# PharmacoLearn

**MPC204T Pharmaceutical Process Chemistry, M.Pharm Semester 2**

## Unit 5: Industrial Safety

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### 5.1 Safety as a process parameter

Every earlier unit has carried a safety thread: nitration runaway, hydrogenation gas handling, ozonolysis intermediates. This unit gathers the formal systems under which a pharmaceutical plant keeps people, product and environment safe. The organising idea is the **hierarchy of controls**: hazards are controlled first by elimination and substitution (choose the route that does not use the dangerous reagent, the lesson of Unit 1), then by engineering controls (closed vessels, ventilation, inerting, relief systems), then by administrative controls (procedures, permits, training), and only lastly by personal protective equipment. The syllabus items follow that logic from information (the safety data sheet), through labels and PPE, to fire, to the management systems that hold the whole structure in place, and finally to the effluent that leaves the site.

### 5.2 The MSDS (material safety data sheet)

The material safety data sheet, in current practice the **safety data sheet (SDS)** under the Globally Harmonized System (GHS), is the standardised document that travels with every chemical and tells the user what the material is, what it can do to people and the environment, and how to handle, store, spill and dispose of it. A GHS SDS has sixteen fixed sections, and a process chemist reads certain of them professionally:

1. Identification of the substance and of the supplier
2. Hazards identification (hazard classes, signal word, hazard and precautionary statements)
3. Composition and information on ingredients
4. First aid measures
5. Firefighting measures
6. Accidental release measures
7. Handling and storage
8. Exposure controls and personal protection (including occupational exposure limits)
9. Physical and chemical properties (flash point, boiling point, explosion limits: the numbers process design uses)
10. Stability and reactivity (incompatibilities, conditions to avoid, hazardous decomposition: the numbers thermal hazard assessment uses)
11. Toxicological information
12. Ecological information
13. Disposal considerations
14. Transport information
15. Regulatory information
16. Other information

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In the plant the SDS is not a filing exercise. It is the source document for the risk assessment of every operation, for the selection of PPE (Section 5.4), for storage segregation (oxidising acids away from organics, the mixed acid lesson of Unit 3), for the emergency plan, and for training. The rule taught with this item is simple: no material is charged to a vessel by anyone who has not read its sheet.

## 5.3 Hazard labels of chemicals

Labels translate the SDS onto the container in the hand. Under GHS the elements are: the **product identifier**; **pictograms** in red bordered diamonds, nine in the system, covering physical hazards (flame, flame over circle for oxidisers, exploding bomb, gas cylinder, corrosion), health hazards (skull and crossbones, exclamation mark, health hazard silhouette, corrosion) and the environmental hazard (dead tree and fish); a **signal word**, Danger for the more severe categories or Warning for the less; **hazard statements** (H statements, coded descriptions such as "flammable liquid and vapour" or "causes severe skin burns"); **precautionary statements** (P statements covering prevention, response, storage and disposal); and the supplier's identity. The older diamond systems survive alongside: the NFPA 704 diamond (health, flammability and reactivity quadrants with a special hazards field) on fixed installations and in transport practice, and the transport labels and UN numbers of the dangerous goods rules. For the process chemist the working skill is fluency: to read a drum label at a glance and know that this solvent store, this oxidant and this corrosive cannot share a bund, a pump or a waste stream.

## 5.4 Personal protective equipment (PPE)

PPE is the last line of the hierarchy, worn because the hazard remains after every better control has done its work. In an API plant the standard ensemble is:

- **Eye and face protection:** safety glasses for general areas, chemical goggles for splash risk operations (charging, sampling, line breaking), face shields over goggles for corrosive transfers.
- **Hand protection:** gloves matched to the chemical (nitrile for many organics, heavier laminates for aggressive solvents), changed on schedule and on damage, because a solvent soaked glove is an exposure device, not a protection device.
- **Body protection:** laboratory coats and plant coveralls, chemical resistant aprons and suits for corrosive charging, antistatic and flame retardant clothing where flammable atmospheres are handled.
- **Foot protection:** safety shoes with toe caps and chemical resistant soles; gumboots for washdown and effluent areas.
- **Respiratory protection:** dust masks and respirators with cartridges matched to the hazard for powder handling (potent API work uses powered air purifying or supplied air systems inside containment), and self contained breathing apparatus for emergency response only, by trained teams.
- **Hearing protection** in high noise areas such as compressor and utility halls.

The management content matters as much as the list: PPE is selected from the SDS and the risk assessment, issued personally, fitted (a respirator that does not seal does not protect), inspected, maintained, and its use trained and enforced: PPE is specified last in the hierarchy and audited hardest.

## 5.5 Fire hazards, types of fire and fire extinguishers

Fire needs fuel, oxygen and ignition together (the fire triangle; adding the self sustaining chain reaction gives the tetrahedron), and a pharmaceutical plant stores all three at scale: flammable solvents are the dominant fuel inventory, oxidising reagents and air supply the oxygen side, and ignition arrives by static discharge, electrical fault, hot work or runaway reaction. Prevention follows the triangle: inerting vessels with nitrogen, bonding and earthing against static, flameproof electrical equipment in classified areas, hot

work permits, and solvent inventory discipline.

**Types (classes) of fire,** in the classification used in Indian practice:

| Class | Fuel | Extinguishers suited |
|---|---|---|
| A | Solid combustibles: wood, paper, packaging, many powders | Water, foam, dry powder |
| B | Flammable liquids: solvents, oils | Foam, dry powder, carbon dioxide; never a water jet, which spreads the burning liquid |
| C | Gases: hydrogen, LPG, solvent vapour leaks | Dry powder; first shut off the gas supply |
| D | Metals: sodium, magnesium, aluminium powder, metal hydrides | Special dry powder for metals; water is dangerous here |
| E | Electrical equipment (treated as a class in Indian practice) | Carbon dioxide, dry powder; non conducting agents only |
| F | Cooking and vegetable oils (kitchens and canteens) | Wet chemical extinguishers |

**Extinguisher types** map onto the classes by mechanism: water cools; foam cools and blankets the vapour; dry chemical powder interrupts the chain reaction and coats; carbon dioxide displaces oxygen and cools, leaving no residue, which suits electrical and instrument fires; wet chemical saponifies burning oils. The process plant additions are fixed systems: hydrant and hose reel networks, sprinklers, foam systems over solvent tank farms, gas detection with automatic isolation, and fire walls and bunding that keep a tank fire a tank fire. The syllabus point is selection under pressure: the wrong extinguisher (water on a solvent pool, water on a metal fire) converts an incident into a disaster, so class recognition is trained, not looked up.

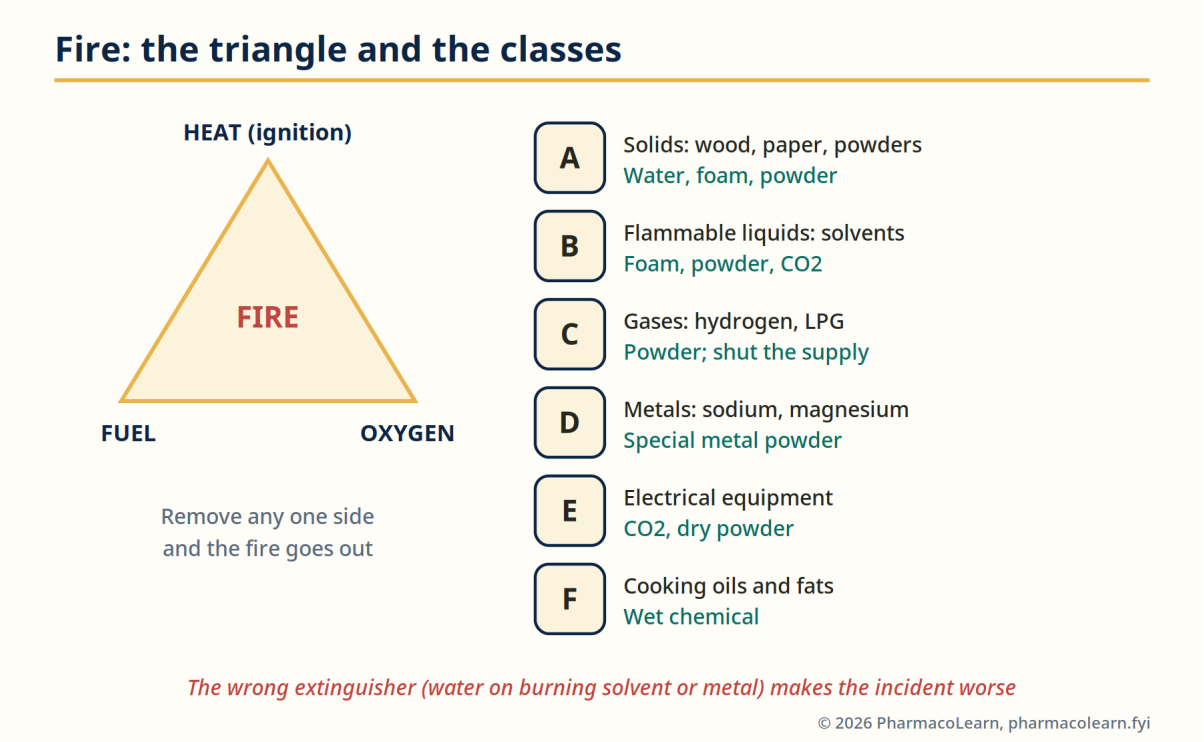


*Figure: The fire triangle and the classes of fire used in Indian practice, each with the extinguishers that suit it and, by omission, those that must never be used.*

## 5.6 OHSAS 18001 and ISO 14001: the management systems

Individual precautions become a system under the two standards the syllabus names. (The syllabus prints "OHSAS 1800"; the standard is **OHSAS 18001**, and for accuracy it should be recorded that OHSAS 18001

was withdrawn in 2018 and replaced by ISO 45001, whose structure it anticipated.)

**OHSAS 18001** specified an occupational health and safety management system: the organisation sets a safety policy, identifies hazards and assesses risks for every activity (the **plan**), implements controls, training, communication and emergency preparedness (**do**), monitors performance, investigates incidents and audits the system (**check**), and reviews and improves it at management level (**act**). The plan do check act cycle is the standard's engine, and its product is the difference between safety as a poster and safety as an audited routine: permits to work, management of change, contractor control and incident investigation all live inside it.

**ISO 14001** applies the same architecture to the **environment**: an environmental policy, identification of environmental aspects and impacts (emissions to air, effluent to water, waste to land, resource consumption), legal compliance obligations, objectives and programmes, operational control, monitoring and management review, again on the plan do check act cycle. In a pharmaceutical plant the two systems share most of their machinery: the same audit calendar, the same corrective action system, the same management review, and the same documentary discipline that GMP already imposes on the production side. Together they answer the regulator, the insurer, the neighbour and the workforce with one voice: hazards and impacts are known, controlled, measured and improving.

## 5.7 Effluents and their management

An API plant's liquid waste is chemically unlike any other industry's: mother liquors carrying product and by products, aqueous washes with solvent traces, scrubber liquors, fermentation broths of high biological oxygen demand, and utility water, in streams that vary batch by batch. **Effluent management** proceeds in layers:

- **At source, the process layer:** the cheapest effluent is the one never made. Solvent recovery by distillation (Unit 2) returns solvent to the process and removes it from the waste; segregating strong streams (mother liquors, first washes) from weak ones (later washes, cooling water) keeps the difficult fraction small, and high strength organic streams are commonly sent for incineration or cement kiln co processing rather than diluted into the treatment plant. The waste intensity of a process is summarised by Sheldon's E factor, kilograms of waste per kilogram of product, linking this section back to the route selection of Units 1 and 4.
- **Primary treatment:** screening, equalisation (blending the variable flow to a steady composition), neutralisation and oil and solids removal.
- **Secondary (biological) treatment:** activated sludge and related systems in which microbial communities consume the dissolved biodegradable load, measured as BOD (biochemical oxygen demand) and COD (chemical oxygen demand); fermentation and wash streams are treated here, and recalcitrant API residues are watched because some are biologically active at low concentration and can inhibit the biomass itself.
- **Tertiary treatment:** polishing by filtration, activated carbon, advanced oxidation or membrane processes to meet discharge standards for COD, total dissolved solids, colour and specific pollutants; in water stressed Indian industrial clusters, treated effluent is increasingly recycled to utilities, and zero liquid discharge configurations (evaporation and crystallisation of the final brine, closing the Unit 2 circle) are required of some pharmaceutical estates.
- **Solid and hazardous residues** run in parallel: distillation residues, spent catalyst (to metal recovery), contaminated filter aids and sludge go to authorised treatment, storage and disposal facilities with manifest tracking, under the hazardous waste rules.

The examination synthesis is that effluent management is process chemistry continued past the factory gate: what the route makes, the plant must treat, and the standards of Section 5.6 are the system that proves it does.

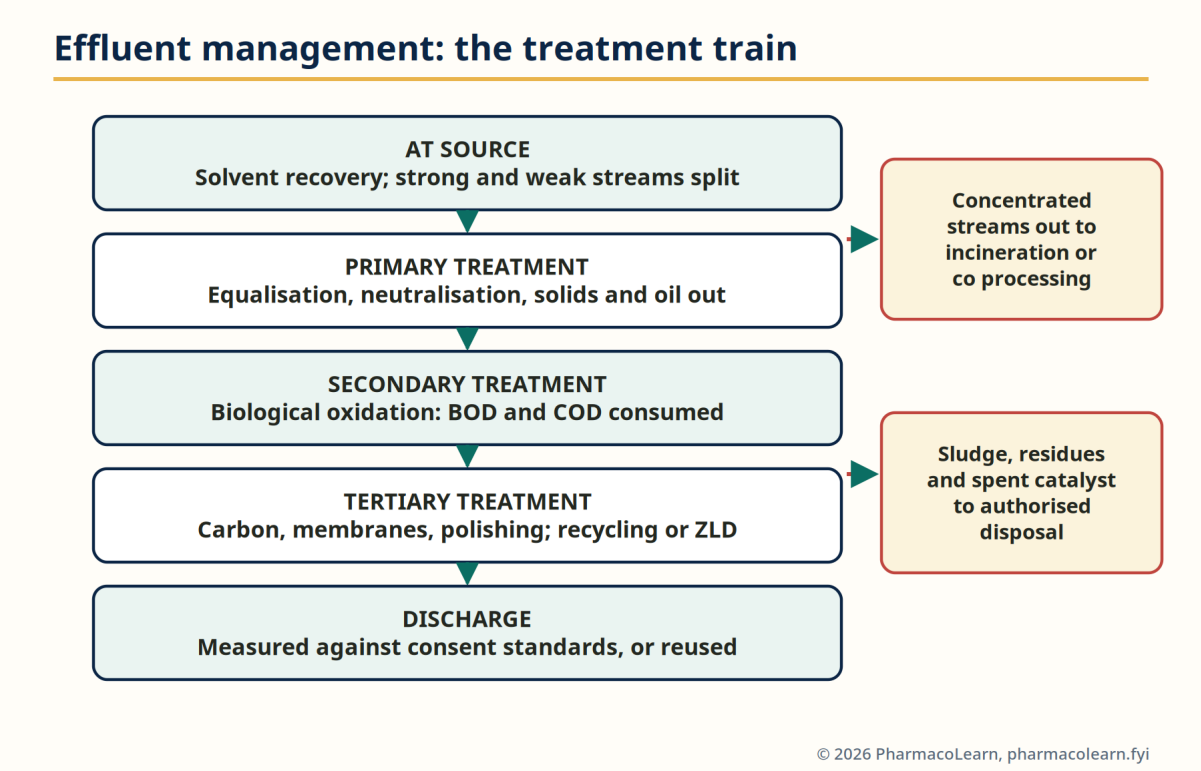


*Figure: Effluent management as a train: reduce and segregate at source, then primary, biological and tertiary treatment, with concentrated streams and residues leaving by their own routes.*

### 5.8 Unit 5 summary

| System | What it carries |
|---|---|
| SDS (16 GHS sections) | The hazard facts for every material, and the source of every risk assessment |
| GHS labels | Pictograms, signal word, H and P statements on the container in the hand |
| PPE | The last line of defence, selected from the SDS, fitted, trained and audited |
| Fire classes A to F | Fuel based classification that decides the extinguisher, and forbids the wrong one |
| OHSAS 18001 (now ISO 45001) | Occupational health and safety as an audited plan do check act system |
| ISO 14001 | Environmental management on the same architecture |
| Effluent management | Source reduction and segregation, primary, biological and tertiary treatment, hazardous residue control |

## Frequently Asked Questions

**Q: What is the difference between a unit operation and a unit process?** A: A unit operation is a physical step that does not change chemical identity, such as extraction, filtration, distillation, evaporation and crystallization, while a unit process is a chemical transformation such as nitration, halogenation, oxidation or reduction.

**Q: Why does a reaction that is safe in the laboratory become dangerous at plant scale?** A: Heat generation scales with volume while heat removal scales with surface area, so the same exothermic

chemistry can outrun its cooling in a large vessel; mixing also slows, operations take longer and the inventory of hazardous material is far greater.

**Q: What are the three stages of scale up and what happens at each?** A: Bench scale (gram quantities: route choice, optimisation, thermal hazard screening), pilot scale (kilogram quantities: the process rehearsed in plant style equipment, engineering data collected, material made for toxicology and trials), and large scale (hundreds of kilograms to tonnes: the validated process run to fixed batch records).

**Q: What is a genotoxic impurity and how is it controlled?** A: A genotoxic impurity is an impurity that can damage DNA, so no safe threshold is assumed; control follows ICH M7, using structural alert assessment and the threshold of toxicological concern (1.5 micrograms per day for lifetime exposure), achieved mainly by designing the impurity out at route selection and demonstrating purge through the process.

**Q: Why are several small extractions better than one large extraction with the same total solvent?** A: Because of the distribution law: each fresh portion of solvent removes a fraction of the solute remaining, so splitting the solvent into portions leaves progressively less solute behind than a single equilibration with the whole volume.

**Q: What is the metastable zone in crystallization and why do processes work inside it?** A: The metastable zone is the band of supersaturation between the solubility curve and the point of spontaneous nucleation, where a solution will grow existing crystals but will not nucleate new ones; seeding a batch inside this zone and generating supersaturation slowly gives controlled growth, consistent crystal size and the correct polymorph.

**Q: What is mixed acid and why is sulfuric acid used in nitration?** A: Mixed acid is concentrated nitric acid with concentrated sulfuric acid; the sulfuric acid generates the nitronium ion electrophile by protonating nitric acid and removing water, absorbs the water formed so the medium stays strongly acidic, and acts as a heat absorbing reaction medium.

**Q: How can the same chlorine give ring chlorinated or side chain chlorinated toluene?** A: Conditions choose the mechanism: a Lewis acid catalyst such as ferric chloride, in the dark, polarises chlorine for electrophilic attack on the ring, giving ortho and para chlorotoluenes, while light, heat or radical initiators give free radical attack on the side chain, giving benzyl chloride and its further chlorination products.

**Q: Why is transfer hydrogenation used when hydrogen gas exists?** A: Transfer hydrogenation replaces hydrogen gas with a donor such as ammonium formate, cyclohexene or isopropanol, so it needs no pressure autoclave or hydrogen supply and runs in ordinary vessels with easy dosing control, at the cost of a stoichiometric donor and its by product; it is favoured at development and smaller scales.

**Q: What do OHSAS 18001 and ISO 14001 have in common?** A: Both are management system standards built on the plan do check act cycle: policy, identification of hazards (OHSAS 18001, occupational health and safety, now succeeded by ISO 45001) or environmental aspects (ISO 14001), objectives, operational controls, monitoring, audit and management review, applied as one audited routine in a well run plant.

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