It's all in how you do it: Annotating process conditions in laboratory chemical hazard recognition and risk management

Leah McEwen, Cornell University
Ye Li, University of Michigan
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It's all in how you do it:
Annotating process conditions in laboratory chemical hazard recognition and risk management
Stakeholders need to make decisions

- **Safety Officers**
  - Following up on emergencies;
  - Advising on laboratory setup and documentation practices;
  - Training researchers;
  - Complying with regulations

- **Researchers**
  - Appreciating complexity of hazard potential beyond intentional chemistry;
  - Determining suitable precautions and mitigations;
  - Assessing ripple effects when adjusting experiments (scale up, substituting reagents, increase temperature, etc.)

- **Educators**
  - Inaugurating safety and prudence into research practice
Lots of moving parts can alter conditions unexpectedly, and trigger unintentional reactions and exposure to hazards.

Caution! tert-Butyllithium 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...
Potential Hazard Triggers

HIGH REACTIVITY CHEMICALS?
- Self-reactive substances
- Powdered metals
- Explosives
- Pyrophorics
- Self-healing substances

ACUTE or CHRONIC HEALTH HAZARDS?
- Acute oral toxicity LD$_{50}$ ≤50 (mg/kg)
- Known human carcinogens
- Reproductive toxins
- Gas, aerosols, or mists

UNKNOWNs?
- Hazards not well classified
- Uncertainty regarding risks

HAZARDOUS PROCESS?
- Pressure other than atmospheric
- High Complexity
- Extreme temperatures
- Large mass or volume

OTHER CONSIDERATIONS?
- Compressed gases
- Select biological agents
- Mechanical/electrical
- Nano materials
- Novice workers
- Radiation

COMPLETE A JHA
Local Conditions Contribute!

Job Hazard Analysis (JHA)

Many professional anecdotes!
Retro-Hazard Analysis

Identify

Threat 1
Threat Control
Threat Control
Hazard and Hazard Source

Threat 2
Threat Control
Threat Control

Threat 3
Threat Control
Threat Control

Assess

Top Event

Consequence 1
Recovery Measure

Recovery Measure

Consequence 2
Recovery Measure

Recovery Measure

Consequence 3
Recovery Measure

Control

Recover

http://www.risktec.co.uk/consulting/bowtie-risk-management.aspx
Lessons Learned

9 Stability and Reactivity

9.1 Reactivities and Incompatibilities

A mixture of acetone and chloroform in a residue bottle exploded. Since addition of chloroform to acetone in presence of a base will result in a highly exothermic reaction, it is thought that a base may have been in the bottle.


Acetone may form explosive mixtures with chromic anhydride, chromyl chloride, hexachloromelamine, hydrogen peroxide, nitric acid and acetic acid, nitrosyl chloride, nitrosyl perchlorate, nitril perchlorate, permensulphuric acid, potassium tert-butoxide, thiodiglycol and hydrogen peroxide.


An explosion occurred during an attempt to prepare bromoform from acetone by the haloform reaction. Acetone ignited when it was accidentally splashed into a sulfuric acid-dichromate solution.

HALOACETYLENE DERIVATIVES

2. Brandsma, 1971, 99

The tendency towards explosive decomposition noted for dihalo-2,4-hexadiyne derivatives appears to be associated more with the co-existence of halo- and acetylene functions in the same molecule, than with its being a polyacetylene. Haloacetyles should be used with exceptional precautions [1]. Explosions may occur during distillation of bromoacetyles when bath temperatures are too high, or if air is admitted to a hot vacuum-distillation residue [2]. Precautions necessary in isolating and handling such compounds on the small (1 g) scale are detailed [3]. Individually indexed compounds are:

1-Bromo-1,2-cyclotridecadien-4,8,10-triyne, 3593
Bromoacetylene, 0647
Bromochloroacetylene, 0575
† 3-Bromopropyne, 1087
* Calcium hypochlorite, : Acetylene, 3918
3-Chloro-1-iodopropyne, 1070
4-Chloro-2-butylnol, 1451
1-Chloro-3-phenylpent-1-en-4-yln-3-ol, 3387
Chloroacetylene, 0648
Chlorocyanooacetylene, 1033
Chloroiodoacetylene, 0595

Bretherick’s Handbook of Reactive Chemical Hazards (7th ed.)
Urben and Bretherick; 2006 Elsevier Ltd.
1. Rationale

• An experiment is a work process
• Many potential triggers and factors for hazards
• Need for discerning, organizing, assessing
• Support documented hazard analysis

• [ecosystems statement]
• [*science value out the safety analysis process]
Why Process Conditions?

• Chemical and laboratory hazards do not exist in isolation (we have GHS, SDS, so what gives?)
• Thinking about safety hazards for one chemical at a time is not enough
• Even thinking about all chemicals in an experiment together are not enough
• Experiments happen in real time and space with real individuals and samples
Local conditions contribute!

- Conditions of experiment and environment
- Procedural operations and actions
- Laboratory practices that impact conditions (e.g., storage, washing, etc)
- Hazard exposure controls in place (e.g., ventilation, PPE, emergency equipment, etc.)

[add procedure paragraph and process diagram to schema]
[overlayed on a lab scene]
Incident Analysis

5. “How do we prevent the hazard from being released?”
   “How do we keep control?”

6. “How do we limit the severity of the event?”
   “How do we minimise the effects?”

7. “How might controls fail?”
   “How could their effectiveness be undermined?”

8. “How do we make sure controls do not fail?”
Post Incident

http://www.risktec.co.uk/consulting/bowtie-risk-management.aspx
Annotating Processes

**Goal:** support scalable laboratory planning by improving documentation relevant to repeatability and oversight

**Goal:** elucidate patterns in combinations of hazard factors that can inform matching of hazard controls and response methods with experimental and laboratory scenarios

**Goal:** identify important chemical hazard analysis and risk management concepts and how they are used in reported data
Annotation by chemical information specialists and safety officers can help identify key concepts and improve searching:
Components

• Concepts
• Data stream
• Entity dictionaries
• Annotations
Concepts

### Participant
- Apparatus
- Body_part
- Equipment
  - Ventilation
  - PPE
- Material
  - Mixture
  - Substance
- Plant
- Animal
- Site

### Attribute
- Participant_role
  - Biological_role
  - Chemical_role
  - Process_role
  - Person_role
- Hazardous_disposition
- Physical_condition
  - Phase
  - Physical_form
- Physical_property
- Control_point
- Duration

### Event
- Action
- Adverse_event
- Biological_effect
- Physical_effect
- Natural_process
- Planned_process

### Relations
- Cause
- Theme
- Associate
- As
- Not_As
- Beyond
- Experience
Entity Dictionaries

- PubChem dictionary
  - Chemicals
  - Identifiers
- Chemical Safety Ontology (CSO) dictionary
  - Safety related entities, attributes, and events
Data Stream

PubChem Annotation Analysis

Text Input:


Output Format: @-html @-bent @-csv @-corrected

Dictionary Group: PubChem_CID

Output:

CFDietN.cf0.CFDietE.cf0.chemicalmolecule.cf02. CFDietA.cf0.chemicalprefix.cf02. CFDietG.cf0. CFDietG_class.cf0. chemicalgeneric.cf02. CFDietM恤. CF
Export annotations

.txt file to be annotated

Annotations in .ann format
Import into annotation tool

<table>
<thead>
<tr>
<th>Line</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Acetone</td>
</tr>
<tr>
<td>2</td>
<td>CID 180</td>
</tr>
<tr>
<td>3</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Health and Symptoms</td>
</tr>
<tr>
<td>5</td>
<td>Symptoms</td>
</tr>
<tr>
<td>6</td>
<td>irritation eyes, nose, throat; headache, dizziness, central nervous system depression; de</td>
</tr>
<tr>
<td>7</td>
<td>from NIOSH-PocketGuide</td>
</tr>
<tr>
<td>8</td>
<td>Carcinogen</td>
</tr>
<tr>
<td>9</td>
<td>Exposure Routes</td>
</tr>
<tr>
<td>10</td>
<td>The substance can be absorbed into the body by inhalation.</td>
</tr>
<tr>
<td>11</td>
<td>from ILO-ICSC</td>
</tr>
<tr>
<td>12</td>
<td>inhalation, ingestion, skin and/or eye contact</td>
</tr>
<tr>
<td>13</td>
<td>from NIOSH-PocketGuide</td>
</tr>
<tr>
<td>14</td>
<td>Fire Hazard</td>
</tr>
<tr>
<td>15</td>
<td>Highly flammable.</td>
</tr>
<tr>
<td>16</td>
<td>from ILO-ICSC</td>
</tr>
<tr>
<td>17</td>
<td>Explosion Hazard</td>
</tr>
<tr>
<td>18</td>
<td>Vapour is explosive.</td>
</tr>
<tr>
<td>19</td>
<td>Heating will cause rise in pressure with risk of bursting.</td>
</tr>
<tr>
<td>20</td>
<td>from ILO-ICSC</td>
</tr>
</tbody>
</table>

13 ed.

An explosion occurred during an attempt to prepare bromoform from acetone by the haliform reaction.

13 ed.

Acetone ignited when it was accidentally splashed into a sulfuric acid-dichromate solution.

NIOSH Pocket Guide to Chemical Hazards & Other Databases CD-ROM.
Department of Health & Human Services, Centers for Disease Prevention & Control.
National Institute for Occupational Safety & Health.
Annotation in BRAT
Building Relationships

Before

CHEMICAL PROFILE: A mixture of acetone and chloroform in a residue bottle exploded.

Since addition of acetone to chloroform in the presence of base will result in a highly exothermic reaction, it is thought that a base was in the bottle (MCA Case History 1661 1970).


The reaction of nitrosyl perchlorate and acetone ignites and explodes.


(REACTIVITY, 1999)
from OSHA Occupational Chemical DB

After

CHEMICAL PROFILE: A mixture of acetone and chloroform in a residue bottle exploded.

Since addition of acetone to chloroform in the presence of base will result in a highly exothermic reaction, it is thought that a base was in the bottle (MCA Case History 1661 1970).


The reaction of nitrosyl perchlorate and acetone ignites and explodes.


(REACTIVITY, 1999)
from OSHA Occupational Chemical DB
Query: Under what conditions could the mixture of Acetone and what molecules cause adverse event?
Workflow

PubChem

Safety relevant text blurbs

Auto-annotation Service (mainly annotating chemicals and TOC terms in PubChem dictionary)

Extract entities, relations, events, and attributes for...

Enabling search, and re-constructing safety related statement.

Human

Select text

Export – import annotations

Annotated text (.txt and .ann files)

Manually annotate/ correct interesting entities, relations, events, and attributes relevant to chemical safety context

Partially annotated text (.txt and .ann files)

BRAT

Text as .txt file

Annotation as .ann file

+
Conclusion: Value of Manual Approach

- Leverage expertise of domain experts
- Identify missing terms in the dictionaries and CSO
- Build relationships to re-construct safety relevant statement
- Correct labels mistakenly assigned by machine
- Feed the terms, labels, and relationships back to dictionaries and ontologies
- Use identified relationships to develop new ways to query PubChem database
Thanks!

- Debbie Decker
- MaryBeth Mulcahy
- Daniel Lowe
- Sammye Sigmann
- Ralph Stuart
- PubChem team
- Many more colleagues for insightful conversation!
Annotations with PubChem and CSO dictionaries (imported in BRAT platform)

CHEMICAL PROFILE: A mixture of acetone and chloroform in a residue bottle exploded.

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The reaction of nitrosyl perchlorate and acetone ignites and explodes.


(REACTIVITY, 1999)
from OSHA Occupational Chemical DB

Acetone may form explosive mixtures with chronic anhydride, chronyl chloride, hexachloroethane, hydrogen peroxide, nitric acid and acetic acid, nitric acid and sulfuric acid, nitrosyl chloride, nitrosyl perchlorate, nitric perchlorate, permanganate, and other substances.

potassium tert-butoxide, thiodiglycol and hydrogen peroxide.

13 ed.
Manual Approach

- Workflow
- Building relationships
- Constructs
The workflow consists of the following steps:

1. **Text from safety relevant sections**
   - Auto-annotation Service (mainly annotating chemicals and TOC terms in PubChem dictionary)
   - Extract entities, relations, events, and attributes for...
   - Enabling search, and re-constructing safety related statement.

2. **Copy/Paste**
   - Text
   - Replace new line breaks ("Option + Enter") with space using TextEditor find/replace
   - Manually annotate/ correct interested entities, relations, events, and attributes relevant to chemical safety context

3. **Text as .txt file**
   - Annotation as .ann file
   - Partially annotated text (.txt and .ann files)

4. **BRAT**
Building Relationships

Before

After
Building Relationships

Before

Acetone may form explosive mixtures with chronic anhydride, chromyl chloride, hexachlororacetic acid, hydrogen peroxide, nitric acid and acetic acid, nitric acid and sulfuric acid, nitrosyl chloride, nitrosyl perchlorate, nitroxy perchlorate, permonosulfuric acid, potassium peroxide, thiodiglycol and hydrogen peroxide.

13 ed.

After

Acetone may form explosive mixtures with chronic anhydride, chromyl chloride, hexachlororacetic acid, hydrogen peroxide, nitric acid and acetic acid, nitric acid and sulfuric acid, nitrosyl chloride, nitrosyl perchlorate, nitroxy perchlorate, permonosulfuric acid, potassium peroxide, thiodiglycol and hydrogen peroxide.
Constructs

**Query:** What biological effect would Acetone cause on which body parts?

**Cause:** Molecule

**Biological effect** (on Theme: Body part)

- irritation
- depression
- headache
- dizziness
- dermatitis

**Body parts:**
- eyes
- nose
- throat
- central nervous system
Constructs

• [queries for combinations of chemicals and conditions]

**Cause:** Molecule  **Theme:** Molecule  to  **Adverse event**

Chromic anhydride
Chromyl chloride
Hyxachloromelamine
... ...

**Cause:** Acetone  **to:**  (Likely) form explosive mixtures

**Query:** What would cause acetone to likely **form explosive mixtures**?
• [rationale, a la EHS]
• [iRAMP, Engr controls, hazard analyses]
• [analyzing incident reports]
• [Identifying process factors]
• [sample blurb]
• [annotated version – html]
• [output tags]
• [Outcome in PubChem, augment auto-annotation]
• [value of manual process to build up]
• [manual annotation workflow]
• [constructs?]