

The Ministry of Health, Labour and Welfare Ministerial Notification No. 65

Pursuant to Paragraph 1, Article 41 of the Pharmaceutical Affairs Law (Law No. 145, 1960), the Japanese Pharmacopoeia (hereinafter referred to as “new Pharmacopoeia”), which has been established as follows*, shall be applied on April 1, 2011. However, in the case of drugs which are listed in the Pharmacopoeia (hereinafter referred to as “previous Pharmacopoeia”) [limited to those listed in the Japanese Pharmacopoeia whose standards are changed in accordance with this notification (hereinafter referred to as “new Pharmacopoeia”)] and drugs which have been approved as of April 1, 2011 as prescribed under Paragraph 1, Article 14 of the same law [including drugs the Minister of Health, Labour and Welfare specifies (the Ministry of Health and Welfare Ministerial Notification No. 104, 1994) as those exempted from marketing approval pursuant to Paragraph 1, Article 14 of the Pharmaceutical Affairs Law (hereinafter referred to as “drugs exempted from approval”)], the Name and Standards established in the previous Pharmacopoeia (limited to part of the Name and Standards for the drugs concerned) may be accepted to conform to the Name and Standards established in the new Pharmacopoeia before and on September 30, 2012. In the case of drugs which are listed in the new Pharmacopoeia (excluding those listed in the previous Pharmacopoeia) and drugs which have been approved as of April 1, 2011 as prescribed under Paragraph 1, Article 14 of the same law (including those exempted from approval), they may be accepted as those being not listed in the new Pharmacopoeia before and on September 30, 2012.

Ritsuo Hosokawa

The Minister of Health, Labour and Welfare

March 24, 2011

(The text referred to by the term “as follows” are omitted here. All of them are made available for public exhibition at the Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare, at each Regional Bureau of Health and Welfare, and at each Prefectural Office in Japan).

*The term “as follows” here indicates the contents of the Japanese Pharmacopoeia Sixteenth Edition from General Notices to Ultraviolet-visible Reference Spectra (pp. 1 - 2131).

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PREFACE

The 15th Edition of the Japanese Pharmacopoeia (JP) was promulgated by Ministerial Notification No. 285 of the Ministry of Health, Labour and Welfare (MHLW) on March 31, 2006.

In July 2006, the Committee on JP established the basic principles for the preparation of the JP 16th Edition, setting out the roles and characteristics of the JP, the definite measures for the revision, and the date of the revision.

At the Committee, the five basic principles of JP, which we refer to as the “five pillars”, were established as follows: 1) Including all drugs which are important from the viewpoint of health care and medical treatment; 2) Making qualitative improvement by introducing the latest science and technology; 3) Promoting internationalization; 4) Making prompt partial revision as necessary and facilitating smooth administrative operation; and 5) Ensuring transparency regarding the revision, and disseminating the JP to the public. It was agreed that the Committee on JP should make efforts, on the basis of these principles, to ensure that the JP is used more effectively in the fields of health care and medical treatment by taking appropriate measurements, including getting the understanding and cooperation of other parties concerned.

It was agreed that the JP should provide an official standard, being required to assure the quality of medicines in Japan in response to the progress of science and technology and medical demands at the time. It should define the standards for specifications, as well as the methods of testing to assure overall quality of all drugs in principle, and it should have a role in clarifying the criteria for quality assurance of drugs that are recognized to be essential for public health and medical treatment.

The JP has been prepared with the aid of the knowledge and experience of many professionals in the pharmaceutical field. Therefore, the JP should have the characteristics of an official standard, which might be widely used by all parties concerned. It should provide information and understanding about the quality of drugs to the public, and it should be conducive to smooth and effective regulatory control of the quality of drugs, as well as promoting and maintaining international consistency and harmonization of technical requirements.

It was also agreed that JP articles should cover

drugs, which are important from the viewpoint of health care and medical treatment, clinical results and frequency of use, as soon as possible after they reach the market.

The target date for the publication of JP 16th Edition (the Japanese edition) was set as April 2011.

JP Expert Committees are organized with the following panels: Panel on the Principles of Revisions; Sub-committee on the Principles of Revisions; Panel on Medicinal Chemicals; Panel on Antibiotics; Panel on Biologicals; Panel on Crude Drugs; Panel on Pharmaceutical Excipients; Panel on Physico-Chemical Methods; Panel on Preparations; Panel on Physical Methods; Panel on Biological Tests; Panel on Nomenclature; Panel on International Harmonization; Panel on Pharmaceutical Water; and Panel on Reference Standards. Furthermore, working groups are established under the Panel on Physico-Chemical Methods, Panel on Preparations and Panel on Biological Tests to expedite discussion on revision drafts.

In the Committee on JP, Takao Hayakawa took the role of chairman from July 2003 to December 2010, and Mitsuru Hashida from January 2011 to March 2011.

In addition to the regular revision every five years in line with the basic principles for the preparation of the JP it was agreed that partial revision should be done as necessary to take account of recent progress of science and in the interests of international harmonization.

In accordance with the above principles, the panels initiated deliberations on selection of articles, and on revisions for General Notices, General Rules for Crude Drugs, General Rules for Preparations, General Tests, Monographs and so on.

Draft revisions covering subjects in General Notices, General Rules for Crude Drugs, General Rules for Preparations, General Tests and Monographs, for which discussions were finished between September 2005 and March 2007, were prepared for a supplement to the JP 15. They were examined by the Committee on JP in April 2007, followed by the Pharmaceutical Affairs and Food Sanitation Council (PAFSC) in June 2007, and then submitted to the Minister of Health, Labour and Welfare. The supplement was named “Supplement I to the JP 15th Edition”, promulgated on September 28, 2007 by Ministerial Notification No. 316 of MHLW, and became effective on October 1,

2007.

Numbers of discussions in the panels to prepare the supplement drafts were as follows: Panel on Principles of Revisions (7); Sub-panel on Principles of Revision (6), Panel on Medicinal Chemicals (33, including the working group); Panel on Antibiotics (9); Panel on Biologicals (8); Panel on Crude Drugs (17); Panel on Pharmaceutical Excipients (7); Panel on Physico-Chemical Methods (12); Panel on Preparations (10); Panel on Physico-Chemical Methods (8); Panel on Biological Tests (7); Panel on Nomenclature (9); Panel on International Harmonization (2); and Panel on Pharmaceutical Water (7).

It should be noted that in the preparation of the drafts for the supplement, generous cooperation was given by the Technical Committee of the Pharmaceutical Manufacturer's Association of Osaka and of Tokyo, the Tokyo Crude Drugs Association, the Japan Pharmaceutical Excipients Council, the Japan Kampo Medicine Manufacturers' Association, the Japan Flavor and Fragrance Materials Association, the Japan Medical Plants Federation, the Japan Pharmaceutical Manufacturers Association, and the Japan Oilseeds Processors Association.

In consequence of this revision, the JP 15th Edition carries 1567 articles, owing to the addition of 90 articles and the deletion of 6 articles.

Draft revisions covering subjects, the addition of specification "Diethylene glycol and related substances" to the Purity of both monographs Glycerin and Concentrated Glycerin was examined by the Committee on JP in September 2007, followed by PAFSC in October 2007, and then submitted to the Minister of Health, Labour and Welfare.

This revision was promulgated on February 21, 2008 by Ministerial Notification No. 32 of MHLW, and became effective.

Draft revisions covering subjects, the addition of specification "Over-sulfated chondroitin sulfate" to the Purity of monograph Heparin Sodium and the resultant addition of Over-sulfated Chondroitin Sulfate Reference Standard to the list of Reference Standards in the General Tests were examined by the Committee on JP in July 2008, followed by PAFSC in October 2008, and then submitted to the Minister of Health, Labour and Welfare.

This revision was promulgated on July 31, 2008 by Ministerial Notification No. 417 of MHLW, and became effective.

Draft revisions covering subjects, the revision of the General Tests connected with the harmonization between the three pharmacopoeias, JP, EP and USP, the revision of the specification of monograph Longuu

and the addition of a monograph Powdered Longgu were examined by the Committee on JP in December 2008, followed by PAFSC in March 2009, and then submitted to the Minister of Health, Labour and Welfare.

This revision was promulgated on March 31, 2009 by Ministerial Notification No. 190 of MHLW, and became effective.

Draft revisions covering subjects in General Rules for Crude Drugs, General Tests and Monographs, for which discussions were completed between April 2007 and March 2009, were prepared for a supplement to the JP 15. They were examined by the Committee on JP in April 2009, followed by PAFSC in June 2009, and then submitted to the Minister of Health, Labour and Welfare.

The supplement was named "Supplement II to JP 15th Edition" and promulgated on September 30, 2009 by Ministerial Notification No. 425 of MHLW, and became effective on October 1, 2009.

Numbers of discussions in the panels to prepare the revision drafts were as follows: Panel on Principles of Revisions (3); Panel on Medicinal Chemicals (23); Panel on Antibiotics (8); Panel on Biologicals (8); Panel on Crude Drugs (21); Panel on Pharmaceutical Excipients (10); Panel on Physico-Chemical Methods (11, including the working group); Panel on Preparations (19, including the working group); Panel on Physico-Chemical Methods (9); Panel on Biological Tests (9); Panel on Nomenclature (6); Panel on International Harmonization (3); and Panel on Pharmaceutical Water (8).

It should be noted that in the preparation of the drafts for the supplement, generous cooperation was given by the Technical Committee of the Pharmaceutical Manufacturer's Association of Osaka and of Tokyo, the Tokyo Crude Drugs Association, the Japan Pharmaceutical Excipients Council, the Home Medicine Association of Japan, the Japan Kampo Medicine Manufacturers' Association, the Japan Flavor and Fragrance Materials Association, the Japan Medical Plants Federation, the Japan Parental Drug Association, the Japan Reagent Association, the Japan Oilseeds Processors Association, and the Association of Membrane Separation Technology of Japan.

In consequence of this revision, the JP 15th Edition carries 1673 articles, owing to the addition of 106 articles and the deletion of 1 article.

Draft revisions covering subjects, the revision of the General Tests connected with the harmonization between the three pharmacopoeias, JP, EP and USP, the addition of specification to the Identification and the

revision in the Purity of two monographs Heparin Calcium and Heparin Sodium, and the several additions to the Reference Standards and the Reagents, Test Solutions were examined by the Committee on JP in August 2009, followed by PAFSC in September 2009, and then submitted to the Minister of Health, Labour and Welfare.

This revision was promulgated on July 30, 2010 by Ministerial Notification No. 322 of MHLW, and became effective.

Draft revisions covering subjects in General Notices, General Rules for Crude Drugs, General Rules for Preparations, General Tests and Monographs, for which discussions were completed between April 2009 and March 2010, were prepared for JP 16. They were examined by the Committee on JP in September 2010, followed by PAFSC in October 2010, and then submitted to the Minister of Health, Labour and Welfare.

Numbers of discussions in the panels to prepare the revision drafts were as follows: Panel on Principles of Revisions (3); Panel on Medicinal Chemicals (20); Panel on Antibiotics (5); Panel on Biologicals (2); Panel on Crude Drugs (10); Panel on Pharmaceutical Excipients (5); Panel on Physico-Chemical Methods (10, including the working group); Panel on Preparations (10, including the working group); Panel on Physico-Chemical Methods (8); Panel on Biological Tests (9, including the working group); Panel on Nomenclature (3); Panel on International Harmonization (1); and Panel on Pharmaceutical Water (4).

It should be noted that in the preparation of the drafts, generous cooperation was given by the Technical Committee of the Pharmaceutical Manufacturer's Association of Osaka and of Tokyo, the Tokyo Crude Drugs Association, the Japan Pharmaceutical Excipients Council, the Home Medicine Association of Japan, the Japan Kampo Medicine Manufacturers' Association, the Japan Flavor and Fragrance Materials Association, the Japan Medical Plants Federation, the Japan Parental Drug Association, the Japan Reagent Association, the Japan Oilseeds Processors Association, and the Association of Membrane Separation Technology of Japan.

In consequence of this revision, the JP 16th Edition carries 1764 articles, owing to the addition of 106 articles and the deletion of 15 articles.

The principles of description and the salient points of the revision in this volume are as follows:

1. The JP 16th Edition comprises the following items, in order: Notification of MHLW; Contents; Preface; General Notices; General Rules for Crude Drugs; General Rules for Preparations; General Tests,

Processes and Apparatus; Official Monographs; then followed by Infrared Reference Spectra and Ultraviolet-visible Reference Spectra; General Information; Table of Standard Atomic Weights 2010 as an appendix; and a Cumulative Index.

2. The articles in General Rules for Preparations, Official Monographs, Infrared Reference Spectra and Ultraviolet-visible Reference Spectra are respectively placed in alphabetical order in principle.

3. The following items in each monograph are put in the order shown below, except that unnecessary items are omitted depending on the nature of the drug:

- (1) English title
- (2) Commonly used name(s)
- (3) Latin title (only for crude drugs)
- (4) Title in Japanese
- (5) Structural formula or empirical formula
- (6) Molecular formula and molecular mass
- (7) Chemical name
- (8) CAS Registry Number
- (9) Origin
- (10) Limits of the content of the ingredient(s) and/or the unit of potency
- (11) Labeling requirements
- (12) Method of preparation
- (13) Description/Description of crude drugs
- (14) Identification tests
- (15) Specific physical and/or chemical values
- (16) Purity tests
- (17) Loss on drying or Ignition, or Water
- (18) Residue on ignition, Total ash or Acid-insoluble ash
- (19) Tests being required for pharmaceutical preparations and other special tests
- (20) Isomer ratio
- (21) Assay or the content of the ingredient(s)
- (22) Containers and storage
- (23) Expiration date
- (24) Others

4. In each monograph, the following physical and chemical values representing the properties and quality of the drug are given in the order indicated below, except that unnecessary items are omitted depending on the nature of drug:

- (1) Alcohol number
- (2) Absorbance
- (3) Congealing point
- (4) Refractive index
- (5) Osmolarity
- (6) Optical rotation
- (7) Viscosity

- (8) pH
- (9) Specific gravity
- (10) Boiling point
- (11) Melting point
- (12) Acid value
- (13) Saponification value
- (14) Ester value
- (15) Hydroxyl value
- (16) Iodine value

5. Identification tests comprise the following items, which are generally put in the order given below:

- (1) Coloration reactions
- (2) Precipitation reactions
- (3) Decomposition reactions
- (4) Derivatives
- (5) Infrared and/or ultraviolet-visible absorption spectrometry
- (6) Special reactions
- (7) Cations
- (8) Anions

6. Purity tests comprise the following items, which are generally put in the order given below, except that unnecessary items are omitted depending on the nature of drug:

- (1) Color
- (2) Odor
- (3) Clarity and/or color of solution
- (4) Acidity or alkalinity
- (5) Acidity
- (6) Alkalinity
- (7) Chloride
- (8) Sulfate
- (9) Sulfite
- (10) Nitrate
- (11) Nitrite
- (12) Carbonate
- (13) Bromide
- (14) Iodide
- (15) Soluble halide
- (16) Thiocyanate
- (17) Selenium
- (18) Cationic salts
- (19) Ammonium
- (20) Heavy metals
- (21) Iron
- (22) Manganese
- (23) Chromium
- (24) Bismuth
- (25) Tin
- (26) Aluminum
- (27) Zinc

- (28) Cadmium
- (29) Mercury
- (30) Copper
- (31) Lead
- (32) Silver
- (33) Alkaline earth metals
- (34) Arsenic
- (35) Foreign matters
- (36) Related substances
- (37) Residual solvent
- (38) Other impurities
- (39) Readily carbonizable substances

7. The following paragraphs of General Notices were revised:

- (1) Paragraph 3: The sentence “The distinction of the preparations name of Fine Granules and Powders follows according to the definition in the section of “Powders” of General Rules for Preparations.” was deleted according to the revision of General Rules for Preparations.
- (2) Paragraph 4: Exemplified name of preparations was revised in accordance with the current status of listed monographs.
- (3) Paragraph 8: Atomic masses the JP refers to was revised to the table of “Standard Atomic Weights 2010”.
- (4) Paragraph 9: Being often used two units, pS·cm⁻¹ and CFU, were added.
- (5) Paragraph 16: The definition of water used to measure the number of drops of a dropping device was revised in accordance with the revision of Paragraph 20.
- (6) Paragraph 20: The provision of water used for the test of drugs was revised according to the revision of monograph Purified Water.
- (7) Other descriptions were improved.

8. To Paragraph 1 of General Rules for Crude Drugs the following items were added:

- (1) Aluminum Silicate Hydrate with Silicon Dioxide
- (2) Brown Rice
- (3) Koi
- (4) Sesame

9. The General Rules for Preparations was revised as follows in general:

The addition of dosage forms which had not have been prescribed, the classification of dosage forms based on the route and/or site of administration, and the definition of individual dosage forms and the tests to be applied to them.

10. The following items in General Tests, Processes and Apparatus were revised:

- (1) 2.01 Liquid Chromatography
- (2) 2.46 Residual Solvents Test
- (3) 2.51 Conductivity Measurement
- (4) 2.54 pH Determination
- (5) 2.58 X-Ray Powder Diffraction Method
- (6) 3.01 Determination of Bulk and Tapped Densities
- (7) 4.01 Bacterial Endotoxins Test
- (8) 4.05 Microbial Limit Test
- (9) 4.06 Sterility Test
- (10) 5.02 Microbial Limit Test for Crude Drugs
- (11) 6.03 Particle Size Distribution Test for Preparations
- (12) 6.07 Insoluble Particulate Matter Test for Injections
- (13) 6.08 Insoluble Particulate Matter Test for Ophthalmic Solutions
- (14) 7.02 Test Methods for Plastic Containers
- (15) 8.01 Sterilization and Aseptic Manipulation

11. The title of the following item in General Tests, Processes and Apparatus was revised:

8.01 Sterilization and Aseptic Manipulation

12. The following Reference Standards were added:

Atorvastatin Calcium
 Alendronate Sodium
 Glimepiride
 Sarpogrelate Hydrochloride
 Donepezil Hydrochloride
 Trehalose
 Nateglinide
 Fexofenadine Hydrochloride
 Fluvoxamine Maleate
 Propiverine Hydrochloride
 Pemirolast Potassium
 Rabeprazole Sodium
 Risedronic Acid

13. The following Reference Standard was revised in Japanese title:

Tyrosine

14. The following Reference Standards were deleted from the list of 9.01 Reference Standards:

Astromicin Sulfate
 Insulin
 Sisomicin Sulfate
 Cefapirin Sodium
 Cefuroxime Sodium
 Netilmicin Sulfate

15. The intended use of each individual Reference Standard was deleted from the list of 9.01 Reference

Standards.

16. Some of the names of the reagents or test solutions under 9.41 Reagents, Test Solutions were maintained.

17. To the each individual item in the General Tests, Processes and Apparatus, chapter and section numbers were putted.

18. The following substans were newly added to the Official Monographs:

Aciclovir Syrup
 Aciclovir Injection
 Aciclovir for Syrup
 Acetylcysteine
 Atorvastatin Calcium Hydrte
 Atorvastatin Calcium Tablets
 Amikacin Sulfate for Injection
 Alendronate Sodium Hydrate
 Alendronate Sodium Injection
 Alendronate Sodium Tablets
 L-Isoleucine, L-Leucine and L-Valine Granules
 Ebastine
 Ebastine Orally Disintegrating Tablets
 Ebastine Tablets
 Carvedilol
 Carvedilol Tablets
 Candesartan Cilexetil
 Candesartan Cilexetil Tablets
 Quinapril Hydrochloride
 Quinapril Hydrochloride Tablets
 Glimepiride
 Glimepiride Tablets
 L-Glutamic acid
 Sarpogrelate Hydrochloride
 Sarpogrelate Hydrochloride Fine Granules
 Sarpogrelate Hydrochloride Tablets
 Diazepam Tablets
 Purified Water in Containers
 Sterile Water for Injection in Containers
 Spironolactone Tablets
 Zolpidem Tartrate Tablets
 Tamsulosin Hydrochloride Extended-release Tablets
 Tamoxifen Citrate
 Precipitated Calcium Carbonate Fine Granules
 Precipitated Calcium Carbonate Tablets
 Temocapril Hydrochloride
 Temocapril Hydrochloride Tablets
 Terbinafine Hydrochloride
 Terbinafine Hydrochloride Cream
 Terbinafine Hydrochloride Solution
 Terbinafine Hydrochloride Spray
 Doxazosin Mesilate Tablets

Donepezil Hydrochloride
 Donepezil Hydrochloride Fine Granules
 Donepezil Hydrochloride Tablets
 Trehalose Hydrate
 Nateglinide
 Nateglinide Tablets
 L-Lactic Acid
 Sodium L-Lactate Solution
 Haloperidol Fine Granules
 Pioglitazone Hydrochloride Tablets
 L-Histidine
 L-Histidine Hydrochloride Hydrate
 Famotidine Injection
 Fexofenadine Hydrochloride
 Butenafine Hydrochloride
 Butenafine Hydrochloride Cream
 Butenafine Hydrochloride Solution
 Butenafine Hydrochloride Spray
 Pravastatin Sodium Fine Granules
 Pravastatin Sodium Solution
 Pravastatin Sodium Tablets
 Fluconazole
 Fluvoxamine Maleate
 Fluvoxamine Maleate Tablets
 Flecainide Acetate
 Flecainide Acetate Tablets
 Propiverine Hydrochloride
 Propiverine Hydrochloride Tablets
 Probucol Fine Granules
 Probucol Tablets
 L-Proline
 Betamipron
 Pemirolast Potassium
 Pemirolast Potassium for Syrup
 Pemirolast Potassium Tablets
 Beraprost Sodium
 Beraprost Sodium Tablets
 Mupirocin Calcium Ointment
 Methotrexate Capsules
 Mosapride Citrate Powder
 Rabeprazole Sodium
 Risperidone
 Risperidone Fine Granules
 Risperidone Oral Solution
 Risperidone Tablets
 Sodium Risedronate Hydrate
 Sodium Risedronate Tablets
 Roxatidine Acetate Hydrochloride Extended-release
 Tablets
 Roxatidine Acetate Hydrochloride for Injection
 Oregedokuto Extract
 Aluminum Silicate Hydrate with Silicon Dioxide
 Koi

Brown Rice
 Sesame
 Saikokeishito Extract
 Saibokuto Extract
 Shakuyakukanzoto Extract
 Juzentaihoto Extract
 Shosaikoto Extract
 Shoseiryuto Extract
 Mukoi-Daikenchuto Extract
 Chutosan Extract
 Bakumondoto Extract
 Rikkunshito Extract

19. The following monographs were revised:

Zinc Oxide Ointment
 Ajmaline Tablets
 Ascorbic Acid Powder
 Ascorbic Acid Injection
 Aspirin Tablets
 Acetylcholine Chloride for Injection
 Azelastine Hydrochloride Granules
 Adrenalin
 Adrenalin Solution
 Opium Tincture
 Opium Alkaloids Hydrochloride Injection
 Opium Alkaloids and Atropine Injection
 Opium Alkaloids and Scopolamine Injection
 Weak Opium Alkaloids and Scopolamine Injection
 Meglumine Sodium Amidotrizoate Injection
 Amitriptyline Hydrochloride Tablets
 Aminophylline Injection
 L-Alanine
 L-Arginine Hydrochloride Injection
 Allopurinol
 Sulfur and Camphor Lotion
 Sodium Iotalamate Injection
 Meglumine Iotalamate Injection
 Isoniazid Injection
 Isoniazid Tablets
 Idoxuridine Ophthalmic Solution
 Imipramine Hydrochloride
 Irsogladine Maleate Fine Granules
 Indigocarmine Injection
 Insulin Human (Genetical Recombination)
 Indometacin Capsules
 Indometacin Suppositories
 Ursodeoxycholic Acid Granules
 Ecabet Sodium Granules
 Estradiol Benzoate Injection
 Estradiol Benzoate Injection (Aqueous Suspension)
 Estriol Tablets
 Estriol Injection (Aqueous Suspension)
 Etacrynic Acid Tablets

Ethanol for Disinfection	Purified Water
Etizolam Fine Granules	Sterile Purified Water in Containers
Ethinylestradiol	Water for Injection
Ethinylestradiol Tablets	Dried Aluminum Hydroxide Gel Fine Granules
Etilefrine Hydrochloride Tablets	Suxamethonium Chloride Injection
Edrophonium Chloride Injection	Suxamethonium Chloride for Injection
Ephedrine Hydrochloride Injection	Spironolactone
Ephedrine Hydrochloride Tablets	Sulpyrine Injection
10% Ephedrine Hydrochloride Powder	Sulfobromophthalein Sodium Injection
Ergometrine Maleate Hydrochloride Injection	Isotonic Sodium Chloride Solution
Ergometrine Maleate Hydrochloride Tablets	Cefaclor
10% Sodium Chloride Injection	Cefaclor Compound Granules
Hydrochloric Acid Lemonade	Cefaclor Fine Granules
Compound Oxycodone Injection	Cefazolin Sodium Hydrate
Compound Oxycodone and Atropine Injection	Cefatrizine Propylene Glycolate for Syrup
Fructose Injection	Cefalexin
Potash Soap	Cefalexin for Syrup
Carmellose	Cefalotin Sodium
Carmellose Calcium	Cefixime Hydrate
Carmellose Sodium	Cefepime Dihydrochloride Hydrate
Xylitol Injection	Cefcapene Pivoxil Hydrochloride Hydrate
Diagnostic Sodium Citrate Solution	Cefcapene Pivoxil Hydrochloride Fine Granules
Sodium Citrate Injection for Transfusion	Cefditoren Pivoxil Fine Granules
Glycerin and Potash Solution	Cefdinir Fine Granules
Absorptive Cream	Ceftibuten Hydrate
Hydrophilic Cream	Cefteram Pivoxil Fine Granules
Clindamycin Hydrochloride	Cefpodoxime Proxetil
Cresol Solution	Cefroxadine for Syrup
Saponated Cresol Solution	Sevoflurane
Clofibrate Capsules	D-Sorbitol Solution
Clomifene Citrate Tablets	Tacrolimus Hydrate
Chlordiazepoxide Powder	Talc
Chlordiazepoxide Tablets	Sodium Bicarbonate Injection
Chlorpheniramine Maleate Powder	Simple Syrup
Chlorpheniramine Maleate Tablets	Thiamazole Tablets
Chlorpropamide Tablets	Thiamine Chloride Hydrochloride Powder
Chlorpromazine Hydrochloride Injection	Thiamine Chloride Hydrochloride Injection
Ketoconazole Solution	Thiopental Sodium for Injection
Ketoconazole Cream	Sodium Thiosulfate Injection
10% Codeine Phosphate Powder	Nitrogen
Codeine Phosphate Tablets	Tipepidine Hibenazate Tablets
Compound Salicylic Acid Spirit	L-Tyrosine
Oxygen	Testosterone Enanthate Injection
Diazepam	Deslanoside Injection
Digitoxin Tablets	Dehydrocholic Acid Injection
Diclofenamide Tablets	Dopamine Hydrochloride Injection
Distigmine Bromide Tablets	Triclofos Sodium Syrup
Dydrogesterone Tablets	Trihexyphenidyl Hydrochloride Tablets
Zinostatin Stimalamer	Trimethadione Tablets
1% Dihydrocodeine Phosphate Powder	Tolnaftate Solution
Dimenhydrinate Tablets	Tolbutamide Tablets
Silver Nitrate Ophthalmic Solution	Droxidopa Fine Granules
Water	Troxipide Fine Granules

Rape Seed Oil
Naphazoline and Chlorpheniramine Solution
Nicardipine Hydrochloride Injection
Nicotinic Acid Injection
Nicomol Tablets
Carbone Dioxide
Nicergoline Powder
Nitroglycerin Tablets
Neostigmine Methylsulfate Injection
Noradrenaline Injection
Norgestrel and Ethinylestradiol Tablets
Baclofen Tablets
Papaverine Hydrochloride Injection
Calcium Paraaminosalicylate Granules
Bisacodyl Suppositories
Hydralazine Hydrochloride Powder
Hydralazine Hydrochloride Tablets
Hydralazine Hydrochloride for Injection
Piperazine Phosphate Tablets
Famotidine Powder
Faropenem Sodium for Syrup
Phenytoin Powder
Phenytoin Tablets
Phenobarbital
10% Phenobarbital Powder
Liquefied Phenol
Phenolated Water
Phenolated Water for Disinfection
Phenol and Zinc Oxide Liniment
Phenolsulfonphthalein Injection
Glucose Injection
Prazepam Tablets
Flurazepam Capsules
Prednisolone Tablets
Prednisolone Sodium Succinate for Injection
Procaine Hydrochloride Injection
Prochlorperazine Maleate Tablets
Propylthiouracil Tablets
Flopropione Capsules
Probenecid
Probenecid Tablets
Flomoxef Sodium
Betamethasone Valerate and Gentamicin Sulfate Cream
Betamethasone Sodium Phosphate
Pethidine Hydrochloride Injection
Perphenazine Tablets
Perphenazine Maleate Tablets
Benzalkonium Chloride Solution
Benzyl Alcohol
Benzethonium Chloride Solution
Formalin Water
Mercurochrome Solution
D-Mannitol Injection
Yellow Beeswax
Minocycline Hydrochloride
Minocycline Hydrochloride Tablets
Minocycline Hydrochloride for Injection
Alum Solution
10% *dl*-Methylephedrine Hydrochloride Powder
Methyltestosterone Tablets
Methyldopa Tablets
Metenolone Enanthate Injection
Metronidazole Tablets
Mepivacaine Hydrochloride
Mefruside Tablets
Meropenem Hydrate
Morphine Hydrochloride Tablets
Morphine Hydrochloride Injection
Morphine and Atropine Injection
Folic Acid Tablets
Folic Acid Injection
Meglumine Sodium Iodamide Injection
Iodine Tincture
Dilute Iodine Tincture
Dental Iodine Glycerin
Compound Iodine Glycerin
Iodine, Salicylic Acid and Phenol Spirit
Latamoxef Sodium
Lanatoside C Tablets
Liothyronine Sodium Tablets
L-Lysine Hydrochloride
L-Lysine Acetate
Lidocaine Injection
Rifampicin Capsules
Riboflavin Powder
Riboflavin Sodium Phosphate Injection
Zinc Sulfate Ophthalmic Solution
Magnesium Sulfate Mixture
Magnesium Sulfate Injection
Ringer's Solution
Dibasic Sodium Phosphate Hydrate
Reserpine Tablets
Reserpine Injection
Levallorphan Tartrate Injection
Levothyroxine Sodium Tablets
Sweet Hydrangea Leaf
Aloe
Powdered Aloe
Foeniculated Ammonia Spirit
Epimedium Herb
Fennel Oil
Turmeric
Powdered Turmeric
Bearberry Leaf
Uva Ursi Fluidextract

Corydalis Tuber
 Powdered Corydalis Tuber
 Polygala Root
 Powdered Polygala Root
 Pueraria Root
 Kamishoyosan Extract
 Glycyrrhiza Extract
 Crude Glycyrrhiza Extract
 Agar
 Platycodon Fluidextract
 Catalpa Fruit
 Apricot Kernel
 Apricot Kernel Water
 Bitter Tincture
 Keishibukuryogan Extract
 Safflower
 Red Ginseng
 Magnolia Bark
 Powdered Magnolia Bark
 Goshajinkigan Extract
 Euodia Fruit
 Condurango
 Condurango Fluidextract
 Bupleurum Root
 Saireito Extract
 Saffron
 Gardenia Fruit
 Powdered Gardenia Fruit
 Cornus Fruit
 Jujube Seed
 Eleutherococcus Senticosus Rhizome
 Sodium Bicarbonate and Bitter Tincture Mixture
 Cimicifuga Rhizome
 Magnolia Flower
 Shimbuto Extract
 Senega Syrup
 Toad Venom
 Atractylodes Lancea Rhizome
 Perilla Herb
 Alisma Rhizome
 Powdered Alisma Rhizome
 Uncaria Hook
 Powdered Polyporus Sclerotium
 Citrus Unshiu Peel
 Capsicum
 Powdered Capsicum
 Capsicum Tincture
 Peach Kernel
 Powdered Peach Kernel
 Orange Peel Syrup
 Orange Peel Tincture
 Ipecac
 Powdered Ipecac

Ipecac Syrup
 Eucommia Bark
 Ginseng
 Powdered Ginseng
 Hachimijiogan Extract
 Honey
 Mentha Water
 Glehnia Root and Rhizome
 Hangekobokuto Extract
 Angelica Dahurica Root
 Atractylodes Rhizome
 Poria Sclerotium
 Belladonna Extract
 Sinomenium Stem and Rhizome
 Saposhnikovia Root and Rhizome
 Moutan Bark
 Powdered Moutan Bark
 Hochuekkito Extract
 Nux Vomica Extract
 Nux Vomica Extract Powder
 Nux Vomica Tincture
 Oyster Shell
 Powdered Oyster Shell
 Ryokeijutsukanto Extract
 Scopolia Extract
 Scopolia Extract Powder
 Royal Jelly

20. The following monographs were deleted:

Astromicin Sulfate
 Isophane Insulin Injection (Aqueous Suspension)
 Insulin
 Insulin Injection
 Insulin Zinc Injection (Aqueous Suspension)
 Insulin Zinc Protamine Injection (Aqueous Suspension)
 Crystalline Insulin Zinc Injection (Aqueous Suspension)
 Amorphous Insulin Zinc Injection (Aqueous Suspension)
 Sisomicin Sulfate
 Cefapirin Sodium
 Cefuroxime Sodium
 Netilmicin Sulfate
 Bufexamac
 Bufexamac Cream
 Bufexamac Ointment

21. The following monographs were changed in Japanese title:

Absorptive Cream
 Hydrophilic Cream
 Sterile Purified Water in Containers
 Cefixime Hydrate

L-Tyrosine
 L-Lysine Hydrochloride
 L-Lysine Acetate

22. The following monographs were revised in the content limit more precise:

Ajmaline Tablets
 Ascorbic Acid Powder
 Ascorbic Acid Injection
 Aspirin Tablets
 Acetylcholine Chloride for Injection
 Meglumine Sodium Amidotrizoate Injection
 Amitriptyline Hydrochloride Tablets
 Aminophylline Injection
 Sodium Iotalamate Injection
 Meglumine Iotalamate Injection
 Isoniazid Tablets
 Isoniazid Injection
 Idoxuridine Ophthalmic Solution
 Imipramine Hydrochloride
 Indigocarmine Injection
 Indometacin Capsules
 Indometacin Suppositories
 Estradiol Benzoate Injection
 Estradiol Benzoate Injection (Aqueous Suspension)
 Estriol Tablets
 Estriol Injection (Aqueous Suspension)
 Etacrynic Acid Tablets
 Ethinylestradiol Tablets
 Edrophonium Chloride Injection
 Ephedrine Hydrochloride Tablets
 Ephedrine Hydrochloride Injection
 Ergometrine Maleate Tablets
 Ergometrine Maleate Injection
 Fructose Injection
 Xylitol Injection
 Clofibrate Capsules Extract
 Clomifene Citrate Tablets
 Chlordiazepoxide Powder
 Chlordiazepoxide Tablets
 Chlorpropamide Tablets
 Chlorpromazine Hydrochloride Injection
 Codeine Phosphate Tablets
 Digoxin Tablets
 Diclofenamide Tablets
 Distigmine Bromide Tablets
 Dimenhydrinate Tablets
 Dydrogesterone Tablets
 Suxamethonium Chloride Injection
 Suxamethonium Chloride for Injection
 Sulpyrine Injection
 Sulfobromophthalein Sodium Injection
 D-Sorbitol Solution

Sodium Bicarbonate Injection
 Thiamazole Tablets
 Thiamine Chloride Hydrochloride Powder
 Thiamine Chloride Hydrochloride Injection
 Thiopental Sodium for Injection
 Sodium Thiosulfate Injection
 Tipepidine Hibenazate Tablets
 Testosterone Enanthate Injection
 Deslanoside Injection
 Dehydrocholic Acid Injection
 Dopamine Hydrochloride Injection
 Triclofos Sodium Syrup
 Trihexyphenidyl Hydrochloride Tablets
 Trimethadione Tablets
 Tolnaftate Solution
 Tolbutamide Tablets
 Nicardipine Hydrochloride Injection
 Nicotinic Acid Injection
 Nicomol Tablets
 Nitroglycerin Tablets
 Neostigmine Methylsulfate Injection
 Noradrenaline Injection
 Norgestrel and Ethinylestradiol Tablets
 Baclofen Tablets
 Papaverine Hydrochloride Injection
 Bisacodyl Suppositories
 Hydralazine Hydrochloride Powder
 Hydralazine Hydrochloride Tablets
 Hydralazine Hydrochloride for Injection
 Piperazine Phosphate Tablets
 Glucose Injection
 Prazepam Tablets
 Flurazepam Capsules
 Prednisolone Tablets
 Prednisolone Sodium Succinate for Injection
 Procaine Hydrochloride Injection
 Prochlorperazine Maleate Tablets
 Propylthiouracil Tablets
 Probenecid Tablets
 Pethidine Hydrochloride Injection
 Perphenazine Tablets
 Perphenazine Maleate Tablets
 Benzalkonium Chloride Solution
 Benzethonium Chloride Solution
 D-Mannitol Injection
 Methyl dopa Tablets
 Metenolone Enanthate Injection
 Mefruside Tablets
 Morphine Hydrochloride Tablets
 Morphine Hydrochloride Injection
 Folic Acid Tablets
 Folic Acid Injection
 Lanatoside C Tablets

Liothyronine Sodium Tablets
 Lidocaine Injection
 Riboflavin Powder
 Riboflavin Sodium Phosphate Injection
 Magnesium Sulfate Injection
 Reserpine Tablets
 Reserpine Injection
 Levallorphan Tartrate Injection
 Levothyroxine Sodium Tablets

23. The monographs which 'Method of preparation' was revised according to the revision of General Rules for Preparations were as follows:

Ascorbic Acid Powder
 Irsogladine Maleate Fine Granules
 Etizolam Fine Granules
 10% Ephedrine Phosphate Powder
 Chlordiazepoxide Powder
 Chlorpheniramine Maleate Powder
 Ketoconazole Solution
 Ketoconazole Cream
 1% Codeine Phosphate Powder
 1% Dihydrocodeine Phosphate Powder
 Dried Aluminum Hydroxide Gel Fine Granules
 Cefaclor Fine Granules
 Cefatrizine Propylene Glycolate for Syrup
 Cefalexin for Syrup
 Cefcapene Pivoxil Hydrochloride Fine Granules
 Cefditoren Pivoxil Fine Granules
 Cefdinir Fine Granules
 Cefteram Pivoxil Fine Granules
 Cefroxadine for Syrup
 Droxidopa Fine Granules
 Troxipide Fine Granules
 Nicergoline Powder
 Hydralazine Hydrochloride Powder
 Famotidine Powder
 Faropenem Sodium for Syrup
 Phenytoin Powder
 10% Phenobarbital Powder
 Betamethazone Valerate and Gentamicin Sulfate Cream
 10% *dl*-Methylephedrine Hydrochloride Powder
 Riboflavine Powder

24. The monographs which 'Particle size' was deleted according to the revision of General Rules for Preparations were as follows:

Azelastine Hydrochloride Granules
 Ursodeoxycholic Acid Granules
 Ecabet Sodium Granules
 Chlorpheniramine Maleate Powder
 Cefaclor Compound Granules
 Nicergoline Powder

Calcium Paraaminosalicylate Granules
 10% Phenobarbital Powder

25. The monographs which 'Method of preparation' was revised according to the revision of the monograph "Water" were as follows:

Adrenaline Solution
 Opium Tincture
 Opium Alkaloids Hydrochloride Injection
 Opium Alkaloids and Atropine Injection
 Opium Alkaloids and Scopolamine Injection
 Weak Opium Alkaloids and Scopolamine Injection
 Meglumine Sodium Amidotrizoate Injection
 L-Arginine Hydrochloride Injection
 Sulfur and Camphor Lotion
 Sodium Iotalamate Injection
 Meglumine Iotalamate Injection
 Ethanol for Disinfection
 10% Sodium Chloride Injection
 Hydrochloric Acid Lemonade
 Compound Oxycodone Injection
 Compound Oxycodone and Atropine Injection
 Potash Soap
 Diagnostic Sodium Citrate Solution
 Sodium Citrate Injection for Transfusion
 Glycerin and Potash Solution
 Absorptive Cream
 Hydrophilic Cream
 Cresol Solution
 Saponated Cresol Solution
 Compound Salicylic Acid Spirit
 Silver Nitrate Ophthalmic Solution
 Isotonic Sodium Chloride Solution
 Simple Syrup
 Deslanoside Injection
 Naphazoline and Chlorpheniramine Solution
 Phenolated Water for Disinfection
 Phenolated Water
 Phenol and Zinc Oxide Liniment
 Phenolsulfonphthalein Injection
 Benzalkonium Chloride Solution
 Benzethonium Chloride Solution
 Formalin Water
 Mercurochrome Solution
 Alum Solution
 Morphine and Atropine Injection
 Meglumine Sodium Iodamide Injection
 Iodine Tincture
 Dilute Iodine Tincture
 Dental Iodine Glycerin
 Compound Iodine Glycerin
 Iodine, Salicylic Acid and Phenol Spirit
 Zinc Sulfate Ophthalmic Solution

Magnesium Sulfate Mixture
 Ringer's Solution
 Foeniculated Ammonia Spirit
 Uva Ursi Fluidextract
 Glycyrrhiza Extract
 Crude Glycyrrhiza Extract
 Platycodon Fluidextract
 Apricot Kernel Water
 Bitter Tincture
 Condurango Fluidextract
 Sodium Bicarbonate and Bitter Tincture Mixture
 Senega Syrup
 Orange Peel Syrup
 Orange Peel Tincture
 Ipecac Syrup
 Mentha Water
 Belladonna Extract
 Nux Vomica Extract
 Nux Vomica Extract Powder
 Nux Vomica Tincture
 Scopolia Extract
 Scopolia Extract Powder

26. Monographs in which the test "Content determination" was changed to "Assay" were as follows:

Aloe
 Powdered Aloe
 Turmeric
 Powdered Turmeric
 Uva Ursi
 Uva Ursi Fluidextract
 Corydalis Tuber
 Powdered Corydalis Tuber
 Apricot Kernel
 Magnolia Bark
 Powdered Magnolia Bark
 Bupleurum Root
 Gardenia Fruit
 Powdered Gardenia Fruit
 Cornus Fruit
 Toad Venom
 Perilla Herb
 Uncaria Hook
 Capsicum
 Powdered Capsicum
 Capsicum Tincture
 Peach Kernel
 Powdered Peach Kernel
 Ipecac
 Powdered Ipecac
 Ipecac Syrup
 Moutan Bark
 Powdered Moutan Bark

Royal Jelly
 Those who were engaged in the preparation of JP 16 are as follows:
 Norio Aimi
 Fumiaki Akahori
 Teruo Amagasa
 Mitsuo Aoki
 Kiichi Aonuki
 Nobuo Aoyagi**
 Hiroshi Asama
 Toshiki Asano
 Kazuhide Ashizawa
 Shinichiro Aso
 Yukio Aso
 Hiroyuki Arai
 Keiko Arimoto
 Takashi Bamba
 Masahiko Chikuma
 Makoto Emura
 Hiroyuki Fuchino
 Shigeyuki Fujikura
 Kiyoshi Fukuhara
 Akihiko Fujise
 Goro Funamoto
 Yukihiro Goda
 Takashi Goto
 Noriaki Habasaki
 Takashi Hakamatsuka
 Ruri Hanajiri
 Kentaro Hanada
 Toshikazu Harada
 Kouji Hasegawa
 Mitsuru Hashida*
 Susumu Hashimoto
 Harumi Hatano
 Rika Hatano
 Takao Hayakawa*
 Masahiro Hayashi
 Yoshinori Hayashi
 Kenji Higuchi
 Katsuhito Hiramatsu
 Yuuki Hirata
 Fusayoshi Hirayama
 Takashi Hiroshima
 Yukio Hiyama
 Naoki Hosono
 Kenji Hosoya
 Kunimoto Hotta
 Akihiro Hurukawa
 Masashi Hyuga
 Takanori Ichikawa
 Nobukazu Igoshi
 Kazuhiko Ikegami

Koichi Inubushi	Kumiko Kusuyama
Kenichi Inui	Masako Maeda
Akiko Ishii	Midori Makita
Tsuneo Ishizuka	Masahiko Marumoto
Shigeru Itai	Yoshihisa Matsuda
Chizuko Itoh	Norio Matsuki
Yuji Ito	Eiichi Mikami
Takashi Itoh	Satoshi Minobe
Masao Izaki	Takao Mitsushashi
Kenichi Izutsu	Tsuyoshi Miura
Akemi Kai	Tsuyoshi Miyagawa
Kazuaki Kakehi	Hiroto Miyamoto
Takemine Kanai	Naoki Miyata
Motoko Kanke	Tamaki Miyazaki
Hirohito Katayama	Michinao Mizugaki
Haru Kato	Taiichi Mizuta
Kumiko Kato	Mitsuo Mori
Yoshiaki Kato	Kaoru Morikawa
Noriko Katori	Seiki Morimoto
Satoshi Kawada	Katsuhiko Morisawa
Nobuo Kawahara	Osamu Morita
Urao Kawakami	Takashi Morita
Toru Kawanishi	Toshimi Murai
Yoshihiko Kawarasaki	Masashi Muroi
Nana Kawasaki	Hiroaki Nagashige
Toshisuke Kawasaki	Takahiro Naito
Yoshiaki Kawashima	Sinsaku Nakagawa
Keiji Kijima	Emi Nakajima
Yutaka Kikuchi	Hiroshi Nakamura
Yuuichi Kikuchi	Tatsuya Nakano
Yasuhiro Kishimoto	Tatsumi Nakashima
Mitsukazu Kitada	Mitsuo Nanaura
Fumiyuki Kiuchi	Masaaki Naotsuka
Junko Kizu	Masao Nasu
Takashi Kobayashi	Shingo Niimi
Yukari Koga	Yutaka Nishihara
Masayoshi Kohase	Hiroshi Nishimura
Tatsuo Koide	Atsushi Nukanobu
Shigeo Kojima	Sumiaki Oba
Hiroyasu Kokubo	Shukichi Ochiai
Katsuko Komatsu	Yasumitsu Ogura
Hitoshi Komatsubara	Atsuyuki Ohtsuki
Akio Komura	Ryozo Oishi
Tetsuya Konda	Satoshi Okada
Toshifumi Konda	Minoru Okada
Kenji Kondo	Norio Okahana
Seizo Kondo	Kimiya Okazaki
Kenichi Kumasaka	Akira Okonogi
Takao Kunisada	Tsuneo Okubo
Masaaki Kurihara	Haruhiro Okuda
Hiroyuki Kurita	Takamasa Okugawa
Haruo Kuriyama	Yuko Osumi
Fumiyo Kusu	Masami Otsuka

Tadashi Ouchi
 Kazuhiro Owada
 Kenji Saiki
 Yukio Saito
 Yoshikazu Sakagami
 Eiji Sakai
 Tomoaki Sakamoto
 Shingou Sakurai
 Tomofumi Santa
 Hideki Sasaki
 Hiroshi Sasaki
 Kunio Sasaki
 Tomoko Sasaki
 Tsuguo Sasaki
 Kazumichi Sasaoki
 Motoyoshi Satake
 Kyoko Sato
 Michiko Sekiguchi
 Setsuko Sekita
 Yasuo Shimada
 Kesamitsu Shimizu
 Kozo Shimoda
 Kyoko Shimura
 Osamu Shirokizawa
 Osamu Shirota
 Takuji Shoda
 Junya Souma
 Takashi Sonobe
 Keiichi Sudo
 Shoko Sueyoshi
 Shinji Sugaya
 Daisuke Sugiura
 Hisakazu Sunada
 Hideyo Suzuki
 Mikio Suzuki
 Shinichi Tadaki
 Nobuo Taguchi
 Toshio Takachi
 Wataru Takada
 Yoshikazu Takahashi
 Kunihiro Takai
 Masaki Takao
 Kikuo Takatera
 Osami Takeda
 Tadahiro Takeda
 Yasushi Takeda
 Hirohumi Takeuchi
 Toyoshige Tanabe
 Haruo Tanaka
 Masaaki Tanaka
 Toshihiro Tanaka
 Kenichi Tanamoto**
 Tsuyoshi Tanimoto

Yoshikazu Tashiro
 Katsuhide Terada
 Reiko Teraoka
 Keijiro Terashita
 Susumu Terabayashi
 Masafumi Teshigawara
 Hiroshi Tokunaga
 Kiyoshi Tomioka
 Motowo Tomita
 Hiroyuki Tomitsuka
 Yosuke Tsuji
 Hiroyuki Tsujimoto
 Kazunori Tsutsui
 Hideya Tuge
 Eriko Uchida
 Yoshimasa Uehara
 Atsuhiko Uetake
 Kazuichi Umemoto
 Masaaki Wada
 Eiji Watanabe
 Haruo Watanabe
 Takehiko Yajima
 Toshiyasu Yamada
 Teruhide Yamaguchi
 Tetsuji Yamaguchi
 Keiichi Yamamoto
 Keiji Yamamoto
 Tosuke Yamamoto
 Chikamasa Yamashita
 Takeshi Yamazaki
 Masato Yasuhara
 Shiho Yasuo
 Hikaru Yoden
 Hitoo Yoshida
 Kumi Yoshida
 Sumie Yoshioka
 Chikako Yomota
 Etsuo Yonemochi

*: Chairman, the Committee on JP

** : Acting Chairman, the Committee on JP

GENERAL NOTICES

1. The official name of this pharmacopoeia is 第十六改正日本薬局方, and may be abbreviated as 日局十六, 日局16, JP XVI or JP 16.

2. The English name of this pharmacopoeia is The Japanese Pharmacopoeia, Sixteenth Edition.

3. Among drugs, the Japanese Pharmacopoeia Drugs (the JP Drugs) are those specified in the monographs. The title names and the commonly used names adopted in the monographs should be used as official names. In the drug monographs, in addition to English name, chemical names or Latin names can be mentioned in the titles, as appropriate.

4. “Crude Drugs and related drugs” are placed together in the posterior part of the Official Monographs. These include: Crude Drugs being applied the requirements of the General Rules for Crude Drugs, or Powders, Extracts, Tinctures, Syrups, Spirits, Fluidextracts or Suppositories containing Crude Drugs as the active ingredient, combination preparations containing Crude Drugs as the principal active ingredient.

5. Drugs are to be tested according to the provisions given in the pertinent monographs, General Notices, General Rules for Crude Drugs, General Rules for Preparations, and General Tests for their conformity to the Japanese Pharmacopoeia. However, the items of “Description” and “Storage” under Containers and storage in the monographs on preparations are given for information, and should not be taken as indicating standards for conformity.

6. In principle, unless otherwise specified, animals used for preparing the JP Drugs or their source materials must be healthy.

7. In this English version, the JP Drugs described in the monographs begin with a capital letter.

8. The molecular formulas or constitution formulas in parentheses () after the name of drugs or chemicals designate chemically pure substances. Atomic masses adopted in the Japanese Pharmacopoeia conform to the table of “Standard Atomic Weights 2010”. Molecular masses are indicated to two decimal places rounded from three decimals.

9. The following abbreviations are used for the principal units.

meter	m
centimeter	cm
millimeter	mm
micrometer	μm

nanometer	nm
kilogram	kg
gram	g
milligram	mg
microgram	μg
nanogram	ng
picogram	pg
Celsius degree	$^{\circ}\text{C}$
mole	mol
millimole	mmol
square centimeter	cm^2
liter	L
milliliter	mL
microliter	μL
megahertz	MHz
per centimeter	cm^{-1}
newton	N
kilopascal	kPa
pascal	Pa
pascal second	$\text{Pa}\cdot\text{s}$
millipascal second	$\text{mPa}\cdot\text{s}$
square millimeter per second	mm^2/s
lux	lx
mole per liter	mol/L
millimole per liter	mmol/L
mass per cent	%
mass parts per million	ppm
mass parts per billion	ppb
volume per cent	vol%
volume parts per million	vol ppm
mass per volume per cent	w/v%
microsimens per centimeter	$\mu\text{S}\cdot\text{cm}^{-1}$
endotoxin unit	EU
colony forming unit	CFU

Note: “ppm” used in the Nuclear Magnetic Resonance Spectroscopy indicates the chemical shift, and “w/v%” is used in the formula or composition of preparations.

10. The unit used for expressing the potency of drug is recognized as the quantity of drug. Usually it is expressed by a definite quantity of a definite standard substance which shows a definite biological activity, and differs according to each drug. The units are determined, in principle, by comparison with each reference standard by means of biological methods. The term “Unit” used for the JP articles indicates the unit

defined in the Japanese Pharmacopoeia.

11. The statement “Being specified separately.” in the monographs means that the tests are to be specified when the drugs are granted approval based on the Pharmaceutical Affairs Law.

12. When an assurance that a product is of the JP Drug quality is obtained consistently from data derived from the manufacturing process validation studies, and from the records of appropriate manufacturing process control and of the test results of the quality control, some of the test items in the monograph being performed for the release of a product may be omitted as occasion demands.

13. The test methods specified in the Japanese Pharmacopoeia can be replaced by alternative methods which give better accuracy and precision. However, where a difference in test results is suspected, only the result obtained by the procedure given in the Pharmacopoeia is effective for the final judgment.

14. The details of the biological test methods may be changed insofar as they do not affect the essential qualities of the test.

15. The temperature for the tests or storage is described, in principle, in specific figures. However, the following expressions may be used instead.

Standard temperature, ordinary temperature, room temperature, and lukewarm are defined as 20°C, 15 – 25°C, 1 – 30°C, and 30 – 40°C, respectively. A cold place, unless otherwise specified, shall be a place having a temperature of 1 – 15°C.

The temperature of cold water, lukewarm water, warm water, and hot water are defined as not exceeding 10°C, 30 – 40°C, 60 – 70°C, and about 100°C, respectively.

The term “heated solvent” or “hot solvent” means a solvent heated almost to the boiling point of the solvent, and the term “warmed solvent” or “warm solvent” usually means a solvent heated to a temperature between 60°C and 70°C. The term “heat on or in a water bath” indicates, unless otherwise specified, heating with a boiling water bath or a steam bath at about 100°C.

Cold extraction and warm extraction are usually performed at temperatures of 15 – 25°C and 35 – 45°C, respectively.

16. To measure the number of drops, a dropping device which delivers 20 drops of water weighing 0.90 – 1.10 g at 20°C shall be used.

17. The term “in vacuum” indicates, unless otherwise specified, a pressure not exceeding 2.0 kPa.

18. The acidity or alkalinity of a solution, unless otherwise specified, is determined by blue or red litmus papers. To indicate these properties more pre-

cisely, pH values are used.

19. The terms in Table 1 are used to express the degree of cutting of Crude Drugs or fineness of powder Drugs.

Table 1

Sieve No.	4	6.5	8.6	18	50	100	200
Nominal Designation of sieve	4750 μm	2800 μm	2000 μm	850 μm	300 μm	150 μm	75 μm
Names of the drugs which pass through the respective sieves	Coarse cutting	Moderately fine cutting	Fine cutting	Coarse powder	Moderately fine powder	Fine powder	Very fine powder

20. The water to be used in the tests of drugs shall be the water suitable for performing the relevant test, such as the water not containing any substance that would interfere with the test.

21. As for wording “solution of a solute”, where the name of the solvent is not stated, the term “solution” indicates a solution in water.

22. For solution an expression such as “(1 in 3)”, “(1 in 10)”, or “(1 in 100)” means that 1 g of a solid is dissolved in, or 1 mL of a liquid is diluted with the solvent to make the total volume of 3 mL, 10 mL or 100 mL, respectively. For the liquid mixture an expression such as “(10:1)” or “(5:3:1)” means that the respective numbers of parts, by volume, of the designated liquids are to be mixed.

23. The term “weigh accurately” means to weigh down to the degree of 0.1 mg, 0.01 mg or 0.001 mg by taking into account the purpose of the test and using a relevant weighing device. The term “weigh exactly” means to weigh to the given decimal places.

24. A value of “n” figures in a test of a JP Drug shall be obtained by rounding off a value of “n + 1” figures.

25. Unless otherwise specified, all tests of the drugs shall be performed at the ordinary temperature and observations of the results shall follow immediately after the operations. However, the judgment for a test which is affected by temperature should be based on the conditions at the standard temperature.

26. The terms “immediately”/“at once” used in the test of a JP Drug mean that the procedure is to be performed within 30 seconds after the preceding procedure.

27. In the section under the heading Description, the term “white” is used to indicate white or practically white, and “colorless” is colorless or practically colorless. Unless otherwise specified, the test of color is carried out by placing 1 g of a solid drug on a sheet of

white paper or in a watch glass placed on white paper. A liquid drug is put into a colorless test tube of 15-mm internal diameter and is observed in front of a white background through a layer of 30 mm. For the test of clarity of liquid drugs the same procedure is applied with either a black or white background. For the observation of fluorescence of a liquid drug, only a black background shall be used.

28. In the section under the heading Description, the term “odorless” is used to indicate odorless or practically odorless. Unless otherwise specified, the test of odor shall be carried out by placing 1 g of a solid drug or 1 mL of a liquid drug in a beaker.

29. In the section under the heading Description, solubilities are expressed by the terms in Table 2. Unless otherwise specified, solubility means the degree of dissolution of a JP Drug, previously powdered in the case of a solid drug, within 30 minutes in a solvent at $20 \pm 5^\circ\text{C}$, by vigorous shaking for 30 seconds each time at 5-minute intervals.

Table 2

Descriptive term	Volume of solvent required for dissolving 1 g or 1 mL of solute
Very soluble	Less than 1 mL
Freely soluble	From 1 mL to less than 10 mL
Soluble	From 10 mL to less than 30 mL
Sparingly soluble	From 30 mL to less than 100 mL
Slightly soluble	From 100 mL to less than 1000 mL
Very slightly soluble	From 1000 mL to less than 10000 mL
Practically insoluble, or insoluble	10000 mL and over

30. In the test of a drug, the term “dissolve” or “miscible” indicates that it dissolves in, or mixes in arbitrary proportion with the solvent to form a clear solution or mixture. Insoluble materials other than the drug including fibers should not be detected or practically invisible, if any.

31. Identification is the test to identify the active ingredient(s) of the drug based upon its specific property.

32. Purity is the test to detect impurities/contaminants in drugs, and it, as well as other requirements in each monograph, specifies the purity of the drug usually by limiting the kind/nature and quantity of the impurities/contaminants. The impurities/contaminants subject to the purity test are those supposed to generate/contaminate during the manufacturing process or storage, including hazardous agents

such as heavy metals, arsenic, etc. If any foreign substances are used or supposed to be added, it is necessary to perform tests to detect or limit the presence of such substances.

33. The term “constant mass” in drying or ignition, unless otherwise specified, means that the mass difference after an additional 1 hour of drying or ignition is not more than 0.10% of the preceding mass of the dried substance or ignited residue. For crude drugs, the difference is not more than 0.25%. However, when the difference does not exceed 0.5 mg in a chemical balance, 0.05 mg in a semi-microbalance, or 0.005 mg in a microbalance, the constant mass has been attained.

34. Assay is the test to determine the composition, the content of the active ingredients, and the potency unit of medicine by physical, chemical or biological procedures.

35. In stating the appropriate quantities to be taken for assay, the use of the word “about” indicates a quantity within 10% of the specified mass. The word “dry” in respect of the sample indicates drying under the same conditions, as described in Loss on drying in the monograph.

36. For the content of an ingredient determined by Assay in the monographs, if it is expressed simply as “not less than a certain percentage” without indicating its upper limit, 101.0% is understood as the upper limit.

37. The container is the device which holds drugs. The stopper or cap, etc., is considered as part of the container. The containers have no physical and chemical reactivity affecting the specified description and quality of the contents.

38. A well-closed container protects the contents from extraneous solids and from loss of the drug under ordinary or customary conditions of handling, shipment, and storage.

Where a well-closed container is specified, it may be replaced by a tight container.

39. A tight container protects the contents from extraneous solids or liquids, from loss of the contents, and from efflorescence, deliquescence, or evaporation under ordinary or customary conditions of handling, shipment, and storage.

Where a tight container is specified, it may be replaced by a hermetic container.

40. A hermetic container is impervious to air or any other gas under ordinary or customary conditions of handling, shipment, and storage.

41. The term “light-resistant” means that it can prevent transmittance of light affecting in the specified properties and quality of the contents and protect the

contained medicament from the light under ordinary or customary conditions of handling, shipment, and storage.

42. For the JP Drugs, the contents or potency in terms of units of the active ingredient(s), or the specified expiration date in the monographs have to be shown on the immediate container or wrapping of them.

43. The origin, numerical value or physical properties of the JP Drugs, being stipulated by the special

labeling requirements in the monographs, have to be shown on the immediate container or wrapping of them.

44. The harmonized General Tests and Monographs among the Japanese Pharmacopoeia, the European Pharmacopoeia and the United States Pharmacopeia are preceded by the statement as such.

The parts of the text, being not harmonized, are surrounded by the symbols (♦ ♦).

—**Abbreviations**—

CS: Colorimetric Stock Solution

RS: Reference Standard

TS: Test Solution

VS: Refer to a solution listed in Standard Solutions for Volumetric Analysis <9.21>.

GENERAL RULES FOR CRUDE DRUGS

1. Crude drugs in the monographs include medicinal parts obtained from plants or animals, cell inclusions and secretes separated from the origins, their extracts, and minerals. General Rules for Crude Drugs and Crude Drugs Test are applicable to the following:

Acacia, Achyranthes Root, Agar, Akebia Stem, Alisma Rhizome, Aloe, Alpinia Officinarum Rhizome, Aluminum Silicate Hydrate with Silicon Dioxide, Amomum Seed, Anemarrhena Rhizome, Angelica Dahurica Root, Apricot Kernel, Aralia Rhizome, Areca, Artemisia Capillaris Flower, Asiasarum Root, Asparagus Tuber, Astragalus Root, Atractylodes Lancea Rhizome, Atractylodes Rhizome, Bear Bile, Bearberry Leaf, Belladonna Root, Benincasa Seed, Benzoin, Bitter Cardamon, Bitter Orange Peel, Brown Rice, Bupleurum Root, Burdock Fruit, Calumba, Capsicum, Cardamon, Cassia Seed, Catalpa Fruit, Chrysanthemum Flower, Cimicifuga Rhizome, Cinnamon Bark, Citrus Unshiu Peel, Clematis Root, Clove, Cnidium Monnieri Fruit, Cnidium Rhizome, Coix Seed, Condurango, Coptis Rhizome, Cornus Fruit, Corydalis Tuber, Crataegus Fruit, Cyperus Rhizome, Digenea, Dioscorea Rhizome, Dolichos Seed, Eleutherococcus Senticosus Rhizome, Ephedra Herb, Epimedium Herb, Eucommia Bark, Euodia Fruit, Fennel, Forsythia Fruit, Fritillaria Bulb, Gambir, Gardenia Fruit, Gastrodia Tuber, Gentian, Geranium Herb, Ginger, Ginseng, Glehnia Root and Rhizome, Glycyrrhiza, Gypsum, Hemp Fruit, Honey, Houttuynia Herb, Immature Orange, Imperata Rhizome, Ipecac, Japanese Angelica Root, Japanese Gentian, Japanese Valerian, Jujube, Jujube Seed, Koi, Leonurus Herb, Lilium Bulb, Lindera Root, Lithospermum Root, Longan Aril, Longgu, Lonicera Leaf and Stem, Loquat Leaf, Lycium Bark, Lycium Fruit, Magnolia Bark, Magnolia Flower, Mallotus Bark, Mentha Herb, Moutan Bark, Mulberry Bark, Nelumbo Seed, Notopterygium, Nuphar Rhizome, Nutmeg, Nux Vomica, Ophiopogon Tuber, Oriental Bezoar, Oyster Shell, Panax Japonicus Rhizome, Peach Kernel, Peony Root, Perilla Herb, Peucedanum Root, Pharbitis Seed, Phellodendron Bark, Picrasma Wood, Pinellia Tuber, Plantago Herb, Plantago Seed, Platycodon Root, Pogostemon Herb, Polygala Root, Polygonatum Rhizome, Polygonum Root, Polyporus Sclerotium,

um, Poria Sclerotium, Powdered Acacia, Powdered Agar, Powdered Alisma Rhizome, Powdered Aloe, Powdered Amomum Seed, Powdered Atractylodes Lancea Rhizome, Powdered Atractylodes Rhizome, Powdered Calumba, Powdered Capsicum, Powdered Cinnamon Bark, Powdered Clove, Powdered Cnidium Rhizome, Powdered Coix Seed, Powdered Coptis Rhizome, Powdered Corydalis Tuber, Powdered Cyperus Rhizome, Powdered Dioscorea Rhizome, Powdered Fennel, Powdered Gambir, Powdered Gardenia Fruit, Powdered Gentian, Powdered Geranium Herb, Powdered Ginger, Powdered Ginseng, Powdered Glycyrrhiza, Powdered Ipecac, Powdered Japanese Angelica Root, Powdered Japanese Gentian, Powdered Japanese Valerian, Powdered Longgu, Powdered Magnolia Bark, Powdered Moutan Bark, Powdered Oyster Shell, Powdered Panax Japonicus Rhizome, Powdered Peach Kernel, Powdered Peony Root, Powdered Phellodendron Bark, Powdered Picrasma Wood, Powdered Platycodon Root, Powdered Polygala Root, Powdered Polyporus Sclerotium, Powdered Poria Sclerotium, Powdered Processed Aconite Root, Powdered Rhubarb, Powdered Rose Fruit, Powdered Scutellaria Root, Powdered Senega, Powdered Senna Leaf, Powdered Smilax Rhizome, Powdered Sophora Root, Powdered Sweet Hydrangea Leaf, Powdered Swertia Herb, Powdered Tragacanth, Powdered Turmeric, Powdered Zanthoxylum Fruit, Processed Aconite Root, Processed Ginger, Prunella Spike, Pueraria Root, Quercus Bark, Red Ginseng, Rehmannia Root, Rhubarb, Rose Fruit, Rosin, Royal Jelly, Safflower, Saffron, Saposhnikovia Root and Rhizome, Sappan Wood, Saussurea Root, Schisandra Fruit, Schizonepeta Spike, Scopolia Rhizome, Scutellaria Root, Senega, Senna Leaf, Sesame, Sinomenium Stem and Rhizome, Smilax Rhizome, Sophora Root, Sweet Hydrangea Leaf, Swertia Herb, Toad Venom, Tragacanth, Tribulus Fruit, Trichosanthes Root, Turmeric, Uncaria Hook, Zanthoxylum Fruit, Zedoary.

2. Crude drugs are usually used in the forms of whole crude drugs, cut crude drugs or powdered crude drugs.

Whole crude drugs are the medicinal parts or their ingredients prepared by drying and/or simple processes, as specified in the monographs.

Cut crude drugs are small pieces or small blocks prepared by cutting or crushing of the whole crude drugs, and also coarse, medium or fine cutting of the crude drugs in whole, and, unless otherwise specified, are required to conform to the specifications of the whole crude drugs used as original materials.

Powdered crude drugs are coarse, medium, fine or very fine powder prepared from the whole crude drugs or the cut crude drugs; usually powdered crude drugs as fine powder are specified in the monographs.

3. Unless otherwise specified, crude drugs are used in dried form. The drying is usually carried out at a temperature not exceeding 60°C.

4. The origin of crude drugs is to serve as the criteria. Such statements as 'other species of the same genus' and 'allied plants' or 'allied animals' appearing in the origin of crude drugs usually indicate plants or animals which may be used as materials for crude drugs containing the same effective constituents.

5. Description in each monograph for crude drugs usually covers the crude drug derived from its typical original plant or animal and includes statements of characteristic properties of the crude drug. As for the color, odor and solubility, apply correspondingly to the prescription of the General Notices, except the

odor which is to serve as the criteria. The taste and aspects obtained by microscopic observation are to serve as the criteria.

6. Powdered crude drugs, otherwise specified, may be mixed with diluents so as to attain proper content and potency.

7. Powdered crude drugs do not contain fragments of tissues, cells, cell inclusions or other foreign matter alien to the original crude drugs or cut crude drugs.

8. Crude drugs are as free as possible from contaminants and other impurities due to molds, insects and other animals and from other foreign matters, and are required to be kept in a clean and hygienic state.

9. Crude drugs are preserved under protection from moisture and insect damage, unless otherwise specified. In order to avoid insect damage, suitable fumigants may be used to preserve crude drugs, provided that the fumigants are so readily volatilized as to be harmless at the usual dosage of the crude drugs, and such fumigants that may affect the therapeutic efficacy of the crude drugs or interfere with the testing are precluded.

10. Crude drugs are preserved in well-closed containers unless otherwise specified.

GENERAL RULES FOR PREPARATIONS

[1] General Notices for Preparations

(1) General Notices for Preparations present general rules for pharmaceutical dosage forms.

(2) In [2] Monographs for Preparations, dosage forms are classified mainly by administration routes and application sites, and furthermore are subdivided according to their forms, functions and characteristics.

Those preparations containing mainly crude drugs as active raw materials are described under [3] Monographs for Preparations Related to Crude Drugs.

(3) In Monographs for Preparations and Monographs for Preparations Related to Crude Drugs, dosage forms, which are generally or widely used, are described. However, any other appropriate dosage forms may be used where appropriate. For example, a dosage form suitable for a particular application may be designated by combining an administration route and a name of a dosage form listed in these chapters.

(4) In these monographs, preparation characteristics are specified for the dosage forms. The preparation characteristics are confirmed by appropriate tests.

(5) In the case of preparations, functions that control the release rate of active substance(s) may be added for the purpose of controlling the onset and duration of therapeutic effects and/or decreasing adverse or side effects. The preparations modified in release rate must have an appropriate function of controlled release for the intended use. The added functional modification must generally be displayed on the pack insert and on the direct container or packaging of these preparations.

(6) Pharmaceutical excipients are substances other than active substances contained in preparations, and they are used to increase the utility of the active substance(s) and preparation, to make formulation process easier, to keep the product quality, to improve the usability, and so forth. Suitable excipients may be added for these purposes. The excipients to be used, however, must be pharmacologically inactive and harmless in the administered amount and must not interfere with the therapeutic efficacy of the preparations.

(7) Purified water to be used for preparations is Purified Water or Purified Water in Containers, and water for injection is Water for Injection or Water for Injection in Containers.

Vegetable oils to be used for preparations are usually edible oils listed in the Pharmacopoeia. When starch is called for, unless otherwise specified, any kind of starch listed in the Pharmacopoeia may be used.

In addition, ethanol specified in vol% is prepared by adding Purified Water or Water for Injection to ethanol at the specified vol%.

(8) Even non-sterile preparations should be prepared with precautions to prevent contamination and growth of microorganisms, and they are applied to the test of Microbial Limit Test <4.05>, if necessary.

(9) The test for Content Uniformity under the Uniformity of Dosage Units <6.02> and the Dissolution Test <6.10> are not intended to apply to the crude drug component of preparations which are prepared using crude drugs or preparations related to crude drugs as raw materials.

(10) Containers and packaging for preparations must be suitable for their proper use and for ensuring safe application, as well as for maintaining the quality of the preparations. To protect preparations that may be susceptible to oxygen in the air, deoxidants or containers made of low-gas-permeability material may be used. For preparations susceptible to degradation by moisture, packages with desiccants or moisture-proof packaging using low-moisture-permeability materials for containers may be used. For preparations susceptible to degradation by evaporation of water, containers of low-moisture-permeability material may be used.

Preparations for single-dose use are referred to as “preparations in single-dose packages”.

(11) Unless otherwise specified, preserve preparations at room temperature. Store them in light-resistant containers or packaging, if light affects the quality of the preparation.

[2] Monographs for Preparations

(1) In the Monographs for Preparations, the definitions of dosage forms, manufacturing methods, test methods, containers and packaging, and storage are described.

(2) The descriptions of the test methods and the containers and packaging in these monographs are fundamental requirements, and the manufacturing methods represent commonly used methods.

1. Preparations for Oral Administration

(1) Immediate-release dosage forms are preparations showing a release pattern of active substance(s) that is not intentionally modified and is generally dependent on the intrinsic solubility of the active substance.

(2) Modified-release dosage forms are preparations showing a release pattern of active substance(s) that is suitably modified for the desired purpose by means of a specific formulation design and/or manufacturing method. Modified-release dosage forms include enteric-coated and extended-release preparations.

(i) Enteric-coated (delayed-release) preparations

Enteric-coated preparations are designed to release the bulk of the active substance(s) not in stomach but mainly in small intestine, in order to prevent degradation or decomposition of the active substance(s) in stomach or to decrease the irritation of the active substance(s) on stomach. Enteric-coated preparations are generally coated with an acid-insoluble enteric film.

(ii) Extended-release preparations

Extended-release preparations are designed to control the release rate and release period of active substance(s) and to restrict the release to appropriate sites in the gastrointestinal tracts in order to decrease the dosing frequency and/or to reduce adverse or side effects. Extended-release preparations are generally prepared by using suitable agents that prolong the release of the active substance(s).

(3) Oral dosage forms such as capsules, granules and tablets can be coated with appropriate coating agents, such as sugars, sugar alcohols, or polymers, for the purpose of enabling the ingestion easy or of preventing degradation of the active substance(s).

1-1. Tablets

(1) Tablets are solid preparations having a desired shape and size, intended for oral administration. Orally Disintegrating Tablets, Chewable Tablets,

Effervescent Tablets, Dispersible Tablets and Soluble Tablets are included in this category.

(2) Tablets are usually prepared by the following procedures. Enteric-coated or extended-release tablets can be prepared by appropriate methods.

(i) Mix homogeneously active substance(s) and excipients such as diluents, binders and disintegrators, granulate with water or a binder solution by a suitable method, mix with a lubricant, and then compress into a desired shape and size.

(ii) Mix homogeneously active substance(s) and excipients such as diluents, binders, and disintegrators, and then directly compress with a lubricant, or compress after adding active substance(s) and a lubricant to granules previously prepared from excipients and then mixing homogeneously.

(iii) Mix homogeneously active substance(s) and excipients such as diluents and binders, moisten with a solvent, form into a certain shape and size or mold the mixed mass into a certain shape and size, and then dry by a suitable method.

(iv) Plain Tablets are usually prepared according to (i), (ii) or (iii).

(v) Film-coated Tablets can be prepared, usually, by coating Plain Tablets with thin films using suitable film coating agents such as polymers.

(vi) Sugar-coated Tablets can be prepared, usually, by coating Plain Tablets using suitable coating agents including sugars or sugar alcohols.

(vii) Multiple-layer Tablets can be prepared by compressing granules of different compositions to form layered tablets by a suitable method.

(viii) Pressure-coated Tablets can be prepared by compressing granules to cover inner core tablets with different compositions.

(3) Unless otherwise specified, Tablets meet the requirements of Uniformity of Dosage Units <6.02>.

(4) Unless otherwise specified, Tablets meet the requirements of Dissolution Test <6.10> or Disintegration Test <6.09>. For Effervescent tablets from which active substance(s) are dissolved before use and Soluble tablets, these tests are not required.

(5) Well-closed containers are usually used for the preparations. For preparations susceptible to degradation by moisture, a moisture-proof container or packaging may be used.

1-1-1. Orally Disintegrating Tablets/Orodispersible Tablets

(1) Orally Disintegrating Tablets are tablets which are quickly dissolved or disintegrated in the oral cavity.

(2) Orally Disintegrating Tablets shows an appropriate disintegration.

1-1-2. Chewable Tablets

(1) Chewable Tablets are tablets which are administered by chewing.

(2) Chewable Tablets must be in shape and size avoiding danger of suffocation.

1-1-3. Effervescent Tablets

(1) Effervescent Tablets are tablets which are quickly dissolved or dispersed with bubbles in water.

(2) Effervescent tablets are usually prepared using suitable acidic substances and carbonates or hydrogen carbonates.

1-1-4. Dispersible Tablets

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

1-1-5. Soluble Tablets

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

1-2. Capsules

(1) Capsules are preparations enclosed in capsules or wrapped with capsule bases, intended for oral administration. Capsules are classified into Hard Capsules and Soft Capsules.

(2) Capsules are usually prepared by the following methods. Enteric-coated or extended-release capsules can be prepared by a suitable method. Coloring agents, preservatives, etc. may be added to the capsule bases.

(i) Hard Capsules: A homogeneous mixture of active substance(s) with diluents and other suitable excipients, or granules or formed masses prepared by a suitable method, are filled into capsule shells as they are or after slight compression.

(ii) Soft Capsules: Active substance(s) and suitable excipients (including solvents) are mixed, enclosed by a suitable capsule base such as gelatin plasticized by addition of glycerin, D-sorbitol, etc. and molded in a suitable shape and size.

(3) Unless otherwise specified, Capsules meet the requirements of Uniformity of Dosage Units <6.02>.

(4) Unless otherwise specified, Capsules meet the requirements of Dissolution Test <6.10> or Disintegration Test <6.09>.

(5) Well-closed containers are usually used for Capsules. For Capsules susceptible to degradation by moisture, a moisture-proof container or packaging may be used.

1-3. Granules

(1) Granules are preparations prepared by granulation, intended for oral administration. Effervescent Granules are included in this category.

(2) Granules are usually prepared by the following

methods. Granules can be coated using suitable coating agents if necessary. Extended-release or enteric-coated granules can also be prepared by a suitable method.

(i) To powdery active substance(s) add diluents, binders, disintegrators, or other suitable excipients, mix to homogenize, and granulate by a suitable method.

(ii) To previously granulated active substance(s) add excipients such as diluents, and mix to homogenize.

(iii) To previously granulated active substance(s) add excipients such as diluents, and granulate by a suitable method.

(3) Among Granules, the preparations may be referred to as "Fine Granules" if, when Particle Size Distribution Test for Preparations <6.03> is performed, all granules pass through a No. 18 (850 μm) sieve, and not more than 10% of which remain on a No. 30 (500 μm) sieve.

(4) Unless otherwise specified, the Granules in single-dose packages meet the requirements of Uniformity of Dosage Units <6.02>.

(5) Unless otherwise specified, Granules comply with Dissolution Test <6.10> or Disintegration Test <6.09>. However, this provision is not to be applied to Effervescent granules, which are dissolved before use, and Disintegration Test <6.09> is not required for the Granules not more than 10% of which remain on a No. 30 (500 μm) sieve when the test is performed as directed under Particle Size Distribution Test for Preparations <6.03>.

(6) Among Granules, the particulate preparations may be referred to as "Powders" if, when the Particle Size Distribution Test for Preparations <6.03> is performed, all granules pass through a No. 18 (850 μm) sieve, and not more than 5% remain on a No. 30 (500 μm) sieve.

(7) Well-closed containers are usually used for Granules. For the preparations susceptible to degradation by moisture, a moisture-proof container or packaging may be used.

1-3-1. Effervescent Granules

(1) Effervescent granules are granules which are quickly dissolved or dispersed with bubbles in water.

(2) Effervescent granules are usually prepared using suitable acidic substances and carbonates or hydrogen carbonates.

1-4. Powders

(1) Powders are preparations in powder form, intended for oral administration.

(2) Powders are usually prepared by homogene-

ously mixing active substance(s) with diluents or other suitable excipients.

(3) Unless otherwise specified, the Powders in single-dose packages meet the requirements of Uniformity of Dosage Units <6.02>.

(4) Unless otherwise specified, Powders meet the requirements of Dissolution Test <6.10>.

(5) Well-closed containers are usually used for Powders. For the preparations susceptible to degradation by moisture, a moisture-proof container or packaging may be used.

1-5. Liquids and Solutions for Oral Administration

(1) Liquids and Solutions for Oral Administration are preparations in liquid form or flowable and viscous gelatinous state, intended for oral administration. Elixirs, Suspensions, Emulsions and Lemonades are included in this category.

(2) Liquids and Solutions for Oral Administration are usually prepared by dissolving, emulsifying or suspending active substance(s) in Purified Water together with excipients, and by filtering if necessary.

(3) For Liquids and Solutions for Oral Administration which are apt to deteriorate, prepare before use.

(4) Unless otherwise specified, the preparations in single-dose packages meet the requirement of Uniformity of Dosage Units <6.02>.

(5) Tight containers are usually used for Liquids and Solutions for Oral Administration. For the preparations susceptible to degradation by evaporation of water, a low-moisture-permeability container or packaging may be used.

1-5-1. Elixirs

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

(2) Elixirs are usually prepared by dissolving solid active substance(s) or their extractives in ethanol and Purified Water, adding aromatic agents and sucrose, other sugars or sweetening agents, and clarifying by filtration or other procedure.

1-5-2. Suspensions

(1) Suspensions are liquid preparations of active substance(s) suspended finely and homogeneously in a vehicle, intended for oral administration.

(2) Suspensions are usually prepared by adding suspending agent or other suitable excipients and Purified Water or oil to solid active substance(s), and suspending homogeneously as the whole by a suitable method.

(3) Mix homogeneously before use, if necessary.

(4) Unless otherwise specified, Suspensions meet

the requirements of Dissolution Test <6.10>.

1-5-3. Emulsions

(1) Emulsions are liquid preparations of active substance(s) emulsified finely and homogeneously in a liquid vehicle, intended for oral administration.

(2) Emulsions are usually prepared by adding emulsifying agents and Purified Water to liquid active substance(s), and emulsifying finely and homogeneously by a suitable method.

(3) Mix homogeneously before use, where necessary.

1-5-4. Lemonades

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

1-6. Syrups

(1) Syrups are viscous liquid or solid preparations containing sugars or sweetening agents, intended for oral administration. Preparations for Syrups are included in this category.

(2) Syrups are usually prepared by dissolving, mixing, suspending or emulsifying active substance(s) in a solution of sucrose, other sugars or sweetening agents, or in Simple Syrup. Where necessary, the mixture is boiled, and filtered while hot.

(3) For Syrups which are apt to deteriorate, prepare before use.

(4) Unless otherwise specified, Syrups in single-dose packages meet the requirements of Uniformity of Dosage Units <6.02>.

(5) Unless otherwise specified, Syrups in which active substance(s) is suspended meet the requirements of Dissolution Test <6.10>.

(6) Tight containers are usually used for Syrups. For the preparations susceptible to degradation by evaporation of water, a low-moisture-permeability container or packaging may be used.

1-6-1. Preparations for Syrups

(1) Preparations for Syrups are preparations in form of granules or powders, which become syrups by adding water. They may be termed "Dry Syrups".

(2) Preparations for Syrup are usually prepared with sugars or sweetening agents as directed under 1-3. Granules or 1-4. Powders.

(3) Preparations for Syrups are usually to be used after having been dissolved or suspended in water.

(4) Unless otherwise specified, the Preparations for Syrups other than preparations which are to be used after having been dissolved meet the requirements of Dissolution Test <6.10> or Disintegration Test <6.09>. However, Disintegration Test <6.09> is not required for the Preparations, if, when the Particle Size Distribution Test for Preparations <6.03> is

performed, not more than 10% of the total amount remains on a No. 30 (500 mm) sieve.

(5) Well-closed containers are usually used for Preparations for Syrups. For the Preparations for Syrups susceptible to degradation by moisture, a moisture-proof container or packaging may be used.

1-7. Jellies for Oral Administration

(1) Jellies for Oral Administration are non-flowable gelatinous preparations having a certain shape and size, intended for oral administration.

(2) Jellies for oral application are usually prepared by mixing active substance(s) with suitable excipients and polymer gel base, gelatinizing and forming into a certain shape and size by a suitable method.

(3) Unless otherwise specified, Jellies for Oral Administration meet the requirements of Uniformity of Dosage Units <6.02>.

(4) Unless otherwise specified, Jellies for Oral Administration meet the requirements of Dissolution Test <6.10> or show an appropriate disintegration.

(5) Tight containers are usually used for Jellies for Oral Administration. For the preparations susceptible to degradation by evaporation of water, a low-moisture-permeability container or packaging may be used.

2. Preparations for Oro-mucosal Application

2-1. Tablets for Oro-mucosal Application

(1) Tablets for Oro-mucosal Application are solid preparations having a certain form, intended for oral cavity application.

Troches/Lozenges, Sublingual Tablets, Buccal Tablets, Mucoadhesive Tablets and Medicated Chewing Gums are included in this category.

(2) Tablets for Oro-mucosal Application are prepared as directed under 1-1. Tablets.

(3) Unless otherwise specified, Tablets for Oro-mucosal Application meet the requirements of Uniformity of Dosage Units <6.02>.

(4) Tablets for Oro-mucosal Application have an appropriate dissolution or disintegration.

(5) Well-closed containers are usually used for Tablets for Oro-mucosal Application. For the preparations susceptible to degradation by moisture, a moisture-proof container or packaging may be used.

2-1-1. Troches/Lozenges

(1) Troches/Lozenges are tablets for oro-mucosal application, which are gradually dissolved or disintegrated in the mouth, and are intended for application locally to the oral cavity or the throat.

(2) Troches/Lozenges must be in shape and size avoiding danger of suffocation.

2-1-2. Sublingual Tablets

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

2-1-3. Buccal Tablets

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

2-1-4. Mucoadhesive Tablets

(1) Mucoadhesive Tablets are tablets for oro-mucosal application that are applied by adhesion to the oral mucosa.

(2) Mucoadhesive Tablets are usually prepared by using hydrophilic polymers to form hydrogel.

2-1-5. Medicated Chewing Gums

(1) Medicated Chewing Gums are tablets for oro-mucosal application, releasing active substance(s) by chewing.

(2) Medicated Chewing Gums are usually prepared using suitable gum bases such as vegetable resin, thermoplastic resin and elastomer.

2-2. Sprays for Oro-mucosal Application

(1) Sprays for Oro-mucosal Application are preparations that are applied active substance(s) by spraying into the oral cavity in mist, powder, foam or paste forms.

(2) Sprays for Oro-mucosal Application are usually prepared by the following methods:

(i) Dissolve or suspend active substance(s) and suitable excipients in a solvent, filter, where necessary, and fill into a container together with liquefied or compressed gas.

(ii) Dissolve or suspend active substance(s) and suitable excipients in a solvent, fill into a container, and fit with a pump for spraying.

(3) Unless otherwise specified, metered-dose types among Sprays for Oro-mucosal Application have an appropriate uniformity of delivered dose.

(4) Tight containers or pressure-resistant containers are usually used for Sprays for Oro-mucosal Application.

2-3. Semi-solid Preparations for Oro-mucosal Application

(1) Semi-solid Preparations for Oro-mucosal Application are preparations in cream, gel or ointment forms, intended for application to the oral mucosa.

(2) Semi-solid Preparations for Oro-mucosal Application are usually prepared by emulsifying active substance(s) together with excipients using "Purified

Water” and oil component such as petrolatum, or by homogenizing active substance(s) together with suitable excipients using polymer gel or oil and fats as the base.

(i) Creams for oro-mucosal application are prepared as directed under 11-5. Creams.

(ii) Gels for oro-mucosal application are prepared as directed under 11-6. Gels.

(iii) Ointments for oro-mucosal application are prepared as directed under 11-4. Ointments.

For Semi-solid Preparations for Oro-mucosal Application which are apt to deteriorate, prepare before use.

(3) Sufficient amounts of suitable preservatives to prevent the growth of microorganisms may be added for Semi-solid Preparations for Oro-mucosal Application filled in multiple-dose containers.

(4) Semi-solid Preparations for Oro-mucosal Application have a suitable viscosity to apply to the oral mucosa.

(5) Tight containers are usually used for Semi-solid Preparations for Oro-mucosal Application. For the preparations susceptible to degradation by evaporation of water, a low-moisture-permeability container or packaging may be used.

2-4. Preparations for Gargle

(1) Preparations for Gargle are liquid preparations intended to apply locally to the oral and throat cavities. Solid type preparations to be dissolved in water before use are also included in this category.

(2) Preparations for Gargle are usually prepared by dissolving active substance(s) in a solvent together with suitable excipients, and filtering where necessary. The solid preparations are prepared as directed under 1-1. Tablets or 1-3. Granules.

(3) Unless otherwise specified, Preparations for Gargle in single-dose packages meet the requirements of Uniformity of Dosage Units <6.02>.

(4) Tight containers are usually used for Preparations for Gargle. For the preparations susceptible to degradation by evaporation of water, a low-moisture-permeability container or packaging may be used.

3. Preparations for Injection

3-1. Injections

(1) Injections are sterile preparations to be administered directly into the body through skin, muscle or blood vessel, usually in form of a solution, a suspension or an emulsion of active substance(s), or of a solid that contains active substance(s) to be dissolved or suspended before use.

Parenteral Infusions, Implants/Pellets and Prolon-

ged-Release Injections are included in this category.

(2) Injections in solution, suspension or emulsion form are usually prepared by the following methods.

(i) Dissolve, suspend or emulsify active substance(s) with or without excipients in Water for Injection or an aqueous or nonaqueous vehicle homogeneously, fill into containers for injection, seal, and sterilize.

(ii) Dissolve, suspend or emulsify active substance(s) with or without excipients in Water for Injection or an aqueous or nonaqueous vehicle, and filtrate aseptically, or prepare aseptically a homogeneous liquid, fill into containers for injection, and seal.

Every care should be taken to prevent contamination with microorganisms. The overall processes of preparing injections, from the preparation of active solution to the sterilization, should be completed as rapidly as possible, taking into consideration the composition of the injection and the storage conditions. The concentration of active substance(s) expressed in % represents w/v%.

Injections that are to be dissolved or suspended before use and are designated in the name as “for injection” may be accompanied by a suitable vehicle to dissolve or suspend the supplied preparation (hereinafter referred to as “vehicle attached to preparation”).

(3) Injections may be prepared as Freeze-dried Injections or Powders for Injections to prevent degradation or deactivation of the active substance(s) in solution.

(i) Freeze-dried Injections

Freeze-dried Injections are usually prepared by dissolving active substance(s) with or without excipients such as diluents in Water for Injection, sterilizing the solution by aseptic filtration, filling the filtrate directly into individual containers for injection and being freeze-dried, or dividing the filtrate in special containers, being freeze-dried and transferred into individual containers for injection.

(ii) Powders for Injections

Powders for injections are usually prepared by filtrating aseptically a solution of active substance(s), obtaining powders by crystallization from the solution or mixing additionally the powders with sterilized excipients, and filling the powders into individual containers for injections.

(4) To prevent errors in the preparation with vehicles attached or administration of injections, or bacterial or foreign matter contamination, or for the purpose of urgent use, prefilled syringes or cartridges may be prepared.

(i) Prefilled Syringes for Injections

Prefilled Syringes for injections are usually prepared by dissolving, suspending or emulsifying active substance(s) with or without excipients in a vehicle, and filling into syringes.

(ii) Cartridges for Injections

Cartridges for Injections are usually prepared by dissolving, suspending or emulsifying active substance(s) with or without excipients in a vehicle, and filling into cartridges.

The cartridges are used by fixing in an injection device for exclusive use.

(5) Vehicles used in Injections or attached to preparations must be harmless in the amounts usually administered and must not interfere with the therapeutic efficacy of the active substance(s).

The vehicles are classified into the following two groups. They should meet each requirement.

(i) Aqueous vehicles: As the vehicle of aqueous injections, Water for Injection is usually used. 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 Bacterial Endotoxins Test <4.01>.

When the Bacterial Endotoxins Test <4.01> is not applicable to aqueous vehicles, the Pyrogen Test <4.04> may be applied instead.

(ii) Non-aqueous vehicles: Vegetable oils are usually used as vehicles for non-aqueous injections. These oils, unless otherwise specified, are clear at 10°C, the acid value is not more than 0.56, the saponification value is between 185 and 200, and the iodine value falls between 79 and 137. They meet the requirements of Mineral Oil Test <1.05>.

Several suitable organic solvents other than vegetable oils may be used as non-aqueous vehicles.

(6) Unless otherwise specified, any coloring agent must not be added solely for the purpose of coloring the preparations.

(7) Sodium chloride or other excipients may be added to aqueous injections to adjust them isotonic to blood or other body fluids. Acids or alkalis may be added to adjust the pH.

(8) Injections supplied in multiple-dose containers may be added sufficient amounts of suitable preservatives to prevent the growth of microorganisms.

(9) Unless otherwise specified, Injections and vehicles attached to preparations other than those used exclusively for intracutaneous, subcutaneous or intramuscular administration meet the requirements of

Bacterial Endotoxins Test <4.01>. In the case where the Bacterial Endotoxins Test <4.01> is not applicable, Pyrogen Test <4.04> may be applied instead.

(10) Unless otherwise specified, Injections and vehicles attached to preparations meet the requirements of Sterility Test <4.06>.

(11) Containers of Injections are colorless and meet the requirements of Test for Glass Containers for Injections <7.01>. Where specified in individual monographs, these containers may be replaced by colored containers meeting the requirements of Test for Glass Containers for Injections <7.01> or by plastic containers for aqueous injections meeting the requirements of Test Methods for Plastic Containers <7.02>.

(12) Unless otherwise specified, rubber stoppers used for glass containers of 100 mL or more of aqueous infusions meet the requirements of Test for Rubber Closure for Aqueous Infusions <7.03>.

(13) Unless otherwise specified, Injections and vehicles attached to preparations meet the requirements of Foreign Insoluble Matter Test for Injections <6.06>.

(14) Unless otherwise specified, Injections and vehicles attached to preparations meet the requirements of Insoluble Particulate Matter Test for Injections <6.07>.

(15) Unless otherwise specified, the actual volume of Injections meets the requirements of Test for Extractable Volume of Parenteral Preparations <6.05>.

(16) Unless otherwise specified, Injections to be dissolved or suspended before use meet the requirements of Uniformity of Dosage Units <6.02>.

(17) Suspensions for injection are usually not to be injected into the blood vessels or spinal cord, and emulsions for injection are not to be injected into the spinal cord.

(18) The maximum size of particles observed in suspensions for injection is usually not larger than 150 μm , and that of particles in emulsions for injection is usually not larger than 7 μm .

(19) The following information, unless otherwise specified, must be written on the package leaflet, or the container or wrapper.

(i) In cases where the vehicle is not specified, the name of the employed vehicle, with the exception of Water for Injection, sodium chloride solution not exceeding 0.9 w/v% and those vehicles in which acids or alkalis are used in order to adjust the pH.

(ii) In case of vehicle attached to preparation, the name of the vehicle, content volume, ingredients and quantities or ratios, and a statement of the presence of the vehicle on the outer container or outer wrapper.

(iii) Name and quantity of stabilizers, preserva-

tives, and diluents if added. In the case where nitrogen or carbon dioxide is filled in the container to replace the air inside, a statement of this replacement is not required.

(20) For ampoules or other containers of 2 mL or less, the designations "injection", "for injection" and "aqueous suspension for injection" may be replaced by "inj.", "for inj." and "aq. susp. for inj.", respectively.

For ampoules 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 abbreviated in the same way as above, when the information is printed directly on the surface of ampoules or containers.

(21) Hermetic containers or tight containers which are able to prevent microbial contamination are usually used for the preparations. For the preparations susceptible to degradation by evaporation of water, a low-moisture-permeability container or packaging may be used.

3-1-1. Parenteral Infusions

(1) Parenteral Infusions are usually injections of not less than 100 mL, intended for intravenous administration.

(2) Parenteral Infusions are mainly administered for the purpose of water supply, correction of electrolyte abnormality and nutritional support, and they are also used by mixing with other injections for treatments by continual infusion.

3-1-2. Implants/Pellets

(1) Implants/Pellets are solid or gel-like form injections, intended for subcutaneous or intramuscular administration by means of an implant device or operative treatment, for the purpose of releasing active substance(s) for a long period of time.

(2) Implants/Pellets are usually prepared in a form of pellet, microsphere or gel using biodegradable polymers.

(3) Unless otherwise specified, Implants/Pellets meet the requirements of Uniformity of Dosage Units <6.02>.

(4) Implants/Pellets have an appropriate function of controlled release.

(5) Implants/Pellets are not required the requirements of Foreign Insoluble Matter Test for Injections, Insoluble Particulate Matter for Injections and Test for Extractable Volume of Parenteral Preparations.

3-1-3. Prolonged Release Injections

(1) Prolonged Release Injections are injections to be used for intramuscular administration, for the purpose of releasing active substance(s) for a long period

of time.

(2) Prolonged Release Injections are usually prepared by dissolving or suspending active substance(s) in a non-aqueous vehicle such as vegetable oil, or by suspending microspheres prepared with biodegradable polymers.

(3) Prolonged Release Injections have an appropriate function of controlled release.

4. Preparations for Dialysis

4-1. Dialysis Agents

(1) Dialysis Agents are preparations in liquid, or in solid which are to be dissolved before use, intended for peritoneal dialysis or hemodialysis.

They are classified into Peritoneal dialysis agents and Hemodialysis agents.

(2) Unless otherwise specified, Dialysis Agents meet the requirements of Bacterial Endotoxins Test <4.01>.

(3) The solid preparations which are to be dissolved before use among Dialysis agents have an appropriate uniformity of dosage units.

4-1-1. Peritoneal Dialysis Agents

(1) Peritoneal Dialysis Agents are sterile dialysis agents, intended to be used for peritoneal dialysis.

(2) Peritoneal Dialysis Agents are usually prepared by dissolving active substance(s) with suitable excipients in a vehicle to make a certain volume, or by filling active substance(s) combined with suitable excipients in a container, and sealing it. Sterilize if necessary. Every care should be taken to prevent microbial contamination. The overall processes from preparation to sterilization for preparing the agents should be completed as rapidly as possible, taking into consideration the composition of the agents and the storage conditions. The concentration of Peritoneal dialysis agents expressed in % represents w/v%. In the case of solid preparations which are dissolved before use, prepare as directed under 1-1. Tablets or 1-3. Granules.

(3) If necessary, pH adjusting agents, isotonic agents or other excipients may be added.

(4) Unless otherwise specified, the vehicle used for Peritoneal dialysis agents is Water for Injection.

(5) Unless otherwise specified, Peritoneal Dialysis Agents meet the requirements of Sterility Test <4.06>.

(6) Unless otherwise specified, Peritoneal Dialysis Agents meet the requirements of (4) Parenteral infusions under Test for Extractable Volume of Parenteral Preparations <6.05>. The mass (g) of content may convert to the volume (mL) by dividing by the density.

(7) Unless otherwise specified, Peritoneal Dialysis Agents meet the requirements of Foreign Insoluble Matter Test for Injections <6.06>.

(8) Unless otherwise specified, Peritoneal Dialysis Agents meet the requirements of Insoluble Particulate Matter Test for Injections <6.07>.

(9) Colorless containers meeting the requirements of Test for Glass Containers for Injections <7.01> are used for Peritoneal Dialysis Agents. Where specified otherwise, the colored containers meeting the requirements of Test for Glass Containers for Injections <7.01> or the plastic containers for aqueous injections meeting the requirements of Test Methods for Plastic Containers <7.02> may be used.

(10) Unless otherwise specified, the rubber closures of the containers meet the requirements of Test for Rubber Closure for Aqueous Infusions <7.03>.

(11) Hermetic containers, or tight containers which are able to prevent microbial contamination are usually used for Peritoneal Dialysis Agents. For the preparations susceptible to degradation by evaporation of water, a low-moisture-permeability container or packaging may be used.

4-1-2. Hemodialysis Agents

(1) Hemodialysis agents are dialysis agents to be used for hemodialysis.

(2) Hemodialysis Agents are usually prepared by dissolving active substance(s) with excipients in a vehicle to make a certain volume, or by filling active substance(s) with excipient(s) in a container. In the case of the solid preparations to be dissolved before use, prepare as directed under 1-1. Tablets or 1-3. Granules.

(3) If necessary, pH adjusting agents, isotonic agents or other excipients may be added.

(4) Unless otherwise specified, the vehicle used for Hemodialysis agents is Water for Injection or water suitable for dialysis.

(5) Tight containers which are able to prevent microbial contamination are usually used for Hemodialysis Agents. For the preparations susceptible to degradation by evaporation of water, a low-moisture-permeability container or packaging may be used.

5. Preparations for Inhalation

5-1. Inhalations

(1) Inhalations are preparations intended for administration as aerosols to the bronchial tubes or lung.

Inhalations are classified to Dry Powder Inhalers, Inhalation Liquid Preparations and Metered-dose Inhalers.

(2) For administration of Inhalations, suitable devices or apparatus are used, or they are placed in containers which have a appropriate function of inhalation device.

5-1-1. Dry Powder Inhalers

(1) Dry Powder Inhalers are preparations which deliver a constant respiratory intake, intended for administration as solid particle aerosols.

(2) Dry Powder Inhalers are usually prepared by pulverizing active substance(s) into fine particles. Where necessary, lactose or other suitable excipients are added to make homogenous mixture.

(3) Metered-dose types among Dry Powder Inhalers have an appropriate uniformity of delivered dose of the active substance(s).

(4) The particles of active substance(s) in Dry Powder Inhalers have an aerodynamically appropriate size.

(5) Well-closed containers are usually used for Dry Powder Inhalers. For the preparations susceptible to degradation by moisture, a moisture-proof container or packaging may be used.

5-1-2. Inhalation Liquid Preparations

(1) Inhalation Liquid Preparations are liquid inhalations which are administered by an inhalation device such as operating nebulizers.

(2) Inhalation Liquid Preparations are usually prepared by mixing active substance(s) with a vehicle and suitable isotonic agents and/or pH adjusting agents to make a solution or suspension, and by filtering where necessary.

(3) Sufficient amounts of suitable preservatives may be added to Inhalation Liquid Preparations to prevent the growth of microorganisms.

(4) Tight containers are usually used for Inhalation Liquid Preparations. For the preparations susceptible to degradation by evaporation of water, a low-moisture-permeability container or packaging may be used.

5-1-3. Metered-dose Inhalers

(1) Metered-dose Inhalers are preparations which deliver a constant dose of active substance(s) from the container together with propellant filled in.

(2) Metered-dose Inhalers are usually prepared by dissolving active substance(s) with a suitable dispersing agents and stabilizers in a vehicle to make a solution or suspension, and by filling in pressure-resistant containers together with liquid propellant, and setting metering valves.

(3) Metered-dose Inhalers have an appropriate uniformity of delivered dose of active substance(s).

(4) Particles of active substance(s) in Metered-dose Inhalers have an aerodynamically appropriate size.

(5) Pressure-resistant and hermetic containers are usually used for Metered-dose Inhalers.

6. Preparations for Ophthalmic Application

6-1. Ophthalmic Liquids and Solutions

(1) Ophthalmic Liquids and Solutions are sterile preparations of liquid, or solid to be dissolved or suspended before use, intended for application to the conjunctival sac or other ocular tissues.

(2) Ophthalmic Liquids and Solutions are usually prepared by dissolving, suspending active substance(s) in a vehicle after adding excipients to make a constant volume, or mixing active substance(s) and excipients, and filling into containers. The overall processes, from preparation to sterilization, should be completed with sufficient care to prevent microbial contamination as rapidly as possible, taking into consideration the composition of the preparations and the storage conditions. The concentration of active substance expressed in % represents w/v%.

Ophthalmic Liquids and Solutions to be dissolved or suspended before use and designated in the name as "for ophthalmic application" may be accompanied by a vehicle for dissolving or suspending the preparation (hereinafter referred to as "vehicle attached to preparation").

(3) Vehicles to prepare Ophthalmic Liquids and Solutions or vehicle attached to the preparations must be harmless in the amounts usually administered and must not interfere with the therapeutic efficacy of the active substance(s).

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

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

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

(4) Unless otherwise specified, any coloring agents must not be added solely for the purpose of coloring Ophthalmic Liquids and Solutions or vehicles attached to the preparations.

(5) Sodium chloride or other excipients may be added to Ophthalmic Liquids and Solutions to adjust them isotonic to lacrimal fluid. Acids or alkalis may be also added to adjust the pH.

(6) Unless otherwise specified, Ophthalmic Liquids and Solutions and vehicles attached to the preparations meet the requirements of Sterility Test <4.06>.

(7) Sufficient amounts of appropriate preservatives to prevent the growth of microorganisms may be added to the preparations filled in multiple dose containers.

(8) Unless otherwise specified, Ophthalmic Liq-

uids and Solutions prepared in aqueous solutions or the vehicles attached to the preparations meet the requirements of Foreign Insoluble Matter Test for Ophthalmic Solutions <6.11>.

(9) Unless otherwise specified, Ophthalmic Liquids and Solutions and the vehicles attached to the preparations meet the requirements of Insoluble Particulate Matter Test for Ophthalmic Solutions <6.08>.

(10) The maximum particle size observed in Ophthalmic suspensions is usually not larger than 75 μm .

(11) Transparent tight containers, which do not disturb the test of Foreign Insoluble Matter Test for Ophthalmic Solutions <6.11>, are usually used for Ophthalmic Liquids and Solutions. For the preparations susceptible to degradation by evaporation of water, a low-moisture-permeability container or packaging may be used.

6-2. Ophthalmic Ointments

(1) Ophthalmic Ointments are sterile preparations of semi-solid, intended for application to the conjunctival sac or other ocular tissues.

(2) Ophthalmic Ointments are usually prepared by mixing homogeneously solution of or finely powdered active substance(s) with petrolatum or other bases, and filling into containers. The overall processes, from preparation to sterilization, should be completed with sufficient care to prevent microbial contamination as rapidly as possible, taking into consideration the composition of the preparations and the storage conditions.

(3) Sufficient amounts of suitable preservatives may be added to Ophthalmic Ointments filled in multiple dose containers to prevent the growth of microorganisms.

(4) Unless otherwise specified, Ophthalmic Ointments meet the requirements of Sterility Test <4.06>, and unless otherwise specified, the test is carried out by the Membrane filtration method.

(5) Unless otherwise specified, Ophthalmic Ointments meet the requirements of Test for Metal Particles in Ophthalmic Ointments <6.01>.

(6) The maximum particle size of active substance(s) in Ophthalmic Ointments is usually not larger than 75 μm .

(7) Ophthalmic Ointments have a suitable viscosity for applying to the ocular tissues.

(8) Tight containers which are able to prevent microbial contamination are usually used for Ophthalmic Ointments. For the preparations susceptible to degradation by evaporation of water, a low-moisture-permeability container or packaging may be used.

7. Preparations for Otic Application

7-1. Ear Preparations

(1) Ear Preparations are liquid, semi-solid, or solid preparations which are to be dissolved or suspended before use, intended for application to the external or internal ear.

(2) Ear Preparations are usually prepared by filling in containers with liquids in which active substance(s) and excipients are dissolved or suspended in a vehicle to make a constant volume, or with powders in which active substance(s) and excipients are mixed. The overall processes, from preparation to sterilization, should be completed with sufficient care to prevent microbial contamination as rapidly as possible, taking into consideration the composition of the preparations and the storage conditions. The concentration of active substance of Ear Preparations expressed in % represents w/v%.

In the case where the sterile preparations are prepared, proceed as directed under 6-1. Ophthalmic Liquids and Solutions.

Ear Preparations which are to be dissolved or suspended before use and designated in the name as "for otic preparation" may be accompanied by a vehicle to dissolve or suspend (hereinafter referred to as "vehicle attached to preparation").

(3) Vehicles used for Ear Preparations or the vehicle attached to the preparation are classified into the following two groups.

(i) Aqueous vehicles: As the vehicles for the aqueous preparations or the vehicles attached to the preparations, Purified Water or suitable aqueous vehicles are used. For the sterile preparations, Sterilized Purified Water or suitable sterilized aqueous vehicles are used as the vehicle attached to the preparations.

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

(4) Unless otherwise specified, any coloring agents must not be added solely for the purpose of coloring Ear Preparations or vehicle attached to the preparations.

(5) Sufficient amounts of suitable preservatives to prevent the growth of microorganisms may be added to the preparations filled in multiple dose containers.

(6) Unless otherwise specified, sterile Ear preparations and the vehicles attached to the sterile preparations meet the requirements of Sterility Test <4.06>.

(7) Tight containers are usually used for Ear Preparations. For the preparations susceptible to degradation by evaporation of water, a low-moisture-

permeability container or packaging may be used.

8. Preparations for Nasal Application

8-1. Nasal Preparations

(1) Nasal Preparations are preparations intended for application to the nasal cavities or nasal mucous membrane.

Nasal preparations are classified into Nasal dry powder inhalers and Nasal Liquid Preparations.

(2) Where necessary, Nasal Preparations are sprayed for inhalation by using a suitable atomizing device such as spray-pump.

(3) Unless otherwise specified, metered-dose type preparations among Nasal Preparations show the appropriate uniformity of delivered dose.

8-1-1. Nasal Dry Powder Inhalers

(1) Nasal Dry Powder Inhalers are fine powdered preparations, intended for application to the nasal cavities.

(2) Nasal Dry Powder Inhalers are usually prepared by pulverizing active substance(s) into moderately fine particles, or by mixing homogeneously with excipients where necessary.

(3) Well-closed containers are usually used for Nasal Dry Powder Inhalers. For the preparations susceptible to degradation by moisture, a moisture-proof container or packaging may be used.

8-1-2. Nasal Liquids and Solutions

(1) Nasal Liquids and Solutions are liquid preparations, or solid preparations to be dissolved or suspended before use, intended for application to the nasal cavities.

(2) Nasal Liquids and Solutions are usually prepared by dissolving or suspending active substance(s) in a vehicle together with excipients, and filtering where necessary. Isotonic agents and/or pH adjusting agents may be used.

(3) Nasal Liquids and Solutions, which are to be dissolved or suspended before use and designated in the name as "for nasal application", may be accompanied by a vehicle to dissolve or suspend.

(4) Sufficient amounts of suitable preservatives to prevent the growth of microorganisms may be added to the preparations filled in multiple dose containers.

(5) Tight containers are usually used for Nasal Liquids and Solutions. For the preparations susceptible to degradation by evaporation of water, a low-moisture-permeability container or packaging may be used.

9. Preparations for Rectal Application

9-1. Suppositories for Rectal Application

(1) Suppositories for Rectal Application are semi-

solid preparations of a desired shape and size, intended for intrarectal application, which release active substance(s) by melting at body temperature or dissolving or dispersing gradually in the secretions.

(2) Suppositories for Rectal Application are usually prepared by mixing homogeneously active substance(s) and excipients such as dispersing agents and emulsifying agents, dissolving or suspending uniformly in a base which is liquefied by warming, filling a constant volume of the resultant material into containers, and molding it into a shape and size. Lipophilic bases or hydrophilic bases are usually used.

(3) Suppositories for Rectal Application are usually a conical- or spindle-shaped.

(4) Unless otherwise specified, Suppositories for Rectal Application meet the requirements of Uniformity of Dosage Units <6.02>.

(5) Suppositories for Rectal Application show an appropriate release.

(6) Well-closed containers are usually used for Suppositories for Rectal Application. For the preparations susceptible to degradation by moisture, a moisture-proof container or packaging may be used.

9-2. Semi-solid Preparations for Rectal Application

(1) Semi-solid Preparations for Rectal Application are preparations which are in a form of cream, gel or ointment intended for application to around or inside of the anus.

(2) Semi-solid Preparations for Rectal Application are usually prepared by emulsifying active substance(s) with excipients in Purified Water and oil component such as vaseline, or by homogeneously mixing active substance(s) and excipients in a base of polymer gel or grease.

(i) Creams for rectal application: Prepare as directed under 11-5. Creams.

(ii) Gels for rectal application: Prepare as directed under 11-6. Gels.

(iii) Ointments for rectal application: Prepare as directed under 11-4. Ointments.

For the preparations which are apt to deteriorate, prepare before use.

(3) Sufficient amounts of suitable preservatives to prevent the growth of microorganisms may be added to the Preparations filled in multiple dose containers.

(4) Semi-solid Preparations for Rectal Application have a suitable viscosity for applying to the rectum.

(5) Tight containers are usually used for Semi-solid Preparations for Rectal Application. For the preparations susceptible to degradation by evaporation of water, a low-moisture-permeability container or packaging may be used.

9-3. Enemas for Rectal Application

(1) Enemas for Rectal Application are preparations in liquid form or viscous and gelatinous state, intended for application via the anus.

(2) Enemas for Rectal Application are usually prepared by dissolving or suspending active substance(s) in Purified Water or a suitable aqueous vehicle to make a given volume, and filling in containers. Dispersing agents, stabilizers and/or pH adjusting agents may be used.

(3) Tight containers are usually used for Enemas for Rectal Application. For the preparations susceptible to degradation by evaporation of water, a low-moisture-permeability container or packaging may be used.

10. Preparations for Vaginal Application

10-1. Tablets for Vaginal Use

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

(2) Tablets for Vaginal Use are usually prepared as directed under 1-1. Tablets.

(3) Unless otherwise specified, Tablets for Vaginal Use meet the requirements of Uniformity of Dosage Units <6.02>.

(4) Tablets for Vaginal Use show an appropriate release.

(5) Well-closed containers are usually used for Tablets for Vaginal Use. For the preparations susceptible to degradation by moisture, a moisture-proof container or packaging may be used.

10-2. Suppositories for Vaginal Use

(1) Suppositories for Vaginal Use are semi-solid preparations of a desired shape and size, intended for application to the vagina, which release active substance(s) by melting at body temperature or by dissolving or dispersing gradually in the secretions.

(2) Suppositories for Vaginal Use are prepared according to 9-1. Suppositories for Rectal Application.

(3) Suppositories for Vaginal Use are usually spherical or ovoid shaped.

(4) Unless otherwise specified, Suppositories for Vaginal Use meet the requirements of Uniformity of Dosage Units <6.02>.

(5) Suppositories for Vaginal Use show an appropriate release.

(6) Well-closed containers are usually used for Suppositories for Vaginal Use. For the preparations susceptible to degradation by moisture, a moisture-proof container or packaging may be used.

11. Preparations for Cutaneous Application

(1) Preparations for Cutaneous Application also include Transdermal Systems which are intended for percutaneous absorption to deliver active substance(s) to the systemic circulation through the skin. The release rate of active substance(s) from Transdermal Systems is generally appropriately controlled.

11-1. Solid Preparations for Cutaneous Application

(1) Solid Preparations for Cutaneous Application are solid preparations intended for application to the skin (including scalp) or nails. Powders for Cutaneous Application are included in this category.

(2) Unless otherwise specified, Solid Preparations for Cutaneous Application in single-dose packages meet the requirements of Uniformity of Dosage Units <6.02>.

(3) Well-closed containers are usually used for Solid Preparations for Cutaneous Application. For the preparations susceptible to degradation by moisture, a moisture-proof container or packaging may be used.

11-1-1. Powders for Cutaneous Application

(1) Powders for Cutaneous Application are powdery solid preparations intended for external application.

(2) Powders for Cutaneous Application are usually prepared by mixing homogeneously active substance(s) and excipients such as diluents and pulverizing the mixture.

11-2. Liquids and Solutions for Cutaneous Application

(1) Liquids and Solutions for Cutaneous Application are liquid preparations intended for application to the skin (including scalp) or nails. Liniments and Lotions are included in this category.

(2) Liquids and Solutions for Cutaneous Application are usually prepared by mixing active substance(s) and excipients in a vehicle, and filtering if necessary.

For the preparations which are apt to deteriorate, prepare before use.

(3) Unless otherwise specified, Liquids and Solutions for Cutaneous Application in single-dose packages meet the requirements of Uniformity of Dosage Units <6.02>, except for emulsified or suspended preparations.

(4) Tight containers are usually used for Liquids and Solutions for Cutaneous Application. For the preparations susceptible to degradation by evaporation of water, a low-moisture-permeability container or packaging may be used.

11-2-1. Liniments

(1) Liniments are liquid or muddy preparations in-

tended for external application to the skin by rubbing.

11-2-2. Lotions

(1) Lotions are external liquids in which active substance(s) are dissolved, emulsified or finely dispersed in an aqueous vehicle.

(2) Lotions are usually prepared by dissolving, suspending or emulsifying active substance(s) in Purified Water with excipients and making homogeneous as a whole.

(3) Lotions in which the components have separated out during storage may be used after mixing to re-homogenize them, provided that the active substance(s) has not deteriorated.

11-3. Sprays for Cutaneous Application

(1) Sprays for Cutaneous Application are preparations intended for spraying active substance(s) onto the skin in mists, powders, foams or paste state.

Sprays for Cutaneous Application are classified into Aerosols for Cutaneous Application and Pump Sprays for Cutaneous Application.

(2) Sprays for Cutaneous Application are usually prepared by dissolving or suspending active substance(s) in a vehicle, filtering where necessary, and filling in containers.

(3) Unless otherwise specified, metered-dose type sprays show an appropriate uniformity of delivered dose.

11-3-1. Aerosols for Cutaneous Application

(1) Aerosols for Cutaneous Application are sprays which atomize active substance(s) together with liquefied or compressed gas filled in containers.

(2) Aerosols for Cutaneous Application are usually prepared by dissolving or suspending active substance(s) in a vehicle, filling with liquefied propellants in pressure-resistant containers, and setting a continuous spray valve. If necessary, dispersing agents and stabilizers may be used.

(3) Pressure-resistant containers are usually used for Aerosols for Cutaneous Application.

11-3-2. Pump Sprays for Cutaneous Application

(1) Pump Sprays for Cutaneous Application are sprays which atomize active substance(s) in containers by pumping.

(2) Pump Sprays for Cutaneous Application are usually prepared by dissolving or suspending active substance(s) with excipients in a vehicle, filling in containers and setting pumps to the containers.

(3) Tight containers are usually used for Pump Sprays for Cutaneous Application. For the preparations susceptible to degradation by evaporation of water, a low-moisture-permeability container or packaging may be used.

11-4. Ointments

(1) Ointments are semi-solid preparations to be applied to the skin, which dissolve or disperse active substance(s) in a base. There are two types, hydrophobic ointments and hydrophilic ointments.

(2) Hydrophobic ointments are usually prepared by warming to melt hydrophobic bases such as fatty oils, waxes or paraffin, adding and mixing active substance(s) in the bases to be dissolved or dispersed, and kneading the whole to make homogeneous.

Hydrophilic ointments are usually prepared by warming to melt hydrophilic bases such as macrogol, adding and mixing active substance(s) in the bases, and kneading the whole to make homogeneous.

For Ointments which are apt to deteriorate, prepare before use.

(3) Ointments have a suitable viscosity for application to the skin.

(4) Tight containers are usually used for Ointments. For the preparations susceptible to degradation by evaporation of water, a low-moisture-permeability container or packaging may be used.

11-5. Creams

(1) Creams are semi-solid preparations to be applied to the skin, which are in the form of oil-in-water or water-in-oil emulsions. Hydrophobic preparations in the form of water-in-oil emulsions may be termed "Oily creams".

(2) Creams are usually prepared by mixing homogeneously and emulsifying an oil-phase component and a water-phase component, both warmed, of which either one contains the active substance(s). These components have the following constituents.

Oil-phase component: Vaseline, fatty alcohols, etc., with or without emulsifying agent(s) or other suitable excipients.

Water-phase component: Purified Water with or without emulsifying agent(s) or other suitable excipients.

For Creams which are apt to deteriorate, prepare before use.

(3) Creams have a suitable viscosity for applying to the skin.

(4) Tight containers are usually used for Creams. For the preparations susceptible to degradation by evaporation of water, a low-moisture-permeability container or packaging may be used.

11-6. Gels

(1) Gels are gelatinous preparations intended for application to the skin.

There are Aqueous Gels and Oily Gels.

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

(i) Aqueous Gels: To active substance(s) add polymers, other excipients and Purified Water, dissolve or suspend, and gelatinize by warming and cooling or by adding a gelatinizing agents.

(ii) Oily Gels: To active substance(s) add liquid oily bases such as glycols, fatty alcohols and other excipients, and mix.

(3) Gels have a suitable viscosity for application to the skin.

(4) Tight containers are usually used for Gels. For the preparations susceptible to degradation by evaporation of water, a low-moisture-permeability container or packaging may be used.

11-7. Patches

(1) Patches are preparations intended to be attached on the skin.

Patches are classified into Tapes/Plasters and Cataplasms/Gel Patches.

(2) Patches are usually prepared by mixing active substance(s) homogeneously with a base such as a polymer or a mixture of polymers, spreading on a backing layer or liner, and cutting into a given size. Percutaneous absorption type preparations may be prepared by using a release rate-controlling membrane. Where necessary, adhesive agents or penetration enhancers may be used.

(3) Unless otherwise specified, Patches of Transdermal Systems meet the requirements of Uniformity of Dosage Units <6.02>.

(4) Patches have a suitable adhesion for application to the skin.

(5) Patches which are regulated the release rate have an appropriate function of controlled release.

11-7-1. Tapes/Plasters

(1) Tapes/Plasters are patches which are prepared with bases of practically no water contain.

Plasters are included in this category.

(2) Tapes/Plasters are usually prepared by mixing homogeneously active substance(s) with or without excipients and a base of non water-soluble natural or synthetic polymers such as resins, plastics or rubber, and spreading on a cloth or spreading and sealing on a cloth or plastic film, cutting into a given size. The preparations may be also prepared by filling a mixture of active substance(s) and a base with or without other excipients in releasers composed with a release-controlling film, supporter and liner.

(3) Well-closed containers are usually used for Tapes/Plasters. For the preparations susceptible to degradation by moisture, a moisture-proof container

or packaging may be used.

11-7-2. Cataplasms/Gel Patches

(1) Cataplasms/Gel Patches are patches using water containing bases.

(2) Cataplasms/Gel patches are usually prepared by mixing active substance(s), Purified Water, and Glycerin or other liquid materials, or by mixing and kneading natural or synthetic polymers, which are soluble in water or absorbent of water, with Purified Water, adding active substance(s), mixing the whole homogeneously, spreading on a cloth or film, and cutting into a given size.

(3) Tight containers are usually used for Cataplasms/Gel Patches. For the preparations susceptible to degradation by evaporation of water, a low-moisture-permeability container or packaging may be used.

[3] Monographs for Preparations Related to Crude Drugs

Preparations Related to Crude Drugs

(1) Preparations related to crude drugs are preparations mainly derived from crude drugs. Extracts, Pills, Spirits, Infusions and Decoctions, Teabags, Tinctures, Aromatic Waters, and Fluidextracts are included in this category.

Definitions, methods of preparations, test methods, containers and packaging, and storage of these preparations are described in this chapter.

(2) The descriptions of the test methods and the containers and packaging in this chapter are fundamental requirements, and the preparation methods represent commonly used methods.

1. Extracts

(1) Extracts are preparations, prepared by concentrating extractives of crude drugs. There are following two kinds of extracts.

(i) Viscous extracts

(ii) Dry extracts

(2) Unless otherwise specified, Extracts are usually prepared as follows.

(i) Crude drugs, pulverized to suitable sizes, are extracted for a certain period of time with suitable solvents by means of cold extraction or warm extraction, or by percolation as directed in (ii) of (2) under 6. Tinctures. The extractive is filtered, and the filtrate is concentrated or dried by a suitable method to make a millet jelly-like consistency for the viscous extracts, or to make crushable solid masses, granules or powder for the dry extracts.

Extracts, which are specified the content of active substance(s), are prepared by assaying active substance(s) in a portion of sample and adjusting, if necessary, to specified strength with suitable diluents.

(ii) Weigh crude drugs, pulverized to suitable sizes, according to the prescription and heat for a certain period of time after adding 10 – 20 times amount of water. After separating the solid and liquid by centrifugation, the extractive is concentrated or dried by a suitable method to make a millet jelly-like consistency for the viscous extracts, or to make crushable solid masses, granules or powder for the dry extracts.

(3) Extracts have order and taste derived from the crude drugs used.

(4) Unless otherwise specified, Extracts meet the requirements of Heavy Metals Limit Test <1.07> when the test solution and the control solution are prepared as follows.

Test solution: Ignite 0.30 g of Extracts to ash, add 3 mL of dilute hydrochloric acid, warm, and filter. Wash the residue with two 5-mL portions of water. Neutralize the combined filtrate and washings (indicator: a drop of phenolphthalein TS) by adding ammonia TS until the color of the solution changes to pale red, filter where 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 these preparations.

2. Pills

(1) Pills are spherical preparations, intended for oral administration.

(2) Pills are usually prepared by mixing drug substance(s) uniformly with diluents, binders, disintegrators or other suitable excipient(s) and rolling into spherical form by a suitable method. They may be coated with a coating agent by a suitable method.

(3) Unless otherwise specified, Pills comply with Disintegration Test <6.09>.

(4) Well-closed or tight containers are usually used for these preparations.

3. Spirits

(1) Spirits are fluid preparations, usually prepared by dissolving volatile drug substance(s) in ethanol or in a mixture of ethanol and water.

(2) Spirits should be stored remote from fire.

(3) Tight containers are used for these preparations.

4. Infusions and Decoctions

(1) Infusions and Decoctions are fluid preparations, usually obtained by macerating crude drugs in water.

(2) Infusions and Decoctions are usually prepared by the following method.

Cut crude drugs into a size as directed below, and transfer suitable amounts to an infusion or decoction apparatus.

Leaves, flowers and whole plants: Coarse cutting

Woods, stems, barks, roots and rhizomes

: Medium cutting

Seeds and fruits: Fine cutting

(i) Infusions: Usually, damp 50 g of crude drugs with 50 mL of water for about 15 minutes, pour 900 mL of hot water to them, and heat for 5 minutes with several stirrings. Filter through a cloth after cooling.

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

Prepare Infusions or Decoctions when used.

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

(4) Tight containers are usually used for these preparations.

5. Teabags

(1) Teabags are preparations, usually packed one-day dose or one dose of crude drugs cut into a size of between coarse powder and coarse cutting in paper or cloth bags.

(2) Teabags are usually used according to the preparation method as directed under 4. Infusions and Decoctions.

(3) Well-closed or tight containers are usually used for these preparations.

6. Tinctures

(1) Tinctures are liquid preparations, 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 by means of either maceration or percolation as described below.

(i) Maceration: Place crude drugs in a suitable container, and add an amount of a solvent, equivalent to the same volume or about three-fourths of the volume of the crude drugs. Stopper container, and

allow the container to stand for about 5 days or until the soluble constituents have satisfactorily dissolved at room temperature with occasional stirring. Separate the solid and liquid by centrifugation or other suitable methods. In the case where about three-fourths volume of the solvent is added, wash the residue with a suitable amount of the solvent, and squeeze the residue, if necessary. Combine the extract and washings, and add sufficient solvent to make up the volume. In the case where the total volume of the solvent is added, sufficient amounts of the solvent may be added to make up for reduced amount, if necessary. Allow the mixture to stand for about 2 days, and obtain a clear liquid by decantation or filtration.

(ii) Percolation: Pour solvent in small portions to crude drugs placed in a container, and mix well to moisten the crude drugs. Stopper container, and allow it to stand for about 2 hours at room temperature. Pack the contents as tightly as possible in an appropriate 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. Then, 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 to the percolator, and continue to percolate until the desired volume has passed. Mix thoroughly, allow standing 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 and specified the content of marker constituent or ethanol, are prepared by assaying the content using a portion of the sample and adjusting the content with a sufficient amount of the percolate or solvent as required on the basis of the result of the assay.

(3) Tinctures should be stored remote from fire.

(4) Tight containers are used for these preparations.

7. Aromatic Waters

(1) Aromatic Waters are clear liquid preparations, saturated essential oils or other volatile substances in water.

(2) Unless otherwise specified, Aromatic Waters are usually prepared by the following process.

Shake thoroughly for 15 minutes 2 mL of an essential oil or 2 g of a volatile substance with 1000 mL of lukewarm purified water, set the mixture aside for 12 hours or longer, filter through moistened filter paper, and add purified water to make 1000 mL. Alterna-

tively, incorporate thoroughly 2 mL of an essential oil or 2 g of a volatile substance with sufficient talc, 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 if necessary, and add sufficient purified water passed through the filter paper to make 1000 mL.

(3) Aromatic Waters have odor and taste derived from the essential oils or volatile substances used.

(4) Tight containers are used for these preparations.

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. Where the content is specified, it takes precedence.

(2) Unless otherwise specified, Fluidextracts are usually prepared from coarse powder or fine cutting of crude drugs by either of following maceration or percolation.

(i) Maceration: Place a certain amounts of crude drugs in a suitable vessel, add a solvent to cover the crude drugs, close the vessel, and allow the vessel to stand at room temperature with occasional stirring for about 5 days or until the soluble constituents have satisfactorily dissolved. Separate the solid and liquid by centrifugation or other suitable method. Usually, reserve a volume of the liquid equivalent to about three-fourths of the total volume, and use it as the first liquid. Wash the residue with appropriate amount of the solvent, combine the washings and the remaining of the first liquid, concentrate if necessary, mix with the first liquid, and use it as solution (A). To the solution (A) add the solvent, if necessary, to make equal amount of the mass of the crude drugs. Allow the mixture to stand for about 2 days, and collect a clear liquid by decantation or filtration.

(ii) Percolation: Mix well 1000 g of the crude drugs with the first solvent to moisten them, 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 of the percolate as the first percolate. Add the second solvent to the percolator, then drip the percolate, and use it as the second percolate.

The period of standing and the flow rate during percolation may be varied depending on the kind and the amount of crude drugs used. The flow rate is usually regulated as follows, depending on the using amount of crude drugs.

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 10000 g	2.0 – 4.0 mL

Concentrate the second percolate, taking care not to lose the volatile substances of the crude drug, mix with the first percolate, and use it as solution (A). To the solution (A) add the second solvent to make 1000 mL, and allow the mixture to stand for about 2 days. Decant the supernatant liquid or filter the liquid to obtain a clear solution.

Fluidextracts for which the content of marker constituent or ethanol is specified are obtained by adjusting the content with a sufficient amount of the second solvent as required on the basis of the result of the assay made with a portion of the solution (A).

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

(4) Unless otherwise specified, Fluidextracts meet the requirements of Heavy Metals Limit Test <1.07> when the test solution and the control solution are prepared as follows.

Test solution: Ignite 1.0 g of Fluidextracts to ash, add 3 mL of dilute hydrochloric acid, warm, and filter. Wash the residue with two 5-mL portions of water. Neutralize the combined filtrate and washings (indicator: a drop of phenolphthalein TS) by adding ammonia TS until the color of the solution changes to pale red, filter if necessary, and add 2 mL of the 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 these preparations.