# Certification of Microcrystalline Cellulose as a humidity reference for gravimetric DVS instruments

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**Application Note 18-02**

## Introduction

The need for a reference material of known and reliable sorption properties was recognized and described first in the European COST 90 project on physical properties of foods [1]. Following the recommendations of the COST 90 project, microcrystalline cellulose (MCC) was made available as a BCR certified reference material in subsequent studies by the Institute for Reference Materials and Measurements IRMM in 1993 [2].

The reference material CRM 302 became a standard for the validation of the humidity calibration of gravimetric water sorption instruments. In 2015, the distribution of the CRM 302 was discontinued. A new MCC reference material was made available, certified as a ProUmid factory standard.

Frequent humidity validation of DVS instruments, using a certified reference material for precise and reliable validation results is highly recommended.

## Microcrystalline cellulose

Microcrystalline cellulose (MCC) is widely used in pharmaceutical applications primarily as a binder or diluent in tablet or capsule formulations. Furthermore, it is also used in cosmetics and food technology.

MCC is an almost white, free flowing fine or granular powder consisting of porous particles. The typical particle size ranges between 20 µm and 300 µm.

Fig. 1: Microcrystalline cellulose bottled in 2 ml vials for certification.

Various grades of MCC are available which differ in particle size, moisture content and field of application.

Although a hygroscopic substance, MCC is considered stable when stored in tightly closed containers under dry and cool conditions. It is generally regarded as a relatively non-toxic and non-irritant material [3].

For certification, bulk cellulose was mixed and bottled into 2 ml glass vials with each vial containing 500 mg of MCC (Fig. 1). Climatic conditions during filling operation were kept between 20 °C - 22 °C and 35 % - 45 % RH at all times.

## Certification method

The certification of the MCC was achieved in three steps:

- Homogeneity study to verify the reliability and repeatability of the generated sorption data.
- Stability study to ensure a certain shelf-life of the reference material.
- Round robin test for the certification of the microcrystalline cellulose.

All measurements were done using ProUmid DVS instruments following a standard procedure.

## Standard Measurement procedure

Humidity cycle settings:

- Sorption from 0 % to 90 % RH, 9 steps, at 25°C
- Desorption from 80 % to 0 % RH, 8 steps, at 25°C

Sample preparation:

- 5 samples per test, each 100 mg MCC
- Preparation of a thin layer of MCC in each sample pan
- Preconditioning at 3.0 % RH for 1 hour after RH has settled to 3.0 %
- Initial weighing of the samples, start of measurement.

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## Homogeneity study

The bulk MCC used for this study is produced from pharmaceutical grade wood pulp under strict quality requirements and is considered to be intrinsically homogeneous. The homogeneity of the bottled material was tested by means of moisture sorption analysis. No evidence for inhomogeneities from the bottling procedure between vials or within a vial was found.

## Stability study

MCC samples were stored under three typical lab storage conditions:

- Constant ambient (lab cupboard), 21 °C - 25 °C, protected from light.
- Changing ambient (window bench), 18 °C - 30 °C, frequent exposure to direct sunlight.
- Refrigerator, 4 °C - 7 °C, protected from light.

No evidence of a significant change in the water sorption properties of the MCC material for the three storage conditions was observed over the test period of 150 weeks. Therefore, only a general recommendation to store the material at dry and cool ambient conditions is given for the MCC reference.

## Round Robin test

For the certification of the MCC to be used as a reference material, first, 10 sets of results were generated in the ProUmid lab. Each set consisted of 5 replicates whereas MCC material from one vial per sample was used. The mean values out of this test series were then validated in a round robin test with 10 participating European laboratories.

The certified water contents and their uncertainties (99.5 % confidence intervals) at 25 °C are summarized in Tab. 1.

Tab. 1: Certified equilibrium water content based on 3 % RH and 25 °C (valid for MCC batch no. 5611262924)

| RH in % | Cycle | Equilibrium water content in dm% | |
|---|---|---|---|
| | | Mean value | Uncertainty |
| 10 | sorption | 0.995 | 0.078 |
| 20 | | 1.910 | 0.090 |
| 30 | | 2.716 | 0.111 |
| 40 | | 3.564 | 0.098 |
| 50 | | 4.515 | 0.123 |
| 60 | | 5.610 | 0.130 |
| 70 | | 6.934 | 0.170 |
| 80 | | 8.721 | 0.209 |
| 90 | | 11.623 | 0.260 |
| 80 | desorption | 9.929 | 0.186 |
| 70 | | 8.197 | 0.188 |
| 60 | | 6.813 | 0.168 |
| 50 | | 5.644 | 0.140 |
| 40 | | 4.592 | 0.117 |
| 30 | | 3.610 | 0.115 |
| 20 | | 2.645 | 0.067 |
| 10 | | 1.434 | 0.085 |

The usage of the MCC reference for humidity validation, with special emphasis on validation parallel to a regular measurement without the need of running a time consuming separate validation test, is described in Application Note 18-03.

## References


[1] W. E. L. Spiess and W. R. Wolf, Results of the COST 90 project on water activity, Physical properties of foods/edited by R. Jowitt et al.(1983).

[2] R. Jowitt and P. J. Wagstaffe, The certification of the water content of microcrystalline cellulose (MCC) at 10 water activities – CRM 302, EC 12429. (1989).

[3] Raymond C. Rowe, Paul J. Sheskey and M. E. Quinn, Handbook of pharmaceutical excipients–7th edition, Pharm. Dev. Technol. 18 (2013): 544.