Chemical Safety and Security Officer Training

Yemen

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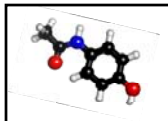
Sandia is a multiprogram laboratory operated by Sandia Corporation, a Lockheed Martin Company, for the United States Department of Energy's National Nuclear Security Administration under contract DE-AC04-94AL85000.

Sandia National Laboratories

Lab Visit

Lunch

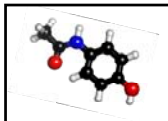
Chemical Toxicology and Physiology



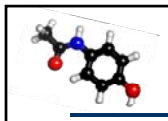
US National Institutes of Health, National Library of Medicine (NIH/NLM) on-line Toxicology Course

I. Basics
II. Toxicokinetics
III. Cellular Toxicology

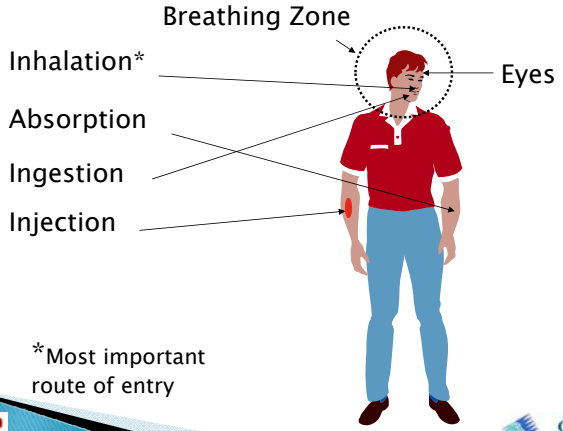
http://sis.nlm.nih.gov/enviro/toxtutor.html



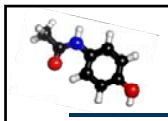
Simplified Physiology



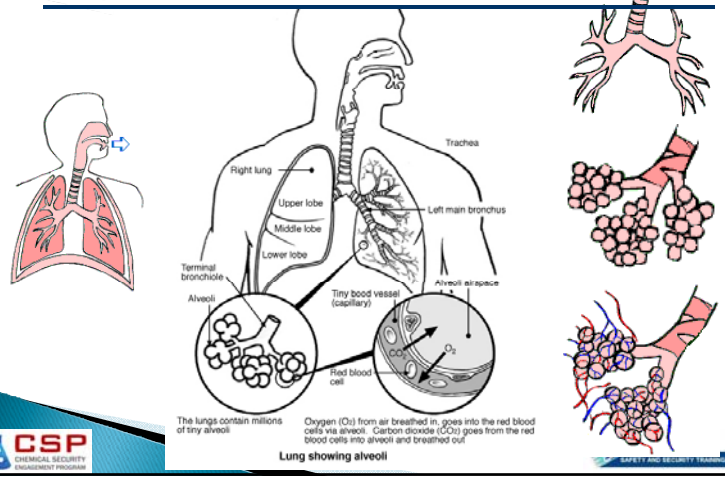
Routes of Exposure



*Most important route of entry



Respiratory System

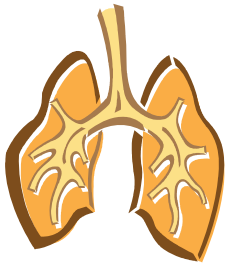


The Lungs Defense Mechanisms

- **Cilia**
  - Mucus traps dirt and foreign particles.
  - Little hairs (**cilia**) beat back and forth in the airways to move mucus and dirt up where it can be expelled by coughing.
- **Macrophages**
  - Special mobile cells that eat up toxins in the airways and lungs
- **Requirements:**
  - Regular supply of air with O_2
  - Open, clear airways

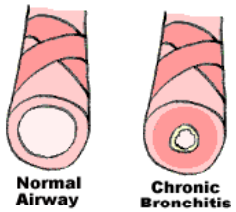
Gas Exchange Region

- About 70 m^2 – the serving area of a tennis court.
- Consists of alveolar duct and alveoli with surfactant to keep open.
- Close contact with capillaries to exchange O_2 for CO_2 and exhale other gases/vapors.



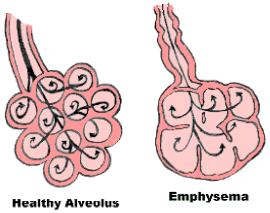
Common Respiratory Issues

Chronic Bronchitis



- Cells inflamed
- Airway narrow and clogged

Emphysema



- Normal elasticity destroyed
- Forcefully blow the air out, pressure on the airways
- Excessive coughing

Aerosol Penetration into the Lung

Size (micrometers)	% Deposition
> 20	100% in upper airways
10 – 20	80% upper, 0+ alveoli
5.0 – 10	50% upper, 50% alveoli
0.1 – 5.0	0+ upper, 90+ alveoli

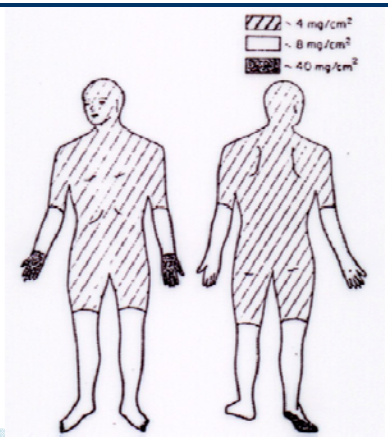
Certain Effects of Chemicals on the Lungs

- **Irritations** – acid mists (HCl)
- **Edema** – phosgene ($COCl_2$)
- **Emphysema** – smoke (esp. tobacco)
- **Fibrosis** – silicon dioxide (SiO_2)
- **Cancer** – asbestos (mesothelioma)

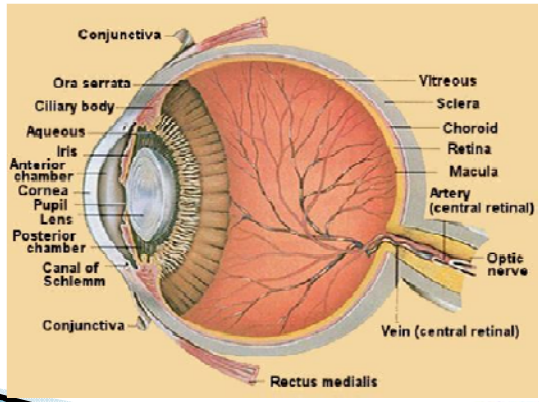
Asphyxiant/Suffocating Agent

- **Physical** – dilute oxygen in air to below 10%, non-irritant gases – methane, N_2, CO_2, Freon®
- **Chemical** – displace oxygen on hemoglobin – cyanide, carbon monoxide

Skin Thickness



The Eyes



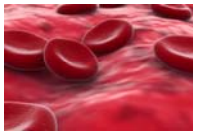
Routes of Exposure

Ingestion (mouth)

- Rare, but contamination can = intake
  - mucociliary action of respiratory tract
- Stomach → GI tract → bloodstream
- Absorbed – systemic injury
- Liver, kidney; Detoxification process
  - Inflammation
  - cirrhosis – fibrotic liver disease
  - malignant tumors
- Factors: physical state, duration

Routes of Exposure

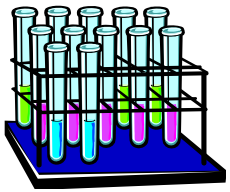
- Injection
  - Directly into bloodstream
    - "sharps", needles, broken glassware
    - skin puncture or injuries
  - Bypasses protective mechanisms
  - Usually rare in workplace
    - primarily associated with bloodborne pathogens (biomedical facilitates)
    - especially hazardous in health care industry

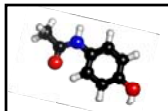


Chemical Toxicology

The World of Chemicals

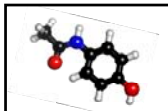
- Universe of Chemicals > 5 Million
- Industrial Inventories ~ 55,000
- Regulated Occupationally ~ 600





Terminology

Toxicants	• Substances that produce adverse biological effects of any nature • May be chemical or physical in nature • Effects may be of various types (acute, chronic, etc.)
Toxins	• Specific proteins produced by living organisms (Mushroom toxin or tetanus toxin) • Most exhibit immediate effects
Poisons	Toxicants that cause immediate death or illness when experienced in very small amounts

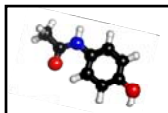


Toxicology

Poisons – the adverse effects of substances on living systems.

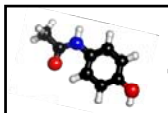
"All substances are poisons; There is none which is not a poison. The right dose differentiates a poison from a remedy…"
– Paracelsus (1493–1541)

Chemical Toxicology – The potential adverse effects and control of chemicals in the workplace.



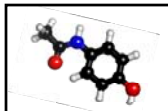
Basic Concepts

- All chemicals have the capacity to be toxic
- All chemicals act in the body according to the principles of chemistry, physics and biology
- Natural chemicals are not inherently harmless
- Synthetic chemicals are not inherently hazardous



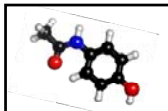
The Dose Makes the Poison

Chemical	Beneficial Dose	Toxic Dose
Aspirin	300-1000 mg	1000-30,000mg
Vitamin A	500 units/d	50,000 units/d
Oxygen	20% in air	50-100% in air



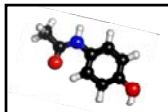
Lethal Dose

Agent	LD_{50} (mg/kg)
Ethyl Alcohol	7060
Sodium Chloride	3000
Naphthalene	1760
Ferrous Sulfate	1500
Aspirin	1000
Formaldehyde	800
Ammonia	350
Dextromethorphan Hydrobromide	350
Caffeine	192
Phenobarbital	150
Chlorpheniramine Maleate	118
DDT	100
Strychnine Sulfate	2
Nicotine	1
Dioxin	0.0001
Botulinus Toxin	0.00001



There are no harmless substances.

Only harmless ways of using substances.

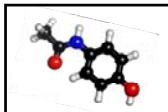


Chemical Toxicology

The study of the effect the chemical has on the body.

Pharmacokinetics

The study of the effect the body has on the chemical.



Factors Influencing Toxicity

- Concentration of toxin
- Duration and frequency of exposure
- Route of exposure
- Environmental factors — temperature, humidity, atmospheric pressure
- Chemical combinations (difficult and expensive to test)

Factors Influencing Toxicity

- Age
- Gender and hormonal status
- Genetic makeup
- State of health—presence of disease or stress
- Nutrition
- Lifestyle

Toxicity Testing Assumptions

- Effects seen in animals apply to humans
- High doses in animals are needed to predict possible hazard to humans

Duration of Exposure

- Acute 1 to 5 days
- Subchronic 14 to 90 days
- Chronic 6 months to lifetime

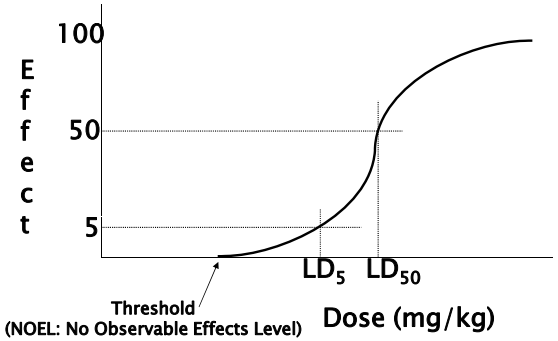
Dose-Response Relationship

With increasing dose, there is an increase in the number affected and/or an increase in the intensity of the effect: e.g., mortality; cancer; respiratory depression; liver pathology

Dose = (Concentration) x (Time)

Dose-Response Relationship

This relationship is unique for each chemical



Slope of Dose-Response Relationship

- Determines tradeoffs between drug effectiveness and toxicity.
- Low doses may be effective without producing toxicity.
  - More patients may benefit from higher doses.
  - Offset by the higher probability that toxicity or death could occur.
- Slope important in comparing toxicity of various substances.
  - For some, a small increase in dose causes a large increase in response.
  - For others, a much larger increase in dose is required to cause the same increase in response.

Dose-Response Relationship

- Fundamental concept in toxicology
- The relationship between the degree of exposure (dose) and the magnitude of the effect (response)
- Provides basis for evaluating a chemical's relative toxicity

Dose and Dosage

- Dose is *quantity* (mg, mL)
- Dosage includes *frequency* (10 mg, 4 times/day)
- Exposure dose – quantity administered
- Absorbed dose – Actual quantity absorbed

Dose-Response Terms

- TD_{lo} – Toxic dose low – lowest dose for effect
- LD_{10} – Lethal dose 10% – dose that causes death in 10% of the test population
- LD_{50} – Lethal dose 50% – dose that causes death in 50% of the test population
- TC_{lo} – Toxic concentration low – used to express toxic concentration *via* inhalation
- LC_{10} – Lethal concentration 10% – dose that causes death in 10% of the test population –*via* inhalation
- LC_{50} – Lethal concentration 50% – concentration that causes death in 50% of the test population *via* inhalation

Dose Units

Mass per weight or surface area of subject:

- Quantity per unit mass (mg/kg)
- Quantity per unit area of skin surface (mg/m^2)

Pharmacokinetics

Rate of:

- Absorption (uptake) – chemical enters
- Distribution (transportation) – spread/storage
- Metabolism (biotransformation) – processing
- Excretion – elimination

Metabolism

One purpose of metabolism is to make the chemical more water soluble so it can be excreted.

Done by adding oxygen molecules in the form of –OH, =O, –COOH, or by conjugation with glutathione, sulfonate, glycine, etc.

Some chemicals are not directly carcinogenic, but are metabolized to intermediates, e.g, epoxides, which are highly carcinogenic.

Metabolism, cont'd.

Chemicals not metabolized are stored in the body (e.g.):

- Lipid soluble materials in fat cells
- Metals are bound to proteins (hemosiderin)
- Dusts are deposited at surface of lung

This is why tattoos stay in place!

Metabolites

Benzene (C_6H_6)
carcinogenic
phenol, S-phenylmercapturic acid in urine

Toluene
CNS depressant
hippuric acid in urine

Ethyl benzene
irritant, dermatitis
mandelic acid in urine

Xylene ($C_6H_4(CH_3)_2$)
CNS, irritant
methyl hippuric acid in urine

Styrene
dermatitis
mandelic acid in urine

Interaction of Chemicals

- Additive Effect
  - Combined effect of 2 chemicals equals sum of each agent alone…(2 + 3 = 5)
- Synergistic Effect
  - Combined effect of 2 chemicals is greater than sum of each agent alone…(2 + 3 = 20)

Interaction of Chemicals

- Potentiation
  - One substance does not have toxic effect on certain organ or system, but when added to another chemical, it makes the latter more toxic…(0 + 2 = 10)
- Antagonism
  - 2 chemicals, when given together, interfere with each other's actions or one interferes with the action of the other chemical…(4 + 6 = 8)

Site of Effects

- Local
  - Effects occurring at site of first contact between biologic system and toxicant
    - Ingestion of caustic substances
    - Inhalation of irritant materials
- Systemic
  - Require absorption and distribution of toxicant to a site distant from entry point where effects are produced; most substances produce systemic effects
    - CCl_4 effects on the liver

Target Organs for Chemicals

Systemic toxin – affects entire body or many organs rather than a specific site, e.g., KCN affects virtually every cell and organ in the body by interfering with the cell's ability to utilize oxygen.

Toxicants – may also affect only specific tissues or organs while not producing damage to the body as a whole. These specific sites are known as Target Organs.

Benzene – a specific organ toxicant that it is primarily toxic to the blood-forming tissues.

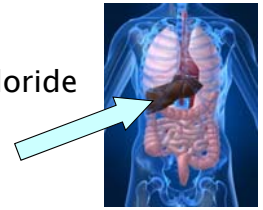
Lead – has three target organs (central nervous system, kidney, and hematopoietic system).

Target Organ Effects

Toxins	Target organ	Signs & Symptoms	Examples
HEPATOTOXIN	LIVER	JAUNDICE	CGl
NEPHROTOXINS	KIDNEY	EDEMA	HALOGENATED HYDROCARBONS
NEUROTOXINS	CNS	NARCOSIS BEHAVIOR	MERCURY
HEMATOPOIETIC SYSTEM	HEMOGLOBIN	CYANOSIS	CO, CS
LUNG AGENTS	PULMONARY TISSUE	COUGH,CHEST TIGHTNESS	SILICA, ASBESTOS
REPRODUCTION TOXIN	REPRODUCTIVE SYSTEM	BIRTH DEFECTS	LEAD
CUTANEOUS AGENTS	SKIN	RASHES; IRRITAION	KETONE
EYE HAZARDS	EYES	CONJUCTIVITIS	ORGANIC SOLVENTS

Target Organs

Liver Diseases



- Fatty liver – carbon tetrachloride
- Cirrhosis – ethanol
- Liver cancer – vinyl chloride and chlorinated solvents/pesticides

Target Organs

Skin

The protective barrier wrapped around the body (surface area about 2 m^2).

Helps maintain temperature, prevents water soluble materials entry, site of excretion, sensory activities, protective coating.

Target Organs

Skin Diseases

- Sensitization – chemical allergy
  - TDI – toluene – 2,4-diisocyanate
- Oil/coal tar acne – chloroacne
  - PCBs-polychlorinatedbiphenyls
- Contact dermatitis – fat soluble solvents
- Leukoderma (depigmentation) – H_20_2
- Allopecia (loss of hair) – thallium

Target Organs

Reproductive and Developmental Disorders

Concern for spermatogenesis, hormonal status, maternal toxicity, and embryo or fetal toxicity.

Target Organs

Spermatogenesis

- Rarely destroys the testes.
- Usually blocks sperm development.
- EGME (ethylene glycol monoethyl ether)
- Completely reversible after exposure ends.

Target Organs

Developmental Effects:

- Lethality – resorptions/stillbirths
- Toxicity – body weight/behavioral effects
- Teratogenicity – malformations (thalidomide)
- Delayed development/structural anomalies/variations

Target Organs

Maternal Toxicity:

- The ovary is more protected than the testes. So, it is not toxicity, but changes in hormonal regulation that is upset
- Endocrine modulation, DDT, and raptor eggs, ovulation, gestation

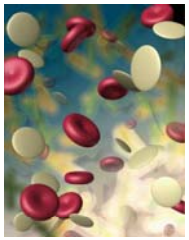
Target Organs

Nervous System:

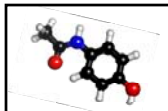
- CNS depression – many organic solvents
- Cholinesterase inhibition – organophosphorus & carbamate pesticides
- Nerve conduction velocity – myelin sheath, peripheral nerve destruction – n-hexane

Target Organs

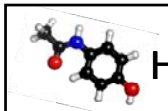
Circulatory System:



- Hemoglobin – CN and CO
- Red cells – lysis or lead poisoning
- Leukemia – benzene
- Arterial blockage – cholesterol, HDL/LDL



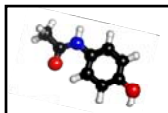
Toxic Effects of Solvents and Vapors



Halogenated Hydrocarbons

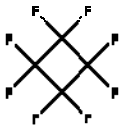
(low flammability, excellent solvents)

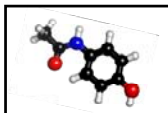
- Acute – CNS depression, defatting skin, myocardium
- Chronic – liver, kidney
- Chlorinated – solvents (CNS/skin/cancer)
  CCl_4–carcinogenic, liver, kidney
- Brominated – fumigant, solvents (CNS/skin)
- Fluorinated – refrigerants (ozone layer/myocardium)



Structure Affects Activity

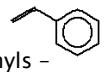
- Useful, but dangerous – i.e., guilty by association, e.g., C_4F_8
- Branched chain isomer – lethal @ 0.5ppm
- Linear isomer – lethal @ 6,100ppm in 4 hr
- Cyclic isomer – essentially non-toxic

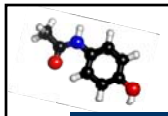




Aromatic Hydrocarbons

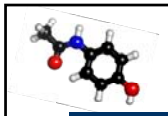
- Benzene – CNS depression, leukemia
- Toluene – CNS depression (glue sniffers)
- Styrene – dermatitis, CNS depression
- Poly-aromatic hydrocarbons – doxin, PCBs, biphenyls – liver/thyroid/skin
- Nitrobenzene – CNS, jaundice (liver effect), methemoglobin – blue lips & fingernails
- Phenol – CNS, liver, kidney, skin effects (absorbed readily through skin)





Aliphatic Alcohols

- Methanol – alcohol dehydrogenase–blindness–treat with ethanol
- Ethanol – CNS depression, fetal alcohol syndrome, liver cirrhosis
- Isopropanol – CNS depression, gastritis



Glycol Ethers

Ethylene glycol monomethyl ether (EGME) $CH_3OCH_2CH_2OH$

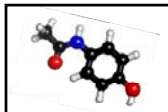
1. Disrupts sperm development
2. Developmental toxin – day 7,8–neural tube; day 10–11–digit/paw effects, brain, liver, and kidney

Ethylene glycol monoethyl ether (EGEE) $CH_3CH_2OCH_2CH_2OH$

1. Testicular degeneration
2. Reproductive/developmental toxins, but less severe

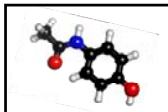
Propylene glycol monomethyl ether (PGME)

– Not a reproductive/developmental toxin



Ketones

- Acetone (dimethyl ketone) – CNS, skin effects
- Methyl ethyl ketone – CNS, skin, reproductive and developmental effects
- Methyl butyl ketone – CNS and peripheral nervous system effects



Pesticides

- Organophosphates – cholinesterase inhibitor; parathion, dursban, dichlorvos,
- Organochlorine – CNS; DDT, aldrin, kepone, mirex
- Carbamates – reversible cholinesterase inhibitor; sevin
- Chlorophenoxy – liver, kidney, CNS; 2,4–D, agent orange, 2,4,5–T
- Pyrethrins – CNS effects; resmethrin

Lab Assessment Exercise

Part 3: Lab Assessments

Break

Safe/Secure Transport of Chemicals

Transport References

UNECE, "Globally Harmonized System Of Classification and Labeling of Chemicals (GHS)," 1st edition, 2003, online, http://www.unece.org/trans/danger/publi/ghs/ghs_rev00/00files_e.html

International Airlines Transportation Association, Dangerous Goods Regulations(DGR), 2008, not online, http://www.iata.org/ps/publications/9065.htm

UN International Maritime Organization (IMO), http://www.imo.org/

European Union (EU) Transport Activities http://europa.eu/

US Department of Transportation (DOT) http://www.dot.gov

International Shipping Fines

- For international shipments fines are severe
  - up $250,000 fine + 5 years prison in US
- Apply to scientists improperly transporting
  - samples
  - test material
  - specimens
- Dangerous Goods Regulations are set by:
  - IATA: International Air Transport Association

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Modes of transport

- Air
- Ship
- Rail
- Road

- Vehicle (car/truck)
  - Cart, Bicycle
  - Hand carry

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Always expect the unexpected

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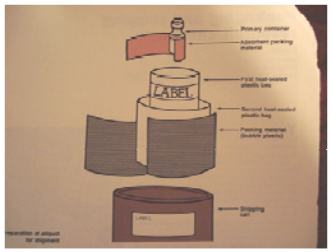
Universal Safety/Security Concept

Container within a Container



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What is a hazardous chemical shipment?

- Infectious substances
- Magnetized material
- Oxidizing substances
- Radioactive substances
- Toxic substances
- Aerosols
- Corrosives
- Dry ice
- Explosives
- Flammables
- Gases
- Flammable liquids
- Flammable solids
- Genetically modified organisms

Are there special shipping requirements?

What are the physical and chemical properties?

dry ice, refrigeration?

Are specific containers required?
size, strength, composition

Specific transport concerns

- Quantities, exclusions, limitations
- Restricted routes:
  tunnels
  bridges
  populated areas

Sender/Shipper Should Know

- Who transports the material?
- How is it transported?
- How is it packaged?
- Are transporters knowledgeable and prepared?
- Is there safety documentation?
- When did it leave, arrival time?
- Did all material depart and arrive as scheduled?

Labels continued

properly and fully identify material

use proper, full chemical name
no abbreviations
ID codes, e.g., UN Numbers

specify
quantities, concentrations,
number of containers

Labels continued

indicate specific hazard class
according to regulations

include
emergency information
contact names
24/7 phone numbers

language(s)
proper universal symbols

Documentation

shipping order
bill of lading
manifest
full shipper, receiver
addresses
packing & labeling
certification
verification of receipt

Documentation continued

Safety Data Sheets

follow up documentation

require incident/accident reports

Handling

Where, how, who opens shipment?

Should package be opened in a hood?

Is material radioactive?

Is monitoring equipment needed?

Is special storage needed on receipt?

Who requires training?

- Managers
- Packers
- Handlers
- Loaders
- Drivers
- All shipping and receiving personnel
- Mailroom personnel

Emergency Preparation

- Transportation accidents/incidents:
  - Organization reports
  - Police reports
  - Emergency contacts
- Spill and leakage control:
  - prevention
  - minimization
  - spill clean up kits
  - PPE
- Emergency contacts
  - Regulation requirements
    - local, national, international

Emergency preparation continued

- Emergency contacts
  - Regulation requirements
    - local, national, international

- Public relations
  - Designate spokesperson beforehand
  - Be responsive to public concerns

Plan ahead

- Have a plan
- Remember:
  - Anticipation
  - Recognition
  - Evaluation
  - Control

Unsafe Transport of Gas Cylinders

Acknowledgement

International Labour Organization (ILO)

International Occupational Safety and Health Centre (CIS)

Programme on Safety and Health at Work and the Environment (SafeWork)

http://www.ilo.org/public/english/protection/safework/cis/index.htm

Any Questions?

REACH and the Global Harmonized System for the Labeling of Chemicals

REACH

Registration, Evaluation, Authorisation of Chemicals

2007 EU regulation; replaces 40 existing acts to create a single system for all chemicals

- requires authorization to use, manufacture and import
- to track and manage chemical risks and provide safety information
- proposes to integrate REACH with GHS
- creates European Chemical Agency (ECHA, Helsinki, Finland

REACH

Life of the chemical from

Cradle-to-the-Grave

Manufacturing

Importing

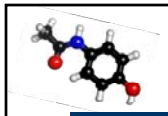
Marketing

Use

Waste stream

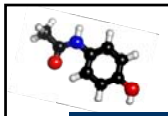
REACH

- Comprehensive legislation to ensure European authorities know and condone what chemicals are used as they enter the EU supply train
- Objective is to protect human health and the environment by recognizing and classifying hazardous chemicals so they are handled safely
- REACH & GHS are not equivalent or optional but separate legislation with parallel requirements



REACH

- The responsibility for proving whether a chemical is hazardous or non-hazardous is on the manufacturer and supplier not the government
- The responsibility also includes documentation, tests, classification, risk exposure, labeling, safety data sheets
- ECHA will store the information in the International Uniform Chemical information Database (IUCLID)

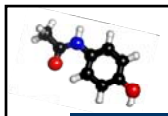


REACH

Four Steps

1. Registration
2. Evaluation
3. Authorization
4. Restriction

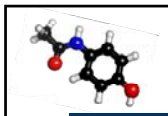
ECHA maintains database



REACH: Registration

Importers and manufacturers of substances in quantities over 1 ton/yr must register their substance with ECHA

- Registration began June 2007
  - December 1, 2010
    - ≥ 1000 tons per year
      - carcinogenic, mutagenic, or reproductive toxin ≥ 1 ton per year
      - substances classified as dangerous for aquatic environment ≥ 100 tons per year
  - June 1, 2013
    - manufactured or imported at 100-1000 tons per year
  - June 1, 2018
    - manufactured or imported at 1-100 tons per year



REACH: Evaluation

Authorities will review registration and request further information or testing to determine the impact of the substance on human health and the environment

Decides next steps:

- action for authorization
- align classification & label
- other action

REACH: Authorization

Decisions on what substances require an authorization or restriction are carried out for substances that pose the most concern, such as carcinogens and mutagens

Three steps:

- SVHC (Substances of Very High Concern)
  - carcinogenic, mutagenic and reprotoxic substances, persistent, bio-accumulative and toxic
- Prioritize
- Authorization provided

REACH: Restriction

- Limit uses
  - Where no viable alternative exists, a research and development plan to derive a suitable alternative is developed
- Ban substance
  - where there is an unacceptable risk to human health and the environment.

REACH: Concern

A potential concern may be creating country specific safety data sheets and labels that are compatible with the GHS proposal

REACH: Resources

About REACH: http://guidance.echa.europa.eu/

http://ec.europa.eu/environment/chemicals/reach/reach_intro.htm

REACH Help: http://echa.europa.eu/help_en.asp#helpdesks

About ECHA: http://ec.europa.eu/echa

Globally Harmonized System for Classification and Labeling of Chemicals (GHS)

International UN standardization for classification, safety data sheet format, and labeling of chemicals using pictograms, signal words, and hazard warnings

US OSHA is reviewing GHS for adoption

GHS

- United Nations proposed system to internationally standardize chemical communication
- Countries will adopt on their own timeframe
- 2008 – UN goal for world-wide implementation

GHS Implementation

Intergovernmental Forum on Chemical Safety (IFCS) – adopted GHS implementation goal of 2008. The US participates and agreed to work toward this goal

Japan, Korea, New Zealand – various stages of adopting & implemented GHS

European Union – 2010 deadline for GHS substance classification

Canada – Assessing how to adopt and implement GHS

United States – OSHA proposed rulemaking at end of 2009. DOT has adopted some parts, still working on others.

GHS Benefits

- Uniform Communication
- Better Safety
- Improved International Trade
- Lower cost

GHS Changes

MSDS now named: "SDS" (Safety Data Sheet)

Labels will be standardized with:

- signal words
- hazard statements
- precautionary statements
- pictograms
- elimination of US, Canadian and EU labels

GHS Labeling

Information required on a GHS label:

- Pictograms
- Signal words
- Hazard statements
- Precautionary statements and pictograms
- Product identifier
- Supplier information

Changes to (M)SDS

GHS name: Safety Data Sheet (SDS)

- Format:
  - 16 sections required in specified order (as per ANSI MSDS format in US Regulations presentation)
- Reclassification:
  - (MSDS) Health & Physical Hazards
  - (SDS) Environmental Hazards
- Building Block Approach
  - each country can select portions of GHS to adopt
  - Not every country will require all categories or all hazards

Examples of GHS Pictograms

Differences between REACH and GHS

- REACH and GHS have different scopes but there are many links between the two regulations
- REACH aims to produces information on hazards, risks, and risk management
- GHS aims to harmonize classification and labeling of materials
- GHS is a UN recommendation which applies across countries, including the EU

Differences between REACH and GHS

- REACH intends to replace current EU classification criteria with GHS. REACH has provisions for safety data sheets based on GHS.
- GHS intends to apply classification and labeling beginning December 1, 2010, when the new GHS regulation will be available.
- Substances will be phased in the first 3.5 years. Mixtures will be given an additional 4.5 years for reclassification.

Globally Harmonized System

Resources

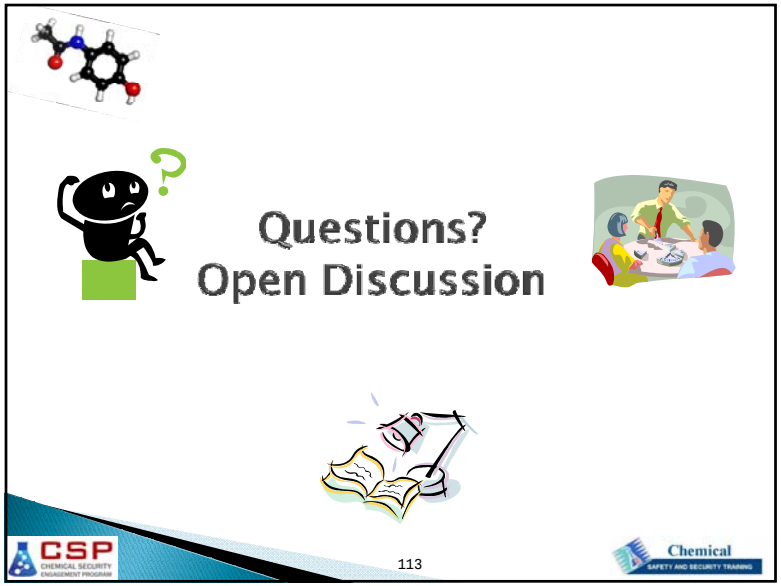
http://www.unece.org/trans/danger/publi/ghs/ghs_rev02/02files_e.html

http://www.unece.org/trans/danger/publi/ghs/presentation_e.html

http://www.osha.gov/dsg/hazcom/ghs.html

Lab Assessment Exercise

Part 4: Lab Improvements


Questions?
Open Discussion
CSP
CHEMICAL SECURITY ENGAGEMENT PROGRAM
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Chemical
SAFETY AND SECURITY TRAINING