## 1.2.1 Melting point and melting range

**2025-01**

### A. Determination of melting point and melting range of pulverizable substances

The *melting range* of a solid substance is the range between the corrected temperature at which the substance begins to collapse or forms droplets on the wall of a transparent glass capillary tube and the corrected temperature at which it is completely melted, as shown by the disappearance of the solid phase.

The statement in a monograph "melting range *a-b* °C" means that the melting range determined by the method below must fall within these limits.

The *melting point* of a substance is the corrected temperature at which the solid substance is completely melted to a liquid or a decomposed state.

#### Apparatus

A suitable apparatus for the determination consists of a controlled source of heat, either a metal heating block with one or more compartments for capillary tubes or a glass vessel with an appropriate liquid and fitted with a suitable means of heating and stirring. The apparatus is equipped with a temperature sensor or a suitable certified thermometer allowing readings at least to the nearest 0.1 °C.

The controlled source of heat should be capable of raising the temperature of the sample at a rate of 1 °C/min or less. The accuracy of the equipment is at most +/- 0.5°C.

Standardized thermometers should cover the range -10 to +250 °C, the length of one degree on the scale being not less than 0.8 mm.

Thermometers used for determination of melting points may be calibrated for total or partial immersion. A *total-immersion thermometer* should read correctly when it is immersed at least to the end of the liquid column in the medium, the temperature of which is to be measured. A *partial-immersion thermometer* should read correctly when it is immersed to a prescribed depth and when the emergent liquid column is under prescribed conditions. When total-immersion thermometers are used partially immersed, an auxiliary thermometer is required for the determination of the emergent-stem correction. These two thermometers should be surrounded with a glass tube above the surface of the heating material.

Samples are introduced into the equipment in glass capillary tubes, closed at one end. The dimensions are chosen according to the manufacturer’s requirements, typically with an external diameter of 1.3-1.5 mm and a wall thickness of 0.1 – 0.3 mm. In some, apparatus glass slides are used instead of capillary tubes.

In case of visual detection, a suitable magnifying glass should be used for observation of the capillary tube.

Other apparatus or methods may be used provided they are capable of equal accuracy and have been calibrated against the method of *The International Pharmacopoeia* by means of the WHO Melting Point Reference Substances.

#### Recommended procedure

Spread a small quantity of the finely powdered substance in a thin layer and dry it in a vacuum desiccator over silica gel, desiccant, R, phosphorus pentoxide R or other suitable desiccant for 24 hours, or at a temperature specified in the monograph. Coarse crystals might lead to false results. If necessary, crush the sample into a fine powder.

Transfer a quantity of the dried powder to a dry capillary tube and pack the powder carefully by tapping the tube on a hard surface (ensure the capillary tube bottom is not damaged or cracked). Pack the sample column tightly to a height of about 4-6 mm. Introduce the capillary tube into the controlled source of heat at a temperature of 5 °C below the expected lower limit of the melting range, the rise of temperature being regulated beforehand to 1 °C per minute, unless either the temperature of the introduction of the capillary tube into the bath or the rate of temperature rise are otherwise specified in the monograph. If a bath with a suitable liquid is used, the capillary tube should be fitted in the bath in such a way that its closed end is at the level of the middle of the bulb of the standard thermometer.

When a thermometer calibrated for partial immersion is used, care must be taken that it is immersed exactly to its immersion mark when the readings are taken.

Unless otherwise specified in the monograph, readings are taken of the temperature at which the substance is observed to collapse or form droplets on the wall of the tube and of the temperature at which it is completely melted as indicated by the disappearance of the solid phase. In case of instrumental detection, follow the instrument manufacturer’s requirements for the determination of the melting point.

To the temperature readings, add the correction for deviation of the standard thermometer. When thermometers calibrated for total immersion are used and partially immersed, also add to the readings of the standard thermometer the emergent-stem correction, which is obtained as follows:

Before starting the determination of the melting range, an auxiliary thermometer is attached so that the bulb touches the standard thermometer at a point midway between the graduation for the expected melting point and the surface of the heating material. When the substance has melted, the temperature is read on the auxiliary thermometer. The correction to be added to the temperature reading of the standard thermometer is calculated from the following formula:

$0.00015\ N(T-t)$

where $T$ is the temperature reading of the standard thermometer;

$t$ is the temperature reading of the auxiliary thermometer;

$N$ is the number of degrees of the scale of the standard thermometer between the surface of the heating material and the level of the mercury.

When needed, the emergent-stem correction for thermometers calibrated for partial immersion may be calculated from the same formula as above, but replacing $T$ by $T_s$, which is the mean temperature of the emergent-stem of the thermometer at the time of calibration.

Both the above-mentioned corrections for emergent-stem and any deviation of the standard thermometer may conveniently be replaced by calibration of the apparatus by means of the WHO Melting Point Reference Substances.

### System suitability

Carry out a system suitability test before the measurements, for example, by choosing a suitable reference material with a melting point close to that expected for the test substance.

### B. Determination of melting point of low melting solids

The melting point of fats, waxes, etc. is the corrected temperature at which the column of substance in the capillary tube becomes transparent or moves upwards, when tested by the method described below.

### Apparatus

A similar apparatus to the glass vessel with an appropriate liquid, as described under A for the determination of melting point and melting range of pulverizable substances, should be used with the following modifications:

water should be used in the heating vessel;

an accurately standardized thermometer should cover the range -10 to +100 °C; and

a glass capillary tube should be used, open at both ends, about 80 mm long, having an external diameter of 1.4 mm to 1.5 mm and an internal diameter of 1.0 mm to 1.2 mm.

### Recommended procedure

Unless otherwise specified in the monograph, melt the substance at as low a temperature as possible and then suck the liquid up to a height of about 10 mm in the capillary tube. Cool the charged tube at 10 °C or lower for 24 hours. If the monograph specifies that the melting point is to be determined without previous melting of the substance, charge the capillary tube by pushing it into the unmelted substance so that a column about 10 mm long is forced in. The determination may then be immediately carried out.

Attach the tube to the thermometer in the water bath by means of a rubber band or otherwise so that the lower end of the capillary tube is at the level of the middle of the bulb of the thermometer and the distance between the lower end of the capillary tube and the water level is about 20 mm. Heat the bath with constant stirring, the heating being regulated so that the temperature rises, at a temperature of 5 °C below the expected melting point, which is about 1 °C per minute.

### C. Qualification of the equipment

The qualification is carried out periodically according to the instrument manufacturer's requirements, using WHO Melting Point Reference Substances. These are selected to cover the temperature range that is used on the equipment. Use capillary tubes with the same dimensions as those used for sample measurement.

WHO Melting Point Reference Substances.

| Substance | Assigned melting point [1] |
|---|---|
| Biphenyl M.P. | 69.2 °C |
| Vanillin M.P. | 83.2 °C |

| | |
|---|---|
| Benzil M.P. | 95.9 °C |
| Acetanilide M.P. | 115.7 °C |
| Phenacetin M.P. | 136.0 °C |
| Benzanilide M.P. | 164.7 °C |
| Sulfanilamide M.P. | 165.9 °C |
| Sulfapyridine M.P. | 192.7 °C |
| Dicyanodiamide M.P. | 210.2 °C |
| Saccharin M.P. | 230.0 °C |
| Caffeine M.P. | 237.2 °C |
| Phenolphthalein M.P. | 263.1 °C |

[1] The exact melting points assigned to the substances can be found in the leaflets accompanying the standards.

These substances are available from the WHO collaborating host organization for International Chemical Reference Substances: European Directorate for the Quality of Medicines & HealthCare, 7 allée Kastner, CS 30026, F-67081 Strasbourg, France; fax: +33 (0)3 88 41 27 71 – for the attention of EDQM Sales Section; email: orders@edqm.eu; website: http://www.edqm.eu.