Administrative notice
January 28, 2022

To: Pharmaceutical Affairs Section, Prefectural Health Department (Bureau)

Pharmaceutical Evaluation Division, Pharmaceutical Safety and
Environmental Health Bureau
Ministry of Health, Labour and Welfare

Rationalization of descriptions in the specification column in approval application forms for prescription drugs

The rationalization of descriptions in the specification column in marketing approval application forms for prescription drugs (excluding in-vitro diagnostics; the same shall apply hereinafter) is specified in "Handling of Changes to Approved Product Information Pertaining to the Quality of Drugs" (PSEHB/PED Notification No. 0309-1 and PSEHB/CND Notification No. 0309-1 jointly issued by the Director of the Pharmaceutical Evaluation Division and the Director of the Compliance and Narcotics Division, Pharmaceutical Safety and Environmental Health Bureau, Ministry of Health, Labour and Welfare dated March 9, 2018).

In light of a study conducted under the sub-theme "Rationalization of pharmaceutical product lifecycle management" under a research project on regulatory science of pharmaceuticals and medical devices funded by AMED Research Grants in FY 2020 entitled "Regulatory science on novel techniques for manufacturing and controlling qualified pharmaceuticals and their lifecycle management," examples of rationalized descriptions for the specifications of residual solvents, test for preparations, ICP atomic emission spectrometry/mass spectrometry, identification test (infrared spectrophotometry), identification test (ultraviolet-visible spectrophotometry), and identification test (qualitative test) are summarized in Attachments 1 to 6. It is now permissible to rationalize descriptions by referring to Attachments 1 to 6. Please inform relevant business operators under your jurisdiction.

If you intend to rationalize descriptions for test methods of approved prescription drugs for which no description examples are provided, please use procedural consultations for drugs provided by the Pharmaceutical and Medical Devices Agency prior to the change procedure for the time being, from the viewpoint of confirming the idea of rationalization and the appropriateness of the description.

Examples of rationalized descriptions for residual solvents

[Description of residual solvents for Piperacillin Hydrate in the Japanese Pharmacopoeia Eighteenth Edition]	[Example of rationalized description of residual solvents for Piperacillin Hydrate]
Residual solvents (GC) Transfer exactly 10 mg of Piperacillin Hydrate to an about 3-mL vial, add exactly 1 mL of saturated sodium hydrogen carbonate solution to dissolve and seal the vial tightly. After heating this at 90°C for 10 minutes, use the gas inside the container as the sample gas. Separately, measure exactly 1 mL of ethyl acetate, dissolve in water to make exactly 200 mL. Pipet 10 mL of this solution, add water to make exactly 20 mL. Pipet 2 μL of this solution in an about 3-mL vial containing exactly 1 mL of saturated sodium hydrogen carbonate solution, and stop the vial tightly. Run the procedure similarly to the sample, and use the gas as the standard gas. Perform the test with exactly 0.5 mL each of the sample gas and standard gas as directed under Gas Chromatography <2.02> according to the following conditions, and determine the peak area of ethyl acetate by the automatic integration method: the peak area of ethyl acetate obtained from the sample gas is not larger than that from the standard gas. Operating conditions Detector: A hydrogen flame-ionization detector. Column: A glass column 3 mm in inside diameter and 1 m in length, packed with porous styrene-divinyl benzene copolymer for gas chromatography (average pore diameter of 0.0085 μm, 300 – 400 m^2/g) with the particle size of 125 to 150 μm. Column temperature: A constant temperature of about 145°C. Carrier gas: Nitrogen. Flow rate: Adjust so that the retention time of ethyl acetate is about 4 minutes. Split ratio: 1:15 System suitability System performance: Take 1 mL of saturated sodium hydrogen carbonate solution in an about 3-mL vial, add 2 μL each of ethyl acetate solution (1 in 400) and acetone solution (1 in 400), and stop the vial tightly. When the procedure is run under the above operating conditions, acetone and ethyl acetate are eluted in this order with the resolution between these peaks being not less than 2.0.	Residual solvents **Test method**: Gas chromatography, headspace method, hydrogen flame-ionization detector, peak area **Specification value/acceptance criterion**: Not more than 0.045% for ethyl acetate **Analytical procedure** Sample solution: Dissolve Piperacillin Hydrate in saturated sodium hydrogen carbonate solution (10 mg/mL). Standard solution: A mixture of saturated sodium hydrogen carbonate solution and ethyl acetate solution (1 in 400) (500:1). Heating conditions: 90°C, 10 minutes. Injection volume of sample gas and standard gas: 0.5 mL. Operating conditions Detector: A hydrogen flame-ionization detector. Column: A glass column, porous styrene-divinyl benzene copolymer (average pore diameter of 0.0085 μm, 300 – 400 m^2/g), 3 mm in inside diameter, 1 m in length. Column temperature: About 145°C. Carrier gas: Nitrogen. Flow rate: The retention time of ethyl acetate is about 4 minutes. Split ratio: 1:15 System suitability System performance: Acetone and ethyl acetate are eluted in this order from a mixture of saturated sodium hydrogen carbonate solution, ethyl acetate solution (1 in 400) and acetone solution (1 in 400) (500:1:1), with the resolution being not less than 2.0. System repeatability: The relative standard deviation of ethyl acetate from a mixture of saturated sodium hydrogen carbonate solution and ethyl acetate solution (1 in 400) (500:1) (6 replicates) is not more than 10%.

System repeatability: Take 1 mL of saturated sodium hydrogen carbonate solution in an about 3-mL vial, add 2 μL of ethyl acetate solution (1 in 400), stop the vial tightly, and perform the test under the above operating conditions. When the procedure is repeated 6 times, the relative standard deviation of the peak area of ethyl acetate is not more than 10%.	Precautions Operate accurately and exactly as necessary.

[Description of residual solvents for ○△○△○ according to the Japanese Pharmacopoeia Eighteenth Edition]	[Example of rationalized description of residual solvents for ○△○△○]
Residual solvents (GC) Take accurately about 0.5 g of the substance to be tested, transfer to about 20 mL-vial, dissolve in exactly 5 mL of benzyl alcohol, and seal the vial tightly. After heating this at 120°C for 15 minutes, use the gas inside the container as the sample gas. Separately, weigh accurately about 0.5 g each of ethanol and ethyl acetate, add benzyl alcohol to make exactly 50 mL each, and use these solutions as the ethanol standard stock solution and ethyl acetate standard stock solution, respectively. Pipet 2 mL of the ethanol standard stock solution and 1 mL of the ethyl acetate standard stock solution, and add benzyl alcohol to make exactly 100 mL. Transfer exactly 5 mL of this solution into an about 20 mL-vial, seal the vial tightly, proceed in the same manner as for the sample, and use this gas as the standard gas. Perform the test with exactly 1 mL each of the sample gas and standard gas as directed under Gas Chromatography <2.02> according to the following conditions, and determine the peak areas A_{Ta} and A_{Sa} of ethanol and the peak areas A_{Tb} and A_{Sb} of ethyl acetate, respectively, and calculate the amounts of ethanol and ethyl acetate by the following formula: not more than 0.2% and not more than 0.1%, respectively. Amount (%) of ethanol = $M_{Sa} / M_T \times A_{Ta} / A_{Sa} \times 0.2$ Amount (%) of ethyl acetate = $M_{Sb} / M_T \times A_{Tb} / A_{Sb} \times 0.1$ M_{Sa}: Amount (g) of ethanol taken M_{Sb}: Amount (g) of ethyl acetate taken M_T: Amount (g) of the substance to be tested taken Operating conditions Detector: A hydrogen flame-ionization detector. Column: A fused silica column 0.25 mm in inside diameter and 60 m in length, coated inside surface with polyethylene glycol for gas chromatography 0.5 μm in thickness. Column temperature: 70°C for 15 minutes, then up to 240°C at a rate of 30°C per minute, and hold at 240°C for 15 minutes. Injection port temperature: 200°C Detector temperature: 250°C	Residual solvents **Test method**: Gas chromatography, headspace method, hydrogen flame-ionization detector, peak area **Specification value/acceptance criterion**: Not more than 0.2% for ethanol, not more than 0.1% for ethyl acetate Ethanol (%) = $M_{Sa} / M_T \times A_{Ta} / A_{Sa} \times 0.2$ Ethyl acetate (%) = $M_{Sb} / M_T \times A_{Tb} / A_{Sb} \times 0.1$ M_{Sa}: Amount (g) of ethanol taken M_{Sb}: Amount (g) of ethyl acetate taken M_T: Amount (g) of the substance to be tested taken A_{Ta} and A_{Sa}: Peak areas of ethanol from the sample solution and standard solution A_{Tb} and A_{Sb}: Peak areas of ethyl acetate from the sample solution and standard solution **Analytical procedure** Sample solution: A solution of the substance to be tested in benzyl alcohol (0.1 g/mL). Standard solution: Dilute ethanol and ethyl acetate with benzyl alcohol (0.2 mg/mL and 0.1 mg/mL). Heating conditions: 120°C, 15 minutes. Injection volume of sample gas and standard gas: 1 mL. Operating conditions Detector: A hydrogen flame-ionization detector. Column: A fused silica column, polyethylene glycol (coated 0.5 μm in thickness), 0.25 mm in inside diameter, 60 m in length Column temperature: 70°C for 15 minutes, then up to 240°C at a rate of 30°C per minute, and hold at 240°C for 15 minutes. Injection port temperature: 200°C Detector temperature: 250°C Carrier gas: Helium.

Carrier gas: Helium. Flow rate: Adjust so that the retention time of ethanol is about 7 minutes. Split ratio: 1:40 Time span of measurement: About 2 times as long as the retention time of ethanol (15 minutes). System suitability System performance: When the procedure is run with the standard gas under the above operating conditions, ethyl acetate and ethanol are eluted in this order with the resolution between these peaks being not less than 10. System repeatability: When the test is repeated 6 times with the standard gas under the above operating conditions, the relative standard deviation of the peak area of ethanol is not more than 10%.	Flow rate: The retention time of ethanol is about 7 minutes. Split ratio: 1:40 Time span of measurement: About 2 times as long as the retention time of ethanol. System suitability System performance: Ethyl acetate and ethanol are eluted in this order from the standard gas, with the resolution being not less than 10. System repeatability: The relative standard deviation of ethanol from the standard gas (6 replicates) is not more than 10%. Precautions Operate accurately and exactly as necessary.

Example of rationalized description for tests for preparations

[Acemetacin Tablets in the Japanese Pharmacopoeia Eighteenth Edition]	[Example of rationalized description for Acemetacin Tablets]
Uniformity of dosage units Perform the test according to the following method: it meets the requirement of the Content uniformity test. To 1 tablet of Acemetacin Tablets add 3 mL of water, and shake until the tablet is disintegrated. Add 15 mL of methanol, shake for 20 minutes, and add methanol to make exactly *V* mL so that each mL contains about 1.2 mg of acemetacin ($C_{21}H_{18}ClNO_6$). Centrifuge this solution, filter the supernatant liquid, discard the first 10 mL of the filtrate, pipet 5 mL of the subsequent filtrate, add exactly 1 mL of the internal standard solution, add methanol to make 50 mL, and use this solution as the sample solution. Proceed as directed in the Assay. Amount (mg) of acemetacin ($C_{21}H_{18}ClNO_6$) $= M_S \times Q_T / Q_S \times V / 25$ M_S: Amount (mg) of acemetacin for assay taken Internal standard solution — A solution of hexyl parahydroxybenzoate in methanol (1 in 250).	**Uniformity of dosage units** **Test method**: Content uniformity test, liquid chromatography, ultraviolet absorption photometer, peak area **Specification value/acceptance criterion**: Conforming Acemetacin (mg) = $M_S \times Q_T / Q_S \times V / 25$ Q_T: Ratio of acemetacin in the sample solution to the internal standard Q_S: Ratio of acemetacin in the standard solution to the internal standard M_S: Amount (mg) of acemetacin for assay taken **Analytical procedure** Sample solution: To 1 Acemetacin Tablet add 3 mL of water, shake with methanol, and add methanol to make *V* mL (about 1.2 mg/mL as the theoretical concentration of acemetacin). Separate the solid and the liquid from this solution, add the internal standard solution to the filtrate, and dilute with methanol (about 0.12 mg/mL of acemetacin). Standard solution, internal standard solution, operating conditions, system suitability, precautions: Proceed as directed in the Assay. The volume of the standard solution is equivalent to 25/V times as much as the sample solution.

[Acemetacin Tablets in the Japanese Pharmacopoeia Eighteenth Edition]	[Example of rationalized description for Acemetacin Tablets]
Dissolution When the test is performed at 50 revolutions per minute according to the Paddle method, using 900 mL of 2nd fluid for dissolution test as the dissolution medium, the dissolution rate in 45 minutes of Acemetacin Tablets is not less than 80%. Start the test with 1 tablet of Acemetacin Tablets, withdraw not less than 20 mL of the medium at the specified minute after starting the test, and filter through a membrane filter with a pore size not exceeding 0.45 μm. Discard not less than 10 mL of the first filtrate, pipet *V* mL of the subsequent filtrate, add the dissolution medium to make exactly *V'* mL so that each mL contains about 33 μg of acemetacin ($C_{21}H_{18}ClNO_6$), and use this solution as the sample solution. Separately, weigh accurately about 17 mg of acemetacin for assay, previously dried at 105°C for 2 hours, dissolve in the dissolution medium to make exactly 100 mL. Pipet 4 mL of this solution, add the dissolution medium to make exactly 20 mL, and use this solution as the standard solution. Determine the absorbances, A_T and A_S, of the sample solution and standard solution at 319 nm as directed under Ultraviolet-visible Spectrophotometry *<2.24>*. Dissolution rate (%) with respect to the labeled amount of acemetacin ($C_{21}H_{18}ClNO_6$) $= M_S \times A_T / A_S \times V' / V \times 1 / C \times 180$ M_S: Amount (mg) of acemetacin for assay taken C: Labeled amount (mg) of acemetacin ($C_{21}H_{18}ClNO_6$) in 1 tablet	**Dissolution** **Test method**: Dissolution test, paddle method, ultraviolet-visible spectrophotometry, absorbance **Specification value/acceptance criterion**: Not less than 80% (45 minutes) Acemetacin (%) $= M_S \times A_T / A_S \times V' / V \times 1 / C \times 180$ M_S: Amount (mg) of dried acemetacin for assay taken A_T: Sample solution A_S: Standard solution C: Labeled amount (mg) of acemetacin in 1 tablet V: Collected volume of the sample solution V': Prepared volume of the sample solution **Analytical procedure** Sample solution: Dilute the filtrate with the dissolution medium (theoretical concentration of acemetacin: about 33 μg/mL). Standard solution: Dissolve acemetacin for assay in the dissolution medium (about 33 μg/mL). Dissolution medium and amount of dissolution medium: 2nd fluid for dissolution test, 900 mL. Revolution speed: 50 revolutions per minute. Wavelength: 319 nm. **Precautions** Operate accurately and exactly as necessary. Acemetacin for assay: Dry at 105°C for 2 hours.

[Acemetacin Tablets in the Japanese Pharmacopoeia Eighteenth Edition]	[Example of rationalized description for Acemetacin Tablets]
Assay Weigh accurately the mass of not less than 20 Acemetacin Tablets, and powder. Weigh accurately a portion of the powder, equivalent to about 0.6 g of acemetacin ($C_{21}H_{18}ClNO_6$), add 120 mL of methanol, shake for 20 minutes, and add methanol to make exactly 200 mL. Centrifuge this solution, filter the supernatant liquid, discard the first 10 mL of the filtrate, pipet 2 mL of the subsequent filtrate, add exactly 1 mL of the internal standard solution, add methanol to make 50 mL, and use this solution as the sample solution. Separately, weigh accurately about 30 mg of acemetacin for assay, previously dried at 105°C for 2 hours, and dissolve in methanol to make exactly 25 mL. Pipet 5 mL of this solution, add exactly 1 mL of the internal standard solution, add methanol to make 50 mL, and use this solution as the standard solution. Perform the test with 10 μL each of the sample solution and standard solution as directed under Liquid Chromatography according to the following conditions, and calculate the ratios, Q_T and Q_S, of the peak area of acemetacin to that of the internal standard. Amount (mg) of acemetacin ($C_{21}H_{18}ClNO_6$) $= M_S \times Q_T / Q_S \times 20$ M_S: Amount (mg) of acemetacin for assay taken Internal standard solution — A solution of hexyl parahydroxybenzoate in methanol (1 in 250). Operating conditions Detector: An ultraviolet absorption photometer (wavelength 254 nm). Column: A stainless steel column 4.6 mm in inside diameter and 25 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μm in particle diameter). Column temperature: A constant temperature of about 40°C. Mobile phase: To 6 g of acetic acid (100) add water to make 1000 mL, and adjust the pH to 3.2 with a solution of 1.36 g of sodium acetate trihydrate in 100 mL of water. To 200 mL of this solution add 300 mL of acetonitrile. Flow rate: Adjust so that the retention time of acemetacin is about 7 minutes. System suitability System performance: Dissolve 75 mg of acemetacin and 75 mg of indometacin in 50 mL of methanol. To 4 mL of this solution add 1 mL of	**Assay** **Test method**: Liquid chromatography, ultraviolet absorption photometer, peak area Acemetacin (mg) = $M_S \times Q_T / Q_S \times 20$ M_S: Amount (mg) of acemetacin for assay taken Q_T: Ratio of acemetacin in the sample solution to the internal standard Q_S: Ratio of acemetacin in the standard solution to the internal standard **Analytical procedure** Sample solution: Powder not less than 20 tablets. Disperse the powder with methanol, and further dilute with methanol (theoretical concentration of acemetacin: about 3 mg/mL). Separate the solid and the liquid from this solution, add the internal standard solution to the filtrate, and dilute with methanol (about 0.12 mg/mL of acemetacin). Standard solution: Dissolve acemetacin for assay in methanol, add the internal standard solution, and dilute with methanol to make a volume 1/20 times that of the sample solution (about 0.12 mg/mL of acemetacin). Add the internal standard solution so that it is the same as the amount of the internal standard relative to the theoretical amount of acemetacin in the sample solution. Internal standard solution: Dissolve hexyl parahydroxybenzoate in methanol (4 mg/mL). Injection volume: 10 μL. Operating conditions Wavelength: 254 nm. Column: Octadecylsilanized silica gel (5 μm), 4.6 mm in inside diameter, 25 cm in length. Column temperature: About 40°C. Mobile phase: A mixture of acetonitrile and diluted acetic acid (3 in 500) adjusted to pH 3.2 with a solution of sodium acetate trihydrate (13.6 g/L) (3:2). Flow rate: The retention time of acemetacin is about 7 minutes. System suitability System performance: Acemetacin, indomethacin and the internal standard are eluted in this order from a solution of acemetacin (0.12 mg/mL), indomethacin (0.12 mg/mL) and the internal standard (80 μg/mL) in methanol, with the resolutions between the peaks of acemetacin and

the internal standard solution, and add methanol to make 50 mL. When the procedure is run with 10 μL of this solution under the above operating conditions, acemetacin, indometacin and the internal standard are eluted in this order with the resolutions between the peaks of acemetacin and indometacin and between the peaks of indometacin and the internal standard being not less than 3, respectively. System repeatability: When the test is repeated 6 times with 10 μL of the standard solution under the above operating conditions, the relative standard deviation of the ratio of the peak area of acemetacin to that of the internal standard is not more than 1.0%.	indomethacin and between the peaks of indomethacin and the internal standard being not less than 3 each. System repeatability: The relative standard deviation of the ratio of acemetacin in the standard solution to the internal standard (6 replicates) is not more than 1.0%. **Precautions** Operate accurately and exactly as necessary. Acemetacin for assay: Dry at 105°C for 2 hours.

Example of rationalized description for ICP Atomic Emission Spectrometry/Mass Spectrometry

Guideline for drafting the Japanese Pharmacopoeia (1)	**Example of rationalized description**
ICP atomic emission spectrometry	**ICP atomic emission spectrometry**
Assay	Assay
Weigh accurately about ○○ mg of the substance to be tested, add △ mL of ○ acid, heat to dissolve, cool, and add water to make exactly ○△ mL. Pipet □ mL of this solution, add △ mL of ○ acid and water to make exactly ○× mL, and use this solution as the sample solution. Dilute △ mL of ○ acid with water to make exactly ○× mL, and use this solution as the blank solution. Pipet ○ mL, △ mL, × mL and □ mL of Standard Element # Solution (× ppm), add water to each to make exactly ○× mL, and use these solutions as the standard solution (1) for element #, standard solution (2) for element #, standard solution (3) for element # and standard solution (4) for element #, respectively. Perform the test with the sample solution, the blank solution and the standard solution (1) for element #, standard solution (2) for element #, standard solution (3) for element # and standard solution (4) for element # as directed under Inductively Coupled Plasma-Atomic Emission Spectrometry <2.63> according to the following conditions, and determine the content of element # using the calibration curve obtained from the emission intensities of the blank solution and standard solutions for element #.	Test method: Inductively coupled plasma-atomic emission spectrometry, emission intensity Specification value/acceptance criterion: Determine the content of element # from the calibration curve obtained from the emission intensities of the blank solution and standard solutions for element #. Analytical procedure Sample solution: Dissolve the substance to be tested in ○ acid by heating, cool, and dilute with water and ○ acid. (A mixture of water and ○ acid (○/△), about ▽ μg/mL of element #) Blank solution: A mixture of water and ○ acid (○/△). Standard solution for element # (diluted with water): Element # ●, ▲, ▼, ■ μg/mL.
Operating conditions Wavelength: Element # ○○○. ○○○ nm	Operating conditions Wavelength: Element # ○○○. ○○○ nm
System suitability System repeatability: When the test is repeated 6 times with the standard solution (1) for element # under the above operating conditions, the relative standard deviation of the emission intensity of element # is not more than ○%.	System suitability System repeatability: The relative standard deviation of the emission intensity of element # from the standard solution for element # (● μg/mL) (6 replicates) is not more than ○%.
	Precautions: Operate accurately and exactly as necessary.

Guideline for drafting the Japanese Pharmacopoeia (2)	**Example of rationalized description**
ICP atomic emission spectrometry	**ICP atomic emission spectrometry**
Purity, element #	Purity, element #
Weigh accurately ○○ mg of the substance to be tested, add △ mL of ○ acid, and heat to decompose in a microwave digestion apparatus. After cooling, wash the decomposition vessel several times with water, add water to make exactly ○× mL, and use this solution as the sample solution. Add water to △ mL of ○	Test method: Inductively coupled plasma-atomic emission spectrometry, emission intensity Specification value/acceptance criterion:

acid to make exactly ○× mL, and use this solution as the blank solution. Pipet ○ mL of Standard Element # Solution (× ppm), add × mL of ○ acid, add water to make exactly ○× mL, and use this solution as the standard stock solution for element #. To exactly ○ mL, △ mL, × mL and □ mL of the standard stock solution for element # add △ mL of ○ acid and water to make exactly ○× mL, and use these solutions as the standard solution (1) for element #, standard solution (2) for element #, standard solution (3) for element # and standard solution (4) for element #, respectively. Perform the test with the sample solution, the blank solution and the standard solution (1) for element #, standard solution (2) for element #, standard solution (3) for element # and standard solution (4) for element # as directed under Inductively Coupled Plasma-Atomic Emission Spectrometry <2.63> according to the following conditions, and determine the content of element # from the calibration curve obtained from the emission intensities of the blank solution and the standard solution (1) for element #, standard solution (2) for element #, standard solution (3) for element # and standard solution (4) for element #: not more than ○.○ ppm.	Determine the content of element # from the calibration curve obtained from the emission intensities of the blank solution and standard solutions for element #. Element # Not more than ○.○ ppm. Analytical procedure Sample solution: To the substance to be tested add ○ acid, heat to decompose (about ◎ mg/mL) in a microwave digestion apparatus, cool, and dilute with water. (A mixture of water and ○ acid (○/△), about ▽ μg/mL) Blank solution: A mixture of water and ○ acid (○/△). Standard solution for element #: A solution of element # ●, ▲, ▼, ■ μg/mL in a mixture of water and ○ acid (○/△).
Operating conditions Wavelength: Element # ○○○.○○○ nm.	Operating conditions Wavelength: Element # ○○○.○○○ nm.
System suitability System repeatability: When the test is repeated 6 times with the standard solution (1) for element # under the above operating conditions, the relative standard deviation of the emission intensity of element # is not more than ○%.	System suitability System repeatability: The relative standard deviation of the emission intensity of element # from the standard solution for element # (● μg/mL) (6 replicates) is not more than ○%.
	Precautions: Operate accurately and exactly as necessary.

Guideline for drafting the Japanese Pharmacopoeia (3)	**Example of rationalized description**
ICP mass spectrometry	**ICP mass spectrometry**
Element #, assay	Element #, assay
Weigh accurately about ○○ mg of the substance to be tested, add △ mL of ○ acid and × mL of □ acid, and heat gradually on a hot plate. After no brown gas is generated and the reaction solution becomes light yellow and clear, allow to cool. After cooling, add exactly □ mL of the internal standard solution to this solution, then add water to make ○× mL, and use this solution as the sample solution. To △ mL of ○ acid add exactly × mL of □ acid and □ mL of the internal standard solution, add water to make ○× mL, and use this solution as the blank solution. Pipet ○ mL, △ mL, □ mL and × mL of Standard Element # Solution (× ppm), add exactly △ mL of ○ acid, × mL of □ acid and □ mL of the internal standard solution, add water to make ○× mL, and use these	Test method: Inductively coupled plasma-mass spectrometry, ion count ratio Specification value/acceptance criterion: Determine the content of element # from the calibration curve obtained from the ion counts of the blank solution and standard solutions for element #. Analytical procedure Sample solution: To the substance to be tested add ○ acid and □ acid (a mixture of ○ acid and □ acid (○/△), about ◎ mg/mL for the substance to be tested), heat gradually on a hot plate until no brown gas is generated and the reaction

solutions as the standard solution (1) for element #, standard solution (2) for element #, standard solution (3) for element # and standard solution (4) for element #, respectively. Perform the test with the sample solution, the blank solution and the standard solution (1) for element #, standard solution (2) for element #, standard solution (3) for element # and standard solution (4) for element # as directed under Inductively Coupled Plasma-Mass Spectrometry <2.63> according to the following conditions, and determine the content of element # from the ion count ratios of the blank solution and the standard solution (1) for element #, standard solution (2) for element #, standard solution (3) for element # and standard solution (4) for element # to the internal standard.	solution becomes light yellow and clear, and allow to cool. After cooling, add the internal standard solution, and dilute with water. (A mixture of water, ○ acid and □ acid (○/△/×), about ▽ μg/mL for the substance to be tested, about ◇ ng/mL for element $) Blank solution: A mixture of water, ○ acid and □ acid (○/△/×). Standard solution for element #: A solution of element # ●, ▲, ▼, ■ μg/mL, element $ ◇ ng/mL in a mixture of water, ○ acid and □ acid (○/△/×).
Internal standard solution: Pipet △ mL of Standard Element $ Solution (× ppm), and add water to make exactly △× mL.	Internal standard solution: A solution of element $ ◆ ng/mL.
Operating conditions Measurement m/z: Element # m/z ○, element $ m/z △	Operating conditions Measurement m/z: Element # m/z ○, element $ m/z △
System suitability System repeatability: When the test is repeated 6 times with the standard solution (1) for element # under the above operating conditions, the relative standard deviation of the ion count ratio of element # to the internal standard is not more than ○%.	System suitability System repeatability: The relative standard deviation of the ion count ratio of element # to the internal standard in the standard solution for element # (● μg/mL) (6 replicates) is not more than ○%.
	Precautions: Operate accurately and exactly as necessary.

Guideline for drafting the Japanese Pharmacopoeia (4)	**Example of rationalized description**
ICP mass spectrometry	**ICP mass spectrometry**
Purity, elements #1, #2 and #3	Purity, elements #1, #2 and #3
Weigh accurately ○○ mg of the substance to be tested, add △ mL of ○ acid, and heat to decompose in a microwave digestion apparatus. After cooling, wash the decomposition vessel several times with water, add exactly ○ mL of the internal standard solution, add water to make ○× mL, and use this solution as the sample solution. To △ mL of ○ acid add exactly ○ mL of the internal standard solution, add water to make ○× mL, and use this solution as the blank solution. Pipet ○ mL each of Standard Element #1, #2 and #3 Solutions (× ppm), add × mL of ○ acid, add water to make ○△ mL, and use these solutions as the standard stock solutions for elements #1, #2 and #3. Pipet ○ mL, △ mL, × mL and □ mL of the standard stock solutions for elements #1, #2 and #3, respectively, add exactly △ mL of ○ acid and ○ mL of the internal standard solution, add water to make exactly ○× mL, and use these solutions as the standard solution (1), standard solution (2), standard solution (3) and standard solution (4) for elements #1, #2 and #3. *Each standard element solution may be mixed as long as they do not interfere with each other*. Perform the test with the sample solution, the blank solution and each standard solution (1), standard solution (2), standard solution (3) and standard solution (4) as directed under Inductively Coupled Plasma-Mass Spectrometry <2.63> according to the following conditions, and calculate the contents of elements #1, #2 and #3 from the ion count ratios of the blank solution and the standard solution (1), standard solution (2), standard solution (3) and standard solution (4) for elements #1, #2 and #3 to the internal standard: Not more than ○.○ ppb each.	Test method: Inductively coupled plasma-mass spectrometry, ion count ratio Specification value/acceptance criterion: Determine the content of element # from the calibration curve obtained from the ion counts of the blank solution and elements #1, #2 and #3. Element #1 not more than ○. ○ ppb, element #2 not more than ○. ○ ppb, element #3 not more than ○. ○ ppb Analytical procedure Sample solution: To the substance to be tested add ○ acid, heat to decompose in a microwave digestion apparatus (about ◎ mg/mL), cool, add the internal standard solution, and dilute with water. (A mixture of water and ○ acid (○/△), about ▽ μg/mL for the substance to be tested, ◇ ng/mL for element $) Blank solution: A mixture of water and ○ acid (○/△), ◇ ng/mL for element $. Standard solution for element #: A solution of element #1, #2 or #3 ●, ▲, ▼, ■ μg/mL, element $ ◇ ng/mL in a mixture of water and ○ acid (×/□).
Internal standard solution: Pipet ○ μL of Standard Element $ Solution (× ppm), and add water to make exactly △× mL.	Internal standard solution: A solution of element $ ◆ ng/mL.
Operating conditions Measurement m/z: Element #1 m/z ○, element #2 m/z △, and element #3 m/z ×, element $ m/z □. Use collision reaction cell gas (name of the gas, if necessary).	Operating conditions Measurement m/z: Element #1 m/z ○, element #2 m/z △, element #3 m/z ×, element $ m/z □. Use collision reaction cell gas (name of the gas, if necessary).
System suitability System repeatability: When the test is repeated 6 times with the standard solutions (1) of elements #1, #2 and #3 under the above operating conditions, the relative standard deviation of the ion count ratio of element # to the internal standard is not more than ○%.	System suitability System repeatability: The relative standard deviation of the ion count ratio of element # to the internal standard from the standard solutions for elements #1, #2 and #3 (● μg/mL) (6 replicates) is not more than ○%.

	Precautions: Operate accurately and exactly as necessary.

Case example (an example of ICP atomic emission spectrometry (internal standard method))	**Example of rationalized description**
ICP atomic emission spectrometry	**ICP atomic emission spectrometry**
Purity, element #	Purity, element #
Weigh accurately ○○ mg of the substance to be tested, add △ mL of ○ acid, and heat to decompose in a microwave degradation apparatus. After cooling, wash the decomposition vessel several times with water, add exactly ○ mL of the internal standard solution, add water to make ○× mL, and use this solution as the sample solution. To △ mL of ○ acid add exactly ○ mL of the internal standard solution, add water to make exactly ○× mL, and use this solution as the blank solution. Pipet ○ mL of Standard Element # Solution (× ppm), add × mL of ○ acid, add water to make exactly ○× mL, and use this solution as the standard stock solution for element #. To exactly ○ mL, △ mL, × mL and □ mL of the standard stock solution for element # add exactly △ mL of ○ acid and ○ mL of the internal standard solution to each, add water to make exactly ○× mL, and use these solutions as the standard solution (1) for element #, standard solution (2) for element #, standard solution (3) for element # and standard solution (4) for element #, respectively. Perform the test with the sample solution, the blank solution and the standard solution (1) for element #, standard solution (2) for element #, standard solution (3) for element #, and standard solution (4) for element # as directed under Inductively Coupled Plasma-Atomic Emission Spectrometry <2.63> according to the following conditions, and determine the content of element # from the emission intensity ratio of the blank solution and the standard solution (1) for element #, standard solution (2) for element #, standard solution (3) for element # and standard solution (4) for element # to the internal standard: not more than ○.○ ppm.	Test method: Inductively coupled plasma-atomic emission spectrometry, emission intensity ratio Specification value/acceptance criterion: Determine the content of element # from the calibration curve obtained from the emission intensities of the blank solution and standard solutions for element #. Element # Not more than ○.○ ppm. Analytical procedure Sample solution: To the substance to be tested add ○ acid, heat to decompose in a microwave digestion apparatus (about ◎ mg/mL), cool, add the internal standard solution, and dilute with water. (A mixture of water and ○ acid (○/△), about ▽ μg/mL for the substance to be tested, ◇ μg/mL for element $) Blank solution: A mixture of water and ○ acid (○/△), ◇ μg/mL for element $. Standard solution for element #: A solution of element # ●, ▲, ▼, ■ μg/mL, element $ ◇ μg/mL in a mixture of water and ○ acid (○/△).
Internal standard solution: Pipet △ mL of Standard Element $ Solution (× ppm), and add water to make exactly △× mL.	Internal standard solution: A solution of element $ ◆ μg/mL.
Operating conditions Wavelength: Element # ○○○.○○○ nm.	Operating conditions Wavelength: Element # ○○○.○○○ nm.
System suitability System repeatability: When the test is repeated 6 times with the standard solution (1) for element # under the above operating conditions, the relative standard deviation of the emission intensity of element # is not more than ○%.	System suitability System repeatability: The relative standard deviation of the emission intensity of element # from the standard solution for element # (● μg/mL) (6 replicates) is not more than ○%.
	Precautions: Operate accurately and exactly as necessary.

Example of rationalized description for identification, infrared spectrophotometry

JP monograph	Example of rationalized description
Identification, infrared spectrophotometry	**Identification, infrared spectrophotometry**
(1) Reference spectrum method **Example 1: Codeine Phosphate Hydrate** Determine the infrared absorption spectrum of Codeine Phosphate Hydrate, previously dried at 105°C for 4 hours, as directed in the potassium bromide disk method under Infrared Spectrophotometry <2.25>, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wave numbers.	**(1) Reference spectrum method** **Example 1: Codeine Phosphate Hydrate** Test method: Infrared spectrophotometry, potassium bromide disk method Specification/acceptance criterion: Coincide with the reference spectrum. Sample preparation: Dry Codeine Phosphate Hydrate (105°C, 4 hours).
Example 2: Cyanamide Drop one or two drops of a solution of Cyanamide in acetone (1 in 100) onto a potassium bromide disk prepared as directed in the potassium bromide disk method under Infrared Spectrophotometry <2.25>, and air-dry the disk. Determine the infrared absorption spectrum of the disk as directed in the film method under Infrared Spectrophotometry <2.25>, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wave numbers.	**Example 2: Cyanamide** Test method: Infrared spectrophotometry, film method Specification/acceptance criterion: Coincide with the reference spectrum. Sample preparation: Add a solution of Cyanamide in acetone (1 in 100) dropwise to a potassium bromide disk, and air-dry.
Example 3: Dimercaprol Determine the infrared absorption spectrum of Dimercaprol as directed in the liquid film method under Infrared Spectrophotometry <2.25>, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wave numbers.	**Example 3: Dimercaprol** Test method: Infrared spectrophotometry, liquid film method Specification/acceptance criterion: Coincide with the reference spectrum. Sample preparation: Use the substance to be tested as the sample.

(2) Method specifying wave numbers **Example 1: Chlordiazepoxide Tablets** Weigh a portion of powdered Chlordiazepoxide Tablets, equivalent to 0.01 g of Chlordiazepoxide, add 10 mL of diethyl ether, shake vigorously, and centrifuge. Evaporate 5 mL of the supernatant liquid by warming on a water bath to dryness. Determine the infrared absorption spectrum of the residue as directed in the potassium bromide disk method under Infrared Spectrophotometry <2.25>: it exhibits absorption at the wave numbers of about 1625 cm^{-1}, 1465 cm^{-1}, 1265 cm^{-1}, 850 cm^{-1} and 765 cm^{-1}.	**(2) Method specifying wave numbers** **Example 1: Chlordiazepoxide Tablets** Test method: Infrared spectrophotometry, potassium bromide disk method Specification/acceptance criterion: Absorbance at the wave numbers of about 1625 cm^{-1}, 1465 cm^{-1}, 1265 cm^{-1}, 850 cm^{-1} and 765 cm^{-1} Sample preparation: Powder Chlordiazepoxide Tablets, disperse with diethyl ether (about 1 mg/mL as chlordiazepoxide), centrifuge, take 5 mL of the supernatant liquid, and evaporate on a water bath.
Example 2: Purified Sodium Hyaluronate Ophthalmic Solution To 1 volume of Purified Sodium Hyaluronate Ophthalmic Solution, equivalent to 7.5 mg of purified sodium hyaluronate $[(C_{14}H_{20}NNaO_{11})_n]$, add 2 volumes of acetone, shake well, and centrifuge at 3000 rpm for 10 minutes. Remove the acetone, wash the precipitate with a mixture of acetone and water (5:1), dry the precipitate under reduced pressure (not exceeding 0.67 kPa) at 60°C for 5 hours using phosphorus (V) oxide as a desiccant, and determine the infrared absorption spectrum as directed in ATR method under Infrared Spectrophotometry <2.25>: it exhibits absorption at the wave numbers of about 1605 cm^{-1}, 1404 cm^{-1}, 1375 cm^{-1}, 1150 cm^{-1}, 1025 cm^{-1} and 945 cm^{-1}.	**Example 2: Purified Sodium Hyaluronate Ophthalmic Solution** Test method: Infrared spectrophotometry, ATR method Specification/acceptance criterion: Absorption at the wave numbers of about 1605 cm^{-1}, 1404 cm^{-1}, 1375 cm^{-1}, 1150 cm^{-1}, 1025 cm^{-1} and 945 cm^{-1} Sample preparation: To 1 volume of Purified Sodium Hyaluronate Ophthalmic Solution, equivalent to 7.5 mg of purified sodium hyaluronate $[(C_{14}H_{20}NNaO_{11})_n]$, add 2 volumes of acetone, centrifuge, remove the acetone, wash the precipitate with a mixture of acetone and water (5:1), and dry under reduced pressure (not exceeding 0.67 kPa) at 60°C for 5 hours using phosphorus (V) oxide as a desiccant.
Example 3: Hypromellose Acetate Succinate Determine the infrared absorption spectrum of Hypromellose Acetate Succinate as directed in the ATR method under Infrared Spectrophotometry <2.25>: it exhibits absorption at the wave numbers of about 2840 cm^{-1}, 1737 cm^{-1}, 1371 cm^{-1}, 1231 cm^{-1} and 1049 cm^{-1}.	**Example 3: Hypromellose Acetate Succinate** Test method: Infrared spectrophotometry, ATR method Specification/acceptance criterion: Absorption at the wave numbers of about 2840 cm^{-1}, 1737 cm^{-1}, 1371 cm^{-1}, 1231 cm^{-1} and 1049 cm^{-1} Sample preparation: Use the substance to be tested as the sample.

(3) If differences appear between spectra **Example 1: L-Glutamic Acid** Determine the infrared absorption spectrum of L-Glutamic Acid as directed in the potassium bromide disk method under Infrared Spectrophotometry <2.25>, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wave numbers. If any difference appears between the spectra, dissolve L-Glutamic Acid in a small amount of water, evaporate water at 60°C under reduced pressure, and perform the test in the same manner with the dried residue.	**(3) If differences appear between spectra** **Example 1: L-Glutamic Acid** Test method: Infrared spectrophotometry, potassium bromide disk method Specification/acceptance criterion: Coincide with the reference spectrum. Sample preparation: Use the substance to be tested as the sample. Sample repreparation (if differences appear between spectra): Dissolve in water, and dry under reduced pressure at 60°C.
(4) Setting of multiple test methods and if differences appear between spectra **Example 1: Montelukast Sodium** Determine the infrared absorption spectrum of Montelukast Sodium as directed in the paste method under Infrared Spectrophotometry <2.25>, and compare the spectrum with the Reference Spectrum or the spectrum of Montelukast Sodium for Identification RS: both spectra exhibit similar intensities of absorption at the same wave numbers. Or, perform the test by the potassium bromide disk method or the ATR method, and compare the spectrum with the spectrum of Montelukast Sodium for Identification RS: both spectra exhibit similar intensities of absorption at the same wave numbers. If any difference appears between the spectra, dissolve Montelukast Sodium and Montelukast Sodium for Identification RS in toluene, add heptane, shake, then allow to stand, and remove the supernatant liquid by decantation. Dry the residue at 75°C for 16 hours under reduced pressure, and perform the test by paste method, potassium bromide disk method or the ATR method.	**(4) Setting of multiple test methods and if differences appear between spectra** **Example 1: Montelukast Sodium** Test method: Infrared spectrophotometry, paste method, potassium bromide disk method, or ATR method Specification/acceptance criterion: The spectrum agrees with the Reference Spectrum or the Spectrum of Reference Standard (paste method). The spectrum agrees with that of the Reference Standard (potassium bromide disk method, ATR method). The spectrum agrees with the Reference Spectrum or the Spectrum of the Reference Standard (sample repreparation). Preparation of the sample and reference standard: Use Montelukast Sodium as the sample. Sample repreparation (if differences appear between spectra): Dissolve Montelukast Sodium and Reference Standard in toluene, add heptane, mix, allow to stand, and remove the supernatant liquid. Dry under reduced pressure at 75°C for 16 hours

Example of rationalized description for identification, ultraviolet-visible spectrophotometry

Guideline for drafting the Japanese Pharmacopoeia	Example of rationalized description
Identification, ultraviolet-visible spectrophotometry	**Identification, ultraviolet-visible spectrophotometry**
(1) Reference spectrum method Determine the absorption spectrum of a solution of the substance to be tested in ethanol (95) (1 in ○○) as directed under Ultraviolet-visible Spectrophotometry <2.24>, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wavelengths.	**(1) Reference spectrum method** Test method: Ultraviolet-visible spectrophotometry Specification value/acceptance criterion: Coincide with the Reference Spectrum Analytical procedure: Sample solution: A solution in ethanol (95) (1 in ○○).
(2) Comparison with the spectrum of the Reference Standard Determine the absorption spectrum of a solution of the substance to be tested in ethanol (95) (1 in ○○) as directed under Ultraviolet-visible Spectrophotometry <2.24>, and compare with the spectrum of a solution of ** RS prepared in the same manner: both spectra exhibit similar intensities of absorption at the same wavelengths.	**(2) Comparison with the spectrum of the Reference Standard** Test method: Ultraviolet-visible spectrophotometry Specification value/acceptance criterion: Coincide with the spectrum of the Reference Standard. Analytical procedure: Sample solution: A solution in ethanol (95) (1 in ○○). Standard solution: A solution of ** RS in ethanol (95) (1 in ○○).
(3) Method specifying the wavelength of absorption maximum Determine the absorption spectrum of a solution of the substance to be tested in ethanol (95) (1 in ○○) as directed under Ultraviolet-visible Spectrophotometry <2.24>: it exhibits maxima between ○○○ nm and ○○○ nm, and between □□□ nm and □□□ nm. (no case example in JP monographs)	**(3) Method specifying the wavelength of absorption maximum** Test method: Ultraviolet-visible spectrophotometry, Specification value/acceptance criterion: Maximum absorption wavelengths ○○○-○○○ nm and □□□-□□□ nm Analytical procedure: Sample solution: A solution in ethanol (95) (1 in ○○).
(4) Method specifying the wavelength of absorption maximum and the absorbance ratio at the wavelength of absorption maximum (example with Propafenone Hydrochloride Tablets)	**(4) Method specifying the wavelength of absorption maximum and the absorbance ratio at the wavelength of absorption maximum** (example with Propafenone Hydrochloride Tablets)

To a quantity of Propafenone Hydrochloride Tablets, equivalent to 0.3 g of Propafenone Hydrochloride, add 60 mL of water, and disintegrate by warming. After cooling, centrifuge, and to 3 mL of the supernatant liquid add water to make 500 mL. Determine the absorption spectrum of this solution as directed under Ultraviolet-visible Spectrophotometry <2.24>: it exhibits maxima between 247 nm and 251 nm, and between 302 nm and 306 nm. Separately, determine both maximal absorbances, A1 and A2, of the solution, the ratio of A1/A2 is between 2.30 and 2.55.	Test method: Ultraviolet-visible spectrophotometry Specification value/acceptance criterion: Absorption maximum wavelengths ○○○-○○○ nm (A1) and □□□-□□□ nm (A2), absorbance ratio A1/A2 = #.##-#.## Analytical procedure: Sample solution: Add water to Propafenone Hydrochloride Tablets, disintegrate by warming, cool, and dilute the supernatant liquid with water (about ○.○○ mg/mL).

Examples of rationalized description for identification (qualitative test)

[1] Color reaction:

Description in the JP	Example of rationalized description	Remarks
Taltirelin Hydrate Dissolve 30 mg of Taltirelin Hydrate in 10 mL of water. To 0.5 mL of this solution add 2 mL of a solution of 4-nitrobenzenediazonium fluoroborate (1 in 2000) and 3 mL of boric acid-potassium chloride-sodium hydroxide buffer solution (pH 9.0): a red color is produced.	**Test method:** Color reaction **Specification value/acceptance criterion:** A red liquid **Analytical procedure** Sample solution: A solution of Taltirelin Hydrate in water (3 mg/mL). Reaction: To 1 volume of the sample solution add 4 volumes of a solution of 4-nitrobenzenediazonium fluoroborate (1 in 2000) and 6 volumes of boric acid-potassium chloride-sodium hydroxide buffer solution, pH 9.0.	Example of description for drug substance
Taltirelin Tablets Powder Taltirelin Tablets. To a portion of the powder, equivalent to 30 mg of Taltirelin Hydrate, add 10 mL of water, shake for 15 minutes, and filter. To 0.5 mL of the filtrate add 2 mL of a solution of 4-nitrobenzendiazonium fluoroborate (1 in 2000) and 3 mL of boric acid-potassium chloride-sodium hydroxide buffer solution (pH 9.0): a red color is produced.	**Test method:** Color reaction **Specification value/acceptance criterion:** A red liquid **Analytical procedure** Sample solution: To Taltirelin Tablets add water, filter, and use the filtrate (about 3 mg/mL of taltirelin hydrate). Reaction: To 1 volume of the sample solution add 4 volumes of a solution of 4-nitrobenzenediazonium fluoroborate (1 in 2000) and 6 volumes of boric acid-potassium chloride-sodium hydroxide buffer solution, pH 9.0.	Example of description for drug product (tablets)

[2] Precipitation reaction:

Description in the JP	Example of rationalized description	Remarks
Tiaramide Hydrochloride Dissolve 5 mg of Tiaramide Hydrochloride in 5 mL of 0.1 mol/L hydrochloric acid TS, and add 3 drops of Dragendorff's TS: an orange precipitate is formed.	**Test method:** Precipitation reaction **Specification value/acceptance criterion:** An orange precipitate **Analytical procedure** Sample solution: A solution of Tiaramide Hydrochloride in 0.1 mol/L hydrochloric acid TS (about 1 mg/mL). Reaction: Add Dragendorff's TS.	Example of description for drug substance

[3] Degradation reaction:

Description in the JP	Example of rationalized description	Remarks
Flomoxef Sodium Decompose 0.01 g of Flomoxef Sodium as directed under Oxygen Flask Combustion Method <1.06>, using a mixture of 0.5 mL of 0.01 mol/L	**Test method:** Decomposition reaction, oxygen flask combustion method **Specification value/acceptance criterion:** A blue-purple liquid	Example of description for drug substance

sodium hydroxide TS and 20 mL of water as the absorbing liquid. To 2 mL of the test solution so obtained add 1.5 mL of a mixture of alizarin complexone TS, acetic acid-potassium acetate buffer solution (pH 4.3) and cerium (III) nitrate TS (1:1:1): blue-purple color develops.	**Analytical procedure** Test solution: A solution of Flomoxef Sodium decomposed with the absorbing liquid (5 mL of 0.01 mol/L sodium hydroxide TS and 200 mL of water per 0.1 g of Flomoxef Sodium). Reaction: To 4 volumes of the test solution add 3 volumes of a mixture of alizarin complexone TS, acetic acid-potassium acetate buffer solution, pH 4.3 and cerium (III) nitrate TS (1:1:1).	

[4] Nuclear magnetic resonance spectrum:

Description in the JP	Example of rationalized description	Remarks
Alprazolam Dissolve 0.05 g of Alprazolam in 0.7 mL of deuterochloroform for nuclear magnetic resonance spectroscopy, and determine the spectrum of this solution using tetramethylsilane for nuclear magnetic resonance spectroscopy as an internal reference compound, as directed under Nuclear Magnetic Resonance Spectroscopy <2.21> (^{1}H): it exhibits a single signal A at around δ2.6 ppm, doublet signals B and C at around δ 4.0 ppm and δ5.4 ppm, and a broad signal D between δ7.1 ppm and 7.9 ppm. The ratio of integrated intensity of each signal, A:B:C:D, is about 3:1:1:8.	**Test method:** Nuclear magnetic resonance spectroscopy, ^{1}H **Specification value/acceptance criterion:** δ2.6 ppm: A single signal A δ4.0 ppm and δ5.4 ppm: Doublet signals B and C Between δ7.1 and 7.9 ppm: A broad signal D Ratio of integrated intensity of each signal, A:B:C:D = 3:1:1:8 **Analytical procedure** Sample solution: Dissolve Alprazolam in the diluent (about 0.07 g/mL). Diluent: Deuterochloroform for nuclear magnetic resonance spectroscopy. Internal reference compound: Tetramethylsilane for nuclear magnetic resonance spectroscopy Frequency: Not less than 400 MHz.	Example of description for drug substance

[5] Chromatography

- Liquid chromatography

Description in the JP	Example of rationalized description	Remarks
Tacalcitol Lotion Perform the test with 30 μL each of the sample solution and standard solution, both are obtained in the Assay, as directed under Liquid Chromatography <2.01> according to the following conditions: the retention time of the principal peaks in the chromatograms obtained from the sample solution and standard solution is the same, and both adsorption spectra of these peaks exhibit similar intensities of absorption at the same wavelengths.	**Test method:** Liquid chromatography, photodiode array detector, absorption spectrum, retention time **Specification value/acceptance criterion:** The retention times of the principal peaks from the sample solution and standard solution are the same, and the absorption spectrum of the sample solution agrees with that of the standard solution. **Analytical procedure** Sample solution: Proceed as directed in the Assay.	Example of description for drug product

Operating conditions Column, column temperature, mobile phase, and flow rate: Proceed as directed in the operating conditions in the Assay. Detector: A photodiode array detector (wavelength: 265 nm; spectrum range of measurement: 210 – 400 nm). System suitability System performance: Proceed as directed in the system suitability in the Assay.	Standard solution: Proceed as directed in the Assay. Injection volume: 30 μL. Operating conditions Column, column temperature, mobile phase, and flow rate: Proceed as directed in the operating conditions in the Assay. Detector: A photodiode array detector (wavelength: 265 nm; spectrum range of measurement: 210 – 400 nm). System suitability System performance: Proceed as directed in the system suitability in the Assay.	

- Thin-layer chromatography

Description in the JP	Example of rationalized description	Remarks
Acrinol Hydrate Shake 0.5 g of Acrinol Hydrate with 5 mL of diethyl ether, 1 mL of acetic acid (100) and 5 mL of water, separate the water layer, and use the water layer as the sample solution. Dissolve 5 mg of acrinol in 1 mL of acetic acid (100) and 5 mL of water, and use this solution as the standard solution. Perform the test with these solutions as directed under Thin-layer Chromatography <2.03>. Spot 5 μL each of the sample solution and standard solution on a plate of silica gel for thin-layer chromatography. Develop the plate with a mixture of diethyl ether, ethanol (95) and acetic acid (100) (40:10:1) to a distance of about 10 cm, and air-dry the plate. Examine under ultraviolet light (main wavelength: 365 nm): the spots from the sample solution and the standard solution exhibit a blue fluorescence and show the same Rf value.	**Test method:** Thin-layer chromatography **Specification value/acceptance criterion:** The spots from the sample solution and the standard solution exhibit a blue fluorescence and show the same Rf value. **Analytical procedure** Sample solution: A water layer after adding diethyl ether (10 mL per g of Acrinol Hydrate), acetic acid (100) (2 mL per g of Acrinol Hydrate) and water (10 mL per g of Acrinol Hydrate) to Acrinol Hydrate. Standard solution: Dissolve acrinol in acetic acid (100) (1 mL per 5 mg of Acrinol Hydrate) and water (1 mL per mg of Acrinol Hydrate). Spot volume: 5 μL Thin-layer plate: Silica gel Developing solvent: A mixture of diethyl ether, ethanol (95) and acetic acid (100) (40:10:1) Developing distance: About 10 cm Main wavelength: 365 nm	Example of description for drug substance Example of description for liquid/liquid extraction
Ascorbic Acid and Calcium Pantothenate Tablets To a quantity of powdered Ascorbic Acid and Calcium Pantothenate Tablets, equivalent to 3 mg of Calcium Pantothenate, add 20 mL of ethanol (95), shake vigorously for 10 minutes, centrifuge, and use the supernatant liquid as the sample solution. Separately, dissolve 3 mg of calcium pantothenate in 20 mL of ethanol (95), and use this solution as the standard solution. Perform the test with these solutions as directed under Thin-layer Chromatography <2.03>. Spot 10 μL each of the sample solution and standard solution on a plate of silica gel for thin-layer	**Test method:** Thin-layer chromatography **Specification value/acceptance criterion:** One of the spots obtained from the sample solution and the spot from the standard solution are purple in color, and their Rf values are the same. **Analytical procedure** Sample solution: To Ascorbic Acid and Calcium Pantothenate Tablets add the diluent (about 0.15 mg/mL of calcium pantothenate), the supernatant liquid.	Example of description for drug product Example of description for pretreatment of drug product

Description in the JP	Example of rationalized description	Remarks
chromatography. Develop the plate with a mixture of ethyl acetate, methanol and dilute acetic acid (5:3:2) to a distance of about 10 cm, and air-dry the plate. Spray evenly a solution of ninhydrin in ethanol (95) (1 in 200) on the plate, and heat the plate at 120°C for 20 minutes: one of the spots obtained from the sample solution and the spot from the standard solution are purple in color, and their Rf values are the same.	Standard solution: Dissolve calcium pantothenate in the diluent (about 0.15 mg/mL). Diluent: Ethanol (95). Spot volume: 10 μL. Thin-layer plate: Silica gel Developing solvent: A mixture of ethyl acetate, methanol and dilute acetic acid (5:3:2). Developing distance: About 10 cm Chromogenic reagent: A solution of ninhydrin in ethanol (95) (1 in 200). Heating temperature and time: 20 minutes at 120°C after spraying chromogenic reagent.	Description of chromogenic reagent, heating temperature and time of thin-layer plate
Iohexol Dissolve 0.1 g of Iohexol in 10 mL of methanol, and use this solution as the sample solution. Perform the test with the sample solution as directed under Thin-layer Chromatography <2.03>. Spot 10 μL of the sample solution on a plate of silica gel with fluorescent indicator for thin-layer chromatography. Develop the plate with a mixture of 1-butanol, water and acetic acid (100) (50:25:11) to a distance of about 12 cm, and air-dry the plate. Examine under ultraviolet light (main wavelength: 254 nm): the number of principal spots obtained from the sample solutions is two, and their Rf values are about 0.2 and about 0.3, respectively.	**Test method:** Thin-layer chromatography, Rf value **Specification value/acceptance criterion:** The number of principal spots is two, and their Rf values are about 0.2 and about 0.3. **Analytical procedure** Sample solution: Dissolve Iohexol in methanol (about 10 mg/mL). Spot volume: 10 μL Thin-layer plate: Silica gel with fluorescent indicator Developing solvent: A mixture of 1-butanol, water and acetic acid (100) (50:25:11) Developing distance: About 12 cm Main wavelength: 254 nm	Example of description for drug substance When the Rf value of the sample solution is specified

[6] Cations and anions:

Description in the JP	Example of rationalized description	Remarks
Chlorpromazine Hydrochloride Dissolve 0.5 g of Chlorpromazine Hydrochloride in 5 mL of water, add 2 mL of ammonia TS, and heat on a water bath for 5 minutes. Cool, filter, and render the filtrate acidic with dilute nitric acid: the solution responds to Qualitative Tests <1.09> (2) for chloride.	**Test method:** Qualitative test **Specification value/acceptance criterion:** Qualitative Tests (2) for chloride. **Analytical procedure** Sample solution: Dissolve Chlorpromazine Hydrochloride in water (10 mL per g of Chlorpromazine Hydrochloride), add ammonia TS (4 mL per g of Chlorpromazine Hydrochloride), heat on a water bath for 5 minutes, cool, and filter. Reaction: Acidify the sample solution with dilute nitric acid.	Example of description for drug substance