

Sterile Formulations

Introduction to Sterile Formulations

Introduction

- Sterile formulations are pharmaceutical preparations free from all living microorganisms, including bacteria, fungi, and spores.
- These are essential for dosage forms that bypass the body's natural barriers (e.g., skin, mucous membranes), especially in the eyes, bloodstream, internal organs, and parenteral tissues.

Importance of Sterility

- Sterile formulations are required when:
 - The product is injected directly into the body (IV, IM, SC).
 - Used in the eyes or lungs.
 - Applied to open wounds or internal cavities.
- Even minimal contamination can lead to severe adverse effects or death, especially in immunocompromised patients.

Common Sterile Dosage Forms

- Injectables (solutions, suspensions)
- IV infusions
- Ophthalmic solutions/suspensions
- Inhalation solutions
- Irrigation fluids
- Implants

Key Characteristics

1. **Sterile:** No live microorganisms.
2. **Pyrogen-free:** No fever-causing substances (like endotoxins).
3. **Particulate-free:** No visible or microscopic particles.
4. **Isotonic and pH-adjusted:** To match physiological conditions.
5. **Stable:** Chemically and microbiologically over shelf life.

Manufacturing Methods

1. Aseptic Processing:

- Drug and components sterilized separately.
- Combined in a sterile environment.
- Used for heat-sensitive drugs.

2. Terminal Sterilization:

- Entire product is sterilized after filling/sealing.
- Preferable when possible due to higher reliability.

Cleanroom Standards

- Sterile manufacturing must occur in cleanrooms under controlled conditions:
 - **Class 100 / ISO 5** for critical areas.
 - Positive pressure, HEPA-filtered air.
 - Environmental monitoring.
 - Gowning and hygiene protocols.

Injectables (Parenteral Preparations)

Definition:

- Injectables are sterile preparations intended for administration into the body through injection.
- They are introduced directly into the bloodstream, muscles, tissues, or body cavities.

Routes of Administration:

- Intravenous (IV)
- Intramuscular (IM)
- Subcutaneous (SC)
- Intradermal
- Intrathecal (into cerebrospinal fluid)
- Intra-articular (into joints)

Types of Injectable Preparations:

Type	Description
Solution for injection	Clear, sterile, aqueous or oily solution
Suspension for injection	Sterile suspension of drug particles

Emulsion for injection	O/W or W/O sterile emulsions
Powder for reconstitution	Sterile dry powder reconstituted before use
Depot injections	Long-acting formulations in oily base

Ideal Characteristics:

- Must be sterile, pyrogen-free, and particulate-free
- Isotonic with blood plasma (~0.9% NaCl equivalent)
- pH adjusted (usually 4.5–8) for drug stability and compatibility
- Must be prepared in aseptic conditions using Good Manufacturing Practices (GMP)

Composition:

- **Active drug**
- **Vehicle:** Water for injection (WFI), oils (for IM use), or co-solvents like propylene glycol
- **Buffers:** To maintain pH
- **Tonicity agents:** NaCl, dextrose
- **Stabilizers:** Antioxidants (ascorbic acid), chelating agents (EDTA)
- **Preservatives:** Benzyl alcohol, methylparaben (for multi-dose vials only)

Advantages:

- Rapid onset of action
- 100% bioavailability
- Suitable for unconscious or vomiting patients
- Controlled and localized delivery

Disadvantages:

- Invasive and painful
- Requires trained personnel
- Risk of infection if contaminated
- Higher production cost

Methods of Preparation:

A. Solution-based Injectable:

1. Dissolve drug and excipients in WFI under aseptic conditions.

2. Adjust pH using buffer solutions.
3. Adjust tonicity (e.g., with NaCl).
4. Sterile filtration through 0.22 μm membrane filter.
5. Aseptically fill into sterile vials or ampoules.
6. Seal immediately (e.g., flame-seal ampoules).
7. Terminal sterilization (e.g., autoclaving at 121°C for 15–20 min), unless already sterile-filtered.

B. Powder for Injection:

1. Dissolve and filter drug solution.
2. Sterile fill into vials.
3. Lyophilize (freeze-dry) to remove water.
4. Seal under vacuum or inert gas (nitrogen).
5. Label: "Reconstitute with ____ before use."

Examples:

- Adrenaline injection (IV, IM)
- Ceftriaxone injection (powder for reconstitution)
- Insulin injection (SC)

Eye Drops (Ophthalmic Solutions)

Definition:

- Eye drops are sterile aqueous or oily solutions intended for instillation into the conjunctival sac of the eye.

Requirements:

- Sterile
- Isotonic ($\approx 0.9\%$ NaCl)
- pH 6.5–7.5 (close to tear fluid pH)
- Non-irritating and preservative-free in unit-dose
- Free from foreign particles

Composition:



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