Developing and testing of a new balance for monitoring lyophilization in vials

4th ISL-FD International Conference
Dublin, Ireland 17-19th October 2007

Developing and testing of a new balance for monitoring lyophilisation in vials

Alberto Vallan, Marco Parvis,
Dipartimento di Elettronica, Politecnico di Torino;

Antonello A. Barresi, Valeria Rasetto
Dipartimento di Scienza dei Materiali e Ingegneria Chimica, Politecnico di Torino;
Corso Duca degli Abruzzi 24 – 10129 Torino, Italy; e-mail: antonello.barresi@polito.it

This new patented balance has been designed to be installed inside any freeze-dryer to monitor the lyophilization process and to determine in real time the end of the primary drying without interfering with the ongoing lyophilization process.

The balance can be placed in the vacuum chamber of a freeze dryer where it can weigh up to 15 of the vials which are being lyophilized. The weighed vials lay on the tray with all the other lyophilized vials during all the lyophilization process except for few seconds during the actual weighing so that the measurement can be considered representative of the whole batch. This represent a remarkable innovation with respect to other available monitoring approaches, which require either the removal of the vials via an air thigh duct or alter the thermal transfer on the weighed vials.

The balance has a range of 2 kg, a mass resolution of few milligrams and an uncertainty of few tens of milligrams over a wide temperature range (-40 °C, +40 °C). The balance is also equipped with auxiliary temperature probes (up to three thin thermocouples in the current version), which can be inserted inside the weighed vials to monitor the temperature within the liophilized substance during the process. A wireless transmission approach ensure the temperature probes do not affect the weigh measurement and the negligible sensor dimension make its effect on the liphilization process almost negligible thus ensuring the thermal measurement are representative of the complete process.

The balance has been tested in a pilot-scale freeze dryer (Lyobeta–Telstar), equipped with other control thermocouples, Pirani and Baratron pressure sensors and a mass spectrometer for the measurement of the composition of the chamber atmosphere

The experimental data have been obtained from various cycles carried out with batches composed of 50 to 700 vials, filled with a 10% w/w sucrose solution. The tests highlighted a good agreement between the trends of the measured mass and temperature. In particular, in correspondence of the increase of the product temperature at the end of primary-drying, the balance starts measuring an almost constant value of the weighed mass. This suggests that the final point of the sublimation phase could be detected just using the on-line measurement of the mass measured by the developed balance.

A very good agreement was also observed with the estimation of the sublimation front carried out using our Dynamic Parameter Estimator method, and advanced tool derived from classic manometric temperature measurement.