

# GENERAL RULES FOR PREPARATIONS

## 1. General Notices for Preparations

(1) In stating the amount of content in pharmaceutical preparations, the use of an expression “not less than 95% and not more than 105%” or “not less than 95% and not more than 110%”, for example, indicates that it is usually prepared so as to contain the labeled amount of the chemically pure substance or one corresponding to it and that it is quantitatively determined in the above range.

(2) In the manufacture of any official preparation, personnel engaged in the processing of medicinal products should be completely familiar with the description, composition and action of the used drugs. There should be a cleaning routine for all equipment and manufacturing areas. Every care should be exercised in the preparation of all products, to prevent contamination risks of all kinds. In particular, use purified water with precautions against bacterial contamination. The details of the procedure of preparation may be altered as occasion demands, such as coating to granules, pills, powders or tablets with a suitable coating agent, or changing constitution ratio of bases only of ophthalmic ointments, suppositories, plasters and pressure sensitive adhesives, or ointments to adjust their physical properties properly, provided the finished preparation complies with the specifications prescribed by the Pharmacopoeia.

(3) Unless otherwise specified, suitable excipients such as diluents, stabilizers, preservatives, buffering agents, corrigents, suspending agents, emulsifiers, aromatics, solubilizing agents, coloring agents, and viscous agents may be added as occasion demands to pharmaceutical preparations to assure the property and quality of the products during storage. These substances, however, must be non-toxic and harmless in the amount administered and must not interfere with the therapeutic efficacy or the test of the preparations.

(4) Vegetable oil referred to in the manufacture of any official preparation usually indicates the edible vegetable oil incorporated in the Pharmacopoeia. When starch is called for, any kind of starch incorporated in the Pharmacopoeia may be used, unless otherwise specified.

Moreover, ethanol specified in vol% is prepared by adding purified water or water for injection to ethanol at the specified vol%.

(5) Functions which control the releasing rate of objective drugs from preparation may be added to official preparations for the purpose of controlling efficacy revelation time or decreasing side-effect. Unless otherwise specified, however, the function added preparations must meet the correspondent drug-release requirements.

Unless otherwise specified, state the function added to official preparation on a package insert and direct container or package for the preparation.

(6) When a high level of sterility assurance is maintained consistently, based on the records derived from validation studies of the manufacturing process and the in-process controls, the sterility test usually required for the release of the product may be omitted.

(7) Unless otherwise specified, preserve official preparations preferably at room temperature.

## 2. Aerosols

(1) Aerosols are preparations for use by expelling a solution or suspension of a medicine under a pressure of liquefied or compressed gas filled in a common or different container.

Aerosols are used for topical application, space spray, inhalation, oral administration, etc. Modes of expelling are available in vapor, powder, foam and paste, depending on the purpose of use.

(2) Hermetic containers are used for preservation.

## 3. 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 lukewarm 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.

#### 4. Capsules

(1) Capsules are preparations in which liquefied, suspended, pasty, powdered or granulated drugs are enclosed in capsules or wrapped with capsule bases. There are two kinds of capsules which are:

(i) Hard capsules (ii) Soft capsules

(2) Capsules are usually prepared by the following methods.

(i) Hard capsules: Drugs or uniform mixtures of drugs with diluents and other suitable excipients, granules prepared by a suitable method, or granules coated with a suitable coating agent are filled as they are or prepared lightly into hard capsules.

(ii) Soft capsules: Drugs or mixtures of drugs and suitable diluents, etc. are enclosed by an approved suitable capsule base such as gelatin plasticized by addition of glycerin, sorbitol, etc., and molded in a suitable shape. If necessary, coloring agents, preservatives, etc. may be added to capsule bases.

(3) Unless otherwise specified, Capsules meet the requirements of the Dissolution Test or the Disintegration Test.

(4) Unless otherwise specified, Capsules meet the requirements of the Content Uniformity Test or the Mass Variation Test.

(5) Well-closed or tight containers are used for preservation.

#### 5. Cataplasms

(1) Cataplasms are pasty preparations or those spread on cloth, intended for external application to supply moist warmth. They usually contain finely powdered drugs and essential oils.

(2) Unless otherwise specified, Cataplasms are usually prepared by mixing glycerin, water, or other suitable liquid materials with finely powdered drugs,

adding essential oils, and kneading the mixture until homogeneity is attained.

(3) Pasty cataplasms which have separated out one or more of their components during storage are re-homogenized before use unless the ingredients have deteriorated.

(4) Tight containers are used for preservation.

#### 6. Elixirs

(1) Elixirs are usually clear, sweetened, and aromatic liquid preparations, containing ethanol, intended for oral use.

(2) Elixirs are usually prepared by dissolving drugs or their extractives in ethanol and purified water, adding aromatic agents and sucrose, other sugars or sweetening agents, and clarifying by filtration or other procedures.

(3) Tight containers are used for preservation.

#### 7. Extracts

(1) Extracts are usually prepared by evaporating the extractives of crude drugs. There are two kinds of Extracts which are:

(i) viscous extracts (ii) dry extracts

(2) In the manufacture of Extracts, unless otherwise specified, crude drugs, in coarse powder, are usually extracted for a certain period of time with suitable solvents by cold extraction or warm extraction, or by percolation as directed in (2) under Tinctures.

The extractive is filtered, and the filtrate is concentrated or dried in a suitable method to produce a millet jelly-like consistency in the case of a viscous extract, and to make crushable solid masses, granules or powder in the case of a 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 crude drugs used.

(4) Unless otherwise specified, Extracts meet the requirements of the Heavy Metals Limit Test when the test solution and the control solution are prepared as follows.

Test solution: Ignite 0.3 g of Extracts to ash, warm with 3 mL of dilute hydrochloric acid, and filter. Wash the residue with two 5 mL portions of water. Neutralize the combined filtrate and washings by adding ammonia TS, filter, if necessary, and add 2 mL of

dilute acetic acid and water to make 50 mL.

Control solution: Proceed with 3 mL of dilute hydrochloric acid in the same manner as directed in the preparation of the test solution, and add 3.0 mL of Standard Lead Solution and water to make 50 mL.

(5) Tight containers are used for preservation.

## 8. Fluidextracts

(1) Fluidextracts are liquid percolates of crude drugs, usually prepared so that each mL contains soluble constituents from 1 g of the crude drugs.

(2) Fluidextracts are usually prepared by the percolation process. Mix well 1000 g of coarse powder or fine cutting of the crude 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 crude 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 crude drugs used. The flow rate is usually regulated as follows, depending on the amount of the crude drugs used.

Mass of crude drug	Volume of solution running per minute
Not more than 1000 g	0.5 - 1.0 mL
Not more than 3000 g	1.0 - 2.0 mL
Not more than 10,000 g	2.0 - 4.0 mL

Concentrate the second percolate, taking care not to lose the volatile ingredients of the crude 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 the active ingredient is specified are obtained by adjusting the content of the active ingredient with a sufficient amount of the second solvent, as required on the basis of the result of the assay made with a portion of (A).

Use the specified solvent only in cases where there is no distinction between the first and the second sol-

vent.

(3) Fluidextracts have odor and taste derived from the crude drugs used.

(4) Unless otherwise specified, Fluidextracts meet the requirements of the Heavy Metals Limit Test when the test solution and the control solution are prepared as follows.

Test solution: Ignite 1.0 g of Fluidextracts to ash, warm with 3 mL of dilute hydrochloric acid, filter, and wash the residue with two 5 mL portions of water. Neutralize the combined filtrate and washings by adding ammonia TS, filter, if necessary, and add 2 mL of dilute acetic acid and water to make 50 mL.

Control solution: Proceed with 3 mL of dilute hydrochloric acid as directed in the preparation of the test solution, and add 3.0 mL of Standard Lead Solution and water to make 50 mL.

(5) Tight containers are used for preservation.

## 9. Granules

(1) Granules are prepared in a form of granules with a drug or mixture of drugs.

(2) Granules are prepared, usually, by mixing uniformly a drug or mixture of drugs with or without adding diluents, binders, disintegrators or other suitable excipients, and granulating by a suitable method so that the products are preferably equal in particle size.

(3) When the Particle Size Distribution Test is performed with granules, all the granules pass through a No. 10 (1700  $\mu\text{m}$ ) sieve, not more than 5% of total granules remain on a No. 12 (1400  $\mu\text{m}$ ) sieve, and not more than 15% of total granules pass through a No. 42 (355  $\mu\text{m}$ ) sieve.

(4) Unless otherwise specified, Granules comply with the Dissolution Test or the Disintegration Test, provided that this provision does not apply to granules not more than 5% of which remain on a No. 30 (500  $\mu\text{m}$ ) sieve when shaken with a No. 30 sieve as directed in the Particle Size Distribution Test.

(5) Unless otherwise specified, Granules for single-dose use meet the requirements of the Content Uniformity Test or the Mass Variation Test.

(6) Well-closed or tight containers are used for preservation.

## 10. Infusions and Decoctions

(1) Infusions and Decoctions are liquid preparations usually obtained by macerating crude drugs in

purified water.

(2) Infusions and Decoctions are usually prepared by the following method. Cut crude drugs as directed below, and transfer 50 g to an infusion or decoction apparatus.

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

Woods, barks, roots, and rhizomes: Medium cutting

Seeds and fruits: Fine cutting

Infusions: Damp an amount of crude 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.

Decoctions: Heat, with several stirrings, an amount of crude drugs with 950 mL of purified water for 30 minutes, and filter through cloth while warm.

Sufficient purified water is further added to the filtrate through the residue to make 1000 mL of an infusion or decoction.

Prepare Infusions or Decoctions before use.

(3) Infusions and Decoctions have odor and taste derived from the crude drugs used.

(4) Tight containers are used for preservation.

## 11. Injections

(1) Injections are solutions, suspensions or emulsions of drugs or such preparations that contain drugs to be dissolved or suspended before use. They are sterile preparations to be administered directly into the skin or the body through the skin or mucous membrane.

(2) Unless otherwise specified, Injections are prepared by dissolving, suspending or emulsifying a prescribed amount of a drug in a prescribed volume of the solvent, or by distributing a prescribed amount of a drug in hermetic containers for Injections. Every care should be taken to prevent contamination. The entire process of preparing Injections including preparation of the solution, filling, sealing and sterilization, should be completed as rapidly as possible, usually within 8 hours. The concentrations of Injections are expressed in terms of percentage, w/v%.

Water for injection prepared by Reverse Osmosis-Ultrafiltration shall be sterilized by heating before use. This provision does not apply to Injections and attached solvent, if they are sterilized by heating in the process of manufacture.

Drugs to be dissolved or suspended before use and designated in the title as "for injection" may be accompanied by a suitable solvent.

(3) Solvents used in the preparation of Injections or attached to Injections must be harmless in the amounts usually administered and must not interfere with the therapeutic efficacy or with testing.

The solvents are classified into the following two major groups. They should meet the following requirements.

(i) Aqueous vehicles: As the solvent of aqueous injections, water for injection is usually used. Unless otherwise specified, isotonic sodium chloride solution, Ringer's solution, or other suitable aqueous solutions may be used instead. Unless otherwise specified, these aqueous vehicles other than those 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 monographs, compliance with the Bacterial Endotoxins Test is not required.

When the Bacterial Endotoxins Test is not applicable to aqueous vehicles with a volume of more than 10 mL, the Pyrogen Test may be used.

(ii) Nonaqueous vehicles: Vegetable oils are usually used as solvents for nonaqueous injections. These oils, unless otherwise specified, are clear at 10°C and have no odor or taste suggesting rancidity. The acid value is not more than 0.56, iodine value is between 79 and 137, and the saponification value falls in the range between 185 and 200. They meet the requirements of the Mineral Oil Test.

Several suitable organic solvents other than the vegetable oils may be used as nonaqueous vehicles.

(4) 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  $\mu\text{m}$ . As a rule, suspensions for injection are not to be injected into the vessels or spinal cord, and emulsions for injection, not into the spinal cord.

(5) Unless otherwise specified, no coloring agent may be added solely for the purpose of coloring the preparations. Unless otherwise specified, suitable diluents may be added to the preparations to be dissolved before use.

(6) Unless otherwise specified, 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.

(7) Unless otherwise specified, sufficient amounts of suitable preservatives to prevent the growth of microorganisms are added to Injections filled in multiple dose containers.

(8) Unless otherwise specified, Injections other

than those used exclusively for intracutaneous, subcutaneous or intramuscular administration meet the requirements of the Bacterial Endotoxins Test. For Injections for which endotoxin limits are not specified in the individual monographs, compliance with the Bacterial Endotoxins Test is not required.

When the Bacterial Endotoxins Test is not applicable to Injections with a volume of more than 10 mL, the Pyrogen Test may be used.

(9) Unless otherwise specified, 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.

(10) Usual containers of Injections are colorless and meet the requirements of the Glass Containers for Injections. Where specified in individual monographs, these containers may be replaced by colored containers meeting the requirements of the Glass Containers for Injections or by plastic containers for aqueous injections meeting the requirements of the Test Methods for Plastic Containers.

(11) Unless otherwise specified, rubber stoppers used for glass containers of 100 mL or more of aqueous infusions meet the requirements of the Rubber Closures for Aqueous Infusions.

(12) Unless otherwise specified, Injections meet the requirements of the Foreign Insoluble Matter Test for Injections.

(13) Unless otherwise specified, Injections meet the requirements of the Insoluble Particulate Matter Test for Injections.

#### Method 1: Light Obscuration Particle Count Test

The limits of the number of insoluble particles by this method are as follows: For large-volume injections labeled as containing 100 mL or more, the limits are not more than 25 particles per mL equal to or greater than 10  $\mu\text{m}$ , and not more than 3 particles per mL equal to or greater than 25  $\mu\text{m}$ . For small-volume injections labeled as containing less than 100 mL, the limits are not more than 6000 particles per container equal to or greater than 10  $\mu\text{m}$ , and not more than 600 particles per container equal to or greater than 25  $\mu\text{m}$ .

#### Method 2: Microscopic Particle Count Test

The limits of the number of insoluble particle by this method are as follows: For large-volume injections labeled as containing 100 mL or more, the limits are not more than 12 particles per mL equal to or greater than 10  $\mu\text{m}$ , and not more than 2 particles per

mL equal to or greater than 25  $\mu\text{m}$ . For small-volume injections labeled as containing less than 100 mL, the limits are not more than 3000 particles per container equal to or greater than 10  $\mu\text{m}$ , and not more than 300 particles per container equal to or greater than 25  $\mu\text{m}$ .

When Method 1 is not applicable (as in the case where it is impossible to prepare 25 mL of sample solution or the estimate obtained by Method 1 exceed the specific limit because of protein preparation), Method 2 is used. These tests are not applied to emulsion type or suspension type injections.

(14) Unless otherwise specified, the actual volume of an injection contained in a single-dose container is slightly larger than the labeled volume and capable of providing this volume on injection. The following table shows the volumes to be filled in excess in a single-dose container.

Labeled volume (mL)	Excess volume	
	For mobile liquids	For viscous liquids
0.5 or less	0.10 mL	0.12 mL
More than 0.5 and not exceeding 1	0.10 mL	0.15 mL
More than 1 and not exceeding 2	0.15 mL	0.25 mL
More than 2 and not exceeding 5	0.30 mL	0.50 mL
More than 5 and not exceeding 10	0.50 mL	0.70 mL
More than 10 and not exceeding 30	0.60 mL	0.90 mL
More than 30	2 vol%	3 vol%

The average actual volume of 10 Injections is not more than 107% of the sum of the labeled volume and the excess volume indicated above. The actual individual volume is not less than the labeled volume, and the number of Injections containing more than 115% of the sum of the labeled volume and excess volume is one or naught.

(15) Unless otherwise specified, Injections to be dissolved or suspended before use meet the requirements of the Content Uniformity Test or the Mass Variation Test.

(16) Unless otherwise specified, the written, printed, or graphic matter in the package, the container, or the wrapper must 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 alkalies 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 exceeding 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) Hermetic containers are used for preservation. Plastic containers for aqueous injections may be used when specified in an individual monograph.

## 12. Lemonades

(1) Lemonades are sweet, sour, and usually clear liquid preparations intended for oral use.

(2) Unless otherwise specified, Lemonades are usually prepared by dissolving hydrochloric acid, citric acid, L-tartaric acid, or lactic acid in simple syrup and purified water, and filtering if necessary.

Prepare Lemonades before use.

(3) Tight containers are used for preservation.

## 13. 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 drugs 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.

(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.

## 14. Liquids and Solutions

(1) Liquids and Solutions are liquid preparations intended for oral or external use. They are not identical with any other preparations under General Rules for Preparations.

(2) Liquids and Solutions are prepared direct with a medicine or by dissolving a medicine in a solvent.

(3) Tight containers are used for preservation.

## 15. Lotions

(1) Lotions are usually homogeneous suspensions or solutions of drugs in aqueous vehicles intended for external application to the skin by inunction.

(2) Unless otherwise specified, Lotions are usually prepared by adding a drug with solvents, emulsifying agents, suspending agents, etc. to an aqueous vehicle and mixing to complete uniformity by a suitable method.

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.

## 16. Ointments

(1) Ointments are usually homogeneous, semi-solid preparations for external application, of such consistency that they may be applied to the skin by inunction.

(2) Unless otherwise specified, Ointments are usually prepared by mixing homogeneously drugs with fats, fatty oils, lanolin, petrolatum, paraffin, waxes, resins, plastics, glycols, higher alcohols, glycerin, water, emulsifying agents, suspending agents, or other suitable excipients, or with above excipients emulsified in a suitable way as bases.

Prepare before use in the case of Ointments which are apt to deteriorate.

Ointments which are prepared with emulsified bases may be described as Cream.

(3) Ointments are free from rancid odor.

(4) Tight containers are used for preservation.

## 17. Ophthalmic Ointments

(1) Ophthalmic Ointments are aseptic ointments intended for the application to the conjunctiva.

(2) Ophthalmic Ointments are usually prepared by the following method. Solution of drugs or finely powdered drugs are thoroughly mixed with petrolatum or

other suitable materials as a base, and are distributed into collapsible tubes or other tight containers. Sufficient care should be taken to prevent any kinds of contamination, and to proceed as fast as possible in the manufacturing of products.

(3) Drug particles in Ophthalmic Ointments are usually not larger than  $75\ \mu\text{m}$  in size.

(4) Unless otherwise specified, Ophthalmic Ointments meet the requirements of the Sterility Test, and unless otherwise specified, carry out the test by Membrane filtration method.

(5) Unless otherwise specified, Ophthalmic Ointments meet the requirements of the Test of Metal Particles in Ophthalmic Ointments.

The requirement is met if a total of not more than 50 metal particles, each measuring  $50\ \mu\text{m}$  or more in any dimension, is found in the 10 samples, and if not more than one sample is found to contain more than 8 such particles. If Ophthalmic Ointments fail the foregoing test, repeat the test on 20 additional samples of Ophthalmic Ointments. The requirement is met if a total of not more than 150 metal particles, each measuring  $50\ \mu\text{m}$  or more in any dimension, is found in the 30 samples, and if not more than three samples are found to contain more than 8 such particles each.

(6) Tight containers are used for preservation.

## 18. Ophthalmic Solutions

(1) Ophthalmic Solutions are aseptic preparations intended for application to the conjunctiva. They are solutions or suspensions of drugs, or preparations which contain drugs to be dissolved or suspended before use.

(2) Unless otherwise specified, Ophthalmic Solutions are prepared either by dissolving or suspending a prescribed amount of a drug in a prescribed volume of a solvent, or by placing a prescribed amount of a drug in tight containers. Every caution is required to avoid contamination in preparing Ophthalmic Solutions. The entire process of preparing Ophthalmic Solutions should be completed as rapidly as possible. The concentrations of Ophthalmic Solutions are expressed in terms of percentage of drugs, w/v%.

Preparations to be dissolved or suspended before use and designated as "for ophthalmic solutions" may be accompanied by a suitable solvent.

(3) Solvents used in the preparation of Ophthalmic Solutions or attached to Ophthalmic Solutions must be harmless in the amounts usually administered and must not interfere with therapeutic efficacy, or with testing.

Solvents for Ophthalmic Solutions are classified into the following two major groups. They should meet the following requirements.

(i) Aqueous vehicles: The usual vehicle for aqueous ophthalmic solutions is purified water or suitable aqueous solutions. Solvents constituted to Ophthalmic Solutions are sterilized purified water or suitable sterilized aqueous solutions.

(ii) Nonaqueous vehicles: The vehicles for nonaqueous ophthalmic solutions are the nonaqueous solvents for injection.

(4) The usual particle size observed in suspensions for Ophthalmic Solutions is not larger than  $75\ \mu\text{m}$ .

(5) Unless otherwise specified, no coloring agent may be added solely for the purpose of coloring the preparations. Unless otherwise specified, a suitable diluent may be added to the preparations to be dissolved before use.

(6) Unless otherwise specified, sodium chloride or other suitable substances, or nontoxic and harmless acids or alkalies, may be added to aqueous preparations to render them isotonic with lachrymal liquid, or to adjust the pH, respectively.

(7) Unless otherwise specified, Ophthalmic Solutions meet the requirements of the Sterility Test. In the case of drugs to be dissolved before use, carry out the test using the solution obtained by dissolving the content in the attached solvent.

(8) Ophthalmic Solutions prepared as aqueous solution and aqueous vehicles attached to Ophthalmic Solutions to be prepared before use should be clear and free from foreign insoluble matter when inspected with the unaided eye at a position of luminous intensity of 3000 to 5000 luxes under an incandescent electric bulb. The containers of Ophthalmic Solutions should have a transparency which does not interfere with the test for foreign matter.

(9) Unless otherwise specified, Ophthalmic Solutions meet the Insoluble Particulate Matter Test for Ophthalmic Solutions. The limit of the particulates is not more than 1 particle per mL equal to or greater than  $300\ \mu\text{m}$ .

(10) Tight containers are used for preservation.

## 19. Pills

(1) Pills are spherical masses.

(2) Pills are usually prepared by mixing drugs uniformly with diluents, binders, disintegrators or other suitable excipients, and rolling into spherical form by a suitable method.

(3) Unless otherwise specified, Pills comply with

the Dissolution Test or the Disintegration Test.

(4) Well-closed or tight containers are used for preservation.

## 20. Plasters and Pressure Sensitive Adhesives

(1) Plasters and Pressure Sensitive Adhesives are 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 skin.

(2) Unless otherwise specified, Plasters and Pressure Sensitive Adhesives are usually prepared by mixing bases such as water soluble or insoluble, natural or artificial high molecular compound, or their mixture uniformly with drugs and kneading or sealing on a cloth or film into a suitable shape.

Unless otherwise specified, Plasters and Pressure Sensitive Adhesives 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 plasters.

(3) Well-closed containers are used for preservation.

## 21. Powders

(1) Powders are preparations in powdered form.

(2) Powders are usually prepared by uniformly mixing drugs with or without diluents, binders, disintegrators or other suitable excipients by a suitable method to produce a pulverized or finely granulated form.

(3) When the Particle Size Distribution Test is performed with Powders, all the powders pass through a No. 18 (850  $\mu\text{m}$ ) sieve and not more than 5% of total powders remain on a No. 30 (500  $\mu\text{m}$ ) sieve. Powders with not more than 10% of total passing through a No. 200 (75  $\mu\text{m}$ ) sieve may be described as Fine Granules.

(4) Unless otherwise specified, Powders for single-dose use meet the requirements of the Content Uniformity Test or the Mass Variation Test.

(5) Well-closed or tight containers are used for preservation.

## 22. Spirits

(1) Spirits are usually alcoholic or hydroalcoholic solutions of volatile drugs.

(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.

## 23. Suppositories

(1) Suppositories are solid preparations intended for insertion into the rectal or vaginal cavity. Suppositories are usually prepared by molding bases into a suitable shape.

Suppositories melt or soften at body temperature or dissolve slowly in the secretions.

(2) Unless otherwise specified, Suppositories are usually prepared by mixing drugs with fat-type bases, watermiscible bases or other suitable materials, and, if necessary, with emulsifying agents, suspending agents, etc. into a homogeneous mass, and molding it into a suitable shape or coating it with a suitable coating agent, or prepared as a liquid form-fill-seal.

(3) Rectal suppositories are usually conical or spindle-shaped, and Vaginal suppositories are globular or oval.

(4) Unless otherwise specified, Suppositories meet the requirements of the Content Uniformity Test or the Mass Variation Test.

(5) Well-closed or tight containers are used for preservation.

## 24. Suspensions and Emulsions

(1) Suspensions and Emulsions are usually liquid preparations of finely divided drugs suspended or emulsified uniformly in liquid vehicles, respectively.

(2) Suspensions and Emulsions are usually prepared by the following method.

**Suspensions:** Suspensions are prepared by adding suspending agents or other suitable excipients and purified water or oil to solid drugs, and suspending to complete uniformity by a suitable method.

**Emulsions:** Emulsions are prepared by adding emulsifying agents and purified water to liquid drugs, and emulsifying to complete uniformity by a suitable method.



If necessary, preservatives, stabilizers, etc., may be added.

Prepare before use in the case of Suspensions or Emulsions which are apt to deteriorate.

- (3) Mix uniformly before use, if necessary.
- (4) Tight containers are used for preservation.

## 25. Syrups

(1) Syrups are oral liquid preparations. Syrups are solutions of sucrose, or viscous liquids or suspensions of drugs containing sucrose, other sugars or sweetening agents.

Syrups include preparations which are dissolved or suspended before use depending on the properties of the drugs.

(2) Unless otherwise specified, 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.

Syrups may be prepared in the form of preparations which are dissolved or suspended before use depending on the properties of the drugs.

(3) Unless otherwise specified, Syrups which are dissolved or suspended before use and are for single-dose use (divided dosage forms) meet the requirements of the Content Uniformity Test or the Mass Variation Test.

- (4) Tight containers are used for preservation.

## 26. Tablets

(1) Tablets are prepared by compressing drugs directly, or by forming or molding drugs dampened with a solvent into a desired shape and size.

(2) Tablets are usually prepared by the following procedures:

(i) Drugs are first rendered granular in a suitable method with or without uniform admixture with a diluent, binder, disintegrator, and other suitable excipients. The resultant granules are provided with additives such as a lubricant, and compressed into a desired shape and size.

(ii) Tablets may also be prepared either by direct compression of a drug with or without a diluent, binder, disintegrator, and other suitable excipients, or by compression after drugs with or without suitable excipients have been added to previously prepared inactive granules.

(iii) Tablets may also be prepared by drying the admixture by a suitable method after forming or molding drugs, uniformly mixed with a diluent, binder and other suitable excipients and dampened with a solvent, into a desired shape and size.

(3) Unless otherwise specified, Tablets meet the requirements of the Dissolution Test or the Disintegration Test.

(4) Unless otherwise specified, Tablets meet the requirements of the Content Uniformity Test or the Mass Variation Test. The requirements for coated tablets are provided in each monograph.

(5) Well-closed or tight containers are used for preservation.

## 27. Tinctures

(1) Tinctures are liquid preparations, and usually prepared by extracting crude 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 crude drugs either by maceration or by percolation as described below.

**Maceration:** Place crude drugs in a suitable container, and add about three-fourths of the total volume of a solvent to be used. 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 volume. Allow the mixture to stand for about 2 days, and obtain a clear liquid by decantation or filtration.

**Percolation:** Pour the solvent in small portions on crude drugs placed in a container, and mix well to moisten the crude drugs. Stopper 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 crude 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 crude 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 used for preservation, remoting from fire.

## 28. Troches

(1) Troches are usually preparations of suitable shape to dissolve or disintegrate slowly in the mouth, and are intended for application to the mouth or the throat.

(2) Troches are usually prepared by the following procedures:

(i) Drugs are first rendered granular by a suitable method with or without uniform admixing with a dil-

uent, binder, and other suitable excipients. The resultant granules are provided with additives such as a lubricant, and compressed into a desired shape and size.

(ii) Troches may also be prepared either by direct compression of drugs with or without a diluent, binder or other suitable excipients, or by compression of drugs with or without suitable excipients after they have been uniformly mixed with previously prepared inactive granules.

(iii) Troches are also prepared by mixing drugs with a diluent such as sucrose, binder, moistening agent, other suitable excipients, etc., to make a homogeneous paste, spreading the paste, stamping out or cutting into a suitable shape and drying.

(3) Unless otherwise specified, Troches meet the requirements of the Content Uniformity Test and the Mass Variation Test.

(4) Well-closed or tight containers are used for preservation.