Safety Starts with U

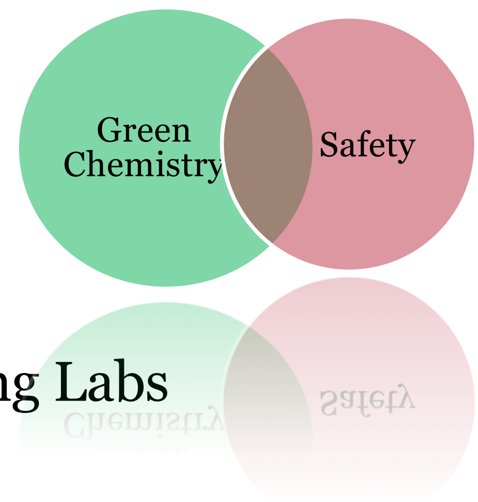
Green Chemistry's Role in Promoting Safety

Jane E. Wissinger

256th ACS National Meeting, Boston, MA
Sunday, August 19, 2018
Boston Convention Center, Room 103
2:20-2:50 PM

Overview

- Intersecting Goals of Chemical Safety and Green Chemistry
- Assessing Risk
- Green Chemistry & RAMP
- Examples in the Organic Chemistry Teaching Labs
- Ideas for implementation U of MN Joint Safety Team



Definitions & Goals

Safety in the Chemistry Enterprise

- "The practice of chemistry must be done safely so as to minimize adverse impacts on human health and/or the environment"

Protect

Green Chemistry

- "Green Chemistry is the design of chemical products and processes that reduce or eliminate the use and generation of hazardous substances."

Prevent

https://www.acs.org/content/acs/en/policy/publicpolicies/science-policy/safety-in-the-chemistry-enterprise.html
https://www.epa.gov/greenchemistry/basics-green-chemistry

12 Principles of Green Chemistry

3. **Less Hazardous Chemical Syntheses**

   Wherever practicable, synthetic methods should be designed to use and generate substances that possess little or no toxicity to human health and the environment.

4. **Designing Safer Chemicals**

   Chemical products should be designed to affect their desired function while minimizing their toxicity.

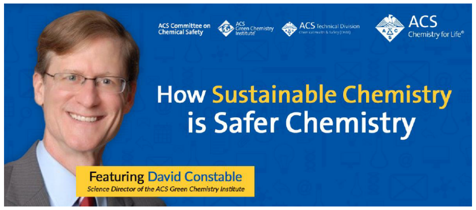
5. **Safer Solvents and Auxiliaries**

   The use of auxiliary substances (e.g., solvents, separation agents, etc.) should be made unnecessary wherever possible and innocuous when used.

12. **Inherently Safer Chemistry for Accident Prevention**

   Substances and the form of a substance used in a chemical process should be chosen to minimize the potential for chemical accidents, including releases, explosions, and fires.

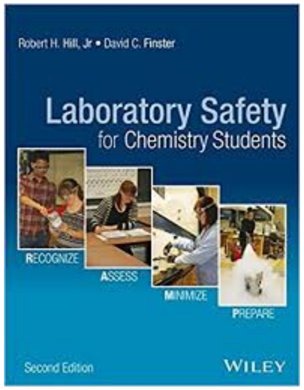
12 Principles of Green Engineering



1. **Inherent Rather Than Circumstantial**
   Designers need to strive to ensure that all materials and energy inputs and outputs are as inherently nonhazardous as possible.
2. **Prevention Instead of Treatment**
   It is better to prevent waste than to treat or clean up waste after it is formed.
3. **Design for Separation**
   Separation and purification operations should be designed to minimize energy consumption and materials use.
4. **Maximize Efficiency**
   Products, processes, and systems should be designed to maximize mass, energy, space, and time efficiency.
5. **Output-Pulled Versus Input-Pushed**
   Products, processes, and systems should be "output pulled" rather than "input pushed" through the use of energy and materials.
6. **Conserve Complexity**
   Embedded entropy and complexity must be viewed as an investment when making design choices on recycle, reuse, or beneficial disposition.
7. **Durability Rather Than Immortality**
   Targeted durability, not immortality, should be a design goal.
8. **Meet Need, Minimize Excess**
   Design for unnecessary capacity or capability (e.g., "one size fits all") solutions should be considered a design flaw.
9. **Minimize Material Diversity**
   Material diversity in multicomponent products should be minimized to promote disassembly and value retention.
10. **Integrate Material and Energy Flows**
    Design of products, processes, and systems must include integration and interconnectivity with available energy and materials flows.
11. **Design for Commercial "Afterlife"**
    Products, processes, and systems should be designed for performance in a commercial "afterlife."
12. **Renewable Rather Than Depleting**
    Material and energy inputs should be renewable rather than depleting.

https://www.acs.org/content/acs/en/greenchemistry/what-is-green-chemistry/principles/12-principles-of-green-engineering.html

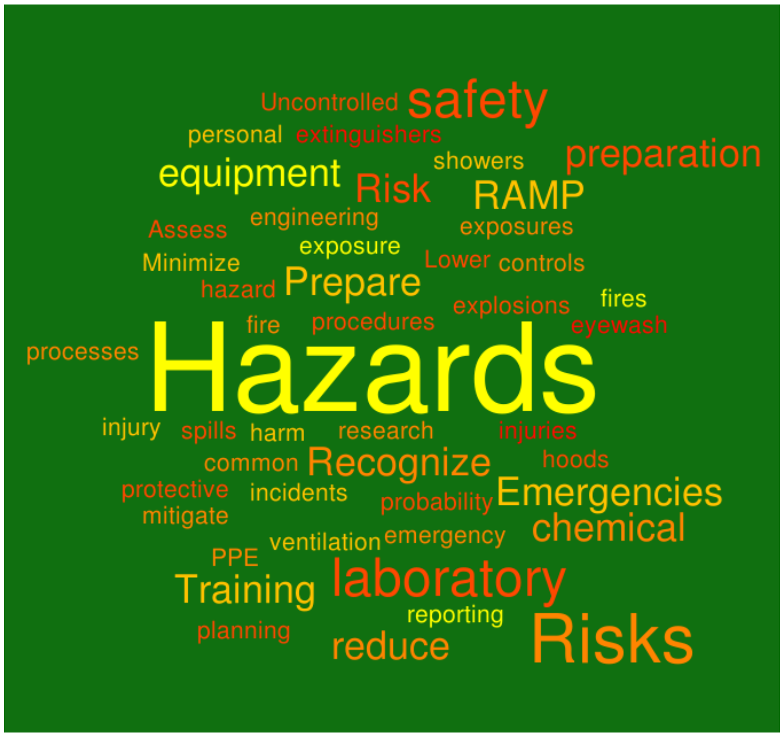
RAMP: Safety education guidelines for working in the laboratory



- **Recognize the hazards**
  - use of hazard rating systems to identify hazards
- **Assess the Risks of Hazards**
  - Risk is the probability of suffering injury or harm from exposure to a hazard. Students should be able to determine the relative severity of a specific hazard and to give an estimate of the likelihood of exposure under certain circumstances.
- **Minimize the Risk of Hazards**
  - Identify ways risk can be lowered. This may involve using appropriate engineering controls (equipment such as hoods, ventilation systems, and safety interlocks), administrative controls (procedures, processes, and training), and personal protective equipment (PPE) to reduce or mitigate the hazard.
- **Prepare for Emergencies from Uncontrolled Hazards**
  - Students should be able to explain how to respond to common emergencies that could occur in laboratories, such as fires, explosions, chemical exposures, injuries, and chemical spills.

Word Cloud Overlaps

RAMP



Green Principles

What is different from where safety culture is now?

How does a green chemistry mindset promote safety?

Recognize

- SDS – similar starting places (GHS)

- Green Chemistry Metrics (Analyze)
  - Compare processes for design
  - Type of reaction
  - Atom economy (intrinsic/inherent)
  - Focus NOT just on yield of desired products, but possible by-products and their hazards/waste handling
  - Energy and water use considerations

New Resources for Learning Chemcial Toxicology Promoted by Green Chemists

- Teaching chemists appropriate level of toxicology
  - Better understanding promotes safer design of processes and products

  - Relationship of MW to toxicity
  - Relationship of $LogK_{ow}$ to toxicity
  - ADME (Absorption, Distribution, Metabolism, Excretion)

https://modrn.yale.edu/ https://modrn.yale.edu/education

Assess the Risk

Definition:

$$\text{Risk} = f\,(\text{exposure, hazard})$$

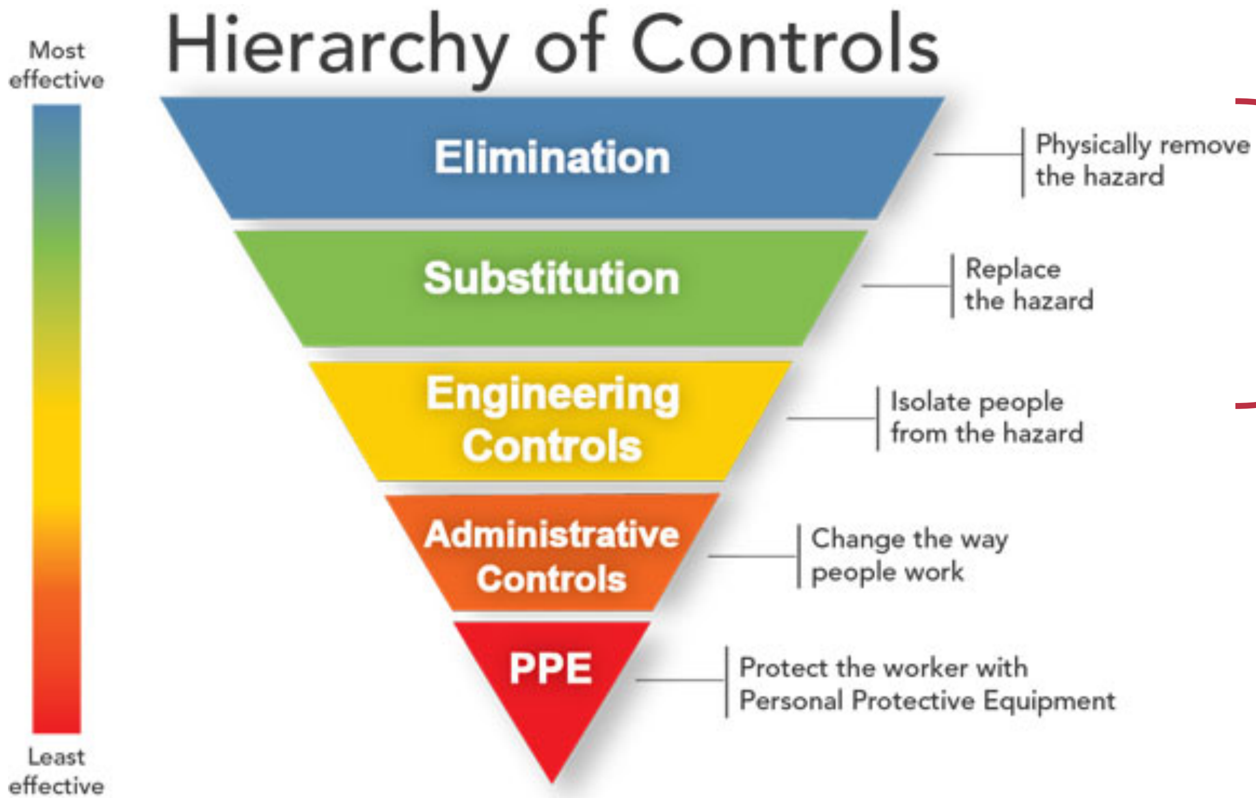
Definition:

Green Chemistry is the design of chemical products and processes that reduce or eliminate the use and generation of hazardous substances.

Thus: GC strategy is to minimize risk by reducing the HAZARD

Alternative approach to minimizing exposure: PPE, fume hoods, etc..

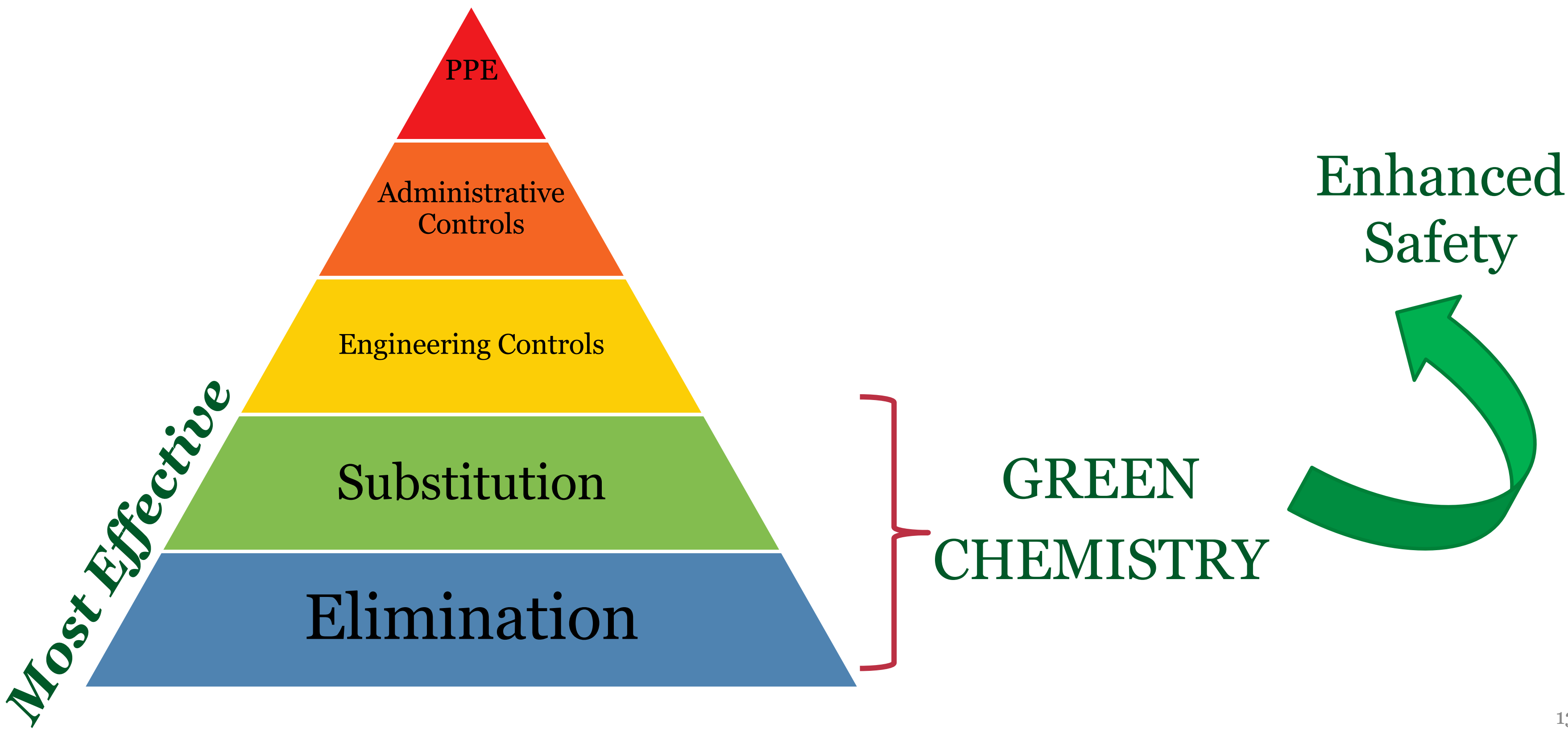
NIOSH
National Institute for Occupational Safety and Health



GREEN CHEMISTRY

https://en.wikipedia.org/wiki/Hierarchy_of_hazard_controls

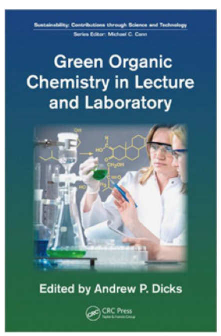
Green Chemistry → Most effective strategy should be the first strategy



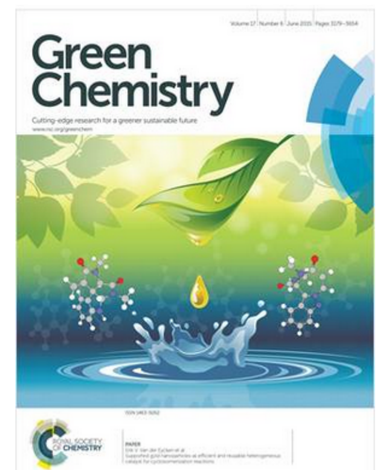
Strategies for Elimination or Substitution

- Increasing amount of literature examples/resources
- Solvent replacements
- Solventless reaction examples

ACS Sustainable Chemistry & Engineering



beyondbenign
green chemistry education



Solvent Selection Guides

Preferred	Usable	Undesirable
Water	Cyclohexane	Pentane
Acetone	Heptane	Hexane(s)
Ethanol	Toluene	Di-isopropyl ether
2-Propanol	Methylcyclohexane	Diethyl ether
1-Propanol	Methyl *t*-butyl ether	Dichloromethane
Ethyl acetate	Isooctane	Dichloroethane
Isopropyl acetate	Acetonitrile	Chloroform
Methanol	2-MethylTHF	Dimethyl formamide
Methyl ethyl ketone	Tetrahydrofuran	*N*-Methylpyrrolidinone
1-Butanol	Xylenes	Pyridine
t-Butanol	Dimethyl sulfoxide	Dimethyl acetate
	Acetic acid	Dioxane
	Ethylene glycol	Dimethoxyethane
		Benzene
		Carbon tetrachloride

Fig. 1 Pfizer solvent selection guide for medicinal chemistry.

GSK Solvent Selection Guide 2009

Classification	Solvent	CAS number	Melting point °C	Boiling point °C	Waste recycling, incineration, VOC, and biotreatment issues	Environmental Impact fate and effects on the environment	Health acute and chronic effects on human health and exposure potential	Flammability & Explosion storage and handling	Reactivity/ Stability factors affecting the stability of the solvent	Life Cycle Score Environmental impacts to produce the solvent	Legislation Flag alerts regulatory restrictions
Greenest	Water	7732-18-5	0	100	4	10	10	10	10	10	
Alcohols	1-Butanol	71-36-3	-89	118	5	7	5	8	9	5	
	2-Butanol	78-92-2	-115	100	4	6	8	7	9	6	
	Ethanol/IMS	64-17-5	-114	78	3	8	8	6	9	9	
	t-Butanol	75-65-0	25	82	3	9	6	6	10	8	
	Methanol	67-56-1	-98	65	4	9	5	5	10	9	
	2-Propanol	67-63-0	-88	82	3	9	8	6	8	4	
	1-Propanol	71-23-8	-127	97	4	7	5	7	10	7	
	2-Methoxyethanol	109-86-4	-85	124	3	8	2	7	6	7	
Ester	t-Butyl acetate	540-88-5	-78	95	6	9	8	6	10	8	
	Isopropyl acetate	108-21-4	-73	89	5	7	7	6	9	7	
	Propyl acetate	109-60-4	-92	102	5	7	8	6	10	4	
	Dimethyl carbonate	616-38-6	-1	91	4	8	7	6	10	8	
	Ethyl acetate	141-78-6	-84	77	4	8	8	4	8	6	
	Methyl acetate	79-20-9	-98	57	3	9	7	4	9	7	
Ketone	Methylisobutyl ketone	108-10-1	-84	117	6	6	6	7	8	2	
	Acetone	67-64-1	-95	56	3	9	8	4	9	7	
	Methylethyl ketone	78-93-3	-87	80	3	7	8	4	8	3	
Organic Acids	Propionic acid	79-09-4	-21	141	4	8	6	8	8	7	
	Acetic acid (glacial)	64-19-7	17	118	4	8	6	8	7	8	
Aromatics	p-Xylene	106-42-3	-13	138	7	2	6	5	10	7	
	Toluene	108-88-3	-95	111	6	3	4	4	10	7	
	Benzene	71-43-2	6	80	5	6	1	3	10	7	
Hydrocarbons	Isooctane	540-84-1	-107	99	6	4	8	3	10	7	
	Cyclohexane	110-82-7	7	81	5	5	7	2	10	7	
	Heptane	142-82-5	-91	98	6	3	8	3	10	7	
	2-Methylpentane	107-83-5	-153	60	5	4	7	2	10	7	
	Hexane	110-54-3	-95	69	5	3	4	2	10	7	
	Petroleum spirit	8032-32-4	-73	55	6	2	2	3	10	7	
Ethers	t-Butyl methyl ether	1634-04-4	-109	55	4	5	5	3	9	8	
	Cyclopentyl methyl ether	5614-37-9	-140	106	6	4	4	5	8	4	
	2-Methyl THF	96-47-9	-137	78	4	5	4	3	6	4	
	Diethyl ether	60-29-7	-116	35	4	4	5	2	4	6	
	Bis(2-methoxyethyl) ether	111-96-6	-68	162	4	5	2	8	4	6	
	1,4-Dioxane	123-91-1	12	102	3	4	4	4	5	6	
	Tetrahydrofuran	109-99-9	-108	65	3	5	6	3	4	4	
	1,2-Dimethoxyethane	110-71-4	-58	85	4	5	2	4	4	7	
	Diisopropyl ether	108-20-3	-86	68	4	3	8	1	1	9	
Dipolar aprotics	Dimethyl sulfoxide	67-68-5	19	189	5	5	7	9	2	6	
	Dimethyl formamide	68-12-2	-61	153	4	6	2	9	9	7	
	N-Methylformamide	123-39-7	-4	200	4	6	2	10	10	7	
	N-Methyl pyrrolidone	872-50-4	-24	202	5	6	3	9	8	4	
	Dimethyl acetamide	127-19-5	-20	165	5	6	2	10	8	2	
	Acetonitrile	75-05-8	-45	82	2	6	6	6	10	3	
Chlorinated	Carbon tetrachloride	56-23-5	-23	77	4	5	3	4	10	7	
	Dichloromethane	75-09-2	-95	40	3	6	4	6	9	7	
	Chloroform	67-66-3	-64	61	3	6	3	6	9	6	
	1,2-Dichloroethane	107-06-2	-36	84	4	4	2	6	10	7	

Legislation Flag

- Substitution recommended - There are no current restrictions but future regulatory restrictions may apply
- Substitution recommended - existing regulatory restrictions apply
- Must be substituted - A regulatory ban applies

GSK SSG-MC-02 September 2010

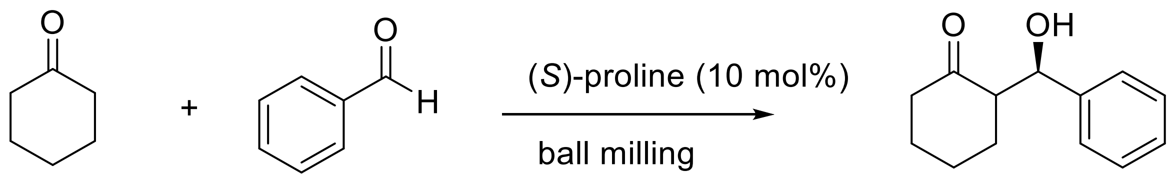
GlaxoSmithKline

ACS Green Chemistry Institute®

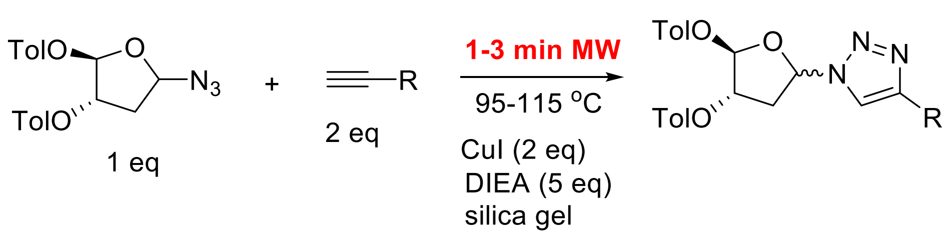
Pharmaceutical Roundtable

Scoring Information				
Safety	Health	Env (Air)	Env (Water)	Env (Waste)
3	6	6	3	6
3	6	6	2	7
2	6	5	4	7
		6	6	10
2	5	6	4	6
3	5	5	5	3
4	4	6	2	6

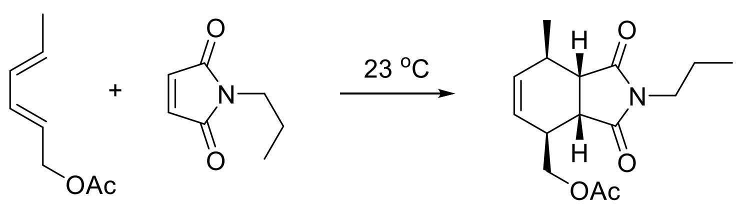
Elimination/Substitution → Minimizing (Hazardous) Waste and Innovative Chemistry



Ball Milling



Microwave



Solvent	time (h)	yield %
Water	8	81
toluene	144	79
methanol	48	82

Aqueous Reactions

Simple Techniques to Make Everyday Lab Work Greener (Safer)

This document was prepared by:

Green Chemistry Initiative

www.chem.utoronto.ca/green

Graduate student organization

Solvent Selection

1 **Use dry ice/isopropanol for cooling baths**

Reaches essentially the same temperature as dry ice/acetone (-77°C vs. -78°C), but the lower volatility of isopropanol minimizes vapor emissions and inhalation, and makes the bath last longer.

2 **Use heptane instead of hexanes**

Heptane has almost identical chemical properties to hexane, but is significantly less toxic due to the odd number of carbons, which alter its metabolic product in the body.

3 **Use 2-MeTHF instead of THF**

2-MeTHF is indirectly derived from bio-based renewable feedstocks. Its chemical properties are very similar to THF but it is immiscible with water, making separations, recycling, and drying easier. See D. F. Aycock , *Org. Process Res. Dev.* **2007**, *11*, 156–159 for more information.

4 **Substitute DCM in column chromatography**

One of the largest contributors to chlorinated solvent waste is chromatography. While selecting a new solvent system may seem challenging, J. P. Taygerly, et al. (*Green Chem.* **2012**, *14*, 3020-3025) have already done the work for you.

Simple Techniques to Make Everyday Lab Work Greener (Safer)

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www.chem.utoronto.ca/green

Waste Reduction

5 **Recycle wash solvents**

Wash solvents are ideal for recycling because dryness and purity isn't as important. Simply wash your glassware as usual, collecting the liquid in a separate container. When it's full, transfer to the rotovap and distill into a clean collection flask.

6 **Recycle solvents isolated from distillation/rotovaping**

If you are going to remove the solvent anyway, why not reuse it? When you are done your purification step, do a quick check of the purity of the solvent. If pure: reuse it for another reaction or as a wash solvent. This is ideal for single-solvent systems, azeotropes, and solvent mixtures with >10°C difference in boiling point.

7 **Use a closed-loop cooling system for condensers**

Closed-loop cooling systems eliminate wastewater and accidental laboratory flooding. Use a commercially available chilled water recirculator, an aluminum condenser, or for high-boiling liquids simply use air.

8 **Use Dry Column Vacuum Chromatography to purify large samples**

This is a relatively new technique that can dramatically reduce the amount of silica and solvents used. For larger purifications, it's faster than flash chromatography and the columns can easily be recycled. For more information see D. S. Pedersen and C. Rosenbohm, *Synthesis* **2001**, *16*, 2431-2434.

Energy Reduction

9 **Close your fume hood**

A variable volume fume hood is 60% more energy efficient when the sash is closed.

10 **Turn off/unplug stuff when you are done with it**

It just makes sense.

Precautions for Substitutions

- Like scaling, replacements must be done carefully and thoughtfully
  - Regrettable substitutions (BPS for BPA)
  - Alternatives Assessment
    - Life cycle/systems thinking approach
    - Scale

Minimize the Risks of the Hazards

- If the hazards are reduced, type of controls can be reconsidered:
  - Engineering controls (hoods)
  - PPE (error on caution – gloves)

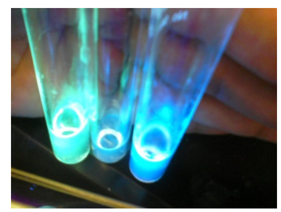
Prepare for Emergencies from Uncontrolled Hazards

12. Inherently Safer Chemistry for Accident Prevention

    Substances and the form of a substance used in a chemical process should be chosen to minimize the potential for chemical accidents, including releases, explosions, and fires.

Green Organic Chemistry Laboratory

- 2002 – token green experiment
- 2018 – A green approach
  - Modern
  - Green Solvents (water, ethyl acetate, alcohols)
    - Reduce exposure
    - Reduced halogenated/heavy metal waste
  - Greener Reactions
    - Less potential for accidents
    - More variety (polymer-supported rxns, solventless)
    - New techniques
  - Student interest in research
  - GTA interest in applying to their research



Reduced Waste/Less Hazardous Waste

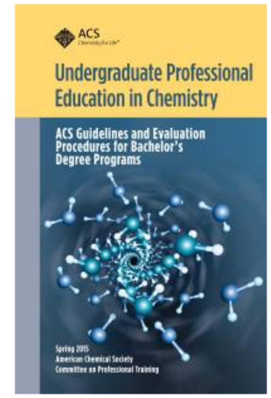
- Concerted effort to teach students how to wash glassware with minimal acetone (VIDEO)
  - Track acetone use per experiment – can tell where the most waste is generated
  - Track waste containers per semester
    - ***0.92 L down to 0.56 L per student***

- Less Concern for Hazardous Waste
  - Example: strong oxidizers in organic waste
  - Emphasis on not overfilling waste containers

Student Response to Inclusion of Green Chemistry

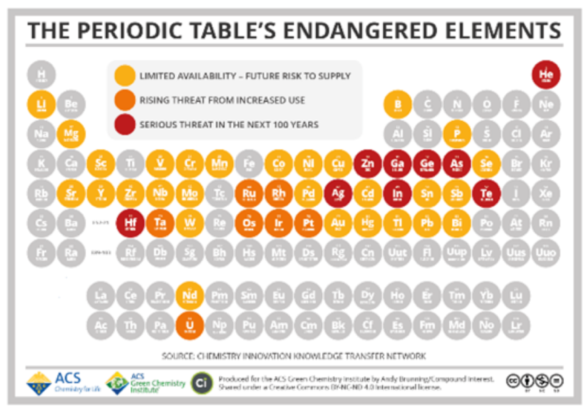
Statement	% positive responses
I value the inclusion of green chemistry in the 2311 curriculum	92.6
The fact that the product will be used in a research group rather than thrown away is important to me	71.6
I appreciate learning about chemistry that is currently employed in industry	87.9

CPT Supplement on Green Chemistry



- What's in this supplement?
  - ***Making the case for green and sustainable chemistry.***
    - SAFER chemistry departments
    - Preparing students for future careers
    - Modern and innovative
    - Chemical enterprise contributions to sustainability

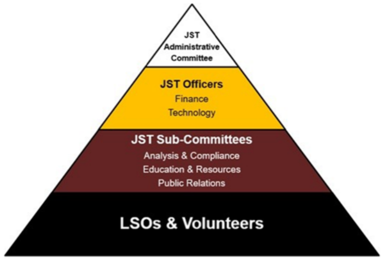
- Practical Examples – Like Safety (cross disciplinary)
  - General Chemistry
  - Analytical Chemistry
  - Biochemistry
  - Inorganic Chemistry
  - Organic Chemistry
  - Physical Chemistry



Incorporation into a Safety Culture

Safety Starts with U

University of Minnesota



Joint Safety Team Organization

JST is compiled of Lab Safety Officers (LSOs) from each research group (~ 80 people) as well as volunteer undergraduates, graduates, and postdocs.

Mission Statement

Mission Statement:	Student-led initiative to improve the safety culture in the CHEM and CEMS department at the University of Minnesota*

CARE

Compliance Define and enforce standard roles and expectations through biannual lab audits

Awareness Enhance safety through signage, safety moments, posters, and email communication

Resources Provide easy access to information and establish a system for maintaining records

Education Provide frequent and relevant training

University of Minnesota
Driven to Discover℠

1. Awareness

- Signs around department
- Stall wall moments
- Safety Moments BEFORE all seminars and presentation
- Safety Note in weekly news letter

Add Green Chemistry Based Examples

Stall Moment – Choose a safer solvent

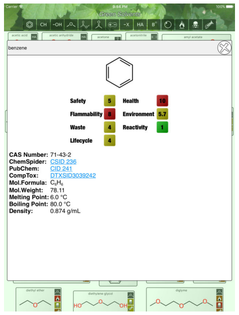
Preferred	Usable	Undesirable
Water	Cyclohexane	Pentane
Acetone	Heptane	Hexane(s)
Ethanol	Toluene	Di-isopropyl ether
2-Propanol	Methylcyclohexane	Diethyl ether
1-Propanol	TBME	Dichloromethane
Ethyl Acetate	Isooctane	Dichloroethane
Isopropyl acetate	Acetonitrile	Chloroform
Methanol	2-MeTHF	NMP
MEK	THF	DMF
1-Butanol	Xylenes	Pyridine
t-Butanol	DMSO	DMAc
	Acetic Acid	Dioxane
	Ethylene Glycol	Dimethoxyethane
		Benzene
		Carbon tetrachloride

Or solventless

The Pfizer solvent guide

2. Resources

- Working with Stockroom/vendors to have safer solvents on hand
  - Heptane versus hexane
  - methyl THF versus diethyl ether or methylene chloride



- 2-Iphone Mobile App – Green Solvents

- ACS-GCI Pharmaceutical Roundtable

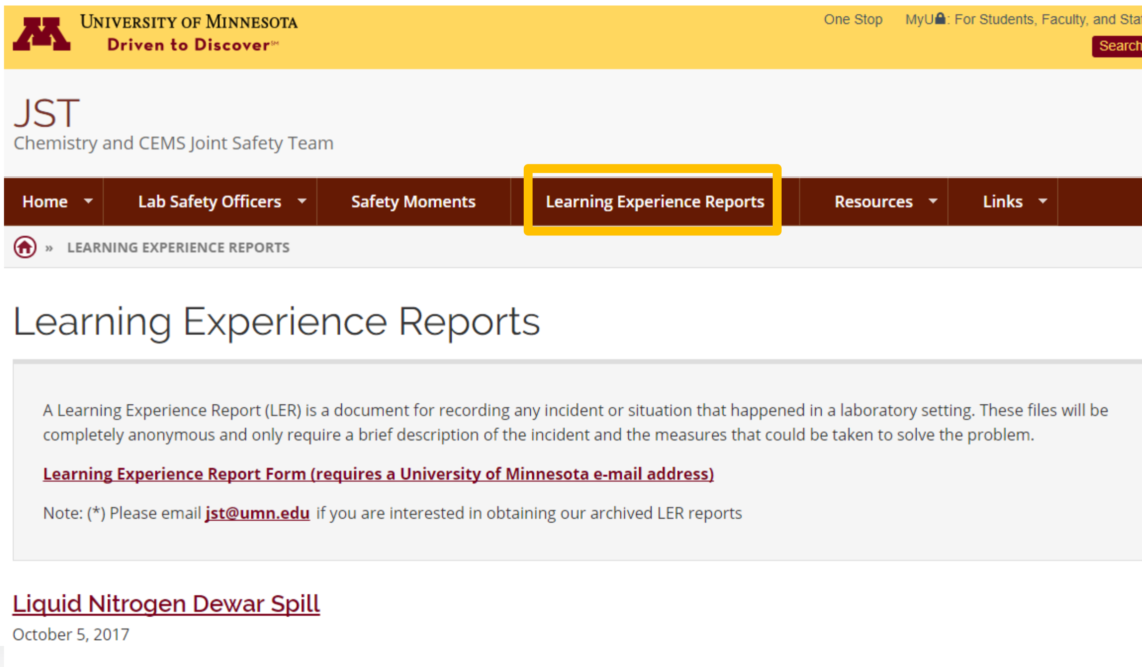
  https://www.acs.org/content/dam/acsorg/greenchemistry/industriainnovation/roundtable/acs-gci-pr-solvent-selection-guide.pdf

- GlaxoSmithKline (GSK) expanded and quick guides

  http://www.rsc.org/suppdata/gc/c0/c0gc00918k/c0gc00918k.pdf

JST Website

Provide a central location for safety resources



Green LER - "I found using 1,3-dioxolane was an excellent replacement solvent for methylene chloride"

www.jst.umn.edu

3. Education

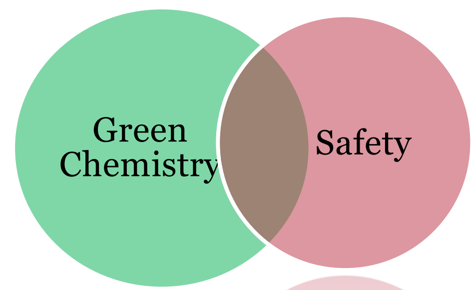
- Scaffold in Green Chemistry with Safety Training Courses – everyone has to complete
  - Introduction to Research Safety
  - Chemical Safety
  - Management

- Emphasize in TA Training

- Include chemical toxicology training

Conclusion

- Green Chemistry Goals and Safety Goals are complimentary



- **Mindset** of utilizing green chemistry when possible will **enhance** safety of chemists and the environment

Acknowledgements

- Anna Sitek – U of MN Research Safety Professional
- U of MN Joint Safety Team (JST)

Joint Safety Team

Departments of Chemistry and
Chemical Engineering and Materials Science

Questions? Comments? Contact JST@umn.edu or visit us at jst.umn.edu
The JST thanks Dow Chemical Company for their support

Safety Starts with U

Safety in the Chemistry Enterprise Policy Statement (2016-2019)

- Chemical management and regulatory policy should foster technological innovation and a globally competitive US chemical industry. Advancing research and **applying appropriate green and sustainable principles will lead to economically viable technical innovations.** To this end, ACS supports the government implementation of:
- An expedited, rigorous treatment of regulatory applications for **inherently safer chemical products and processes.** The government should work with industry, academia, scientific organizations, public interest groups, and other stakeholders to develop guidelines for use in such a regulatory process.

https://www.acs.org/content/acs/en/policy/publicpolicies/science-policy/safety-in-the-chemistry-enterprise.html

Education is Key to Assessing Risk

- **Safety**
  - Compliance with regulations
  - Review of experimental procedures (SOPs)
  - Use of Globally Harmonzied System (GSH) and Consumer Product Safety Commission (CPSC)

- **Green Chemistry Initiatives**
  - Work with EHS personnel (AASHE – Association for the Advancement of Sustainability in Higher Education, Anna Sitek (UMN), U of MN facilities)
  - Teach Appropriate Level Toxicology (simple bioavailabilities properties)
  - Solvent Replacement Guides (many to choose from)
  - Safer Reagent Guides (GCI – Pharmaceutical Roundtable)
  - Designing a Safer Chemical Game (Yale Green Chemistry Institute)