV—Threshold limit value