



# OFFICIAL METHOD

## Determination of the Disintegration Time of Tablets

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**Health Products and Food Branch**

## I. APPLICATION

This method shall be used to measure the disintegration time of uncoated, plain coated and enteric coated tablets, intended to be swallowed whole, as described in Section C.01.015 of the *Food and Drug Regulations*.

## II. APPARATUS

- (1) A device for raising and lowering the basket-rack assembly, vertically along its axis, in the immersion fluid at a constant frequency between 28 and 32 cycles per minute through a distance of not less than 5.0 cm and not more than 6.0 cm.
- (2) A basket-rack assembly (see Figures I and II) containing six open-ended glass tubes, each  $7.75 \pm 0.25$  cm long and having an inside diameter of not less than 21.0 mm and not more than 22.5 mm and a wall approximately 2 mm thick. The tubes are held in a vertical position by two superimposed plastic plates each about 9 cm in diameter and 6 mm in thickness, with six holes, each about 24 in diameter, equidistant from the centre of the plate and equally spaced from one another. These holes are bored completely through the lower plate, but only through the lower 4 mm of the upper plate. The upper 2 mm of the plate contains six 21 mm diameter holes concentric with the 24 mm holes in the bottom portion of the plate, thereby forming a lip to retain the glass tubes. Alternatively the holes may be bored through the upper plate which is then covered with a stainless steel disk perforated by six holes about 22 mm in diameter which fit over the tubes. Attached to the underside of the lower plate in woven stainless steel wire cloth made from wire 0.635 mm in diameter having mesh apertures of about 2.0 mm and which retains the tubes. The plates are held rigidly in position, 77.5 mm apart, by means of 3 metal bolts, about 6.0 mm in diameter, passing through the upper and lower plates. A metal rod, about 8 cm in length and 7 mm in diameter, is also fixed to the centre of the upper plate and provided with a suitable means to suspend the assembly from the raising or lowering device (NOTE 1).
- (3) Six slatted and perforated cylindrical disks  $9.5 \pm 0.15$  mm thick and  $20.7 \pm 0.15$  mm in diameter. Each disk is made of a suitable transparent plastic material having a specific gravity of between 1.18 and 1.20. Five 2 mm holes extend between the ends of the disk, one of the holes being through the cylinder axis and the others parallel with it, equally spaced on a 6 mm radius around it. Equally spaced on the sides of the disk are four V-shaped notches. The dimensions of each notch are such that the openings on the bottom of the disk are 1.6 mm square and those on the top are 9.5 mm wide and 2.55 mm deep at the centre (and about 1.3 mm deep at the ends). All surfaces of the disk are smooth.

- (4) Six plungers each consisting of two plastic disks and a 3.2 mm diameter stainless steel rod approximately 9 cm in length. The lower disk is cylindrical and smooth,  $7.5 \pm 0.15$  mm thick and  $20.7 \pm 0.15$  mm in diameter. Six holes,  $4.0 \pm 0.1$  mm in diameter, are bored through the disk symmetrically distributed in a circle around the axis of the disk. One end of the stainless steel rod is permanently embedded in the centre and flush with the lower edge of the disk. The upper disk is smooth and approximately 7.5 mm thick. The lower half has a diameter of  $20.7 \pm 0.15$  mm and the upper half has a diameter of approximately 24 mm. This provides for an indent to enable the seating of the plunger in the glass tube. Twelve holes  $2.4 \pm 0.1$  mm in diameter, are bored through the disk symmetrically in two circles around the axis. A 3.2 mm hole is bored through the axis of the disk, through which the stainless steel rod is inserted such that when the apparatus is assembled the lower edge of the bottom disk is  $2.8 \pm 0.1$  cm from the bottom of the glass tube.
- (5) A cylindrical glass jar having an outside diameter of about 15 cm and a height of 20-21 cm.
- (6) A water bath or other suitable means of maintaining the test fluid in the jar at  $37 \pm 2^\circ\text{C}$ .

FIGURE I

Diagram of Assembled Apparatus

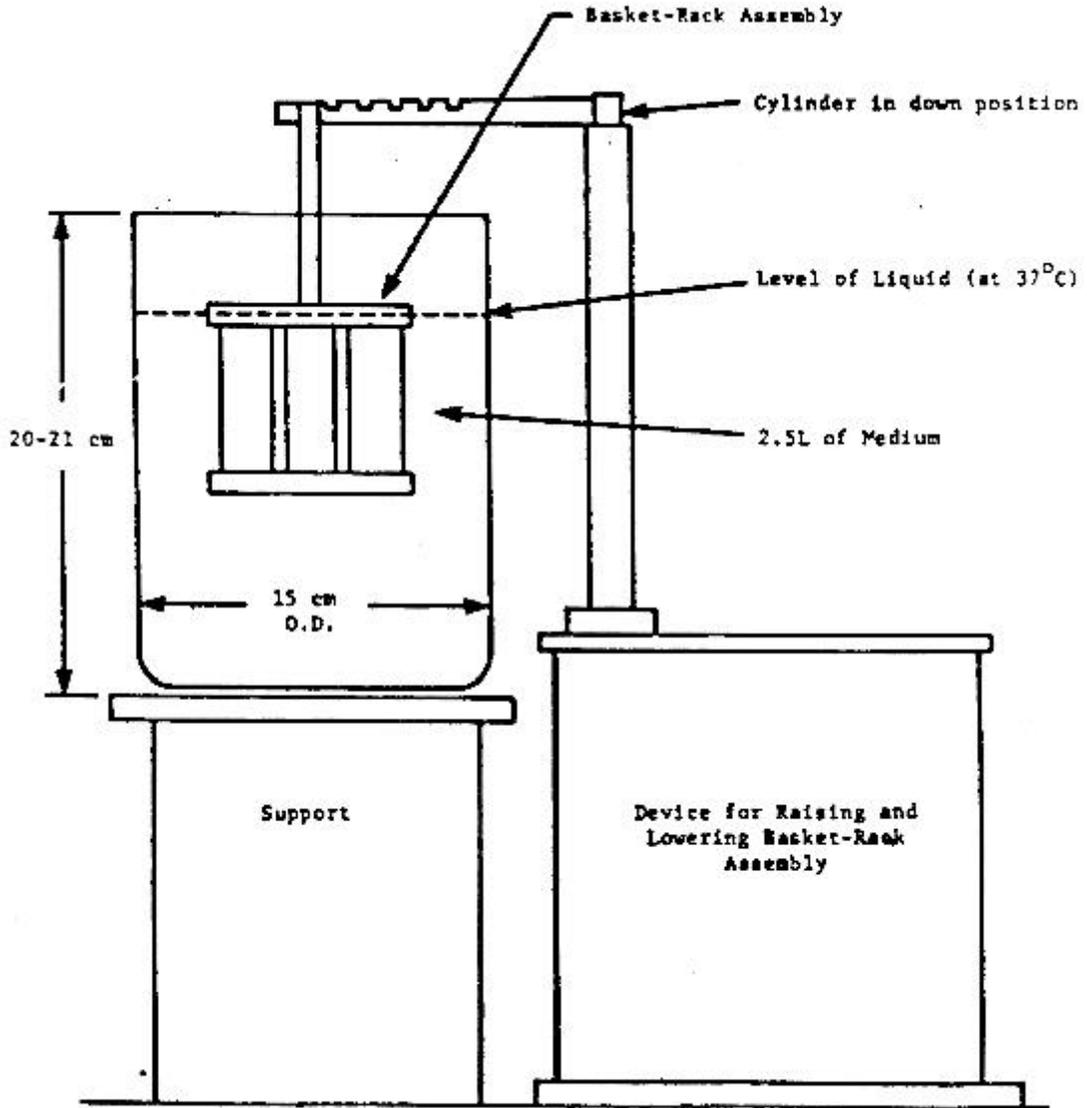
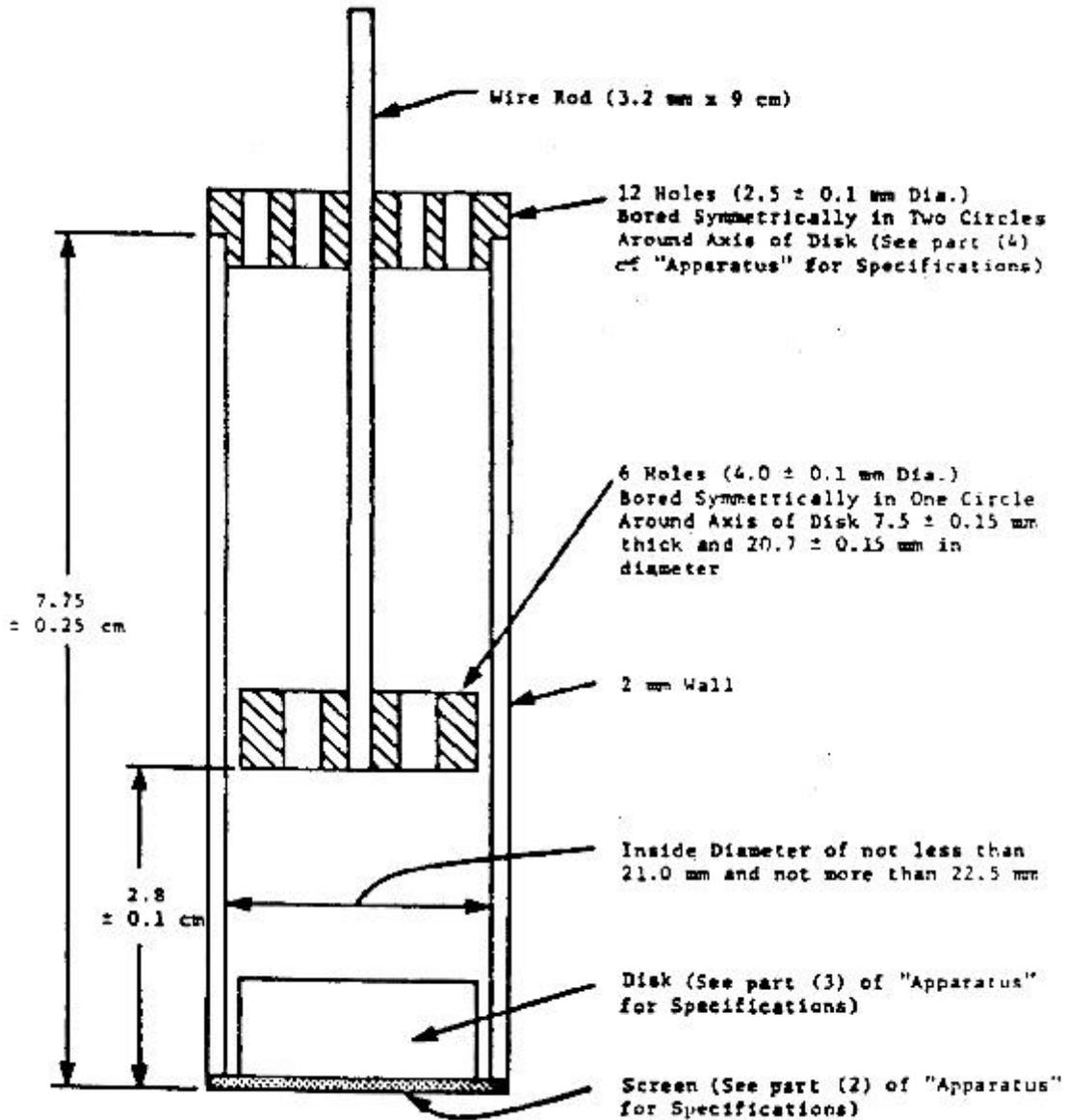


FIGURE II

Diagram of Glass Tube, Plastic Disk and Plunger



### III. MATERIALS AND SOLUTIONS

- (1) Water. Use distilled water.
- (2) Hydrochloric Acid. Use ACS reagent grade.
- (3) Sodium Chloride. Use ACS reagent grade.
- (4) Pepsin. Use FCC grade.
- (5) Potassium Phosphate, Monobasic. Use ACS reagent grade.
- (6) Pancreatin. Use USP grade.
- (7) Hydrochloric Acid Solution (0.1 M). Dilute 8.5 ml of hydrochloric acid to 1000 ml with water, **or** dilute a commercial volumetric solution with water to obtain a final concentration of 0.1 M.
- (8) Sodium Hydroxide Solution (0.2 M). Use ACS reagent grade. Dissolve 8 g of sodium hydroxide in, and dilute to 1000 ml with, carbon dioxide-free water, **or** dilute a commercial volumetric solution with carbon dioxide-free water to give a final concentration of 0.2 M.
- (9) Simulated Gastric Fluid. Dissolve 2.0 g of sodium chloride and 3.2 g of pepsin in 500 ml of water, add 7.0 ml of hydrochloric acid and dilute to 1000 ml with water. The pH is about 1.2. (NOTE 2).
- (10) Simulated Intestinal Fluid. Dissolve 6.8 g of potassium phosphate, monobasic, in 250 ml of water. Mix with 190 ml of Sodium Hydroxide Solution (0.2 M) and 400 ml of water. Add 10.0 g of pancreatin, mix and adjust the pH of the resulting solution to  $7.5 \pm 0.1$  with Sodium Hydroxide Solution (0.2 M). dilute with water to 1000 ml. (NOTE 2).

### IV. PROCEDURE

The test shall be carried out in accordance with the following instructions:

#### Uncoated and Plain Coated Tablets

- (1) assemble the apparatus when the device for raising and lowering the basket-rack assembly is at rest and its cylinder is in the extreme down position;

- (2) with 2.5 L of water in the cylindrical jar, adjust the apparatus until the level of fluid in the jar coincides approximately with the mid-line of the upper plastic plate (see Figure II);
- (3) maintain the temperature of the fluid at  $37 \pm 2^\circ\text{C}$  by a suitable means as indicated under APPARATUS (6);
- (4) remove the basket-rack assembly from the water and disassemble;
- (5) select at random six tablets from the sample and place one in each of the tubes of the basket-rack assembly;
- (6) place a plastic disk on each tablet, ensuring the orientation specified under APPARATUS (3) and then a plunger as specified under APPARATUS (4), (See Figure I);
- (7) re-insert the assembly in the water and set the machine in motion;
- (8) the plastic disks should travel up and down freely, exerting a gentle rubbing action on each tablet;
- (9) after 45 or 60 minutes (see (10) and (11) below), remove the basket-rack assembly from the water;
- (10) uncoated tablets pass the test if each of the six uncoated tablets disintegrates (NOTE 3) in not more than 45 minutes;
- (11) plain coated tablets pass the test if each of the six plain coated tablets disintegrates in not more than 60 minutes. If any of the tablets has not disintegrated at the end of 60 minutes, repeat the test on a further six plain coated tablets, replacing the water in the cylindrical jar with Hydrochloric Acid Solution (0.1 M). The tablets pass the test if each of the six tablets disintegrates within 60 minutes in this acid medium.

### **Enteric Coated Tablets**

- (1) assemble the apparatus as described in (1) to (3) under "Uncoated and Plain Coated Tablets", using 2.5 L of Simulated Gastric Fluid in place of water;
- (2) remove the basket-rack assembly from the Simulated Gastric Fluid and disassemble;
- (3) select at random six tablets from the sample and place one in each of the tubes of the basket-rack assembly;
- (4) place a plunger in each tube as specified under Apparatus (4) and as shown in Figure II (omitting the plastic disk);

- (5) insert the assembly in the Simulated Gastric fluid and set the machine in motion;
- (6) at the end of 60 minutes of operation, remove the basket-rack assembly from the fluid and gently rinse with water;
- (7) enteric coated tablets fail the test if any now show distinct evidence of disintegration;
- (8) replace the Simulated Gastric Fluid in the jar with 2.5 L of Simulated Intestinal Fluid;
- (9) remove the plungers, place a plastic disk on each tablet ensuring the orientation specified under APPARATUS (3);
- (10) re-insert the plunger as specified under APPARATUS (4);
- (11) continue the test by setting the machine in motion;
- (12) after 60 minutes remove the basket-rack assembly from the fluid;
- (13) enteric coated tablets pass the test if each of the six tablets disintegrates (NOTE 3) in not more than 60 minutes in the Simulated Intestinal Fluid

## V. NOTES

1. The design of the basket-rack assembly may be varied somewhat provided that the specifications for the glass tubes, disks, plungers, plunger position and wire mesh are maintained.
2. Stock solution of the digestive fluids may be prepared; however, the enzymes must be omitted to avoid decomposition. The pepsin or pancreatin shall be added to the respective stock solution in the proper quantity just before use.
3. Disintegration is considered to be that state in which any residue, except fragments of insoluble coating, remaining on the screen is a soft mass having no palpably firm core.

The method described above, being comprised of seven pages including Figures I and II and identified as DO-25, DETERMINATION OF THE DISINTEGRATION TIME OF TABLETS and dated July 5, 1989, is hereby designated the "official method" referred to in Section C.01.015 of the *Food and Drug Regulations*.