

Chemical Risk Management and Basic Toxicology

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Contents

- Chemical hazards
- Sources of information
- Risk assessment
- Risk management
- Protective and safety measures
- Emergency procedures
- Waste management

Chemical hazards

Risks encountered when handling chemicals

- Fire
- Explosions (and implosions)
- Poisoning (acute or chronic)
- Chemical burns
- Asphyxia
- Cuts and other injuries
- Electrocutation

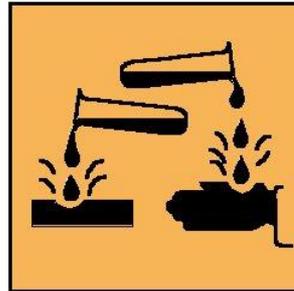
Sources of information

Identification of chemical hazards

Hazard pictograms (on containers, outdated)



Flammable



Corrosive



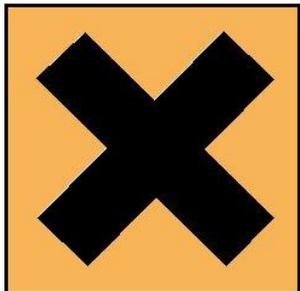
Explosive



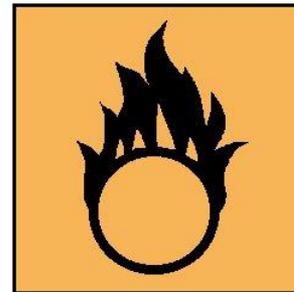
Toxic



Polluting



Harmful



Oxidizing

Identification of chemical hazards

The R and S phrases (EU and international)

No longer used since 1st June 2017

R (risk) and S (safety) phrases, their numbers, and their meanings can be found on:
<https://www.msds-europe.com/r-phrases-s-phrases/>

Identification of chemical hazards

Hazard pictograms (rooms)



Flammable materials



Corrosive materials



Explosive materials



Toxic materials



Electrical hazard



Biological hazard



Laser radiation



Radioactive materials

Identification of chemical hazards

The GHS pictograms (global harmonized system)



- Since 20th January 2009
- Transition period until 2015
- Applied globally (via UN)

Identification of chemical hazards

The "new" GHS pictograms



Flammable



Corrosive



Environmentally
damaging



Explosive



Toxic



Oxidizing



Irritant



Health
hazard



Compressed
gas

Identification of chemical hazards

The GHS hazard statements: physical hazards

- H200: Unstable explosive
- H201: Explosive; mass explosion hazard
- H202: Explosive; severe projection hazard
- H203: Explosive; fire, blast or projection hazard
- H204: Fire or projection hazard
- H205: May mass explode in fire
- H220: Extremely flammable gas
- H221: Flammable gas
- H222: Extremely flammable aerosol
- H223: Flammable aerosol
- H224: Extremely flammable liquid and vapour
- H225: Highly flammable liquid and vapour
- H226: Flammable liquid and vapour
- H227: Combustible liquid
- H228: Flammable solid
- H229: Pressurized container: may burst if heated
- H230: May react explosively even in the absence of air
- H231: May react explosively even in the absence of air at elevated pressure and/or temperature
- H240: Heating may cause an explosion
- H241: Heating may cause a fire or explosion
- H242: Heating may cause a fire
- H250: Catches fire spontaneously if exposed to air
- H251: Self-heating; may catch fire
- H252: Self-heating in large quantities; may catch fire
- H260: In contact with water releases flammable gases which may ignite spontaneously
- H261: In contact with water releases flammable gas
- H270: May cause or intensify fire; oxidizer
- H271: May cause fire or explosion; strong oxidizer
- H272: May intensify fire; oxidizer
- H280: Contains gas under pressure; may explode if heated
- H281: Contains refrigerated gas; may cause cryogenic burns or injury
- H290: May be corrosive to metals

Identification of chemical hazards

The GHS hazard statements: health hazards

- H300: Fatal if swallowed
- H301: Toxic if swallowed
- H302: Harmful if swallowed
- H303: May be harmful if swallowed
- H304: May be fatal if swallowed and enters airways
- H305: May be harmful if swallowed and enters airways
- H310: Fatal in contact with skin
- H311: Toxic in contact with skin
- H312: Harmful in contact with skin
- H313: May be harmful in contact with skin
- H314: Causes severe skin burns and eye damage
- H315: Causes skin irritation
- H316: Causes mild skin irritation
- H317: May cause an allergic skin reaction
- H318: Causes serious eye damage
- H319: Causes serious eye irritation
- H320: Causes eye irritation
- H330: Fatal if inhaled
- H331: Toxic if inhaled
- H332: Harmful if inhaled
- H333: May be harmful if inhaled
- H334: May cause allergy or asthma symptoms or breathing difficulties if inhaled
- H335: May cause respiratory irritation
- H336: May cause drowsiness or dizziness

Identification of chemical hazards

The GHS hazard statements: health hazards

- H340: May cause genetic defects
- H341: Suspected of causing genetic defects
- H350: May cause cancer
- H351: Suspected of causing cancer
- H360: May damage fertility or the unborn child
- H361: Suspected of damaging fertility or the unborn child
- H361d: Suspected of damaging the unborn child
- H362: May cause harm to breast-fed children
- H370: Causes damage to organs
- H371: May cause damage to organs
- H372: Causes damage to organs through prolonged or repeated exposure
- H373: May cause damage to organs through prolonged or repeated exposure

Identification of chemical hazards

The GHS hazard statements: environmental hazards

- H400: Very toxic to aquatic life
- H401: Toxic to aquatic life
- H402: Harmful to aquatic life
- H410: Very toxic to aquatic life with long lasting effects
- H411: Toxic to aquatic life with long lasting effects
- H412: Harmful to aquatic life with long lasting effects
- H413: May cause long lasting harmful effects to aquatic life
- H420: Harms public health and the environment by destroying ozone in the upper atmosphere

Identification of chemical hazards

The GHS precautionary statements: general

- P101: If medical advice is needed, have product container or label at hand.
- P102: Keep out of reach of children.
- P103: Read label before use.

The GHS precautionary statements: prevention

- P201: Obtain special instructions before use.
- P202: Do not handle until all safety precautions have been read and understood.
- P210: Keep away from heat/sparks/open flames/hot surfaces. - No smoking.
- P211: Do not spray on an open flame or other ignition source.
- P220: Keep/Store away from clothing/.../combustible materials.
- P221: Take any precaution to avoid mixing with combustibles...
- P222: Do not allow contact with air.
- P223: Keep away from any possible contact with water, because of violent reaction and possible flash fire.
- P230: Keep wetted with...
- P231: Handle under inert gas.
- P232: Protect from moisture.
- P233: Keep container tightly closed.
- P234: Keep only in original container.
- P235: Keep cool.
- P240: Ground/bond container and receiving equipment.
- P241: Use explosion-proof electrical/ventilating/lighting/.../equipment.
- P242: Use only non-sparking tools.
- P243: Take precautionary measures against static discharge.
- P244: Keep reduction valves free from grease and oil.

Identification of chemical hazards

The GHS precautionary statements: prevention

- P250: Do not subject to grinding/shock/.../friction.
- P251: Pressurized container: Do not pierce or burn, even after use.
- P260: Do not breathe dust/fume/gas/mist/vapours/spray.
- P261: Avoid breathing dust/fume/gas/mist/vapours/spray.
- P262: Do not get in eyes, on skin, or on clothing.
- P263: Avoid contact during pregnancy/while nursing.
- P264: Wash ... thoroughly after handling.
- P270: Do not eat, drink or smoke when using this product.
- P271: Use only outdoors or in a well-ventilated area.
- P272: Contaminated work clothing should not be allowed out of the workplace.
- P273: Avoid release to the environment.
- P280: Wear protective gloves/protective clothing/eye protection/face protection.
- P281: Use personal protective equipment as required.
- P282: Wear cold insulating gloves/face shield/eye protection.
- P283: Wear fire/flame resistant/retardant clothing.
- P284: Wear respiratory protection.
- P285: In case of inadequate ventilation wear respiratory protection.
- P231 + P232: Handle under inert gas. Protect from moisture.
- P235 + P410: Keep cool. Protect from sunlight.

Identification of chemical hazards

The GHS precautionary statements: response

- P301: IF SWALLOWED:
- P302: IF ON SKIN:
- P303: IF ON SKIN (or hair):
- P304: IF INHALED:
- P305: IF IN EYES:
- P306: IF ON CLOTHING:
- P307: IF exposed:
- P308: IF exposed or concerned:
- P309: IF exposed or if you feel unwell:
- P310: Immediately call a POISON CENTER or doctor/physician.
- P311: Call a POISON CENTER or doctor/physician.
- P312: Call a POISON CENTER or doctor/physician if you feel unwell.
- P313: Get medical advice/attention.
- P314: Get medical advice/attention if you feel unwell.
- P315: Get immediate medical advice/attention.
- P320: Specific treatment is urgent (see ... on this label).
- P321: Specific treatment (see ... on this label).
- P322: Specific measures (see ... on this label).
- P330: Rinse mouth.
- P331: Do NOT induce vomiting.
- P332: If skin irritation occurs:
- P333: If skin irritation or rash occurs:
- P334: Immerse in cool water/wrap in wet bandages.
- P335: Brush off loose particles from skin.
- P336: Thaw frosted parts with lukewarm water. Do not rub affected area.
- P337: If eye irritation persists:
- P338: Remove contact lenses, if present and easy to do. Continue rinsing.

Identification of chemical hazards

The GHS precautionary statements: response

- P340: Remove victim to fresh air and keep at rest in a position comfortable for breathing.
- P341: If breathing is difficult, remove victim to fresh air and keep at rest in a position comfortable for breathing.
- P342: If experiencing respiratory symptoms:
- P350: Gently wash with plenty of soap and water.
- P351: Rinse cautiously with water for several minutes.
- P352: Wash with plenty of soap and water.
- P353: Rinse skin with water/shower.
- P360: Rinse immediately contaminated clothing and skin with plenty of water before removing clothes.
- P361: Remove/Take off immediately all contaminated clothing.
- P362: Take off contaminated clothing and wash before reuse.
- P363: Wash contaminated clothing before reuse.
- P370: In case of fire:
- P371: In case of major fire and large quantities:
- P372: Explosion risk in case of fire.
- P373: DO NOT fight fire when fire reaches explosives.
- P374: Fight fire with normal precautions from a reasonable distance.
- P375: Fight fire remotely due to the risk of explosion.
- P376: Stop leak if safe to do so.
- P377: Leaking gas fire: Do not extinguish, unless leak can be stopped safely.
- P378: Use ... for extinction.
- P380: Evacuate area.
- P381: Eliminate all ignition sources if safe to do so.
- P390: Absorb spillage to prevent material damage.
- P391: Collect spillage.

Identification of chemical hazards

The GHS precautionary statements: response

- P301 + P310: IF SWALLOWED: Immediately call a POISON CENTER or doctor/physician.
- P301 + P312: IF SWALLOWED: Call a POISON CENTER or doctor/physician if you feel unwell.
- P301 + P330 + P331: IF SWALLOWED: rinse mouth. Do NOT induce vomiting.
- P302 + P334: IF ON SKIN: Immerse in cool water/wrap in wet bandages.
- P302 + P350: IF ON SKIN: Gently wash with plenty of soap and water.
- P302 + P352: IF ON SKIN: Wash with plenty of soap and water.
- P303 + P361 + P353: IF ON SKIN (or hair): Remove/Take off immediately all contaminated clothing. Rinse skin with water/shower.
- P304 + P340: IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing.
- P304 + P341: IF INHALED: If breathing is difficult, remove victim to fresh air and keep at rest in a position comfortable for breathing.
- P305 + P351 + P338: IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
- P306 + P360: IF ON CLOTHING: rinse immediately contaminated clothing and skin with plenty of water before removing clothes.
- P307 + P311: IF exposed: Call a POISON CENTER or doctor/physician.
- P308 + P313: IF exposed or concerned: Get medical advice/attention.
- P309 + P311: IF exposed or if you feel unwell: Call a POISON CENTER or doctor/physician.
- P332 + P313: If skin irritation occurs: Get medical advice/attention.
- P333 + P313: If skin irritation or rash occurs: Get medical advice/attention.
- P335 + P334: Brush off loose particles from skin. Immerse in cool water/wrap in wet bandages.
- P337 + P313: If eye irritation persists: Get medical advice/attention.
- P342 + P311: If experiencing respiratory symptoms: Call a POISON CENTER or doctor/physician.
- P370 + P376: In case of fire: Stop leak if safe to do so.
- P370 + P378: In case of fire: Use ... for extinction.
- P370 + P380: In case of fire: Evacuate area.
- P370 + P380 + P375: In case of fire: Evacuate area. Fight fire remotely due to the risk of explosion.
- P371 + P380 + P375: In case of major fire and large quantities: Evacuate area. Fight fire remotely due to the risk of explosion.

Identification of chemical hazards

The GHS precautionary statements: storage

- P401: Store ...
- P402: Store in a dry place.
- P403: Store in a well-ventilated place.
- P404: Store in a closed container.
- P405: Store locked up.
- P406: Store in corrosive resistant/... container with a resistant inner liner.
- P407: Maintain air gap between stacks/pallets.
- P410: Protect from sunlight.
- P411: Store at temperatures not exceeding ... oC/...oF.
- P412: Do not expose to temperatures exceeding 50 oC/122oF.
- P413: Store bulk masses greater than ... kg/... lbs at temperatures not exceeding ... oC/...oF.
- P420: Store away from other materials.
- P422: Store contents under...
- P402 + P404: Store in a dry place. Store in a closed container.
- P403 + P233: Store in a well-ventilated place. Keep container tightly closed.
- P403 + P235: Store in a well-ventilated place. Keep cool.
- P410 + P403: Protect from sunlight. Store in a well-ventilated place.
- P410 + P412: Protect from sunlight. Do no expose to temperatures exceeding 50 celcius degress.
- P411 + P235: Store at temperatures not exceeding ...Keep cool.

The GHS precautionary statements: disposal

- P501: Dispose of contents/container to...

Identification of chemical hazards

Safety data sheets (SDS) / former material safety data sheets (MSDS)

- Delivered with all chemicals
- ...often thrown away...

➤ Contain 16 sections

- Identification
- Hazard(s) identification
- Composition/ information on ingredients
- First-aid measures
- Fire-fighting measures
- [Accidental release measures](#)
- Handling and storage
- Exposure control/ personal protection
- Physical and chemical properties
- Stability and reactivity
- Toxicological information
- Ecological information
- Disposal considerations
- Transport information
- Regulatory information
- Other information.

➤ Keep all (M)SDS on file and ready for use

➤ Available on websites of all major chemical resellers

➤ **READ THEM!!**

Identification of chemical hazards

« Unorthodox » labeling of chemical containers

- Concerns wash bottles, solutions prepared in the lab, etc.
 - Products synthesized in the lab
 - All containers NEED to be clearly labeled
-
- Include sufficient information
 - The name is NOT ENOUGH (an abbreviation even less so)
 - A chemical formula is more appropriate
 - Use stickers of hazard pictograms! (often available for free)

Identification of chemical hazards

Unknown samples / products

- Newly synthesized products
 - Non-identified products arising from side reactions (even of well-known reactions)
-
- Handle with extreme care
 - **EVERY uncharacterized product should be considered as toxic!**
 - If the structure is known, certain structural motifs should ring the alarm bells (cf. toxicology)
 - **In case of doubt, use maximum caution!**

Identification of chemical hazards

Unknown samples / products

- Example: *Organic Process Research & Development* **2003**, 7, 225
- Editorial : « Dangers of the Unknown »

chose to read had a safety theme. The dangers of scale-up are illustrated by the following account from Darryl D. Desmarteau of Clemson University!

He needed $S_2O_6F_2$ for some work on the fluorosulphate radical and therefore scaled up the reaction of SO_3 and F_2 to 900 g using a catalytic reactor. The temperature controller was not working too well and when this happens a significant by-product, $FOSO_2F$, arises. As a result, the 900 g of $S_2O_6F_2$ produced also gave 200 g of this by-product which was separated and collected in a cold trap, then transferred to a metal cylinder and allowed to warm to room temperature. He then went for a couple of beers with a friend before returning to the lab. About 2 h later, judging that the compound had warmed, he removed the cylinder and laid it on its side in the fume hood and labeled it. He was just reaching to pick it up when the cylinder exploded with incredible force, instantly removing the chemist's left-hand and part of the forearm, and also part of his right-hand. The face shield and safety glasses were destroyed and his wristwatch was embedded in the ceiling!

The chemist said that from this he learnt two lessons:

- (1) It's what you do not know that will get you (i.e. forewarned is forearmed).
- (2) If he had had two more beers, he may not have lost his hand, since the explosion may have occurred before he returned to the lab!

The other chapter, which fascinated me, was from William J Middleton formerly of DuPont. Whilst working on Freon refrigerants he came across some extremely toxic fluorine compounds such as perfluoropinacol, prepared from hexafluoroacetone. A single drop of perfluoropinacol on the skin of a guinea pig is sufficient to kill it. Middleton had made over 500 g before this was realised. It was only by good fortune and excellent hygiene practices by DuPont employees that no one was poisoned by this material before it was ultimately destroyed. So fluorine compounds can be amongst the least toxic (e.g., blood substitutes) and the most toxic, too.

Risk assessment

Assessment = a global approach

- Numerous sources of information on chemical hazards are available
 - BUT: Certain hazards only appear during manipulation
 - A correct risk assessment need to take into account all aspects, in particular:
 - Before, during, and after use!!
 - Typically, a chemical reaction might create new hazards...
 - Hazards that might appear at any moment need to be identified and FORESEEN

Risk assessment

Hazards appearing during reactions

- Exothermicity, thermal runaway (explosions!)
- Gas evolution (explosions, fires if flammable gases, intoxication...)
- Pressure rise (explosion)

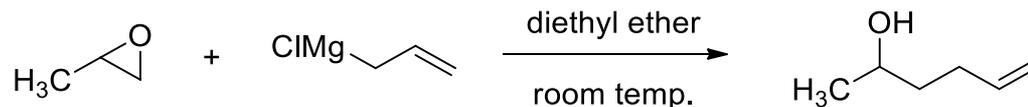
Hazards due to equipment failures

- Overheating, thermal runaway (Failed temperature sensor, ...)
- Overpressure, explosion (Failed pressure controller, ...)
- Solvent vapours (Cooling failure)
- Overboiling (stirring failure)
- Electrocution (Electrical cables, perforations, water, ...)

Risk assessment

Example: Grignard reaction

The following transformation, a simple epoxide opening by an organomagnesium reagent, has ended in an explosion.



Hazards:

- Acute and chronic toxicity of propylene oxide
- Reactivity of organomagnesium reagent (reacts violently with water, flammable in contact with air)

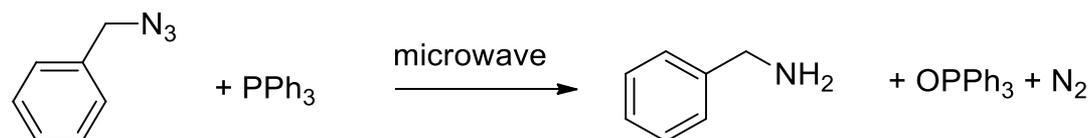
Safety measures: gloves, fume hood, handling of solutions using syringes and argon atmosphere. **NEVERTHELESS THERE WAS AN EXPLOSION.**

The researcher did not take into account the exothermicity of the reaction!

Risk assessment

Example: Staudinger reduction

The reduction of organic azides by phosphines is an efficient and clean reaction, in that it transforms a potentially toxic and explosive starting material (azide) into a phosphine oxide (low toxicity) and nitrogen gas. It is strongly accelerated under microwave heating.



Reactions in laboratory microwaves take place in sealed tubes: the risk of overpressure in the case of gas formation is obvious.

Solution: the apparatus is fitted with a pressure gauge that will shut down microwave irradiation in case of a rapid pressure rise.

Nevertheless, there was a violent explosion (destroying the microwave cavity)

Reaction kinetics were ignored, as well as the lack of expansion volume available, resulting in a too rapid pressure increase.

Risk assessment

Example: Perchloric acid on silica gel (Namur, sept. 2017)

Literature procedure :

Preparation of $\text{HClO}_4/\text{SiO}_2$ Catalyst:[30] HClO_4 (1.8 g, 12.5 mmol, as a 70 % aq. solution) was added to a suspension of SiO_2 (230–400 mesh, 23.7 g) in Et_2O (70.0 mL). The mixture was concentrated and the residue was heated at 100 °C for 72 hours under vacuum to furnish $\text{HClO}_4/\text{SiO}_2$ (0.5 mmol/g) as a free flowing powder (50 mg, 0.025 mmol of HClO_4).

Researchers, unaware of the explosive nature of perchloric acid when dry, replaced heating by an oil bath with a short heating using a heat gun. A violent explosion occurred, shattering the side of a fume cupboard and wounding 2 researchers in the face.

Potential severe injuries to eyes were avoided thanks to the use of safety glasses.

The risk of explosion of anhydrous perchloric acid is not mentioned on the aqueous solution used in the procedure. No assessment of the stability after drying was undertaken.

GHS H Statement:

Causes severe skin burns and eye damage.

May cause fire or explosion;
strong oxidizer.



Risk assessment

Conclusion

- Gather all available information on the substances used
 - Labels, catalogues, (M)SDS, internet ...
- Take into account all products formed during the reaction
 - Labels, catalogues, (M)SDS, literature, internet ...
- Beware of unknown products and side-products
 - **In case of doubt, assume the worst!**
- Take into account all other aspects of the reaction
 - Exothermicity, gas evolution, explosive mixtures ...
 - Foresee all hazards linked to the equipment (failures, breakage, ...)

Risk management

Risk management

Introduction

- After having identified the hazards linked to every substance...
- After having identified all the risk arising from chemical reactions...
 - A risk management strategy covers all the measures that are implemented in order to minimize the hazards and their impact
 - Laboratory cleanliness, personal protective equipment, tidiness, etc.

Risk management

Laboratory notebook

- Standardized layout
- Mandatory to write down all experiments (BEFORE starting them!)
- Prime importance for intellectual property
- **MUST contain a description of all hazards linked to the experiments**
- **MUST contain a description of all hazard containment measures**
- **MUST contain all measures to be taken in the case of an accident**
- Will be used in the case of an investigation
- **Needs to contain waste disposal information**

Risk management

Good laboratory practice

- Clothes covering arms and legs;
 - closed shoes;
 - hair (or scarves) attached ;
 - labcoat with pressure buttons;
 - safety glasses / goggles
- = minimum precautions

Might add gloves (different types), masks (dust), face screen, etc.

- Never eat or drink in a laboratory
 - Never use pipettes with your mouth
 - Do not smoke
-
- Wash your hands! (use hand cream if needed)

Risk management

C&EN 11 May 2009

NEGLIGENCE CAUSED UCLA DEATH

SAFETY: State safety and health agency faults university for training lapses, unsafe practices

NEGLIGENCE OF LAB SAFETY by the department of chemistry and biochemistry at UCLA led to the Dec. 29, 2008, accident and subsequent death of researcher Sheharbano (Sheri) Sangji, says the state agency charged with investigating the incident.

In particular, the California Division of Occupational Safety & Health (Cal/OSHA) cited the department in a report released on May 4 for lacking both safety training and training documentation; failing to ensure employees wore appropriate personal protective equipment (PPE), such as lab coats; and failing to correct unsafe conditions and work practices identified in an Oct. 30, 2008, laboratory safety inspection.

Among the findings of the October lab inspection was that PPE was not fully used in the lab in which the 23-year-old Sangji worked. She was not wearing a lab coat in December when pyrophoric material she was handling splashed and ignited her clothing.

Sangji's supervisor, professor Patrick Harran, says that he did address the PPE issues with his group. "My expectation is that everyone is to wear a lab coat and wear protective gear on their eyes," he says, adding that a lab coat is specifically ordered for everyone who joins

Sangji, Sheri's sister. Naveen and her family would still like to know more about the circumstances that led to the fire.

The Cal/OSHA citations carry a total fine of \$31,875. It is the largest fine levied by the agency in seven investigations since 2006 that involved academic research labs or the chemical or biotechnology industry. For incidents that involve a fatality, Cal/OSHA routinely forwards its findings to the local district attorney's office to evaluate whether criminal prosecution is warranted.

"I think Cal/OSHA did everything they could" within their regulatory structure to penalize UCLA, says Neal Langerman, the founder of the company Advanced Chemical Safety and a consultant to the American Chemical Society Committee on Chemical Safety.

UCLA will not contest the findings or appeal the fine, it says in its statement. The university also outlined the steps it is taking to address the deficiencies, including requiring written safety assessments of laboratory procedures. The assessments include quantifying hazards, assessing potential risks, and specifying appropriate PPE. The university is



Langerman says the safety culture in academia generally lags far behind that in industry and that even minor incidents in academic labs are far too frequent and treated as too routine.

The Cal/OSHA report says that, when the incident occurred, Sangji was drawing approximately 20 mL of 1.7 mol/L *tert*-butyllithium in pentane into a 60-mL syringe when the syringe plunger was either ejected or pulled out of the syringe. An undetermined amount of the liquid splashed onto her hands, arms, and torso. The ensuing fire burned more than 40% of her body. One of the post-doctoral researchers used his lab coat to extinguish the flames and called for help. Sangji died of her injuries on Jan. 16

Risk management

Les conséquences de l'accident (C&EN 30 January 2012)

SYSTEMIC FAILURES CITED IN LAB DEATH

REPORT: State investigator alleges safety and training breakdown at UCLA

Photo shows what remains of the 60-mL plastic syringe Sangji was using to transfer more than 50 mL of tert-butyllithium when she pulled the plunger out of the barrel.



NEW DETAILS of the circumstances surrounding the 2009 death of University of California, Los Angeles, chemistry researcher Sheharbano (Sheri) Sangji are outlined in a report by the California Division of Occupational Safety & Health (Cal/OSHA). The report says a “systemic breakdown of overall laboratory safety practices” contributed to the fatal accident. Cal/OSHA sent the report to the Los Angeles County District Attorney’s Office, which filed felony charges in the case on Dec. 27, 2011 ([C&EN, Jan. 2, page 7](#)).

The report—obtained by C&EN but first made public by the *Los Angeles Times* on Jan. 20—describes a seemingly ineffective environmental health and safety program at UCLA in which fixing problems identified during lab safety inspections and wearing personal protective equipment were viewed as optional.

UCLA administrators assert that the report is biased. It “reached the conclusion that the [state’s] investigator set out to reach,” says Kevin S. Reed, vice chancellor for legal affairs.

An attorney representing chemistry professor Patrick G. Harran, who faces prison time for the charges against him, alleges the report contains “numerous errors” but declined to give examples. The lethal incident occurred in Harran’s lab.

The report provides insight into how Sangji, who was 23 at the time, was trained to handle the pyrophoric chemical *tert*-butyllithium (tBuLi). Sangji died from injuries sustained in a fire that started when the plunger came out of a syringe she was using to transfer tBuLi.

According to the report, Sangji had not handled pyrophoric reagents prior to her job at UCLA. Harran told a Cal/OSHA investigator, however, that he checked Sangji’s technique by observing her use an air-sensitive nonpyrophoric reagent.

The report goes on to say that Sangji then sought help with the tBuLi procedure from then-postdoctoral researcher Paul Hurley. Hurley told the Cal/OSHA investigator he could not recall his specific interactions with Sangji, but the approach he described for handling tBuLi was similar to what is known about Sangji’s actions leading to the accident. His description included details that are counter to safety recommendations for handling the hazardous chemical by its manufacturer.

The report is the second prepared by Cal/OSHA. The first report resulted in fines levied against UCLA for multiple safety regulation violations. Harran and the university are scheduled for arraignment on the felony charges on Feb. 2.—JYLLIAN KEMSLEY

& MORE ONLINE

Read the Cal/OSHA report at cenm.galileo.com/report.

Risk management

Laboratory tidiness

- chemicals need to be stored in ventilated and safe storage rooms;
 - in the laboratory in cupboards, ideally ventilated and fire-proof;
 - a **limited amount** of flammable liquids per room;
 - no flammable substances to be stored on benches and in fume hoods;
 - only dilute aqueous solutions are allowed;
 - and all containers need to be appropriately labeled.
-
- Minimal amount of chemicals, especially flammable ones, in fume hoods!
 - Avoid proximity of incompatible substances during storage
 - Acids and bases, inflammable compounds and oxidizing agents, reducing and oxidizing agents...

Risk management

Explosive substances



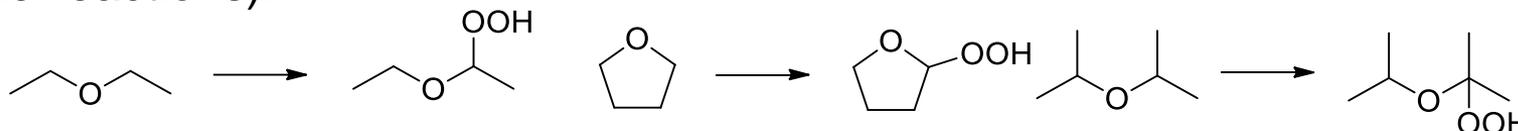
- substances giving rise to explosion under the influence of external factors;
- Shocks, friction, sparks, heat;
- Store cold, in the absence of light
- Handle in the absence of flames, sparks, heat
- Avoid shocks and friction (spatula!)
- Handle behind a blast shield or use a face shield
- Beware of organic and inorganic substances containing the following bonds:
 - O-O, N-O, N-N ou N(O)-halogen (simples or double)
 - peroxides (hydrogen peroxide, organic peroxides, peracids, ozonides, etc...)
 - chlorates and perchlorates
 - nitrated products (TNT !) and nitrates (ammonium nitrate → AZF !)
 - azides and diazonium salts, diazomethane
 - chloramines
 - ...

Risk management

Hidden explosives



- Ether type solvents are spontaneously oxidized in contact with air;
- they form peroxides that detonate spontaneously when dry;
- they are stored in the presence of stabilizers (chemists: beware of unexpected side-reactions).



- Store in the absence of light and open as little as possible;
- Peroxide test sticks are available;
- Methods for the safe decomposition of peroxides are described.

- **PREFER THE USE OF LESS OXIDIZABLE ETHERS**
- MTBE, 2-methylTHF, ...

Organic Process Research & Development **2004**, 8, 815

During any chemical reaction, and particularly during the work-up, where aqueous acid or base extractions may be involved, it is easy to remove the stabilisers. Many procedures then follow this with an evaporation to dryness (as did the submitted paper). This is a procedure you will find difficult to repeat, since you may have perished during the explosion resulting from the first evaporation.

Risk management

Flammable substances



Flammable substances are (formerly F-):

- Substances that ignite spontaneously:
 - Pyrophoric liquids and solids (White P, phosphines, organoaluminiums, ...)
 - Store in the absence of air (inert gas)
 - Gases mixed with air (butane, ...)
 - Avoid contact with air
- Substances that form flammable gases in contact with water
 - inorganic hydrides (NaH , CaH_2 , LiAlH_4 , ...), amides (NaNH_2), ...
 - store and handle in the absence of humidity (even that of air !)
- Liquids with a flash point $\leq 21^\circ\text{C}$
 - nearly ALL solvents except water
 - Store and handle away from flames, heat sources, sparks ...

Risk management

Flammable substances



Highly flammable substances (formerly F+) are:

- Liquids with b.p. ≤ 35 °C and flash point ≤ 0 °C

Flash point = temperature at which sufficient vapor is in equilibrium with the liquid to allow ignition in the presence of a flame or spark

| | b.p. | Flash point |
|-------------------------|-------|-------------|
| • butane C_4H_{10} | - 0°5 | - 60° |
| • ether $(CH_3CH_2)_2O$ | 34° | - 45° |
| • methanol CH_3OH | 65° | 10° |
| • ethanol CH_3CH_2OH | 79° | 12° |
| • acetone CH_3COCH_3 | 56° | -20° |

Risk management

Flammable substances



Fire triangle:



Sources of energy:

- Hot surface
- Flame
- Friction
- Short circuit
- Electrical current
- Static discharges
- Lightning
- Sun
- Chemical reaction

In general:

- Easy to prevent
- Have to be eliminated first

In case of fire

Fire hazard

In the case of fire

- 1) If possible, cut off the energy supply or the fuel supply
- 2) Extinguish the fire (vide infra)

If this fails:

- 3) Ring the fire alarms and evacuate (or help to evacuate) the premises

Fire hazard

How to extinguish a fire

1) Is it possible to cut off the fuel or energy supply?

Examples:

Switch off the electricity supply or gas supply

Burning gas cylinder : close the main valve

Solvent pouring on a heat source : cut off solvent source

2) Eliminate the oxidizing agent (= air) by using:

- A fire blanket
- Extinguishers
- Water
- Sand or an inert solid

In case of failure to extinguish the fire:

3) Ring the fire alarms and evacuate (or help to exvacuate) the premises

Fire hazard

Types of fire



A = solid (dry) :
paper, wood, plastics...



B = liquid (organic) :
solvent, oil, electrical appliance...



C = gas :
gas (liquefied)...



D = metal (! Divided !):
sodium, aluminium, nickel....

Fire hazard

Types of fire

Grey exting.

CO₂

Red extinguisher

powder

Fire hose
or extinguisher

H₂O 

Liquid (B)



Gas (C)

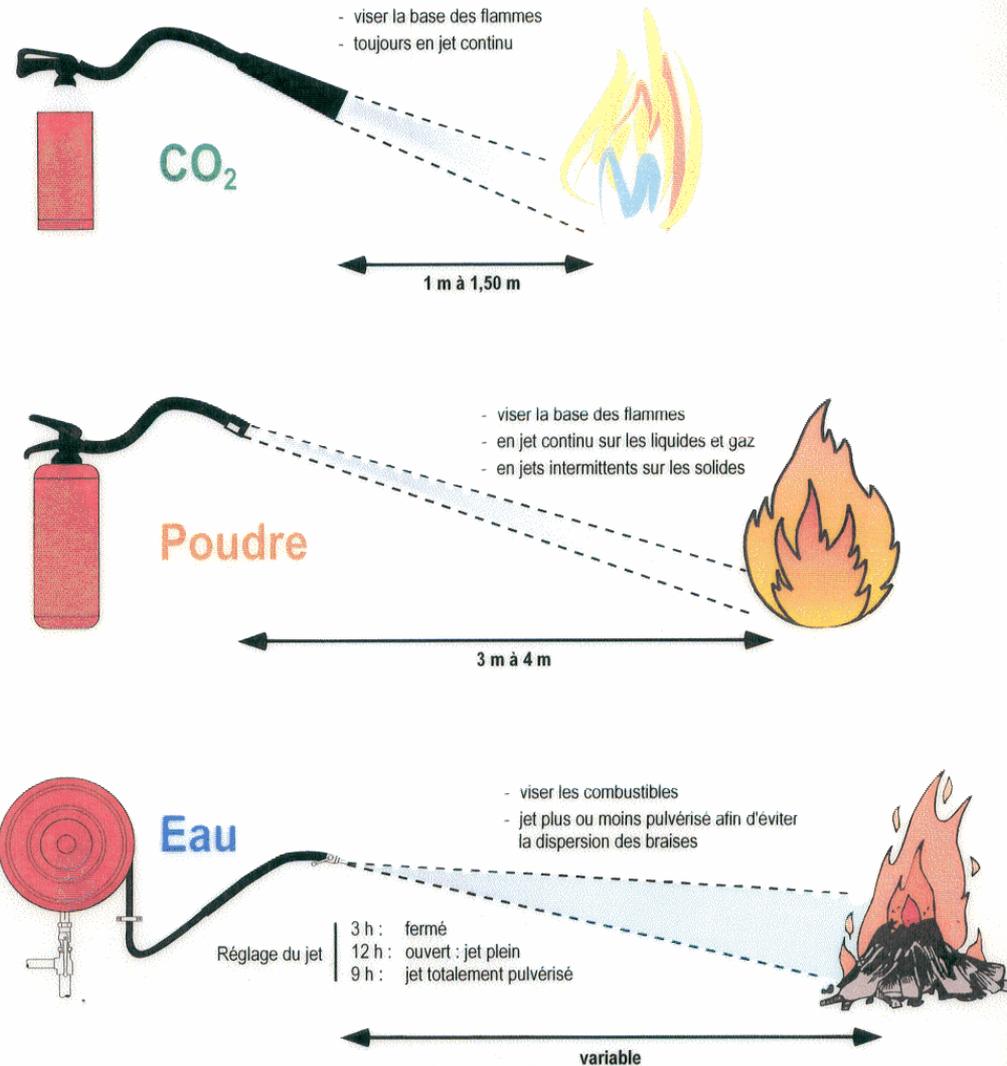


Solid (A)



- Follow fire extinguisher training if available
- Difficult choices in a stressful situation : determine the appropriate extinguisher, its location and its use before starting the experiment !!!!

How to handle different extinguishers



Fire hazard

Metal fires

1) Reducing metals

Na, K, Li, Mg, Ca, Zn, ...

Use sand to extinguish. **Avoid water at all cost:** formation of hydrogen gas, aggravated fire and explosions might occur!!!

2) Non-reducing metals

Mainly Raney nickel or palladium on charcoal

Extinguish with water, then dissolve nickel/palladium with dilute HCl solution.

Fire hazard

Special cases

1) Clothes on fire

Do not run!

Call for help (loudly)

Roll on the floor

Use a safety shower

Extinguish using a blanket, labcoat...or powder extinguisher

2) Oil fire (similar to classical domestic frying pan fire)

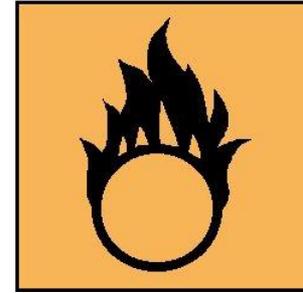
Extinguish with a fire blanket or a wet cloth

Open only when completely cooled down to room temperature

NEVER USE WATER!!!!!!

Risk management continued

Risk management



Oxidizing agents

Oxidizing agents (formerly O) accelerate combustion

Their presence increases the risk of fire

- Keep away from flammable substances!
- Avoid contact with clothes, wipes, etc...

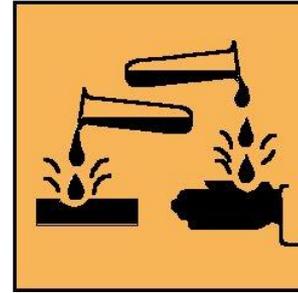
Examples: strong inorganic oxidizing agents (permanganates, perchlorates, peroxides, nitrates, fluorine, ...)

Dioxygen (liquid) !!

Pressurized oxygen cylinders need to be handled with special care (specific manometers, absence of organic lubricants on all connections).

Risk management

Corrosive substances



Substances that destroy living tissue and materials

Acids : hydrochloric, sulfuric, phenol...

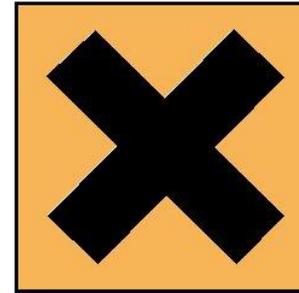
Bases : sodium hydroxide, potassium hydroxide, carbonates...

Acidic salts: AlCl_3 , ...

Halogens : chlorine, bromine, iodine,...

- Avoid contact with skin and eyes
- Do not breathe vapors or fumes, use fume hoods
- Wear gloves (of the correct type!)
- Immediately remove contaminated gloves and clothes
- If exposed, rinse immediately and abundantly with water

Risk management



Irritants

Substances causing weak alterations by irritation of the exposed organs (formerly Xi)

Lungs: ammonia, formaldehyde, ...

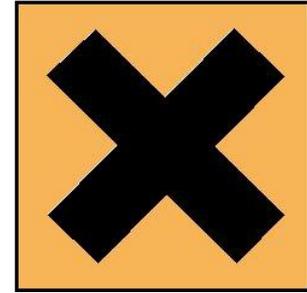
Eyes : Benzyl bromide, ...

Skin : pentane, ...

- Avoid contact with skin and eyes
- Do not breathe vapors or fumes, use fume hoods
- Wear gloves (of the correct type!)
- Immediately remove contaminated gloves and clothes
- If exposed, rinse immediately and abundantly with water

Risk management

Harmful substances



Formerly harmful : Xn

or

Corrosive (C) cat. 2

or

Toxic (T) cat. 4 (LD50 from 0,5 to 2g / kg)

Cause weak health issues:

pyridine, dichloromethane, ...

- Avoid contact and ingestion
- In case of unwellness, see a physician
- In case of exposure, rinse immediately and abundantly with water

Risk management

Toxic substances



Formerly toxic (T) and highly toxic (T+) cat. 1, 2 and 3

Cause severe lesion by ingestion or death by ingestion, inhalation
Or skin contact :

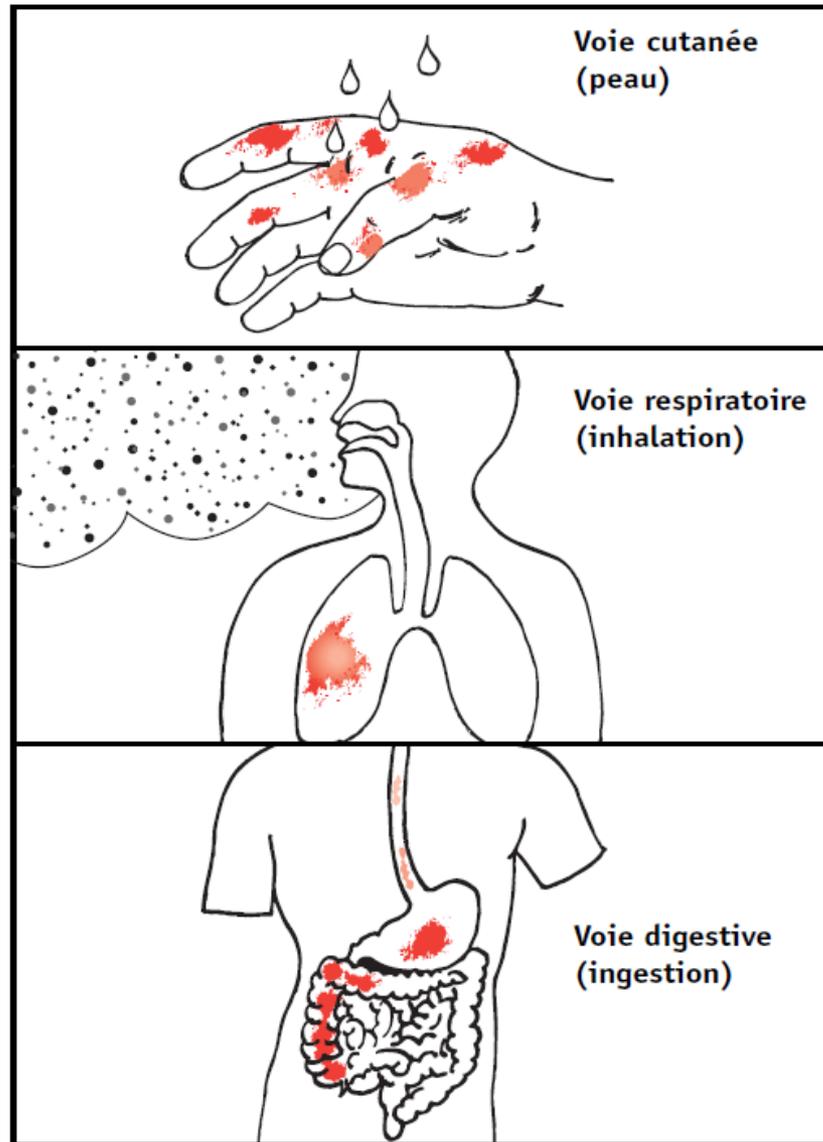
Chlorine gas, heavy metals and their salts (Hg, Pb, ...), Carbon tetrachloride, ...

Cause mortal lesions by ingestion, inhalation or skin contact :
thallium (TI) and its salts, Hydrocyanic acid and cyanides (HCN, KCN,...), methyl
cyanoformate ($\text{NC-COOCH}_3 = \text{Zyklon-B}$), alkaloids (strychnine, brucine, ...), etc.

- Avoid all contact and ingestion
- In case of unwellness, see a physician

Toxicology of acute toxicity

Exposure types

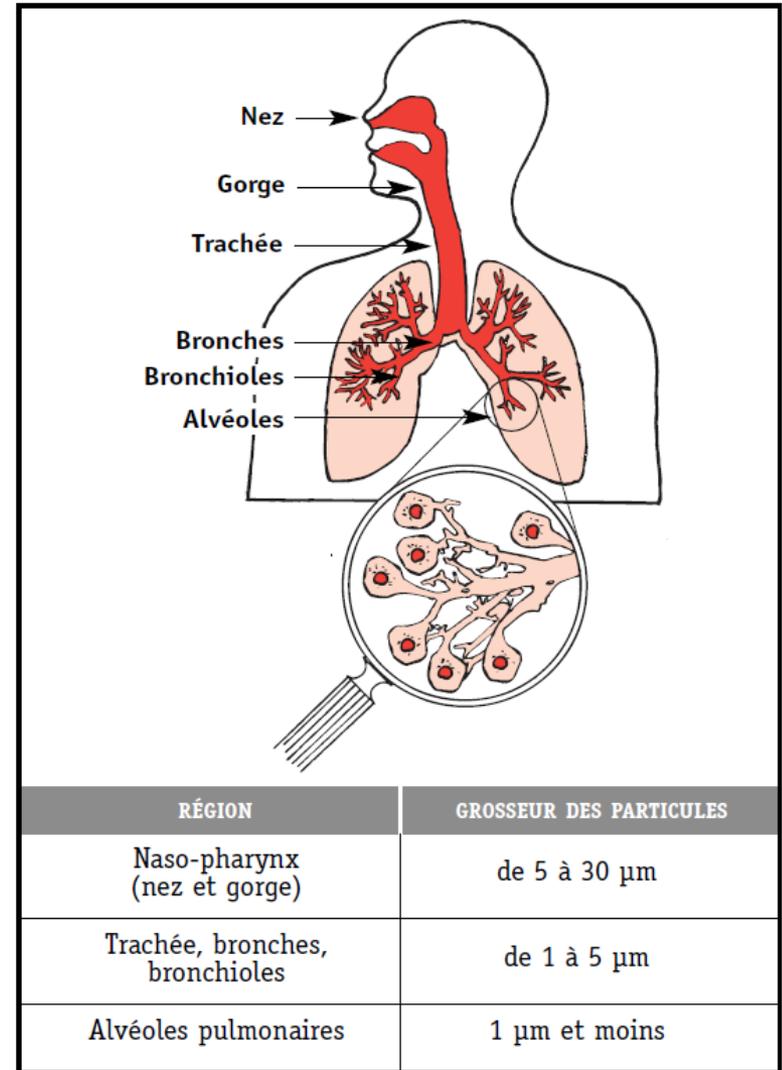


| SUBSTANCE | ÉTAT PHYSIQUE | VOIE RESPIRATOIRE | VOIE CUTANÉE | VOIE DIGESTIVE |
|---------------------|---------------|-------------------|--------------|----------------|
| Acide phosphorique | Solide | Faible | Faible | Faible |
| Alcool éthylique | Liquide | Oui | Faible | Oui |
| Béryllium | Solide | Oui | Faible | Faible |
| Chlorpyrifos | Solide | Oui | Oui | Oui |
| Mercure | Liquide | Oui | Oui | Faible |
| Monoxyde de carbone | Gaz | Oui | Non | Non |
| Toluène | Liquide | Oui | Oui | Oui |

Exposure by inhalation

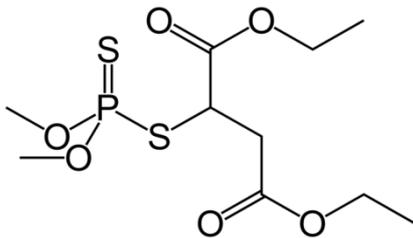
Solubility and particle size

| SUBSTANCE | SOLUBILITÉ DANS L'EAU | ABSORPTION | REMARQUE |
|--------------------------------------|-----------------------|---|--|
| Dioxyde de soufre (SO ₂) | Très soluble | Pénètre peu profondément dans le système respiratoire | Se limite au nez. Absorption par le mucus et le tissu. |
| Monoxyde de carbone (CO) | Peu soluble | Pénètre profondément dans le système respiratoire | Passe dans le sang et est distribué dans l'organisme. |



Skin exposure

Variable permeability of the skin (case of malathion)



Insecticide
Parasympathomimetic
Weakly toxic towards
humans

| Région | Absorption (%) |
|------------------|----------------|
| Front | 23,2 |
| Avant-bras | 6,8 |
| Dos de la main | 12,5 |
| Paume de la main | 5,8 |
| Abdomen | 9,4 |
| Plante du pied | 6,8 |

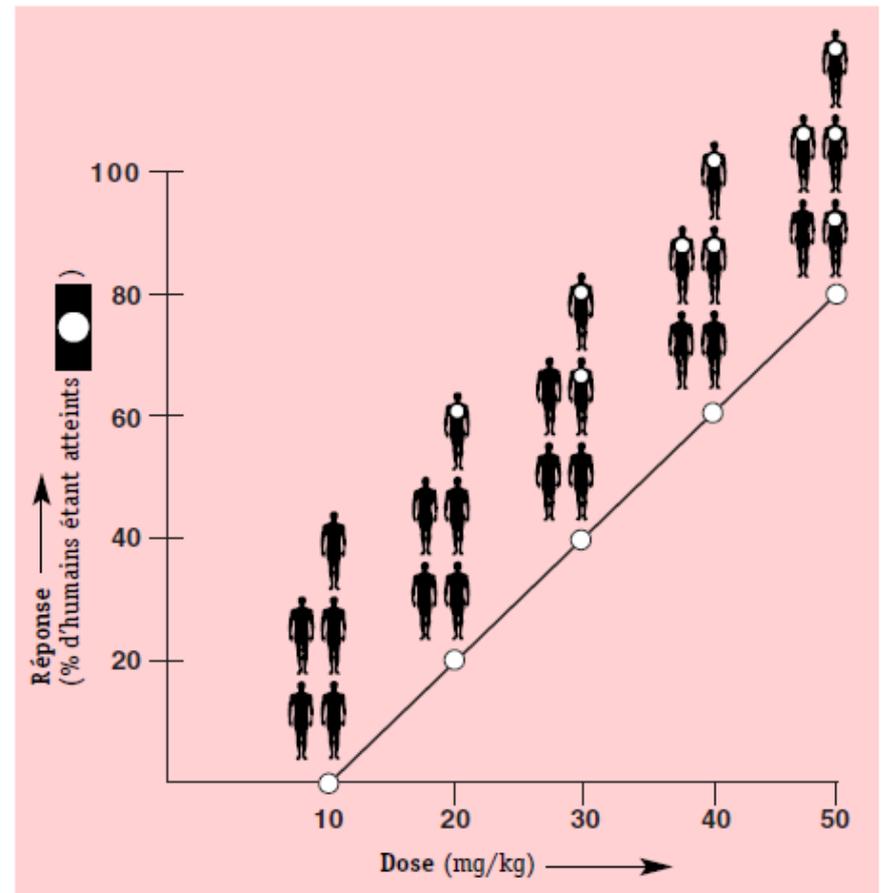
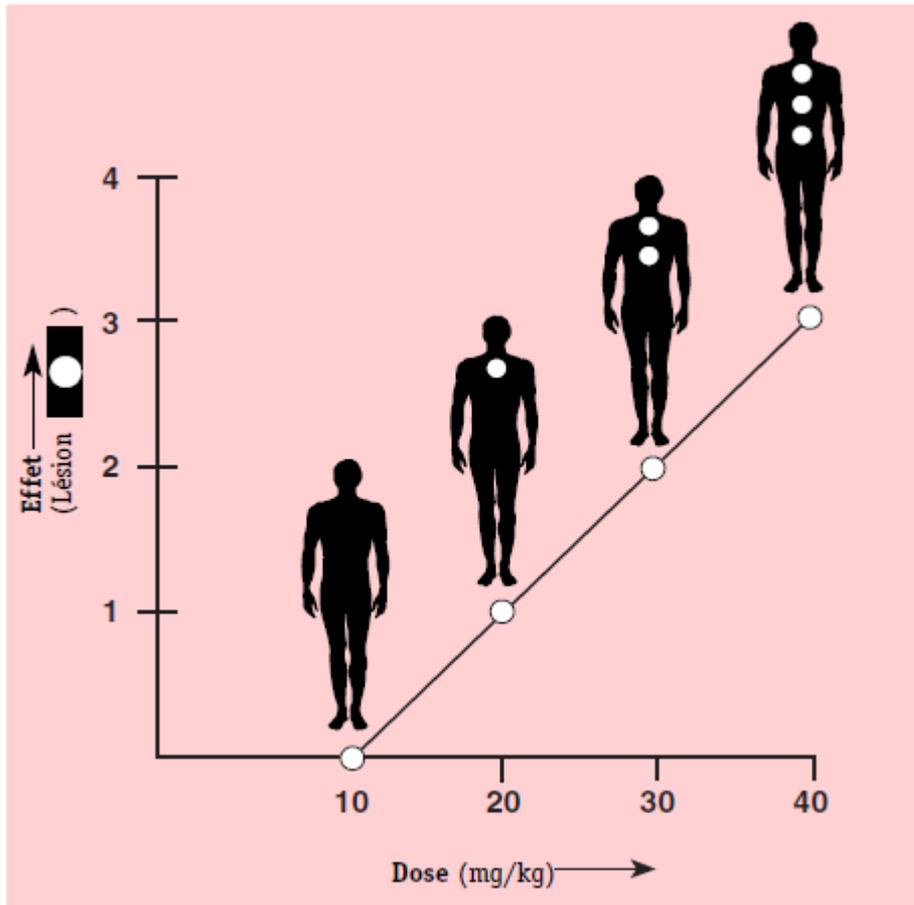
Also depends on:

- Solubility of the molecule
- Hydration of the skin
- Skin lesions
- ...

Toxicodynamics

Dose-effect and dose-response relationships

➤ All is poison ! (Paracelsus)



Toxicodynamics

Intrinsic toxic properties

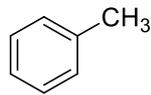
➤ Linked to chemical structure and reactivity!

Aromatic compounds are DNA intercalating agents

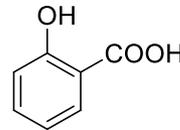
Physicochemical properties entailing side-effects



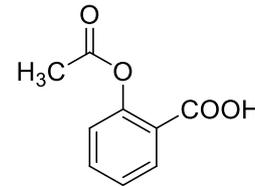
benzene
carcinogen



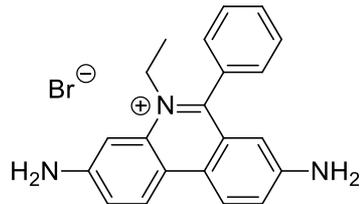
toluene
no carcinogenic
properties known (!)



salicylic acid
stomach burns
ulcers

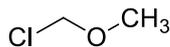


acetylsalicylic acid
drug

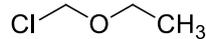


ethidium bromide

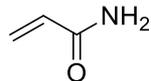
Electrophiles and alkylating agents (of DNA)



MOMCl
carcinogen

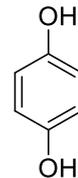


EOMCl
no carcinogenic
properties documented (!)

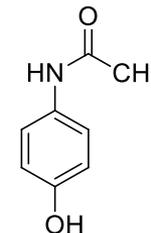


acrylamide
carcinogen, neurotoxic

Metabolized to form electrophiles



hydroquinone
toxic
(R22, 40, 41, 43, 50,68)



paracetamol
drug

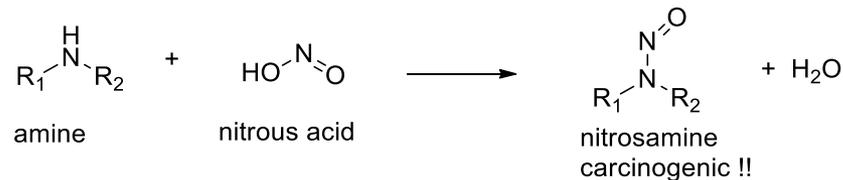
Toxicodynamics

Intrinsic toxic properties

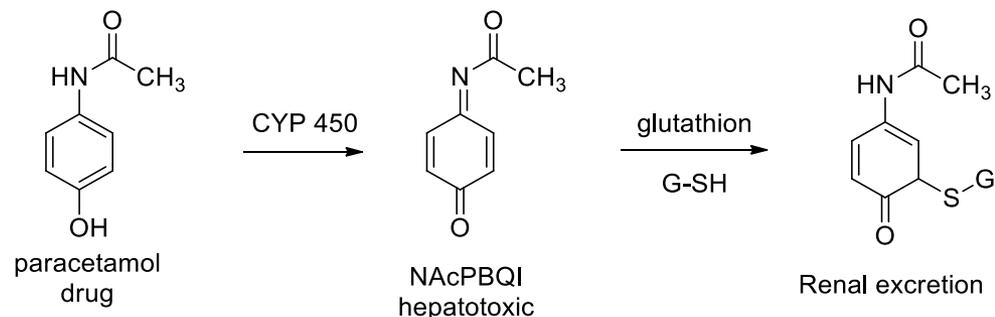
➤ Direct toxicity

Example : CN^- (ingested) \rightarrow HCN (g) \rightarrow Fe(III)-CN hemoglobine (asphyxia)

➤ Indirect toxicity (protoxic)



➤ Indirect toxicity (metabolic): even for alkanes!



Toxicodynamics

Genetic factors

- Essentially due to different gene expression of genes coding for certain enzymes among different populations
- Example : alcohol dehydrogenases (asian populations, intolerance towards ethanol)

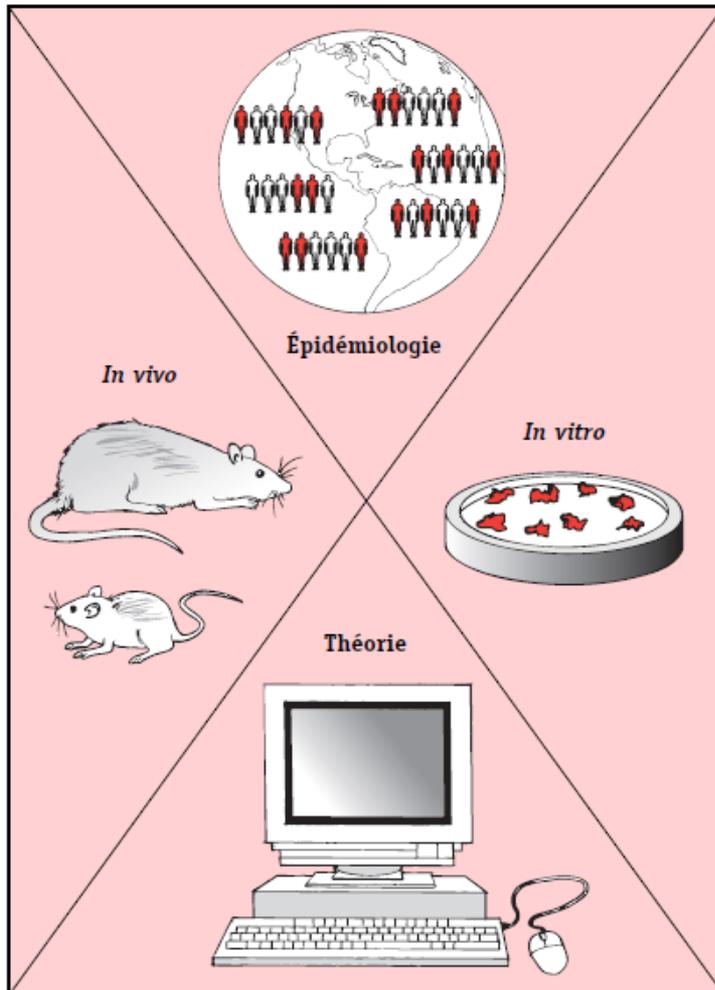
Physiopathological factors

- Age
- Sex
- Nutritional state
- Overall health
- Pregnancy
- Environment (addition, synergy potentialisation, antagonism)

| INTERACTION | | MODÈLE | EFFET |
|-----------------|------------------|--------------|--------------------|
| Additivité* | Addition | $1 + 2 = 3$ | Aucune interaction |
| Supraadditivité | Synergie | $1 + 2 = 5$ | Augmentation |
| | Potentialisation | $0 + 3 = 5$ | |
| Infraadditivité | Antagonisme | $0 + 3 = 2$ | Diminution |
| | | $-2 + 3 = 1$ | |

Evaluation of toxic effects

Study types (qualitative and/or quantitative)

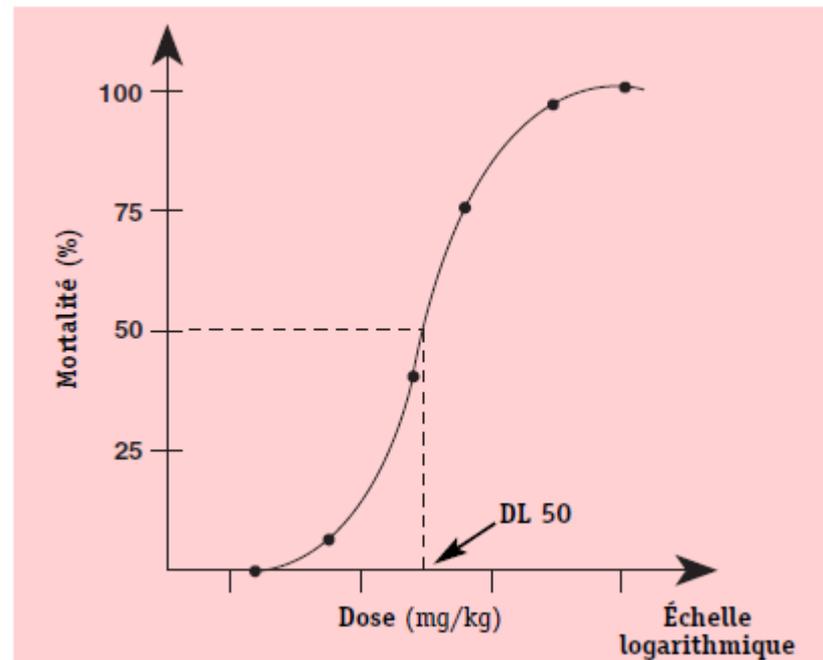


| FORME D'INTOXICATION | FRÉQUENCE D'ADMINISTRATION | DURÉE DE L'EXPOSITION |
|----------------------|----------------------------|-----------------------|
| AIGUË | Unique | < 24 heures |
| SUBAIGUË | Répétée | ≤ 1 mois |
| SUBCHRONIQUE | Répétée | de 1 à 3 mois |
| CHRONIQUE | Répétée | > 3 mois |

Evaluation of toxic effects

Acute toxicity– LD₅₀

| | | EFFET | |
|------------|-----------|--|--|
| | | AIGU | CHRONIQUE |
| EXPOSITION | AIGUË | <p>Effet à court terme à la suite d'une exposition à court terme (ex. : irritation cutanée causée par le contact avec une solution très diluée d'acide sulfurique)</p> | <p>Effet à long terme à la suite d'une exposition à court terme (ex. : trouble respiratoire persistant à la suite d'une courte inhalation d'une forte concentration de chlore)</p> |
| | CHRONIQUE | <p>Effet à court terme à la suite d'une exposition à long terme (ex. : sensibilisation cutanée à l'éthylènediamine à la suite d'un contact pendant plusieurs années)</p> | <p>Effet à long terme à la suite d'une exposition à long terme (ex. : cancer du foie, du poumon, du cerveau et du système hématopoïétique causé par l'exposition à des doses élevées de chlorure de vinyle pendant plusieurs années)</p> |



Risk management continued

Risk management



Health hazards (chronic toxicity)

Formerly highly toxic (T+)

Includes: Carcinogens, mutagens, toxic towards reproduction, specific toxicity towards organs by single or repeated exposure, respiratory sensitizers

Benzene, epoxides, dimethylsulfate, Ethidium bromide, ...
Hexane (peripheral nervous system)!

- Avoid all contact and ingestion
- In case of unwellness, see a physician

Toxicology of chronic toxicity

Evaluation of toxic effects

Chronic toxicity – long term studies (including offspring!)

| PRODUIT (UTILISATION) | ESPÈCE ANIMALE | DOSE LÉTHALE (g/kg) ¹ | | CONCENTRATION LÉTHALE (ppm/4 h) ² |
|--|-------------------|----------------------------------|--------------|--|
| | | VOIE ORALE | VOIE CUTANÉE | |
| Acétone (solvant) | lapin | 5,34 | 20,00 | --- |
| | rat | 5,80 | --- | 29 853,00 |
| | souris | 3,00 | --- | --- |
| Acroléine (fabrication de polymères) | hamster | --- | --- | 25,40 |
| | lapin | --- | 0,20 | --- |
| | rat | 0,046 | --- | 8,30 |
| | souris | 0,028 | --- | --- |
| Méthanol (solvant) | lapin | 14,41 | 15,80 | --- |
| | rat | 6,20 | --- | 64,00 |
| | souris | 7,30 | --- | --- |

| Valeurs limites d'exposition | longue | courte | classifi cation |
|---------------------------------|------------|--------|--------------------|
| acétone | 750 | 1000 | |
| acétonitrile | 40 | 60 | |
| acide formique | 5 | 10 | |
| oxyde diéthyle | 100 | 200 | |
| octane | 300 | 375 | |
| pentane | 500 | 750 | |

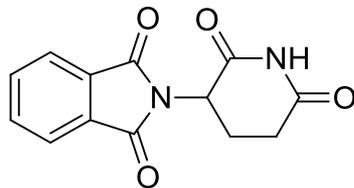
1. Quantité exprimée en gramme par kilogramme (g/kg).

2. Concentration dans l'air exprimée en partie par million (ppm) pour une période de quatre heures (4 h).

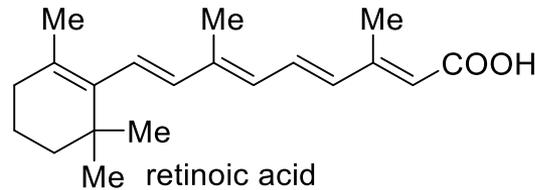
Type of toxicity

Teratogens

Alters embryonic/foetal organogenesis leading to malformations



thalidomide



retinoic acid

Mutagens (potential carcinogens)

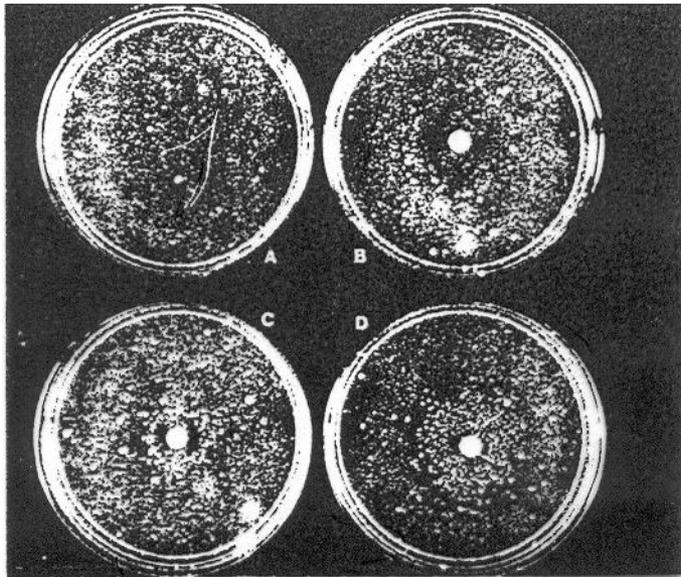
Causes mutations of the genome

- Chemical (all electrophiles – alkyl halides and sulfonates, epoxides, Michael acceptors, ... ; all intercalating agents – ethidium bromide, ... + all compounds whose metabolites are mutagenic !!)
- Physical (ionizing radiation, UV radiation, ... others?)

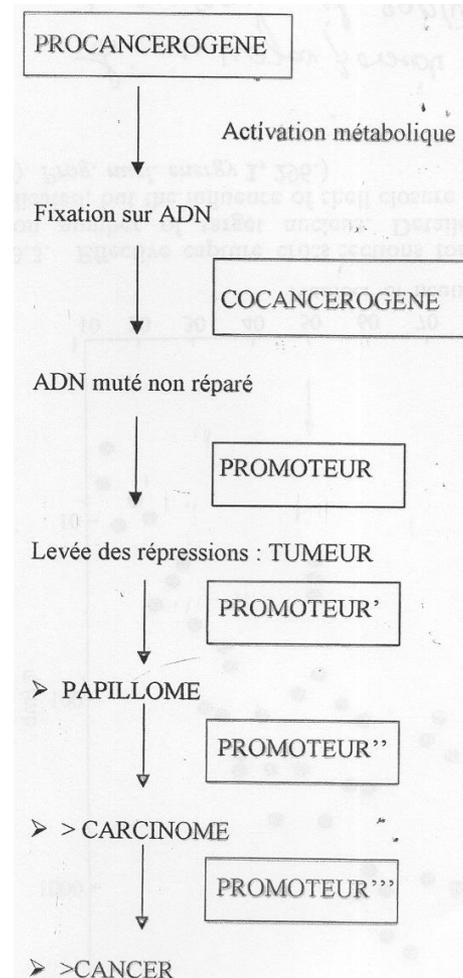
Type of toxicity

Mutagenesis test (Ames)

Culture of auxotrophic *Salmonella typhimurium* (histidine) in histidine-poor medium + mutagenic substance: appearance of autotrophic mutant strains



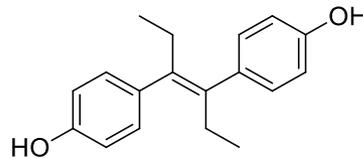
Mutagenesis and cancer



Nature of toxic effects

Transmitted toxicity

The case of diethylstilbestrol (DES) or distilbene (numerous media reports)

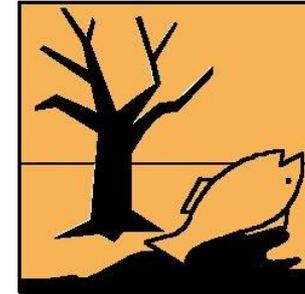


Vaginal cancers and infertility within women whose mother had been treated with DES !!

Highly publicized « second generation » lawsuits (incl. UCB Pharma)

Risk management continued

Risk management



Environmental hazards

Substances which are not compatible with the environment
Substances that interfere with ecosystems

Could be ANY of the previous.
However, few are labeled as such : sodium azide, ...

- Destroy or decompose any waste
- Recycle
- Specific waste containers

- Importance of waste management!

Risk management



Pressurized gases

All cylinders containing pressurised gases
Argon, nitrogen, carbon dioxide, hydrogen, butane...

BUT: also all pressurized reactors, autoclaves, Parr hydrogenators, sealed tubes,...

- Avoid shocks (violent pressure losses)
- Cylinders **HAVE TO BE ATTACHED** solidly to wall or bench
- Absence of any leakages (intoxication/asphyxia)
- Specific precautions for oxygen

- Respect all safety recommendations for the use of cylinders and pressure gauges
- Use in ventilated rooms or in fume hoods

Risk management

In case of accident or emergency

CALL FOR HELP!!!! And stay calm...

Internal phone number : **5000**

European emergency phone number: 112

If possible, eliminate the source of danger

Clearly indicate the location of injured persons if possible.

In case of asphyxia, ventilate the premises and evacuate the victims

In case of intoxication, contact the anti-poisoning center : 070 245245

In case of electrocution, turn off the main electrical switch before acting

In case of chemical or thermal burns, wash abundantly with cool water (>15 min)

Waste management

Solvents

Organic solvents:

- **NEVER THROW IN THE SINK**

Collect and eliminate using dedicated waste containers

- Halogenated solvents separated from
- Non-halogenated solvents

Non-toxic aqueous waste:

Can be poured into the sink **ONLY** if:

- pH is NEUTRAL (neutralize acids and bases before disposal)

Reactive aqueous waste

Collect in separated containers

- Oxidizing solutions
- Reducing solutions

Toxic aqueous, liquid or solid waste:

Collect and dispose of in *clearly labeled* containers!

(heavy metal salts, azides, cyanides, ...)

Waste management: new labeling system

Types of solid waste

- SW1. Mercury and its compounds (mercury lamps, UV lamps, .)
- SW2. Nanomaterials,
- SW3. CMR, toxic or harmful, (gloves, paper, pipettes, tips,)
- SW4. Non-CMR,
- SW5. Silica gel,
- SW6. Contaminated (empty) containers
- SW7. Synthesis media,
- SW8. Unused, partially used containers
- SW9. Other waste (milliQ cartridges, pH probes,

Waste management: new labeling system

Types of liquid waste

- LW1. Mercury and its compounds,
- LW2. Nanomaterials,
- LW3. Heavy metals (Cd, Cr, plomb, Ni, As, ...),
- LW4. CMR (Phenol, BET, CCl₄, ...),
- LW5. Oils,
- LW6. Explosives (picric acid, azides, perchlorates, peroxides...),
- LW7. Alkaline and alkaline-earth metals,
- LW8. Photographic developer and fixer,
- LW9. Toxic, harmful, harmful to the environment,
- LW10. Acids (HCl, HNO₃, H₂SO₄, H₃PO₄, ...),
- LW11. Bases, (NaOH, NH₃, KOH, ...),
- LW12. Halogenated solvents, (perchloroethylene, trichloroethylene, dichloromethane, chloroform, ...),
- LW13. Non-halogenated solvent (toluene, acetone, ethers, alcohols, alkanes, ketones, white spirit,...).

Waste management: new labeling system

Solid waste decision flowchart

SW1 Le déchet à collecter contient-il du mercure ou dérivés mercuriels ?

Non

SW2 Le déchet à collecter est-il contaminé par des nanomatériaux ?

Non

SW3 Le déchet à collecter est-il contaminé par un produit CMR, toxique ou nocif ?*

Non

SW4 Le déchet à collecter est-il contaminé par un produit hors CMR, toxique ou nocif ?

Oui

20 L

Oui

*Tout solide minéral ou organique contenant : BET, Acrylamide, Formol, Phénol, CCl₄,....

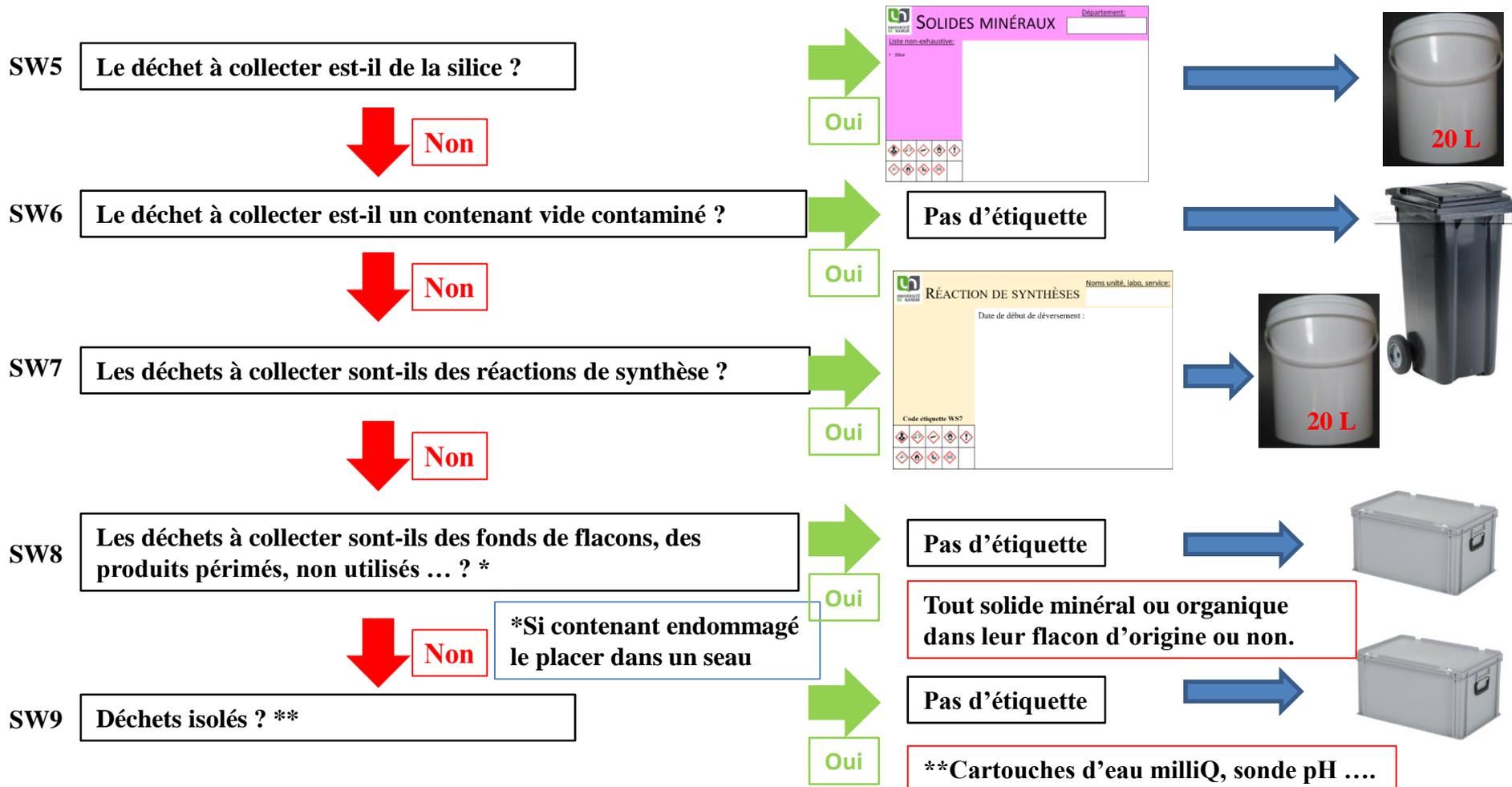
Oui

30 L

Oui

Waste management: new labeling system

Solid waste decision flowchart



Waste management: new labeling system

Flowcharts, labels, user guide, waste containers

For all questions related to chemical waste of any kind, in order to receive the flowcharts for solid and liquid waste, the waste containers and the labels for the latter, please contact:

Thierry Mayenne
dechets-dangereux@unamur.be

For all other safety, well-being or waste management-related queries, contact:

Service de Prévention (SerP)
sippt@unamur.be

For sources of safety and other information (in French):
<https://terranostra.unamur.be/sippt>

Back in the lab

When returning to the lab after this lecture...

- Find the location of all safety equipment (extinguishers, showers, alarms, ...)
- Check the evacuation plan of your floor and information thereon
- Check if your chemicals are stored and labeled correctly
- When planning your next experiment, evaluate the risk before starting it!
- When doing dangerous experiments, warn your colleagues...
- ...as well as trained first-aiders !
- Find the correct procedures to apply in the case of an accident...
- ...before it takes place!