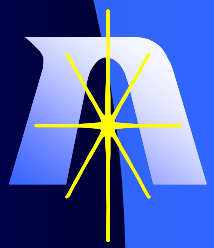
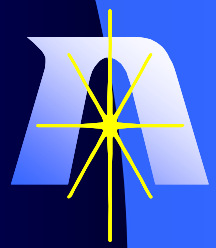
STERIEL DOSAGE FORMS



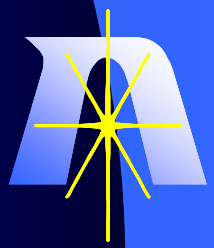
COURSE CONTENTS

- Parenteral preparations
- Ophthalmic preparations
- Radiopharmaceutics
- Enhalations
- Good Manufacture Practice (GMP)



PARENTERAL PREPARATIONS

- **Definitions related to the topic:**
  - Parenteral Products
  - Sterilization & Sterile Product
  - Pyrogen
  - SVP
  - LVP
  - Single dose container
  - Multiple dose container
  - Hermetically sealed container



PARENTERALS

para: outside

enteron: intestine

These are the preparations which are given other than oral routes.

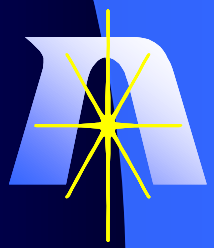
Injections:

These are

- Sterile,
- Pyrogen free preparations intended to be administered parenterally (outside alimentary tract).

Background

- **Contamination** – Any effect or action that has a negative impact on a product's integrity making it unfit for use
  - Chemical composition
  - pH
  - Sterility (e.g. microorganism contamination)
  - Pyrogenicity
  - Physical appearance
  - Particulate matter (e.g. dust, glass or precipitation)



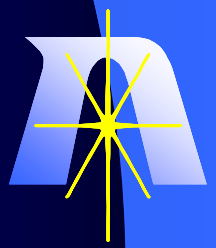
Background (cont.)

- **Sources of product contamination**
- **People (most common)**
  - Touch contamination
  - Generation of particulates from shedding cells or hair
- **Air Supply**
  - Heating, Ventilation and Air Conditioning (HVAC)
- **Infiltration**
  - Particles from adjacent spaces (e.g. entrance, hall)
- **Internal generation**
  - Walls, floors, ceilings, packaging, equipment

Background (cont.)

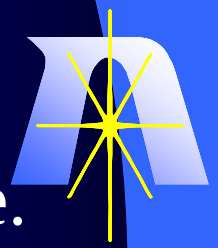
- **Sterility**
- The complete destruction of all living organisms and their spores or their complete removal from the formulation.

- *All* parenterals, as well as otic, nasal, ophthalmic solutions, must be sterile, including packaging materials



Background (cont.)

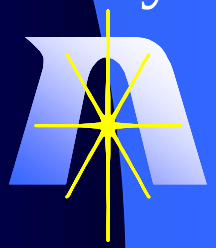
- **Aseptic Technique**
  - The technique for preparation and manipulation of compounded sterile products and parenteral preparations that prevents contamination.
- **Importance of Aseptic Technique**
  - Parenteral administration bypasses the skin and gastrointestinal tract, the bodies natural barriers to infection.
  - Giving a patient a contaminated product can cause serious adverse effects including **DEATH.**
  - Parenteral medications account for >40% of all medications administered in institutional practice.



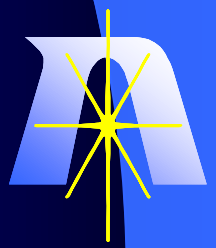
Why Parenteral?

Parenteral Route Is Used because

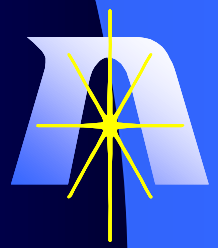
1) Rapid action
2) Oral route can not be used
3) Not effective except as injection
4) Many new drugs particularly those derived from new development in biotechnologically can only be given by parenteral as they are inactivated in GIT if given orally.
5) New drugs require to maintain potency & specificity so that they are given by parenteral.



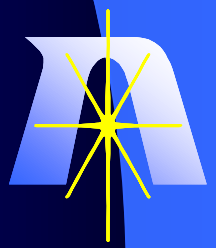
- **Advantages:**
  - Quick onset of action.
  - Suitable for the drugs which are not administered by oral route.
  - Useful for unconscious or vomiting patients.
  - Duration of action can be prolonged by modifying formulation.
  - Suitable for nutritive like glucose & electrolyte.
  - Suitable for the drugs which are inactivated in GIT or HCl (GI fluid).
  - Bypass hepatic first pass effect.



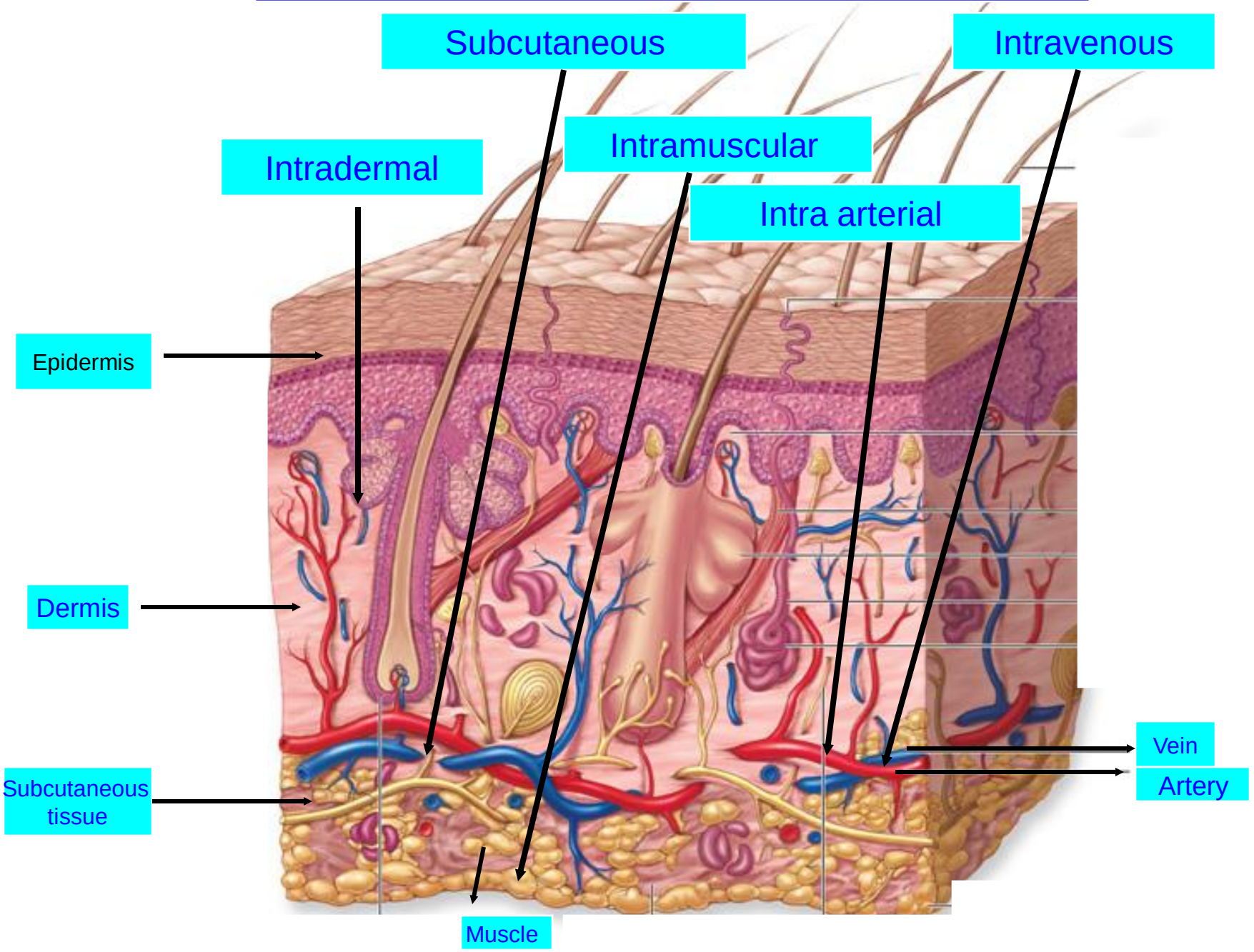
- **Disadvantages:**
  - Once injected cannot be controlled (retreat)
  - Injections may cause pain at the site of injection
  - Only trained person is required
  - If given by wrong route, difficult to control adverse effect
  - Difficult to save patient if overdose
  - Sensitivity or allergic reaction at the site of injection
  - Requires strict control of sterility & non pyrogenicity than other formulation.

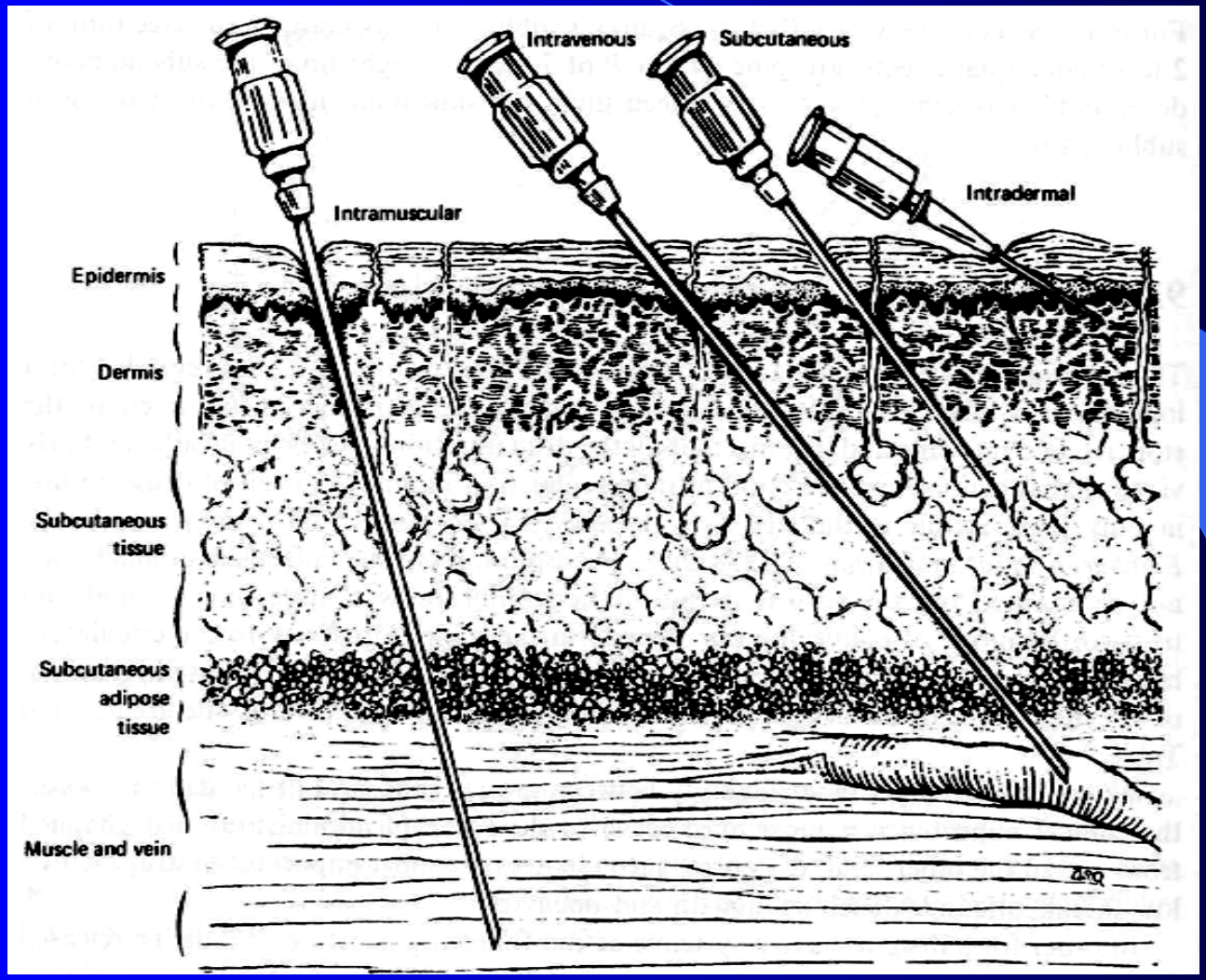


- **Necessities of Parenteral preparations:**
  - Sterility (must)
  - Free from Pyrogen (must)
  - Free from particulate matter (must)
  - Clarity (must)
  - Stability (must)
  - Isotonicity (should)
  - Solvents or vehicles used must meet special purity and other standards.
  - Restrictions on buffers, stabilizers, antimicrobial preservative. Do not use coloring agents.
  - Must be prepared under aseptic conditions.
  - Specific and high quality packaging.



Routes of Parenteral Administration

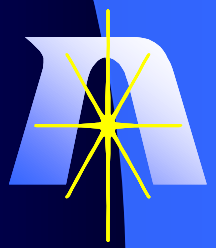



Intravenous
Subcutaneous
Intramuscular
Intradermal
Epidermis
Dermis
Subcutaneous tissue
Subcutaneous adipose tissue
Muscle and vein

Parental Routes of Administration:

Most Common:
1. Subcutaneous (**SC; SQ ;Sub Q**)
2. Intramuscular (IM)
3. Intravenous (IV)

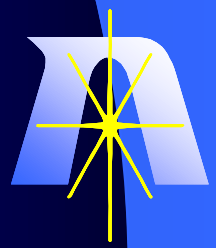
Others:
4. Intra-arterial (IA)
5. Intrathecal
6. Intraarticular
7. Intrapleural
8. Intracardial
9. Intradermal (Diagnostic)



Subcutaneous (SC; SQ ;Sub Q):

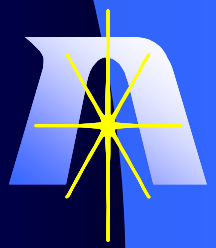
- The injection is given under the skin
- Need to be isotonic
- Upto 2 ml is given

- **Given:**
  - Vaccines
  - Insulin
  - Scopolamine
  - Epinephrine



- **Intramuscular (IM):**
  - Striated muscle fibre
  - 0.5 to 2 ml sometimes upto 4 ml
  - Preferably isotonic
  - Can be use for delay or prolonged effect by:
    a- administration of the drug in suspension form
    b- use of oil vehicle

- **Principle sites:**
  - Gluteal (buttocks), Deltoid (upper arms) and Vastus lateralis (lateral thigh)
- **Given:**
  - Solutions
  - Emulsions
  - Oils
  - Suspension

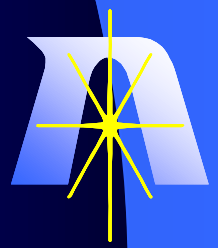


Intravenous (IV):

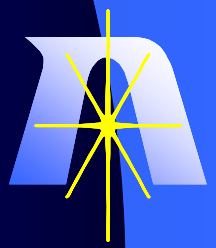
- Into the vein
- 1 to 1000 ml
- Injection rate of 1ml/ 10 sec. Give rapid effect
- Need trained person in administration.

Given:

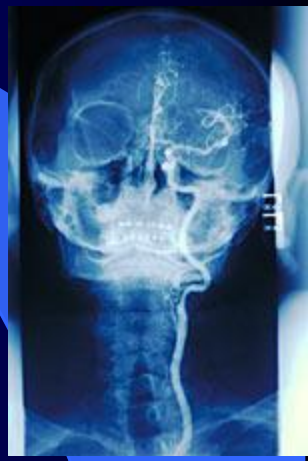
- Aqueous solutions
- Hydro alcoholic solutions
- Emulsions
- Liposome



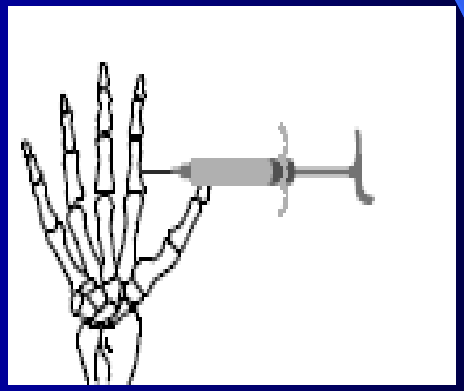
- **Intravenous (IV) (cont.):**
- IV infusion of large volume fluids (100- 1000 ml) has become increasingly popular. This technique is called as **Venoclysis.**
- This is used to supply electrolytes & nutrients to restore blood volume & to prevent tissue dehydration.
- Combination of parenteral dosage forms for administration as a unit product is known as an IV admixture.



- **Intra-arterial (IA):**
  - Direct into the artery
  - 2 to 20 ml
  - there effect is mainly localized rather than generalized as in I.V.
  - Mostly used for diagnostic purposes such as arteriogram and also for anti-neoplastic drugs.
  - Solutions & emulsions can be administered
- **Given:**
  - Radio opaque media
  - Antineoplastic



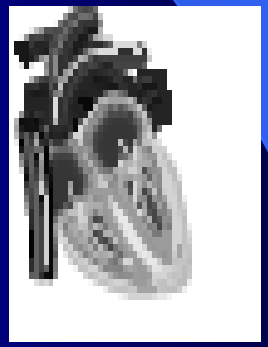
- **Intrathecal:**
  - Also called intra-spinal
  - Directly given into the spinal cord
  - 1 to 4 ml
  - Must be isotonic
- **Given:**
  - Local anesthetic (LA)
  - Analgesics
  - Neuroleptics
- **Intra-articular**
  - inside the joints
  - Used for corticosteroids and LA



- **Intrapleural:**
  - Given directly into the pleural cavity or lung
  - Used for fluid withdrawal
  - 2 to 30 ml
- **Given:**
  - LA
  - Narcotics
  - Chemotherapeutic agents

Intracardial:

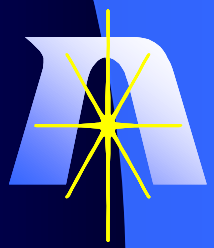
- Directly given into the heart
- 0.2 to 1 ml



Given:

- Cardiotonics
- Calcium salts as a calcium channel blockers

- **Intradermal:**
  - Also called as diagnostic testing
  - 0.05 ml
  - Should be isotonic
- **Given:**
  - Diagnostic agents

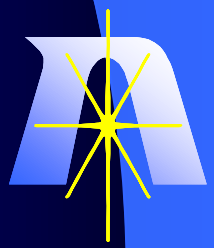


- N.B.

♣Parenteral drugs for Intra-spinal routs must be in solution form.

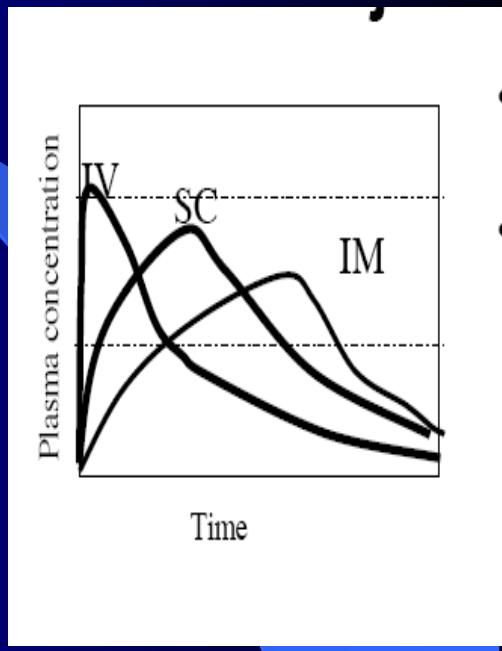
♣ For IV must be solution or emulsion.

♣ For IM, SC, I.D may be solution , suspension or emulsion.



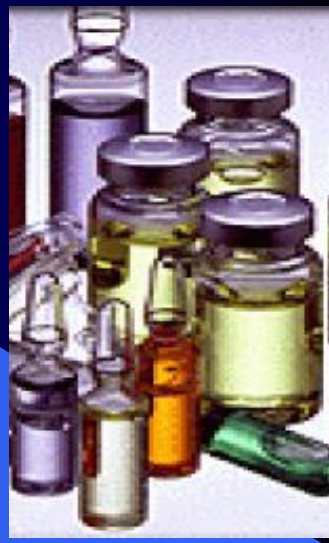
Pharmacokinetics of parenteral

- Simple solution:
  - IV > SC > IM
- Delayed release
- ❖ Choice of solvent; oil decrease release
- ❖ Injection of suspensions
- ❖ Controlled release formulations



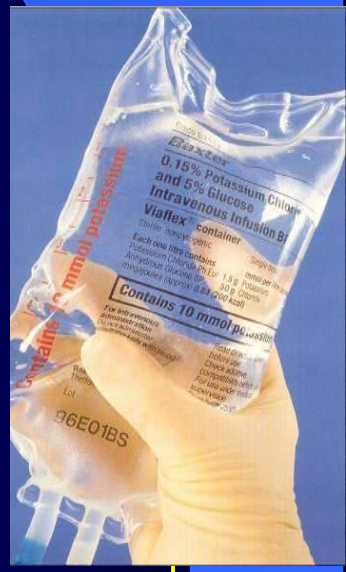
Types of Parenteral Preparation

- They can classified according to:



1. Type of Packaging

1-Single dose units (ampoules, pre-filled disposable
- syringes)
2-Infusion solution
3-Multiple dose units (vials)



2. Volume

1-Small volume parenterals (SMP) of less than 100 ml.

2-Large volume parenterals (LVP) of 100 ml or more

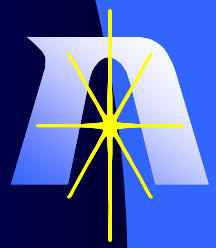
Types of Parenteral Preparation

- **Clinical Use**

  1-Irrigation solution
  2-Dialysis solution
  4-Diagnostic agent
  5-Ophthalmic products

- **Physical State**

  1-Sterile Solutions
  2-Sterile Suspensions
  3-Sterile Emulsions
  4-Sterile Solid



Types (cont.)

- **1- Injections:**

  It is a sterile drug *solution* or emulsion in a suitable vehicle, *with/out* added substance(s) intended for parenteral administration.
  Its volume ranges from **0.5-ml** (atropine SO_4) -to-**1000 ml** (dextrose).
  According to the No. of doses, it is classified as:
  a- Single dose unit
  b- Multiple dose unit

Types (cont.)

- **2- Infusion Fluids:**

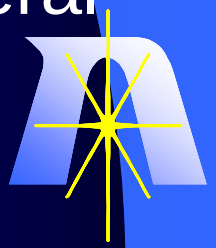
I.V. fluid found in single dose injection characterized by their method of administration as:

a)- Basic nutrition (Dextrose inj.)

b)- Restoration of electrolyte balance (Ringer solution containing Na, Ca, K ions)

c)- Fluid replacement therapy (a combination such as dextrose and NaCl)

d)- Injection for special use (Total parenteral nutrition.)



Types (cont.)

- **3- Sterile solids:**

  Owing to the instability of some drugs in solution form ,they prepared as dry powder which reconstitute before use with its specific vehicle.

  Sterile drug: Product *contains no buffer or additives* such as Na Nafcillin.
  Sterile drug for injection: Product that *contains buffer, diluents & additives* such as Amphotericin B for injection.

Types

- **4- Parenteral Suspensions**
- As parenteral solutions in addition to the presence of :
  1. Insoluble drug powder

  2-Suspending and/or viscosity improving agent such as MC, CMC, gelatin to ensure dose uniformity.

  3-Flocculating agent to prevent caking (precipitation of materials at the bottom of the container).

  4-Wetting agent Tween 80 also helps to keep solid as suspension.

  ♣♣In parenteral suspension, the particle size should be less than 10 um. The solid content usually about 0.5-5%

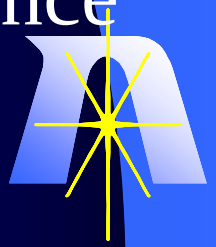
Types

- **4- Parenteral Suspensions (cont.)**
- **Advantages:**

  1- suitable for insoluble drugs
  2- increase chemical stability
  3- possible depot effect

  Disadvantages:

  1-Difficult formulation and manufacture
  2-Patient discomfort
  3-Difficult dose uniformity and maintenance of physical stability



Types

- **Characters Parenteral Suspensions :**

  Syringe -ability;

  It refer the handling character of suspension (ease of drawing from container into syringe)

  Inject- ability:

  The properties of suspension to flow from the needle of syringe

  Both affected by:

  1-viscosity

  2- particle characters

  3- particles distribution

Types

- **5- Parenteral Emulsion**
- Are used to provide
  1- A concentrated source of calories and essential oil for IV administration (parenteral nutrition)
  2- As a vehicle for drugs intended for prolonged release
  3- delivery of oily substances through IV

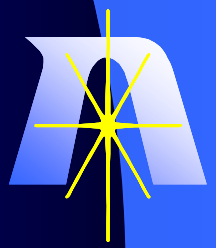
- Oily phase The most commonly used oil are vegetable oil as sesame, cotton seed …..etc

  •The ideal size of droplets are 0.5 to 1μm

  •The oil must be stored at low temp.

Official Types of Injections

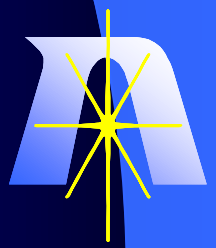
1. ***Injection:*** liquid preparations that are drug substances or their solutions (e.g. Insulin Injection, USP).
2. ***For injection***: Dry solids that upon addition of suitable vehicles yield solutions complying the requirements for injections (e.g. Cefuroxime for injection, USP)
3. ***Injectable emulsion***: liquid preparation of drug dissolved or dispersed in a suitable emulsion medium (e.g., Propofol, USP



Official Types of Injections

4. ***Injectable suspension***: liquid preparation of solid suspended in a suitable liquid medium (e.g. Methylprednisolone Acetate Suspension, USP)

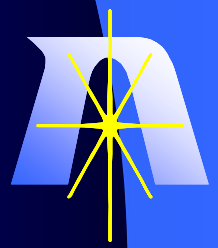
5. ***For injectable suspension***: Dry solid that upon addition of suitable vehicle yields preparation comply with the requirements for *injectable suspensions* (e.g. Impenem and Cilastatin for Injectable Suspension, USP)



Sterilization

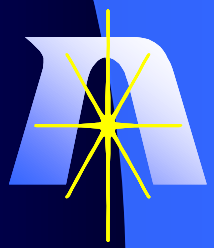
- Sterility: absence of life or absolute freedom from microbial contamination.

- Sterilization: Inactivation or elimination of all viable organism and their spores.



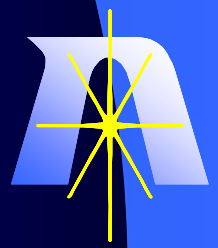
Methods of Sterilization

- 1. Steam
- 2. Dry heat
- 3. Filtration
- 4. Gas
- 5. Ionizing radiation
- NOTE: end product must pass sterility test.



Methods of Sterilization

- **1. Steam sterilization:**
- Method: Applying steam under high pressure
- Equipment: Autoclave (steam sterilizer)
- Mechanism of microbial destruction: denaturation and coagulation of some of organism's essential protein.
- In presence of moisture, MO are destroyed at lower temp. than dry heat.
- Most commonly applied temp. is 121°C.



Methods of Sterilization

- **1. Steam sterilization (cont.):**
- Latent period; is the time needed for the moist heat to penetrate the load, and time should be adjusted to count for this peroid.
- **Applications:**
  - Ampoules,
  - Bulk solutions,
  - Glassware,
  - Surgical dressing

Methods of Sterilization

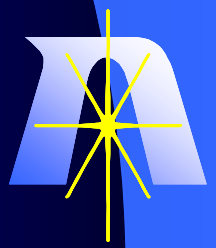
- **1. Steam sterilization (cont.):**
- Advantages:

  Rapid, inexpensive, effective, large volume
- Disadvantages:

  1. cannot use for oily preparation

  2. cannot use for moisture sensitive preparations

  3. cannot kill spores



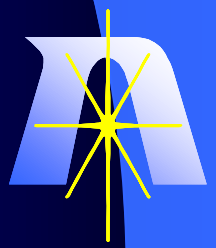
Methods of Sterilization

- **2. Dry Heat Sterilization:**
- Method: using heated air
- Equipment: Oven
- Mechanism of microbial destruction: dehydration of microbial cell after oxidation
- Usually conducted at 150 to 170°C for not less than 2 hours
- **Application:** Generally employed for substances that are not effectively sterilized by moist heat such as fixed oil, glycerol, petrolatum, heat stable powder.

Methods of Sterilization

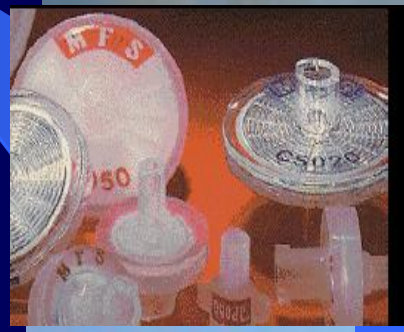
- **2. Dry Heat Sterilization (cont.):**
- Advantages and disadvantages

Sterilization by means of heat requires higher temperature and longer exposures than sterilization by steam. Heat transfer is slow, small volumes of oil and thin layers of powder should be used.



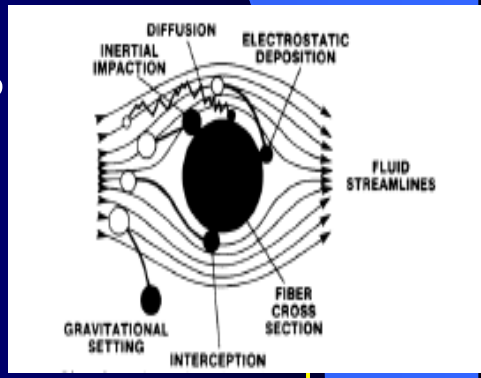
Methods of Sterilization

- **3. Sterilization by filtration:**
- Method: physical removal of MO by adsorption on the filter medium or sieving mechanism.
- Equipment: filter medium
- NB; preparations filtered by this method must undergo extensive validation and monitoring as the effectiveness of the filtered product can be greatly affected by microbial load in the solution being filtered



Methods of Sterilization

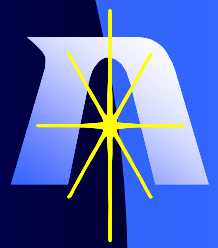
- **3. Sterilization by filtration:**
- Example: Millipore filter which is a thin plastic membrane of cellulose ester containing uniform pores constituting up to 80% of membrane's volume.
- Pore size range from 14 to 0.025µm
- NB. Small bacteria is 0.2 µm, poliovirus is of 0.025 µm



Methods of Sterilization

- **3. Sterilization by filtration:**
- Advantages and disadvantages:

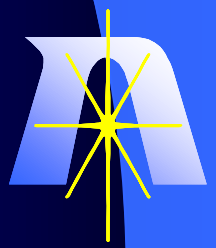
  1. depend on filter media
  2. thermolabile solutions can be sterilized.
  3. speed of filtration of small volumes



Methods of Sterilization

- **4. Gaseous sterilization**
- Method: use of gas, such as Ethylene Oxide
- Equipment: special oven, for admission of gas and humidity
- Application:

  Thermolabile powder, plastic (e.g. syringes), polymers, ophthalmic prep., tubing sets.

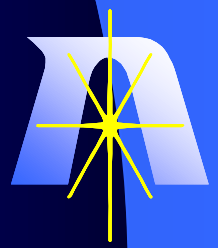


Methods of Sterilization

- **4. Gaseous sterilization**
- Ethylene Oxide (EO)
- Used to sterilize heat-senstive materials, MO and spores.
- Used in combination with CO2 to avoid explosion, >3% EO in air is explosive.
- Mechanism of action of EO is alkylation of hydroxyl, carbonyl and amino groups of bacterial enzyme.

Methods of Sterilization

- **4. Gaseous sterilization(cont.):**
- Disadvantages
  1. Explosive hazards
  2. Toxic
  3. Not appropriate for solutions



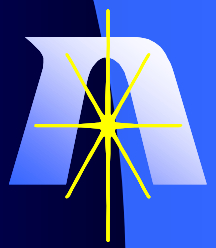
Methods of Sterilization

- **5. Radiation sterilization**
- Equipment: Ultraviolet lamp; for surface strelization

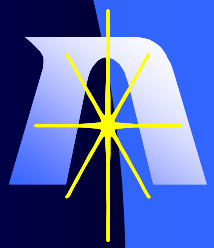
  - Ionization (Beta rays, Gamma rays, X-rays)
- Application:

  Thermolabile drugs (powder)
- Disadvantages:

  1. Highly specialized equipment required
  2. Effect of irradiation on product and their containers

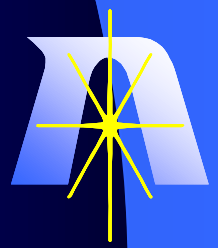


Formulation of Parenteral

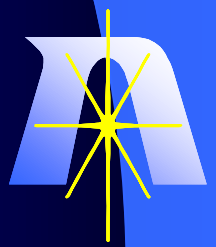


Formulation of Parenteral:

1. Therapeutic agents
2. Vehicles
   i. Water
   ii. Water miscible vehicles
   iii. Non- aqueous vehicles
3. Added substances (Additives)
   i. Antimicrobials
   ii. Antioxidants
   iii. Buffers
   iv. Bulking agents
   v. Chelating agents
   vi. Protectants
   vii. Solubilizing agents
   viii. Surfactants
   ix. Tonicity- adjusting agents



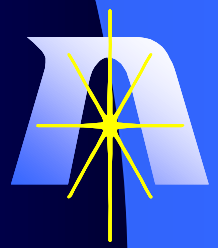
- **During the formulation of parenteral products, the following factors are critical:**
  - (a) **The vehicle in which the drug is dissolved or dispersed**
  - **(b) Volume (dose) of the injection**
  - **(c) Adjustment to isotonicity**
  - ***(d)*** **Adjustment of pH**
  - **(e) Stabilisers**
  - **(f) Preservatives**
  - ***(g) Adjustment of specific gravity (for spinal anaesthesia)***
  - **(h) Concentration units**



Formulation of Parenteral

1.Therapeutic ingredients:

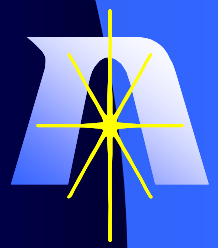
- Insulin
- Antibiotics
- Anticancer
- Steroids
- Vaccines
- Antipyretic
- Analgesics
- Anti- inflammatory
- LVP's like Dextrose, NaCl or combination etc….



Formulation of Parenteral

2.Solvents:

- Water
  - Should meet compendial requirements
- Water miscible vehicles
  - Ethyl alcohol, PEG, PG
- Non aqueous vehicles
  - Fixed oils

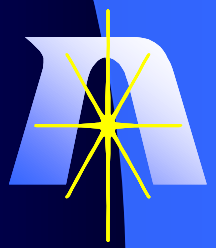


Formulation of Parenteral

Solvents

Solvents used must be:

- Non-irritating
- Non-toxic
- Non-sensitizing
- No pharmacological activity
- Not affect activity of medicinal agent

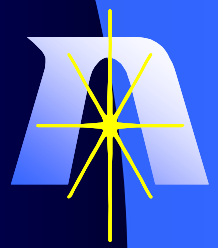


Formulation of Parenteral

Aqueous solvents

The preferred vehicle is water as it is well tolerated by the body and easy to administer.

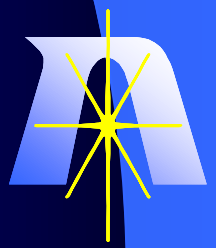
- **Water for Injection (WFI).**
- **Sterile Water for Injection (SWFI).**
- **Bacteriostatic Water for Injection (BWFI).**
- **Sodium chloride injection (USP)**
- **Sterile Water for Inhalation.**
- **Sterile Water for Irrigation**



Formulation of Parenteral

- **1- Water for injection (WFI):**
  - It is the water intended to be used in the manufacture of injectable products, which are to be sterilized after their preparation.
  - It is the most frequently used solvent.
  - It contains no added substances.
  - It is NOT used for the dilution of packaged parenteral products.
  - Although it is not required to be sterile, it should be free from pyrogens.
  - It must be clear, colorless and odorless.

- Prepared by distillation or reverse osmosis



Formulation of Parenteral

- **1. WFI (cont.)**
- The total number of dissolved solids must not exceed 10 ppm.
- Unless it is used within 24 hrs of its collection, WFI should be discarded or maintained sterile or stored in tight containers at:
  1- 25.0 ºC for small volumes or
  2- 80.0 ºC for larger tanks
  (below and above the range at which microbial growth occurs)

Formulation of Parenteral

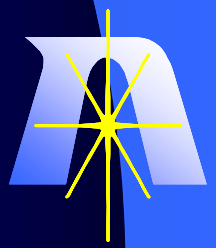
- **2. Steriel water for injection (SWFI):**
- Sterile Water for Injection (USP) is a sterile, non-pyrogenic preparation of water for injection which contains no antimicrobial agent or added buffer and is supplied only in single-dose containers.
- ***Uses:*** used to dilute or dissolve already-sterilized and packaged injectable medications such as the dry powders of Na phenobarbitol & Ampicillin Na.
- It is added under *aseptic conditions.*

Formulation of Parenteral

- 2. Steriel water for injection (cont.)
- **Characterized by:**
  - ♣ It must be pyrogen-free.
  - ♣ Doesn't contain antimicrobial agent.
  - ♣ It must be isotonic when intended for Intra-vascular.

Formulation of Parenteral

- **3- Bacteriostatic water for injection (BWFI):**
- Bacteriostatic Water for Injection (USP) is a sterile, nonpyrogenic preparation of water for injection containing 0.9% (9 mg/mL) of benzyl alcohol added as a preservative.
- It is supplied in a multiple-dose container from which repeated withdrawals may be made to dilute or dissolve drugs for injection. The pH is 5.7 (4.5 to 7.0).



Formulation of Parenteral

- **3- Bacteriostatic water for injection (BWFI):**
- ***N.B. If the patient will receive more than 5mL of parenteral preparation, BWFI is NOT the vehicle of choice.*** ***Why?***

  To avoid excessive and/or toxic concentrations of antimicrobial agent(s) which would be injected along with the medication.

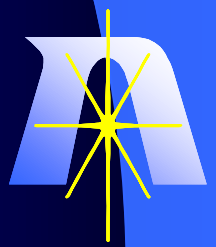
  N.B. The added bacteriostatic(s) should be compatible (doesn't interact) with the drug.

Formulation of Parenteral

- **4- Sodium Chloride Injection, USP:**
- Is a sterile isotonic solution of NaCl in water for injection.
- Contains no antimicrobial agent.
- May be used as a sterile vehicle in solutions or suspensions of drugs for parenteral administration.

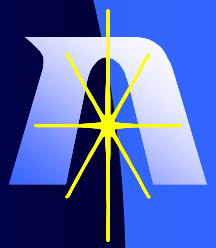
Formulation of Parenteral

- **Preservatives:** Multidose containers must have preservatives unless prohibited by monograph.
- Large volume parenterals (LVP) must not contain preservative because it may be dangerous to human body if it contain in high doses.



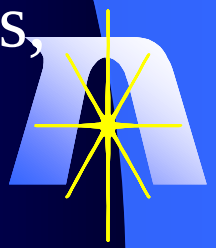
Formulation of Parenteral

- **Solubilizing agents:**
  - Used to increase solubility of slightly soluble drugs
  - they acts by any one of the following:
    - solubilizers,
    - emulsifiers or
    - wetting agents.
- **Examples:**
  - Dimethylacetamide, Ethyl alcohol, Glycerin, PEG – 400

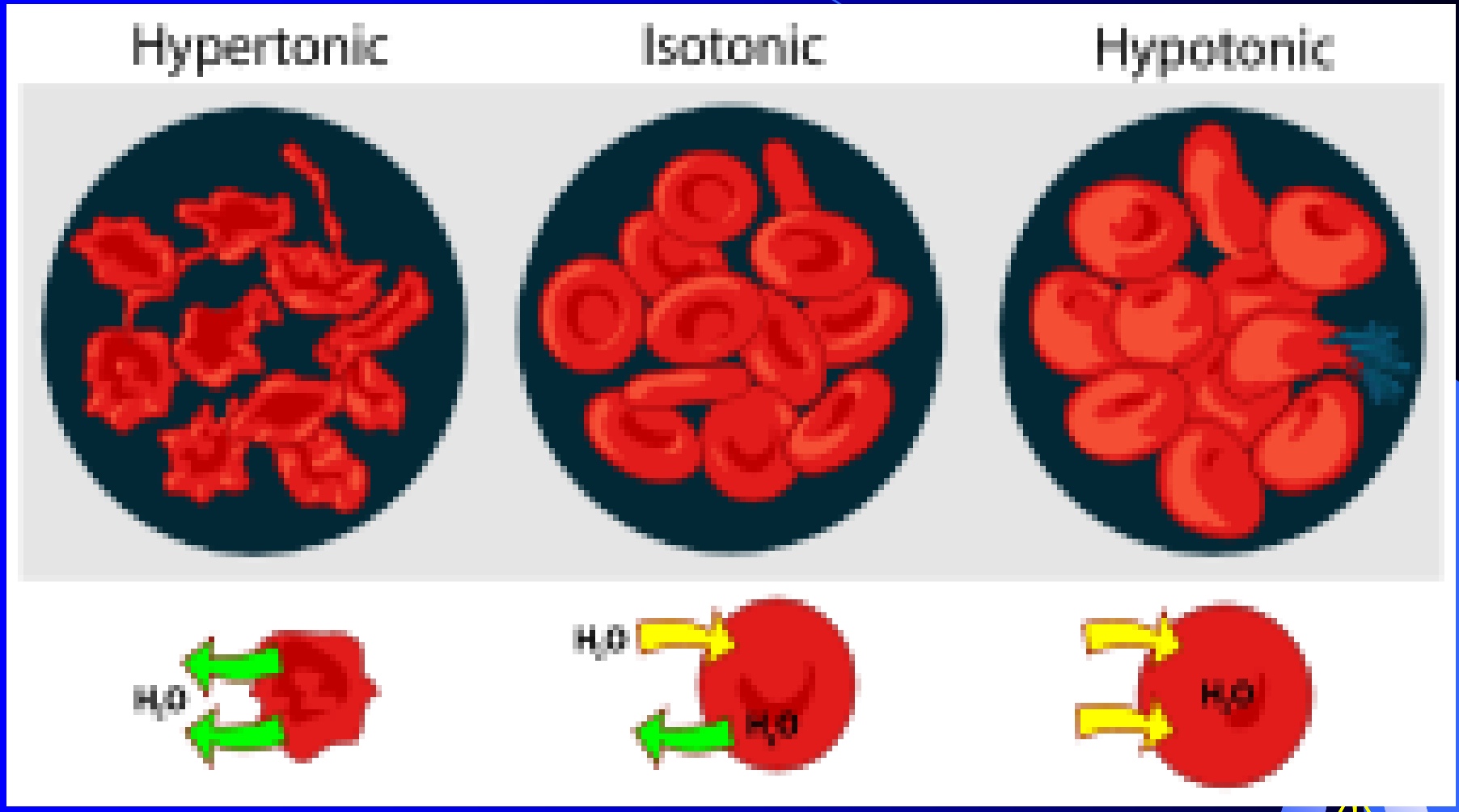


Formulation of Parenteral

- **Tonicity- adjusting agents:**
- The osmotic pressure of blood is approximately 300 milliOsmoles/L and ideally any sterile solution would be formulated to have the same osmolarity e.g., 0.9% w/v Sodium Chloride iv solution has an osmolarity of 308 mOsmole/L and 5% w/v Dextrose iv solution has an osmolarity of 280 mOsmol/L.
- Intravenous solutions that have larger osmolarity values (hypertonic) or smaller osmolarity values (hypotonic) may cause damage to red blood cells, pain, and tissue irritation.



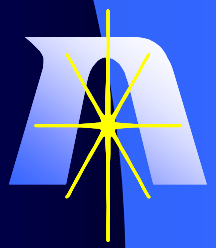
Effect of different solutions on blood cells



Formulation of Parenteral

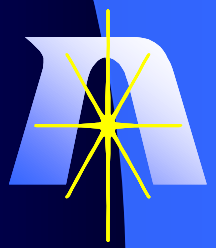
- **Tonicity- adjusting agents:**
- Osmolarity adjustment is made usually by using sodium chloride, glucose or mannitol using one of the following methods;

  - • The freezing point depression method
  - • Sodium chloride equivalent
  - Examples: Mannitol, Dextrose, Sodium chloride, Sorbitol, boric acid.



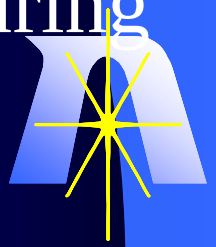
Formulation of Parenteral

- **PH-adjusting agent**
- As parenteral formulations are administered directly to tissues and systemic circulation, formulations prepared should not vary significantly from physiological pH, which is about 7.4. In certain cases however, acidic or alkaline solutions may be needed to solubilize drugs.
- The acceptable **pH range is 3-10.5 for IV preparations and 4-9 for other routes.**
- Buffers are included in injections to maintain the pH of the packaged product. However, the buffer used in the injection must allow the body fluids to change the product pH after injection.
- Examples: Acetate, citrate and phosphate buffers are commonly used in parenteral products.



Formulation of Parenteral

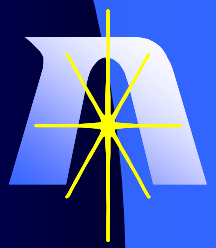
- **Anti-microbial agent**
- Aqueous preparations which are prepared using aseptic precautions and which cannot be terminally sterilized may contain a suitable antimicrobial preservative in an appropriate concentration.
- Are added to multiple dose vials to inhibit the growth of microbial organisms which may occur accidentally and contaminate the product during use.



Formulation of Parenteral

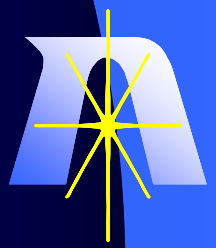
- **Anti-microbial agent**
- No antimicrobial preservative is added when:
  - The volume to be injected in a single dose exceeds 15mL unless otherwise justified
  - The preparation is intended for administration by routes where for medical reasons an antimicrobial preservative is not acceptable
  - If the drug formulation itself has sufficient antimicrobial activity

    0.01
- **Examples;** Benzalkonium Chloride, Benzyl alcohol



Background; Definitions

- **SINGLE DOSE PREPARATIONS**
- The British Pharmacopoeia (B.P.) 1998 define single dose preparations as:
- ‘The volume of the injection in a single dose container is sufficient to permit the withdrawal and administration of the nominal dose using a normal technique’.
- **MULTIPLE DOSE PREPARATIONS (BP 2004)**
- Multidose preparations are multidose aqueous injections which contain a suitable antimicrobial preservative at an appropriate concentration except when the preparation itself has adequate antimicrobial properties.



PACKAGING OF PARENTERAL

- A. Single dose container
- B. Multiple dose container

Packaging of Parenterals

1. single dose container

- Glass ampoules are the most commonly used single dose containers and can range from sizes of 1 to 50mL.

Ampules

Packaging of Parenterals
1. single dose container

- Hermetic (sealed by heat fusion) container holding a quantity of sterile drug intended to be used as a single dose.
- It could be ampoules or vials; however, glass ampoules are the most commonly used single dose containers and can range from sizes of 1 to 50mL
- The type of glass used is indicated in the individual monograph of that preparation.

Packaging of Parenterals

1. single dose container

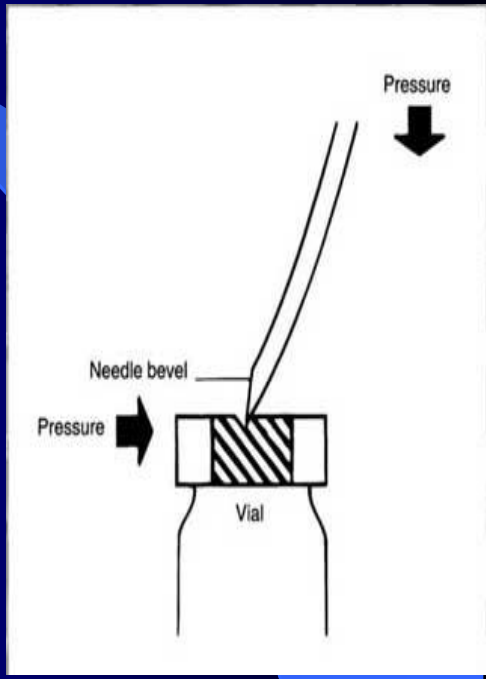
- Unit dose-disposable syringe

Packaging of Parenterals
2. Multiple dose container

- A hermetic container that permits withdrawal of successive portions of contents without changing the strength, quality, or purity of the remaining portion.

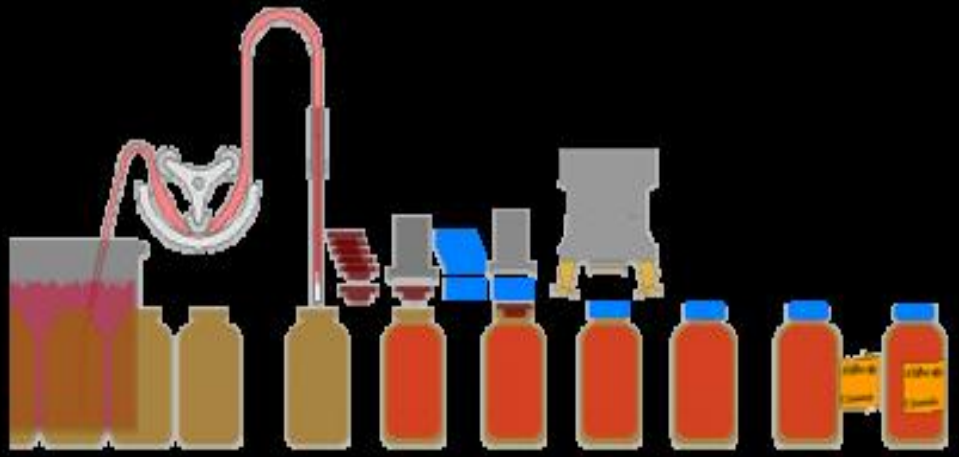
Packaging of Parenterals
2. Multiple dose container

- Affixed with rubber closures to permit penetration of a hypodermic needle without removal or destruction of the closure.
- Upon withdrawing the needle from the container, the closure reseals and protect the contents from airborne contamination.
- They are required to contain antibacterial preservative.
- NOT allow to withdraw more than 30 ml.



Packaging of Parenterals

- N.B
- The beyond-use date for an opened or entered (e.g., needle-punctured) multiple-dose container with antimicrobial preservatives is 28 days
- Single and multiple dose containers usually contain slight excess of volume over labeled size or volume (*Why*?)



Packaging (filling) and labeling of liquid parenterals

Packaging components:

Packaging components are the major source of particulate matter, Pyrogen and Stability problems.

Types of packaging:

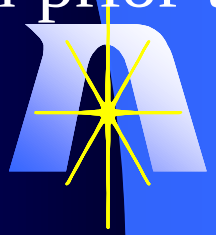
1- Glass
2- Plastic
3. Rubber

1. Glass

- Factors controlling the effect of glass on the products:
  1- Types of the product
  2- PH of aqueous solution.
  3- Constituents of aqueous solution
  4- Sterilization technique (as heat sterilization cause change in color , stability, pH ….etc)

1. Glass

- **Types of glass**
- ***Type I***: Commonly known as neutral glass. It has a high resistance to hydrolysis and withstands autoclaving, weathering and solution of pH of up to 8.
- ***Type II (sulphated glass)***: Containers may be treated with moist sulphur dioxide at high temperature to create a neutral surface film with high hydrolytic resistance. Lower resistance to autoclaving than for type I glass.
- ***Type III (soda glass)***: little resistance to hydrolysis and should only be used for powders for reconstitution prior to injection and for non aqueous preparations.



N.B.

- Ppt in glass may be due to alkali leached from glass & metallic ion leaching (Dextrose +KcL soln→ ppt of silica + alumina)

- Glass usually sterilized by dry heat.

- The type of glass used is indicated in the individual monograph of that preparation.

- **2. Plastic**

2- plastic:

- Polymers as polyethylene – polypropylene.

Disadvantages of plastics:

1- Substance can be leakage from plastic into solution

2- Ingredients from solution can be adsorbed by plastics

3- May be permeable to moisture

N.B

leaching or sorption depends upon the contact period between the plastic and the product

3- Rubber:

Usually used as closures.

Advantages:

- Good elasticity
- Ability to reseal after puncture
- Adaptability to various shape

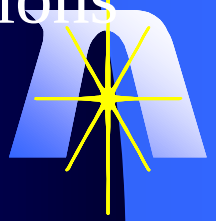
3. Rubber

- **Disadvantages:**

- Discoloration, turbidity, degradation of incompatible solution.
- Physical & chemical instability in presence of SAA.
- Adsorption of preservatives
- Coring (cutting of a piece of rubber from the closure by the needle)

Packaging and Product: Not Always Perfect Together

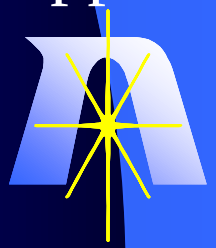
- Modern biopharmaceuticals such as proteins and peptides, are molecules with unique chemical, physical, and mechanical properties.
- Proteins are sensitive to heat, light, and chemical contaminants. Minute concentrations of metals, plasticizers, and other materials from biopharma packaging may deactivate or denature therapeutic proteins.
- The seriousness of chemical contamination is compounded by the extremely low concentrations of most protein drugs.



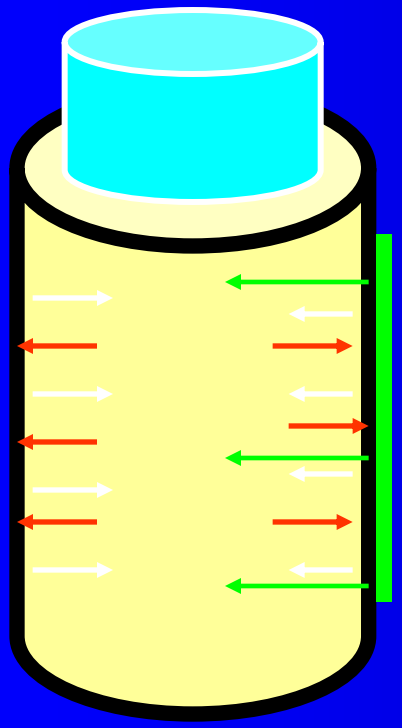
Packaging and Product: Not Always Perfect Together

- Proteins and peptides have a tendency to adsorb onto the surface of packaging containers and closures which, due to the small amount of drug present, can essentially remove all active material from the drug formulation. In situations where the drug desorbs back into solution, the interaction could cause the drug to lose potency.

- Many biopharmaceuticals are sensitive to silicone oil, a material commonly used to lubricate rubber stoppers during fill/finish to facilitate insertion of the stopper into the vial.



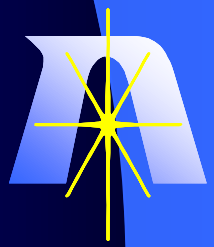
Sources of Contamination from Containers



- **Extractable**
  - Compounds that can be extracted from container-closure system in the presence of an appropriate solvent(s).
- **Leachable**
  - Compounds that leach from container-closure system as a result of direct contact with the formulation of the drug product. Can get interaction with a product component to produce an impurity that requires stability monitoring.

- The potential impact of extractables and leachables on drug products is significant, especially with highly active biopharmaceutical drug products that may contain about femptograms of active ingredient.

- Example; Di-ethylhexyl phthalate (DEHP)
  - Plasticizer in PVC; detected, for example, in TPN fat emulsions probably via infusion tubing set
  - Neonates have particular sensitivity to DEHP

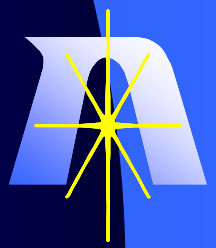


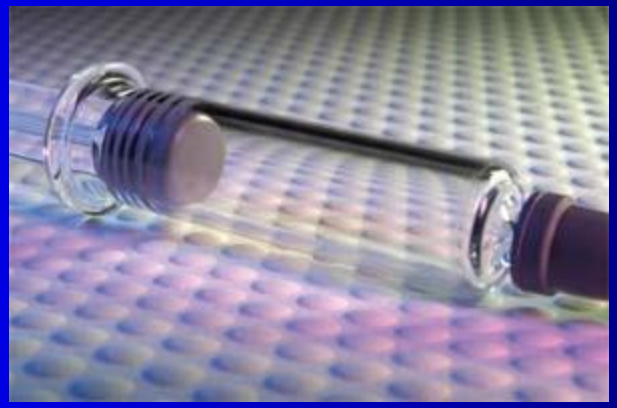
Fluorocarbon film

- Fluorocarbon film coatings provide the best combination of protection from extractables from the packaging material while providing a high level of barrier protection for the drug product, therefore minimizing leachables.

- Fluorocarbon films significantly reduce adsorption of the drug onto the stopper, which is critical for maintaining the product's potency and shelf life. In addition, fluorocarbon films provide extra lubricity for proper vial seating, without the need for silicone oil.

- Fluoroelastomer films, which are made from highly inert materials, also significantly reduce the possibility of extractables migrating from the rubber stopper into the biopharmaceutical product.

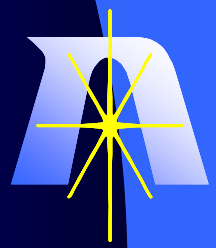


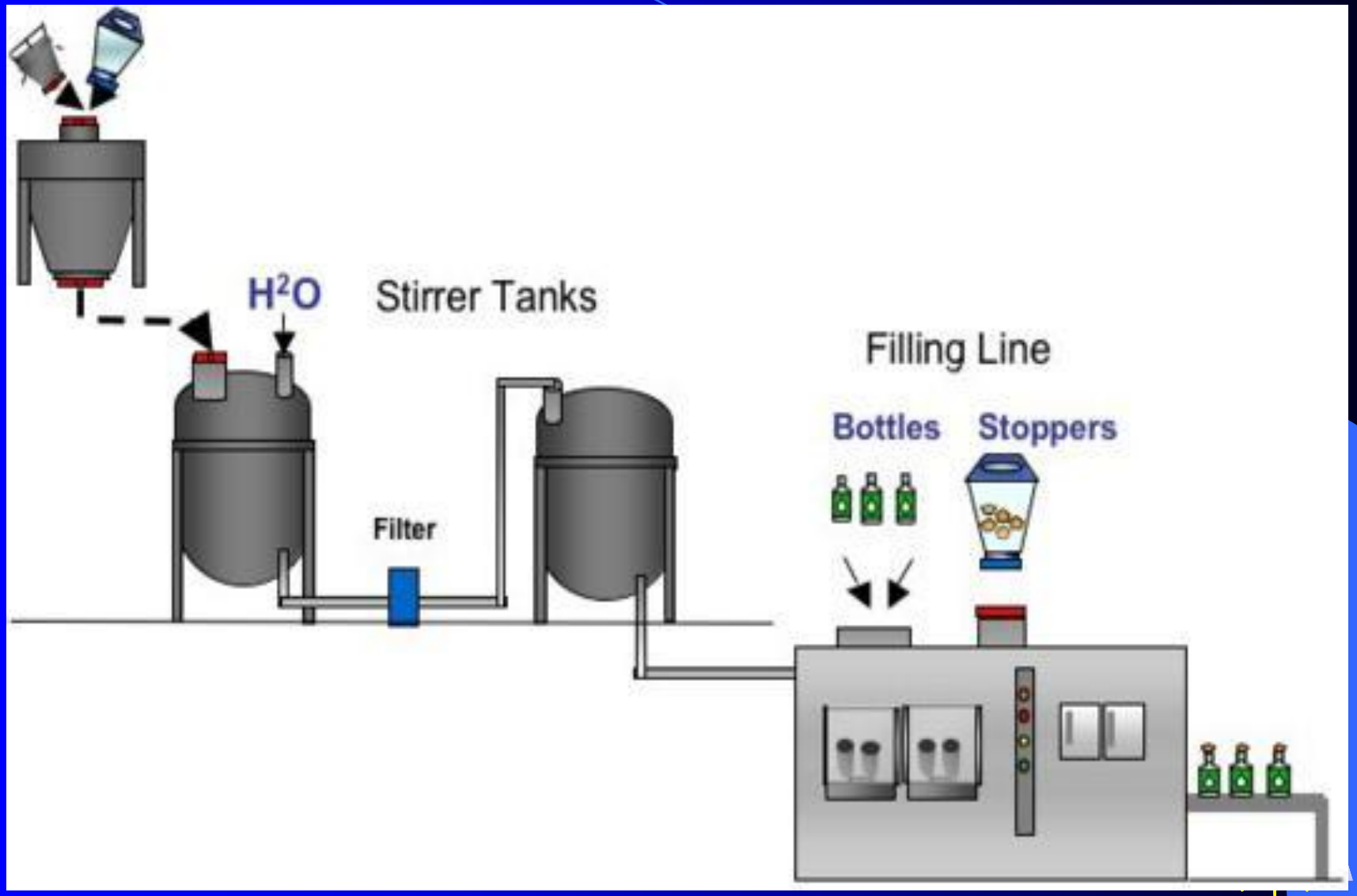


The Art of Making Parenterals

General steps involved

1. Cleaning
2. Preparation of bulk products
3. Filtration
4. Filling of solution or product in ampoule or vial
5. Sealing
6. Sterilization
7. Tests for Quality control




H²O
Stirrer Tanks
Filter
Filling Line
Bottles
Stoppers

Preparation of product: Clarification and sterilization :

1- Thermostable →Filtration → subdivided into the final container→ sealed→ terminal sterilization by autoclave.

2- Thermolabile→ filtration for sterilization→ subdivided into the final container→ sealed

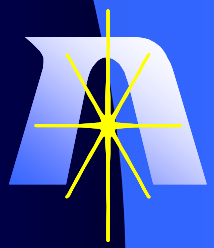
Sterilization of packing components:

Glass → Dry heat (170°C for 2 hr)

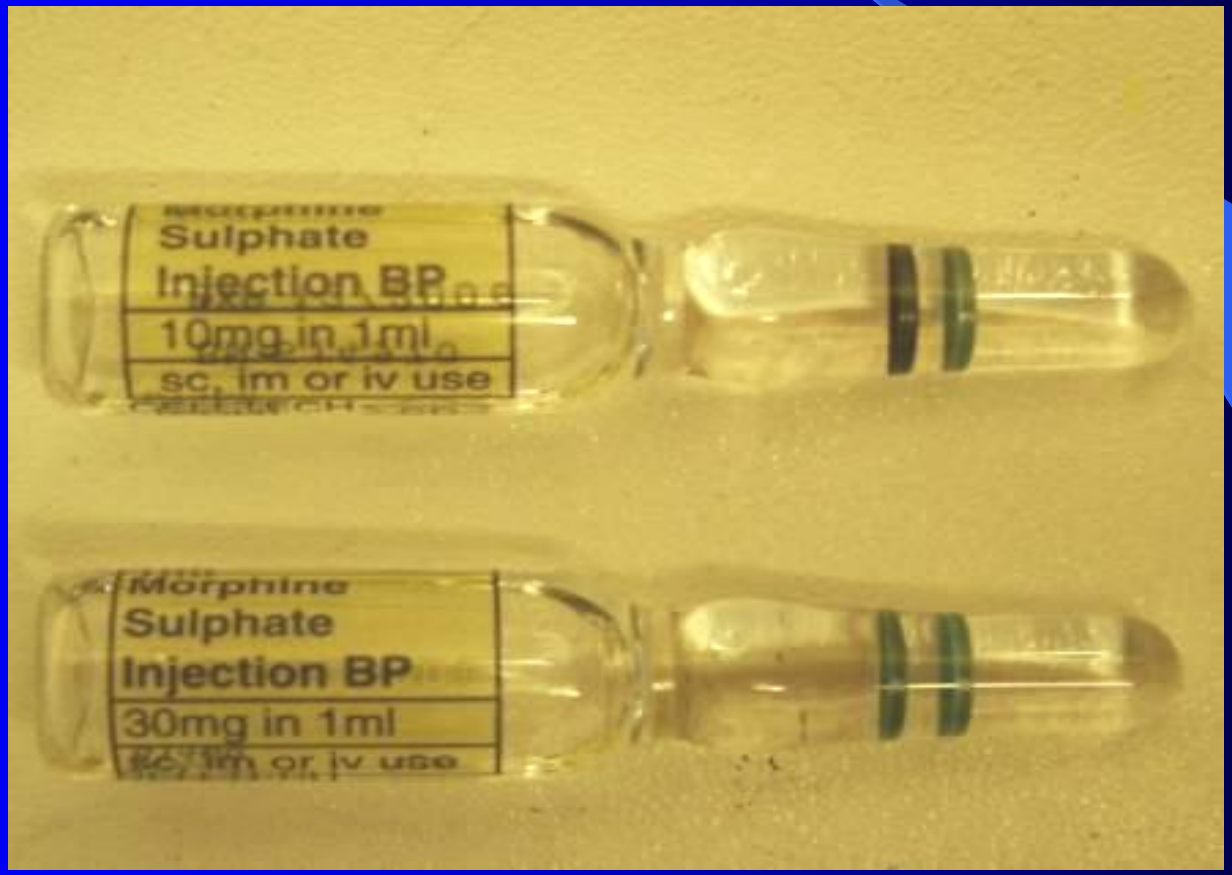
rubber → autoclave (120ºC for 10min)

plastic → EO (450mg/L for 4hr) after being washed and rapped

- **LABELING:**
  - Name of product
  - Quantity of the product
  - % of drug or amount of drug in specified volume of amount of drug and volume of liquid to be added
  - Name and quantity of all added substances
  - Mfg. license no.
  - Batch no.
  - Manufacturer/Distributor
  - Mfg. & Expiration date
  - Retail price (incl. of all taxes)
  - Mfger. address
  - **Veterinary product should be so labeled**

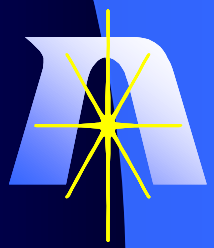


labeling


Sulphate
Injection BP
10mg in 1ml
sc, im or iv use
Morphine
Sulphate
Injection BP
30mg in 1ml

Must check each individual monogram for:

- Type of container:
  - Glass
  - Plastic
  - Rubber closure
- Type of glass
  - Type I
  - Type II
  - Type III
  - NP
- Tests for glass containers
  - Powdered Glass test
  - Water Attack test
- Package size
- Special storage instructions



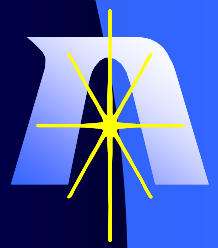
STERILITY TESTING FOR PARENTERAL PRODUCTS

1. Sterility testing - definition

- Sterility testing attempts to reveal the presence or absence of viable micro-organisms in a sample number of containers taken from batch of product. Based on results obtained from testing the sample a decision is made as to the sterility of the batch.

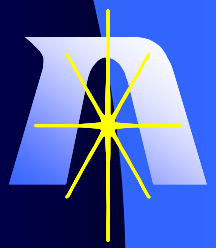
Sterility testing

- Is made after the product exposition to the one of the possible sterilization procedures
- Can only provide partial answers to the state of sterility of the product batch under test
- Is inadequate as an assurance of sterility for a terminally sterilized product



Major factors of importance in sterility testing

- The environment in which the test is conducted
- The quality of the culture conditions provided
- The test method
- The sample size
- The sampling procedure



Sterility test

- a- Pyrogen test
  b- Clarity test
  c- Safety test
  d- leaker test (immerse the ampl. in a dye (methylene blue) → apply vacuum inside the ampl. → if dye go inside ∴ there is leakage)

Two official methods are applied to determine sterilization:

1- Transfer the samples to sterile culture medium.

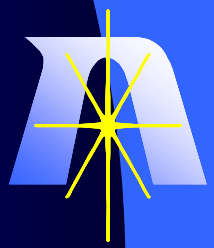
2- Membrane filtration procedure.

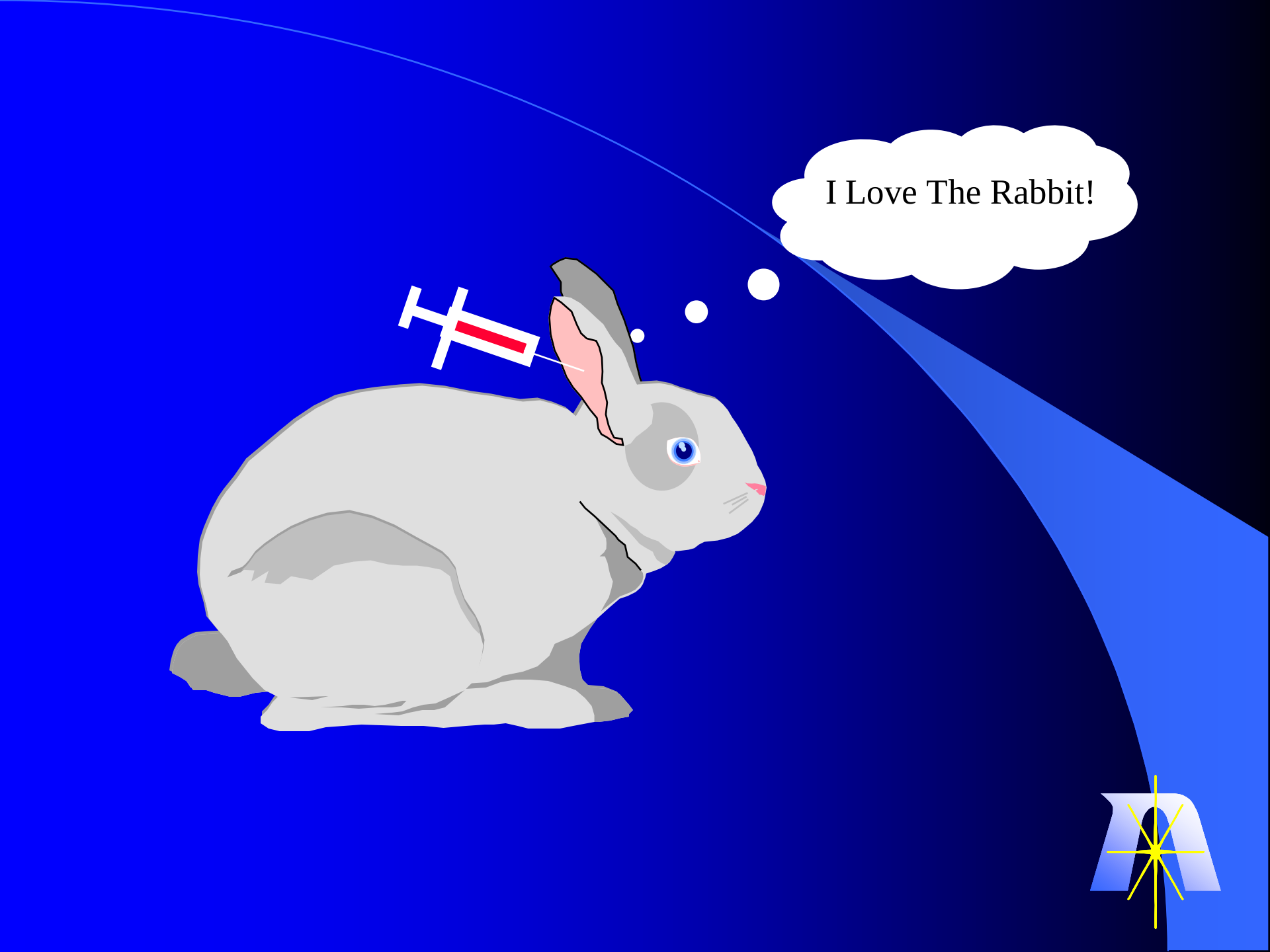
In both methods use two sterile culture media:

a- Thioglycollate which incubated at 32 °C for 2 weeks

b- Soybean casein digest incubated at 22 °C for 2 weeks

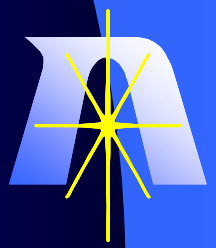
PYROGENS AND PYROGEN TESTING




I Love The Rabbit!

Pyrogens

- Pyrogenic - means producing fever (febrile)
- Pyrogens - fever inducing substances
  - Having nature
    - **Endogenous (inside body)**
    - **Exogenous (outside body)**
  - Exogenous pyrogens –
    - mainly lipopolysaccharides
    - bacterial origin, but not necessary

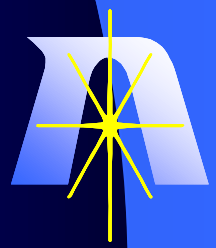


Structure of endotoxins

- Produced mostly by gram-negative bacteria
- Endotoxin-complex of pyrogenic **lipopolysaccharide**, a protein and inert lipid;
- lipid part of the lipopolysaccharide is the main pyrogenic agent; polysaccharide part increases solubility.

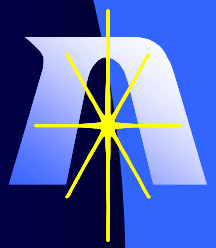
Sources of pyrogen contamination

- Solvent-possibly the most important source
- The medicament
- The apparatus
- The method of storage between preparation and sterilization



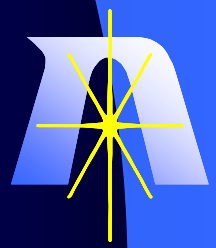
The endotoxin characteristics

- Thermostable
- Water-soluble
- Unaffected by the common bactericides
- Non-volatile
- These are the reasons why pyrogens are difficult to destroy once produced in a product



Tests for pyrogenic activity

- Test for pyrogens = Rabbit test
- Bacterial endotoxins



Test for pyrogens = Rabbit test

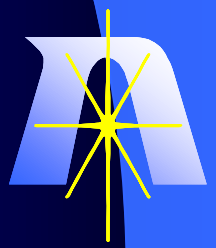
- The development of the test for pyrogens reach in 1920
- A pyrogen test was introduced into the USP XII (1942)
- The test consists of measuring the rise in body temperature in healthy rabbits by the intravenous injection of a sterile solution of the substance under the test.

Why the Rabbit?

- Reproducible pyrogenic response
- Other species not predictable
- Similar threshold pyrogenic response to humans

Rabbit Pyrogen Test

- Rabbits must be healthy and mature
- New Zealand or Belgian Whites used
- Either sex may be used
- Must be individually housed between 20 and 23°C



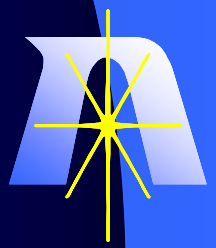
Rabbit test

- Selection of animals (healthy, adult, not less than 1,5 kg,…)
- Housing of animals (environmental problems: presence of strangers (unknown place), noise, T, …)
- Equipment and material used in test (glassware, syringes, needles)
- Retaining boxes (comfortable for rabbits as possible)
- Thermometers (standardized position in rectum, precision of 0.1°C)


Pyrogen Test

Rabbit test

- **Preliminary test (Sham Test)**
  - Intravenous injection of sterile pyrogen-free saline solution
  - To exclude any animal showing an unusual response to the trauma (shock) of injection
  - Any animal showing a temperature variation greater than 0.5°C is not used in the main test
  - All glassware, syringes and needles must be pyrogen free by heating at 250 °C for not less than 30 min.



Rabbit test -

- Main test:
  - Group of 3 rabbits
  - Preparation and injection of the product:
    - Warming the product to 37±2°C
    - Dissolving or dilution
    - Injection site: ear vein
    - The injected volume: about 10 ml per kg of body weight over 10 min. duration
    - Record temperature at 30-min intervals for 3 hours

Rabbit test

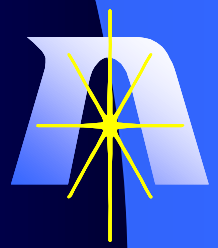
- **Interpretation of the results:**
  - The test is carried out on the first group of 3 rabbits; if necessary on further groups of 3 rabbits to a total of 4 groups, depending on the results obtained.
  - Intervals of passing or failing of products are on the basis of summed temperature response

The result of pyrogen test:

No.of Rabbits	Individual Tempt. rise (°c)	Tempt. Rise in group (°c)	Test
3 rabbits	0.5	1.4	Passes
If above not passes 3+5 = 8 rabbits	0.5	3.3	Passes
If above test not passes perform the test again			

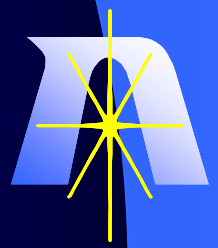
If above test not passes, the sample is said to be pyrogenic or go thr' the sources of contamination of pyrogen.

- **Disadvantages of rabbit test**
  - High variability in response.
  - Difficulty in controlling all factors.
  - Antipyretic drugs such as aspirin, acetaminophen and morphine mask pyrogenic effect (i.e., misleading in results).
  - Some other drugs have their inherent pyrogenic effect.



Bacterial endotoxins

- To detect or quantify endotoxins of gram-negative bacterial origin
- Reagent: Amoebocyte lysate from horseshoe crab (*Limulus polyphemus* or *Tachypleus tridentatus*).
- The name of the test is also *Limulus amebocyte lysate* (LAL) test



Limulus polyphemus = horseshoe crab

Mechanism of LAL

- The test is based on the primitive blood-clotting mechanism of the horseshoe crab

enzymes located with the crab's amebocyte

blood cells

endotoxins

↓

initiation of an enzymatic coagulation cascade

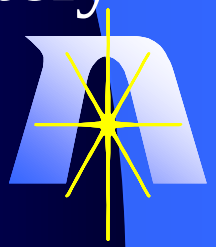
↓

proteinaceous gel

Particulate Matter Monitoring

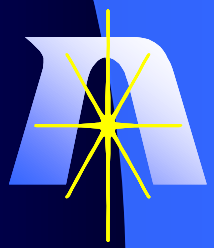
Definition:

- Unwanted mobile insoluble matter other than gas bubbles present in the given product.
- It may be dangerous when the particle size is larger than R.B.C. & may block the blood vessel.
- This type of products are immediately rejected from the batch.



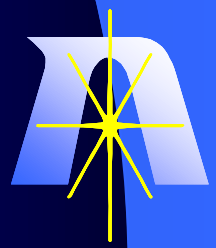
- The limit test for particulate matter is prescribed in I.P. 1996 (A- 125)
- **Biological risk:**

  - Inflammatory response
  - Antigenic response
  - Occlusion of blood vessels
- **Sources of particles**
  - Excipients
  - Processes
  - Packaging materials



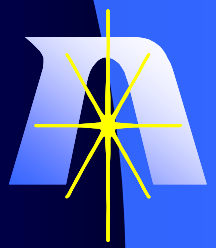
Permitted limits of particulate matter

Particle size in micrometer (equal to or larger than)	Max.No.of particles per ml
10 25 50	50 5 Nil



Sources of particulate matter

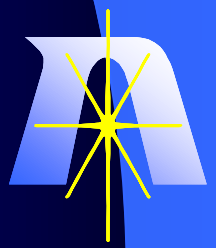
- **Intrinsic contamination:**
  - Originally present in products
    - e.g. Barium ions may react or leach with Sulphur ion which are already present in formulation may produce barium sulphate crystals.
- **Extrinsic contamination:**
  - Material comes from outside or environment
    - e.g. coming off the material from body & cloths of person
    - Entry of particle from ceiling , walls & furniture
    - May be in the form of cotton, glass rubber, plastics, tissues, insect fragments, bacterial contamination, dust, papers etc…



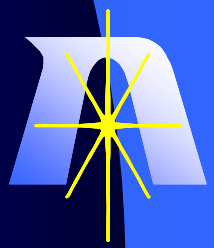
Methods of monitoring particulate matter contamination

- Visual method
- Coulter counter method
- Filtration method
- Light blockage method

- **Visual method:**
  - Simple method
  - Filled container are examined against strong illuminated screen by holding neck & rotating it slowly or inverted it to keep out the foreign matter.
- **Coulter counter method:**
  - It is used for detection of particles less than 0.1 micrometer in diameter.
  - Based on electrode resistance.
  - Sample is evaluated between two electrode & if particle found the resistance of electrode is increased.



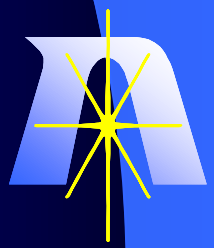
- **Filtration method:**
  - It is used for counting the particles in hydraulic fluids.
  - Sample passed through filter
  - Material is collected on filter
  - Evaluated under microscope.
  - Disadvantage:
    - Skilled & trained person is required



Significance of Particulate Matter monitoring

- Its presence may causes:
  - Septicemia
  - Fever & blockage of blood vessels
- Quality of product may affect

- **As per USP**
  - LVP : Not more than 50 particles/ ml (size 10 or more than 10 micrometer) & 5 particles/ ml (size more than 25 micrometer)
  - SVP: 10,000 particles/ container of size 10 micrometer or greater & not more than 1000 particles/ container greater than 25 micrometer.

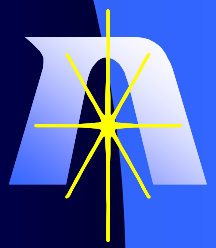


Large Volume Parenterals LVP's

Preparations for IV Fluids:

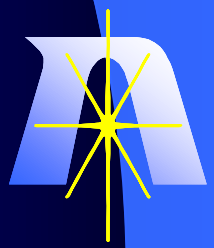
- LVP's which are administered by IV route are commonly called as IV fluids.
- Purposes:
  - Body fluids,
  - Electrolyte replenisher
- Volume supplied:

  100 to 1000 ml

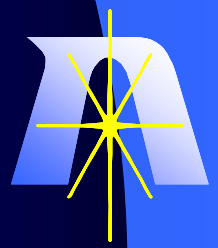


- **According to their basic use, LVPS can be classified into:**

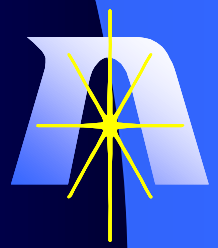
1-Basic nutrition.
2-Restoration of electrolyte imbalance.
3-Body's fluid replacement.
4-Blood and blood products.
5-Drug carriers.
6-Parenteral nutrition.
7-Special (miscellaneous) use.



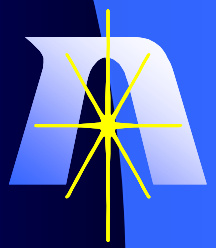
- Precautions / necessities in manufacturing:
  - Free from foreign particles
  - Free from micro organisms
  - Isotonic with body fluids
  - As they are in LVP no bacteriostatic agents are added (To avoid the possible toxicity of the high concentration of the added preservative).
  - Free from pyrogens



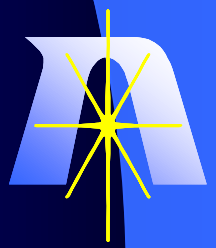
- **Examples of LVPs:**
  - **Dextrose injection :** Available in 2 , 5 , 10 , 25 & 50 % w/v solution.
  - Used for
    - Fluids replenisher
    - Electrolyte replenisher
  - **Sodium chloride & Dextrose injection:**
    - Contains
      - **0.11 to 0.9 % Sodium chloride**
      - **2.5 to 5.0 % Dextrose**
  - Used for
    - Fluids replenisher,
    - Electrolyte replenisher
    - Nutrient replenisher



- **Examples of LVP's:**
- **Sodium chloride injection IP:**
  - 0.9 % conc.
  - Also known as normal saline solution
  - Used as
    - Isotonic vehicle
    - Fluids replenisher,
    - Electrolyte replenisher
- **Sodium lactate injection IP:**
  - Contains 1.75 to 1.95 % w/v of sodium lactate
  - Used as
    - Fluids replenisher,
    - Electrolyte replenisher

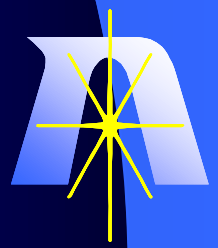


- **Examples of LVPs:**
- **Mannitol injection IP:**
  - Contains 5, 10 , 15, 20 % of mannitol
  - Used as :
    - Diagnostic aid
    - Renal function determination
    - As a diuretic
- **Mannitol & Sodium chloride injection IP:**
  - Contains 5, 10 , 15, 20 % of mannitol & 0.45 % of Sodium chloride
  - Used as :
    - As a diuretic



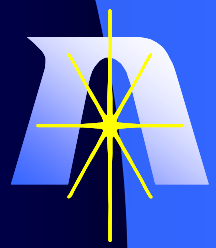
. Ringer's Injection, USP:

- Is a sterile solution of sodium chloride, potassium chloride and calcium chloride in water for injection (WFI).
- It is isotonic with physiological fluids
- Used as vehicle for other drugs or alone as electrolyte replenisher and plasma volume expander.



- **Lactated Ringer’s Injection, USP:**
- Lactated Ringer's solution is abbreviated as "LR" or "RL". It is also known as **Ringer's lactate solution**
- Has different quantities of the three salts in Ringer’s injection, and it contains sodium lactate.
- Used as fluid and electrolyte replenisher and systemic alkalizer.

- Common uses :
  - Used in surgery patients
  - In replacement therapy
  - Providing basic nutrition
  - For providing TPN
  - As a vehicle for other drug subs.



Total Parenteral Nutrition

- **TPN** stands for Total Parenteral Nutrition. This is a complete form of nutrition, containing protein, sugar, fat and added vitamins and minerals as needed for each individual.
- Total Parenteral Nutrition (TPN) may be defined as provision of nutrition for metabolic requirements and growth through the parenteral route.

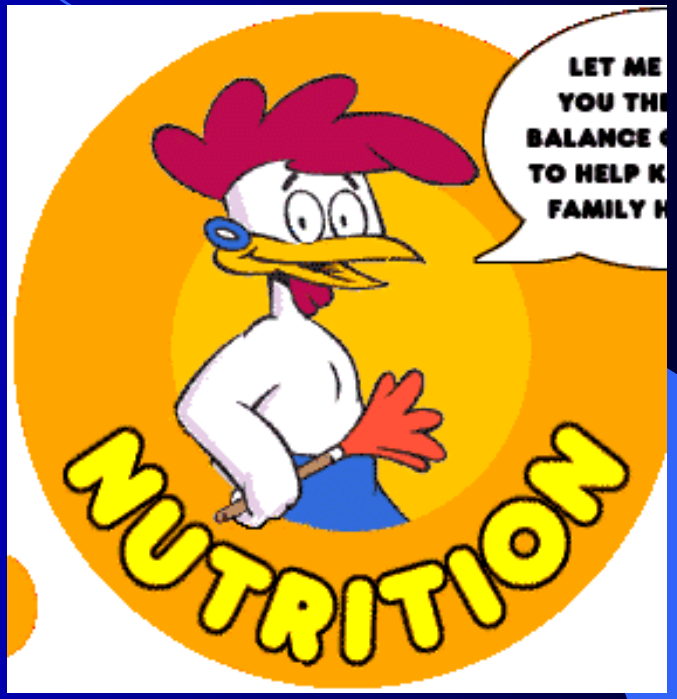
Total Parenteral Nutrition (TPN) (Intravenous Nutrition)

- They are available as ready-to-mix kits.

- Parenteral Nutrition (PN) can be used to supplement ordinary or tube feeding.

Nutritional Requirements

- Amino acids
- Glucose
- Lipid
- Minerals
- Vitamins
- Water and electrolytes
- Trace elements



- ***Components of TPN solutions:***

(1) Protein as crystalline amino acids.

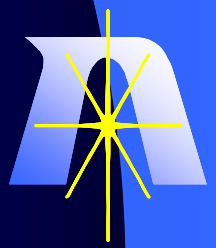
(2) Fats as lipids.

(3) Carbohydrate as glucose.

(4) Electrolytes–Sodium, potassium, chloride, calcium and magnesium.

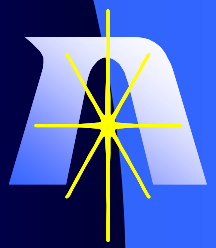
(5) Metals/Trace elements–Zinc, copper, manganese, chromium, selenium.

(6) Vitamins A, C, D, E, K, thiamine, riboflavin, niacin, pantothenic acid, pyridoxine, biotin, choline and folic acid.



Why it is necessary?

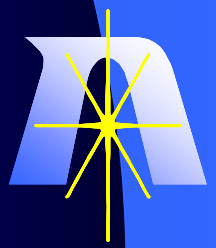
- TPN might be necessary if:
  - A patient is severely undernourished, and needs to have surgery, radiotherapy or chemotherapy;
  - A patient suffers from chronic diarrhea and vomiting;
  - A baby's gut is too immature;
  - A patient's (their "gastrointestinal tract") is paralysed, for example after major surgery.



When is it necessary?

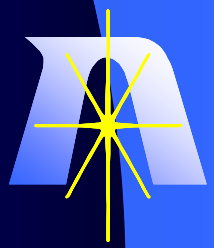
- TPN is normally used following surgery, when feeding by mouth or using the gut is not possible,
- When a person's digestive system cannot absorb nutrients due to chronic disease, or, alternatively, if a person's nutrient requirement cannot be met by enteral feeding (tube feeding) and supplementation.

- Short-term TPN may be used if a person's digestive system has shut down (for instance by Peritonitis), and they are at a low enough weight to cause concerns about nutrition during an extended hospital stay.
- Long-term TPN is occasionally used to treat people suffering the extended consequences of an accident or surgery.
- Most controversially, TPN has extended the life of a small number of children born with nonexistent or severely birth-deformed guts.



- GENERAL INDICATIONS
  - Patient who can't eat
  - Patient who won't eat
  - Patient who shouldn't eat
  - Patient who can't eat enough

    "*If the gut works, use it.*"



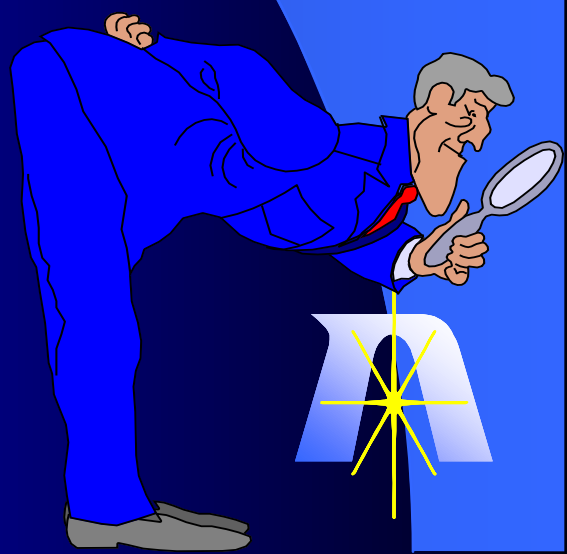
Indications for TPN

Short-term use

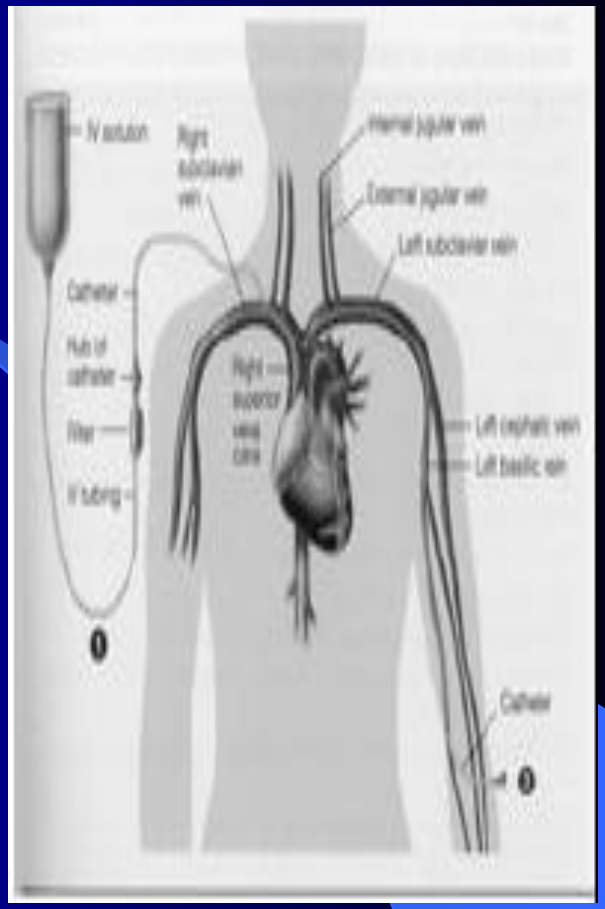
- Bowel (intestinal) injury /surgery
- Bowel disease
- Severe malnutrition
- Nutritional preparation prior to surgery.
- Malabsorption - bowel cancer

Long-term use

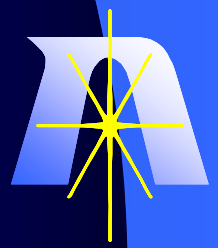
- Prolonged Intestinal Failure
- Crohn's Disease
- Bowel resection



- The solution is administer through superior venacava which is accessed by the subclavian vein near the heart. WHY?
- The preferred method of delivering TPN is with a medical **infusion pump**.
- A **sterile** bag of nutrient solution, between 500 mL and 4 L is provided.
- The pump infuses a small amount (0.1 to 10 mL/hr) continuously in order to keep the vein open.



- Feeding schedules vary, but one common regimen ramps (rises) up the nutrition over a few hours, levels off the rate for a few hours, and then ramps it down over a few more hours, in order to simulate a normal set of meal times.
- Occasionally, other drugs are added as well, sometimes unnecessarily.
- Insulin may be included, WHY?

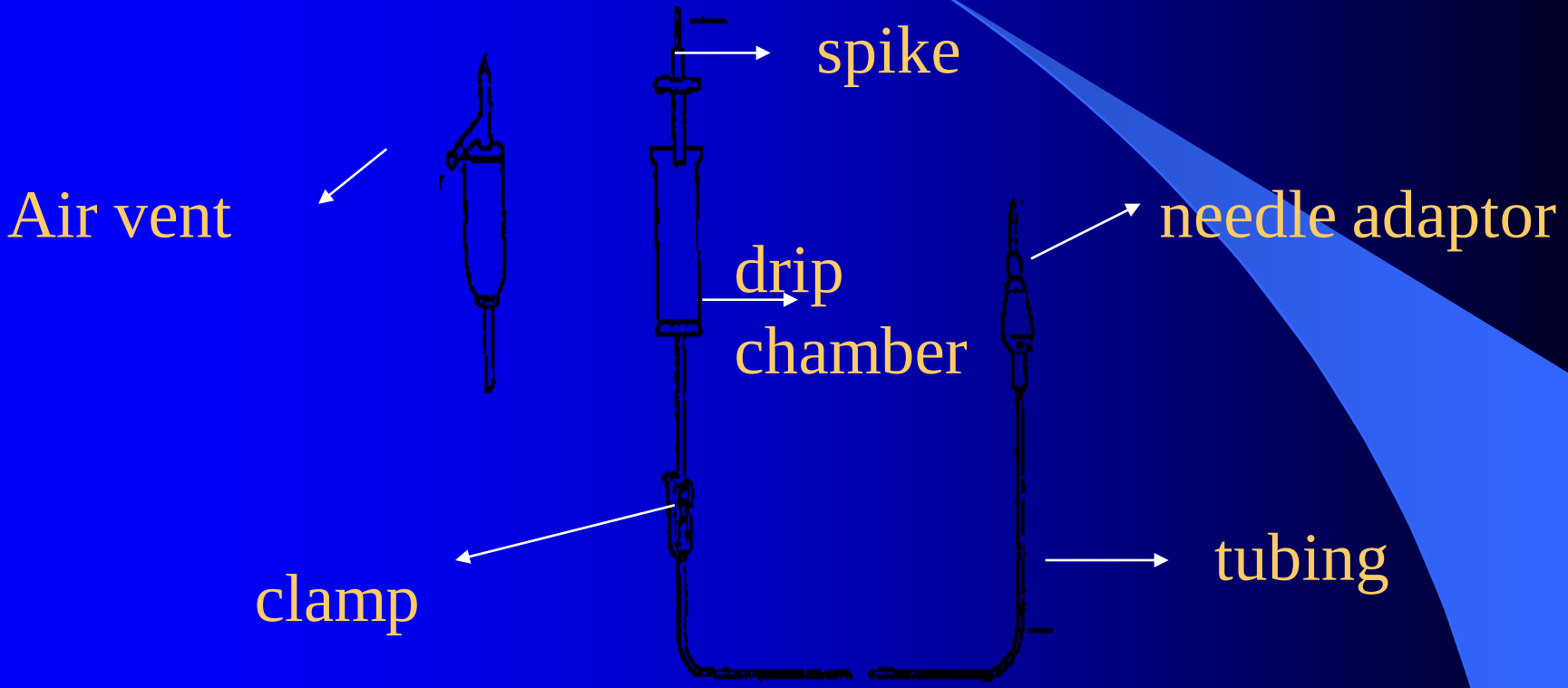


Complications of TPN

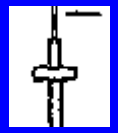
- Sepsis
- Air embolism
- Clotted catheter line
- Catheter displacement
- Fluid overload
- Hyperglycaemia

IV administration set:

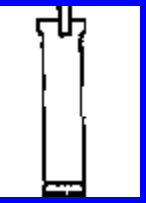
IV administration set:



Basic component of IV administration set

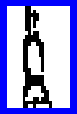


Spike→ to enter the rubber closure of the IV system



Drip chamber→ to allow setting uninterrupted air free flow

Long polyethylene tubing→ connect with Injection set

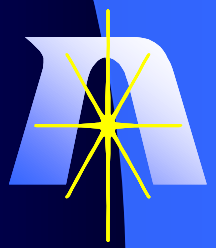


Needle adapter → (rigid plastic) to enter the vein

Clamp-like device → to adjust the tubing diameter and hence the flow rate

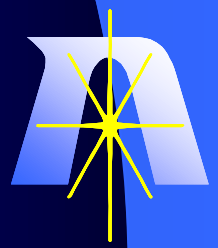
Irrigation Solution

- They are topical solutions used to flush (clean) open wounds or body cavities. Although they often labeled using the same terms for injections,
  - They never given parenterally.
  - They are available in the form of:
    - Single use unit (never recapped to avoid contamination).
    - Multiple use units with screw cap e.g. NaCl irrigation solution

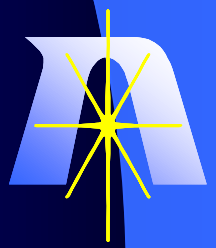


DIALYSIS FLUIDS

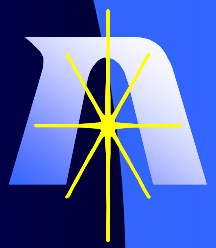
- **Dialysis** is the process in which substances are separated from one another due to their difference in diffusibility (distribution) throught membrane.
- The fluids used in dialysis are known as **dialysis fluids.**



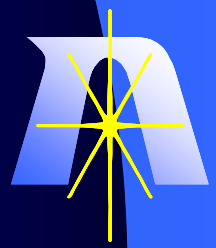
- General uses :
  - Renal failure
    - waste product is removed
    - Maintain electrolytes
    - Also called as *haemodialysis* or ***intraperitoneal dialysis***
  - Transplantation of kidney
  - Poisoning cases



- *Haemodialysis:*
  - To remove toxins from blood
  - In haemodialysis, the blood from artery is passed thr' artificial dialysis membrane, bathed in dialysis fluid.
  - The dialysis membrane is permeable to urea, electrolytes & dextrose but not to plasma proteins & lipids
  - So excess of urea is passed out from blood thr' dialysis fluid.



- After dialysis blood is returned back to the body circulation thr’ vein.
- A kidney unit may require more than 1200 litres of solution / week.
- So haemodialysis fluid is prepared in conc. form then it is diluted with deionised water or dist. water before use.



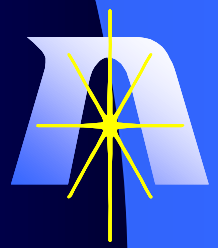
COMPOSITION

Composition of Concentrated Haemodialysis Fluid BPC

Dextrose monohydrate ----------	8.0 gm
Sodium acetate ----------	19.04 gm
Lactic acid ----------	0.4 ml
Sodium chloride ----------	22.24 gm
Potassium chloride ----------	0.4 gm
Freshly boiled & cooled water -q.s.	100 ml

Dilute 1 liter of conc. solution with 39 liters of water to make 40 litres.

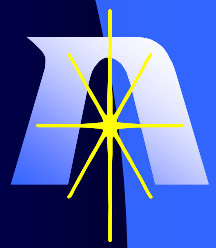
Storage: store in warm place as it is liable to convert into crystals on storage.



IV ADMIXTURES

- **Definition:**
  - When two or more sterile products are added to an IV fluid for their administration, the resulting combination is known as IV admixture.
  - In hospitals, prepared by nurses by combining or mixing drugs to the transfusion fluids.
  - The drugs may be admixed in one syringe or are incorporated into bottles of LV transfusion fluids.

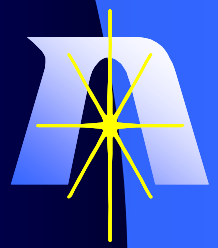
- **Care :**
  - Microbial contamination
  - Incompatibility
    - Physical : change in color
    - Chemical : hydrolysis, oxidation, reduction etc..
    - Therapeutic: undesirable antagonistic or synergistic effect



- **Methods for safe & effective use of IV admixture:**
  - Proper training to nurses & pharmacists
  - Instruction regarding labeling
  - Information for stability & compatibility to the hospital pharmacy dept.
  - Information for the formulation skills to the pharmacist.
  - Must prepared under ASEPTIC conditions

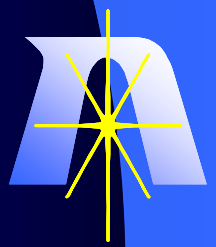
Aseptic Technique

- Importance of Aseptic Technique
  - Parenteral administration bypasses the skin and gastrointestinal tract, the bodies natural barriers to infection
  - Giving a patient a contaminated product can cause serious adverse effects including **DEATH**



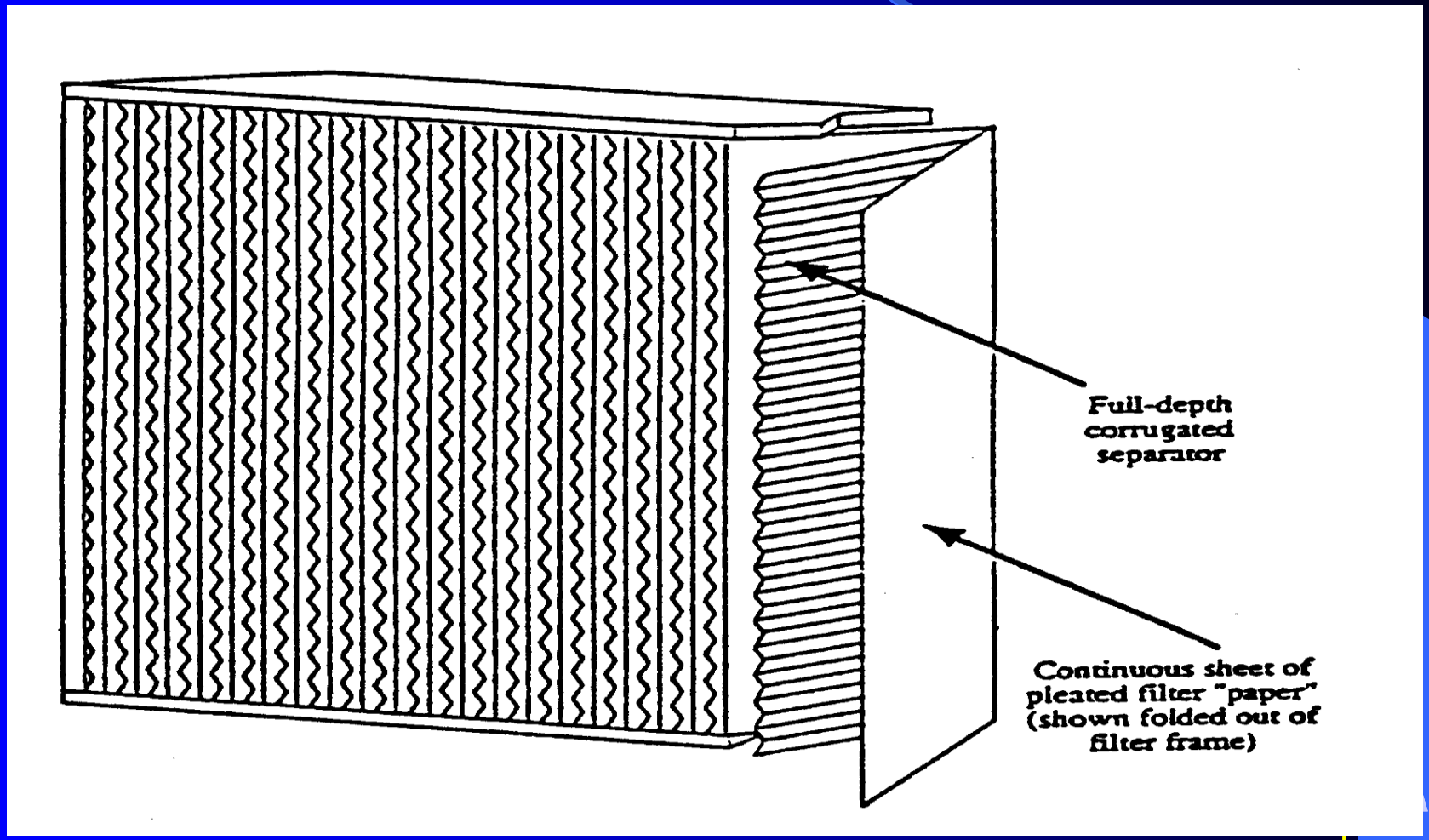
Laminar Air Flow Hoods

- The underlying principle of a laminar air flow hood is that a constant flow of HEPA filtered air at a rate of approximately 90 linear feet per minute physically sweeps the work area and prevents the entry of contaminated air
- The hood workspace is used to prevent the contamination of compounded sterile products and parenteral preparations
- The space between the HEPA filter and sterile product being prepared is referred to as the critical work surface
- **HEPA** filter - **H**igh **E**fficiency **P**articulate **A**ir filter removes 99.97% of all air particles 0.3mm or larger



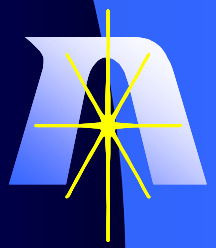
Laminar Air Flow Hoods (cont.)

HEPA Filter in Frame



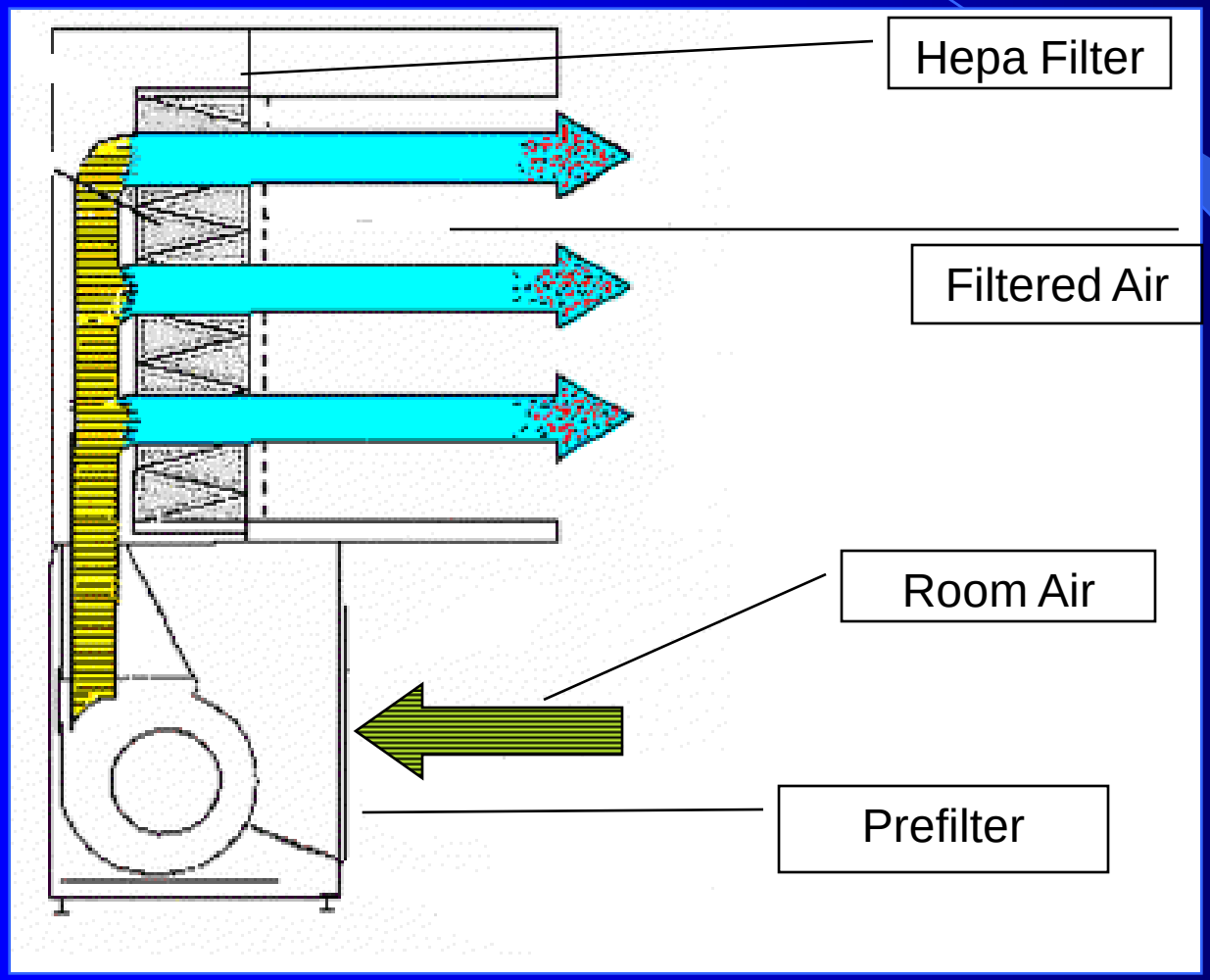
Laminar Air Flow Hoods (cont.)

- **Horizontal Flow (Laminar Flow Hood)**
  - Air blows towards worker
  - Used for non-chemotherapy preparations
- **Vertical Flow (Biological Safety Cabinet or Chemotherapy Hood)**
  - Air blows from top down to maintain sterility and protect the worker
  - Used to make chemotherapy



Laminar Air Flow Hoods (cont.)

Horizontal Laminar Air Flow Hood



Laminar Air Flow Hoods (cont.)

Vertical Laminar Flow Hood

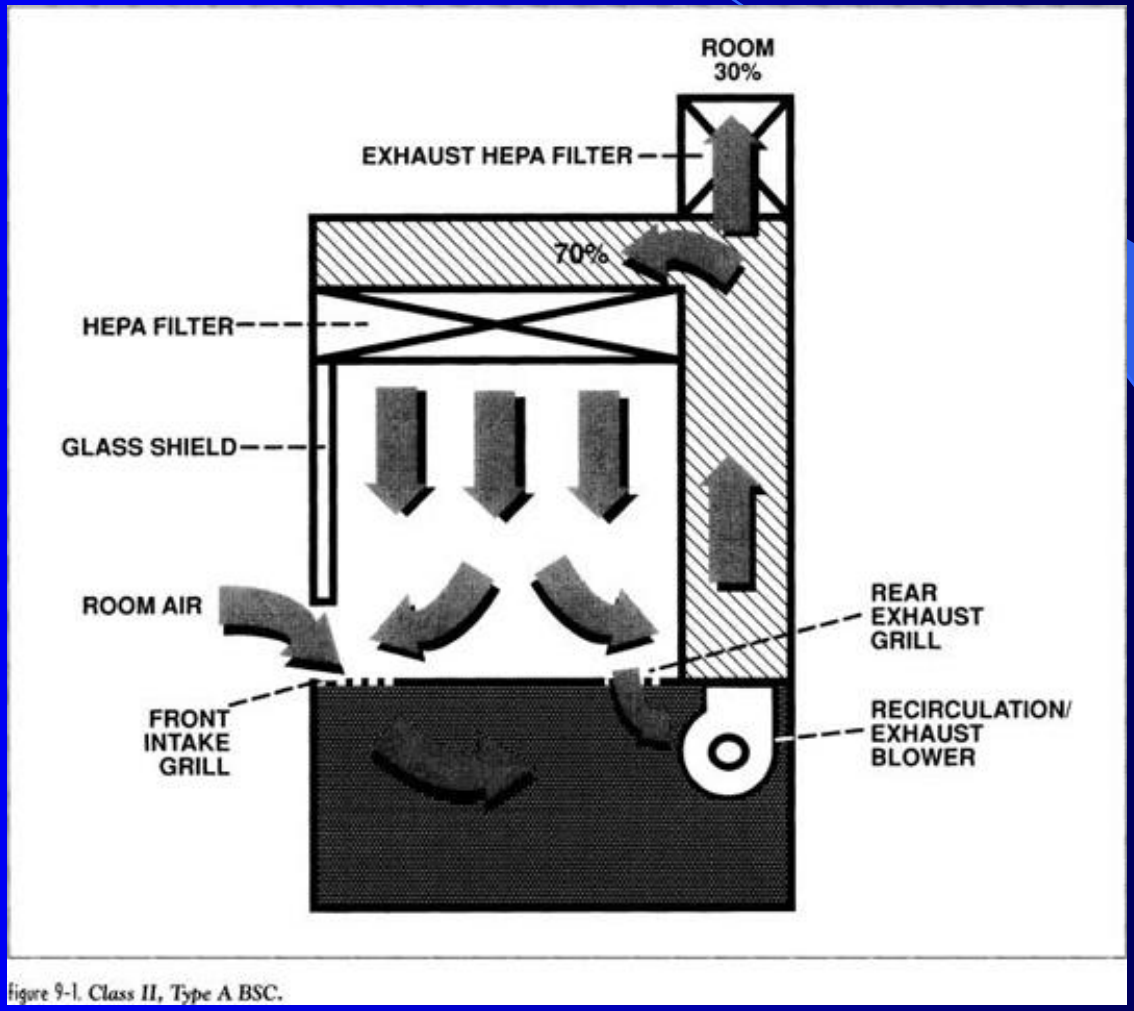
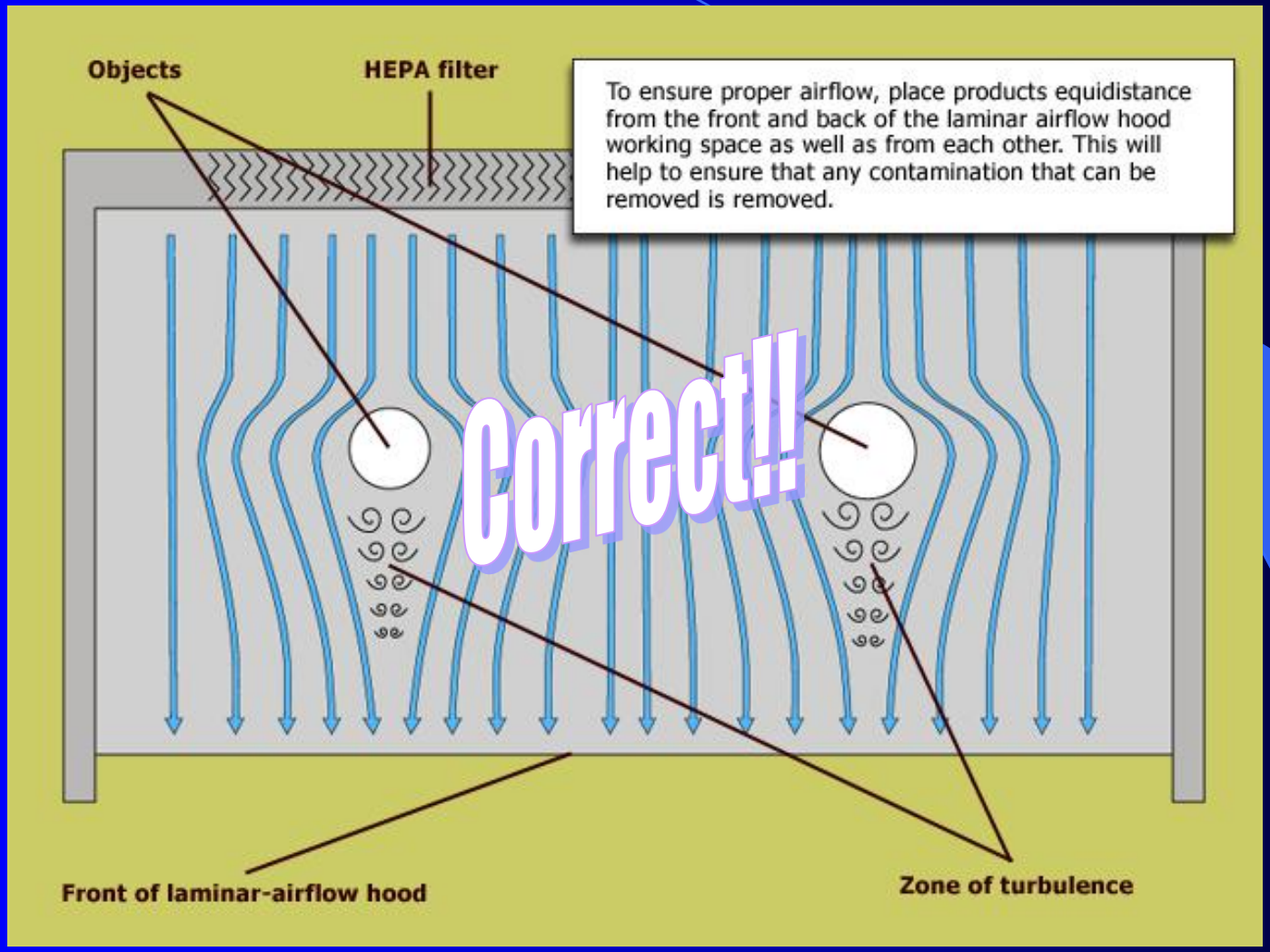
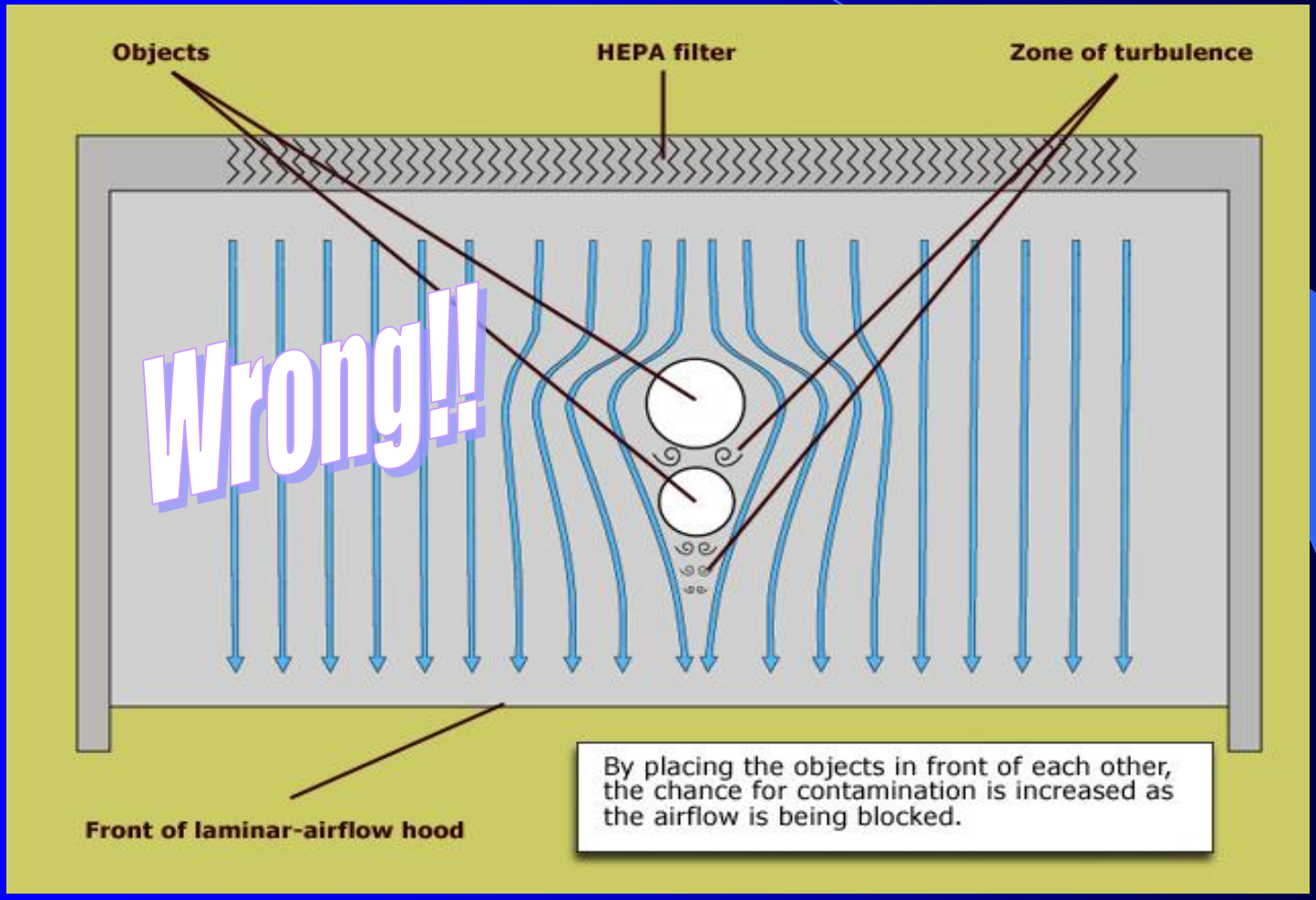


figure 9-1. *Class II, Type A BSC.*

Correct placement of items in a laminar flow hood



Incorrect placement of items in a laminar flow hood



Formulation of Parenteral

- **Reverse Osmosis:**
- It works by using pressure to force a solution through a membrane, retaining the solute on one side and allowing the pure solvent to pass to the other side. This is the reverse of the normal osmosis process, which is the natural movement of solvent from an area of low solute concentration, through a membrane, to an area of high solute concentration when no external pressure is applied.