
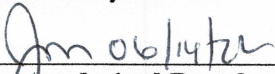
	Standard Operating Procedure		SOP Number D-725	Revision 6
	Loss on Drying		Effective Date 06/29/22	Page Page 1 of 6
Written by/ Date  06/08/22		Reviewed by/ Date SAS 06/08/22		Approved by/ Date  06/14/22
Title: QC Laboratory Director		Title: Analytical Development Scientist		Title: Analytical Development Manager

1.0 Purpose

The purpose of this procedure is to define the process used for the determination of volatile chemical loss during drying under a specified set of conditions.

2.0 Scope

This procedure applies to the determination of loss on drying as a percentage of weight for powder samples. This procedure follows Loss on Drying USP<731> guidelines. Unless otherwise noted in a monograph or pharmacopeia, LOD should only be performed on solids whose melting point is above the temperature used for drying. Other forms of moisture determination should be used when this is not the case.

3.0 Responsibility

- 3.1 It is the responsibility of QC and Analytical Chemists to follow this procedure.
- 3.2 It is the responsibility of QC Laboratory Management to implement this procedure and to ensure that the procedure is being followed.
- 3.3 It is the responsibility of QC Laboratory and/or Analytical Development Management to keep this procedure current with latest Ion Labs practices.

4.0 Definitions

- 4.1 **LOD** – Loss on Drying
- 4.2 **QC** – Quality Control

5.0 References

- 5.1 D-725-F1, Form, LOD Test Record
- 5.2 D-725-F2, Form, Halogen Moisture Analyzer Test Record
- 5.1 USP<731>, Method, Loss on Drying

6.0 Procedure

- 6.1 Equipment
 - 6.1.1 VWR Symphony™ Vacuum oven or equivalent
 - 6.1.2 Mettler Toledo Halogen Moisture Analyzer HE73 or equivalent
 - 6.1.3 ¼ HP vacuum pump
 - 6.1.4 Analytical Balance
 - 6.1.5 Temperature probe
- 6.2 Supplies
 - 6.2.1 30mL 34/12 Kimax Weigh Bottle or equivalent
 - 6.2.2 Watch Glass, 12.5cm diameter
 - 6.2.3 Mettler Toledo SmartCal Sachets
 - 6.2.4 Aluminum Sample Pans
- 6.3 Testing – Drying Oven

Note: If a monograph is available to give conditions for testing LOD for a material then the monograph conditions supersede Ion Labs standard conditions.

- 6.3.1 Equilibrate the oven to 105°C or appropriate temperature. Use a calibrated digital thermometer to confirm temperature of oven.
- 6.3.2 If the melting point of the sample is below 105°C then adjust temperature 5 to 10°C below the melting point.
- 6.3.3 Dry a clean watch glass or Weigh Bottle before adding sample.
- 6.3.4 Weigh a clean and dry watch glass or weigh bottle on the analytical balance.
- 6.3.5 Print the tare weight of the watch glass or weigh bottle.
- 6.3.6 Mix the substance to be tested and, if it is in the form of large particles, reduce the particle size to about 2 mm by crushing before weighing. Apply a 1 to 2 g test sample to the tared container.
- 6.3.7 By gentle, sidewise shaking, distribute the test specimen as evenly as practicable to a depth of about 5 mm generally, and NMT 10 mm in the case of low bulk density materials.
- 6.3.8 Print the sample weight.
- 6.3.9 The weight of the tare and sample is the initial weight.
- 6.3.10 Place the open container holding sample into a pre-equilibrated oven.
- 6.3.11 If necessary, apply 20 +/- 4 inches of vacuum and dry for 2 hours. Once vacuum is applied, ensure oven temperature is at testing conditions.
- 6.3.12 After allotted time, be sure to cap samples to keep them from drawing moisture from the air and move the sample to a desiccator to cool for 20 minutes or until the sample has equilibrated to room temperature. Use caution when moving samples as they may be hot. Weigh the sample again after cooling. This is the final weight of container and sample.
- 6.3.13 Print the final container and sample weight.

6.3.14 The % LOD is determined by the following equation:

$$\%LOD = \frac{\text{initial weight} - \text{final weight}}{\text{sample weight}} \times 100\%$$

6.3.15 Record results on Form D-725-F1 LOD Test Record.

6.4 Cautionary Measures when using a drying oven

6.4.1 Cautionary measures should be taken when drying multiple samples concurrently.

6.4.2 A recommended maximum of 10 samples should be dried in the oven at the same time.

6.4.3 Care should be taken when drying samples with higher moisture content with those containing lower moisture contents and hygroscopic in nature.

6.5 Testing – Halogen Moisture Analyzer

6.5.1 Monthly Check

6.5.1.1 Level Instrument.

6.5.1.2 Place empty sample pan into the sample pan handler. Place sample pan handler into the draft shield, ensuring the tongue of the sample pan handler lies exactly in the slot of the draft shield. The pan must lie flat in the pan holder.

6.5.1.3 Close lid. The instrument will tare automatically.

6.5.1.4 Remove a SmartCal stick from blister pack, open and distribute contents evenly over the sample pan. Close lid.

6.5.1.5 Press menu and select “CAL”. In “CAL” menu, select “S.CAL”.

6.5.1.6 Set temperature that closely matches the preferred application.

Confirm entry with the backwards arrow button.

6.5.1.7 Compare the test results to the below table and evaluate whether the result meets the control limits

Drying Temperature (°C)	SmartCal Control Limits
70	3.2 - 4.4%
100	5.2 - 6.4%
130	7.4 - 8.8%
160	9.9 - 11.7%

6.5.1.8 Capture monthly check in instrument logbook/ notebook.

6.5.1.9 If the test falls outside of the above control limits, take the following measures:

6.5.1.9.1 After instrument has cooled down, repeat the test and ensure all steps have been carried out correctly.

6.5.1.9.2 If the failure persists, perform a temperature and weight adjustment and perform an additional SmartCal test.

6.5.1.9.3 If the result continues to fail, reference Troubleshooting guide in instrument manual.

6.5.2 Performing a simple measurement

6.5.2.1 Let instrument warm up for one hour.

6.5.2.2 Place empty sample pan into the sample pan handler. Place sample pan handler into the draft shield, ensuring the tongue of the sample pan handler lies exactly in the slot of the draft shield. The pan must lie flat in the pan holder.

6.5.2.3 Close lid. The instrument will tare automatically.

6.5.2.4 Open lid and place specimen into sample pan. A minimum of 0.5 grams of sample is required. Ensure the sample is distributed evenly to

obtain good analysis results.

6.5.2.5 Close the heating module lid. The drying and measuring process starts automatically.

6.5.2.6 Results will automatically print.

6.5.2.7 Capture results on Form D-725-F2 Halogen Moisture Analyzer Test Record.

7.0 Revision History

Revision	Date	Description of Changes	CCR #	By
0	10/05/10	New procedure.	-	-
1	01/26/12	Updated SOP format	-	-
2	02/21/13	Reformatted	-	-
3	08/28/13	Two forms added, updated instrument and supply information, more detailed instruction on use of the vacuum oven and electronic moisture analyzer, removed USP <921> references	13-764	B. Johns
4	01/05/16	Biennial review: Reformatted SOP. Removed electronic moisture analyzer instructions and form. Added use of temperature probe. Added tolerances.	16-0023	N. Zhang
5	02/04/19	Scheduled review: updated responsibilities, fixed typos, clarified areas	19-0117	J. Maignan
6	06/06/22	Update to reflect current practices. Added additional instruction to incorporate Halogen Moisture analyzer. Updated logo and format.	CC-22-0159	J. Sassman

**LOD Test Record**

Form: D-725-F1

CCR No. CC-22-0159

Revision: 4

Sample Prep

Sample Name:

Sample Batch/ lot Number:

Test Date:

Equipment

Balance ID #:

Oven ID #:

Thermometer ID #:

Data / Parameters

Container Weight (g):

Sample Weight (g):

Final Weight (g):

Run Time:

Operating Temp (+/-2°C):

Pressure (20 inHg +/-4):

Cooling (Desiccator) Time:

Notebook Reference:

% LOD:

$$\frac{(\text{Initial Weight} - \text{Final Weight})}{\text{Sample Weight}} \times 100$$

% LOD:

Specifications:

Determination (circle one):

Pass**Fail**

Comments:

Performed By/Date: _____

Reviewed By/Date: _____



Halogen Moisture Analyzer Test Record

Form: D-725-F2

CCR No. CC-22-0159

Revision: 0

Sample Prep

Sample Name:

Sample Batch/ lot Number:

Test Date:

Equipment

Analyzer ID #:

Date last monthly check performed/
Notebook and page reference:

Analyzer Result Tape:

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% Moisture:

Specifications:

Determination (circle one):

Pass

Fail

Comments:

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Performed By/Date: _____

Reviewed By/Date: _____