GENERAL NOTICES

1. The official name of this pharmacopoeia is 第十八改正日本薬局方, and may be abbreviated as 日局十八, 日局18, JP XVIII or JP 18.

2. The English name of this pharmacopoeia is The Japanese Pharmacopoeia, Eighteenth 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 monograph should be used as official names. In the drug monograph, in addition to English name, chemical name or Latin name can be mentioned in the title, as appropriate.

4. Crude Drugs and their related products are placed together in ''Crude Drugs and Related Drugs'' in the posterior part of the Official Monographs. These include: Extracts, Powders, Tinctures, Syrups, Spirits, Fluidextracts or Suppositories containing Crude Drugs as the active ingredient, and combination preparations containing Crude Drugs as the principal active ingredient.

5. The JP 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 headings of ''Description'' and in addition ''Containers and storage'' and ''Shelf life'' in the monographs on preparations are given for information, and should not be taken as indicating standards for conformity. Nevertheless, Containers under ''Containers and storage'' in the monograph on preparations containing crude drugs as main active ingredients are the 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 ''Atomic Weights of the Elements 2015'' (IUPAC)-Standard Atomic Weights 2017 (Atomic Weights Subcommittee of the Chemical Society of Japan). However, the atomic masses of the elements whose atomic weight is indicated with an interval in the 2015 table conform to the table of ''Atomic Weights of the Elements 2007'' (IUPAC)-Standard Atomic Weights 2010 (Atomic Weights Subcommittee of the Chemical Society of Japan).

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	°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	Pa·s
millipascal second	mPa·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%
microsiemens per centimeter	$\mu S \cdot cm^{-1}$
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 the JP Drugs 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 Law on Securing Quality, Efficacy and Safety of Products including Pharmaceuticals and Medical Devices.

12. From the point of view of quality assurance, requirements that should be noted on manufacturing processes, if appropriate in addition to the specifications, are shown in the heading ''Manufacture'' in monograph. It may contain requirements regarding control of materials, manufacturing processes and intermediates, and requirements regarding tests in process and omission of tests for the release. The fulfilment of requirements mentioned in this heading are confirmed based on the information obtained during the establishment of manufacturing method at the development stage, the control of manufacturing processes, or the tests for the release. Also even in the case of absence of the heading ''Manufacture'' in monograph, it is important to note appropriate controls of materials, manufacturing processes and intermediates in individual drugs.

13. 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, the performance of some test items in the monograph at release on a product may be omitted as occasion demands. Moreover, the quality evaluation of final products (drug substances and drug products) based on in-process data including in-process testing results and monitoring data on process parameters can replace specifications and test methods in the monograph or performing the test methods, if appropriate.

14. 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.

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

16. 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.

17. 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.

18. The term ''in vacuum'' indicates, unless otherwise specified, a pressure not exceeding 2.0 kPa.

19. The acidity or alkalinity of a solution, unless otherwise specified, is determined by blue or red litmus papers. To indicate these properties more precisely, pH values are used.

20. 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

21. 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.

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

23. 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.

24. The term ''weigh accurately'' means to weigh down to the degree of 0.1 mg, 10 μg, 1 μg or 0.1 μg 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.

25. A value of ''n'' figures in a test of the JP Drugs shall be obtained by rounding off a value of ''n + 1'' figures.

26. Unless otherwise specified, all tests of the JP 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.

27. The terms ''immediately''/''at once'' used in the test of the JP Drugs mean that the procedure is to be performed within 30 seconds after the preceding procedure.

28. 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.

29. 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.

30. 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 the JP Drugs, previously powdered in the case of a solid drug, within 30 minutes in a solvent at 20 ± 5°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

31. 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.

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

33. 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.

34. In principle, the JP Drug Products are controlled appropriately according to the direction under Elemental Impurities of the General Tests. When elemental impurities in the drug products are appropriately controlled in accordance with the direction, it is not necessary to perform the tests on elemental impurities such as heavy metals and arsenic specified in the monographs including, but not limited to, those of drug products, drug substances and excipients.

35. In principle, unless specified in the monograph, the JP Drugs are controlled appropriately according to the direction under Residual Solvents of the general tests.

36. Concerning harmful substances reported as intentionally contaminated to drugs, the control requirement for the presence or absence of contamination is described in the heading ''Potential adulteration'' in the monograph, as necessary. These substances are controlled by tests on materials, manufacturing processes, intermediates, or final products. The necessity and frequency of the tests are specified separately on individual drugs depending on the control strategy established as part of quality risk management.

37. 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, 50 μg in a semi-microbalance, or 5 μg in a

microbalance, the constant mass has been attained.

38. 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.

39. 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.

40. 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.

41. Sterility means a condition when no target microorganism is detected by the specified method. Sterilization means a process whereby killing or removal of all living microorganisms in an object to be sterilized is accomplished. Aseptic technique is controlled technique to maintain the aseptic condition.

42. The container is the device which holds the JP 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.

43. 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.

44. 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.

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

46. 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.

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

48. 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.

49. 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 (◆ ◆ or ◇ ◇).

—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>*.

The JP 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. (See the General Notices 5.)