PHARMACEUTICAL AEROSOLS

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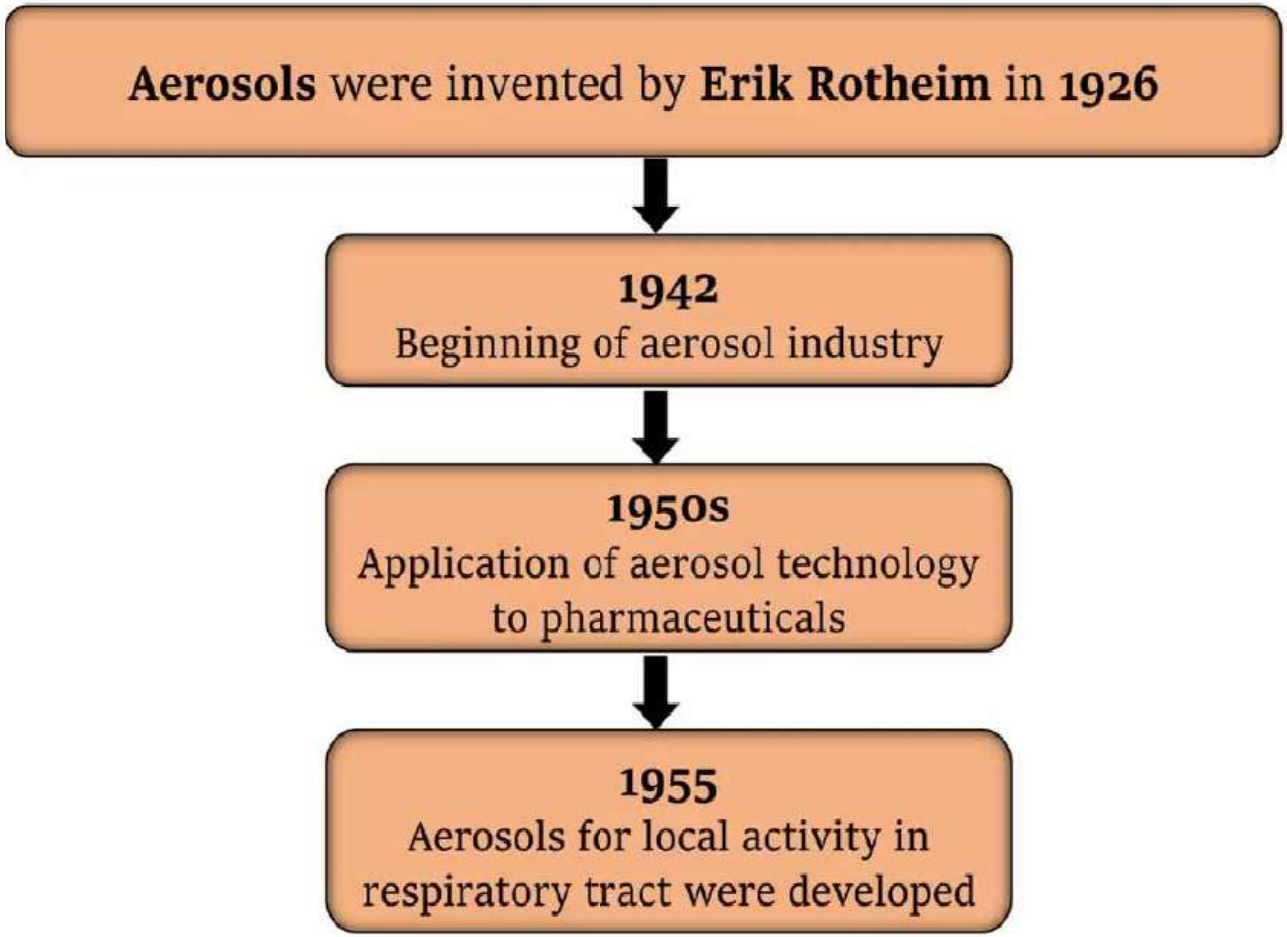
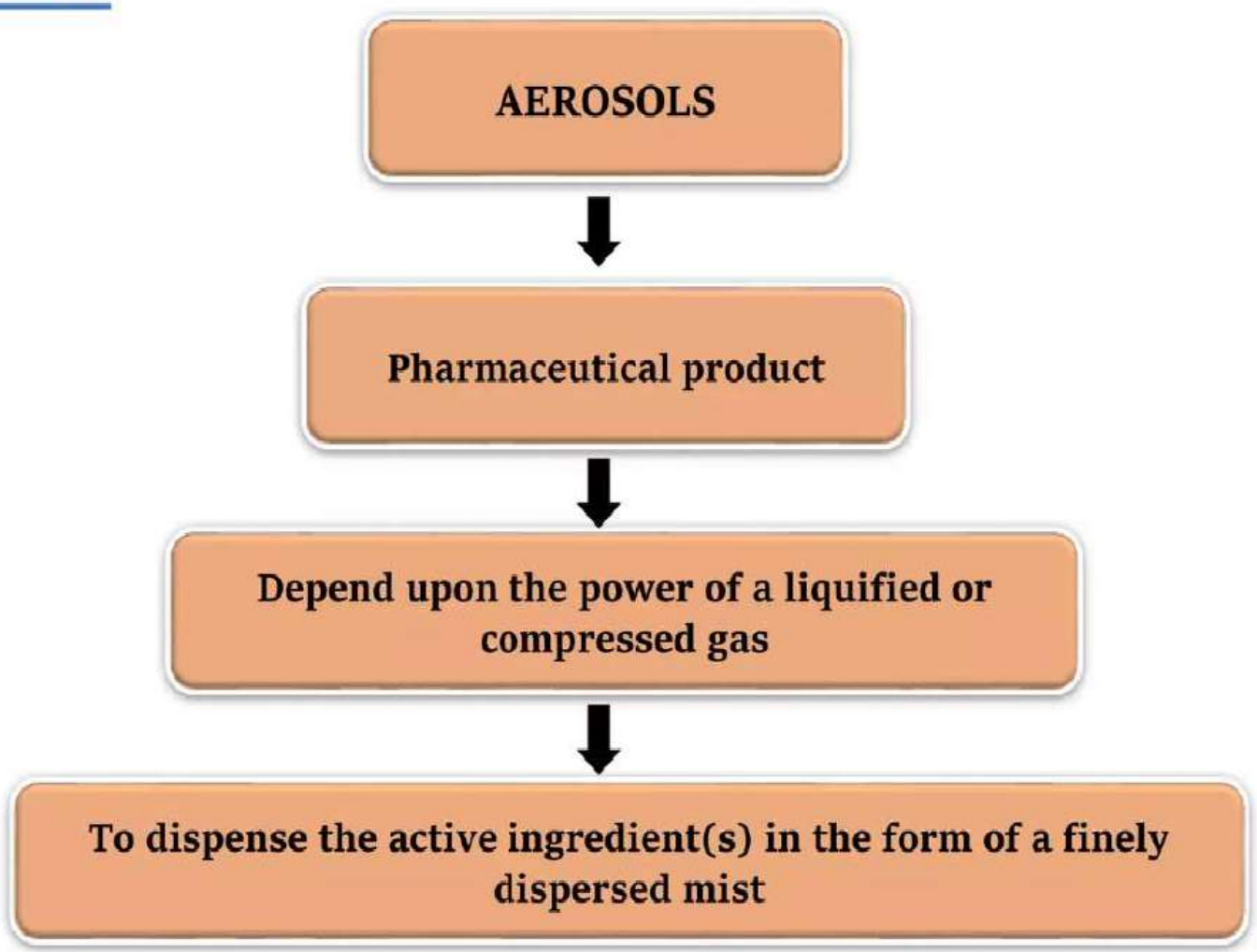
Background


Aerosols were invented by **Erik Rotheim** in **1926**
1942
Beginning of aerosol industry
1950s
Application of aerosol technology to pharmaceuticals
1955
Aerosols for local activity in respiratory tract were developed

Definition


AEROSOLS
Pharmaceutical product
Depend upon the power of a liquified or compressed gas
To dispense the active ingredient(s) in the form of a finely dispersed mist

Advantages of using Aerosols

- Dose removal without contamination of the bulk
- Enhanced stability for substances affected by oxygen and/or moisture
- Sterility is maintained
- Minimum or no irritation due to application
- Dose lowering in case of steroid therapy
- Circumvention of first pass effect
- Application of medication in a thin layer
- **Tamperproof** system.

Disadvantages of using Aerosols

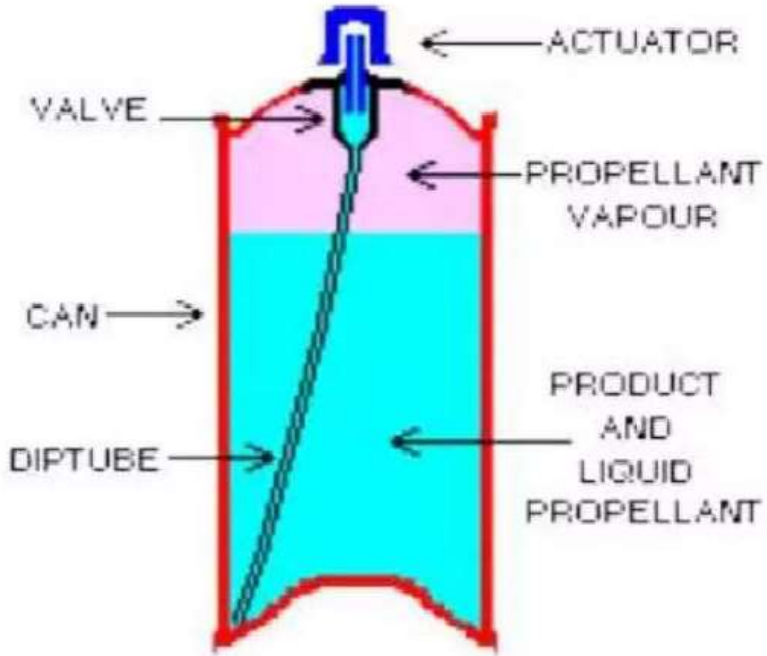
- Costly
- Difficult disposal of container due to flammable propellants
- Allergic in some cases
- Explosive
- Some formulations are difficult to formulate as aerosols
- In some cases propellants may cause toxic reactions.

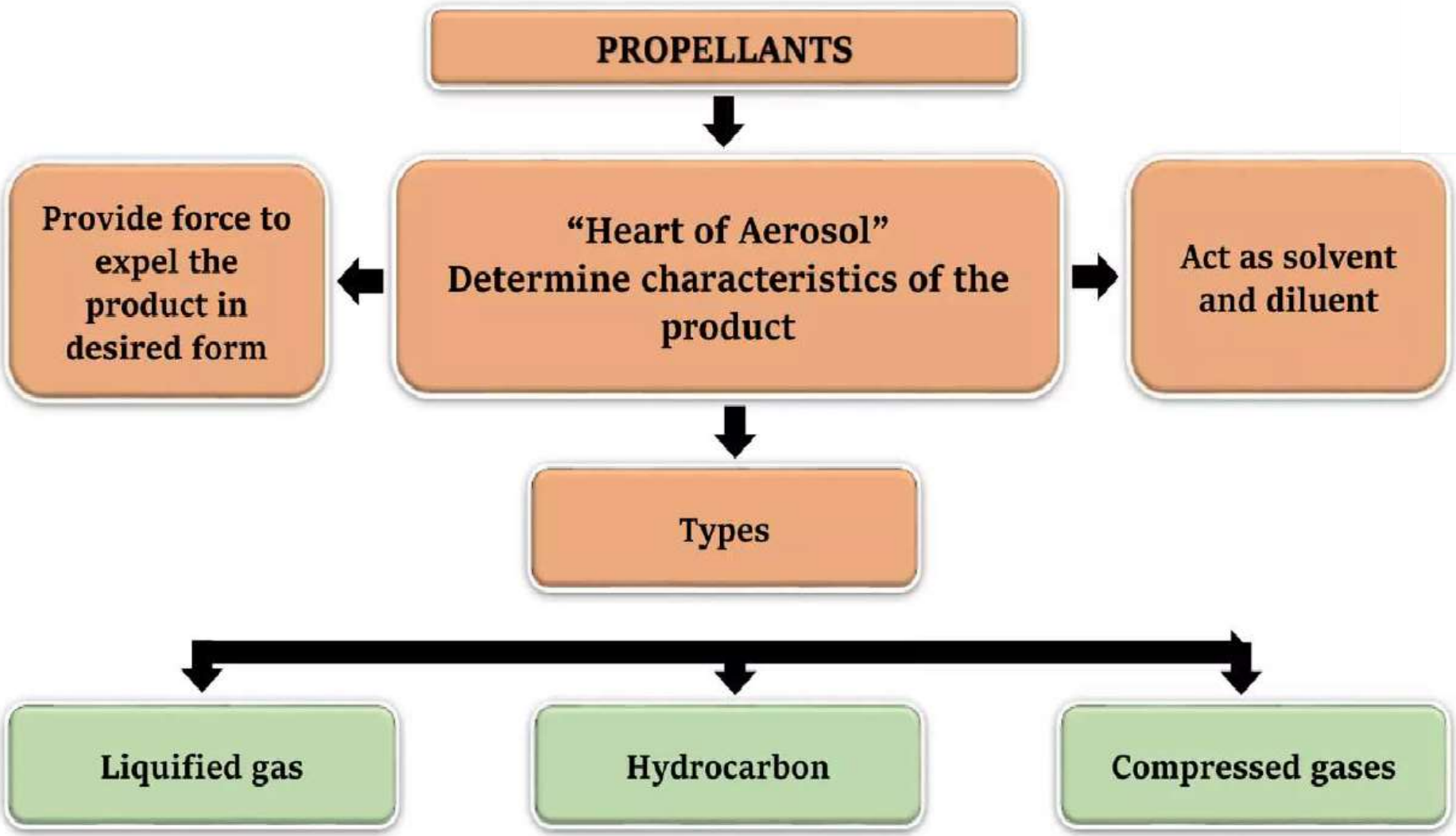
Desired characteristics

- Less explosive.
- Uniform and constant dose delivery.
- Non allergic.
- Economic/Low cost.
- Easy to handle.
- Non Breakable.
- Eco-friendly

Components of Aerosol

- Propellant
- Container
- Valve
- Actuator
- Product concentrate




PROPELLANTS
Provide force to expel the product in desired form
"Heart of Aerosol"
Determine characteristics of the product
Act as solvent and diluent
Types
Liquified gas
Hydrocarbon
Compressed gases

Liquified gases

- Widely used propellant
- Relatively inert, nontoxic and non flammable
- Immediately separate into a liquid and a vapor phase
- Maintain a constant pressure within the container
- Contains are maintained in fine mist or foam form
- Examples – Chlorofluorocarbons (CFCs)
  Hydrochlorofluorocarbons (HCFCs)
  Hydrofluorocarbons (HFCs)

- FCs are widely used in inhalational and oral aerosols.

Hydrocarbons

- Flammable
- Less toxic
- Less dense
- More Soluble
- Chemically more stable
- More economic
- Examples – Butane

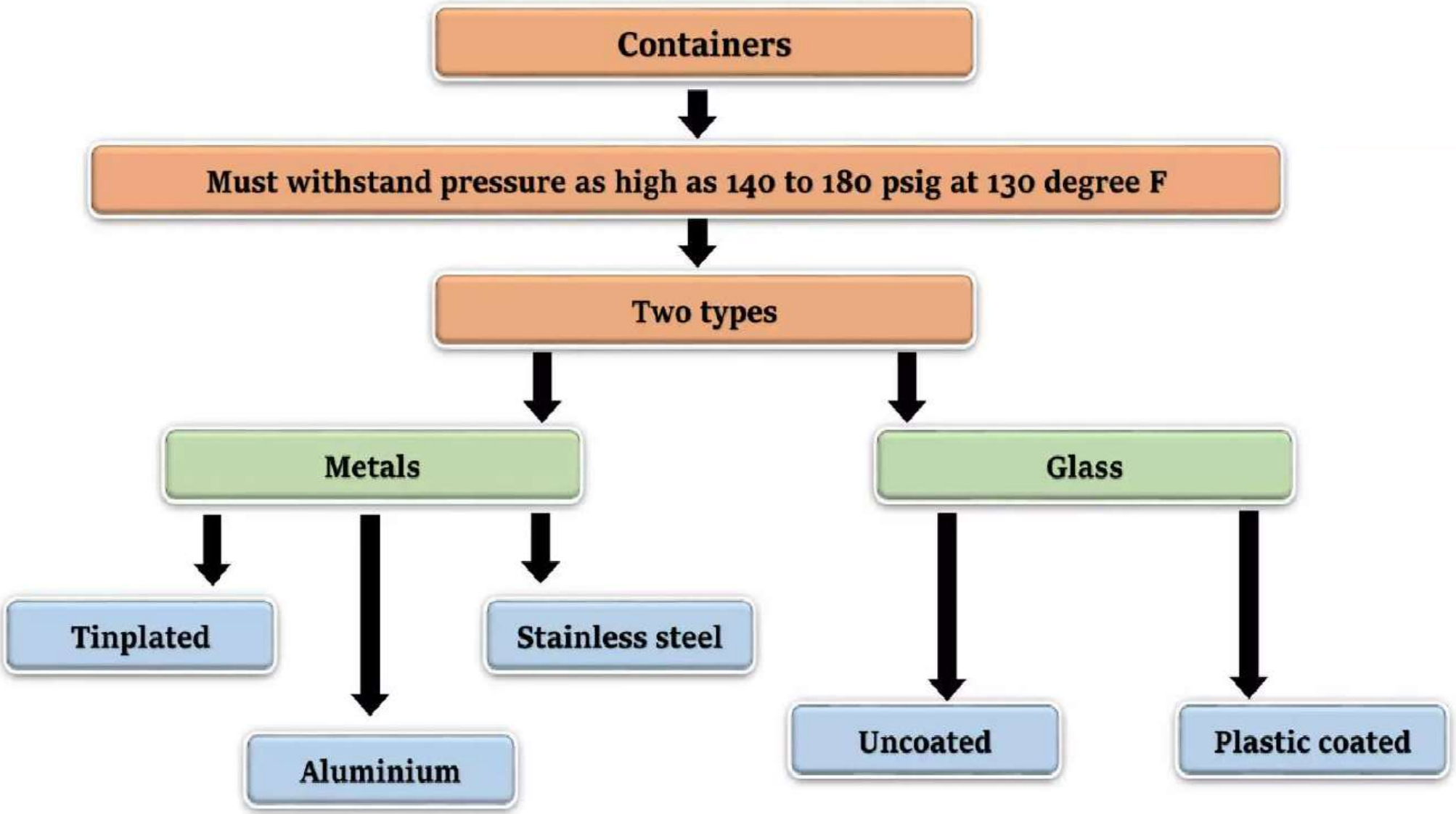
  Propane
- Earlier restricted to use with foams and water based aerosols
- Development of "Vapor tap" and "Aquasol valve" extended their use.

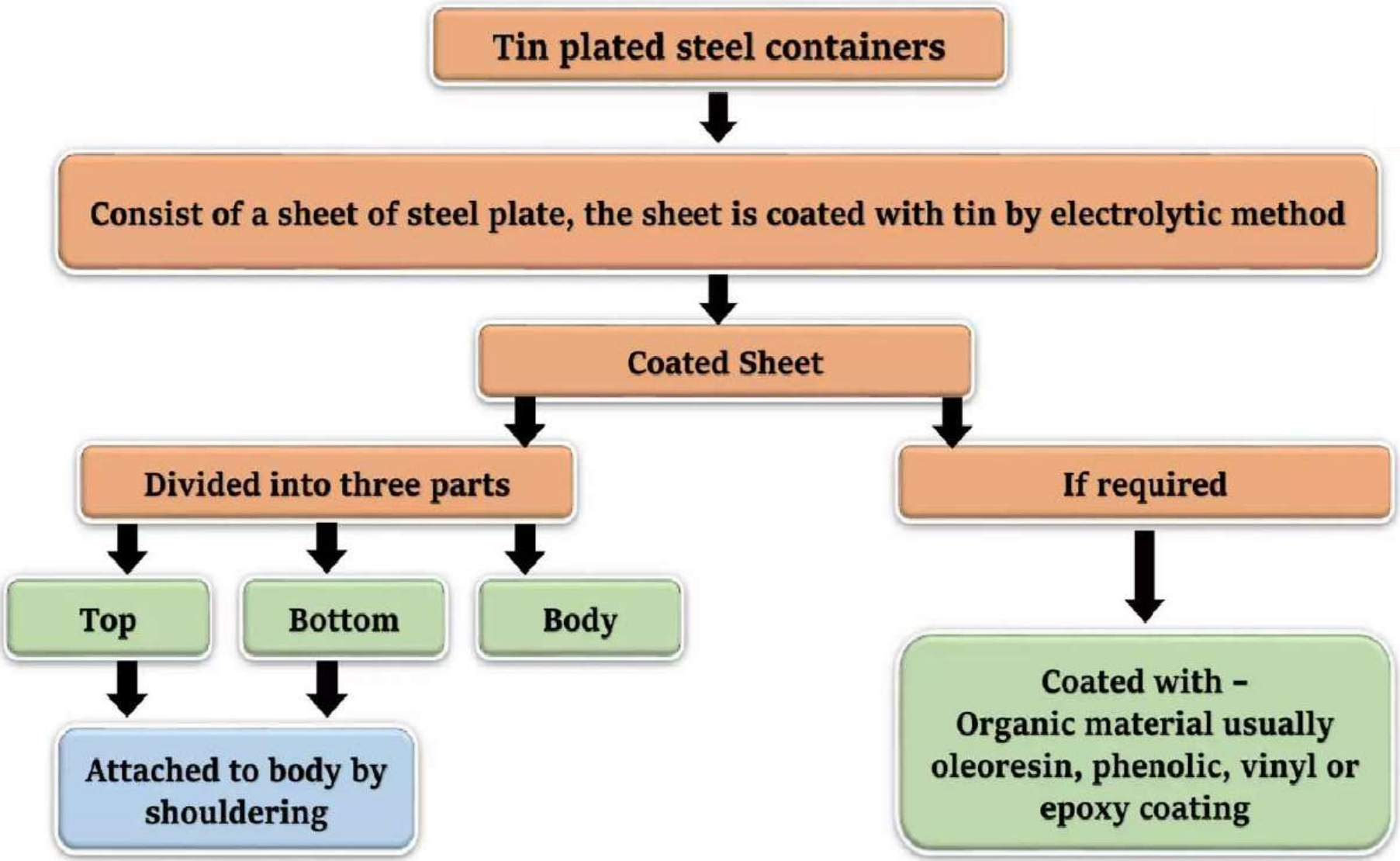
Compressed Gases

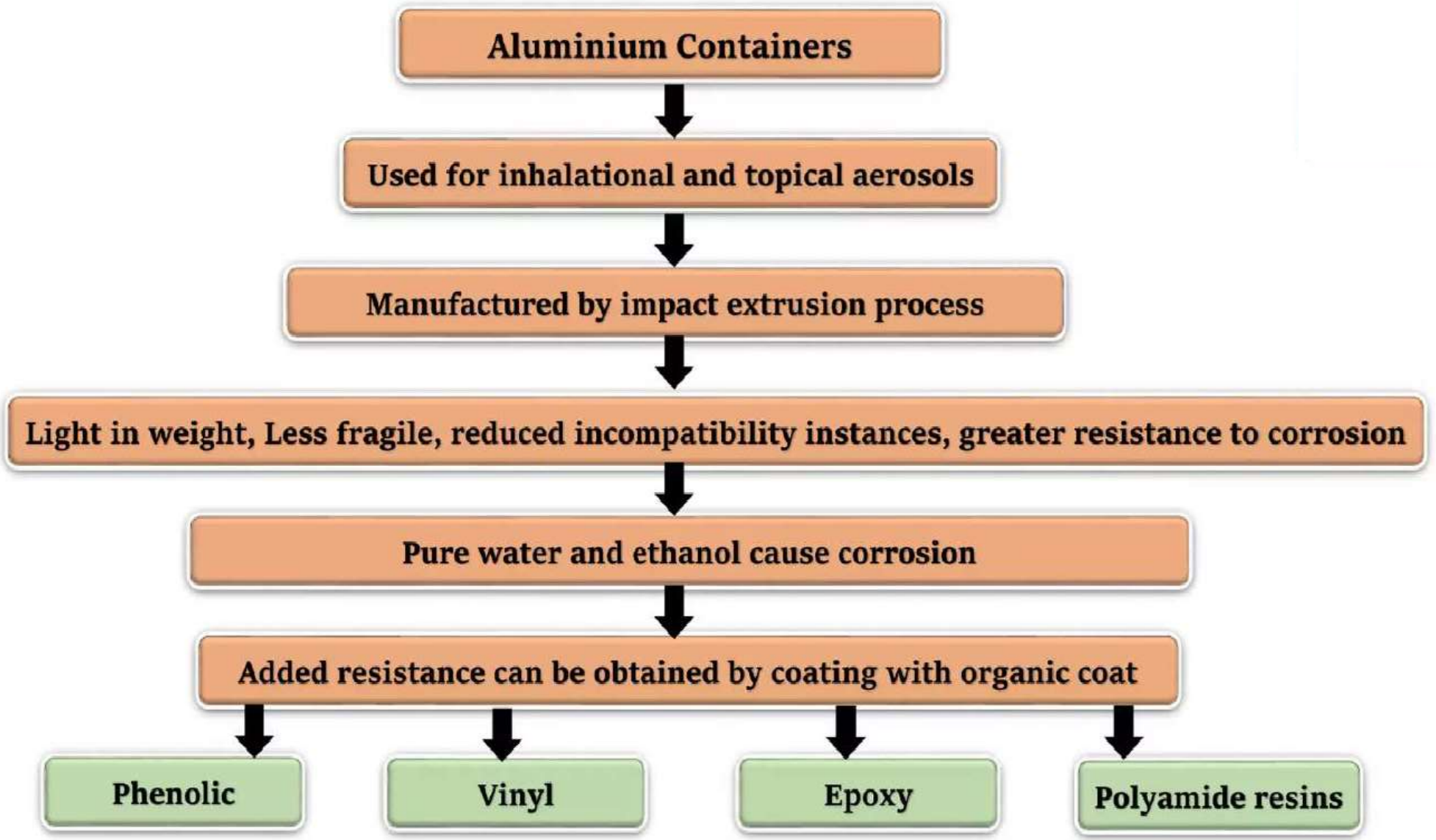
- Have little expansion power
- Fairly wet spray is produced
- Foam is less stable as compared to liquified gases
- Do not have a *chilling effect*
- Used mostly in topical pharmaceutical aerosol products
- Examples – Nitrogen
  Nitrous oxide
  Carbon dioxide

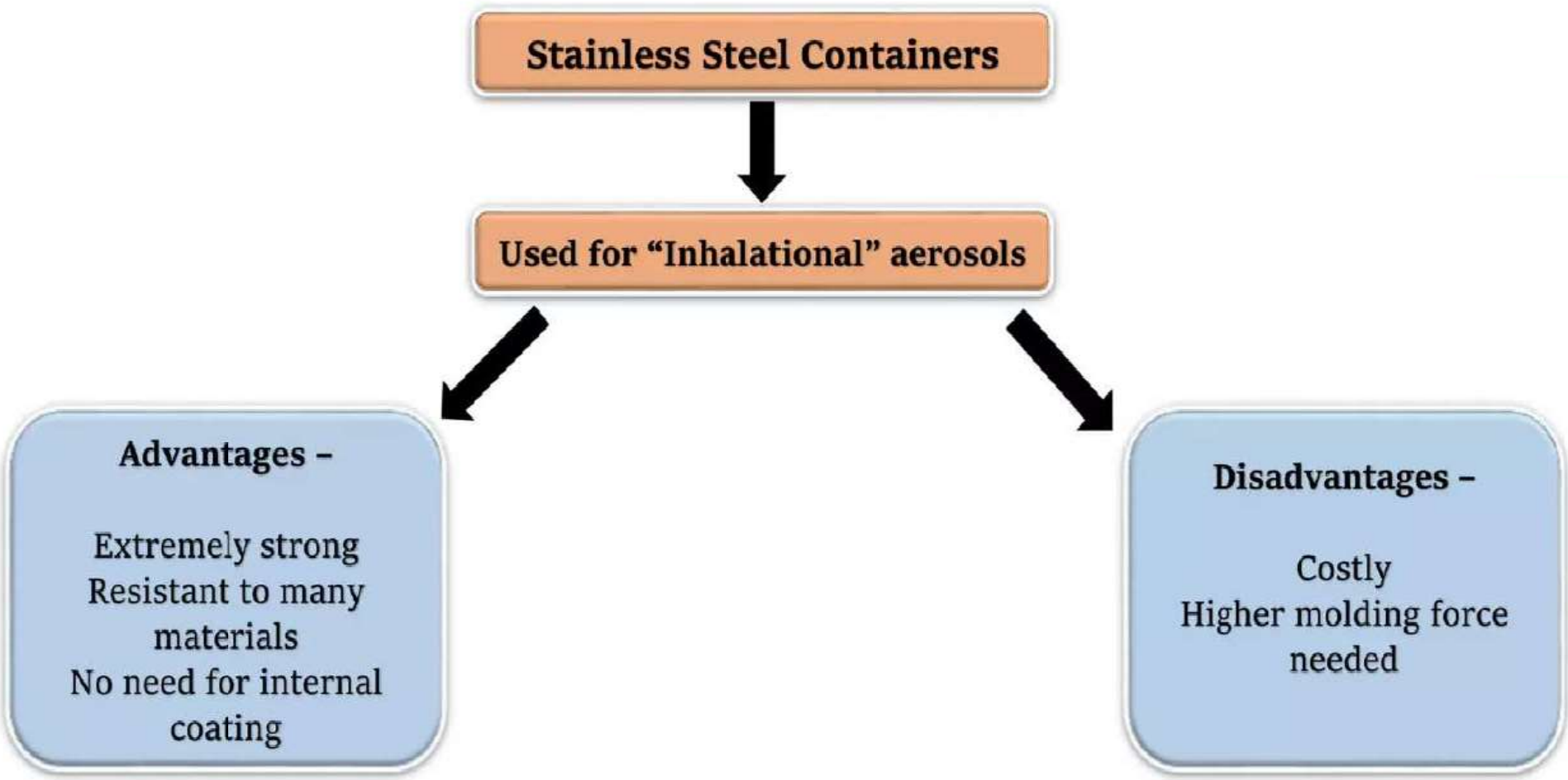
Common rules of nomenclature

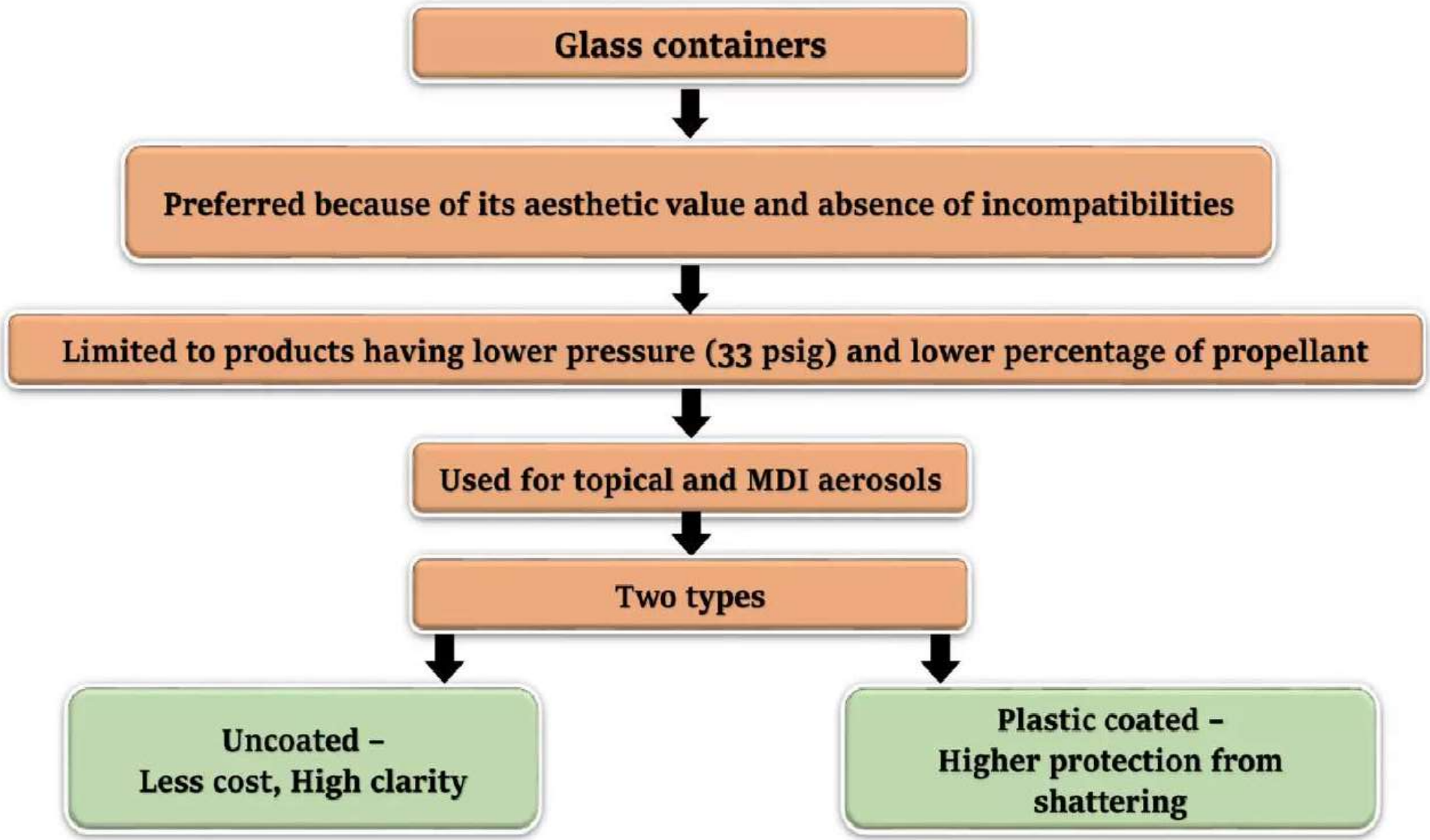
- All propellants are designated by **three** digits
- When the first digit is zero, the propellant is designated by last two digits
- Example – Propellant 011 is Propellant 11
- The first digit is one fewer than the number of carbon atoms in the compound
- First digit – Zero indicates methane derivative
- First digit – One indicates Ethane derivative
- First digit – Two indicates Propane derivative
- The second digit is one more than the number of hydrogen atoms in the compound
- For cyclic compounds a "C" is used before the number

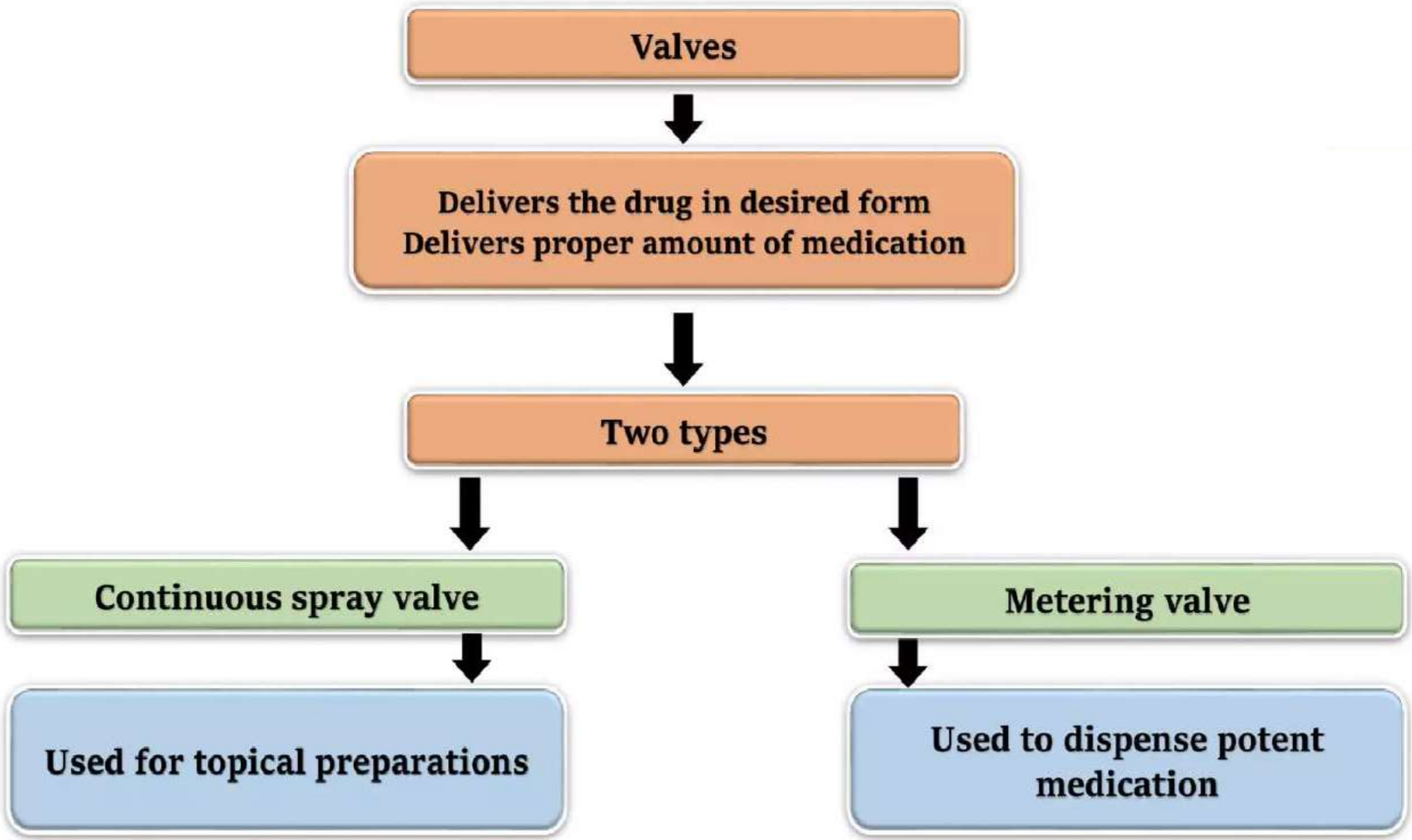

Containers
Must withstand pressure as high as 140 to 180 psig at 130 degree F
Two types
Metals
Glass
Tinplated
Aluminium
Stainless steel
Uncoated
Plastic coated

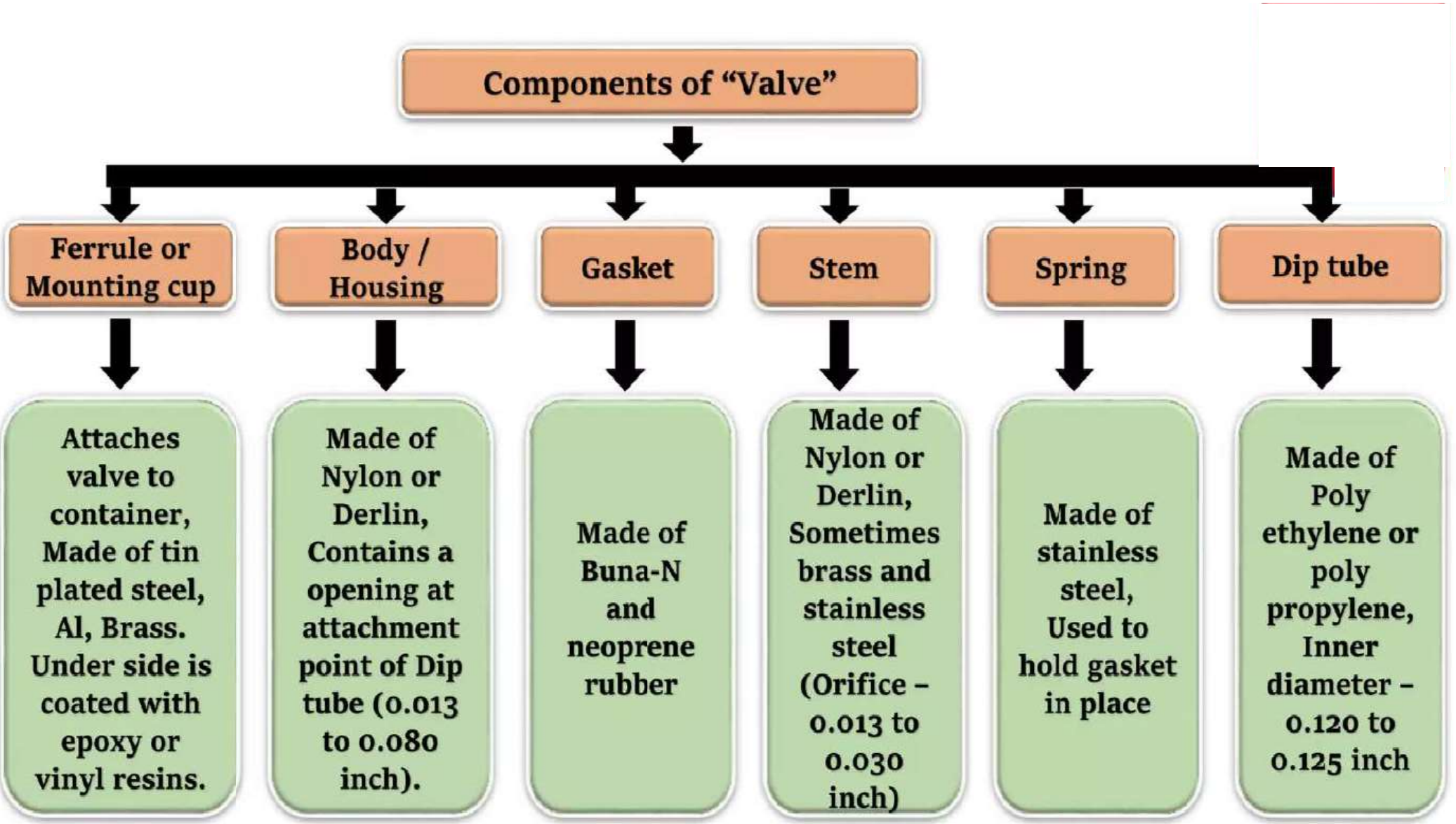

Tin plated steel containers
Consist of a sheet of steel plate, the sheet is coated with tin by electrolytic method
Coated Sheet
Divided into three parts
If required
Top
Bottom
Body
Attached to body by shouldering
Coated with –
Organic material usually oleoresin, phenolic, vinyl or epoxy coating

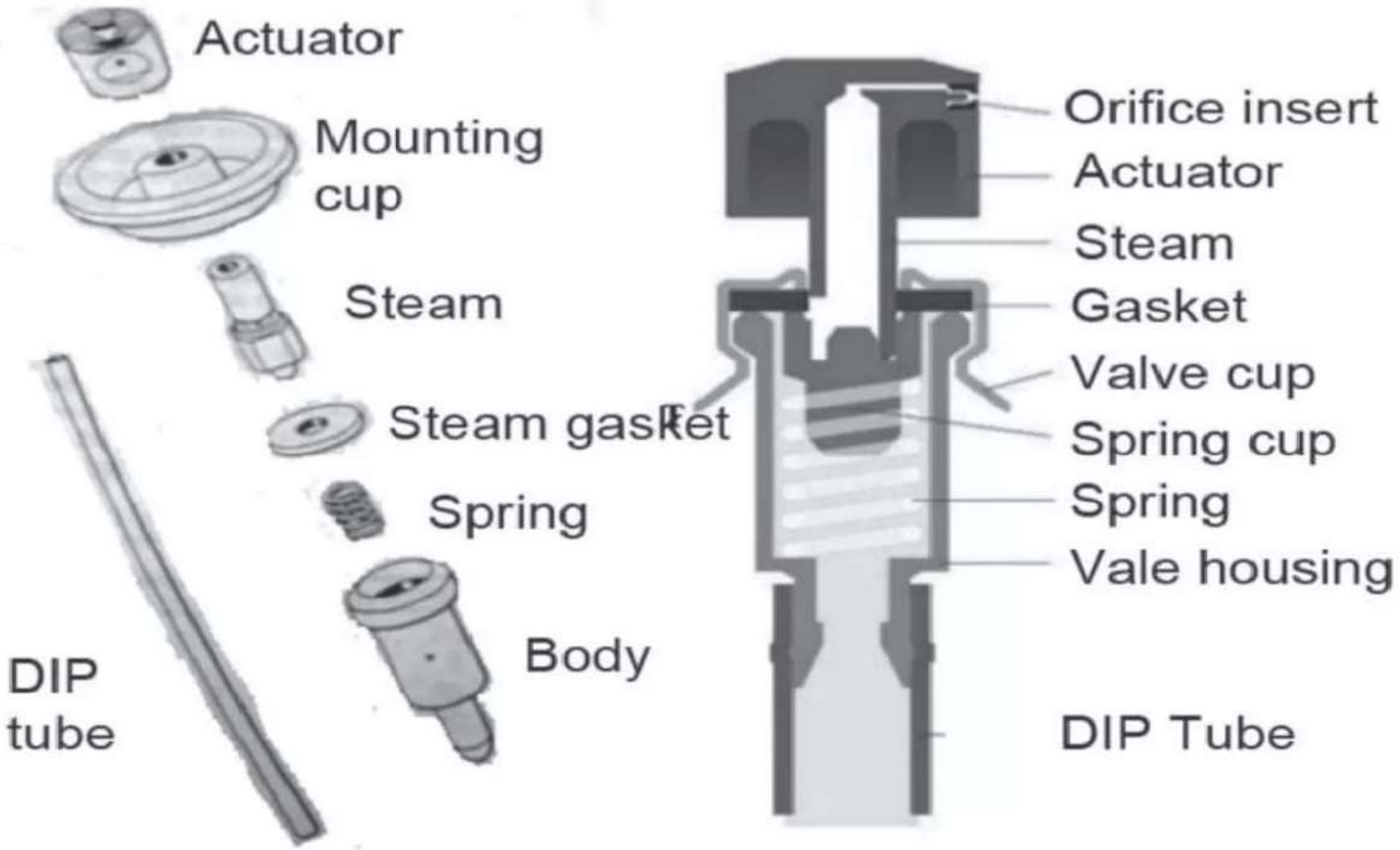

Aluminium Containers
Used for inhalational and topical aerosols
Manufactured by impact extrusion process
Light in weight, Less fragile, reduced incompatibility instances, greater resistance to corrosion
Pure water and ethanol cause corrosion
Added resistance can be obtained by coating with organic coat
Phenolic
Vinyl
Epoxy
Polyamide resins

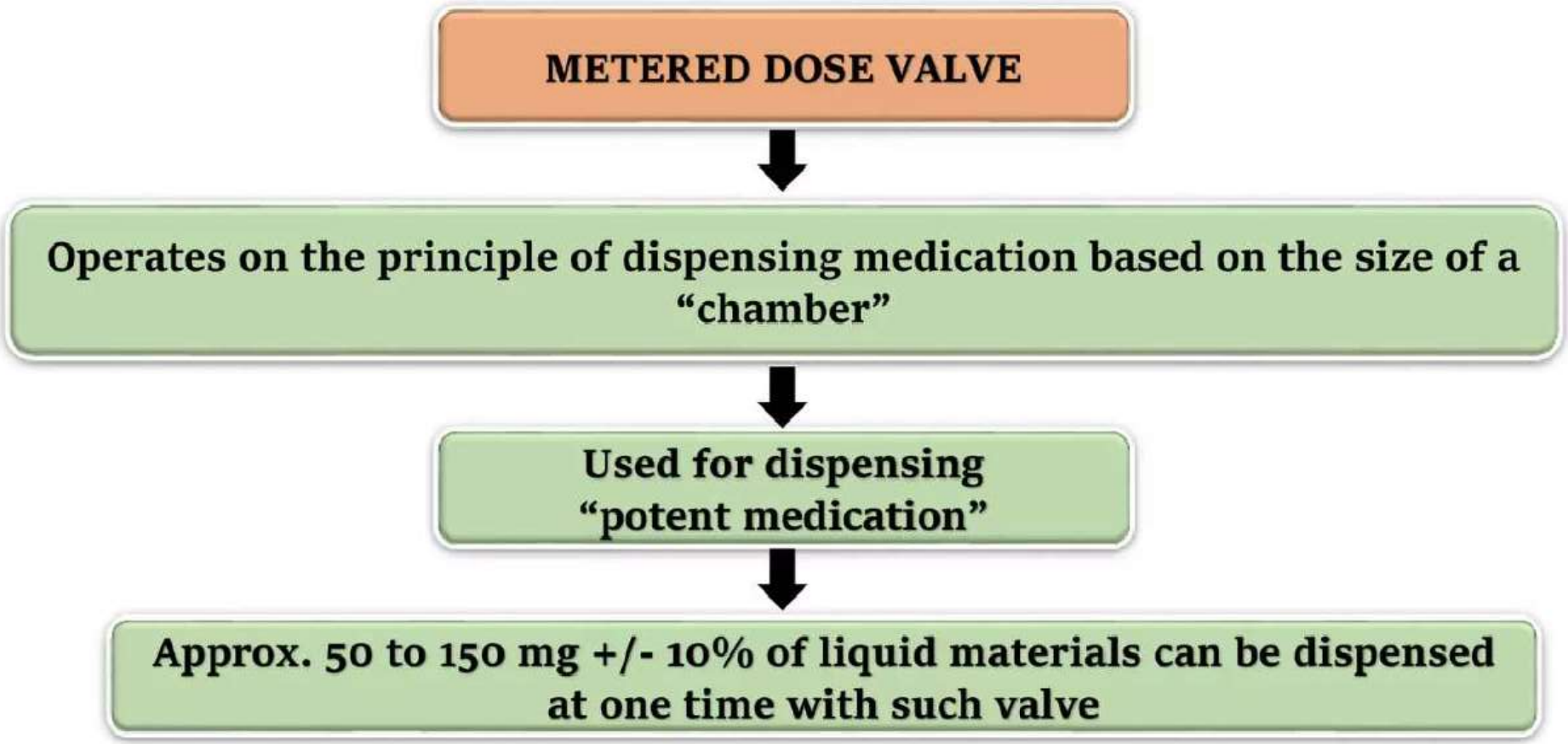

Stainless Steel Containers
Used for "Inhalational" aerosols
Advantages –
Extremely strong
Resistant to many materials
No need for internal coating
Disadvantages –
Costly
Higher molding force needed

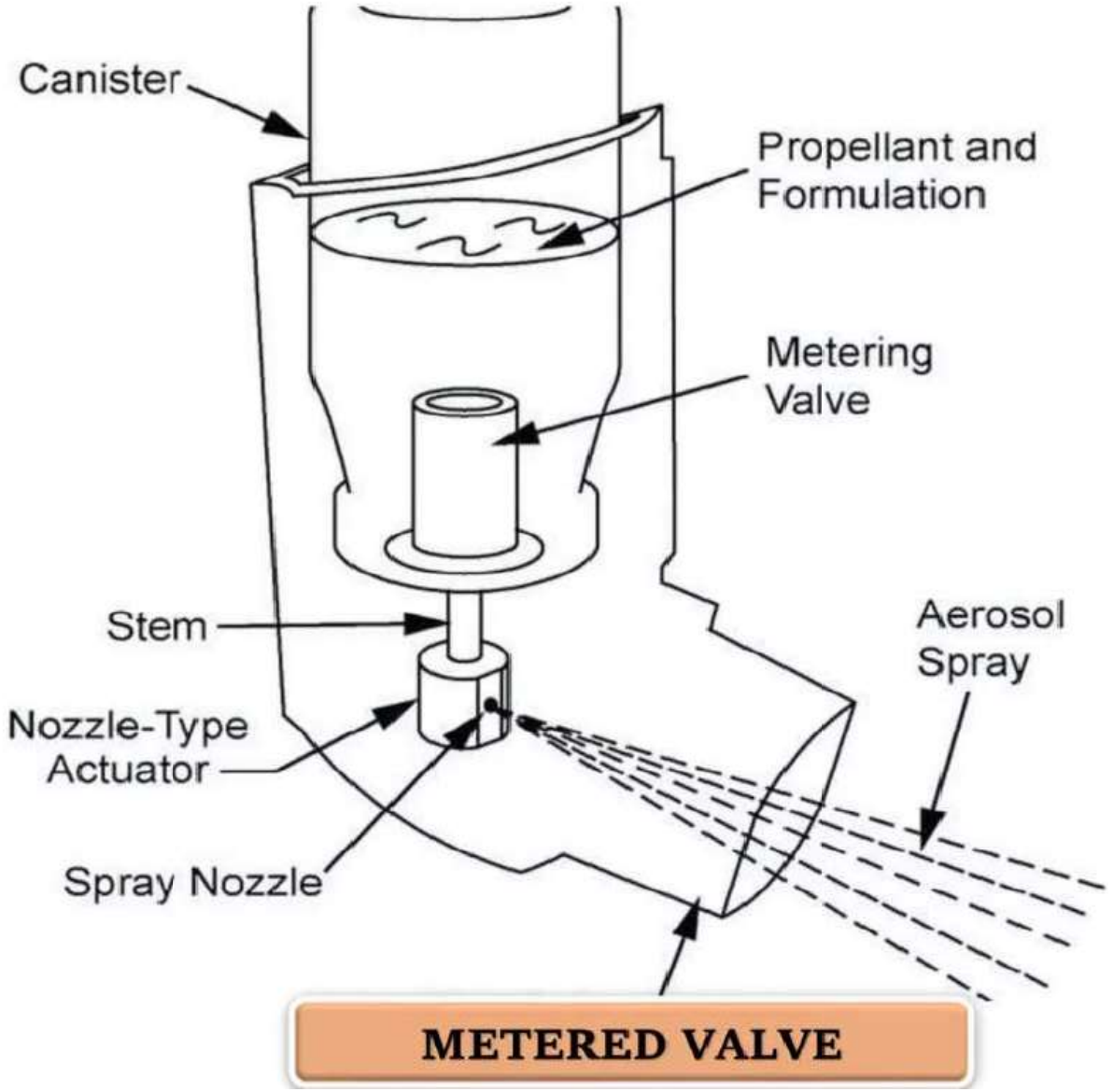

Glass containers
Preferred because of its aesthetic value and absence of incompatibilities
Limited to products having lower pressure (33 psig) and lower percentage of propellant
Used for topical and MDI aerosols
Two types
Uncoated –
Less cost, High clarity
Plastic coated –
Higher protection from
shattering

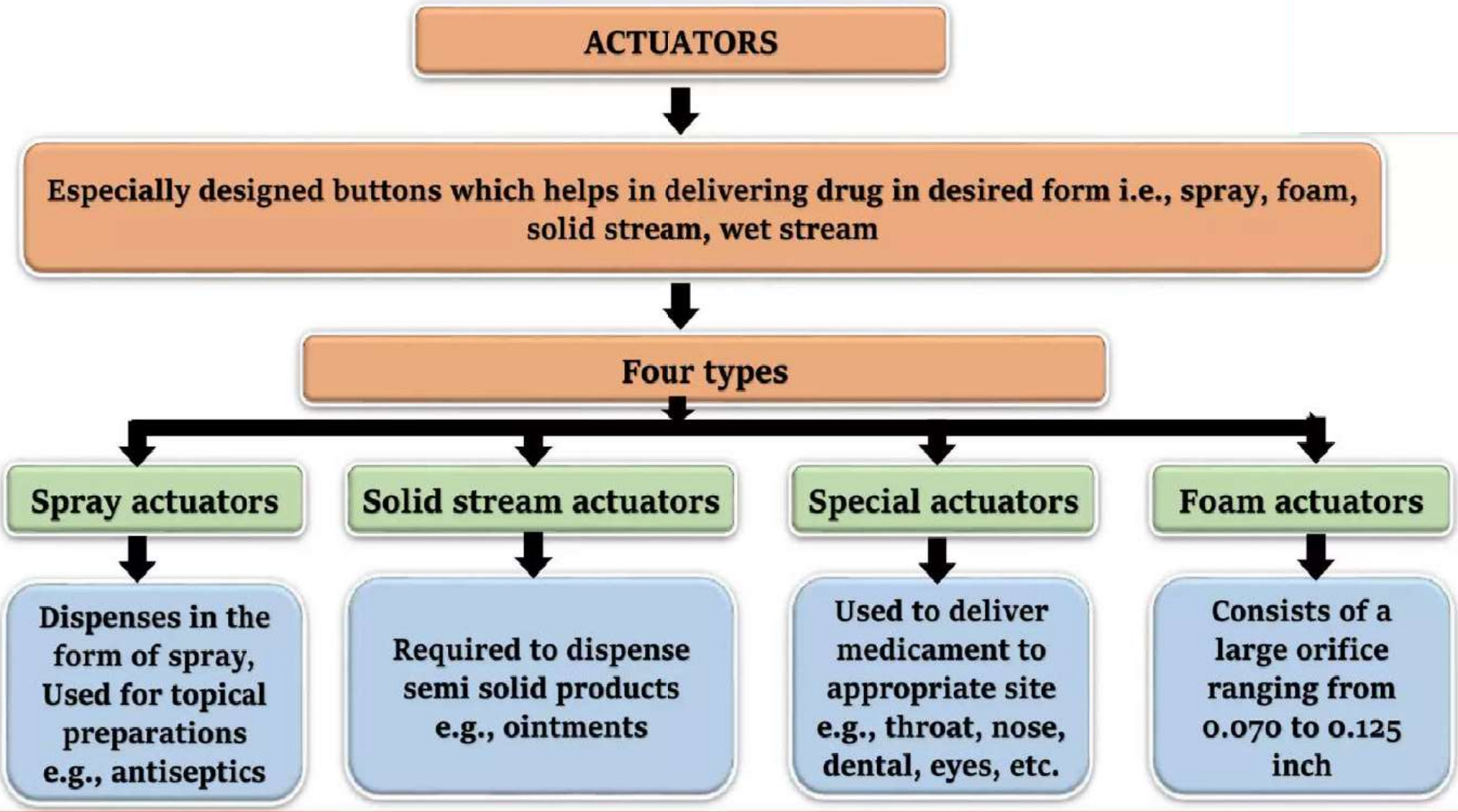

Valves
Delivers the drug in desired form
Delivers proper amount of medication
Two types
Continuous spray valve
Used for topical preparations
Metering valve
Used to dispense potent medication

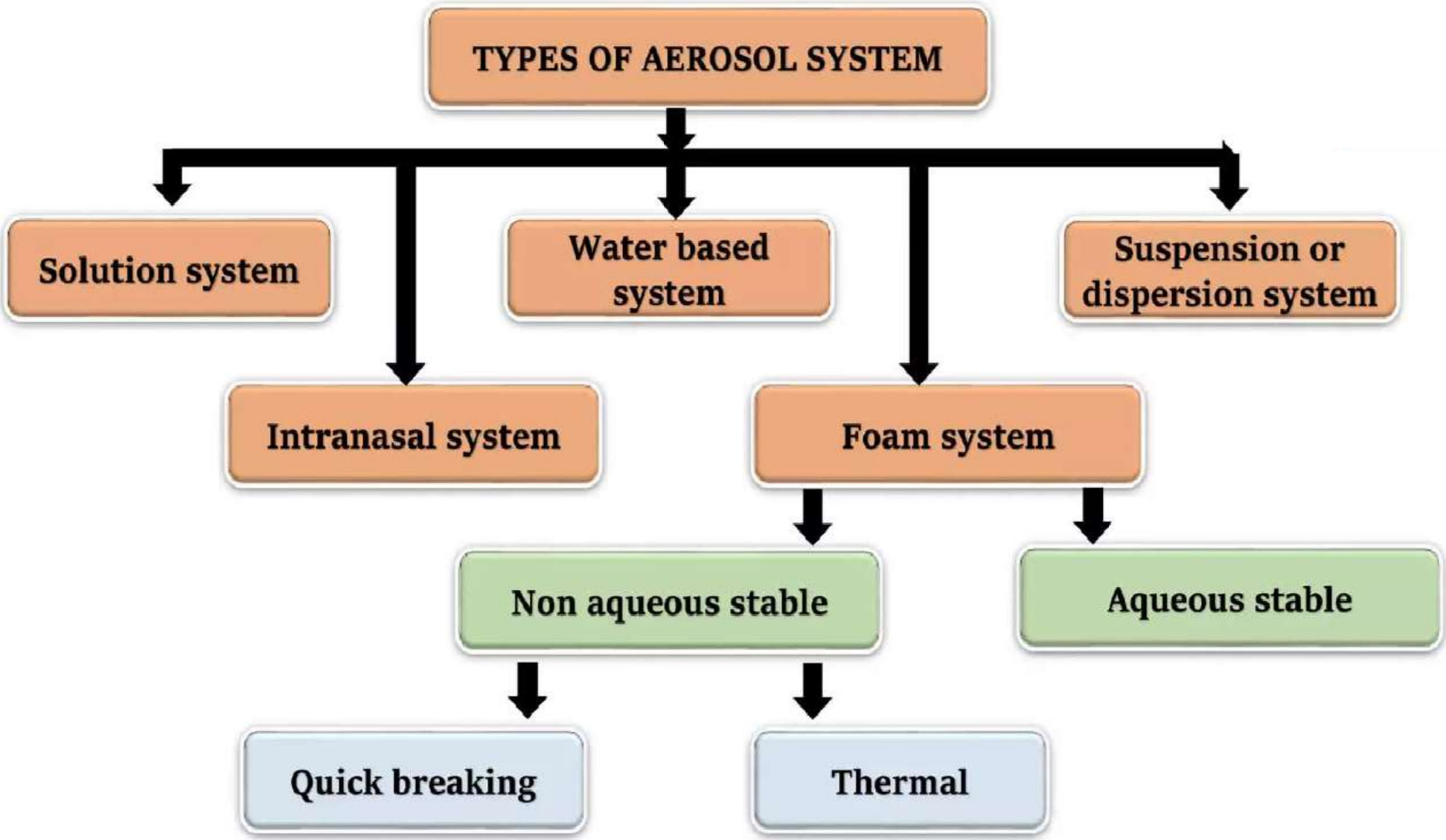

Components of "Valve"
Ferrule or Mounting cup
Attaches valve to container, Made of tin plated steel, Al, Brass. Under side is coated with epoxy or vinyl resins.
Body / Housing
Made of Nylon or Derlin, Contains a opening at attachment point of Dip tube (0.013 to 0.080 inch).
Gasket
Made of Buna-N and neoprene rubber
Stem
Made of Nylon or Derlin, Sometimes brass and stainless steel (Orifice – 0.013 to 0.030 inch)
Spring
Made of stainless steel, Used to hold gasket in place
Dip tube
Made of Poly ethylene or poly propylene, Inner diameter – 0.120 to 0.125 inch


Actuator
Mounting cup
Steam
Steam gasket
Spring
Body
DIP tube
Orifice insert
Actuator
Steam
Gasket
Valve cup
Spring cup
Spring
Vale housing
DIP Tube


METERED DOSE VALVE
Operates on the principle of dispensing medication based on the size of a "chamber"
Used for dispensing "potent medication"
Approx. 50 to 150 mg +/- 10% of liquid materials can be dispensed at one time with such valve


Canister
Propellant and Formulation
Metering Valve
Stem
Aerosol Spray
Nozzle-Type Actuator
Spray Nozzle
METERED VALVE


ACTUATORS
Especially designed buttons which helps in delivering drug in desired form i.e., spray, foam, solid stream, wet stream
Four types
Spray actuators
Solid stream actuators
Special actuators
Foam actuators
Dispenses in the form of spray, Used for topical preparations e.g., antiseptics
Required to dispense semi solid products e.g., ointments
Used to deliver medicament to appropriate site e.g., throat, nose, dental, eyes, etc.
Consists of a large orifice ranging from 0.070 to 0.125 inch


TYPES OF AEROSOL SYSTEM
Solution system
Water based system
Suspension or dispersion system
Intranasal system
Foam system
Non aqueous stable
Aqueous stable
Quick breaking
Thermal

Solution system

- Also referred as "**Two phase system**"
- Consists of vapor and liquid phase
- If active ingredient is soluble in propellant no other solvent is needed
- Vapor pressure of system is reduced by addition of less volatile solvents such as –

  Ethanol, Acetone, Propylene glycol, Glycerin
- Amount of propellant may vary from 5% (for foams) to 95% (for inhalations)
- **General formula** **Weight %**

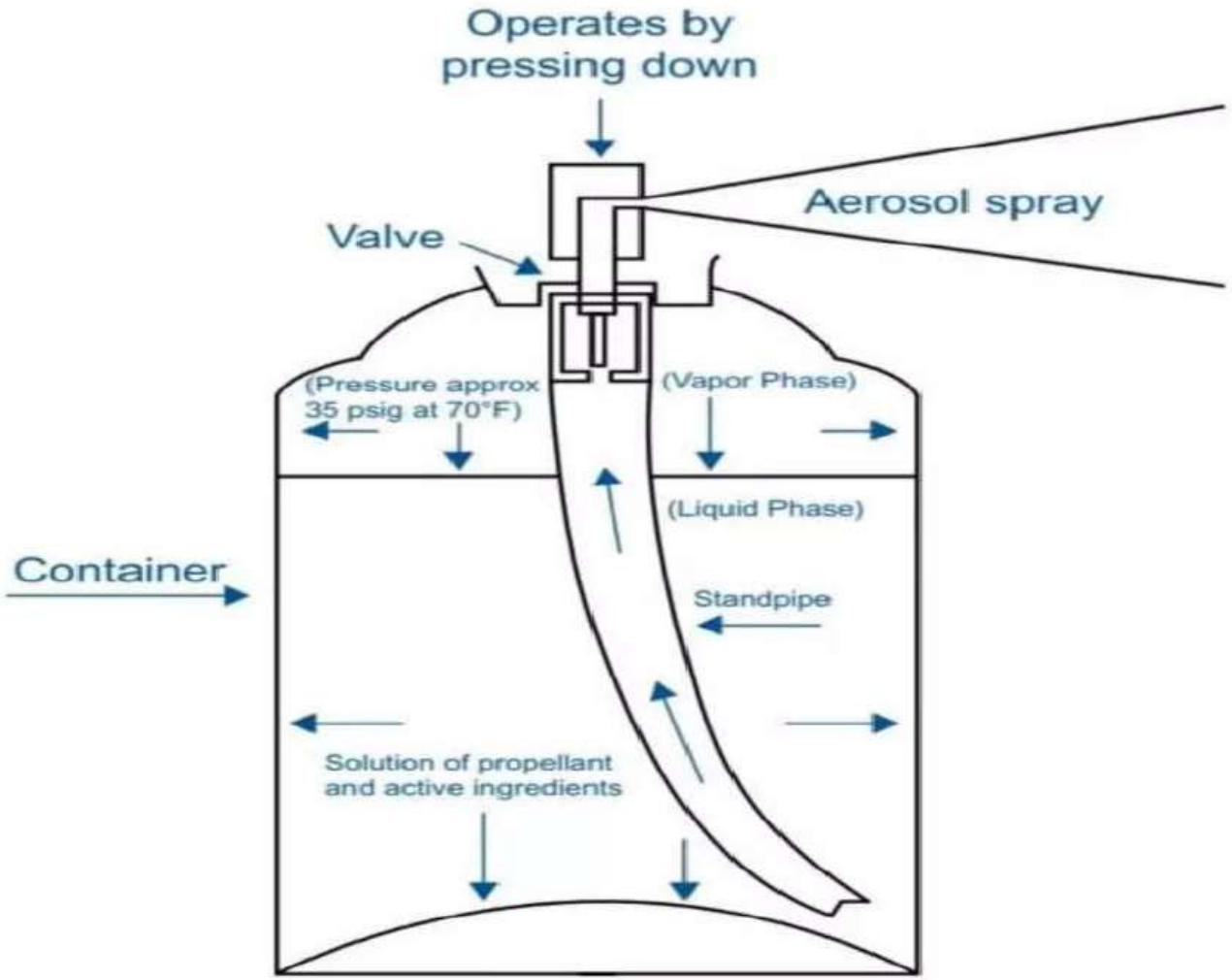
  Active drug to 10-15

  Propellant 12/11 (50:50) to 100

Contd.

- Depending on water content, final product may be solution or three phase system
- Solution aerosols produce a fine to coarse spray
- Hydrocarbon propellant **A-70** produces drier particles
- Hydrocarbon propellant **A-17** and **A-31** tend to produce a wetter spray
- Useful for topical preparations
- Packaged in plastic coated glass containers

SOLUTION SYSTEM



Water based system

- Large amounts of water can be used to replace all or part of non aqueous solvent
- Spray or foam is produced
- For spray production formulation must consist of dispersion of API and other solvents in **emulsion system** with propellant as external phase
- Since propellant and water are not miscible, a three phase aerosol forms (propellant, water and vapor phases).
- Ethanol can be used as cosolvent to solubilize propellant in water. It also reduces surface tension aiding in the production of smaller particles .
- 0.5 to 2% of surfactant is used to produce a homogenous dispersion.

Contd.

- Surfactants with low water solubility and high solubility in non polar solvents will be most useful e.g., Long chain fatty acid esters of polyhydric compounds including glycol, glycerol and sorbitan esters of oleic, stearic, palmitic and lauric acids
- Propellant concentration varies from about 25 to 60%
- Aquasol system (Aquasol valve) – dispensing fine mist or spray of active ingredient dissolved in water
- No chilling effect, since only active ingredient and water are dispensed, propellant is in vapor state
- Difference between aquasol system and three phase system is aquasol dispenses fairly dry spray with very small particles, non flammability of the product .