MASS VARIATION

Carry out an assay for the active substance(s) on a representative sample of the batch using an appropriate analytical method. This value is result A, expressed as percentage of label claim (see Calculation of Acceptance Value). Assume that the concentration (mass of active substance per mass of dosage unit) is uniform. Select not fewer than 30 dosage units, and proceed as follows for the dosage form designated.

Uncoated or film-coated tablets. Accurately weigh 10 tablets individually. Calculate the active substance content, expressed as percentage of label claim, of each tablet from the mass of the individual tablets and the result of the assay. Calculate the acceptance value.

Hard capsules. Accurately weigh 10 capsules individually, taking care to preserve the identity of each capsule. Remove the contents of each capsule by suitable means. Accurately weigh the emptied shells individually, and calculate for each capsule the net mass of its contents by subtracting the mass of the shell from the respective gross mass. Calculate the active substance content in each capsule from the mass of product removed from the individual capsules and the result of the assay. Calculate the acceptance value.

Soft capsules. Accurately weigh 10 intact capsules individually to obtain their gross masses, taking care to preserve the identity of each capsule. Then cut open the capsules by means of a suitable clean, dry cutting instrument such as scissors or a sharp open blade, and remove the contents by washing with a suitable solvent. Allow the occluded solvent to evaporate from the shells at room temperature over a period of about 30 min, taking precautions to avoid uptake or loss of moisture. Weigh the individual shells, and calculate the net contents. Calculate the active substance content in each capsule from the mass of product removed from the individual capsules and the result of the assay. Calculate the acceptance value.

Solid dosage forms other than tablets and capsules. Proceed as directed for hard capsules, treating each unit as described therein. Calculate the acceptance value.

Liquid ◊or semi-solid◊ dosage forms. Accurately weigh the amount of liquid or semi-solid that is removed from each of 10 individual containers in conditions of normal use. If necessary, compute the equivalent volume after determining the density. Calculate the active substance content in each container from the mass of product removed from the individual containers and the result of the assay. Calculate the acceptance value.

Calculation of Acceptance Value. Calculate the acceptance value (AV) as shown in content uniformity, except that the individual contents of the units are replaced with the individual estimated contents defined below.

$x_1, x_2, ..., x_n$ = individual estimated contents of the dosage units tested;

where

$$x_i = w_i \times \frac{A}{\overline{W}}$$

$w_1, w_2, ..., w_n$ = individual masses of the dosage units tested;

A = content of active substance (percentage of label claim) obtained using an appropriate analytical method (assay);

$\overline{W}$ = mean of individual masses ($w_1, w_2, ..., w_n$).

CRITERIA

Apply the following criteria, unless otherwise specified.

Solid, semi-solid and liquid dosage forms. The requirements for dosage uniformity are met if the acceptance value of the first 10 dosage units is less than or equal to $L1$ per cent. If the acceptance value is greater than $L1$ per cent, test the next 20 dosage units and calculate the acceptance value. The requirements are met if the final acceptance value of the 30 dosage units is less than or equal to $L1$ per cent and no individual content of the dosage unit is less than $(1 - L2 \times 0.01)M$ or more than $(1 + L2 \times 0.01)M$ in calculation of acceptance value under content uniformity or under mass variation. Unless otherwise specified, $L1$ is 15.0 and $L2$ is 25.0.

04/2012:20941

2.9.41. FRIABILITY OF GRANULES AND SPHEROIDS

This chapter describes 2 methods for determination of the friability of granules and spheroids, which may be used during development studies. It is recognised, however, that many methods with equal suitability may be used.

This test is intended to determine, under defined conditions, the friability of granules and spheroids. Friability is defined as a reduction in the mass of the granules or spheroids or in the formation of fragments of granules or spheroids, occurring when the granules or spheroids are subjected to mechanical strain during handling (tumbling, vibration, fluidisation, etc.). Examples of changes are abrasion, breakage or deformation of granules or spheroids.

METHOD A

Apparatus (fluidised-bed apparatus). The apparatus (see Figure 2.9.41.-1) consists of a glass cylinder (A) with a conical lower part. The cylinder is provided with a sieve lid (B) having an aperture size of 500 µm or any other suitable sieve. The conical end is connected to a U-shaped glass tube (C) that can be disconnected from the cylinder for removal of the granules or spheroids. The U-tube is attached to a T-coupling (D). One inlet of the T-coupling is joined by a silicone tube to a manometer for regulating the compressed-air flow (use compressed air complying with the test for water in the monograph *Medicinal air (1238)*), the other one is connected via a silicone tube to a by-pass flowmeter (E) (0.10-1.00 $m^3 \cdot h^{-1}$).

Procedure. *The following procedure is usually suitable.* Remove the fine particles by sieving (sieve having an aperture size of 710 µm or any other suitable sieve). Introduce about 8.0 g (m_1) of granules or spheroids into the cylinder (A). Close the apparatus with the sieve lid (B). Adjust the flow rate of the compressed air to 0.45 $m^3 \cdot h^{-1}$. After 15 min, remove the granules or spheroids from the apparatus by disconnecting the U-tube and weigh again (m_2). Test 3 samples and calculate the mean value. It is recommended to spray the inside of the apparatus with an antistatic agent every 3 determinations in order to prevent electrostatic charging.

Loss on drying. Dry in an oven at 105 °C, unless otherwise prescribed. Alternatively, other drying conditions as described in general chapter *2.2.32* may be used.

Calculation

$$F = \frac{m_1(100 - T_1) - m_2(100 - T_2)}{m_1} \times 100$$

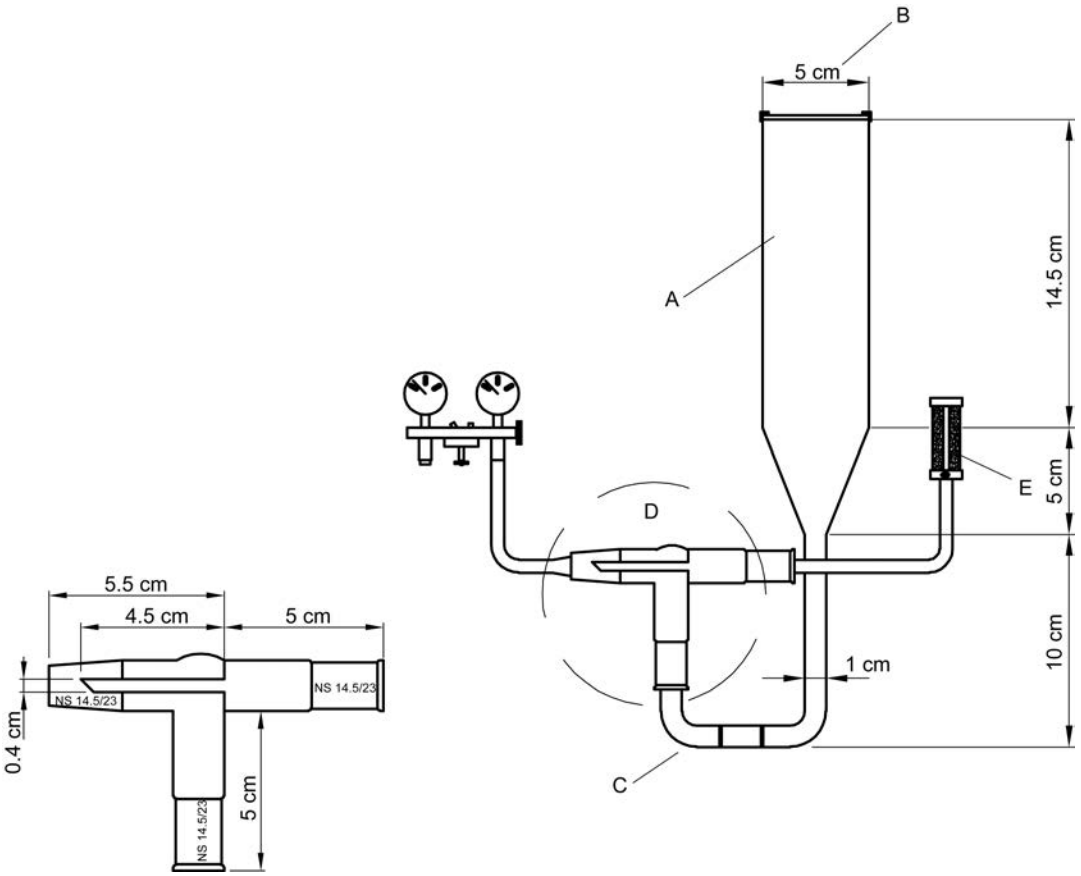

Figure 2.9.41.-1. – *Fluidised-bed apparatus*

F = friability;

T_1 = percentage loss on drying before the test (mean of 2 determinations);

T_2 = percentage loss on drying after the test (mean of 2 determinations);

m_1 = mass of the granules or spheroids before the test, in grams;

m_2 = mass of the granules or spheroids after the test, in grams.

METHOD B

Apparatus (oscillating apparatus). The apparatus (see Figure 2.9.41.-2) consists of a glass container, containing the granules or spheroids to be examined, which is subjected to horizontal oscillations. The frequency and duration of the oscillations can be varied continuously. The frequency can be adjusted, using a scale, to a value in the range 0-400 oscillations/min. The duration can be set to a value in the range 0-9999 s.

Procedure. *The following procedure is usually suitable.* Remove the fine particles by sieving (sieve having an aperture size of 355 µm or any other suitable sieve). In the glass container, weigh about 10.00 g (m_1) of the granules or spheroids. Install the container in the apparatus. Shake for 240 s at the highest frequency for hard granules or spheroids, or for 120 s at a lower frequency (e.g. 140 oscillations/min) for soft granules or spheroids. Sieve (355 µm, or the same sieve as used previously) and weigh the granules or spheroids again (m_2). Test 3 samples and calculate the mean value.

Loss on drying. Dry in an oven at 105 °C, unless otherwise prescribed. Alternatively, other drying conditions as described in general chapter *2.2.32* may be used.

Calculation

$$F = \frac{m_1(100 - T_1) - m_2(100 - T_2)}{m_1} \times 100$$

F = friability;

T_1 = percentage loss on drying before the test (mean of 2 determinations);

T_2 = percentage loss on drying after the test (mean of 2 determinations);

m_1 = mass of the granules or spheroids before the test, in grams;

m_2 = mass of the granules or spheroids after the test, in grams.

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2.9.42. DISSOLUTION TEST FOR LIPOPHILIC SOLID DOSAGE FORMS

APPARATUS

The apparatus (see Figure 2.9.42.-1) consists of:

- A reservoir for the dissolution medium.
- A pump that forces the dissolution medium upwards through the flow-through cell.
- A flow-through cell shown in Figure 2.9.42.-2 specifically intended for lipophilic solid dosage forms such as suppositories and soft capsules. It consists of 3 transparent parts which fit into each other. The lower part (1) is made up of 2 adjacent chambers connected to an overflow device.