**INDUSTRIAL PHARMACY-I**

**UNIT IV-PARENTERALS**

**CLASS:30**

**TOPIC Large volume parenterals and lyophilized products**

**Formulation of large volume parenterals:-**

Large volume injections are intended to be administered by IV Infusion Fluids & are included in the group of sterile products & are known as large volumeParenterals.Theseconsist of single dose injecting a volume of 100 ml or more than 100 ml sometimes additional drugs are added to them by either injecting svp to the administration sets or by piggyback method(small volume infusion of an additional drug is added to the intravenous delivery system).large volume parenteral products include:

1) Infusionfluid(Basicnutrition-Dextroseinj,Fluidreplacementtherapy-Normalsaline)
2) TotalparenteralNutritionsolution(TPN)
3) Intravenousantibiotics
4) Dialysisfluid
5) Irrigationsolutions

Large volume parenterals should be terminally heat sterilized. Apart from water for injection as the main component, other ingredients that should be included are carbohydrates (e.g. dextrose, sucrose and dextran), aminoacids, lipidemulsion,electrolytes (Nacl)andglycerol, sorbitol and mannitol.TheLVParemostlyclearsolutions,exceptfortheoil-in–wateremulsions.The emulsions for infusion are produced by highly specialized method as they are destabilized by heat. This result in many difficulties during production, thus the size of oil droplets should be controlled during heat sterilization.

**ProductionofLVP**:

i) The manufacturing and filling of LVP fluids into containers are carried out in aa high standard clean room environment. High standards are required to prevent these products from getting contaminated with organisms, pyrogens and particulate matter.
ii) The fluids from a bulk container are filled into the product container using high speed filling machine. Before filling the fluid into the container, it is passed through an in-line membrane filter to remove the particulate matter.
iii) After filling, the neck of each glass bottle is immediately sealed with a tight fitting rubber closure held in place with a crimped aluminum cap.
iv) In case plastic bags are used, the pre-formed plastic bags are aseptically filled and heat-sealed immediately.

v) Blow –fill-seal system are adopted to minimizes the problems with product handling, cleaning and particulate contamination.

vi) TheLVPproducts,including irrigation solution and dialysis fluids should be moist heat sterilized immediately after the containers are filled.

**Lyophilization or freeze-drying:-**

Lyophilizationorfreezedryingisaprocessinwhichwaterisremovedfromaproductafter it isfrozen and placed under a vacuum,allowing the ice to change directly from solid to vaporwithout passing through a liquid phase. The process consists of three separate, unique, and interdependent processes like;Freezing, Primary drying (sublimation), and Secondary drying (desorption).

Advantages of Lyophilization

- Ease of processing a liquid, which simplifies aseptic handling.
- Enhanced stability of a drypowder.
- Removal of water without excessive heating of the product.
- Enhanced product stability in a dry state.
- Rapid and easy dissolution of reconstituted

product Disadvantages

- Increased handling and processing time.
- Need for sterile diluents upon reconstitution.
- Cost and complexity of equipment

**StepsinvolvedinformulationofLyophilizedproducts:-**

- Dissolving the drug and excipients in a suitable solvent, generally water for injection (WFI).
- Sterilizing the bulk solution by passing it through a 0.22-micron bacteria-retentive filter.
- Filling into individual sterile containers and partially stoppering the containers under aseptic conditions.
- Transporting the partially stoppered containers to the lyophilizer and loading into the chamber under aseptic conditions.
- Freezing the solution by placing the partially stoppered containers on cooled shelvesin a freeze-drying chamber or pre-freezing in another chamber.
- Applying a vacuum to the chamber and heating the shelves in order to evaporate the water from the frozen state.
- Complete stoppering of the vials usually by hydraulic or screw rod stoppering mechanisms installed in the lyophilizers. There are many new parenteral products, including anti-infectives, biotechnology derived products, and in-vitro diagnostics which are manufactured as lyophilized products.

Additionally,inspectionshavedisclosedpotency,sterilityandstabilityproblems associated with the manufacture and control of lyophilized products