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Draft for comment

REVISION OF METHOD OF ANALYSIS:

5.3 DISINTEGRATION TEST FOR TABLETS AND CAPSULES

(February 2014)

DRAFT FOR COMMENT

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SCHEDULE FOR THE ADOPTION PROCESS OF DOCUMENT QAS/14.572

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5.3 DISINTEGRATION TEST FOR TABLETS AND CAPSULES

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Draft monograph received from a WHO Expert	February 2014
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Collation of comments	April 2014
Presentation to forty-ninth WHO Expert Committee on Specifications for Pharmaceutical Preparations for discussion	October 2014
Further follow-up action as required	

Revision of method of Analysis: 5.3 Disintegration test for tablets and capsules

[Note from the Secretariat.
It is proposed to include a disintegration test for large tablets in the test for disintegration of tablets and capsules. The proposed method is reproduced with permission from The European Pharmacopoeia.
Changes from the current text are indicated in the text by insert or ~~delete~~.]

5.3 DISINTEGRATION TEST FOR TABLETS AND CAPSULES

This test is provided to determine whether tablets or capsules disintegrate within the prescribed time when placed in a liquid medium under the experimental conditions presented below.

For the purposes of this test disintegration does not imply complete dissolution 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 discs, if used, is a soft mass having no palpably firm core.

Use apparatus A for tablets and capsules that are not greater than 18 mm. For larger tablets and capsules use apparatus B.

Test A. Tablets and capsules of normal size

This text is based on the internationally-harmonized texts developed by the Pharmacopoeial Discussion Group (PDG). Some editorial modifications have been made in order to be in line with the style used in The International Pharmacopoeia.

Apparatus. The apparatus (Figure 1) consists of a basket-rack assembly, a 1000 ml, low-form beaker, 138–160 mm in height and having an inside diameter of 97–115 mm for the immersion fluid, a thermostatic arrangement for heating the fluid between 35 °C and 39 °C, 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 75.0–80.0 mm long and having an internal diameter of 20.70–23.00 mm and a wall 1.0–2.8 mm thick; the tubes are held in a vertical position by two plates, each 88–92 mm in diameter and 5.00–8.50 mm in thickness, with six holes, each 22–26 mm in diameter, equidistant from the centre of the plate and equally spaced from one another. Attached to the lower surface of the lower plate is a

woven stainless steel wire mesh, which has a plain square weave with 1.8–2.2 mm apertures and with a wire diameter of 0.570–0.660 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 shown in Figure 1.

Discs. The use of discs is permitted only where specified or allowed. Each tube is provided with a cylindrical disc 9.35–9.65 mm thick and 20.55–20.85 mm in diameter. The disc is made of a suitable, transparent plastic material having a specific gravity of 1.18–1.20. Five parallel 1.9–2.1 mm holes extend between the ends of the cylinder. One of the holes is centered on the cylindrical axis. The other holes are centered 5.8–6.2 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 centres 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 1.5–1.7 mm and its bottom edges lie at a depth of 1.50–1.80 mm from the cylinder's circumference. The parallel side of the trapezoid on the top of the cylinder has a length of 9.2–9.6 mm and its centre lies at a depth of 2.5–2.7 mm from the cylinder's circumference. All surfaces of the disc are smooth. If the use of discs is specified, add a disc to each tube and operate the apparatus as directed under procedure. The discs conform to the dimensions found in Figure 1.

The use of automatic detection employing modified discs is permitted where the use of discs is specified or allowed. Such discs must comply with the requirements of density and dimension given in this chapter.

Procedure. Place one dosage unit in each of the six tubes of the basket and if specified add a disc. Operate the apparatus using water as the immersion fluid unless another liquid is specified and maintain its temperature at 35–39 °C. At the end of the specified time, lift the basket from the fluid and observe the dosage units: all of the dosage units have disintegrated completely. If one or two dosage units fail to disintegrate, repeat the test on 12 additional dosage units. The requirements of the test are met if not less than 16 of the 18 dosage units tested are disintegrated.

Test B – Large tablets and large capsules

This test is reproduced with permission from The European Pharmacopoeia.

Apparatus. The main part of the apparatus (Figure 2) is a rigid basket-rack assembly supporting 3 cylindrical transparent tubes 77.5 ± 2.5 mm long, 33.0 mm ± 0.5 mm in internal diameter, and with a wall thickness of 2.5 ± 0.5 mm. Each tube is provided with a cylindrical disc 31.4 ± 0.13 mm in diameter and 15.3 ± 0.15 mm thick, made of transparent plastic with a relative density of 1.18–1.20. Each disc is pierced by 7 holes, each 3.15 ± 0.1 mm in diameter, 1 in the centre and the other 6 spaced equally on a circle of radius 4.2 mm from the centre of the disc. The tubes are held vertically by 2 separate and superimposed rigid plastic plates 97 mm in diameter and 9 mm thick, with 3 holes. The holes are equidistant from the centre of the plate and equally spaced. Attached to

the under side of the lower plate is a piece of woven gauze made from stainless steel wire 0.63 ± 0.03 mm in diameter and having mesh apertures of 2.0 ± 0.2 mm. The plates are held rigidly in position and 77.5 mm apart by vertical metal rods at the periphery. A metal rod is also fixed to the centre of the upper plate to enable the assembly to be attached to a mechanical device capable of raising and lowering it smoothly at a constant frequency of between 29 and 32 cycles per minute, through a distance of 55 ± 2 mm.

The assembly is suspended in the specified liquid medium in a suitable vessel, preferably a 1 litre beaker. The volume of the liquid is such that when the assembly is in the highest position the wire mesh is at least 15 mm below the surface of the liquid, and when the assembly is in the lowest position the wire mesh is at least 25 mm above the bottom of the beaker and the upper open ends of the tubes remain above the surface of the liquid. A suitable device maintains the temperature of the liquid at 35–39 °C.

The design of the basket-rack assembly may be varied provided the specifications for the tubes and wire mesh are maintained.

Method. Test 6 tablets or capsules either by using 2 basket-rack assemblies in parallel or by repeating the procedure. In each of the 3 tubes, place 1 tablet or capsule and, if prescribed, add a disc; suspend the assembly in the beaker containing the specified liquid. Operate the apparatus using water as the immersion fluid unless another liquid is specified for the prescribed period, withdraw the assembly and examine the state of the tablets or capsules. To pass the test, all 6 of the tablets or capsules must have disintegrated.

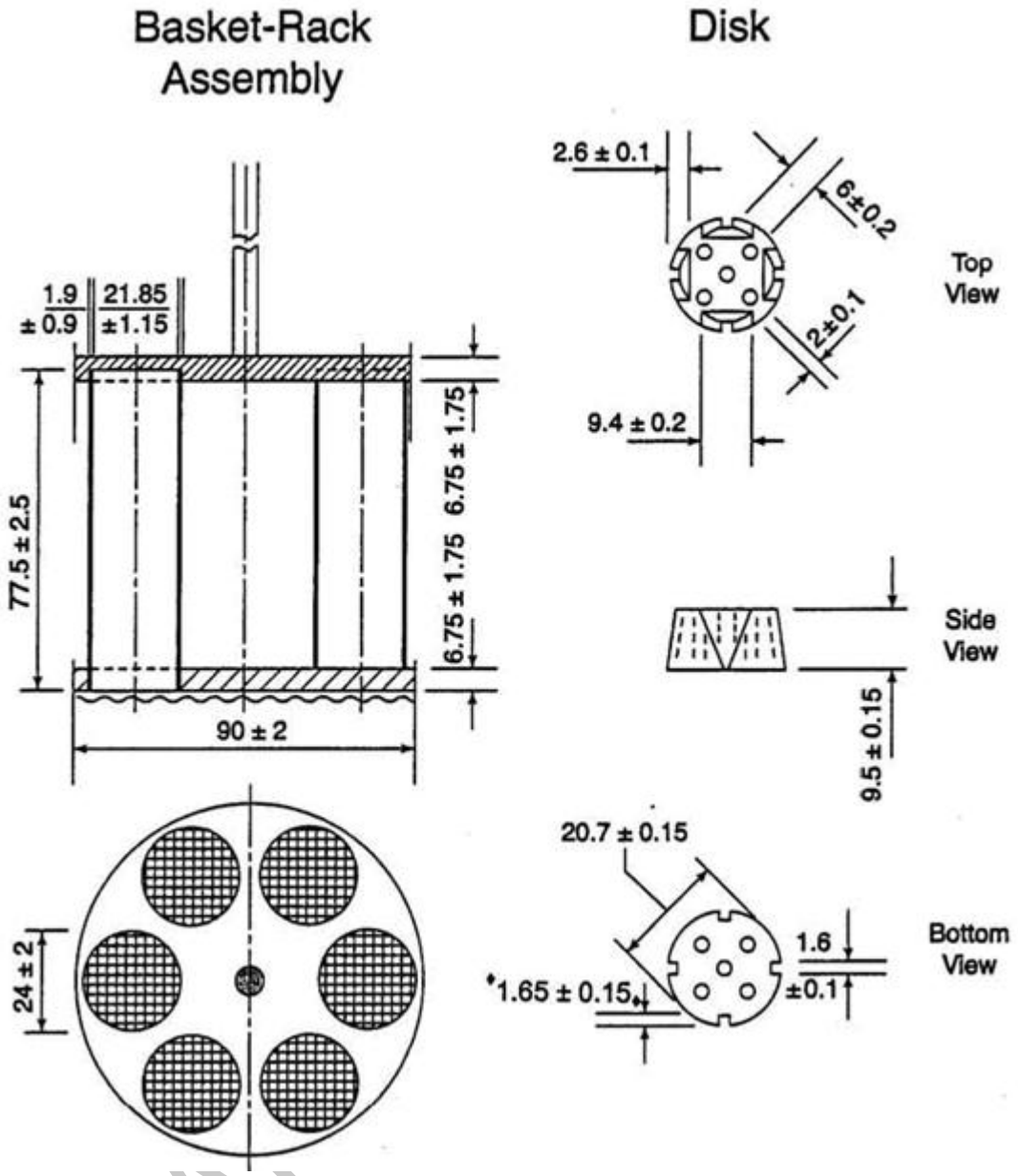

Figure 1. Diagram for disintegration apparatus A (dimensions are expressed in millimeters).

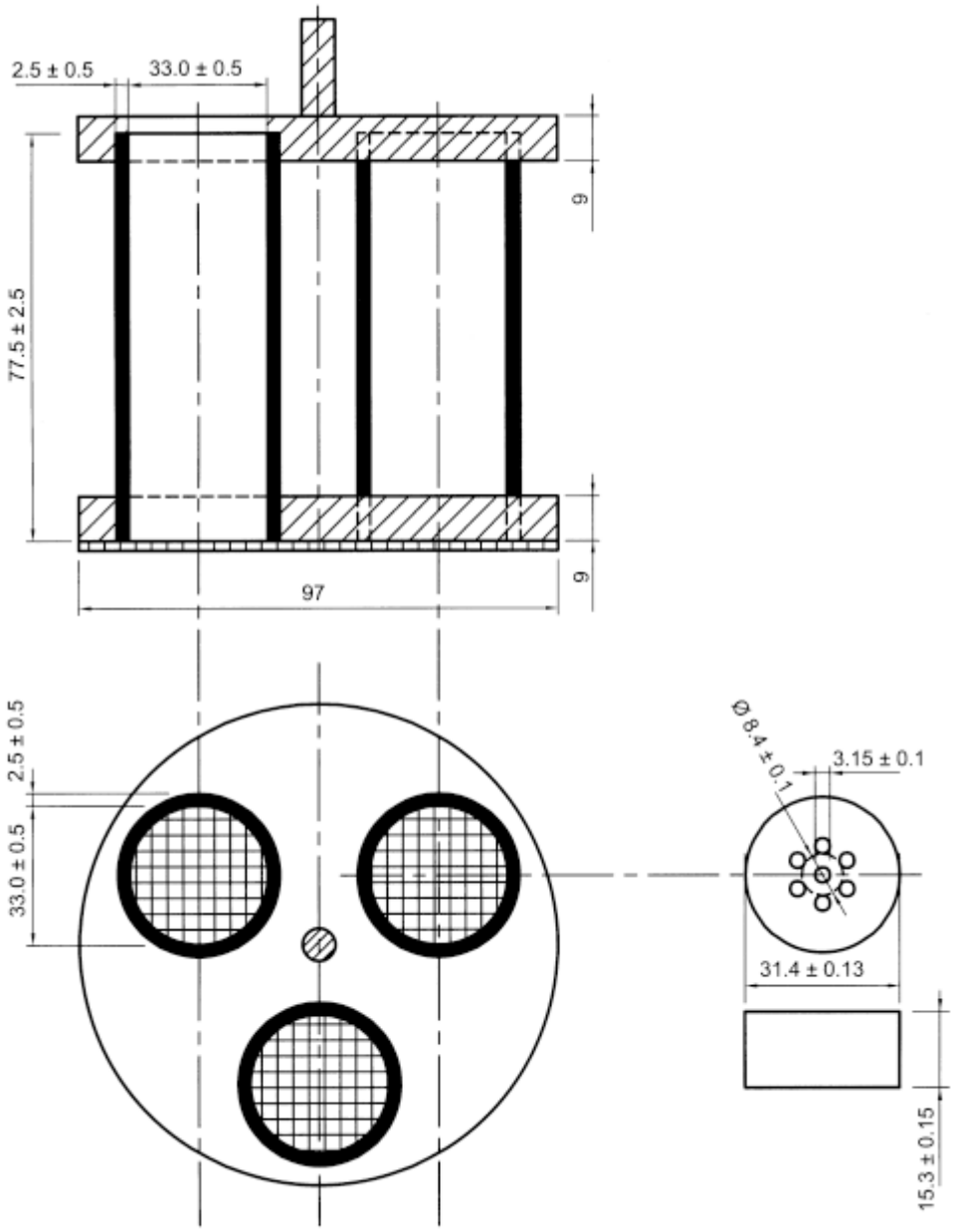

Figure 2.9.1.-2. – *Disintegration apparatus B*
Dimensions in millimetres

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110 Figure 2. Diagram for disintegration apparatus B (dimensions are expressed in millimeters).

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