

The temperature of the gas pycnometer should be between 15° and 30° and should not vary by more than 2° during the course of the measurement. Load the test cell with the substance under examination that has been prepared according to the individual monograph. Where <699D> is indicated, dry the substance under examination as directed for *Loss on drying* in the monograph unless other drying conditions are specified in the monograph *Density of solids* test. Where <699U> is indicated, the substance under examination is used without drying. Use a quantity of powder recommended in the operating manual for the pycnometer. Seal the test cell in the pycnometer, and purge the pycnometer system with the test gas according to the procedure given in the manufacturer's operating instructions. If the sample must be degassed under vacuum, follow the recommendations in the individual monographs and the instructions in the operating manual for the pycnometer.

The measurement sequence above describes the procedure for the gas pycnometer shown in *Figure 1*. If the pycnometer differs in operation or in construction from the one shown in *Figure 1*, follow the operating procedure given in the manual for the pycnometer.

Repeat the measurement sequence for the same powder sample until consecutive measurements of the sample volume,  $V_s$ , agree to within 0.2%. Unload the test cell and measure the final powder weight,  $w$ . Calculate the pycnometric density,  $\rho$ , of the sample according to *Equation 2*.

## <701> DISINTEGRATION

This general chapter is harmonized with the corresponding texts of the *European Pharmacopoeia* and/or the *Japanese Pharmacopoeia*. The texts of these pharmacopoeias are therefore interchangeable, and the methods of the *European Pharmacopoeia* and/or the *Japanese Pharmacopoeia* may be used for demonstration of compliance instead of the present general chapter. These pharmacopoeias 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 ( $\star$ ) to specify this fact.

This test is provided to determine whether tablets or capsules disintegrate within the prescribed time when placed in a liquid medium at the experimental conditions presented below.  $\star$ Compliance with the limits on *Disintegration* stated in the individual monographs is required except where the label states that the tablets or capsules are intended for use as troches, or are to be chewed, or are designed as extended-release dosage forms or delayed-release dosage forms. Determine the type of units under test from the labeling and from observation, and apply the appropriate procedure to 6 or more dosage units. $\star$

For the purposes of this test, disintegration does not imply complete solution of the unit or even of its active constituent. Complete disintegration is defined as that state in which any residue of the unit, except fragments of insoluble coating or capsule shell, remaining on the screen of the test apparatus or adhering to the lower surface of the disk, if used, is a soft mass having no palpably firm core.

### APPARATUS

The apparatus consists of a basket-rack assembly, a 1000-mL, low-form beaker, 138 to 160 mm in height and having an inside diameter of 97 to 115 mm for the immersion fluid, a thermostatic arrangement for heating the fluid be-

tween 35° and 39°, and a device for raising and lowering the basket in the immersion fluid at a constant frequency rate between 29 and 32 cycles per minute through a distance of not less than 53 mm and not more than 57 mm. The volume of the fluid in the vessel is such that at the highest point of the upward stroke the wire mesh remains at least 15 mm below the surface of the fluid and descends to not less than 25 mm from the bottom of the vessel on the downward stroke. At no time should the top of the basket-rack assembly become submerged. The time required for the upward stroke is equal to the time required for the downward stroke, and the change in stroke direction is a smooth transition, rather than an abrupt reversal of motion. The basket-rack assembly moves vertically along its axis. There is no appreciable horizontal motion or movement of the axis from the vertical.

**Basket-Rack Assembly**—The basket-rack assembly consists of six open-ended transparent tubes, each  $77.5 \pm 2.5$  mm long and having an inside diameter of 20.7 to 23 mm and a wall 1.0 to 2.8 mm thick; the tubes are held in a vertical position by two plates, each 88 to 92 mm in diameter and 5 to 8.5 mm in thickness, with six holes, each 22 to 26 mm in diameter, equidistant from the center of the plate and equally spaced from one another. Attached to the under surface of the lower plate is a woven stainless steel wire cloth, which has a plain square weave with 1.8- to 2.2-mm apertures and with a wire diameter of 0.57 to 0.66 mm. The parts of the apparatus are assembled and rigidly held by means of three bolts passing through the two plates. A suitable means is provided to suspend the basket-rack assembly from the raising and lowering device using a point on its axis.

The design of the basket-rack assembly may be varied somewhat, provided the specifications for the glass tubes and the screen mesh size are maintained. The basket-rack assembly conforms to the dimensions found in *Figure 1*.

**Disks**—The use of disks is permitted only where specified or allowed  $\star$ in the monograph. If specified in the individual monograph, $\star$  each tube is provided with a cylindrical disk  $9.5 \pm 0.15$  mm thick and  $20.7 \pm 0.15$  mm in diameter. The disk is made of a suitable transparent plastic material having a specific gravity of between 1.18 and 1.20. Five parallel  $2 \pm 0.1$ -mm holes extend between the ends of the cylinder. One of the holes is centered on the cylindrical axis. The other holes are centered  $6 \pm 0.2$  mm from the axis on imaginary lines perpendicular to the axis and parallel to each other. Four identical trapezoidal-shaped planes are cut into the wall of the cylinder, nearly perpendicular to the ends of the cylinder. The trapezoidal shape is symmetrical; its parallel sides coincide with the ends of the cylinder and are parallel to an imaginary line connecting the centers of two adjacent holes 6 mm from the cylindrical axis. The parallel side of the trapezoid on the bottom of the cylinder has a length of  $1.6 \pm 0.1$  mm, and its bottom edges lie at a depth of 1.5 to 1.8 mm from the cylinder's circumference. The parallel side of the trapezoid on the top of the cylinder has a length of  $9.4 \pm 0.2$  mm, and its center lies at a depth of  $2.6 \pm 0.1$  mm from the cylinder's circumference. All surfaces of the disk are smooth. If the use of disks is specified  $\star$ in the individual monograph, $\star$  add a disk to each tube, and operate the apparatus as directed under *Procedure*. The disks conform to dimensions found in *Figure 1*<sup>1</sup>.

### PROCEDURE

**$\star$ Uncoated Tablets**— $\star$ Place 1 dosage unit in each of the six tubes of the basket and, if prescribed, add a disk. Oper-

<sup>1</sup>The use of automatic detection employing modified disks is permitted where the use of disks is specified or allowed. Such disks must comply with the requirements for density and dimension given in this chapter.

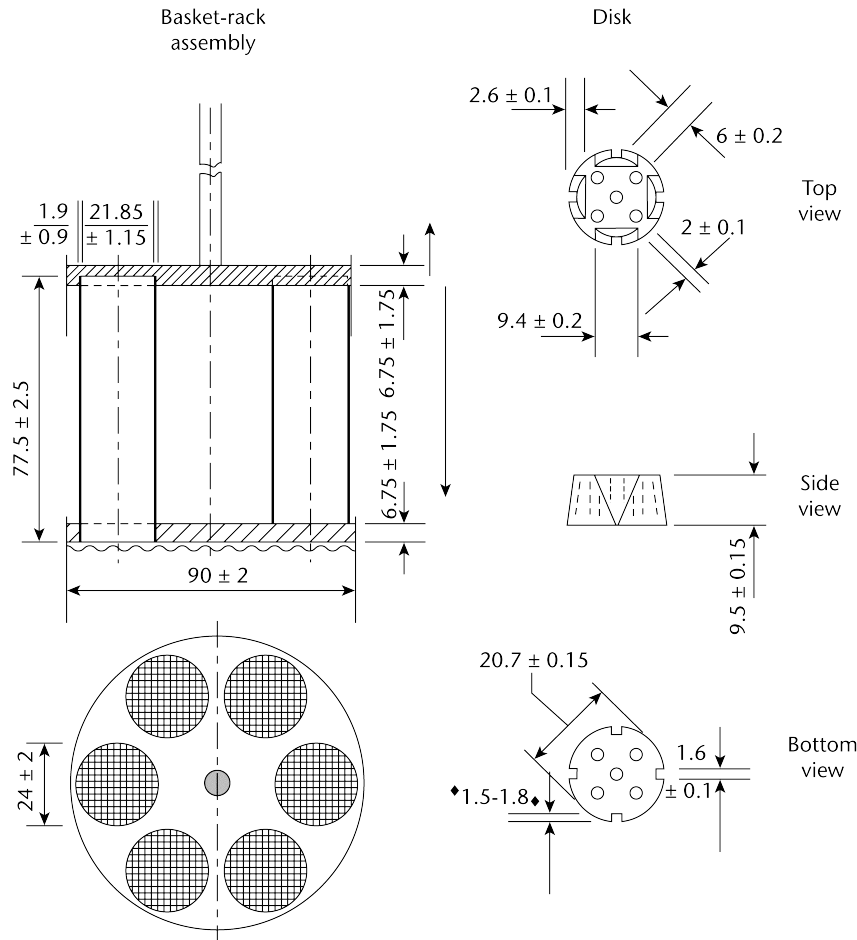


Figure 1. Disintegration apparatus. (All dimensions are expressed in mm.)

ate the apparatus, using water or the specified medium as the immersion fluid, maintained at  $37 \pm 2^\circ$ . At the end of the time limit specified in the monograph, lift the basket from the fluid, and observe the tablets: all of the tablets have disintegrated completely. If 1 or 2 tablets fail to disintegrate completely, repeat the test on 12 additional tablets. The requirement is met if not fewer than 16 of the total of 18 tablets tested are disintegrated.

**Plain-Coated Tablets**—Apply the test for *Uncoated Tablets*, operating the apparatus for the time specified in the individual monograph.

**Delayed-Release (Enteric-Coated) Tablets**—Place 1 tablet in each of the six tubes of the basket and, if the tablet has a soluble external sugar coating, immerse the basket in water at room temperature for 5 minutes. Then operate the apparatus using simulated gastric fluid TS maintained at  $37 \pm 2^\circ$  as the immersion fluid. After 1 hour of operation in simulated gastric fluid TS, lift the basket from the fluid, and observe the tablets: the tablets show no evidence of disintegration, cracking, or softening. Operate the apparatus, using simulated intestinal fluid TS maintained at  $37 \pm 2^\circ$  as the immersion fluid, for the time specified in the monograph. Lift the basket from the fluid, and observe the tablets: all of the tablets disintegrate completely. If 1 or 2 tablets fail to disintegrate completely, repeat the test on 12 additional tablets: not fewer than 16 of the total of 18 tablets tested disintegrate completely.

**Buccal Tablets**—Apply the test for *Uncoated Tablets*. After 4 hours, lift the basket from the fluid, and observe the tablets: all of the tablets have disintegrated. If 1 or 2 tablets fail to disintegrate completely, repeat the test on 12 additional tablets: not fewer than 16 of the total of 18 tablets tested disintegrate completely.

**Sublingual Tablets**—Apply the test for *Uncoated Tablets*. At the end of the time limit specified in the individual monograph: all of the tablets have disintegrated. If 1 or 2 tablets fail to disintegrate completely, repeat the test on 12 additional tablets: not fewer than 16 of the total of 18 tablets tested disintegrate completely.

**Hard Gelatin Capsules**—Apply the test for *Uncoated Tablets*. Attach a removable wire cloth, which has a plain square weave with 1.8- to 2.2-mm mesh apertures and with a wire diameter of 0.60 to 0.655 mm, as described under *Basket-Rack Assembly*, to the surface of the upper plate of the basket-rack assembly. Observe the capsules within the time limit specified in the individual monograph: all of the capsules have disintegrated except for fragments from the capsule shell. If 1 or 2 capsules fail to disintegrate completely, repeat the test on 12 additional capsules: not fewer than 16 of the total of 18 capsules tested disintegrate completely.

**Soft Gelatin Capsules**—Proceed as directed under *Hard Gelatin Capsules*.<sup>+</sup>

## <711> DISSOLUTION

This general chapter is harmonized with the corresponding texts of the *European Pharmacopoeia* and/or the *Japanese Pharmacopoeia*. These pharmacopoeias 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 (<sup>+</sup>) to specify this fact.

This test is provided to determine compliance with the dissolution requirements <sup>+</sup>where stated in the individual monograph<sup>+</sup> for dosage forms administered orally. In this general chapter, a dosage unit is defined as 1 tablet or 1 capsule or the amount specified. <sup>+</sup>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.

**USP Reference Standards** <11>—*USP Chlorpheniramine Maleate Extended-Release Tablets RS*. *USP Prednisone Tablets RS*.<sup>+</sup>

## APPARATUS

### Apparatus 1 (Basket Apparatus)

The assembly consists of the following: a vessel, which may be covered, made of glass or other inert, transparent material<sup>1</sup>; 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  $37 \pm 0.5^\circ$  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 <sup>+</sup>with one of the following dimensions and capacities: for a nominal<sup>+</sup> capacity of 1 L, the height is 160 to 210 mm and its inside diameter is 98 to 106 mm; <sup>+</sup>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<sup>+</sup>. Its sides are flanged at the top. A fitted cover may be used to retard evaporation.<sup>2</sup> 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 <sup>+</sup>given in the individual monograph,<sup>+</sup> within  $\pm 4\%$ .

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  $\mu\text{m}$ ) 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  $25 \pm 2$  mm during the test.

<sup>1</sup> The materials should not sorb, react, or interfere with the specimen being tested.

<sup>2</sup> If a cover is used, it provides sufficient openings to allow ready insertion of the thermometer and withdrawal of specimens.