[Appendix 2]

General Requirements for Pharmaceutical Preparations

(Related to Article 2 Subparagraph 2)

General Requirements for Pharmaceutical Preparations

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I. General Considerations

A. General requirements for pharmaceutical preparations stipulate general definitions of dosage forms, manufacturing method and storage conditions. Name of preparations listed in the monograph are determined appropriately according to the properties and use by combining dosage forms, functions and administration routes etc., according to the General Requirements for Pharmaceutical Preparations.

B. Pharmaceutical preparations are categorized into three levels of classification: top-level, middle-level, and low-level classification. Top-level classification is based on administration route and site of administration. Middle-level classification is based on the description, dosage forms, and physical properties of pharmaceutical preparations from the top-level classification. Low-level classification is based on the function and release characteristics of pharmaceutical preparations from the middle-level classification.
Pharmaceutical preparations, that do not belong to the low-level classification, are deemed to be under the middle-level classification to which they belong.

C. Sterility test may be skipped on release tests if sterility is always guaranteed through validation of the manufacturing process as well as appropriate process management and its records.

D. Pharmaceutical preparations using antimicrobial preservatives meet the requirements for the test according to the Antimicrobial Preservatives Analysis.

E. Unless otherwise specified, pharmaceutical preparations are stored at room temperature. Protect it from light if necessary.

II. Preparation Monograph

1. Preparations for Cutaneous Application

1.1. Aerosols

A. Aerosols are preparations in which the drug substances are sprayed onto the skin, mouth, and tongue in the form of a mist, powder, foam, paste, etc., by using the pressure of liquefied or compressed gas filled into the same or another container.

B. This preparation is usually prepared by dissolving or suspending the drug substance in a solvent, filling with liquefied propellants into pressure-resistant containers, and putting a continuous spray valve. If necessary, dispersing agents and stabilizers may be used.

C. If necessary, flavor enhancers, flavors and fragrance, preservatives, buffering agents, solubilizing agents, emulsifier, suspending agents, or other appropriate excipients may be added.

D. Unless otherwise specified, metered-dose type preparations have an appropriate uniformity in metered spray.

E. Pressure-resistant hermetic containers are used for storage.

1.1.1. Aerosols for Cutaneous Application

A. Aerosols for cutaneous application are aerosol preparations in which the drug substances in aerosols for cutaneous application are sprayed by using the liquefied or compressed gases filled into a container.

B. This preparation is prepared by dissolving or suspending the drug substance in a solvent, filling with liquefied propellants in pressure-resistant containers, and putting a continuous spray valve. If necessary, dispersing agents and stabilizers may be used.

C. Pressure-resistant containers are used for storage.

1.1.2. Pump Sprays for Cutaneous Application

A. Pump sprays for cutaneous application are mist sprays preparations in which the drug substances in container are sprayed by the pump.

B. This preparation is prepared by dissolving and suspending the drug substance and excipients, filling the mixture into a container, and putting a pump to the container.

C. Tight containers are used for storage. Containers or packaging with low water vapor permeability are used if the water evaporation affects the quality of preparation.

1.2. Cataplasma

A. Cataplasmas are preparations for cutaneous application containing the mixture of drug substance and water or those prepared by spreading the mixture on cloth, which are intended to supply wet compress for topical use.

B. This preparation is usually prepared by mixing the drug substance with liquid materials such as purified water and glycerin and making them homogeneous, or mixing natural or synthetic polymer such as water-soluble polymers and absorbent polymers with purified water and adding the drug substances to make them homogeneous, spreading onto a cotton cloth and finally molding.

C. In case of clay-like form where the components have separated during storage, this preparation is re-homogenized before use unless the ingredients have deteriorated.

D. This preparation has an appropriate releasing property, if necessary.

E. This preparation has an appropriate stickiness for applying onto the skin.

F. Tight containers are used for preservation.

1.3. Creams

A. Creams are semi-solid preparations for cutaneous application of semi-solid emulsified in oil-in-water or water-in-oil which are applied onto skin, oral mucosa, around or inside of the anus. Lipophilic preparations emulsified in water-in-oil may be termed “oily creams.”

B. This preparation is usually prepared by mixing homogeneously and emulsifying an oil phase component and a water phase component, both warmed, of which either one contains the drug substance. These components have the following constituents: Petrolatum, fatty alcohols, etc., with or without emulsifiers or other suitable excipients are added to the oil-phase component. And purified water with or without emulsifiers or other suitable excipients are put in the water-phase component.

C. For the preparations filled into multiple-dose containers, suitable preservatives may be added to prevent microbial growth.

D. Creams have an appropriate viscosity for applying onto the skin, oral mucosa, or rectum.

E. Tight containers are used for storage.

1.4. Gels

A. Gels are semi-solid (gel) preparations for cutaneous application consisting of organic macromolecules that interpenetrated by a liquid. This preparation is applied onto skin, oral mucosa, around or inside of the anus. There are two types of this preparation: aqueous and oily.
B. This preparation is usually prepared by the following procedures. If necessary, stabilizing agents may be added.
   1) Aqueous Gel: Polymers, other excipients and purified water are added to the drug substance to dissolve or suspend this mixture. Heat, cool, or add the gelling agents to mix them.
   2) Oily Gel: Liquid oily bases such as glycols, fatty alcohols and other excipients are mixed with the drug substance.
C. For the preparations filled into multiple-dose containers, suitable preservatives may be added to prevent microbial growth.
D. Gels have an appropriate viscosity for applying onto the skin, oral mucosa, or rectum.
E. If necessary, gels are mixed by shaking properly before use.
F. Tight containers are used for storage.

1.5. Liquids and Solutions for Cutaneous Application

A. Liquids and solutions for cutaneous application are liquid preparations for applying to the skin (including scalp) or nails. This preparation includes liniments and lotions.
B. This preparation is generally prepared by adding solvents, excipients, etc. to the drug substance, dissolving, emulsifying or suspending, and filtering them if necessary. Perishable preparations are prepared before use.
C. Unless otherwise specified, this preparation in single-dose package meets the requirements for the test according to the Uniformity of Dosage Units, except for the emulsified or suspended ones.
D. Tight containers are used for storage. Containers or packaging with low water vapor permeability are used if the water evaporation affects the quality of preparation.

1.5.1. Liniments

A. Liniments are usually liquid or clay-like preparations intended for cutaneous application to rub it to the skin.
B. Unless otherwise specified, this preparation is usually prepared by adding the drug substance to water, ethanol, fatty oils, glycerin, soap, emulsifier, suspending agents, other suitable excipients or their mixtures to make it uniform. If necessary, the preparation may be added such as preservatives, flavors and fragrance, and so on.
C. If the components of these liniments are separated during storage, it should be mixed evenly before use unless the ingredients have deteriorated.

1.5.2. Lotions

A. Lotions are preparations in which drug substances are dissolved, emulsified or finely dispersed in an aqueous solvent for external use.
B. This preparation is usually prepared by dissolving, suspending or emulsifying the drug substance in purified water with excipients and making the solution homogeneous. If necessary, the preparation may be added such as preservatives, flavors and fragrance, and so on. Perishable lotions are prepared before use.
C. If the components of these lotions are separated during storage, it should be mixed evenly before use unless the ingredients have deteriorated.

1.6. Ointments

A. Ointments are semi-solid preparations for cutaneous application in which the drug substances are dissolved or dispersed in bases for the application onto skin, oral mucosa, around or inside of the anus by inunction. There are two types: lipophilic ointment and hydrophilic ointment.
   1) Lipophilic ointments: They are usually prepared by melting lipophilic bases such as fatty oils, waxes or paraffin through heating, adding the drug substances, mixing to be dissolved or dispersed, and making the whole mixture homogeneous.
   2) Hydrophilic ointment: They are usually prepared by melting hydrophilic bases such as macrogol through heating, mixing with the drug substances, and making the whole mixture homogeneous. Perishable ointments are prepared before use.
B. The component proportions may be varied to adjust the physical properties provided that the required content of the drug substances is maintained.
C. Ointments have no rancid odor.
D. For those filled into multiple-dose containers, suitable preservatives may be added to prevent microbial growth.
E. This preparation has an appropriate viscosity for applying onto the skin, oral mucosa or rectum.
F. Tight containers are used for storage.

1.7. Pastes

A. Pastes are preparations for cutaneous application similar to Ointments, which contains relatively much drug powder.
B. This preparation is usually prepared by mixing the powdered drug homogeneously with the bases, which are fats, fatty oils, petrolatum, paraffin, waxes, glycerin, water or their mixture.
C. This preparation has no rancid odor.
D. In the case that the preparation is congealed or ingredients are separated during storage, it is uniformly mixed for use, unless the ingredients are deteriorated.
E. Well-closed containers are used for storage.

1.8. Plasters

A. Plasters are topical preparations intended for cutaneous application. They are made by spreading or sealing drugs on a cloth or on/in a plastic film, and applied onto the skin by topically attaching, so that the drug substance can reach topical open wounds on the skin or through the skin.
B. Unless otherwise specified, this preparation is usually prepared by mixing the drug substance with base homogeneously, which is water-soluble or water-insoluble natural or synthetic polymer or mixture thereof, and molding with spreading or sealing. Unless otherwise specified, those prepared from fats, fatty oils, salts of fatty acids, waxes, resins, plastics, purified lanolin, rubber, etc., or a mixture of the above substances, or prepared by mixing the drug substance with the above bases uniformly and as a solid at the ordinary temperature, may be described as Hard Plasters.
C. This preparation has an appropriate releasing property, if necessary.
D. This preparation has an appropriate stickiness for applying to the skin.
E. Well-closed or tight containers are used for storage.

1.9. Solid Dosage Forms for Cutaneous Application

A. Solid dosage forms for cutaneous application is solid preparations for spreading or dispersing to the skin (including scalp) or nails. This preparation includes powders for cutaneous application.

B. Unless otherwise specified, this preparation in single-dose package meets the requirements for the test according to the Uniformity of Dosage Units.

C. Tight containers are used for storage. Containers or packaging with low water vapor permeability are used if the water evaporation affects the quality of preparation.

1.9.1. Powders for Cutaneous Application

A. Powders for cutaneous application are powdery solid preparations intended for cutaneous application.

B. This preparation is prepared by mixing the drug substance with excipients such as diluents, etc., homogenizing, and then powdering.

1.10. Transdermal Systems (Patches)

A. Transdermal systems are preparations for dermal application designed to deliver the drug substance through the skin to the systemic blood circulation. The semisolid mixtures of the drug substance and excipients, which are used by dosing a suitable amount of the mixture on the support materials, are also included in this preparation.

B. This preparation is usually prepared by dissolving or suspending the drug substance in a base, which is water-soluble or water-insoluble natural or synthetic polymer or mixture thereof, adding adhesive, solvent, absorption accelerator, etc. to this mixture if necessary, and spreading on the support materials. The transdermal systems are also prepared by filling the mixture of drug substance and bases or excipients into a Carrier membrane made of a support material and a membrane which controls the release of the drug substance and molding.

C. Unless otherwise specified, transdermal systems meet the requirements for the test which presents the release properties.

D. Unless otherwise specified, this preparation meets the requirements for the test according to the Uniformity of Dosage Units.

E. This preparation has an appropriate stickiness for applying onto the skin.

F. Tight containers are used for storage.

2. Preparations for Dialysis and Irrigation

2.1. Dialysis Agents, Dialysis Solutions

A. Dialysis agents are liquid or solid preparations that are dissolved before use, and are used for peritoneal dialysis or hemodialysis

B. Unless otherwise specified, dialysis agents meet the requirements for the test according to the Bacterial Endotoxins. The Pyrogen test can be applied if it is difficult to apply the Bacterial Endotoxins. In this case, unless otherwise specified, 10 mL of the preparation is used per 10 kg of the body weight of the rabbit.

C. If necessary, pH adjusters, isotonic agents or other excipients may be added.

D. Unless otherwise specified, the solvent used for dialysis agents is Water for Injection

E. Unless otherwise specified, dialysis agents to be dissolved before use, meet the requirements for the test according to the Uniformity of Dosage Units.

F. This preparation includes peritoneal dialysis agents and hemodialysis agents.

2.1.2. Hemodialysis Agents, Hemodialysis Solutions

A. Hemodialysis agents are liquid preparations used for hemodialysis in liquid or solid preparations, which is dissolved before use.

B. This preparation is usually prepared by dissolving the drug substance with suitable excipients in a solvent to make a certain volume, or by filling the drug substance combined with suitable excipients in a container. In the case of solid preparations that are dissolved before use, prepare as directed under Tablets or Granules.

C. Tight containers which can prevent microbial contamination are used for preservation.

2.1.1. Peritoneal Dialysis Agents, Peritoneal Dialysis Solutions

A. Peritoneal dialysis agents are liquid or solid preparations (of aseptic condition), which are dissolved before use, and are used for peritoneal dialysis.

B. This preparation is usually prepared by dissolving the drug substance with suitable excipients in a solvent to make a certain volume, or by filling the drug substance combined with suitable excipients in a container, and sealing it. Sterilize it, if necessary. Adequate precautions should be taken to minimize the risk of microbial contamination, and the entire process, from preparation to sterilization, should be conducted as quickly as possible considering the composition of the preparation and its storage method. The concentration of the drug substance in % represents w/v%. In the case of solid preparations to be dissolved before use, prepare as directed under Tablets or Granules.

C. Unless otherwise specified, this preparation meets the requirements for the test according to the Sterility.

D. Unless otherwise specified, the actual volume of this preparation in a unit-dose container meets the requirements for the test according to the Parenteral Infusions from Extractable Volume of Injections. However, the mass (g) of the content may be divided by the density and converted into a capacity (mL).

E. Unless otherwise specified, this preparation meets the requirements for the test according to the Injections from the Particulate Contamination: Visible Particles.

F. Unless otherwise specified, this preparation meets the requirements for the test according to the Insoluble Particulate Matter in Injections.

G. Suitable containers according to the conditions of the Glass Containers for Injections and the Plastic Containers for Pharmaceutical Use may be used.

H. Unless otherwise specified, elastomeric closures of the containers meet the requirements of the Elastomeric Closures for Injections.

I. Hermetic containers are used for preservation. If necessary, tight containers which can prevent microbial contamination are used for preservation.

2.2. Irrigations

A. Irrigations, intended to bathe or flush body cavities, open wounds or skin, are sterile aqueous solutions in large volumes.

B. Unless otherwise specified, Water for Injection is used in this preparation. If necessary, sodium chloride or other suitable excipients may be added to render them isotonic with blood or other body fluids. If necessary, nontoxic and

harmless acids or alkalis may be added to adjust the pH.

C. Unless otherwise specified, a sufficient amount of suitable preservatives is added to irrigations filled in multiple dose containers to prevent microbial growth.

D. Unless otherwise specified, irrigations meet the requirements for the test according to the Bacterial Endotoxins. The Pyrogen test can be applied if it is difficult to apply the Bacterial Endotoxins. In this case, unless otherwise specified, 10 mL of the preparation is used per kg of the body weight of the rabbit.

E. Unless otherwise specified, this preparation meets the requirements for the test according to the Sterility.

F. Unless otherwise specified, this preparation meets the requirements for the test according to the Parenteral Infusions of the Extractable Volume of Injections.

G. Hermetic containers are used for preservation.

3. Preparations for Inhalation

3.1. Inhalations

A. Inhalants are preparations containing drug substance solubilized or suspended in an appropriate diluent, administered to the respiratory system in vapor, fine particulate, or aerosol phase.

B. Propellants, solubilizing agents, diluents, preservatives, solubilizers, dispersing agents, isotonic agents, pH adjusting agents, stabilizing agents, and other suitable excipients etc. may be added to the drug substance, if necessary.

C. Tight containers or pressure-resistant hermetic containers are used for preservation.

3.1.1. Dry Powder Inhalers

A. Dry powder inhalers are solid particles in a dry powder state prepared to maintain a constant inhalation.

B. When preparing Dry Powder Inhalers, the drug substance is usually used as fine particulates, and if necessary, excipients such as lactose are added for uniformity.

C. Those intended for inhalation of the weighed quantity have a uniform delivery amount indicating appropriate efficacy.

D. The drug substance of this preparation has an appropriate aerodynamic particle diameter.

E. Tight containers are generally used for preservation. Moisture-resistant containers or package are used if moisture affects the quality of preparations.

3.1.2. Inhalation Solutions

A. Inhalation solutions are liquid preparations for inhalation delivered by nebulizers, etc.

B. This preparation is usually prepared by adding appropriate solutions, isotonic agents, or pH adjusting agents, etc. to the drug substance, dissolving or suspending uniformly, and then concentrating if necessary.

C. For those filled in multiple-dose containers, a sufficient amount of suitable preservatives may be added to prevent microbial growth.

D. Tight containers are generally used for preservation.
Store in a container or packaging with low water vapor permeability, if water evaporation affects the quality of the preparation.

3.1.3. Metered Dose Inhalers

A. Metered dose inhalers are metered-dose type preparation for inhalation to spray a constant amount of the drug substance with dispersing agents filled in the container.

B. This preparation is usually prepared as solution or suspension by adding a solvent and appropriate dispersing agents, stabilizers, etc. to the drug substance and attaching a pump filled with the weighed quantity in a compressed container with liquid dispersing agents.

C. This preparation delivers a constant amount of the appropriate drug substance.

D. The drug substance of this preparation has an appropriate aerodynamic particle diameter.

E. Pressure-resistant hermetic containers are usually used for preservation.

4. Preparations for Injection

4.1. Injections

A. Injections are sterile preparations to be administered directly into subcutaneous tissues, intramuscular sites, or the body tissues and organs such as blood vessel in form of a solution, a suspension, an emulsion, or a solid sterile preparation dissolved or suspended in a solvent before use.

B. This preparation is usually prepared by the following methods. Dissolve, suspend or emulsify the drug substance with or without excipients in Water for Injection or an aqueous or non-aqueous solvent uniformly.

1) Fill it into a container for injection, seal, and sterilize.

2) Perform sterile filtration or prepare homogeneous liquid aseptically, fill into a container for injection, and seal it.
Adequate precautions should be taken to minimize the risk of microbial contamination, and the entire process, from preparation to sterilization, should be conducted as quickly as possible considering the composition of injection and its storage method. The concentration of the drug substance in percentage (%) indicates w/v%.
Those to be dissolved or suspended before use and labeled as “for injection” may be accompanied by a suitable solvent or suspension medium.

C. Ampule, vial, pre-filled syringe and cartridge (A cartridge filled with drug solution is put into an exclusive injection device for use.) can be used as containers of injections.

D. Solvents used in this preparation or the enclosed solvent or suspension medium must be harmless and must not affect the therapeutic efficacy. The solvents are divided into the following two major groups and each must meet the following requirements.

1) Aqueous solvents: Water for Injection is used as a solvent for aqueous injections. However, in general, Isotonic Sodium Chloride Injection, Ringer’s Solution or other suitable aqueous solutions may be used instead. The Pyrogen can be applied if it is difficult to apply the Bacterial Endotoxins.

2) Non-aqueous solvents: Vegetable oils are usually used as solvents for non-aqueous injections. This preparation, unless otherwise specified, must be clear at 10°C, the acid value is NMT 0.56, the saponification value falls in the range between 185 and 200, and the iodine value is 79 to 137. They meet the requirements for the test according to the Mineral Oil. Several suitable organic solvents may also be used as non-aqueous solvents.

E. Unless otherwise specified, substances intended only for the purpose of coloring should not be added to this preparation.

F. Sodium chloride or other suitable excipients may be added to aqueous injections to render them isotonic with blood

or other body fluids. Acids or alkalis may be added to adjust the pH.

G. Unless otherwise specified, a sufficient amount of suitable preservatives is added to injections filled in multiple dose containers to prevent microbial growth.

H. Unless otherwise specified, injections and attached solvent or suspension medium meet the requirements for the test according to the Bacterial Endotoxins, except for the ones used exclusively for intradermal, subcutaneous or intramuscular administration. In cases where the Bacterial Endotoxins is not specified in the monograph, this is not applicable. The Pyrogen test can be applied if it is difficult to apply the Bacterial Endotoxins.

I. Unless otherwise specified, injections and attached solvent or suspension medium meet the requirements for the test according to the Sterility. However, this preparation of more than 50 mL should be tested according to the membrane filtration method unless otherwise specified, except for those filled in multiple-dose containers. In the case of injections to be dissolved before use, perform the test with the solution obtained by dissolving the contents in the attached solvent.

J. The containers of injections should be colorless and meet the requirements of the Glass Containers for Injections. However, when specified separately, 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 Plastic Containers for Pharmaceutical Use.

K. Unless otherwise specified, use the elastomeric closure of the injection containers that meets the requirements of the Elastomeric Closures for Injections.

L. Unless otherwise specified, injections and attached solvent or suspension medium meet the requirements for the test according to the Injections from the Particulate Contamination: Visible Particles.

M. Unless otherwise specified, injections and attached solvent or suspension medium meet the requirements for the test according to the Insoluble Particulate Matter in Injections.

N. Unless otherwise specified, the actual volume of an injection in a unit-dose container meets the requirements according to the Extractable Volume of Injections.

O. Unless otherwise specified, the following information should be written on the documents, containers, or packaging attached to this preparation.
   1) Names of solvents used to prepare this injection, if the solvent is not specified in it.
   2) Name, content, component and quantity or ratio of the solvent when it is enclosed to this preparation, and the fact that the solution is attached to the outer container or outer packaging of the injection.
   3) Names and quantities of added stabilizing agents, preservatives, and diluent (However, when the air inside the container is replaced with carbon dioxide or nitrogen, it is not necessary to state it.)

P. 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 less 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.

Q. Unless otherwise specified, this preparation to be dissolved or suspended before use, meets the requirements for the test according to the Uniformity of Dosage Units.

R. Suspension injections are usually not used for intravascular or intrathecal administration, and emulsion injections are not used for intrathecal administration.

S. The maximum size of particles observed in suspensions for injection is less than 150 μm, and the maximum size of the particles in emulsions for injection is less than 7 μm.

T. Hermetic containers are used for preservation.

4.1.1. Freeze-dried Injections

A. This preparation is usually prepared by dissolving the drug substance with or without excipients such as diluents in Water for Injection, sterilizing the solution by aseptic filtration, filling the filtrate directly into containers for injection and then freeze drying, or freeze-drying in a exclusive container for injection, and then transferring it directly into the container.

4.1.2. Implants

A. Implants are aseptic preparations intended to be administered using a special injector or a surgical operation. It is prepared by compressing and molding purified drugs into a certain shape, and sterilizing.

B. Implants are usually prepared by the following procedures.
   1) This drug substance is first rendered granular using a suitable method with or without uniform admixing with a diluent, binder, and other suitable excipients. The resultant granules are compressed into a desired shape and size, and then sterilized.
   2) Implants may also be prepared either by direct compression of the drug substance with or without a diluent, binder, or other suitable excipients, then sterilized. Otherwise, the drug substance with or without suitable excipients is added to the pre-made granules to mix uniformly, compressed into a desired shape and size, and then sterilized.
   3) The drug substance mixed homogeneously with diluents, binders or other excipients is moistened with an appropriate wetting agent to form a mass, molded, dried, and sterilized.

C. Unless otherwise specified, this preparation meets the requirements for the test according to the Sterility.

D. Unless otherwise specified, this preparation meets the requirements for the test according to the Uniformity of Dosage Units.

E. This preparation has an appropriate release property.

F. Hermetic containers or tight containers which are able to prevent microbial contamination are used for preservation.

4.1.3. Parenteral Infusions

A. Parenteral infusions are injections of more than 100 mL, administered intravenously.

B. This preparation is mainly administered for the purpose of hydration, electrolyte adjustment, and nutrition, but it is also used in combination with other injections through continuous infusion for therapeutic purposes.

4.1.4. Powder for Injections

A. This preparation is usually prepared by aseptically filtering and crystallizing the solution of the drug substance to obtain the powder or mixing additionally the powder with sterilized additives, and filling it into a container for injections.

4.1.5. Prolonged Release Injection

A. Prolonged release injections are injected intramuscularly for the purpose of releasing the drug substance over a long period of time.

B. This preparation is usually made by dissolving the drug substance in vegetable oil or microsphere suspensions using biodegradable polymers.

C. This preparation has an appropriate release property.

5. Preparations for Nasal Application

5.1. Nasal Dry Powder Inhalers

A. Nasal dry powder inhalers are powdery preparations for nasal cavity.

B. When preparing nasal dry powder inhalers, the active pharmaceutical ingredient is usually used as fine particulates of an appropriate particle size, and if necessary, excipients are added to obtain a homogeneous mixture.

C. Well-closed containers are used for storage. Moisture-resistant containers or packages are used if moisture affects the quality of preparations.

5.2. Nasal Solutions

A. Nasal solutions are liquid preparation applied to the nasal cavities or nasal mucosa, or solid preparation to be dissolved or suspended before use.

B. This preparation is usually prepared by dissolving or suspending the drug substance and excipients in a solvent, and filtering, if necessary. Isotonic agents, pH adjusting agents, etc. may be used.

C. Among the preparations to be dissolved or suspended before use, those indicated “for nasal application” may be packaged with a solvent to dissolve or suspend.

D. If necessary, this preparation is inhaled by spraying by using a suitable atomizing device such as spray-pump.

E. Unless otherwise specified, metered-dose type preparations have an appropriate uniformity of metered spray.

F. For the preparations filled into multiple-dose containers, suitable preservatives may be added to prevent microbial growth.

G. Tight containers are used for storage.

6. Preparations for Ophthalmic Application

6.1. Ophthalmic Ointments

A. Ophthalmic ointments are semi-solid sterile preparations, applied to the conjunctival sac or other ocular tissues.

B. Ophthalmic ointments are usually prepared by uniformly mixing the solution or fine powder of drug substances with appropriate bases such as petrolatum, and filling it into containers. Adequate precautions should be taken to minimize the risk of microbial contamination, and the entire process, from preparation to sterilization, should be conducted as quickly as possible considering the composition of the preparation and its storage method.

C. For those filled into multiple-dose containers, suitable preservatives may be added to prevent microbial growth.

D. Unless otherwise specified, this preparation meets the requirements for the test according to the Sterility. Unless otherwise specified, the test is carried out using the membrane filtration method.

E. Unless otherwise specified, this preparation meets the requirements for the test according to the Foreign Metallic Matter.

F. Drug particles in ophthalmic ointments are usually not larger than 75 μm in size.

G. This preparation has a suitable viscosity for the application to the ocular tissues.

H. Tight containers which can prevent microbial contamination are usually used for storage.

6.2. Ophthalmic Solutions

A. Ophthalmic solutions are sterile preparations applied to ocular tissues such as conjunctival sacs, or solid sterile preparations that are dissolved or suspended before use, and therefore, should not include any foreign matters.

B. This preparation is usually prepared by dissolving, or suspending the drug substance and excipients in a solvent to make a constant volume, or filling the mixture of the drug substance and excipients into a container. Adequate precautions should be taken to minimize the risk of microbial contamination, and the entire process, from preparation to sterilization, should be conducted as quickly as possible considering the composition of the preparation and its storage method. The concentration of the drug substance in % represents w/v%. Those to be dissolved or suspended on use and labeled as “for ophthalmic solutions” may be packaged with a solvent for dissolving or suspending the preparation.

C. Solvents used to prepare ophthalmic solutions, or solvents or suspensions packaged with the preparation must be harmless and must not affect the therapeutic efficacy of the preparation. Solvents for ophthalmic solutions are classified into the following two types and each of them must meet the following requirements:

1) Aqueous solvents: Purified water or suitable aqueous solvents are used as solvents for aqueous preparations. Sterilized purified water or sterilized aqueous solvents are used as the solvents enclosed with the preparation.

2) Non-aqueous solvents: Vegetable oils are usually used as solvents for non-aqueous preparations. Suitable organic solvents may be also used as non-aqueous solvents.

D. Unless otherwise specified, substances intended only for the purpose of coloring should not be added to this preparation or the solvents or suspensions in this preparation.

E. Sodium chloride or other excipients may be added to this preparation to adjust a tonicity similar to tears. Acids or alkalis may be also added to adjust the pH.

F. Unless otherwise specified, ophthalmic solutions and enclosed solvent or suspension meet the requirements for the test according to the Sterility.

G. For those filled into multiple-dose containers, suitable preservatives may be added to prevent microbial growth.

H. Unless otherwise specified, aqueous solvents or other solvents to be added to ophthalmic solutions meet the requirements for the test according to the Particulate Contamination: Visible Particles.

I. Unless otherwise specified, this preparation and enclosed solvent or suspension meet the requirements for the test according to the Insoluble Particulate Matter in Ophthalmic Solutions.

J. The maximum particle size of suspended ophthalmic solutions is usually not larger than 75 μm.

K. Transparent tight containers that do not affect the Ophthalmic Solutions from the Particulate Contamination:

Visible Particles are usually used for storage.

7. Preparations for Oral Application

7.1. Capsules

A. Capsules are solid dosage forms in which drug substances are filled into capsules either in the form of a liquid, suspension, semi-solid, powder, granule, or encapsulated with capsule shells.

B. There are two types of capsules: hard-shell capsules and soft-shell capsules.
   1) Hard-shell capsules: The capsules are prepared by filling capsules with the drug substance as it is or with suitable excipients such as diluents uniformly mixed, or by filling them into capsules either directly or after light compression following preparing the drug substance in a solid or molded form.
   2) Soft-shell capsules: The capsules are prepared by filling capsules made of gelatin or similar capsule shells, drug substance or with suitable excipients such as glycerin or sorbitol, etc., added to increase the plasticity, and shaped into a specific form by encapsulation.

C. If necessary, coloring agents, antimicrobial preservatives, etc. may be added to capsule shell Extended-release or delayed-release capsules can be prepared by changing the components of capsule shell or applying suitable coating agents to capsules.

D. Unless otherwise specified, this preparation meets the requirements for the test according to the Uniformity of Dosage Units.

E. Unless otherwise specified, this preparation meets the requirements for the test according to the Dissolution or the Disintegration.

F. Capsules are preserved in well-closed containers.

7.2. Extracts

A. Extracts are usually prepared by concentrating extractives of crude drugs. There are two types of extracts:
A) semiliquid extracts and B) powdered extracts.

B. Unless otherwise specified, this preparation is made by adding appropriate menstruums to crude drugs in coarse powder, and it is extracted for a certain period of time by cold extraction or by warm extraction, or by percolation directed in B in 2) of Tinctures.
The extractive is filtered, and the filtrate is concentrated or dried using a suitable method. Semiliquid extracts are made with the same consistency as starch syrups. Powdered extracts are made as crushable solid masses, granules or powder. For the extracts for which the content of drug substances is specified, some of them are weighed and quantified, and if necessary, adjusted to the specified content by adding suitable diluents.

C. Extracts have the odor and the taste of the crude drugs used.

D. Unless otherwise specified, extracts meet the requirements for the test according to Method 5 of the Heavy Metals.

E. Extracts are preserved in tight containers.

7.3. Fluid Extracts

A. Fluid extracts are liquid solutions made by extracting crude drugs and usually contain soluble constituents of 1 g of the crude drugs per in 1mL.

B. This preparation is usually prepared from coarse powder or fine cutting of crude drugs using either of the following the maceration or percolation.
   1) Maceration: Place a certain amount of crude drugs in a suitable container, add a menstruum until the crude drug is sufficiently wet, seal the container, and allow it to stand at room temperature with occasional stirring for about 5 days or until the soluble constituents are sufficiently dissolved. Separate the liquid by centrifugation or other suitable method. Usually, an amount equivalent to about 3/4 of the decoction is used as the first decoction, and it is stored separately. Wash the residue with an appropriate amount of the menstruum, combine the washings with the remaining ¼ of the first decoction, concentrate as necessary, mix with the first decoction. This is referred to as A. Add menstruum, if necessary, to equalize the amount of the crude drugs. Allow the mixture to stand for about 2 days, and then filter to obtain a clear supernatant liquid.
   2) Percolation: Mix well 1 kg of crude drugs, add the first menstruum to moisten it, seal 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 menstruum to cover the crude drugs. Close the lower opening when the decoction begins to drip, and allow the mixture to stand for 2 to 3 days at room temperature. Open the lower opening, and spill the decoction at the rate of 0.5 to 1.0 mL per minute. The 850 mL obtained initially is used as the first decoction and is stored separately. Add the second menstruum to the percolator, then continue to spill and use it as the second menstruum. The rest time and spill rate may vary depending on the type and the amount of the crude drugs used. The spill rate is usually adjusted as follows, depending on the amount of the crude drugs used.

Mass of crude drugs	Spill volume per minute
NMT 1 kg	0.5 to 1.0 mL
NMT 3 kg	1.0 to 2.0 mL
NMT 10 kg	2.0 to 4.0 mL

Next, concentrate the second decoction as much as possible, taking care not to lose the volatile ingredients of the crude drug, then mix with the first decoction, which is referred to as (A). Add (A) and the second menstruum to make 1000 mL, and allow the mixture to stand for 2 days. Decant the clear supernatant liquid or filter it to obtain a clear solution. However, for preparations prepared according to any of the above maceration or percolation, if the content of the drug substance or ethanol is specified, part of (A) is collected and quantified, and the menstruum is added according to the results to adjust the specified content.

C. This preparation has the odor and the taste of the crude drugs used.

D. Unless otherwise specified, this preparation meets the requirements for the test according to Method 5 of the Heavy Metals.

E. Fluid extracts are preserved in tight containers.

7.4. Granules

A. Granules are solid dosage forms that are composed of smaller particles, intended for oral administration.
B. This preparation is usually prepared by the following methods and coated as necessary. Extended-release or delayed-release granules can also be prepared using a suitable method.
   1) Diluents, binders, disintegrants, or other suitable excipients are added to the powdery drug substance, homogenized, and granulated using a suitable method.
   2) Excipients such as diluents are added to the previously granulated drug substance, and homogenized.
   3) Excipients such as diluents are added to the previously granulated drug substance, mixed, and granulated using a suitable method.
C. This preparation meets the requirements for the test according to the Particle Size Distribution Estimation by Analytical Sieving.
D. Unless otherwise specified, granules in single-dose packages meet the requirements for the test according to the Uniformity of Dosage Units.
E. Unless otherwise specified, this preparation meets the requirements for the test according to the Dissolution or the Disintegration.
   However, this does not apply to granules under the application of the Dissolution and those sieved according to the Particle size distribution estimation by analytical sieving and having NMT 5% remaining on a No. 30 (500 μm) sieve.
F. This preparation contains effervescent granules, and the Disintegration or the Dissolution suitable for the preparation's properties is defined separately in the monograph.
G. Granules are usually preserved in well-closed or tight containers.

7.4.1. Effervescent Granules
A. Effervescent granules are granules that release carbon dioxide, producing the characteristic effervescent action and dissolve or disperse in water.
B. This preparation is usually prepared using mixtures of acids, carbonates or bicarbonates.

7.5. Jellies for Oral Administration
A. Jellies for oral administration are gel-like preparations formed to be stiffened.
B. This preparation is generally made by adding and mixing excipients and high-molecular gel bases with the drug substance, gelling it using an appropriate method, and molding it into a certain shape.
C. Unless otherwise specified, this preparation meets the requirements for the test according to the Uniformity of Dosage Units.
D. Unless otherwise specified, this preparation meets the requirements of the Dissolution or has a suitable disintegration.
E. Tight containers are generally used for preservation. Store in a container or packaging with low water vapor permeability, if water evaporation affects the quality of the preparation.

7.6. Liquids and Solutions for Oral Administration
A. Liquids and solutions for oral administration are liquid dosage forms for internal use.
B. This preparation usually uses the drug substance as it is or by dissolving it in solvents.
C. If necessary, flavor enhancers, antimicrobial preservatives, stabilizing agents, buffering agents, or other suitable excipients may be added.
D. Unless otherwise specified, liquids and solutions for oral administration in single-dose packages meet the requirements for the test according to the Uniformity of Dosage Units.
E. Liquids and solutions are preserved in tight containers.

7.6.1. Aromatic Water
A. Aromatic water is a clear aqueous solution saturated with essential oils or other volatile substances.
B. Unless otherwise specified, this preparation is usually prepared by the following process: Mix 2 mL of essential oil or 2 g of a volatile substance with 1000 mL of lukewarm purified water properly and shake for 15 minutes, allow the mixture to stand for at least 12 hours, filter through a filter paper soaked with purified water and add purified water to make 1000 mL. Alternatively, mix 2 mL of essential oil or 2 g of volatile substances with an appropriate amount of talc, refined siliceous earth, or pulped filter-paper well, add 1000 mL of purified water, stir the mixture well for 10 minutes, and then filter. If the filtrate is not clear, repeat the filtration, and add purified water through the filter paper to make 1000 mL.
C. This preparation has odor and taste derived from the drugs used.

7.6.2. Decoctions and Infusions
A. Decoctions and infusions are liquid preparations usually prepared by macerating crude drugs in purified water. This preparation is prepared before use.
B. This preparation is usually prepared by cutting crude drugs as directed below and transferring them to decoction and infusion apparatus.
   Leaves, flowers, and whole parts of plants: Coarse cutting.
   Lignum, caulis, barks, roots, and rhizomes: Moderately fine cutting.
   Seeds and fruits: Fine cutting.
   1) Decoctions: Add 400 to 600 mL of purified water to the usual daily dose of crude drug, stir several times, and heat for around 30 minutes. When the volume of the mixture reaches half, filter it using cotton.
   2) Infusions: Damp 50 g of crude drugs with 50 mL of purified water for about 15 minutes, pour 900 mL of hot purified water, mix by stirring several times, and heat for 5 minutes. Filter it using a cotton after cooling.
C. This preparation has the odor and the taste of the crude drugs used.

7.6.3. Elixirs
A. Elixirs are clear, sweetened, and aromatic liquid preparations containing ethanol.
B. This preparation is usually prepared by dissolving drug substances or extractives in ethanol or purified water, flavoring agents, sucrose, other sugars, or sweetening agents, and then filtering or using other methods to obtain a clear liquid. If necessary, preservatives, solubilizers, coloring agents, etc., may be added.

7.6.4. Emulsions
A. Emulsions are liquid preparations in which drug

substances are well-emulsified.

B. This preparation is usually prepared by adding emulsifier and purified water to the liquid drug substances, and emulsifying it to make a well-mixed preparation using a suitable method. If necessary, preservatives, stabilizing agents, etc. may be added. Perishable emulsions are prepared before use.

C. This preparation is well mixed before use, if necessary.

7.6.5. Lemonades

A. Lemonades are sweet and sour and are generally clear liquid preparations.

B. Unless otherwise specified, this preparation is usually prepared by dissolving either hydrochloric acid, citric acid, tartaric acid or lactic acid into a simple syrup and purified water, and filtering if necessary. Lemonades are prepared before use.

7.6.6. Spirits

A. Spirits are liquid preparations, usually prepared by dissolving volatile drug substances in ethanol or in a mixture of ethanol and water.

B. Unless otherwise specified, this preparation is usually prepared by dissolving drugs in ethanol or in a mixture of ethanol and water.

C. This preparation is kept away from fire.

7.6.7. Suspensions

A. Suspensions are liquid pharmaceutical preparations in which drug substances are well-dispersed or suspended throughout a liquid phase.

B. This preparation is usually prepared by adding a suspending agent or other suitable excipients and purified water or oil to the solid drug substance and suspending them until well-mixed. If necessary, preservatives, stabilizing agents, etc. may be added. Perishable suspensions are prepared before use.

C. This preparation is mixed and homogenized before use, if necessary.

D. This preparation has an appropriate dissolution, if necessary.

7.6.8. Tinctures

A. Tinctures are liquid preparations, usually prepared by macerating crude drugs in ethanol or in a mixture of ethanol and purified water.

B. Unless otherwise specified, this preparation is usually prepared from coarse powder or fine cuttings of crude drugs with either maceration or percolation as described below.

1) Maceration: Place crude drugs in a suitable container, and add about ¾ of the total volume of a menstruum. Seal it, and leave the container at room temperature with occasional stirring for about 5 days or until the soluble ingredients are sufficiently dissolved. Filter the liquid using cotton. Wash the residue with several portions of the menstruum, and press it. Combine the filtrate and the washed liquid to make up the total volume. Allow the mixture to stand for about 2 days, and decant or filter it to obtain a clear liquid.

2) Percolation: Add a small amount of the menstruum to the crude drug in advance, and mix well to moisten the crude drugs. Seal the container, and allow it to stand for 2 hours at room temperature. Pack it as tightly as possible in a suitable percolator, open the lower opening, and slowly pour sufficient menstruum to cover the crude drugs. When the decoction begins to drip, close the lower opening, and allow the mixture to stand for 2 to 3 days at room temperature. Open the opening, and allow the decoction to spill at a rate of 1 to 3 mL per minute. Add an appropriate quantity of the menstruum, and continue to spill until the desired volume has passed. Mix thoroughly and allow it to stand for 2 days to obtain a clear supernatant liquid by decantation or filtration. The rest time and spill rate may vary depending on the type and amount of crude drugs to be percolated.

However, for tinctures prepared according to any of the above methods, if there are specifications for the content of the drug substance and the content of ethanol, a portion of the sample is taken, the drug substance is quantified and the menstruum is added as necessary to adjust the content to the specified content.

C. This preparation is kept away from fire.

7.7. Pills

A. Pills are drug substance-containing spherical bodies intended for oral administration.

B. This preparation is usually prepared by mixing the drug substance uniformly with diluents, binders, disintegrants or other suitable excipients to achieve homogeneity, and then molding it into a spherical shape using 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.

C. Unless otherwise specified, this preparation meets the requirements for the test according to the Dissolution or the Disintegration.

D. Pills are preserved in well-closed or tight containers

7.8. Powders

A. Powders are pharmaceutical preparations made of powder or fine particulates for oral administration.

B. This preparation is usually prepared by mixing the drug substance with diluents or other suitable excipients until a homogeneous mixture is obtained.

C. Unless otherwise specified, powders in single-dose packages (distribution) meet the requirements for the test according to the Uniformity of Dosage Units.

D. Powders have an appropriate dissolution, if necessary.

E. Powders meet the requirements for the test according to the Particle Size Distribution Estimation by Analytical Sieving. Powders that pass through a No. 200 (75 μm) sieve of NMT 10% of the total amount are referred to as fine granules. In this case, powders may be referred to as fine granules.

F. Powders are preserved in well-closed or tight containers.

7.9. Syrups

A. Syrups are viscous liquid or solid preparations containing sugars or sweetening agents, intended for oral administration.

B. This preparation is usually prepared by adding the drug substances in solutions of sucrose, other sugars, sweetening agents, or in simple syrup to dissolve, mix, suspend or emulsify. If necessary, the mixture is boiled and filtered while hot. Unless otherwise specified, flavors and fragrance, preservatives, stabilizing agents, emulsifier, viscosity-increasing agent, coloring agents, suspending

agents, etc., may be added.

C. Perishable preparation is prepared before use.

D. Unless otherwise specified, this preparation in single-dose packages meets the requirements for the test according to the Uniformity of Dosage Units.

E. The suspended syrups have a suitable dissolution if necessary.

F. Syrups are preserved in tight containers.

7.9.1. Preparations for Syrups

A. Preparations for syrups are granular or powdery preparations that turn into a syrup when water is added. It may be referred to as dry syrups.

B. This preparation is usually prepared by using sugars or sweetening agents, according to the method of preparation of granules or powders.

C. This preparation is dissolved or suspended before use.

D. This preparation, which should be suspended for use, has a suitable dissolution if necessary.

E. Well-closed containers are used for preservation. However, store it in moisture-proof containers or packaging if moisture affects the quality of the preparation.

7.10. Tablets

A. Tablets are solid dosage forms made in a certain shape. This preparation can be coated with suitable coating agents, such as sugars, sugar alcohol or polymers to facilitate ingestion or prevent degradation of the active pharmaceutical ingredient. Also, extended-release or delayed-release tablets can be prepared using suitable methods.

B. This preparation is usually prepared by the following procedures. Uncoated tablets are usually prepared according to methods 1), 2) or 3):

1) Add excipients such as diluents, binders and disintegrants to the drug substance and mix until a homogeneous mixture is obtained, and then directly compress and mold it, or add the drug substance and a lubricant to pre-made granules, mix homogeneously, and then compress and mold it.

2) Add excipients such as diluents, binders and disintegrants to the drug substance, granulate with water or a binder solution using a suitable method until a homogeneous mixture is obtained, add a lubricant, mix, and then compress and mold it.

3) Add excipients such as diluents, binders and disintegrants to the drug substance and mix until a homogeneous mixture is obtained. Moisten with a solvent, mold it into a certain shape and size, and then dry it using a suitable method.

4) Film-coated tablets are usually prepared by thinly coating uncoated tablets with a suitable coating agent such as polymers.

5) Sugar-coated tablets are usually prepared by coating uncoated tablets using a coating agent containing sugar or sugar alcohols.

6) Multiple-layer tablets are prepared by stacking granules of different compositions and compressing them using a suitable method.

7) Cored tablets are prepared by covering inner cored tablets with different compositions covering inner cored tablets

C. Unless otherwise specified, this preparation meets the requirements for the test according to the Uniformity of Dosage Units. However, in cases where conformity is required for sugar-coated tablets, it is defined in the monograph.

D. Unless otherwise specified, this preparation meets the requirements for the test according to the Dissolution or Disintegration.

E. This preparation includes chewable tablets, dispersible tablets, effervescent tablets, orally disintegrating tablets, and soluble tablets, and the Disintegration or the Dissolution suitable for the preparation's properties is separately specified in each monograph. However, unless otherwise specified, chewable tablets, effervescent tablets, and soluble tablets are not applicable to these tests.

F. Tablets are usually preserved in well-closed containers.

7.10.1. Chewable Tablets

A. Chewable tablets are tablets which are chewed or crushed prior to swallowing.

B. This preparation is shaped to prevent choking when taken.

7.10.2. Dispersible Tablets

A. Dispersible tablets are tablets administered after having been dispersed in water.

7.10.3. Effervescent Tablets

A. Effervescent tablets are tablets that release carbon dioxide, producing the characteristic effervescent action and dissolve or disperse in water.

B. This preparation is usually prepared using mixtures of acids, carbonates or bicarbonates.

7.10.4. Orally Disintegrating Tablets / Orodispersible Tablets

A. Orally disintegrating tablets are tablets that dissolve or disintegrate quickly in the oral cavity.

B. This preparation has suitable disintegration properties.

7.10.5. Soluble Tablets

A. Soluble tablets are tablets that are administered after having been dissolved in water.

7.11. Tea Bags

A. Tea bags are pharmaceutical preparations, usually made by putting crude drugs in coarse powder to coarse cutting, and packing the daily dose or one-time dose of crude drugs in papers or cloth bags.

B. This preparation is usually made according to the preparation method as directed under Infusions and Decoctions.

C. Tea bags are preserved in well-closed or tight containers.

8. Preparations for Oromucosal Application

8.1. Liquids and Solutions for Oromucosal Application

A. Liquids and solutions for oromucosal application are liquid preparations for oromucosal application.

B. This preparation is usually prepared by mixing the active pharmaceutical ingredient with excipients and purified water or suitable solvents to reach a homogeneous dissolution, emulsification, or suspension. Filter it if necessary.

C. Perishable preparations are prepared before use.

D. Unless otherwise specified, this preparation in single-dose package meets the requirements for the test according to the Uniformity of Dosage Units.

E. Tight containers are used for preservation.

8.1.1. Gargles

A. Gargles are liquid preparations that are applied locally by rinsing the mouth, such as in the oral cavity and pharynx. These preparations include solid preparations that dissolve when used.

B. This preparation is usually prepared by adding solvents and excipients to the drug substances, dissolving it homogeneously, and then filtering it if necessary. Solid preparations, which are dissolved upon use, are manufactured according to the manufacturing method of tablets, granules, and so on.

C. Tight containers are used for preservation.

8.2. Orodispersible Films for Oromucosal Application

A. Orodispersible films for oromucosal application are made of drugs in single or multi-layer of suitable material.

B. Unless otherwise specified, this preparation meets the requirements for the test according to the Uniformity of Dosage Units.

C. The Disintegration or the Dissolution suitable for this preparation is defined in the monograph.

D. Tight containers are used for preservation.

8.3. Semi-solid Preparations for Oromucosal Application

A. Semi-solid preparations for oromucosal application are applied to the oral mucosa, and include creams, gels, and ointments.

B. This preparation is prepared by emulsifying the drug substance and excipients in purified water and oil-based ingredient such as petrolatum or by homogenizing the drug substance and excipients with high-molecular substances.

1) In case of creams for oromucosal application, the cream preparation method applies.
2) In case of gels for oromucosal application, the gel preparation method applies.
3) In case of oinments for oromucosal application, the ointment preparation method applies.

C. For the preparations filled in multiple-dose containers, a sufficient amount of suitable preservatives may be added to prevent microbial growth.

D. This preparation has an appropriate viscosity for application to the oral mucosa.

E. Tight containers are used for preservation. Containers with low water vapor permeability are used, if water evaporation affects the quality of the preparation.

8.4. Sprays for Oromucosal Application

A. Sprays for oromucosal application are preparations to spray the active pharmaceutical ingredient applied orally in the form of mist, powder, foam, or paste.

B. This preparation is prepared by the following method.

1) Dissolve or suspend the drug substance and excipients in a solution, etc., concentrate if necessary, and then fill in a container with liquefied or compressed gas.
2) Prepare the solution or suspension using the drug substance and excipients. Fill it in a container and place the spray pump.

C. Unless otherwise specified, metered-dose type preparations among aerosol preparations have an appropriate uniformity of the metered spray.

D. Tight containers or pressure-resistant containers are used for preservation.

8.5. Tablets for Oromucosal Application

A. Tablets for oromucosal application are solid preparations in a certain shape for oral cavity. This preparation includes troches, sublingual tablets, buccal tablets, mucoadhesive tablets, and medicated chewing gums.

B. This preparation is prepared in compliance with the method of preparation of tablets.

C. Unless otherwise specified, this preparation meets the requirements for the test according to the Uniformity of Dosage Units.

D. Unless otherwise specified, this preparation has a suitable dissolution or disintegration properties.

E. Tight containers are used for preservation. Store it in moisture-resistant containers or packaging, if moisture affects the quality of the preparation.

8.5.1. Buccal Tablets

A. Buccal tablets are tablets for oromucosal application, from which the drug substance is dissolved gradually in the buccal pouch, and absorbed via the oral mucosa membrane.

8.5.2. Medicated Chewing Gums

A. Medicated chewing gums are preparations in a certain shape that allow for the drug substance to be released by chewing.

B. This preparation is usually prepared using suitable gum materials such as vegetable resin, thermoplastic resin and elastomer by the following methods. Medicated chewing gums may be coated by an appropriate coating agent.

1) Gum materials are melted, excipients such as sweetening agents, plasticizers, flavoring agents, etc. are added to the drug substance, and molded into a certain shape.
2) Excipients such as sweetening agents, lubricants, flavoring agents, etc., are added to the drug substances in powdered gum materials, homogenized, compressed, and molded into a certain shape.

C. Unless otherwise specified, this preparation meets the requirements for the test according to the Uniformity of Dosage Units.

D. This preparation has a suitable dissolution or disintegration properties.

8.5.3. Mucoadhesive Tablets

A. Mucoadhesive tablets are preparations that are used by attaching them to the oral mucosa.

B. This preparation is usually prepared by using hydrophilic polymers to form a hydro gel.

8.5.4. Sublingual Tablets

A. Sublingual tablets are tablets for oromucosal application. from which drug substances are quickly dissolved sublingually and absorbed via the oral mucosa membrane.

8.5.5. Troches

A. Troches are preparations that act locally (in the oral cavity, pharynx, etc.) or systemically while being slowly dissolved or disintegrated in a mouth.

B. This preparation is usually prepared in a shape that prevents choking when taken by the following procedures:

1) This drug substance is first rendered granular using a suitable method with or without uniform admixing with a diluent, binder, and other suitable excipients.

The resultant granules are provided with excipients such as a lubricant, and compressed into a desired shape and size.

2) Troches may also be prepared either by direct compression of the drug substance with or without a diluent, binder, or other suitable excipients, or by compression of the drug substance with or without suitable excipients after they have been uniformly mixed with previously prepared granules.

3) Troches may also be prepared by mixing drugs with diluents such as sucrose, binders, moistening agents, other suitable excipients, etc., to obtain a uniformed wet mixture, spreading, stamping out, or cutting it into a suitable shape and drying.

C. Unless otherwise specified, this preparation meets the requirements for the test according to the Uniformity of Dosage Units.

D. If this preparation is required to have a systemic effect, etc., the Disintegration or the Dissolution suitable for the preparation's properties is defined separately in the monograph.

9. Preparations for Otic Application

9.1. Otic Solutions

A. Otic solutions are liquid, semi-solid, or solid preparations dissolved or suspended before use, and are applied to the outer or middle ear.

B. Otic solutions are usually prepared by dissolving, suspending the drug substance and excipients in a solvent to make a constant volume, or filling the mixture of the drug substance and excipients into a container. Adequate precautions should be taken to minimize the risk of microbial contamination, and the entire process should be conducted as quickly as possible considering the composition of the preparation and its storage method. The concentration of the drug substance in % represents w/v%. Those to be dissolved or suspended before use and labeled as “for otic solutions” may be packaged with a solvent for dissolving or suspending the preparation.

C. Solvents used in this preparation or enclosed solvent or suspension are classified into two types as follows:

1) Aqueous solvents: Purified water or suitable aqueous solvents are usually used as solvents for aqueous otic solutions or as solvents or suspensions enclosed with the preparation. For the sterile preparations, sterilized purified water or sterilized aqueous solvents are used.

2) Non-aqueous solvents: Vegetable oils are usually used as the solvents for non-aqueous otic solutions. Suitable organic solvents may be also used as non-aqueous solvents.

D. Unless otherwise specified, substances intended only for the purpose of coloring should not be added to this preparation or the solvents or suspensions in this preparation.

E. For those filled into multiple-dose containers, suitable preservatives may be added to prevent microbial growth.

F. Unless otherwise specified, this preparation and solvents or suspensions added to this sterile preparation meet the requirements for the test according to the Sterility.

G. Tight containers are used for storage.

10. Preparations for Rectal Application

10.1. Enemas for Rectal Application

A. Enemas for rectal application are liquid or viscous gel preparations for applying though the anus.

B. This preparation is generally prepared by dissolving or suspending the drug substance in solvents, etc. using purified waters or appropriate aqueous solvents and filling it into a container. Dispersing agents, stabilizers, or pH adjusters may be used.

C. Tight containers are used for storage. Containers or packaging with low water vapor permeability are used, if the water evaporation affects the quality of preparation.

10.2. Semi-solid Preparations for Rectal Application

A. Semi-solid preparations for rectal application are applied to perianal or intra-anal regions, including creams, gels, or ointments.

B. In the preparations, the drug substance with excipients is emulsified in purified water, petrolatum, etc. or mixed with polymer gel or the fatty oils as the base for efficacy and homogeneity.

1) Creams for rectal application are prepared as directed under Creams.

2) Gels for rectal application are prepared as directed under Gels.

3) Ointments for rectal application are prepared as directed under Ointments.

C. For the preparations filled into multiple-dose containers, suitable preservatives may be added to prevent microbial growth.

D. This preparation has a suitable viscosity for rectal application.

E. Tight containers are used for storage. Containers or packaging with low water vapor permeability are used, if the water evaporation affects the quality of preparation.

10.3. Suppositories

A. Suppositories are solid preparations intended for the application into the rectum, which are usually prepared by mixing the drug substance evenly with the base and molding into a certain shape. This preparation melts or softens at body temperature or dissolve slowly in the body fluids.

B. This preparation is usually prepared by heating a homogeneous mixture of drug substance and excipients such as dispersing agents and emulsifier, dissolving or evenly dispersing in a liquid base, filling in a certain amount into a container, solidifying, and finally molding. Lipophilic or hydrophilic bases are usually used.

C. This preparation is generally a cone or spindle shape.

D. Unless otherwise specified, this preparation meets the requirements for the test according to the Disintegration or the Dissolution.

E. Unless otherwise specified, this preparation meets the requirements for test according to the Uniformity of Dosage Units.

F. Tight containers are used for storage.

11. Preparations for Vaginal Application

11.1. Suppositories for Vaginal Use

A. Suppositories for vaginal use are intended for vaginal application. This preparation is a semi-solid preparation in a certain shape and size, which release the drug substance when being melted by body temperature or slowly dissolved or dispersed in the body fluids.

B. This preparation is prepared as directed under Suppositories.

C. This preparation usually has a round or egg shape.

D. Unless otherwise specified, this preparation meets the requirements for the test according to the Uniformity of Dosage Units.
E. This preparation has suitable dissolution or disintegration properties.
F. Tight containers are used for storage. Containers or packaging with low water vapor permeability are used if the water evaporation affects the quality of preparation.

11.2. Vaginal Tablets

A. Vaginal tablets are solid preparations in a certain shape and size, intended for vaginal application, which release the drug substance when being dissolved or dispersed gradually in the body fluids.
B. This preparation has suitable dissolution or disintegration properties.
C. This preparation is prepared as directed under Tablets.
D. Unless otherwise specified, this preparation meets the requirements for the test according to the Uniformity of Dosage Units.
E. Unless otherwise specified, this preparation is tested as directed under Suppositories when the Disintegration is performed.
F. Tight containers are used for storage. Containers or packaging with low water vapor permeability are used if the water evaporation affects the quality of preparation.