each sample. The mean of these values is then calculated. The exact requirements will depend on the equipment capability and degree of accuracy needed.

Isoperibol Solution Calorimetry

In the isoperibol solution calorimeter, the heat change during the solution process causes a corresponding change in temperature of the solvent–solute system (i.e., solution). This temperature change is measured by a temperature sensor, which is wired to an electrical circuit that records an electrical signal corresponding to the temperature change. Typically, this temperature change in an electronic form is measured at precisely defined time intervals to produce temperature–time data that are collected, analyzed by a computer, and then plotted. A blank run without addition of the solid solute to the solvent normally shows no discernible change in the slope of the temperature–time plot.

For isoperibol solution calorimeters, response is fairly rapid, but corrections must be made for any heat losses to or heat gains from the bath. Therefore, isoperibol solution calorimeters are more advantageous than isothermal solution calorimeters when the solution process is relatively fast. For all measurements of enthalpy of solution using isoperibol solution calorimeters, the choice of solvent is critical. The nature and mass of the solvent and the mass of sample allow the total heat change, corresponding to total dissolution of the solid, to proceed to completion within five min under vigorous stirring at a constant rotational speed within the range of 400–600 revolutions/min.

The effective heat capacity of the calorimeter cell and its contents is determined for every calorimeter run. This determination is accomplished by electrical heating of the contents of the calorimeter cell. The effective heat capacity is determined according to one of two protocols—either by making one determination after ampul breakage or by making one determination before and a second determination after ampul breakage, and then averaging the two results. The accuracy and reliability of the electrical heating are established by the accuracy and reliability of the aforementioned chemical calibrations.

Isothermal Solution Calorimetry

In the isothermal (constant temperature) solution calorimeter, the heat change during the solution process is compensated for by an equal but opposite energy change, such that the temperature of the solvent–solute system (i.e., solution) remains essentially constant. This equal but opposite energy change is measured and, when its sign is reversed, provides the enthalpy of solution. For isothermal calorimeters, response is relatively slow, but the compensation process eliminates the effects of heat losses to or heat gains from the bath. Therefore, isothermal calorimeters are more advantageous than isoperibol calorimetry when the solution process is relatively slow.

Solution Calorimeter Calibration

To ensure the accuracy of the calorimeter, chemical calibrations must be performed on a regular basis. For an endothermic solution process, the calibration of the calorimeter is checked by measuring the heat absorbed during the dissolution of potassium chloride in distilled water at 298.15 K (25.0°). The established enthalpy change in this endothermic process is 235.5 J/g (17.56 kJ/mol). For an exothermic solution process, the calorimeter is checked by measuring the heat evolved during the dissolution of 5 g/L of tromethamine [tris(hydroxymethyl)aminomethane, THAM] in a 0.1 mol/L aqueous hydrochloric acid solution at 298.15 K (25.0°). The established heat for the aforementioned process is –246.0 J/g (–29.80 kJ/mol).

Sample Handling

The chemical and physical stability of solids may decrease with decreasing crystallinity. In particular, solids of low crystallinity, especially amorphous solids, tend to sorb water vapor from the atmosphere, leading to crystallization and a corresponding gain in crystallinity. For these reasons, anhydrous samples whose crystallinity is to be determined must be stored at zero humidity or below critical humidity levels in sealed chambers containing a desiccant, preferably containing an indicator of effectiveness. If crystallinity–humidity studies are to be carried out, the sample is stored in a sealed chamber containing a saturated salt solution to provide a defined relative humidity.■2S (*USP35*)

⟨711⟩ DISSOLUTION

This general chapter is harmonized with the corresponding texts of the *European Pharmacopoeia* and/or the *Japanese Pharmacopoeia*. These pharmacopeias have undertaken not to make any unilateral change to this harmonized chapter.

Portions of the present general chapter text that are national USP text, and therefore not part of the harmonized text, are marked with symbols (✦✦) to specify this fact.

This test is provided to determine compliance with the dissolution requirements ✦where stated in the individual monograph✦ for dosage forms administered orally. In this general chapter, a dosage unit is defined as 1 tablet or 1 capsule or the amount specified. ✦Of the types of apparatus described herein, use the one specified in the individual monograph. Where the label states that an article is enteric-coated, and where a dissolution or disintegration test that does not specifically state that it is to be applied to delayed-release articles is included in the individual monograph, the procedure and interpretation given for *Delayed-Release Dosage Forms* is applied unless otherwise specified in the individual monograph. For hard or soft gelatin capsules and gelatin-coated tablets that do not conform to the *Dissolution* specification, repeat the test as follows. Where water or a medium with a pH of less than 6.8 is specified as the *Medium* in the individual monograph, the same *Medium* specified may be used with the addition of purified pepsin that results in an activity of 750,000 Units or less per 1000 mL. For media with a pH of 6.8 or greater, pancreatin can be added to produce not more than 1750 USP Units of protease activity per 1000 mL.

Change to read:

USP Reference Standards ⟨11⟩—●● (RB 1-Feb-2012) *USP Prednisone Tablets RS.*✦

Change to read:

APPARATUS

Apparatus 1 (Basket Apparatus)

The assembly consists of the following: a vessel, which may be covered, made of glass or other inert, transparent

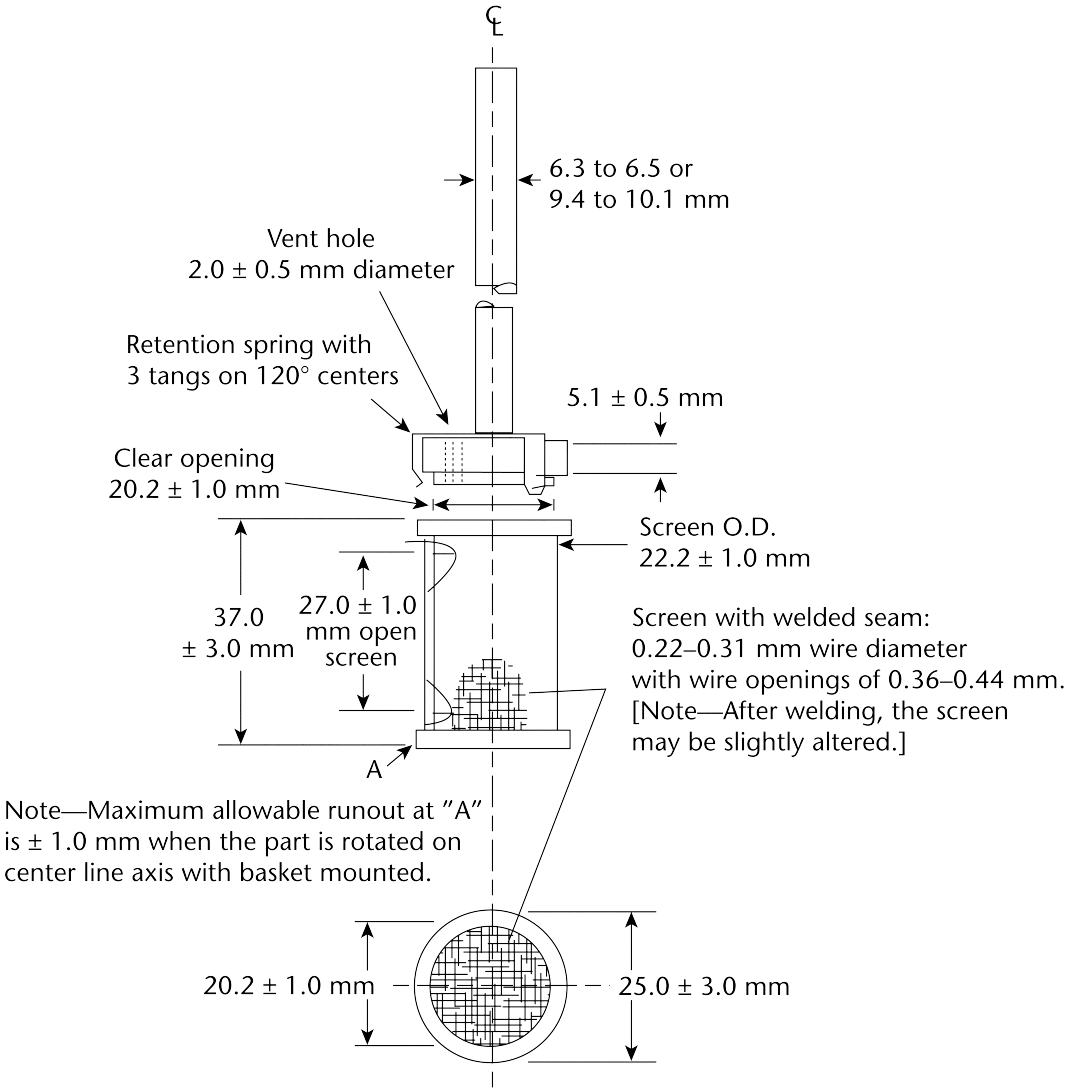

Figure 1. Basket stirring element.

material[1]; a motor; a metallic drive shaft; and a cylindrical basket. The vessel is partially immersed in a suitable water bath of any convenient size or heated by a suitable device such as a heating jacket. The water bath or heating device permits holding the temperature inside the vessel at 37 ± 0.5° during the test and keeping the bath fluid in constant, smooth motion. No part of the assembly, including the environment in which the assembly is placed, contributes significant motion, agitation, or vibration beyond that due to the smoothly rotating stirring element. An apparatus that permits observation of the specimen and stirring element during the test is preferable. The vessel is cylindrical, with a hemispherical bottom and ✦with one of the following dimensions and capacities: for a nominal✦ capacity of 1 L, the height is 160 to 210 mm and its inside diameter is 98 to 106 mm; ✦for a nominal capacity of 2 L, the height is 280 to 300 mm and its inside diameter is 98 to 106 mm; and for a nominal capacity of 4 L, the height is 280 to 300 mm and its inside diameter is 145 to 155 mm✦. Its sides are flanged at the top. A fitted cover may be used to retard evaporation.[2] The shaft is positioned so that its axis is not more than 2 mm at any point from the vertical axis of the vessel and rotates smoothly and without significant wobble that could affect the results. A speed-regulating device is used that allows the shaft rotation speed to be selected and maintained at the specified rate ✦given in the individual monograph✦ within ±4%.

Shaft and basket components of the stirring element are fabricated of stainless steel, type 316, or other inert material, to the specifications shown in *Figure 1*. A basket having a gold coating of about 0.0001 inch (2.5 µm) thick may be used. A dosage unit is placed in a dry basket at the beginning of each test. The distance between the inside bottom of the vessel and the bottom of the basket is maintained at 25 ± 2 mm during the test.

Apparatus 2 (Paddle Apparatus)

Use the assembly from *Apparatus 1*, except that a paddle formed from a blade and a shaft is used as the stirring element. The shaft is positioned so that its axis is not more than 2 mm from the vertical axis of the vessel at any point and rotates smoothly without significant wobble that could affect the results. The vertical center line of the blade passes through the axis of the shaft so that the bottom of the blade is flush with the bottom of the shaft. The paddle conforms to the specifications shown in *Figure 2*. The distance of 25 ± 2 mm between the bottom of the blade and the inside bottom of the vessel is maintained during the test.

[1] The materials should not sorb, react, or interfere with the specimen being tested.
[2] If a cover is used, it provides sufficient openings to allow ready insertion of the thermometer and withdrawal of specimens.

The metallic or suitably inert, rigid blade and shaft comprise a single entity. A suitable two-part detachable design may be used provided the assembly remains firmly engaged during the test. The paddle blade and shaft may be coated with a suitable coating so as to make them inert. The dosage unit is allowed to sink to the bottom of the vessel before rotation of the blade is started. A small, loose piece of nonreactive material, such as not more than a few turns of wire helix, may be attached to dosage units that would otherwise float. An alternative sinker device is shown in *Figure 2a*. Other validated sinker devices may be used.

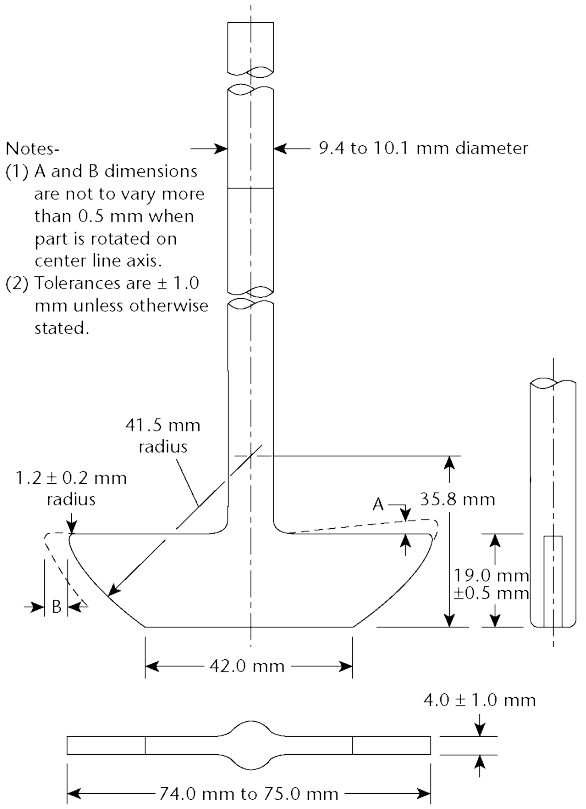

Figure 2. Paddle stirring element.

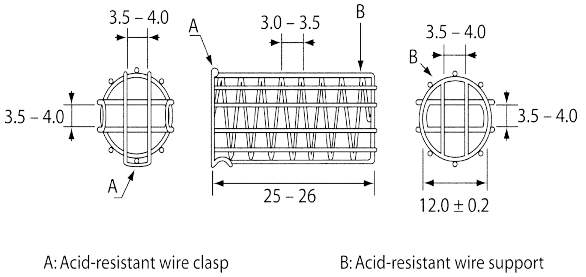

Figure 2a. Alternative sinker. All dimensions are expressed in mm.

Apparatus 3 (Reciprocating Cylinder)

NOT ACCEPTED BY THE JAPANESE PHARMACOPOEIA

The assembly consists of a set of cylindrical, flat-bottomed glass vessels; a set of glass reciprocating cylinders; inert fittings (stainless steel type 316 or other suitable material), and screens that are made of suitable nonsorbing and nonreactive material and that are designed to fit the tops and bottoms of the reciprocating cylinders; and a motor and drive assembly to reciprocate the cylinders vertically inside the vessels and, if desired, index the reciprocating cylinders horizontally to a different row of vessels. The vessels are partially immersed in a suitable water bath of any convenient size that permits holding the temperature at 37 ± 0.5° during the test. No part of the assembly, including the environment in which the assembly is placed, contributes significant motion, agitation, or vibration beyond that due to the smooth, vertically reciprocating cylinder. A device is used that allows the reciprocation rate to be selected and maintained at the specified dip rate ✦given in the individual monograph✦ within ±5%. An apparatus that permits observation of the specimens and reciprocating cylinders is preferable. The vessels are provided with an evaporation cap that remains in place for the duration of the test. The components conform to the dimensions shown in *Figure 3* unless otherwise specified ✦in the individual monograph✦.

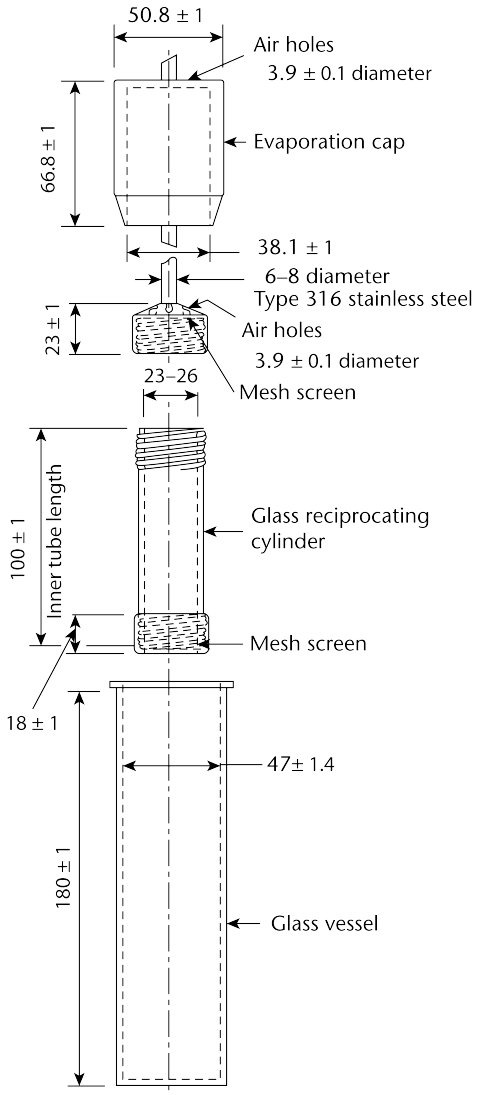

Figure 3. Apparatus 3 (reciprocating cylinder).

Apparatus 4 (Flow-Through Cell)

The assembly consists of a reservoir and a pump for the *Dissolution Medium*; a flow-through cell; and a water bath

that maintains the *Dissolution Medium* at 37 ± 0.5°. Use the specified cell size ✦as given in the individual monograph✦.

The pump forces the *Dissolution Medium* upwards through the flow-through cell. The pump has a delivery range between 240 and 960 mL per hour, with standard flow rates of 4, 8, and 16 mL per minute. It must deliver a constant flow (±5% of the nominal flow rate); the flow profile is sinusoidal with a pulsation of 120 ± 10 pulses per minute. A pump without pulsation may also be used. Dissolution test procedures using a flow-through cell must be characterized with respect to rate and any pulsation.

The flow-through cell (see *Figures 4* and *5*), of transparent and inert material, is mounted vertically with a filter system (specified in the individual monograph) that prevents escape of undissolved particles from the top of the cell; standard cell diameters are 12 and 22.6 mm; the bottom cone is usually filled with small glass beads of about 1-mm diameter with one bead of about 5 mm positioned at the apex to protect the fluid entry tube; and a tablet holder (see *Figures 4* and *5*) is available for positioning of special dosage forms, for example, inlay tablets. The cell is immersed in a water bath, and the temperature is maintained at 37 ± 0.5°.

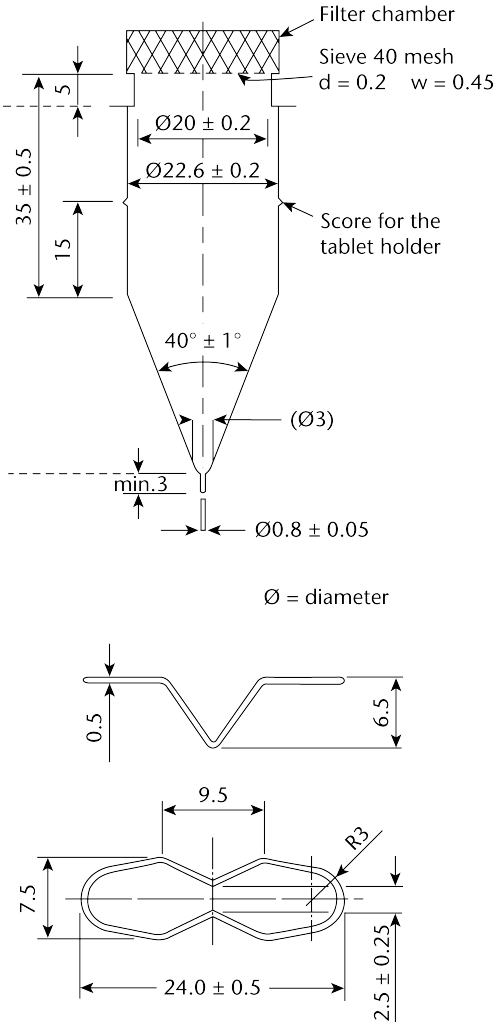

Figure 4. Apparatus 4, large cell for tablets and capsules (top), tablet holder for the large cell (bottom). (All measurements are expressed in mm unless noted otherwise.)

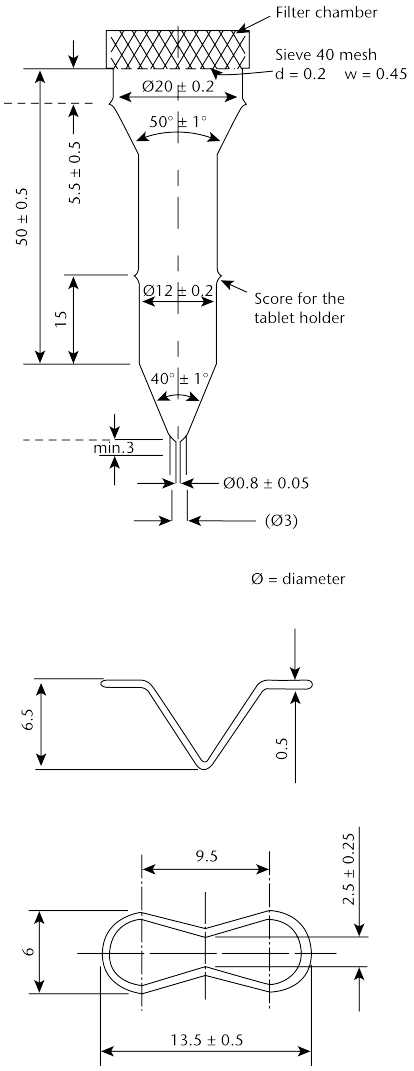

Figure 5. Apparatus 4, small cell for tablets and capsules (top), tablet holder for the small cell (bottom). (All measurements are expressed in mm unless noted otherwise.)

The apparatus uses a clamp mechanism and two O-rings to assemble the cell. The pump is separated from the dissolution unit in order to shield the latter against any vibrations originating from the pump. The position of the pump should not be on a level higher than the reservoir flasks. Tube connections are as short as possible. Use suitably inert tubing, such as polytef, with about 1.6-mm inner diameter and chemically inert flanged-end connections.

APPARATUS SUITABILITY

The determination of suitability of a test assembly to perform dissolution testing must include conformance to the dimensions and tolerances of the apparatus as given above. In addition, critical test parameters that have to be monitored periodically during use include volume and temperature of the *Dissolution Medium,* rotation speed (*Apparatus 1* and *Apparatus 2*), dip rate (*Apparatus 3*), and flow rate of medium (*Apparatus 4*).

Determine the acceptable performance of the dissolution test assembly periodically. ✦The suitability for the individual apparatus is demonstrated by the *Performance Verification Test*.

Performance Verification Test, Apparatus 1 and 2— Test USP Prednisone Tablets RS according to the operating

conditions specified. The apparatus is suitable if the results obtained are within the acceptable range stated in the technical data sheet specific to the lot used and the apparatus tested.

Performance Verification Test, Apparatus 3—•[To come.]• (RB 1-Feb-2012)

Performance Verification Test, Apparatus 4—[To come.]✦

PROCEDURE

Apparatus 1 and Apparatus 2

IMMEDIATE-RELEASE DOSAGE FORMS

Place the stated volume of the *Dissolution Medium* (±1%) in the vessel of the specified apparatus ✦given in the individual monograph✦, assemble the apparatus, equilibrate the *Dissolution Medium* to 37 ± 0.5°, and remove the thermometer. Place 1 dosage unit in the apparatus, taking care to exclude air bubbles from the surface of the dosage unit, and immediately operate the apparatus at the specified rate ✦given in the individual monograph✦. Within the time interval specified, or at each of the times stated, withdraw a specimen from a zone midway between the surface of the *Dissolution Medium* and the top of the rotating basket or blade, not less than 1 cm from the vessel wall. [NOTE—Where multiple sampling times are specified, replace the aliquots withdrawn for analysis with equal volumes of fresh *Dissolution Medium* at 37° or, where it can be shown that replacement of the medium is not necessary, correct for the volume change in the calculation. Keep the vessel covered for the duration of the test, and verify the temperature of the mixture under test at suitable times.] Perform the analysis ✦as directed in the individual monograph✦ using a suitable assay method.[3] Repeat the test with additional dosage form units.

If automated equipment is used for sampling or the apparatus is otherwise modified, verification that the modified apparatus will produce results equivalent to those obtained with the standard apparatus described in this general chapter is necessary.

Dissolution Medium—A suitable dissolution medium is used. Use the solvent specified ✦in the individual monograph✦. The volume specified refers to measurements made between 20° and 25°. If the *Dissolution Medium* is a buffered solution, adjust the solution so that its pH is within 0.05 unit of the specified pH ✦given in the individual monograph✦. [NOTE—Dissolved gases can cause bubbles to form, which may change the results of the test. If dissolved gases influence the dissolution results, dissolved gases should be removed prior to testing.[4]]

Time—Where a single time specification is given, the test may be concluded in a shorter period if the requirement for minimum amount dissolved is met. Specimens are to be withdrawn only at the stated times within a tolerance of ±2%.

✦**Procedure for a Pooled Sample for Immediate-Release Dosage Forms**—Use this procedure where *Procedure for a Pooled Sample* is specified in the individual monograph. Proceed as directed for *Immediate-Release Dosage Forms* under *Apparatus 1 and Apparatus 2* in the *Procedure* section. Combine equal volumes of the filtered solutions of the six or twelve individual specimens withdrawn, and use the pooled sample as the test specimen. Determine the average amount of the active ingredient dissolved in the pooled sample.✦

EXTENDED-RELEASE DOSAGE FORMS

Proceed as directed for *Immediate-Release Dosage Forms*.

Dissolution Medium—Proceed as directed for *Immediate-Release Dosage Forms*.

Time—The test-time points, generally three, are expressed in hours.

DELAYED-RELEASE DOSAGE FORMS NOT ACCEPTED BY THE JAPANESE PHARMACOPOEIA

Use *Method A* or *Method B* and the apparatus specified ✦in the individual monograph✦. All test times stated are to be observed within a tolerance of ±2%, unless otherwise specified.

Method A—

Procedure ✦(unless otherwise directed in the individual monograph)✦—

ACID STAGE—Place 750 mL of 0.1 N hydrochloric acid in the vessel, and assemble the apparatus. Allow the medium to equilibrate to a temperature of 37 ± 0.5°. Place 1 dosage unit in the apparatus, cover the vessel, and operate the apparatus at the specified rate ✦given in the monograph✦.

After 2 hours of operation in 0.1 N hydrochloric acid, withdraw an aliquot of the fluid, and proceed immediately as directed under *Buffer Stage*.

Perform an analysis of the aliquot using a suitable assay method. ✦The procedure is specified in the individual monograph.✦

BUFFER STAGE—[NOTE—Complete the operations of adding the buffer and adjusting the pH within 5 minutes.]

With the apparatus operating at the rate specified ✦in the monograph✦, add to the fluid in the vessel 250 mL of 0.20 M tribasic sodium phosphate that has been equilibrated to 37 ± 0.5°. Adjust, if necessary, with 2 N hydrochloric acid or 2 N sodium hydroxide to a pH of 6.8 ± 0.05. Continue to operate the apparatus for 45 minutes, or for the specified time ✦given in the individual monograph✦. At the end of the time period, withdraw an aliquot of the fluid, and perform the analysis using a suitable assay method. ✦The procedure is specified in the individual monograph. The test may be concluded in a shorter time period than that specified for the *Buffer Stage* if the requirement for the minimum amount dissolved is met at an earlier time.✦

Method B—

Procedure ✦(unless otherwise directed in the individual monograph)✦—

ACID STAGE—Place 1000 mL of 0.1 N hydrochloric acid in the vessel, and assemble the apparatus. Allow the medium to equilibrate to a temperature of 37 ± 0.5°. Place 1 dosage unit in the apparatus, cover the vessel, and operate the apparatus at the rate specified ✦in the monograph✦. After 2 hours of operation in 0.1 N hydrochloric acid, withdraw an aliquot of the fluid, and proceed immediately as directed under *Buffer Stage*.

Perform an analysis of the aliquot using a suitable assay method. ✦The procedure is specified in the individual monograph.✦

BUFFER STAGE—[NOTE—For this stage of the procedure, use buffer that previously has been equilibrated to a temperature of 37 ± 0.5°.] Drain the acid from the vessel, and add to the vessel 1000 mL of pH 6.8 phosphate buffer, prepared by mixing 0.1 N hydrochloric acid with 0.20 M tribasic sodium phosphate (3:1) and adjusting, if necessary, with 2 N hydrochloric acid or 2 N sodium hydroxide to a pH of 6.8 ±

[3] Test specimens are filtered immediately upon sampling unless filtration is demonstrated to be unnecessary. Use an inert filter that does not cause adsorption of the active ingredient or contain extractable substances that would interfere with the analysis.

[4] One method of deaeration is as follows: Heat the medium, while stirring gently, to about 41°, immediately filter under vacuum using a filter having a porosity of 0.45 µm or less, with vigorous stirring, and continue stirring under vacuum for about 5 minutes. Other validated deaeration techniques for removal of dissolved gases may be used.

0.05. [NOTE—This may also be accomplished by removing from the apparatus the vessel containing the acid and replacing it with another vessel containing the buffer and transferring the dosage unit to the vessel containing the buffer.]

Continue to operate the apparatus for 45 minutes, or for the specified time ✦given in the individual monograph✦. At the end of the time period, withdraw an aliquot of the fluid, and perform the analysis using a suitable assay method. ✦The procedure is specified in the individual monograph. The test may be concluded in a shorter time period than that specified for the *Buffer Stage* if the requirement for minimum amount dissolved is met at an earlier time.✦

Apparatus 3 (Reciprocating Cylinder)

NOT ACCEPTED BY THE JAPANESE PHARMACOPOEIA

IMMEDIATE-RELEASE DOSAGE FORMS

Place the stated volume of the *Dissolution Medium* in each vessel of the apparatus, assemble the apparatus, equilibrate the *Dissolution Medium* to 37 ± 0.5°, and remove the thermometer. Place 1 dosage-form unit in each of the six reciprocating cylinders, taking care to exclude air bubbles from the surface of each dosage unit, and immediately operate the apparatus as specified ✦in the individual monograph✦. During the upward and downward stroke, the reciprocating cylinder moves through a total distance of 9.9 to 10.1 cm. Within the time interval specified, or at each of the times stated, raise the reciprocating cylinders and withdraw a portion of the solution under test from a zone midway between the surface of the *Dissolution Medium* and the bottom of each vessel. Perform the analysis as directed ✦in the individual monograph✦. If necessary, repeat the test with additional dosage-form units.

Dissolution Medium—Proceed as directed for *Immediate-Release Dosage Forms* under *Apparatus 1 and Apparatus 2*.

Time—Proceed as directed for *Immediate-Release Dosage Forms* under *Apparatus 1 and Apparatus 2*.

EXTENDED-RELEASE DOSAGE FORMS

Proceed as directed for *Immediate-Release Dosage Forms* under *Apparatus 3*.

Dissolution Medium—Proceed as directed for *Extended-Release Dosage Forms* under *Apparatus 1 and Apparatus 2*.

Time—Proceed as directed for *Extended-Release Dosage Forms* under *Apparatus 1 and Apparatus 2*.

DELAYED-RELEASE DOSAGE FORMS

Proceed as directed for *Delayed-Release Dosage Forms, Method B* under *Apparatus 1 and Apparatus 2* using one row of vessels for the acid stage media and the following row of vessels for the buffer stage media and using the volume of medium specified (usually 300 mL).

Time—Proceed as directed for *Immediate-Release Dosage Forms* under *Apparatus 1 and Apparatus 2*.

Apparatus 4 (Flow-Through Cell)

IMMEDIATE-RELEASE DOSAGE FORMS

Place the glass beads into the cell specified ✦in the monograph✦. Place 1 dosage unit on top of the beads or, if specified ✦in the monograph✦, on a wire carrier. Assemble the filter head, and fix the parts together by means of a suitable clamping device. Introduce by the pump the *Dissolution Medium* warmed to 37 ± 0.5° through the bottom of the cell to obtain the flow rate specified ✦in the individual monograph✦ and measured with an accuracy of 5%. Collect the eluate by fractions at each of the times stated. Perform the analysis as directed ✦in the individual monograph✦. Repeat the test with additional dosage-form units.

Dissolution Medium—Proceed as directed for *Immediate-Release Dosage Forms* under *Apparatus 1 and Apparatus 2*.

Time—Proceed as directed for *Immediate-Release Dosage Forms* under *Apparatus 1 and Apparatus 2*.

EXTENDED-RELEASE DOSAGE FORMS

Proceed as directed for *Immediate-Release Dosage Forms* under *Apparatus 4.*

Dissolution Medium—Proceed as directed for *Immediate-Release Dosage Forms* under *Apparatus 4*.

Time—Proceed as directed for *Immediate-Release Dosage Forms* under *Apparatus 4.*

DELAYED-RELEASE DOSAGE FORMS

Proceed as directed for *Delayed-Release Dosage Forms* under *Apparatus 1 and Apparatus 2,* using the specified media.

Time—Proceed as directed for *Delayed-Release Dosage Forms* under *Apparatus 1 and Apparatus 2*.

INTERPRETATION

Immediate-Release Dosage Forms

Unless otherwise specified ✦in the individual monograph✦, the requirements are met if the quantities of active ingredient dissolved from the dosage units tested conform to *Acceptance Table 1*. Continue testing through the three stages unless the results conform at either S_1 or S_2. The quantity, *Q*, is the amount of dissolved active ingredient ✦specified in the individual monograph✦, expressed as a percentage of the labeled content of the dosage unit; the 5%, 15%, and 25% values in *Acceptance Table 1* are percentages of the labeled content so that these values and *Q* are in the same terms.

Acceptance Table 1

Stage	Number Tested	Acceptance Criteria
S_1	6	Each unit is not less than *Q* + 5%.
S_2	6	Average of 12 units (S_1 + S_2) is equal to or greater than *Q*, and no unit is less than *Q* − 15%.
S_3	12	Average of 24 units (S_1 + S_2 +S_3) is equal to or greater than *Q*, not more than 2 units are less than *Q* − 15%, and no unit is less than *Q* − 25%.

✦Immediate-Release Dosage Forms Pooled Sample— Unless otherwise specified in the individual monograph, the requirements are met if the quantities of active ingredient dissolved from the pooled sample conform to the accompanying *Acceptance Table for a Pooled Sample.* Continue testing through the three stages unless the results conform at either S_1 or S_2. The quantity, *Q*, is the amount of dissolved active ingredient specified in the individual monograph, expressed as a percentage of the labeled content.

Acceptance Table for a Pooled Sample

Stage	Number Tested	Acceptance Criteria
S_1	6	Average amount dissolved is not less than $Q + 10\%$.
S_2	6	Average amount dissolved ($S_1 + S_2$) is equal to or greater than $Q + 5\%$.
S_3	12	Average amount dissolved ($S_1 + S_2 + S_3$) is equal to or greater than Q.

Extended-Release Dosage Forms

Unless otherwise specified ✦in the individual monograph✦, the requirements are met if the quantities of active ingredient dissolved from the dosage units tested conform to *Acceptance Table 2*. Continue testing through the three levels unless the results conform at either L_1 or L_2. Limits on the amounts of active ingredient dissolved are expressed in terms of the percentage of labeled content. The limits embrace each value of Q_i, the amount dissolved at each specified fractional dosing interval. Where more than one range is specified ✦in the individual monograph✦, the acceptance criteria apply individually to each range.

Acceptance Table 2

Level	Number Tested	Criteria
L_1	6	No individual value lies outside each of the stated ranges and no individual value is less than the stated amount at the final test time.
L_2	6	The average value of the 12 units ($L_1 + L_2$) lies within each of the stated ranges and is not less than the stated amount at the final test time; none is more than 10% of labeled content outside each of the stated ranges; and none is more than 10% of labeled content below the stated amount at the final test time.
L_3	12	The average value of the 24 units ($L_1 + L_2 + L_3$) lies within each of the stated ranges, and is not less than the stated amount at the final test time; not more than 2 of the 24 units are more than 10% of labeled content outside each of the stated ranges; not more than 2 of the 24 units are more than 10% of labeled content below the stated amount at the final test time; and none of the units is more than 20% of labeled content outside each of the stated ranges or more than 20% of labeled content below the stated amount at the final test time.

Delayed-Release Dosage Forms

NOT ACCEPTED BY THE JAPANESE PHARMACOPOEIA

Acid Stage—Unless otherwise specified ✦in the individual monograph✦, the requirements of this portion of the test are met if the quantities, based on the percentage of the labeled content, of active ingredient dissolved from the units tested conform to *Acceptance Table 3*. Continue testing through all levels unless the results of both acid and buffer stages conform at an earlier level.

Acceptance Table 3

Level	Number Tested	Criteria
A_1	6	No individual value exceeds 10% dissolved.
A_2	6	Average of the 12 units ($A_1 + A_2$) is not more than 10% dissolved, and no individual unit is greater than 25% dissolved.
A_3	12	Average of the 24 units ($A_1 + A_2 + A_3$) is not more than 10% dissolved, and no individual unit is greater than 25% dissolved.

Buffer Stage—Unless otherwise specified ✦in the individual monograph✦, the requirements are met if the quantities of active ingredient dissolved from the units tested conform to *Acceptance Table 4*. Continue testing through the three levels unless the results of both stages conform at an earlier level. The value of Q in *Acceptance Table 4* is 75% dissolved unless otherwise specified ✦in the individual monograph✦. The quantity, Q, ✦specified in the individual monograph✦ is the total amount of active ingredient dissolved in both the *Acid* and *Buffer Stages*, expressed as a percentage of the labeled content. The 5%, 15%, and 25% values in *Acceptance Table 4* are percentages of the labeled content so that these values and Q are in the same terms.

Acceptance Table 4

Level	Number Tested	Criteria
B_1	6	Each unit is not less than $Q + 5\%$.
B_2	6	Average of 12 units ($B_1 + B_2$) is equal to or greater than Q, and no unit is less than $Q - 15\%$.
B_3	12	Average of 24 units ($B_1 + B_2 + B_3$) is equal to or greater than Q, not more than 2 units are less than $Q - 15\%$, and no unit is less than $Q - 25\%$.

Change to read:

⟨911⟩ VISCOSITY■—CAPILLARY VISCOMETER METHODS

The following procedures are used to determine the viscosity of a Newtonian fluid, i.e. a fluid having a viscosity that is independent of the shearing stress rate or rate of shear. Unless otherwise directed in the individual monograph, use *Method I*.

• **METHOD I. UBBELOHDE-TYPE CAPILLARY VISCOMETER**

Apparatus: The determination may be carried out with an Ubbelohde-type capillary viscometer (*Figure 1*) that has the specifications described in *Table 1* or *Table 2*.

Table 1

Size Number	Nominal Constant of Viscometer (mm^2/s^2)	Measurable Kinematic Viscosity Range (mm^2/s)	Internal Diameter of Tube, R (mm) (±2%)	Volume of Bulb, C (mL) (±5%)	Internal Diameter of Tube, N (mm)
1	0.01	3.5–10	0.64	5.6	2.8–3.2
1A	0.03	6–30	0.84	5.6	2.8–3.2
2	0.1	20–100	1.15	5.6	2.8–3.2
2A	0.3	60–300	1.51	5.6	2.8–3.2
3	1.0	200–1,000	2.06	5.6	3.7–4.3
3A	3.0	600–3,000	2.74	5.6	4.6–5.4
4	10	2,000–10,000	3.70	5.6	4.6–5.4
4A	30	6,000–30,000	4.07	5.6	5.6–6.4
5	100	20,000–100,000	6.76	5.6	6.8–7.5

Table 2

Size Number	Nominal Constant of Viscometer (mm^2/s^2)	Measurable Kinematic Viscosity Range (mm^2/s)	Internal Diameter of Tube, R (mm) (±2%)	Volume of Bulb, C (mL) (±5%)	Internal Diameter of Tube, N (mm)
0	0.001	0.3–1	0.24	1.0	6.0
0C	0.003	0.6–3	0.36	2.0	6.0
0B	0.005	1–5	0.46	3.0	6.0
1	0.01	2–10	0.58	4.0	6.0
1C	0.03	6–30	0.78	4.0	6.0
1B	0.05	10–50	0.88	4.0	6.0
2	0.1	20–100	1.03	4.0	6.0
2C	0.3	60–300	1.36	4.0	6.0
2B	0.5	100–500	1.55	4.0	6.0
3	1.0	200–1,000	1.83	4.0	6.0
3C	3.0	600–3,000	2.43	4.0	6.0
3B	5.0	1,000–5,000	2.75	4.0	6.5
4	10	2,000–10,000	3.27	4.0	7.0
4C	30	6,000–30,000	4.32	4.0	8.0
4B	50	10,000–50,000	5.20	5.0	8.5
5	100	20,000–100,000	6.25	5.0	10.0