

# **General Requirements for Pharmaceutical Preparations**



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## General Requirements for Pharmaceutical Preparations

General rules for preparations prescribe general definition, preparing method and storage conditions. Name of preparations in monographs are determined appropriately according to description and use, in combinations of dosage forms, functions and administration routes and etc. that follow the general rules of preparation

### 1. Aerosols

- 1) Aerosols are preparations for use by expelling active substances under a pressure of liquefied or compressed gas filled in a common or different container. Modes of expelling are available in vapor, powder, foam, and paste, etc., depending on the purpose of use.
- 2) Aerosols are usually prepared by dissolving or suspending active substances in a vehicle, filling with liquefied propellants in pressure-resistant containers, and setting a continuous spray valve. If necessary, dispersing agents and stabilizers may be used.
- 3) If necessary, flavoring agents, aromatic agents, preservatives, buffering agents, solubilizers, emulsifiers, suspending agents, or other suitable excipients may be added.
- 4) For metered-dose type preparations among the aerosol preparations, unless otherwise specified, it has an appropriate uniformity of delivered dose.
- 5) Pressure-resistant hermetic containers are used for preservation.

### 2. Aromatic Waters

- 1) Aromatic Waters are clear saturated solutions of essential oils or other volatile substances in water.
- 2) Unless otherwise specified, Aromatic Waters may be usually prepared by the following process. Shake thoroughly 2 mL of an essential oil or 2 g of a volatile substance with 1000 mL of luke-warm purified water for 15 minutes, set the mixture aside for 12 hours or longer, filter through moistened filter paper, and add purified water to make 1000 mL. Alternatively, incorporate thoroughly 2 mL of an essential oil or 2 g of volatile substances with sufficient refined siliceous earth or pulped filter-paper, add 1000 mL of purified water, agitate thoroughly for 10 minutes, and then filter the mixture. To obtain a clear filtrate, repeat the filtration, and add sufficient water through the filter paper to make 1000 mL.

- 3) Aromatic Waters have odor and taste derived from the drugs used.
- 4) Tight containers are used for preservation.

### 3. Capsules

- 1) Capsules are solid preparations in which liquefied, suspended, semi-solid, powdered or granulated drugs or preparations are enclosed in capsules or wrapped with capsule bases, which are intended for oral administration.
- 2) There are two kinds of capsules, which are hard capsules and soft capsules.
  - (1) Hard capsules: Drug substances or uniform mixtures of drug substances with diluents and other suitable excipients, or granules or preparations prepared by a suitable method, are filled as they are or prepared lightly formed and into hard capsules.
  - (2) Soft capsules: Drug substances or mixtures of drug substances with suitable diluents, etc. are enclosed by a suitable capsule such as gelatin plasticized by addition of glycerin, sorbitol, etc., and molded in a suitable shape.
- 3) If necessary, coloring agents, preservatives, etc. may be added to capsule agents. By changing the components of capsule shells or applying suitable coating agents to capsules, extended-release or enteric-coated capsules can be prepared.
- 4) Unless otherwise specified, Capsules meet the requirements of the Uniformity of Dosage Units.
- 5) Unless otherwise specified, Capsules meet the requirements of the Disintegration Test or the Dissolution Test.
- 6) Well-closed are used for preservation.

### 4. Cataplasmas

- 1) Cataplasmas are pasty preparations containing the mixture of drug substances and water or those prepared by spreading the mixture on cloth, which are intended for external application to supply moist warmth.
- 2) Cataplasmas are usually prepared by mixing active substances with glycerin, purified water, or other suitable liquid materials or mix with high-molecular-mass materials which are soluble in water or absorbent of water until homogeneity is attained and spread it on a cloth and cut it into a given size.
- 3) Cataplasmas which have separated out one or more of their components during storage are re-homogenized before use unless the ingredients have deteriorated.
- 4) Cataplasmas have a suitable viscosity for application to the skin.
- 5) Tight containers are used for preservation.

## 5. Creams

- 1) Creams are external preparations in semi-solid emulsions of water-in-oil or oil-in-water type which is applied to skin, oral mucosa, around or inside of the anus. Hydrophobic preparations in the form of water in oil emulsions may be termed "Oily creams."
- 2) Creams are usually prepared by mixing homogeneously and emulsifying an oil phase component and a water phase component, both warmed, of which either one contains the active substances. These components have the following constituents. Oil-phase component: Vaseline, fatty alcohols, etc., with or without emulsifying agent(s) or other suitable excipients. Water-phase component: Purified Water with or without emulsifying agent(s) or other suitable excipients.
- 3) In creams, sufficient amount of preservations can be added to preparations filled in multiple dose containers, in order to prevent the growth of microorganisms.
- 4) Creams have a suitable viscosity for applying to the skin, oral mucosa, or inside of the anus.
- 5) Tight containers are used for preservation.

## 6. Decoctions and Infusions

- 1) Decoctions and Infusions are liquid preparations usually obtained by macerating herbal drugs in purified water.
- 2) Decoctions and Infusions are usually prepared by the following method. Cut herbal drugs as directed below, and transfer to a decoctions and infusions apparatus.

Leaves, flowers, and whole parts of plants: Coarse cutting.

Lignum, caulis, barks, roots, and rhizomes: Medium cutting.

Seeds and fruits: Fine cutting.

(1) Decoctions: Usually, Heat one-day dose of herbal drugs with 400 - 600 mL of purified water until to lose about a half amount of added water spending more than 30 minutes, and filter through cloth while warm.

(2) Infusions: Damp 50 g of herbal drugs with 50 mL of purified water for about 15 minutes, pour 900 mL of hot purified water, and heat for 5 minutes with several shakings. Filter through cloth after cooling. Prepare Decoctions and Infusions before use.

- 3) Decoctions and Infusions have odor and taste derived from the herbal drugs used.
- 4) Tight containers are used for preservation.

## 7. Dialysis Solutions, Dialysis Agents

- 1) Dialysis Agents are preparations in liquid, or in solid which are to be dissolved before use, and are intended for peritoneal dialysis or hemodialysis.
- 2) Unless otherwise specified, Dialysis Agents meet the requirements of Bacterial Endotoxins Test. Pyrogen Test may be applied instead of Bacterial Endotoxins Test, when it is not applicable. In this case, unless otherwise specified, use 10 mL of the preparation per 10 kg of the body weight of the rabbit.
- 3) If necessary, pH adjusting agents, isotonic agents or other excipients may be added.
- 4) Unless otherwise specified, the vehicle used for Peritoneal dialysis agents is Water for Injection
- 5) Unless otherwise specified, the solid preparations among Dialysis agents, which are to be dissolved before use, meet the requirements of the Uniformity of Dosage Units
- 6) Dialysis Agents are classified into Preritoneal dialysis agents and Hemodialysis agents.

### Peritoneal Dialysis Solutions, Peritoneal Dialysis Agents

- (1) Peritoneal Dialysis Agents are preparations in liquid (of aseptic condition), or in solid which are to be dissolved before use, and are intended for peritoneal dialysis.
- (2) Peritoneal Dialysis Agents are usually prepared by dissolving active substances with suitable excipients in a vehicle to make a certain volume, or by filling active substances combined with suitable excipients in a container, and sealing it. Sterilize if necessary. Every care should be taken to prevent microbial contamination. The overall processes for preparation to sterilization for preparing the agents should be completed as rapidly as possible, taking into consideration the composition of the agents and the storage conditions. The concentration of Peritoneal Dialysis Agents expressed in % represents W/v%. In the case of solid preparations which are dissolved before use, prepare as directed Tablets or Granules.
- (3) Unless otherwise specified, Peritoneal Dialysis Agents meet the requirements of Sterility Test.
- (4) Unless otherwise specified, volume of medical fluid of Peritoneal Dialysis Agents meets the requirements of Parenteral infusion under Determination of Volume of Injection in Containers. The mass(g) of content may convert to the volume(mL) by dividing by the density.

- (5) Unless otherwise specified, Peritoneal Dialysis Agents meet the requirements of Foreign Insoluble Matter Test for Injections.
- (6) Unless otherwise specified, Peritoneal Dialysis Agents meet the requirements of Insoluble particulate Matter Test for Injections.
- (7) Peritoneal Dialysis Agents meet the requirements of Test for Glass Containers for Injections and Test Methods of Plastic Containers may be used.
- (8) Unless otherwise specified, the rubber closures of the containers meet the requirements of Test for Rubber Closure for Aqueous Infusions.
- (9) Hermetic containers or tight containers which are able to prevent microbial contamination are usually used for Peritoneal Dialysis.

#### Hemodialysis Solutions, Hemodialysis Agents

- (1) Dialysis Agents are preparations in liquid or in solid which are to be dissolved before use, intended for hemodialysis.
- (2) Hemodialysis Agents are usually prepared by dissolving active substances with suitable excipients in a vehicle to make a certain volume, or by filling active substances combined with suitable excipients in a container. In the case of solid preparations which are dissolved before use, prepare as directed Tablets or Granules.
- (3) Tight containers which are able to prevent microbial contamination are usually used for Hemodialysis Agents.

## 8. Elixirs

- 1) Elixirs are clear, sweetened, and aromatic liquid preparations, containing ethanol, intended for oral use.
- 2) Elixirs are usually prepared by dissolving drug substances or their extractives in ethanol, purified water, aromatic agents, sucrose, other sugars or sweetening agents, and clarifying by filtration or other procedures. If necessary, preservatives, solubilizers, coloring agents, etc., may be added.
- 3) Unless otherwise specified, Elixirs packaged in unit-dose containers meet the requirements of the Test for Uniformity of Dosage Units.
- 4) Tight containers are used for preservation.

## 9. Emulsions

- 1) Emulsions are liquid preparations of finely divided drugs emulsified.
- 2) Emulsions are prepared by adding emulsifying agents and purified water to liquid drug substances, and emulsifying to complete uniformity by a suitable method.

If necessary, preservatives, stabilizers, etc. may be added. Prepare before use in the case of Emulsions or Suspensions which are apt to deteriorate.

- 3) Mix uniformly before use, if necessary.
- 4) Unless otherwise specified, Emulsions packaged in unit-dose containers meet the requirements of the Test for Uniformity of Dosage Units. However, this test does not apply for local administration of external preparations to skin.
- 5) Tight containers are used for preservation.

## 10. Extracts

- 1) Extracts are usually prepared by concentrating extractives of herbal drugs. There are two kinds of Extracts which are Viscous extracts and Dry extracts
- 2) In the manufacture of Extracts, unless otherwise specified, herbal drugs, in coarse powder, are usually extracted for a certain period of time with suitable solvents by cold extraction or by warm extraction, or by percolation as directed in 2) under Tinctures. The extractive is filtered, and the filtrate is concentrated or dried by a suitable method to produce a millet jelly-like consistency in the case of viscous extract, and to make crushable solid masses, granules or powder in the case of Dry extract.  
Extracts for which the content of the active principle is specified are prepared by assaying the active principle in a sample portion and adjusting, if necessary, with suitable diluents to the specified strength.
- 3) Extracts have odor and taste derived from the herbal drugs used.
- 4) Unless otherwise specified, Extracts meet the requirements when proceed with Method 5 of the Heavy Metals Limit Test.
- 5) Tight containers are used for preservation.

## 11. Fluid Extracts

- 1) Fluid Extracts are liquid percolates of herbal drugs, usually prepared so that each mL contains soluble constituents from 1 g of the herbal drugs.
- 2) Fluidextracts are usually prepared from coarse powder or fine cutting of herbal drugs by either of following maceration or percolation.  
(1) Maceration : Place a certain amounts of herbal drugs in a suitable vessel, add a solvent to cover the herbal drugs, close the vessel, and allow the vessel to stand at room temperature with occasional stirring for about 5 days or until the soluble constituents have satisfactorily dissolved. Separate the solid and liquid by centrifugation or other suitable method. Usually, reserve a volume of the liquid equivalent to about three-fourths of the total

volume, and use it as the first liquid. Wash the residue with appropriate amount of the solvent, combine the washings and the remaining of the first liquid, concentrate if necessary, mix with the first liquid, and use it as solution (A). To the solution (A) add the solvent, if necessary, to make equal amount of the mass of the herbal drugs. Allow the mixture to stand for about 2 days, and collect a clear liquid by decantation or filtration.

(2) Percolation : Mix well 1 kg of coarse powder or fine cutting of the herbal drugs with the first solvent to moisten it, close the container, and allow it to stand for about 2 hours at room temperature. Transfer the content to a suitable percolator, stuff it as tightly as possible, open the lower opening of the percolator, and slowly pour the second solvent to cover the herbal drugs. Close the lower opening when the solvent begins to drop, and allow the mixture to stand for 2 to 3 days at room temperature. Open the lower opening, and allow the percolate to run out at the rate of 0.5 to 1.0 mL per minute. Set aside the first 850 mL as the first percolate. Add the second solvent to the percolator, then drip the percolate, and use it as the second percolate. The time of maceration and the flow rate during percolation may be varied depending on the kind and the amount of the herbal drugs used. The flow rate is usually regulated as follows, depending on the amount of the herbal drugs used.

| Mass of herbal drugs | Volume of solution running per minute |
|----------------------|---------------------------------------|
| Not more than 1 kg   | 0.5 to 1.0 mL                         |
| Not more than 3 kg   | 1.0 to 2.0 mL                         |
| Not more than 10 kg  | 2.0 to 4.0 mL                         |

Concentrate the second percolate, taking care not to lose the volatile ingredients of the herbal drug, mix with the first percolate, and use it as (A). To (A), add second solvent to make 1000 mL, and allow the mixture to stand for 2 days. Decant the supernatant liquid or filter the liquid to obtain a clear solution. Fluidextracts for which the content of marker constituent or ethanol is specified are obtained by adjusting the content with a sufficient amount of the second solvent as required on the basis of the result of the assay made with a portion of the solution (A).

- 3) Fluid Extracts have odor and taste derived from the herbal drugs used.
- 4) Unless otherwise specified, Fluid Extracts meet the requirements when proceed with Method 5 of the Heavy Metals Test.
- 5) Tight containers are used for preservation.

## 12. Gargles

- 1) Gargles are liquid preparations intended to apply locally to the oral and throat cavities. Solid type preparations to be dissolved in water before use are also included in the category.
- 2) Gargles are usually prepared by dissolving Drug substances with suitable excipients in a solvent together with suitable excipients and filtering. In the case of solid preparations which are dissolved before use, prepare as directed Tablets or Granules.
- 3) Tight containers are used for preservation.

## 13. Gels

- 1) Gels are external preparations consisting organic macro-molecules that inter-penetrated by a liquid. This liquid is applied to skin, oral mucosa, around or inside of the anus. Gels can be either aqueous or oily.
  - (1) Aqueous Gel : To drug substances add polymers, other excipients and Purified Water, dissolve or suspend, and gelatinize by warming and cooling or by adding a gelatinizing agents.
  - (2) Oily Gel : To drug substances add liquid oily bases such as glycols, fatty alcohols and other excipients, and mix.
- 3) In gels, sufficient amount of preservations can be added to preparations filled in multiple dose containers, in order to prevent the growth of microorganisms.
- 4) Gels have a suitable viscosity for applying to the skin, oral mucosa, or inside of the anus.
- 5) If necessary, Gels are shaken well before use.
- 6) Tight containers are used for preservation.

## 14. Granules

- 1) Granules are granular preparations prepared by granulation, intended for oral administration.
- 2) Granules are usually prepared by the following methods. Granules can be coated using suitable coating agents if necessary. Extended release or enteric coated granules can also be prepared by a suitable method
  - (1) To powdery drug substances add diluents, binders, disintegrators, or other suitable excipients, mix to homogenize, and granulate by a suitable method
  - (2) To previously granulated drug substances add excipients such as diluents, and mix to homogenize.



- (3) To previously granulated drug substances add excipients such as diluents, and granulate by a suitable method.
- 3) Granules meet the requirements of the Particle Size Distribution Test.
- 4) Unless otherwise specified, Granules packaged in unit-dose containers meet the requirements of the test for Uniformity of Dosage Units.
- 5) Unless otherwise specified, granules meet the requirements of the Dissolution Test or the Disintegration Test, provided that this provision does not apply to granules under the application of the Dissolution Test and to those not more than 5 % of which remain on a No. 30 (500  $\mu\text{m}$ ) sieve as directed in Particle Size Distribution Test.
- 6) Well-closed are used for preservation.
- 7) These preparations including effervescent granules, each disintegration test and migration test that is suitable to its properties has to be regulated separately.

#### Effervescent Granules

- (1) Effervescent granules are granules which are quickly dissolved or dispersed with bubbles in water.
- (2) Effervescent granules are usually prepared using suitable acidic substances and carbonates or hydrogen carbonates.

## 15. Implants

- 1) Implants are aseptic preparations intended to be administered by a special injection or a surgical operation, and to be prepared by compressing or molding purified drugs into a desired shape.
- 2) Preparations are usually prepared by the following procedures.
  - (1) Drug substances are first rendered granular by a suitable method with or without uniform admixture with diluent, binder, or other suitable excipients. The resulting granules are compressed into a desired shape and size, and then sterilized.
  - (2) Implants may be prepared either by direct compression of drug substances only or uniform admixture with binder, disintegrator and other suitable excipients, or by compression after drug substances with or without suitable excipients have been added to previously prepared inactive granules.
  - (3) Implants may be prepared by drying and sterilizing the admixture by a suitable method after forming or molding drug substances, uniformly mixed with diluent, binder and other suitable excipients and dampened with a wetting agent, into a desired shape and size.
- 3) Unless otherwise specified, preparations meet the Sterility Test.

- 4) Unless otherwise specified, preparations meet the requirement of the Uniformity of Dosage Units.
- 5) Implants have an appropriate function of release
- 6) Hermetic containers or tight containers which are able to prevent microbial contamination are used for preservation.

## 16. Inhalations

- 1) Inhalations are preparations containing drug substances solubilized or suspended in an appropriate excipient, administered in vapor-phase, particulate-phase or aerosol-phase by the nasal or oral respiratory.
- 2) If necessary, propellants, additives for dissolution, diluents, preservatives, solubilizers, dispersing agents, isotonic agents, pH adjusting agents, stabilizers, and other suitable excipients etc. may be added to Inhalations.
- 3) Tight containers or Pressure-resistant hermetic containers are used for preservation.

## 17. Injections

- 1) Injections are sterile preparations to be administered directly into the body through skin, muscle or blood vessel, usually in form of solutions, suspensions or emulsions of drugs substances, or of a solid that contains drugs substances to be dissolved or suspended before use.
- 2) Injections in solution, suspension or emulsion form are usually prepared by the following methods. Dissolve, suspend or emulsify active substances with or without excipients in Water for Injection or an aqueous or nonaqueous vehicle homogeneously.
  - (1) Fill into containers for injection, seal, and sterilize.
  - (2) Filtrate aseptically, or prepare aseptically a homogeneous liquid, fill into containers for injection, and seal.

Every care should be taken to prevent contamination with microorganisms. The entire process of preparing Injections from the preparation of the drug solution, to the sterilization, should be completed as rapidly as possible by taking into consideration of the composition of injection and the storage condition. The concentrations of Injections in terms of percentage (%) means w/v%.

Drugs to be dissolved or suspended before use and designated in the title as "for injection" may be accompanied by a suitable solvent or suspension medium.
- 3) Freeze dried Injection or Powder for Injection are usually prepared by the following methods.
 

Freeze dried injections : Freeze dried Injections are usually prepared by dissolving active sub-

stances with or without excipients such as diluents in Water for Injection, sterilizing the solution by aseptic filtration, filling the filtrate directly into individual containers for injection and being freeze dried, or dividing the filtrate in special containers, being freeze dried and transferred into individual containers for injection.

**Powders for Injections :** powders for injections are usually prepared by filtration aseptically a solution of active substances, obtaining powder by crystallization from the solution or mixing additionally the powders with sterilized excipients, and filling the powders into individual containers for injections

- 4) Ampule, vial, pre-filled syringe and cartridge (put cartridge filled with drug solution into a exclusive injection device for use) can be used for containers of Injections.
- 5) Solvents used in the preparation of Injections or attached to a suitable solvent or suspension medium must be harmless in the amounts usually administered and must not interfere with the therapeutic efficacy. The solvents are classified into the following two major groups. They meet the following requirements.
  - (1) Aqueous vehicles for the solvent of aqueous injections, Water for Injection is used. Isotonic Sodium Chloride Injection, Ringer's Solution or other suitable aqueous solutions may be used instead. Bacterial Endotoxins Test is not applicable, Pyrogen Test may be applied instead.
  - (2) Nonaqueous vehicles Vegetable oils are usually used as solvents for nonaqueous injections. These oils, unless otherwise specified, are clear at 10 °C, the Acid Value is not more than 0.56, the Saponification Value falls in the range between 185 and 200, and the Iodine Value is between 79 and 137. They meet the requirements of the Mineral Oil Test. Several suitable organic solvents other than the vegetable oils may be used as nonaqueous vehicles.
- 6) Unless otherwise specified, any coloring agent must not be added solely for the purpose of coloring the preparations.
- 7) Sodium chloride or other suitable excipients may be added to aqueous injections to render them isotonic with blood or other body fluids. Nontoxic and harmless acids or alkalis may be added to them to adjust the pH.
- 8) Unless otherwise specified, sufficient amounts of suitable preservatives to prevent the growth of microorganisms are added to Injections filled in multiple dose containers.
- 9) Unless otherwise specified, Injections or attached to a suitable solvent or suspension medium other than those used exclusively for intracutaneous, subcutaneous or intramuscular administration meet the requirements of the Bacterial Endotoxins Test. For aqueous vehicles for which endotoxin limits are not specified in the individual mono-

graphs, compliance with the Bacterial Endotoxins Test is not required. Bacterial Endotoxins Test is not applicable, Pyrogen Test may be applied instead.

- 10) Unless otherwise specified, Injections, and solvents attached to injections meet the requirements of the Sterility Test. As for Injections having a capacity of 50 mL or more, except Injections filled in multiple dose containers, unless otherwise specified, carry out the test according to the Membrane Filtration Method. In the case of drugs to be dissolved before use, carry out the test with the solution obtained by dissolving the contents in the attached solvent.
- 11) Usual containers of Injections are colorless and meet the requirements of Glass Containers for Injections. When specified in individual monograph, these containers may be replaced by colored containers meeting the requirements of Glass Containers for Injections or by plastic containers for aqueous injections meeting the requirements of the Test Methods for Plastic Containers.
- 12) Unless otherwise specified, rubber stoppers used for glass containers of 100 mL or more of aqueous infusions meet the requirements of Rubber Closures for Aqueous Infusions.
- 13) Unless otherwise specified, Injections or attached to a suitable solvent or suspension medium meet the requirements of the Injections of the Foreign Insoluble Matter Test.
- 14) Unless otherwise specified, Injections or attached to a suitable solvent or suspension medium meet the requirements of the Insoluble Particulate Matter Test for Injections.
- 15) Unless otherwise specified, the actual volume of an injection contained in a unit-dose container meets the requirements of Determination of Volume of Injection in Containers.
- 16) Unless otherwise specified, the written, printed, or graphic matter in the package, the container, or the wrapper include the following information:
  - (i) Names of employed vehicles and added substances, unless the vehicle is Water for Injection, or sodium chloride solution in concentrations not exceeding 0.9 w/v%, or unless the vehicle contains nontoxic and harmless acids or alkalis in order to adjust the pH of the injections.
  - (ii) In the case that dissolving vehicles are attached to the preparations, the presence of such vehicles and their names, quantities, compositions or ratios of the vehicles on the outer containers or outer wrappers.
  - (iii) Names and quantities of added stabilizers, preservatives, and diluents. In the case where nitrogen or carbon dioxide is enclosed in the container to replace the inside air, no statement of this replacement is necessary.
- 17) When information is printed directly on the surface of ampules or other containers of 2 mL or less or ampules or other containers of more than 2

mL and not more than 10 mL, made of glass or similar materials, the designations “injection”, “for injection” and “aqueous suspension for injection” may be replaced by “inj.” “for inj.” and “aq. susp. for inj.”, respectively.

- 18) Unless otherwise specified, the actual masses of drugs to be dissolved or suspended before use meet the requirements of the Uniformity of Dosage Units.
- 19) Suspensions for injection are not to be injected into the vessels or spinal cord, and emulsions for injection, not into the spinal cord.
- 20) The usual size of particles observed in suspensions for injection is not larger than 150  $\mu\text{m}$ , and that of particles in emulsions for injection is not larger than 7  $\mu\text{m}$ .
- 21) Hermetic containers are used for Injections.

## 18. Irrigations

- 1) Irrigations, intended to bathe or wash body cavities, open wounds or skin, are sterile aqueous solutions in large volumes.
- 2) Unless otherwise specified, Water for Injection is used to prepare Irrigations. If necessary, sodium chloride or other suitable excipients may be added to render them isotonic with blood or other bodily fluids. If necessary, nontoxic and harmless acids or alkalis may be added to them to adjust the pH.
- 3) Unless otherwise specified, suitable preservatives in an amount sufficient to prevent the growth of microorganisms are added to Irrigations intended for divided use.
- 4) Unless otherwise specified, Irrigations meet the requirement of the Bacterial Endotoxins Test. When not applicable, the Pyrogen Test may be alternatively used. In this case, unless otherwise specified, use 10 mL of the preparation per 10 kg of the body weight of the rabbit.
- 5) Unless otherwise specified, Irrigations meet the requirement of the Sterility Test.
- 6) Unless otherwise specified, Irrigations meet the requirement of the Determination of Volume of Injection in Containers.
- 7) Hermetic containers are used for preservation.

## 19. Liniments

- 1) Liniments are usually liquid or semisolid preparations intended for external application to the skin by inunction.
- 2) Unless otherwise specified, Liniments are usually prepared by adding active substances to water, ethanol, fatty oils, glycerin, soap, emulsifying agents, suspending agents, other suitable excipients or their mixtures, and kneading the mixture

until homogeneity is attained. If necessary, preservatives, aromatic agents, etc. may be added.

- 3) Liniments which have separated out one or more of their components during storage are rehomogenized before use unless the ingredients have deteriorated.
- 4) Tight containers are used for preservation.

## 20. Lotions

- 1) Lotions are external liquids in which active substances are dissolved, emulsified or finely dispersed in an aqueous vehicle.
- 2) Lotions are usually prepared by dissolving, suspending or emulsifying active substances in Purified Water with excipients and making homogeneous as a whole. If necessary, preservatives, aromatic substances, etc. may be added. Prepare before use in the case of Lotions which are apt to deteriorate.
- 3) Lotions which have separated out one or more of their components during storage are rehomogenized before use unless the ingredients have deteriorated.
- 4) Tight containers are used for preservation.

## 21. Medicated Chewing Gums

- 1) Medicated Chewing Gum is preparation that allows for active substance of the drug to be released with chewing.
- 2) Medicated Chewing Gum are usually prepared using suitable gum bases such as vegetable resin, thermoplastic resin and elastomer by the following methods.
  - (1) Melt gum base and mix with active substances and excipient such as sweetening agents, plasticizer, flavoring agents, etc., and form into a certain shape.
  - (2) Add active substances and excipients such as sweetening agents, plasticizer, flavoring agents to powdery gum base, mix homogeneously and then compress into a certain shape.
- 3) Unless otherwise specified, preparations meet the requirement of the Uniformity of Dosage Units.
- 4) Medicated Chewing Gum have an appropriate dissolution or disintegration
- 5) Well-closed containers are usually used for preservation.

## 22. Nasal Solutions

- 1) Nasal Solutions are liquid preparation applied to the nasal cavities or nasal mucous membrane, or solid preparation to be dissolved or suspended before use.

- 2) Nasal Solutions are usually prepared by dissolving or suspending active substances in a vehicle together with excipients, and filtering if necessary. Isotonic agents or pH adjusting agents may be used.
- 3) Nasal Solutions, which are to be dissolved or suspended before use and designated in the name as "for nasal application", may be accompanied by a vehicle to dissolve or suspend.
- 4) If necessary, Nasal Solutions are sprayed for inhalation by using a suitable atomizing device such as spray-pump.
- 5) Unless otherwise specified, metered-dose type preparations among Nasal Preparations show the appropriate uniformity of delivered dose.
- 6) Sufficient amounts of suitable preservatives to prevent the growth of microorganisms may be added to the preparations filled in multiple dose containers.
- 7) Tight containers are usually used for preservation.

### 23. Ointments

- 1) Ointments are semi-solid preparations which dissolve or disperse active substances that are applied to skin, oral mucosa, around or inside of the anus by inunction.  
There are two types, hydrophobic ointment and hydrophilic ointment.
- 2) Hydrophobic ointments are usually prepared by warming to melt hydrophobic bases such as fatty oils, waxes or paraffin, adding and mixing active substances in the bases to be dissolved or dispersed, and kneading the whole to make homogeneous.  
Hydrophilic ointments are usually prepared by warming to melt hydrophilic bases such as macrogol, adding and mixing active substances in the bases, and kneading the whole to make homogeneous.  
Prepare before use in the case of Ointments which are apt to deteriorate.
- 3) The component proportions may be varied to adjust the physical properties provided that the required content of the active ingredients is maintained.
- 4) Ointments are free from rancid odor.
- 5) Sufficient amounts of suitable preservatives to prevent the growth of microorganisms may be added to the preparations filled in multiple dose containers.
- 6) Ointments have a suitable viscosity for applying to the skin, oral mucosa or inside of the anus
- 7) Tight containers are used for preservation.

### 24. Ophthalmic Ointments

- 1) Ophthalmic Ointments are sterile preparations of semi-solid, intended for the application to the conjunctiva sac or other ocular tissues.
- 2) Ophthalmic Ointments are usually prepared by the mixing homogeneously solution of or finely powdered active substances with petrolatum or other base, and filling into containers. The overall processes, from preparation to sterilization, should be completed with sufficient care to prevent microbial contamination as rapidly as possible, taking into consideration the composition of the preparations and the storage conditions.
- 3) Sufficient amounts of suitable preservatives to prevent the growth of microorganisms may be added to the preparations filled in multiple dose containers to prevent the growth of microorganisms.
- 4) Unless otherwise specified, Ophthalmic Ointments meet the requirements of the Sterility Test, and unless otherwise specified, the test is carried out by Membrane Filtration Method.
- 5) Unless otherwise specified, Ophthalmic Ointments meet the requirements of the Test of Metal Particles in Ophthalmic Ointments.
- 6) Drug particles in Ophthalmic Ointments are usually not larger than 75  $\mu\text{m}$  in size.
- 7) Ophthalmic Ointments have a suitable viscosity for applying to the ocular tissues.
- 8) Tight containers which are able to prevent microbial contamination are usually used for preservation.

### 25. Ophthalmic Solutions

- 1) Ophthalmic Solutions are sterile preparations of liquid, or solid to be dissolved or suspended before use, intended for application to the conjunctival sac or other ocular tissues.
- 2) Ophthalmic Liquids and Solutions are usually prepared by dissolving, suspending active substances in a vehicle after adding excipients to make a constant volume, or mixing active substances and excipients, and filling into containers. The overall processes, from preparation to sterilization, should be completed with sufficient care to prevent microbial contamination as rapidly as possible, taking into consideration the composition of the preparations and the storage conditions. The concentration of active substance expressed in % represents w/v%. Preparations to be dissolved or suspended before use and designated as "for ophthalmic solutions" may be accompanied by a vehicle for dissolving or suspending the preparation.
- 3) Vehicles to prepare Ophthalmic Solutions or vehicle attached to the preparations must be harm-

less in the amounts usually administered and must not interfere with the therapeutic efficacy of the active substances.

Vehicles for Ophthalmic Solutions are classified into the following two groups.

(1) Aqueous vehicles: As the vehicles for the aqueous preparations Purified Water or suitable aqueous vehicles are used. For vehicles attached to the preparations sterilized Purified Water or sterilized aqueous vehicles are used.

(2) Non-aqueous vehicles: As the vehicles for the non-aqueous preparations vegetable oils are usually used. Suitable organic solvents may be also used as the non-aqueous vehicles.

- 4) Unless otherwise specified, any coloring agents must not be added solely for the purpose of coloring Ophthalmic Solutions or vehicles attached to the preparations.
- 5) Sodium chloride or other excipients may be added to Ophthalmic Solutions to adjust them isotonic to lacrimal fluid. Acids or alkalis may be also added to adjust the pH.
- 6) Unless otherwise specified, Ophthalmic Solutions and vehicles attached to the preparations meet the requirements of Sterility Test.
- 7) Sufficient amounts of appropriate preservatives to prevent the growth of microorganisms may be added to the preparations filled in multiple dose containers.
- 8) Ophthalmic Solutions prepared in aqueous solutions or the vehicles attached to the preparations meet the requirements of Foreign Insoluble Matter Test for Ophthalmic Solutions.
- 9) Unless otherwise specified, Ophthalmic Solutions meet the requirements of the Insoluble Particulate Matter Test for Ophthalmic Solutions.
- 10) The maximum particle size observed in Ophthalmic Solutions is usually not larger than 75  $\mu\text{m}$ .
- 11) Transparent tight containers, which do not disturb the test of Foreign Insoluble Matter Test for Ophthalmic Solutions, are usually used for preservation.

## 26. Otic Solutions

- 1) Otic Solutions are liquid, semi-solid, or solid preparations which are to be dissolved or suspended before use, intended for application to the external or internal ear.
- 2) Otic Solutions are usually prepared by filling in containers with liquids in which active substances and excipients are dissolved or suspended in a vehicle to make a constant volume, or with powders in which active substances and excipients are mixed. The overall processes, from preparation to sterilization, should be completed with sufficient care to prevent microbial contamination as rapidly as possible, taking into consideration the composition of the preparations and the storage condi-

tions. The concentration of active substance of Otic Solutions expressed in % represents w/v%. Preparations to be dissolved or suspended before use and designated as "for Otic Solutions" may be accompanied by Otic Solutions and vehicles attached to a suitable solvent or suspension medium.

- 3) Solvents, used in the preparation of Otic Solutions or are attached to a suitable solvent or suspension medium, are classified into the following two major groups.
  - (1) Aqueous vehicles : The usual vehicles for aqueous Otic Solutions or attached to the preparations are purified water or suitable aqueous vehicles. For the sterile preparations, vehicles attached to the preparations, Sterilized Purified Water or sterilized aqueous solvents are used as vehicles attached to the preparations.
  - (2) Non-aqueous vehicles: The vehicles for non-aqueous Otic Solutions is usually vegetable oils. Suitable organic solvents may be also used as the non-aqueous vehicles.
- 4) Unless otherwise specified, any coloring agent may not be added solely to otic solutions or solvents attached to a suitable solvent or suspension medium for the purpose of coloring the preparation.
- 5) Sufficient amounts of suitable preservatives to prevent the growth of microorganisms may be added to the preparations filled in multiple dose containers.
- 6) Tight containers are used for preservation.

## 27. Pastes

- 1) Pastes are topical preparations similar to Ointments. This preparation contains relatively high content of powdered drug.
- 2) Pastes are usually prepared from fats, fatty oils, petrolatum, paraffin, waxes, glycerin or water by mixing homogeneously powdered drug with the foregoing materials as bases.
- 3) Pastes are free from rancid odor.
- 4) In the case that the preparation is congealed or ingredients are separated during storage, use after a uniform mixing, unless the ingredients are deteriorated.
- 5) Well-closed containers are used for preservation

## 28. Pills

- 1) Pills are spherical masses.
- 2) Pills are usually prepared by mixing active substances uniformly with diluents, binders, disintegrators or other suitable excipients, and rolling into spherical form by a suitable method. If necessary, Pills may be coated with sucrose or other

suitable coating agents, or covered with starch, talc or other suitable materials.

- 3) Unless otherwise specified, Pills meet the requirements of the Disintegration Test or the Dissolution Test.
- 4) Well-closed or tight containers are used for preservation.

## 29. Plasters

- 1) Plasters are preparations intended for external application. They are used by spreading or sealing drugs on a cloth or on/in a plastic film, and adhering to the local skin, so that the active ingredients of the drugs can reach affected parts on the skin or under the skin.
- 2) Unless otherwise specified, Plasters are usually prepared by mixing bases such as water soluble or insoluble, natural or synthetic polymers, or their mixture uniformly with drugs, kneading or sealing into a suitable shape.  
Unless otherwise specified, Plasters prepared from fats, fatty oils, salts of fatty acids, waxes, resins, plastics, purified lanolin, rubber, or a mixture of the above substances, or prepared by mixing drugs with the above bases uniformly and as a solid at the ordinary temperature, may be described as Hard Plasters.
- 3) Plasters have a suitable viscosity for applying to the skin.
- 4) Well-closed or tight containers are used for preservation.

## 30. Powders

- 1) Powders are preparations in powdered or finely granulated form.
- 2) Unless otherwise specified, Powders meet the requirements of Powders of the Particle Size Distribution Test. Powders with not more than 10 % of total passing through No. 200 (75  $\mu\text{m}$ ) sieve may be described as Fine Granules.
- 3) Powders are usually prepared by homogeneously mixing active substances with diluents or other suitable excipients.
- 4) Powders in single-dose packages meet the requirements of Uniformity of Dosage Units.
- 5) Well-closed containers are used for preservation.

## 31. Solutions

- 1) Solutions are external preparations intended for application to the skin (including scalp), nails, or toenails. They are not identical with any other preparations under the General Requirements for Pharmaceutical Preparations.

- 2) Solutions are prepared directly with active substances or by dissolving them in solvents.
- 3) If necessary, stabilizers, buffering agents, flavoring agents, preservatives or other suitable excipients may be added.
- 4) Unless otherwise specified, Solutions in single-dose packages meet the requirements of Uniformity of Dosage Units.
- 5) Solutions that are sweet and sour, clear liquid for oral administration can be termed as Lemonades. Unless otherwise specified, Lemonades are prepared by dissolving usually hydrochloric acid, citric acid, tartaric acid or lactic acid into simple syrup or purified water, and filtering if necessary. Lemonades are prepared just before the use (examination).
- 6) Tight containers are used for preservation.

## 32. Spirits

- 1) Spirits, liquid preparations, are usually prepared by dissolving volatile drug substances in ethanol or in a mixture of ethanol and water.
- 2) Unless otherwise specified, Spirits are usually prepared by dissolving drugs in ethanol or in a mixture of ethanol and water.
- 3) Tight containers are used for preservation, removing from fire.

## 33. Suppositories

- 1) Suppositories are solid preparations intended for insertion into the rectal or vaginal cavity. Suppositories are usually prepared by molding uniform mixtures of active substances and bases into a suitable shape.  
Suppositories melt or soften at body temperature or dissolve slowly in the secretions.
- 2) Suppositories are usually prepared by dissolving a mix of homogeneously active substances and excipients such as dispersing agents and emulsifying agents, or by molding it into a shape and size after filling a constant volume of the resultant material into containers by suspending uniformly in a base which is liquefied by warming. Oleaginous bases or hydrophilic bases are usually used.
- 3) Rectal suppositories are usually conical- or spindle-shaped, and vaginal suppositories are usually globular or oval.
- 4) Unless otherwise specified, Suppositories meet the requirements of the Disintegration Test or the Dissolution Test.
- 5) Unless otherwise specified, Suppositories meet the requirements of the Uniformity of Dosage Units.
- 6) Well-closed containers are used for preservation.

## 34. Suspensions

- 1) Suspensions are liquid preparations that its active substance(s) are suspended finely and homogeneously in a vehicle
- 2) Suspensions are usually prepared under suspending homogeneously as the whole by adding suspending agent or other suitable excipients and purified water or oil to solid active substance(s). If necessary, preservatives, stabilizers, etc. may be added. In the case of deterioration, the suspensions are prepared just before the use.
- 3) Mix uniformly before use, if necessary.
- 4) Unless otherwise specified, suspensions packaged in unit-dose meet the requirements of the Test for Uniformity of Dosage Units. However, local administration of external preparation to skin are not relevant (appropriate) to the test.
- 5) Tight containers are used for preservation.

## 35. Syrups

- 1) Syrups are viscous liquid or solid preparations containing sugars or sweetening agents, intended for oral administration.
- 2) Syrups are usually prepared by dissolving, mixing, suspending or emulsifying drugs in solutions of sucrose, other sugars or sweetening agents, or in simple syrup. If necessary, the mixtures are boiled and filtered while hot.  
Unless otherwise specified, aromatic agents, coloring agents, preservatives, stabilizers, suspending agents, emulsifying agents, thickening agents, etc., may be added.
- 3) For Syrups which are apt to deteriorate, prepare before use.
- 4) Unless otherwise specified, Syrups in single-dose packages meet the requirements of Uniformity of Dosage Units.
- 5) Preparations designated as 「for syrups」 are usually dissolved or suspended as in form of granules or powder.

It may be called as dry syrup and is usually prepared by using sugars or sweetening agents, according to the preparation method of granules or powders.

- 6) Tight containers are used for preservation.
- 7) Preparations designated as 「for syrups」 are usually stored in well-closed container.

## 36. Tablets

- 1) Tablets are solid preparations having a desired shape and size, intended for oral administration. Sugar- and film-coated tablets can be prepared by coating core tablets using suitable coating agents,

containing sugars, sugar alcohols and related substances and by coating with thin films using suitable film coating agents, respectively. Enteric coated and extended release tablets can be prepared by suitable methods.

- 2) Tablets are usually prepared by the following procedures. Plain tablets are usually prepared according to (i), (ii) or (iii):
  - (i) Mix homogeneously active substances and excipients such as diluents, binders and disintegrators, granulate with water or a binder solution by a suitable method, mix with a lubricant, and then compress into a desired shape and size.
  - (ii) Mix homogeneously active substances and excipients such as diluents, binders and disintegrators, and then directly compress with a lubricant, or compress after adding active substances and a lubricant to granules previously prepared from excipients and then mixing homogeneously.
  - (iii) Mix homogeneously active substances and excipients such as diluents and binders, moisten with a solvent, form into a certain shape and size, and then dry by a suitable method.
  - (iv) Film-coated Tablets can be prepared, usually, by coating Plain Tablets with thin films using suitable film coating agents such as polymers.
  - (v) Sugar-coated Tablets can be prepared, usually, by coating Plain Tablets using suitable coating Tablets using suitable coating agents including sugars or sugar alcohols.
  - (vi) Multiple-layer Tablets can be prepared by compressing granules of different compositions to form layered tablets by a suitable method.
  - (vii) Pressure-coated Tablets can be prepared by compressing granules to cover inner core tablets with different compositions.
- 3) Unless otherwise specified, Tablets meet the requirements of the Uniformity of Dosage Units.
- 4) Unless otherwise specified, Tablets meet the requirements of the Dissolution Test or the Disintegration Test.
- 5) Well-closed are used for preservation.
- 6) Tablets including Orally Disintegrating Tablets, Buccal Tablet, Effervescent Tablets, Mucoadhesive Tablets, Dispersible Tablets, Sublingual Tablets, Soluble Tablets, Chewable Tablets and Vaginal Tablets specify separately the suitable Disintegration Test or Dissolution Test according to the preparation characteristics in the Monographs. However, Chewable Tablets don't require the Disintegration Test or the Dissolution Tests unless otherwise specified and Vaginal Tablets meet the requirement the Disintegration Test of Suppositories  
When need the Disintegration Test, unless otherwise specified

Orally Disintegrating Tablets / Orodispersible Tablets

- (1) Orally Disintegrating Tablets are tablets which are quickly dissolved or disintegrated in the oral cavity.
- (2) Orally Disintegrating Tablets are shown an appropriate disintegration.

#### Buccal Tablets

- (1) Buccal Tablets are tablets for oro-mucosal application, from which the active substances are dissolved gradually between the cheek and teeth, and absorbed via the oral mucosa.

#### Effervescent Tablets

- (1) Effervescent Tablets are tablets which are quickly dissolved or dispersed with bubbles in water.
- (2) Effervescent Tablets are usually prepared using suitable acidic substances and carbonates or hydrogen carbonates.

#### Mucoadhesive Tablets

- (1) Mucoadhesive Tablets are tablets for oro-mucosal application that are applied by adhesion to the oral mucosa.
- (2) Mucoadhesive Tablets are usually prepared by using hydrophilic polymers to form hydrogel.

#### Dispersible Tablets

- (1) Dispersible Tablets are tablets which are administered after having been dispersed in water.

#### Sublingual Tablets

- (1) Sublingual Tablets are tablets for oro-mucosal application, from which active substances are quickly dissolved sublingually and absorbed via the oral mucosa.

#### Soluble Tablets

- (1) Soluble Tablets are tablets which are administered after having been dispersed in water.

#### Chewable Tablets

- (1) Chewable Tablets are tablets which are administered by chewing.
- (2) Chewable Tablets must be in shape and size avoiding danger of suffocation.

#### Vaginal Tablets

- (1) Vaginal Tablets are solid preparations of a desired shape and size, intended for application to the vagina, which release active substances by dissolving or dispersing gradually in the secretions.

## 37. Teabags

- 1) Teabags are preparations, usually packed one-day dose or one dose of herbal drugs cut into a size of between coarse powder and coarse cutting in paper or cloth bags.
- 2) Teabags are usually used according to the preparation method as directed under Infusions and Decoctions.
- 3) Well-closed or tight containers are used for preservation.

## 38. Tinctures

- 1) Tinctures are liquid preparations, usually prepared by extracting herbal drugs with ethanol or with a mixture of ethanol and purified water.
- 2) Unless otherwise specified, Tinctures are usually prepared from coarse powder or fine cuttings of herbal drugs by means of either maceration or percolation as described below.
  - (1) Maceration: Place herbal drugs in a suitable container, and add about three-fourths of the total volume of a solvent to be used. Place a stopper, and allow the container to stand at ordinary temperature with occasional stirring for about 5 days or until the soluble constituents have satisfactorily dissolved. Filter the liquid through cloth. Wash the residue with several portions of the solvent, and press. Combine the filtrate and washings, and add sufficient solvent to make up the total volume. Allow the mixture to stand for about 2 days, and obtain a clear liquid by decantation or filtration.
  - (2) Percolation: Pour the solvent in small portions on herbal drugs placed in a container, and mix well to moisten the herbal drugs. Place a stopper on the container, and allow it to stand for about 2 hours at room temperature. Pack the contents as tightly as possible in a suitable percolator, open the lower opening, and slowly pour sufficient solvent to cover the herbal drugs. When the percolate begins to drip, close the opening, and allow the mixture to stand for 2 to 3 days at room temperature. Open the opening, and allow the percolate to drip at a rate of 1 to 3 mL per minute. Add an appropriate quantity of the solvent, and continue to percolate until the desired volume has passed. Mix thoroughly, allow to stand for 2 days, and obtain a clear liquid by decantation or filtration. The time of standing and the flow rate may be varied depending on the kind and amount of herbal drugs to be percolated. Tinctures prepared by either of the above methods for which the content of the active ingredient is specified are prepared by assaying the active ingredient using a portion of the sample and adjusting, if necessary, with the percolate or with the solvent to the specified content.



- 3) Tight containers are usually used for Tinctures, removing from fire.

### 39. Transdermal Systems

- 1) Transdermal Systems are preparations applied to the skin that are designed to deliver active substances through the skin to the systemic blood circulation. Transdermal Systems include semisolid mixtures of active substances and excipients which are used by spreading a suitable amount of the mixture on the backing layer.
- 2) Unless otherwise specified, Transdermal Systems are usually prepared by spreading the mixtures of emulsified or suspended active substances and soluble or insoluble high molecular weight of natural or synthetic bases or their mixtures on the liner or backing sheet. If necessary, adhesives agents, solvents or skin permeation enhancers etc., may be added. The transdermal systems are also prepared by filling the mixture of drug substance and bases or excipients in a reservoir made of a backing layer and a membrane which controls the release of active substances.
- 3) Unless otherwise specified, Transdermal Systems meet the requirements of release tests specified.
- 4) Unless otherwise specified, Transdermal Systems meet the requirements of the Uniformity of Dosage Units Test.
- 5) Transdermal systems have a suitable viscosity for applying to the skin.
- 6) Tight containers are used for preservation.

agent, other suitable excipients, etc., to make a homogeneous paste, spreading the paste, stamping out or cutting into a suitable shape and drying.

If necessary, a flavoring agent, aromatic agent, coloring agent, etc., may be added.

- 3) Unless otherwise specified, Troches meet the requirements of the Uniformity of Dosage Units.
- 4) When preparation applied to the whole body is required, proper test such as the dissolution or the disintegration test is regulated.
- 5) Well-closed
- 6) containers are used for preservation.

### 40. Troches

- 1) Troche is prepared in a certain shape to dissolve or disintegrate slowly in the mouth, and is intended for applying either to a part of body such as the mouth or the throat, or to a whole body.
- 2) Troche is usually prepared in shape and size to avoid danger of suffocation by the following procedures:
  - (1) Active substances are first rendered granular by a suitable method with or without uniform admixing with a diluent, binder, and other suitable excipients. The resultant granules are provided with additives such as a lubricant, and compressed into a desired shape and size.
  - (2) Troches may also be prepared either by direct compression of active substances with or without a diluent, binder or other suitable excipients, or by compression of active substances with or without suitable excipients after they have been uniformly mixed with previously prepared inactive granules.
  - (3) Troches are also prepared by mixing drugs with a diluent such as sucrose, binder, moistening

