SUGGESTED ENHANCEMENTS OF GREEN CHEMISTRY ASSESSMENT TOOLS CROWDSOURCED FROM THE ACS COMMITTEE ON CHEMICAL SAFETY

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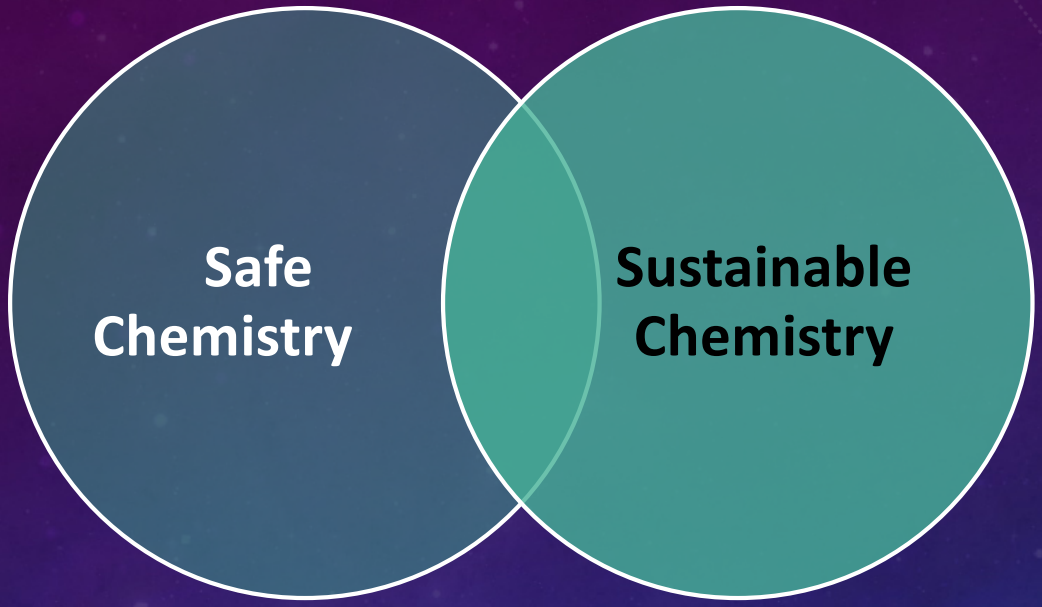

Safe chemistry can be unsustainable chemistry.

Sustainable chemistry needs to be safe chemistry.

SAFE AND SUSTAINABLE FOR WHOM?

- Supplier
- Chemist
- Production engineer/community
- Distributor/retailer
- End user/consumer
- Waste handler
- Environment

Sustainable and green chemistry:

"Chemistry that protects and benefits the economy, people and the planet by finding innovative ways to reduce waste, conserve energy, replace hazardous substances, use more sustainable or renewable feedstocks, and design for end of life or the final disposition of the product."

Safe chemistry:

"Chemistry that protects people and the environment by recognizing hazards, assessing and managing risks, and preparing for contingencies. In order of preference, risks are managed via elimination, substitution, engineering controls, administrative controls and personal protective equipment."

“RAMP”
CHEMICAL SAFETY’S ORGANIZING PRINCIPLE

Recognize the hazards

Assess the risks

Minimize the risks

Plan for emergencies

APPLICATION OF GREEN CHEMISTRY METRICS

Ancillary Environmental Factors	Chemistry Enterprise	Metric Focus/Scope
	Research	Reaction
Material management	↓	
	Development	Synthesis
Personal exposure	↓	
	Production	Process
Waste	↓	
	Commerce	Production
Environmental releases	↓	
	Disposition	Product

Production is within the realm of “process safety,” which includes evaluation of safe process design. Process safety considers the full spectrum of design and risk management opportunities, from reducing potential consequences via Inherently Safer Design (ISD) to reducing risk through process and job design.

CONCERNS WITH GREEN CHEMISTRY METRICS

- Many of then narrowly apply to the reaction/synthesis/process aspects of the chemistry enterprise.
- These tools often overlook key safety factors that could render the “greenest” alternative impractical or unusable.
- In many cases, researchers and engineers assume that safety risks that may arise within green chemistry can be addressed with administrative and engineering controls, rather than averting safety risks altogether through experimental or production design.

SOME GREEN CHEMISTRY METRICS

Assessment tools developed to determine the relative "greenness" of chemical reactions, processes and products

- Yield
- Atom economy (Trost, Barry, *Science,* 1991, *254,* 14-1477)
- E-factor
  (Sheldon, Roger A., 1994, 2000 and in *Green Chem.,* 2017, *19,* 18-43)
- Reaction mass efficiency
  (Constable, et al., 2002, *Green Chemistry,* 4 (6), 521–527)
- Life cycle cost assessment
- EcoScale (Van Aken, et al., *Beilstein J. of Org. Chem.* 2006, 3)
- Green star (Duarte, et al., *J. Chem. Educ.,* 2015, 92, 1024-1034)

NOTES ABOUT GREEN CHEMISTRY METRICS

- Used to compare reactions and processes
- Best thought of as a rough comparison—a first approximation of relative “greenness.”
- A score, in itself, doesn’t have meaning (i.e., a low score doesn’t prohibit the procedure)
- Simplicity and ease of use facilitates utilization
- It is easy to suggest additions, but details and complexity will likely hinder use

In August 2018, the American Chemical Society's Committee on Chemical Safety reviewed two green chemistry assessment tools—EcoScale and Green Star. Multiple suggestions were made to improve the tools. By incorporating safety factors, the tools could be useful in choosing alternatives that optimize both greenness and safety.

PARAMETERS WITH PENALTY POINTS TO CALCULATE THE EcoScale

1. Yield
2. Price of reaction components
3. Safety
4. Technical setup
5. Temperature/time
6. Workup and purification

WASTE GENERATION AND EcoScale's NOTE ABOUT YIELD

Penalty Points = (100 – %yield)/2

"The yield is one of the most important factors… A high yield guarantees an optimal use of resources and usually results in an easy workup procedure as side-products are limited."

Indirectly, yield measures the impact of waste generation. However:

- Yield doesn't account for waste solvents, waste media, waste catalyst and other byproducts
- Waste hazards vary greatly (e.g., instability, PIHs, malodorous)
- Environmental impact of waste varies greatly (e.g., impact of treatment, recycling, indefinite encapsulation)

EcoScale SAFETY PARAMETERS

Safety	Penalty Points
N (dangerous for environment)	5
T (toxic)	5
F (highly flammable)	5
E (explosive)	10
F+ (extremely flammable)	10
T+ (extremely toxic)	10

Penalty points are additive for the characteristics of each component.

MOST POPULAR SUGGESTION TO IMPROVE EcoScale

- Replace current safety parameters with Globally Harmonized System (GHS)-based parameters
- GHS is refined, standardized, well defined, more comprehensive
- Use of GHS will lead to more objective scores

PHYSICAL HAZARDS	ASSOCIATED HAZARD CATEGORY
Explosives	Divisions 1.1-1.6 (with 1.1 being the most hazardous, 1.6 the least hazardous)
Flammable gases	Categories 1 and 2
Flammable aerosols	Categories 1 and 2
Oxidizing gases	Category 1
Gases under pressure	4 Groups include: Compressed gas, Liquefied gas, Dissolved gas, and Refrigerated liquefied gas
Flammable liquids	Categories 1 - 4
Flammable solids	Categories 1 and 2
Self-reactive substances	Types A-G
Pyrophoric solids	Category 1
Pyrophoric liquids	Category 1
Self-heating substances	Categories 1 and 2
Substances which in contact with water emit flammable gases	Categories 1 - 3
Oxidizing liquids	Categories 1 - 3
Oxidizing solids	Categories 1 - 3
Organic peroxides	Types A-G
Substances corrosive to metal	Category 1

HEALTH HAZARDS	ASSOCIATED HAZARD CATEGORY
Acute toxicity	Categories 1-4 (with 1 being the most dangerous)
Skin corrosion	Categories 1A, 1B, 1C, and 2
Skin irritation	Categories 1A, 1B, 1C, and 2
Eye Effects	Categories 1, 2A, and 2B
Sensitization (Skin or Eye)	Category 1A and 1B
Germ cell mutagenicity	Categories 1A, 1B, and 2
Carcinogenicity	Categories 1A, 1B, and 2
Reproductive toxicity	Categories 1A, 1B, 2, and additional category for effects on or via lactation
Target organ systemic toxicity: single	Single: Categories 1-3
and repeated exposure	Repeated: Categories 1 and 2
Aspiration toxicity	Category 1 and 2

ENVIRONMENTAL HAZARDS	ASSOCIATED HAZARD CATEGORY
Acute Aquatic Toxicity	Categories 1 -3
Chronic Aquatic Toxicity	Categories 1 - 4

EcoScale's NOTE ABOUT SAFETY

"Safety is of paramount importance when carrying out organic chemistry experiments. Working with chemicals is never without a risk, and it is necessary to fully understand any potential hazard. …the hazard can increase over time, and photooxidation of ether to generate explosive peroxides is a good example. It must also be emphasized that it takes a long time before the safety profiles of new products are fully characterized. Finally, one should never forget that the combination of certain individual compounds can create a hazardous situation (e.g. exothermic reaction between acids and bases)."

ACS Committee on Chemical Safety suggestion: Add a penalty for chemical incompatibility that risks unsafe reaction conditions.

EcoScale's PENALTIES FOR TECHNICAL SETUP

Penalty points for any beyond-simple extra setup, "including special glassware, equipment for controlled addition of chemicals, pressurized vessels, the application of unconventional techniques such as microwave irradiation, ultrasound or photochemistry, and the need for an inert atmosphere."

OTHER PROCESS/TECHNICAL SETUP PENALTIES TO CONSIDER

- Many different technical setups that merit miscellaneous points (e.g., vacuum techniques, unattended operations, etc.)
- Penalty for needed engineering controls to prevent personal exposure, release or accident
- Penalty for needed personal protective equipment to prevent exposure

Suggestions from the ACS Committee on Chemical Safety

RECOMMENDATIONS TO IMPROVE GREEN CHEMISTRY METRICS —TOWARD A MORE COMPREHENSIVE MODEL

- Consider materials management, including the storage hazards of materials, product and waste: shelf life, storage temperature range, stability
- Use GHS to specify chemical hazards
  - Environmental toxicity should consider environmental mobility, bioaccumulation, and persistence
- Consider chemical incompatibility
- Penalties for additional PPE requirements
- Penalties for required engineering controls
- Make an app for that
- Add post-score validation steps of a) hazard recognition, b) risk assessment (probability and consequence) and c) consideration of contingencies

MAKING GREEN CHEMISTRY SAFER

- Expanded and more nuanced understanding of chemical hazards (i.e., beyond toxicity)
- Better understanding of the risks of exposure and environmental releases, their impacts to human health and the environment, and measures to control them
  - Personal protective equipment
  - Engineering controls
- A more integrative, holistic view—considering ancillary impacts
  - Material management
  - Waste
- Look ahead to scale up, pilot plant, production
  - Managing exothermic reactions
  - Process safety measures of risk management—their complexity and cost, and ways to make them unnecessary
  - Product properties