

Temperature Calibration Methods

Background

Before OptiMlet is put into operation for the first time, it must be calibrated using appropriate reference substances with melting points that are known exactly. In addition, the OptiMelt temperature calibration must be checked, and readjusted if necessary, every six months (minimum) to maintain the instrument within its factory-certified accuracy specifications.

A fresh calibration of the OptiMelt must be performed every 6 months.

Analytical quality control (QC) Laboratories, are required to test their melting point instrumentation on a regular basis, against Certified Reference Standards (CRSs), to determine the **acceptability** of their instruments according to specific QC requirements set forth by Local, National and International Standards and Pharmacopoeia Laboratories.

Temperature Calibration Methodology

Most modern melting point instruments include temperature calibration hardware and procedures to adjust their temperature readings. The calibration methodologies applied by commercial instruments can be divided into three main categories:

Method 1. Using a Calibration Bath

The thermometer is removed from the heating block and immersed in a liquid bath with a well known temperature (i.e. ice bath) . The temperature readings are adjusted to match the temperature of the bath. The thermometer is then reinserted into the heating block.

Method 2. Using a Reference Thermocouple and Electronic Thermometer.

A calibrated thermocouple or Pt/RTD thermometer is inserted into one of the sample slots of the heating block. The melting point apparatus is preheated to a fixed Start temperature. Once the requested Start temperature becomes stable, the readings from the calibrated thermometer are used to correct the temperature display of the instrument.

Method 3. Calibration with a Melting Point Standard

The melting point(s) of one or more CRSs are measured and then compared with their certified values. If the two sets of numbers (i.e. measured vs. expected) deviate from one another beyond the accuracy of the instrument the temperature scale is readjusted accordingly.

The aging of Pt/RTD resistor thermometers has been well documented in the engineering and scientific literatures and has been identified as the leading cause for loss of accuracy in most modern Melting Point (MP) instrumentation.

Calibration methods relying on the use of reference thermometers or calibration baths (**Methods 1 & 2**), though adequate for checking the temperature accuracy of the block's thermometer by itself, are static measurements that do not take into consideration the thermal lag between the thermometer and the capillary samples during the heating process.

Calibrating the temperature readings against CRSs (**Method 3**) accounts not only for drifts in the thermometer readings but also for the unique heat conducting properties of each metal-oven/capillary assembly. As a result, **Method 3** is the ONLY calibration method acceptable for the OptiMelt system. The calibration procedure listed in the OptiMelt's Operations Manual is the only methodology accepted by local, national and international pharmacopoeias for certification and determination of acceptability of melting point instrumentation. The calibration of the thermometer readings according to **Methods 1 & 2** is a convenient way to check the proper operation of the block's thermometer but does not lead to a certifiable calibration procedure according to GLP and GMP practices.

OptiMelt Calibration

Calibration of the OptiMelt is very straightforward: The melting points of three CRSs are measured and then compared with their certified values. If the two sets of numbers (measured vs. expected) deviate from one another beyond the accuracy of the instrument (i.e. $\pm 0.3^{\circ}\text{C}$ below 100°C , $\pm 0.5^{\circ}\text{C}$ below 250°C and $\pm 0.8^{\circ}\text{C}$ below 400°C), the readings are considered unacceptable and the temperature scale must be recalibrated.

Step-by-step calibration instructions and an option to correct the instrument's temperature scale (if necessary) at the end of the procedure are described in detail in the OptiMelt's Operations Manual.

A CRS Kit (SRS Part# O100MPS), traceable to International Pharmacopoeia standards, is available directly from Stanford Research Systems, Inc. and is recommended for calibration and for determination of acceptability.

For additional information on Pharmacopoeia requirements and CRSs, please download the application notes titled: "Pharmacopoeia vs Thermodynamic Melting Point Determinations" and "Melting Point Certified Reference Standards" from the www.thinkSRS.com website.