der ultraviolet light (broad spectrum wavelength): four spots from the sample solution show the same color tone and the same *Rf* value as the corresponding spots from standard solutions (1), (2), (3) and (4).

Containers and storage Containers—Well-closed containers.

Storage—Light-resistant.

Water

常水

H_2O: 18.02

Water usually means tap water and well water.

Description Water occurs as a clear, colorless liquid.

pH 5.8 - 8.6

Purity **(1)** Color and turbidity—View downward 50 mL of Water placed in a Nessler tube against white and black backgrounds: it is clear and colorless.

(2) Odor and taste—Place 100 mL of Water in a 300-mL glass-stoppered Erlenmeyer flask, shake vigorously at ordinary temperature, and check the odor and taste. Then stopper the flask loosely, warm between 40°C and 50°C, and check the odor and taste again as soon as the flask is opened: it has no foreign odor (except a slight chlorine odor) and no foreign taste (except a slight chlorine taste).

(3) Chlorine ion—Pipet 50 mL of Water, and titrate with 0.01 mol/L silver nitrate VS against a white background until a pale red-brown color no longer disappears in the aqueous layer (indicator: 0.5 mL of silver chromate-saturated potassium chromate TS). The concentration of chlorine ion in Water, when calculated from the amount *a* (mL) of 0.01 mol/L silver nitrate VS consumed by using the following equation, is not more than 200 mg/L.

$$\text{The concentration (mg/L) of chlorine ion} = 0.35453 \times a \times \frac{1000}{50}$$

(4) Nitrogen from nitrates—Place 2.0 mL of Water in a 50-mL beaker, add 1 mL of sodium salicylate-sodium hydroxide TS, 1 mL of a solution of sodium chloride (1 in 500) and 1 mL of a solution of ammonium amidosulfate (1 in 1000), and evaporate to dryness on a water bath. After cooling, add 2 mL of sulfuric acid, allow to stand for 10 minutes with occasional shaking, add 10 mL of water, and transfer to a Nessler tube. After cooling, add slowly 10 mL of a solution of sodium hydroxide (2 in 5) and water to make 25 mL. Then view the Nessler tube downward or transversely: the solution has no more color than the following control solution.

Control solution: Pipet 2.0 mL of Standard Nitric Acid Solution, and proceed in the same manner as for the test solution (not more than 10 mg/L).

(5) Nitrogen from nitrites—Place 50 mL of Water in a Nessler tube, add 0.3 g of Griess-Romijin's nitrous acid reagent, dissolve with shaking, and allow to stand for 10 minutes: no light red color develops.

(6) Ammonium—Perform the test using 30 mL of Water as directed under the Ammonium Limit Test. Prepare the control solution with 0.15 mL of Standard Ammonium Solution, dilute with purified water for ammonium limit test to make 30 mL, and proceed in the same manner as for the test solution (not more than 0.05 mg/L).

(7) Cyanide—Place 20 mL of Water in a Nessler tube, add 5 mL of phosphate buffer solution, pH 6.8, and 1.0 mL of diluted sodium toluensulfonchloramide TS (1 in 5), stopper immediately, mix gently, allow to stand for 2 to 3 minutes, add 5 mL of pyridine-pyrazolone TS, mix well, and allow to stand between 20°C and 30°C for 50 minutes: the solution has no more color than the control solution.

Control solution: Pipet 1.0 mL of Standard Cyanide Solution, and dilute with water to make exactly 1000 mL. Place 20 mL of this solution in a Nessler tube, and proceed in the same manner as for the test solution (not more than 0.01 mg/L).

(8) Heavy metals—Proceed with 30 mL of Water, and perform the test according to Method 1. Prepare the control solution with 3.0 mL of Standard Lead Solution (not more than 1 mg/L).

(9) Iron—Prepare the test solution with 50.0 mL of Water according to Method 1, and perform the test according to Method B. Prepare the control solution with 1.5 mL of Standard Iron Solution (not more than 0.3 ppm).

(10) Zinc—Shake 50 mL of Water with 0.5 mL of nitric acid, allow to stand for 1 hour, and use this solution as the sample solution. Separately, dilute 2.0 mL of Standard Zinc Solution with water to make exactly 50 mL, add 0.5 mL of nitric acid, and use this solution as the standard solution. Perform the tests with these solutions as directed under the Atomic Absorption Spectrophotometry according to the following conditions: the absorbance of the sample solution is not more than that of the standard solution (not more than 1 mg/L).

Gas: Combustible gas—Acetylene or hydrogen
Supporting gas—Air
Lamp: Zinc hollow-cathode lamp
Wavelength: 213.9 nm

(11) Cadmium—Shake 50 mL of Water with 0.5 mL of nitric acid, and allow to stand for 1 hour. To this solution add 10 mL of a solution of diammonium hydrogen citrate (1 in 4) and 2 drops of bromothymol blue TS, and add ammonia TS until the color of the solution changes from yellow to green. Then add 10 mL of a solution of ammonium sulfate (2 in 5) and 5 mL of a solution of sodium *N,N*-diethyldithiocarbamate trihydrate (1 in 20), mix, allow to stand for several minutes, add 10.0 mL of 4-methyl-2-pentanone, and shake vigorously. Allow to stand, separate the 4-methyl-2-pentanone layer, and use this solution as the sample solution. Separately, take 0.50 mL of Standard Cadmium Solution, add water to make exactly 50 mL, add 0.5 mL of nitric acid, 10 mL of a solution of diammonium hydrogen citrate (1 in 4) and 2 drops of bromothymol blue TS, proceed in the same manner as for the sample solution, and use this solution as the standard solution. Perform the tests with these solutions as directed under the Atomic Absorption Spectrophotometry according to the following conditions: the absorbance of the sample solution is not more than that of the standard solution (not more than 0.01 mg/L).

Gas: Combustible gas—Acetylene or hydrogen
Supporting gas—Air
Lamp: Cadmium hollow-cathode lamp

Wavelength: 228.8 nm

(12) Copper—Shake 50 mL of Water with 0.5 mL of nitric acid, allow to stand for 1 hour, and use this solution as the sample solution. Separately, dilute 5.0 mL of Standard Copper Solution with water to make exactly 50 mL, add 0.5 mL of nitric acid, and use this solution as the standard solution. Perform the tests with these solutions as directed under the Atomic Absorption Spectrophotometry according to the following conditions: the absorbance of the sample solution is not more than that of the standard solution (not more than 1 mg/L).

Gas: Combustible gas—Acetylene or hydrogen
Supporting gas—Air
Lamp: Copper hollow-cathode lamp
Wavelength: 324.7 nm

(13) Lead—Shake 50 mL of Water with 0.5 mL of nitric acid, and allow to stand for 1 hour. To this solution add 10 mL of a solution of diammonium hydrogen citrate (1 in 4) and 2 drops of bromothymol blue TS, proceed in the same manner as for (11) Cadmium, and use this solution as the sample solution. Separately, dilute 0.50 mL of Standard Lead Solution with water to make 50 mL, add 0.5 mL of nitric acid, 10 mL of a solution of diammonium hydrogen citrate (1 in 4) and 2 drops of bromothymol blue TS, proceed in the same manner as for the sample solution, and use this solution as the standard solution. Perform the tests with these solutions as directed under the Atomic Absorption Spectrophotometry according to the following conditions: the absorbance of the sample solution is not more than that of the standard solution (not more than 0.1 mg/L).

Gas: Combustible gas—Acetylene or hydrogen
Supporting gas—Air
Lamp: Lead hollow-cathode lamp
Wavelength: 283.33 nm

(14) Total hardness—Measure exactly 100 mL of Water, add exactly 1 mL of 0.01 mol/L magnesium chloride VS and 2 mL of ammonia-ammonium chloride buffer solution, pH 10.7, and titrate with 0.01 mol/L disodium dihydrogen ethylenediamine tetraacetate VS (indicator: 0.04 g of eriochrome black T-sodium chloride indicator). Total hardness of Water, when calculated from the amount, a (mL), of 0.01 mol/L disodium dihydrogen ethylenediamine tetraacetate VS by using the following equation, is not more than 300 mg/L.

$$\text{Total hardness (as } CaCO_3\text{) (mg/L)} = (a - 1) \times \frac{1000}{100}$$

(15) Residue on evaporation—Evaporate 100 mL of Water on a water bath to dryness, dry the residue at 105°C for 2 hours, and cool in a desiccator (silica gel): the mass of the residue is not more than 0.050 g (500 mg/L).

(16) Amount of potassium permanganate consumed—Measure exactly 100 mL of Water, add 5 mL of sulfuric acid TS and 10.0 mL of 0.002 mol/L potassium permanganate VS, and boil for 5 minutes. Add 10.0 mL of 0.005 mol/L sodium oxalate VS to decolorize the solution, and titrate immediately with 0.002 mol/L potassium permanganate VS until a light red color persists for 30 seconds. The amount of potassium permanganate consumed, when calculated from the total amount, a (mL), of 0.002 mol/L potassium permanganate VS consumed before and after the addition of 0.005 mol/L sodium oxalate VS by using the following equation, is not more than 10 mg/L.

$$\text{The amount (mg/L) of potassium permanganate consumed} = (a - 10) \times \frac{1000}{100} \times 0.31607$$

(17) Anionic surfactant—Measure exactly 200 mL of Water, add a few drops of phenolphthalein TS and 1 mol/L sodium hydroxide VS until the color of the solution changes to red. Then add 0.5 mol/L sulfuric acid VS to make the red color of the solution disappear, add 25 mL of methylene blue-sulfuric acid-sodium dihydrogenphosphate TS and 10 mL of chloroform, shake for 30 seconds, and allow to stand to separate the chloroform layer from the aqueous layer. Transfer the chloroform layer into another separator. Repeat the same operation with two 10-mL portions of chloroform for the remaining aqueous layer, and add the chloroform extract to the separator into which the first chloroform extract was transferred. Add 50 mL of sulfuric acid-sodium dihydrogenphosphate TS to the combined chloroform extract in the separator, shake vigorously for 30 seconds, allow to stand to separate the chloroform layer from the aqueous layer, and filter the chloroform layer through absorbent cotton. Repeat the same operation twice or more with 5-mL portions of chloroform for the remaining aqueous layer, filter the chloroform extract through the same absorbent cotton, combine each filtrate with the previously filtered chloroform extract, and add chloroform to make exactly 50 mL. View the solution downward or transversely: the solution has no more color than the following control solution.

Control solution: Pipet 10.0 mL of Standard Sodium Dodecylbenzene Sulfonate Solution, add water to make exactly 200 mL, and proceed in the same manner as for the test solution (not more than 0.5 mg/L).

(18) General bacteria and coliform bacilli—Water, when examined by the following procedures, contains not more than 100 general bacteria per mL, i.e., viable bacteria capable of producing colonies on a nutrient agar medium, and none, per 50 mL, of coliform bacilli, i.e., Gram-negative, asporogenic, aerobic or anaerobic bacilli capable of decomposing lactose and producing acids and gases.

Procedures: (i) General bacteria—Introduce 80 mL of Water into a sample bottle which has been autoclaved with 0.02 to 0.05 g of powdered sodium thiosulfate pentahydrate in it, and transfer 1 mL of it to a Petri dish. Add about 15 mL of liquefied nutrient agar kept at 45°C, and mix well while the culture medium is fluid. After cooling, place the dish upside down in an incubator between 35°C and 37°C for 22 to 26 hours, and count the colonies.

(ii) Coliform bacilli—Preliminary test: Transplant 5 tubes containing 10 mL each of Water or 50 mL of Water into a fermention tube, containing twice or three-times concentrated lactose broth, and incubate between 35°C and 37°C for 45 to 51 hours. No gas production indicates the absence of coliform bacilli.

Confirmation test: If a gas is produced in the preliminary test, inoculate immediately the culture medium in a BGLB fermentation tube with 1 loopful of the material, and incubate between 35°C and 37°C for 45 to 51 hours. No gas production indicates the absence of coliform bacilli.

Identification test: If a gas is evolved in the confirmation test, streak immediately EMB plate medium or Endo's plate medium with 1 loopful of the above cultured broth, and incubate between 35°C and 37°C for 24 hours so as to isolate individual colonies. Inoculate lactose broth in a fermentation

tube and a nutrient agar slant with the microorganisms from a typical colony or from not less than 2 subtypical colonies formed, and incubate between 35°C and 37°C. If gas is evolved in the lactose broth fermentation tube within 48 hours, apply Gram-staining to the colonies grown on the nutrient agar slant. Any Gram-negative, asporogenic bacillus indicates the presence of coliform bacilli.

Water for Injection

注射用水

Water for Injection is water prepared by distillation of Water or Purified Water, or by the Reverse Osmosis-Ultrafiltration of Purified Water, to be used for the preparation of injections, or preserved in containers and sterilized.

When Water for Injection is prepared by the Reverse Osmosis-Ultrafiltration, take precaution against microbial permeation through membrane.

Water for Injection for the preparation of injections must be used immediately after preparation. It may be stored overnight avoiding microbial contamination and growth.

Water for Injection preserved in containers and sterilized is used mainly as solvent for injections to be dissolved or suspended before use.

Water for Injection prepared by distillation may be labeled Distilled Water for Injection as commonly used Japanese name.

Purity **(1)** Acid or alkali—To 20 mL of Water for Injection add 0.1 mL of methyl red TS for acid or alkali test: a yellow to orange color develops. To 20 mL of Water for Injection add 0.05 mL of bromothymol blue TS: no blue color develops.

(2) Chloride—To 50 mL of Water for Injection add 3 drops of nitric acid and 0.5 mL of silver nitrate TS: no change occurs.

(3) Sulfate—To 50 mL of Water for Injection add 0.5 mL of barium chloride TS: no change occurs.

(4) Nitrogen from nitrate—Transfer 2.0 mL of Water for Injection to a 50-mL beaker, add 1 mL of sodium salicylate-sodium hydroxide TS, 1 mL of a solution of sodium chloride (1 in 500) and 1 mL of a solution of ammonium amidosulfate (1 in 1000), and evaporate on a water bath to dryness. Cool, dissolve in 2 mL of sulfuric acid, allow to stand for 10 minutes with occasional shaking, add 10 mL of water, and transfer to a Nessler tube. Cool, add 10 mL of a solution of sodium hydroxide (2 in 5) slowly, and add water to make 25 mL: no yellow color develops.

(5) Nitrogen from nitrite—Transfer 10 mL of Water for Injection to a Nessler tube, and add 1 mL of a solution of sulfanilamide in dilute hydrochloric acid (1 in 100) and 1 mL of *N*-(1-naphthyl)-*N'*-diethylethylenediamine oxalate TS: no pale red color develops.

(6) Ammonium—Perform the test as directed under the Ammonium Limit Test, using 30 mL of Water for Injection as the test solution. Prepare the control solution as follows: to 0.15 mL of Standard Ammonium Solution add purified water for ammonium limit test to make 30 mL, and proceed in the same manner as the test solution (not more than 0.05 mg/L).

(7) Heavy metals—To 40 mL of Water for Injection add 2 mL of dilute acetic acid and 1 drop of sodium sulfide TS: no change occurs.

(8) Potassium permanganate-reducing substances—To 100 mL of Water for Injection add 10 mL of dilute sulfuric acid, boil, add 0.10 mL of 0.02 mol/L potassium permanganate VS, and boil again for 10 minutes: the red color does not disappear.

(9) Residue on evaporation—Evaporate 100 mL of Water for Injection on a water bath to dryness, and dry the residue at 105°C for 1 hour: the mass of the residue is not more than 1.0 mg.

For Water for Injection prepared by the Reverse Osmosis-Ultrafiltration for the preparation of injections, perform the test for (8) Total organic carbon described below, instead of (8) Potassium permanganate-reducing substances. For Water for Injection preserved in containers and sterilized, perform the test for (1) Acid or alkali, (2) Chloride, (6) Ammonium and (9) Residue on evaporation according to the following methods:

(1) Acid or alkali—Shake gently 20 mL of Distilled Water for Injection with 0.05 mL of phenol red TS and 0.13 mL of 0.01 mol/L sodium hydroxide VS, and allow to stand for 30 seconds: a red color develops. Shake gently 20 mL of Water for Injection with 0.05 mL of bromothymol blue TS and 0.13 mL of 0.01 mol/L hydrochloric acid VS, and allow to stand for 30 seconds: a yellow color develops.

(2) Chloride—For Water for Injection in containers holding a volume not more than 10 mL, add 2.0 mL of dilute nitric acid to 15 mL of Distilled Water for Injection, and use this solution as the test solution. Separately, to 0.20 mL of 0.001 mol/L hydrochloric acid VS add water to make 15 mL, then add 2.0 mL of dilute nitric acid, and use this solution as the control solution. Mix the test solution and the control solution separately with 0.30 mL each of silver nitrate TS, allow to stand for 5 minutes under the protection from sunlight, and compare the turbidity of the solutions on a black background: the turbidity of the test solution is not thicker than that of the control solution (not more than 0.00005%). For Water for Injection in containers holding a volume exceeding 10 mL, add 3 drops of nitric acid and 0.5 mL of silver nitrate TS to 50 mL of Water for Injection: the solution remains unchanged.

(6) Ammonium—Perform the test as directed under the Ammonium Limit Test, using 30 mL of Water for Injection as the test solution. Prepare the control solution as follows: To 0.6 mL of Standard Ammonium Solution for Water for Injection in containers holding a volume not more than 10 mL, and 0.3 mL of Standard Ammonium Solution for Water for Injection in a volume exceeding 10 mL, add purified water for ammonium limit test to make 30 mL, and proceed in the same manner as the test solution (not more than 0.2 mg/L for Water for Injection in a volume not more than 10 mL, and not more than 0.1 mg/L for that exceeding 10 mL).

(8) Total organic carbon—Perform the test with Water for Injection prepared by the Reverse Osmosis-Ultrafiltration for the preparation of injections, using an apparatus for detection of total organic carbon: it contains not more than 0.50 mg/L of total organic carbon. Use an apparatus which is efficient enough to detect not more than 0.050 mg/L of