Make a compacted bed using the reference powder and again fill the cell with mercury with a planar surface at the top of the cell. Pour out the mercury in a tared beaker and again determine the mass of the mercury (M_B). Calculate the bulk volume (V) of the compacted bed of powder from the following expression:

$$\frac{M_A - M_B}{\rho_{Hg}} \qquad (3)$$

$M_A - M_B$ = difference between the determined masses of mercury in grams,

ρ_{Hg} = density of mercury at the determined temperature in grams per millilitre.

Repeat the procedure twice, changing the powder each time; the range of values for the calculated volume (V) is not greater than 0.01 mL. Use the mean value of the three determined volumes for the calculations.

Apparatus constant (*K*). It is determined using a reference powder with known specific surface area and density as follows:

Calculate the required quantity of the reference powder to be used (expression (1)) using the stated density and the determined volume of the compacted powder bed (expression (3)).

Homogenise and loosen up the powder by shaking it for 2 min in a 100 mL bottle. Prepare a compacted powder bed and measure the flow time of air as previously described. Calculate the apparatus constant (K) from the following expression:

$$\frac{S_{sp} \times \rho \times (1 - \varepsilon) \times \sqrt{\eta}}{\sqrt{\varepsilon^3} \times \sqrt{t}} \qquad (4)$$

S_{sp} = stated specific surface area of the reference powder,

ρ = density of the substance to be examined in grams per millilitre,

ε = porosity of the compacted bed of powder,

t = flow time in seconds,

η = dynamic viscosity of air in millipascal seconds (see Table 2.9.14.-1).

The density of mercury and the viscosity of air over a range of temperatures are shown in Table 2.9.14.-1.

Table 2.9.14.-1.

Temperature (°C)	Density of mercury (g/mL)	Viscosity of air (η) (mPa·s)	$\sqrt{\eta}$
16	13.56	0.01800	0.1342
17	13.56	0.01805	0.1344
18	13.55	0.01810	0.1345
19	13.55	0.01815	0.1347
20	13.55	0.01819	0.1349
21	13.54	0.01824	0.1351
22	13.54	0.01829	0.1353
23	13.54	0.01834	0.1354
24	13.54	0.01839	0.1356

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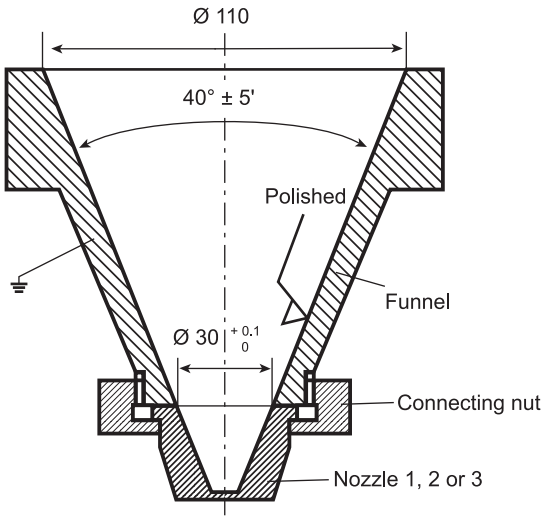
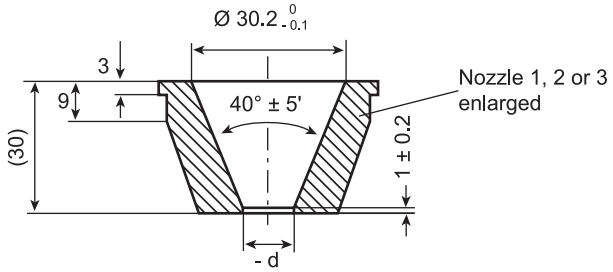
2.9.16. FLOWABILITY

The test for flowability is intended to determine the ability of divided solids (for example, powders and granules) to flow vertically under defined conditions.

APPARATUS

According to the flow properties of the material to be tested, funnels with or without stem, with different angles and orifice diameters are used. Typical apparatuses are shown in Figures 2.9.16.-1 and 2.9.16.-2. The funnel is maintained upright by a suitable device. The assembly must be protected from vibrations.





Nozzle	Diameter (*d*) of the outflow opening (millimetres)
1	10 ± 0.01
2	15 ± 0.01
3	25 ± 0.01

Figure 2.9.16.-1. – *Flow funnel and nozzle. Nozzle is made of stainless, acid-resistant steel (V4A,CrNi)*

Dimensions in millimetres

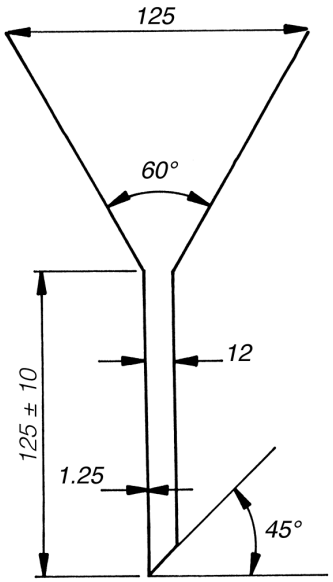


Figure 2.9.16.-2
Dimensions in millimetres

METHOD

Into a dry funnel, whose bottom opening has been blocked by suitable means, introduce without compacting a test sample weighed with 0.5 per cent accuracy. The amount of the sample depends on the apparent volume and the apparatus used. Unblock the bottom opening of the funnel and measure the time needed for the entire sample to flow out of the funnel. Carry out three determinations.

EXPRESSION OF RESULTS

The flowability is expressed in seconds and tenths of seconds, related to 100 g of sample.

The results depend on the storage conditions of the material to be tested.

The results can be expressed as the following:

a) the mean of the determinations, if none of the individual values deviates from the mean value by more than 10 per cent;

b) as a range, if the individual values deviate from the mean value by more than 10 per cent;

c) as a plot of the mass against the flow time;

d) as an infinite time, if the entire sample fails to flow through.

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2.9.17. TEST FOR EXTRACTABLE VOLUME OF PARENTERAL PREPARATIONS(8)

Suspensions and emulsions are shaken before withdrawal of the contents and before the determination of the density. Oily and viscous preparations may be warmed according to the instructions on the label, if necessary, and thoroughly shaken immediately before removing the contents. The contents are then cooled to 20-25 °C before measuring the volume.

SINGLE-DOSE CONTAINERS

Select 1 container if the nominal volume is 10 mL or more, 3 containers if the nominal volume is more than 3 mL and less than 10 mL, or 5 containers if the nominal volume is 3 mL or less. Take up individually the total contents of each container selected into a dry syringe of a capacity not exceeding 3 times the volume to be measured, and fitted with a 21-gauge needle not less than 2.5 cm in length. Expel any air bubbles from the syringe and needle, then discharge the contents of the syringe without emptying the needle into a standardised dry cylinder (graduated to contain rather than to deliver the designated volumes) of such size that the volume to be measured occupies at least 40 per cent of its graduated volume. Alternatively, the volume of the contents in millilitres may be calculated as the mass in grams divided by the density.

For containers with a nominal volume of 2 mL or less, the contents of a sufficient number of containers may be pooled to obtain the volume required for the measurement provided that a separate, dry syringe assembly is used for each container. The contents of containers holding 10 mL or more may be determined by opening them and emptying the contents directly into the graduated cylinder or tared beaker.

The volume is not less than the nominal volume in case of containers examined individually, or, in case of containers with a nominal volume of 2 mL or less, is not less than the sum of the nominal volumes of the containers taken collectively.

MULTIDOSE CONTAINERS

For injections in multidose containers labelled to yield a specific number of doses of a stated volume, select one container and proceed as directed for single-dose containers using the same number of separate syringe assemblies as the number of doses specified.

The volume is such that each syringe delivers not less than the stated dose.

CARTRIDGES AND PREFILLED SYRINGES

Select 1 container if the nominal volume is 10 mL or more, 3 containers if the nominal volume is more than 3 mL and less than 10 mL, or 5 containers if the nominal volume is 3 mL or less. If necessary, fit the containers with the accessories required for their use (needle, piston, syringe) and transfer the entire contents of each container without emptying the needle into a dry tared beaker by slowly and constantly depressing the piston. Determine the volume in millilitres calculated as the mass in grams divided by the density.

The volume measured for each of the containers is not less than the nominal volume.

PARENTERAL INFUSIONS

Select one container. Transfer the contents into a dry measuring cylinder of such a capacity that the volume to be determined occupies at least 40 per cent of the nominal volume of the cylinder. Measure the volume transferred.

The volume is not less than the nominal volume.

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2.9.18. PREPARATIONS FOR INHALATION: AERODYNAMIC ASSESSMENT OF FINE PARTICLES

This test is used to determine the fine particle characteristics of the aerosol clouds generated by preparations for inhalation.

Unless otherwise justified and authorised, one of the following apparatus and test procedures is used.

Stage mensuration is performed periodically together with confirmation of other dimensions critical to the effective operation of the impactor.

(8) This chapter has undergone pharmacopoeial harmonisation. See chapter *5.8. Pharmacopoeial harmonisation.*