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LOSS ON DRYING

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1. PURPOSE

To describe the method for determining the percentage loss on drying. This method is compliant with the current EP and USP.

2. SCOPE

This test method is applicable to Mannitol, empty Gelatin capsules and empty Hypromellose (HPMC) capsules.

3. ASSOCIATED DOCUMENTS

• FM-105 Loss on Drying Test Record

4. REFERENCED DOCUMENTS

- ELB-074 Issue of QC Laboratory Forms (QA Issue)
- FM-010 On the Job Training Record
- SOP-021 Document Control Procedure
- SOP-047 Balances and Certified Masses
- SOP-066 Sample Handling Procedure
- SOP-087 General Laboratory Procedure
- SOP-125 Use of Laboratory Ovens
- SOP-208 QC Laboratory Trending Procedure
- SOP-221 Annual Product Quality Reviews

5. **DEFINITIONS**

Term	Definition	
Dried to Constant Weight	Two consecutive weighings do not differ by more than 0.5mg. The second weighing is following an additional period of drying. (As described in the EP and USP).	

Term	Definition
Specified Time Method	The sample is dried for a specified time.
Desiccant	Chemical agent that absorbs water. In this case the desiccant is Self–Indicating Silica Gel.
LOD	Loss On Drying
НРМС	Hydroxypropyl Methylcellulose (or hypromellose)

6. SAFETY

- 6.1 All appropriate safety precautions should be taken when working in the laboratory.
- 6.2 A lab coat and safety glasses should be worn at all times.
- 6.3 Oven proof gloves are supplied and must be worn when removing or depositing items from the oven. Nitrile gloves are to be worn during weighing.

7. EQUIPMENT AND REAGENTS

- 7.1. Loss On Drying Containers (Bottles) Stainless Steel containers are used in LOD testing. Duplicate results should be performed in the same LOD Container type.
- 7.2. Fan Assisted Oven Ensure that the oven is with calibration for use at 105°C in accordance with SOP-125.
- 7.3. Balance Use a balance with at least 4 decimal places.
- 7.4. Calibrated Timer
- 7.5. Temperature / Humidity Meter

8. **PROCEDURE (Perform in Duplicate)**

- 8.1. GENERAL
 - 8.1.1. Loss on Drying testing is to documented on FM-105 Loss on Drying Test Record. Each copy of the form is to be issued in accordance with ELB-074 Issue of QC Laboratory Forms (QA Issue) prior to use.

8.2. SAMPLE PREPARATION

8.2.1. Wear nitrile gloves when handling loss on drying bottles and lids, heatproof Cotton gloves are supplied for handling hot items.



- 8.2.2. The oven is to be set at $105^{\circ}C \pm 2^{\circ}C$. Ensure the daily temperature check has been performed on the oven as per SOP-125.
- 8.2.3. Label the weighing bottle and lid and dry for at least 30 minutes in the oven.
- 8.2.4. Remove the bottle and lid from the oven and place into a desiccator containing desiccant.
- 8.2.5. Allow to equilibrate for 30 minutes to room temperature.
- 8.2.6. Tare the balance and weigh both the bottle and lid and record. DO NOT TARE THE BALANCE AFTERWARDS.
- 8.2.7. Remove the lid and add the required amount of the sample under evaluation (as detailed below) to the bottle. Replace the lid and record the weight.
 - $1.000g \pm 10\%$ for Mannitol
 - 1 to 2g for Gelatin Capsules
 - 1 to 2g for Hypromellose (HPMC) Capsules
- 8.2.8. Ensure an even distribution of the sample by gently shaking the bottle from side to side. The depth should be no more than 10mm.
- 8.2.9. Place the bottle in the oven, remove the lid and also place it in the oven.
- 8.3. DRIED TO CONSTANT WEIGHT METHOD
 - 8.3.1. After 3 hours place the cover onto the bottle and remove from the oven and place into a desiccator containing desiccant.
 - 8.3.2. Allow to equilibrate for 30 minutes to room temperature.
 - 8.3.3. Weigh the bottle with the lid and record the weight (Tare the balance beforehand).
 - 8.3.4. Place the bottle and the lid back in oven with the lid removed for an additional hour.
 - 8.3.5. Remove from oven, place in a desiccator containing desiccant and repeat steps 8.3.2 to 8.3.4 until there is no more than 0.0005g difference in the weights between any two samples.
 - 8.3.6. Calculate the percent LOD as per section 9.

8.4. SPECIFIED TIME METHOD

Table	84	Sne	cified	Drving	Times
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Sample Description	Time Specified	Temperature (°C)
Mannitol	4 hours	105
Empty Gelatin Capsules (from Capsugel)	4 hours	105
Empty HPMC Capsules (from Capsugel)	4 hours	105

- 8.4.1. After the specified amount of hours (refer to table 8.4 above) place the cover onto the bottle and remove from the oven and place into a desiccator containing desiccant.
- 8.4.2. Allow to equilibrate for 30 minutes to room temperature.
- 8.4.3. Weigh the bottle and lid and record the weight.
- 8.4.4. Calculate the percentage LOD as per section 9.

9. CALCULATIONS

 $%LOD = (W_{S} - W_{D}) \times 100$ (Ws - W_C)

Where:

 W_S = container weight + sample weight W_D = container weight plus dry sample weight W_C = container weight

10. TRENDING

- 10.1. Trending of Loss On Drying results is to be performed in accordance with the current version of SOP-208 QC Laboratory Trending Procedure.
- 10.2. The current Loss On Drying trending data file is saved at the following file path:

P:\Manufacturing\QC Trending\Loss On Drying

The file name for the Loss On Drying trending is 'Loss On Drying Testing Data XXXX to Current' where XXXX is the year the earliest testing in the file was performed.

Note: The data file size should be reviewed at the end of each year, and if required, should be renamed 'Loss On Drying Testing Data XXXX to XXXX' and a new file created for the next year to current.

- 10.3. The trending data file is a protected Microsoft Excel file. The Excel function 'Allow users to Edit Ranges' is used to allow entry of new data. The data entry cells will be reviewed by the QC Laboratory Coordinator or delegate periodically to ensure security of data.
- 10.4. Refer to SOP-221 for requirements for review of Loss on Drying data for QC test samples and refer to relevant Test Protocols for requirements for review of data for development and stability samples.

11. QUALITY RECORDS

- 11.1. FM-105 is to be used to record and report the results.
- 11.2. Use of the laboratory oven is to be recorded in the relevant oven usage logbook.
- 11.3. All test records are to be retained in accordance with the current version of SOP-021.
- 11.4. Training for Loss on Drying testing is to be performed using FM-010 On the Job Training Record.

Version	Date Effective	Section	Description and Rationale
		2, 5 &	Updated to include Hypromellose (HPMC) capsules
		8.2.7	added as per change request OPS-23-015.
		7.5	Temperature/Humidity Datalogger updated to
			Temperature/Humidity Meter as these are now used for
8	02-Jun-23		measurement of laboratory conditions (as per CAR
			939).
			Correct spelling mistake and updated to include
		8.4	Hypromellose (HPMC) capsules added as per change
			request OPS-23-015.
		All	Document updated to use current version of controlled
			template (TE-006-03) in accordance with document
			control procedure requirements.
		1	Statement added to note that the method is compliant to
			EP and USP
		4	ELB-074, FM-010, SOP-066 and SOP-221 added to the
7	15-Dec-21		list of Referenced Documents as needed. FM-183
			removed as this form has been made obsolete.
		6	Safety requirement for appropriate PPE is added, as
			required in handling hot surfaces
		7.1	The use of Stainless Steel Containers is specified as per
			CM-18-011-01 and CAR 634. Added '(Bottles)' as both
			names may be used.

12. CHANGE HISTORY

TM-015-08

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Version	Date Effective	Section	Description and Rationale
		7.2	Added detail that oven is to be calibrated at usage temperature as ovens may be used at different temperatures as per SOP-125.
		8.1	New section added to detail requirement for issue of test form prior to testing.
7	15 Dec 21	8.1.1	Nitrile gloves Specified.
	15-Dec-21	10.4	Reference to FM-183 replaced with SOP-221 as trending of QC data is performed in accordance with the Annual Product Quality Review procedure.
		11.2	Added information to detail requirement to record oven usage in relevant logbooks.
		11.4	Added requirements for training in Loss on Drying.
6	12-Jan-16	8.1.7	Weight to be used for Mannitol testing narrowed in line update of the Mannitol monograph in the USP38.
		4	FM-183 and SOP-208 added to Referenced Documents due to the addition of trending requirements.
		5	Added USP to Dried to Constant Weight definition as this definition is consistent with USP.
5	$05 - \Lambda pr - 12$	7	Added data logger to Equipment section.
5	03-Apr-12	8.2.4	Changed "minimum of 1 hour" to "an additional hour" to be consistent with USP 35/NF 30 Supplement 1 (refer to CR#410).
		10	Added section to describe the trending requirements for Loss On Drying Testing.
4	4 10-Sep-09	4	Changed SOP-099 to SOP-047 as Balance SOP has been updated with a new document number. Also added SOP-125 Use of Laboratory Ovens.
		8.11	Added Table for Specified Drying Times to ensure analysts know the drying time for each sample tested.
		All	Changed formatting to comply with SOP-021
3	01-Mar-09	4	Added section Referenced Documents in accordance with SOP-021
		5	Removed Balance from definitions as the balance required is stated in Equipment section.
		7	Added section Equipment and Reagents to detail the equipment required to perform the test.
		10	Records to be kept for 20 years unless the material is used for clinical trials where it should be kept for 25 years as per SOP-021.
		11	Added section Change History to record all changes made to the document.

END OF DOCUMENT