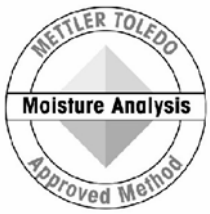
Application Datasheet

METTLER TOLEDO

Moisture Solutions for Pharma

Moisture Method Collection for Pharma Excipients



This document outlines ten moisture methods for pharmaceutical excipients, developed by METTLER TOLEDO. Based on cross-validation they enable you to obtain the same moisture results with HR83 as with the drying oven, but much faster, easier and still fully pharmacopeia-compliant.

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Content

Moisture Method Collection for Pharma Excipients

Exemplary Cross-Validation Graph for Ethyl Cellulose 3

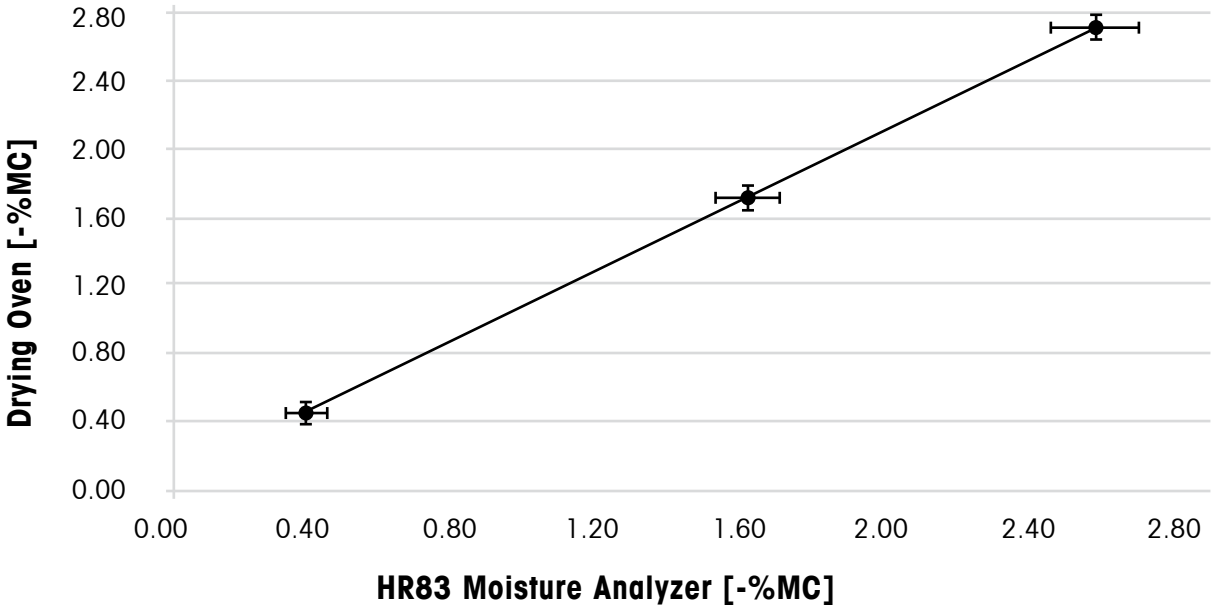
Moisture Determination Methods for:

Aerosil 200 Pharma 4
Avicel PH101 5
Corn Starch 6
Ethyl Cellulose 7
Gelatin 8
Hypromellulose 9
Lactose monohydrate 10
Magnesium Stearate 11
Sodium Saccharin 12
Talc 13

Disclaimer

We carefully tested this method with a METTLER TOLEDO Halogen Moisture Analyzer. However, you should still personally test the information in the application data sheet for its suitability to your intended purpose. Because the use and transfer of an application example are beyond our control, we cannot accept responsibility for this. The general safety rules and precautions of the manufacturer (e.g. for chemicals or solvents) must be observed.

Exemplary Cross-Validation Graph for Ethyl Cellulose



From the exemplary cross-validation graph it becomes evident that moisture results, obtained by applying the moisture method to HR83, excellently match the results of the drying oven for a given substance at different moisture contents. Therefore, the drying oven can be replaced by HR83. Standard deviations of HR83 are within typical tolerances - but results up to 10x faster.

Short explanation concerning the HR83 results:

Two different methods can be used on HR83 to match the drying oven results.
The Standard Method according the Pharma reference customer is based on the same temperature as the drying oven (defined in pharmacopeias) and switch-off criterion 5 (weight loss per unit of time < 1mg/140s). It is FDA audit proven. In the time-optimized method temperature and switch-off criterion were optimized to further reduce analysis time.

Moisture Determination Method for Aerosil 200 Pharma

Description of sample

Synthetic amorphous silicon dioxide, pharma grade from Degussa
Blueish-white powder with very low bulk density

Reference method: Oven

Sample preparation / procedure

Pre-dry weighing bottles with glass lids (at oven temperature) and leave to cool in the desiccator. Weigh 1 g of the sample material into each weighing bottle. Start drying the samples at 145° C in the oven. Remove the contents after the time specified in the pharmacopeia has elapsed, leave to cool in the desiccator, and weigh.
Literature: USP28-NF23 page 3073: NF monograph "Silcon dioxide"

Results (oven)				
Sample weight:	1	[g]		
Drying temperature and time	145	[°C]	4	[hour(s)]
Moisture content (average of 6 measurements)	1.37	[%]	± 0.11	[%]

Moisture determination using the HR83 Halogen Moisture Analyzer

Sample preparation / procedure

Set the HR83. Tare aluminium sample pan. Use a spoon to add the sample to the pan and distribute it evenly by gently shaking the pan. Start the drying process.

Results (HR83 Halogen Moisture Analyzer)

Standard Method according Pharma reference customer				
Sample weight (± 10%):	1	[g]		
Drying program	Standard drying			
End temperature	145	[°C]		
Switch-off criterion	5			
Moisture content (average of 6 measurements)	1.48	[%]	± 0.24	[%]
Measuring time (average of 6 measurements)	3	[min]		

Time-optimized method				
Sample weight (± 10%):	1	[g]		
Drying program	Standard drying			
End temperature	145	[°C]		
Switch-off criterion	3			
Moisture content (average of 6 measurements)	1.50	[%]	± 0.14	[%]
Measuring time (average of 6 measurements)	1:20	[min]		

Moisture Determination Method for Avicel PH101

Description of sample

Microcrystalline cellulose pharma grade, from FMC Biopolymers
White powder

Reference method: Oven

Sample preparation / procedure

Pre-dry weighing bottles with glass lids (at oven temperature) and leave to cool in the desiccator. Weigh 1 g of the sample material into each weighing bottle. Start drying the samples at 105° C in the oven. Remove the contents after the time specified in the pharmacopoeia has elapsed, leave to cool in the desiccator, and weigh. Literature: USP28-NF23 page 2982: NF monograph "Microcrystalline cellulose"

Results (oven)				
Sample weight:	1	[g]		
Drying temperature and time	105	[°C]	3	[hour(s)]
Moisture content (average of 6 measurements)	4.64	[%]	± 0.06	[%]

Moisture determination using the HR83 Halogen Moisture Analyzer

Sample preparation / procedure

Set the HR83. Tare the aluminium sample pan. Use a spoon to add the sample to the pan and distribute it evenly by gently shaking the pan. Start the drying process.

Results (HR83 Halogen Moisture Analyzer)

Standard Method according Pharma reference customer				
Sample weight (± 10%):	2,5	[g]		
Drying program	Standard drying			
End temperature	105	[°C]		
Switch-off criterion	5			
Moisture content (average of 6 measurements)	4.79	[%]	± 0.04	[%]
Measuring time (average of 6 measurements)	6	[min]		

Time-optimized method				
Sample weight (± 10%):	2,5	[g]		
Drying program	Standard drying			
End temperature	105	[°C]		
Switch-off criterion	3			
Moisture content (average of 6 measurements)	4.74	[%]	± 0.06	[%]
Measuring time (average of 6 measurements)	4	[min]		

Moisture Determination Method for Corn Starch

Description of sample

Corn starch, pharma grade
White powder

Reference method: Oven

Sample preparation / procedure

Pre-dry weighing bottles with glass lids (at oven temperature) and leave to cool in the desiccator. Weigh 1 g of the sample material into each weighing bottle. Start drying the samples at 130° C in the oven. Remove the contents after the time specified in the pharmacopeia has elapsed, leave to cool in the desiccator, and weigh. Repeat the process until mass constancy is achieved.
Literature: USP28-NF23 page 3088: NF Monograph "Corn Starch"

Results (oven)				
Sample weight:	1	[g]		
Drying temperature and time	130	[°C]	1.5	[hour(s)]
Moisture content (average of 6 measurements)	11.47	[%]	± 0.05	[%]

Moisture determination using the HR83 Halogen Moisture Analyzer

Sample preparation / procedure

Set the HR83. Tare aluminium sample pan. Use a spoon to put the sample in the pan then distribute it evenly by gently shaking the pan, and weigh. Start the drying process.

Standard Method according Pharma reference customer				
Sample weight (± 10%):	3	[g]		
Drying program	Standard drying			
End temperature	130	[°C]		
Switch-off criterion	5			
Moisture content (average of 6 measurements)	11.81	[%]	± 0.05	[%]
Measuring time (average of 6 measurements)	8:20	[min]		

Time-optimized method				
Sample weight (± 10%):	3	[g]		
Drying program	Standard drying			
End temperature	120	[°C]		
Switch-off criterion	3			
Moisture content (average of 6 measurements)	11.50	[%]	± 0.07	[%]
Measuring time (average of 6 measurements)	7:20	[min]		

Moisture Determination Method for Ethyl Cellulose

Description of sample

Ethyl cellulose Ph Eur from Fluka, viscosity: 10.0 mPa·s
White to cream-white granulates

Reference method: Drying Oven

Sample preparation / procedure

Pre-dry weighing bottles with glass lids (at oven temperature) and leave to cool in the desiccator. Weigh 1 g of the sample material into each weighing bottle. Start drying the samples at 105° C in the oven. Remove the contents after the time specified in the pharmacopeia has elapsed, leave to cool in the desiccator, and weigh.
Literature: USP28-NF23 page 1745

Results (oven)				
Sample weight:	1	[g]		
Drying temperature and time	105	[°C]	2	[hour(s)]
Moisture content (average of 6 measurements)	1.68	[%]	± 0.01	[%]

Moisture determination using the HR83 Halogen Moisture Analyzer

Sample preparation / procedure

Set the HR83. Tare aluminium sample pan. Use a spoon to add the sample to the pan and distribute it evenly by gently shaking the pan. Start the drying process.

Standard Method according Pharma reference customer				
Sample weight (± 10%):	3	[g]		
Drying program	Standard drying			
End temperature	105	[°C]		
Switch-off criterion	5			
Moisture content (average of 6 measurements)	1.68	[%]	± 0.03	[%]
Measuring time (average of 6 measurements)	6:30	[min]		

Time-optimized method				
Sample weight (± 10%):	3	[g]		
Drying program	Standard drying			
End temperature	120	[°C]		
Switch-off criterion	F (1mg/65 sec)			
Moisture content (average of 6 measurements)	1.68	[%]	± 0.06	[%]
Measuring time (average of 6 measurements)	4:30	[min]		

Moisture Determination Method for Gelatin

Description of sample

Gelatin Ph Eur from Fluka
Yellow-brownish granulate

Reference method: Oven

Sample preparation / procedure

Pre-dry weighing bottles with glass lids (at oven temperature) and leave to cool in the desiccator. Weigh 1 g of the sample material into each weighing bottle. Start drying the samples at 105° C in the oven. Remove the contents after the preset time has elapsed, leave to cool in the desiccator, and weigh. Repeat the process until mass constancy is achieved.
Literature: European pharmacopeia 5.02 page 1652: "Gelatin" monograph

Results (oven)				
Sample weight:	1	[g]		
Drying temperature and time	105	[°C]	2	[hour(s)]
Moisture content (average of 6 measurements)	11.57	[%]	± 0.03	[%]

Moisture determination using the HR83 Halogen Moisture Analyzer

Sample preparation / procedure

Set the HR83. Tare aluminium sample pan. Use a spoon to put the sample in the pan then distribute it evenly by gently shaking the pan, and weigh. Start the drying process.

Results (HR83 Halogen Moisture Analyzer)

Standard Method according Pharma reference customer				
Sample weight (± 10%):	4	[g]		
Drying program	Standard drying			
End temperature	105	[°C]		
Switch-off criterion	5			
Moisture content (average of 6 measurements)	11.37	[%]	± 0.06	[%]
Measuring time (average of 6 measurements)	30	[min]		

Time-optimized method				
Sample weight (± 10%):	4	[g]		
Drying program	Rapid drying			
End temperature	130	[°C]		
Switch-off criterion	3			
Moisture content (average of 6 measurements)	11.63	[%]	± 0.07	[%]
Measuring time (average of 6 measurements)	8	[min]		

Moisture Determination Method for Hypromellose

Description of sample

Hypromellose from Sigma-Aldrich
White powder

Reference method: Oven

Sample preparation / procedure

Pre-dry weighing bottles with glass lids (at oven temperature) and leave to cool in the desiccator. Weigh 1 g of the sample material into each weighing bottle. Start drying the samples at 105° C in the oven. Remove the contents after the preset drying time has elapsed, leave to cool in the desiccator, and weigh. Repeat the process until mass constancy is achieved.

Literature: USP28-NF23 page 989: USP monograph "Hypromellose"
European Pharmacopeia 5.2 page 1780: Ph Eur monograph "Hypromellose"

Results (oven)				
Sample weight:	1	[g]		
Drying temperature and time	105	[°C]	2	[hour(s)]
Moisture content (average of 6 measurements)	3.42	[%]	± 0.03	[%]

Moisture determination using the HR83 Halogen Moisture Analyzer

Sample preparation / procedure

Set the HR83. Tare aluminium sample pan. Use a spoon to add the sample to the pan and distribute it evenly by gently shaking the pan. Start the drying process.

Standard Method according Pharma reference customer				
Sample weight (± 10%):	2	[g]		
Drying program	Standard drying			
End temperature	105	[°C]		
Switch-off criterion	5			
Moisture content (average of 6 measurements)	3.45	[%]	± 0.06	[%]
Measuring time (average of 6 measurements)	3	[min]		

Time-optimized method				
Sample weight (± 10%):	2	[g]		
Drying program	Standard drying			
End temperature	130	[°C]		
Switch-off criterion	3			
Moisture content (average of 6 measurements)	3.44	[%]	± 0.07	[%]
Measuring time (average of 6 measurements)	1.5	[min]		

Moisture Determination Method for Lactose monohydrate

Description of sample

Lactose monohydrate, Ph Eur from Fluka
White powder

Reference method: Oven

Sample preparation / procedure

Pre-dry weighing bottles with glass lids and leave to cool in the desiccator. Weigh approx. 1 g of the sample material into each weighing bottle. Start drying the samples at 80° C in the oven. Remove the contents after the time specified in the pharmacopeia has elapsed, leave to cool in the desiccator, and weigh.
Literature: USP28-NF23 page 3024: NF Monograph "Lactose Monohydrate"

Results (oven)				
Sample weight:	2	[g]		
Drying temperature and time	80	[°C]	2	[hour(s)]
Moisture content (average of 6 measurements)	0.06	[%]	± 0.03	[%]

Moisture determination using the HR83 Halogen Moisture Analyzer

Sample preparation / procedure

Set the HR83. Tare the aluminium sample pan. Use a spoon to add the sample to the pan and distribute it evenly by gently shaking the pan. Start the drying process.

Results (HR83 Halogen Moisture Analyzer)

Standard Method according Pharma reference customer				
Sample weight (± 10%):	5	[g]		
Drying program	Standard drying			
End temperature	80	[°C]		
Switch-off criterion	5			
Moisture content (average of 6 measurements)	0.12	[%]	± 0.02	[%]
Measuring time (average of 6 measurements)	3	[min]		

Time-optimized method				
Sample weight (± 10%):	5	[g]		
Drying program	Gentle drying		Ramp:	2:00 min
End temperature	80	[°C]		
Switch-off criterion	F (1 mg / 60 sec)			
Moisture content (average of 6 measurements)	0.06	[%]	± 0.01	[%]
Measuring time (average of 6 measurements)	2	[min]		

Moisture Determination Method for Magnesium Stearate

Description of sample

Magnesium Stearate Ph Eur from Riedel de Haën
White powder

Reference method: Oven

Sample preparation / procedure

Pre-dry weighing bottles with glass lids (at oven temperature) and leave to cool in the desiccator. Weigh 1 g of the sample material into each weighing bottle. Start drying the samples at 105° C in the oven. Remove the contents after the preset time has elapsed, leave to cool in the desiccator, and weigh. Repeat the process until mass constancy is achieved.
Literature: USP28-NF23 USP Monograph "Magnesium Stearate"

Results (oven)				
Sample weight:	2	[g]		
Drying temperature and time	105	[°C]	2	[hour(s)]
Moisture content (average of 6 measurements)	3.69	[%]	± 0.04	[%]

Moisture determination using the HR83 Halogen Moisture Analyzer

Sample preparation / procedure

Set the HR83. Tare aluminium sample pan. Use a spoon to put the sample in the pan then distribute it evenly by gently shaking the pan, and weigh. Start the drying process.

Standard Method according Pharma reference customer				
Sample weight (± 10%):	2	[g]		
Drying program	Standard drying			
End temperature	105	[°C]		
Switch-off criterion	5			
Moisture content (average of 6 measurements)	3.71	[%]	± 0.12	[%]
Measuring time (average of 6 measurements)	17	[min]		

Time-optimized method				
Sample weight (± 10%):	2	[g]		
Drying program	Standard drying			
End temperature	130	[°C]		
Switch-off criterion	F (1 mg / 40 sec)			
Moisture content (average of 6 measurements)	3.68	[%]	± 0.08	[%]
Measuring time (average of 6 measurements)	6	[min]		

Moisture Determination Method for Sodium Saccharin

Description of sample

Sodium Saccharin 40-80 Mesh from JMC Corp. Korea
White granulate

Reference method: Drying Oven

Sample preparation / procedure

Pre-dry weighing bottles with glass lids (at oven temperature) and leave to cool in the desiccator. Weigh 1 g of the sample material into each weighing bottle. Start drying the samples at 105° C in the oven. Remove the contents after the time specified in the pharmacopeia has elapsed, leave to cool in the desiccator, and weigh. Repeat the process until mass constancy is achieved.
Literature: Japanese Pharmacopeia XIV page 1030: "Saccharin Sodium" Monograph

Results (oven)				
Sample weight:	1	[g]		
Drying temperature and time	120	[°C]	4	[hour(s)]
Moisture content (average of 6 measurements)	10.38	[%]	± 0.02	[%]

Moisture determination using the HR83 Halogen Moisture Analyzer

Sample preparation / procedure

Set the HR83. Tare aluminium sample pan. Use a spoon to put the sample in the pan then distribute it evenly by gently shaking the pan, and weigh. Start the drying process.

Results (HR83 Halogen Moisture Analyzer)

Standard Method according Pharma reference customer				
Sample weight (± 10%):	1.5	[g]		
Drying program	Standard drying			
End temperature	120	[°C]		
Switch-off criterion	5			
Moisture content (average of 6 measurements)	10.19	[%]	± 0.09	[%]
Measuring time (average of 6 measurements)	19	[min]		

Time-optimized method				
Sample weight (± 10%):	1.5	[g]		
Drying program	Standard drying			
End temperature	150	[°C]		
Switch-off criterion	4			
Moisture content (average of 6 measurements)	10.37	[%]	± 0.16	[%]
Measuring time (average of 6 measurements)	7	[min]		

Moisture Determination Method for Talc

Description of sample

Talc Ph Eur from Riedel de Haën
Light-gray powder

Reference method: Oven

Sample preparation / procedure

Pre-dry weighing bottles with glass lids (at oven temperature) and leave to cool in the desiccator. Weigh 1 g of the sample material into each weighing bottle. Start drying the samples at 105° C in the oven. Remove the contents after the preset time has elapsed, leave to cool in the desiccator, and weigh. Repeat the process until mass constancy is achieved.

Results (oven)				
Sample weight:	1	[g]		
Drying temperature and time	105	[°C]	2	[hour(s)]
Moisture content (average of 6 measurements)	0.44	[%]	± 0.06	[%]

Moisture determination using the HR83 Halogen Moisture Analyzer

Sample preparation / procedure

Set the HR83. Tare aluminium sample pan. Use a spoon to put the sample in the pan then distribute it evenly by gently shaking the pan, and weigh. Start the drying process.

Standard Method according Pharma reference customer				
Sample weight (± 10%):	4	[g]		
Drying program	Standard drying			
End temperature	105	[°C]		
Switch-off criterion	5			
Moisture content (average of 6 measurements)	0.55	[%]	± 0.03	[%]
Measuring time (average of 6 measurements)	3.5	[min]		

Time-optimized method				
Sample weight (± 10%):	4	[g]		
Drying program	Standard drying			
End temperature	150	[°C]		
Switch-off criterion	3			
Moisture content (average of 6 measurements)	0.52	[%]	± 0.03	[%]
Measuring time (average of 6 measurements)	1.5	[min]		

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