

Summary of Stability Study of Folic Acid

1 Stability summary and conclusions

In accordance with ICH Guidance for industry: ICH Q1A (R2) Stability Testing of New Drug Substances and Products, and Q1E Evaluation of Stability Data, the stability studies performed in support of this application include lots of Folic Acid drug substance stored under variety of conditions. The various studies described in this section can be divided into two sub-categories of testing.

- Accelerated stability studies
- Long term stability studies

1.1 Advice on storage

Preserve in well-closed, light-resistant containers.

2 Post-approval stability protocol and stability commitment

2.1 Accelerated stability study

Duration	0, 1, 2, 3 and 6 months.
Packaging	The same as the actual packaging used for storage and distribution, i.e. polyethylene bags / fiber drum or carton system.
Storage conditions	Temperature 40 ± 2 °C; relative humidity $75 \pm 5\%$.
Test performed	As listed below.

Test	Specification	Method
Appearance	Yellow, yellow-brownish, or yellowish-orange, odorless, crystalline powder.	Visual observation
Water	$\leq 8.5\%$	USP
Assay	95.0% ~ 102.0%	USP

2.2 Long-term stability study

Duration	0, 3, 6, 9, 12, 18, 24 months.
Packaging	The same as the actual packaging used for storage and distribution, i.e. polyethylene bags / fiber drum or carton system.
Storage conditions	Temperature 30 ± 2 °C; relative humidity $75 \pm 5\%$.
Test performed	As listed below.

Test	Specification	Method
Appearance	Yellow, yellow-brownish, or yellowish-orange, odorless, crystalline powder.	Visual observation
Water	$\leq 8.5\%$	USP
Assay	95.0% ~ 102.0%	USP

**3 Tabulated stability data****3.1 Data from accelerated stability study**

Batch number	Manufacturing date
FA17072040	July 11, 2017
FA17072041	July 11, 2017
FA17072042	July 11, 2017

Tabulated Accelerated Study Data for Folic Acid -1

Batch No. FA17072040 Date of initial test: Jul. 25, 2017 40 ± 2 °C, 75 ± 5%RH

Test Frequency	Test Item & Standard		
	Appearance	Assay (%)	Water (%)
	Yellow, yellow-brownish, or yellowish-orange, odorless, crystalline powder.	95.0 - 102.0	≤8.5
0 Month	Complies	97.3	8.2
1 st Month	Complies	98.5	8.3
2 nd Month	Complies	98.2	8.3
3 rd Month	Complies	98.1	8.3
6 th Month	Complies	98.0	8.2

Tabulated Accelerated Study Data for Folic Acid -2

Batch No. FA17072041 Date of initial test: Jul. 25, 2017 40 ± 2 °C, 75 ± 5%RH

Test Frequency	Test Item & Standard		
	Appearance	Assay (%)	Water (%)
	Yellow, yellow-brownish, or yellowish-orange, odorless, crystalline powder.	95.0 - 102.0	≤8.5
0 Month	Complies	98.2	8.3
1 st Month	Complies	98.8	8.3
2 nd Month	Complies	98.4	8.3
3 rd Month	Complies	98.5	8.2
6 th Month	Complies	98.2	8.3

**Tabulated Accelerated Study Data for Folic Acid -3**

Batch No. FA17072042 Date of initial test: Jul. 25, 2017 40±2 °C, 75±5%RH

Test Frequency	Test Item & Standard		
	Appearance	Assay (%)	Water (%)
	Yellow, yellow-brownish, or yellowish-orange, odorless, crystalline powder.	95.0 - 102.0	≤8.5
0 Month	Complies	98.0	8.1
1 st Month	Complies	98.2	8.3
2 nd Month	Complies	98.3	8.2
3 rd Month	Complies	98.3	8.2
6 th Month	Complies	98.2	8.2

3.2 Data from long-term stability study

Batch number	Manufacturing date
FA17072040	July 11, 2017
FA17072041	July 11, 2017
FA17072042	July 11, 2017

Tabulated Long Term Study Data for Folic Acid -1

Batch No. FA17072040 Date of initial test: Jul. 25, 2017 30±2 °C, 75±5%RH

Test Frequency	Test Item & Standard		
	Appearance	Assay (%)	Water (%)
	Yellow, yellow-brownish, or yellowish-orange, odorless, crystalline powder.	95.0 - 102.0	≤8.5
0 Month	Complies	97.3	8.2
3 rd Month	Complies	98.3	8.2
6 th Month	Complies	98.4	8.2
9 th Month	Complies	98.0	8.2
12 th Month	Complies	98.3	8.2
18 th Month	Complies	97.9	8.0
24 th Month	Complies	97.3	8.2



Tabulated Long Term Study Data for Folic Acid -2

Batch No. FA17072041 Date of initial test: Jul. 25, 2017 30 ± 2 °C, 75 ± 5%RH

Test Frequency	Test Item & Standard		
	Appearance	Assay (%)	Water (%)
	Yellow, yellow-brownish, or yellowish-orange, odorless, crystalline powder.	95.0 - 102.0	≤8.5
0 Month	Complies	98.2	8.3
3 rd Month	Complies	98.6	8.3
6 th Month	Complies	98.5	8.2
9 th Month	Complies	98.2	8.3
12 th Month	Complies	98.6	8.2
18 th Month	Complies	98.1	8.1
24 th Month	Complies	97.4	8.2

Tabulated Long Term Study Data for Folic Acid -3

Batch No. FA17072042 Date of initial test: Jul. 25, 2017 30 ± 2 °C, 75 ± 5%RH

Test Frequency	Test Item & Standard		
	Appearance	Assay (%)	Water (%)
	Yellow, yellow-brownish, or yellowish-orange, odorless, crystalline powder.	95.0 - 102.0	≤8.5
0 Month	Complies	98.0	8.1
3 rd Month	Complies	98.3	8.2
6 th Month	Complies	98.7	8.2
9 th Month	Complies	98.0	8.2
12 th Month	Complies	98.4	8.2
18 th Month	Complies	98.3	8.1
24 th Month	Complies	97.4	8.2