Summary of Stability Study of Pyridoxine HCl

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 Pyridoxine HCl 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 Recommended retest period

Based on the stability data, the product has no significant change at accelerated condition, and the long-term data of 48 months' duration show little variation. Therefore, a re-test period of 4 years (48 months) is recommended.

1.2 Advice on storage

Preserve in tight, light-resistant containers, protected from light.

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±5%.
Test performed As listed below.

Test	Specification	Method
Appearance	White or almost white, crystalline powder.	Visual observation
Color of solution	Clear and not more intense than Y7	Ph. Eur.
pH	2.4 ~ 3.0	Ph. Eur.
Related substances (HPLC)	Impurity B: NMT 0.15% Unspecified impurities: NMT 0.10% Total impurities: NMT 0.2%	Ph. Eur.
Loss on drying	NMT 0.5%	Ph. Eur.
Assay	99.0 ~ 101.0%	Ph. Eur.

2.2 Long-term stability study

Duration 0, 3, 6, 9, 12, 18, 24, 36, 48 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 25±2 °C; relative humidity 60±5%.
Test performed As listed below.

Test	Specification	Method
Appearance	White or almost white, crystalline powder.	Visual observation
Color of solution	Clear and not more intense than Y_7	Ph. Eur.
pH	2.4 ~ 3.0	Ph. Eur.
Related substances (HPLC)	Impurity B: NMT 0.15% Unspecified impurities: NMT 0.10% Total impurities: NMT 0.2%	Ph. Eur.
Loss on drying	NMT 0.5%	Ph. Eur.
Assay	99.0 ~ 101.0%	Ph. Eur.

3 Tabulated stability data

3.1 Data from accelerated stability study

Batch number	Manufacturing date
PH12084024	Aug. 8, 2012
PH12084025	Aug. 8, 2012
PH12084026	Aug. 9, 2012

Tabulated Accelerated Study Data for Pyridoxine HCl (VB_6) -1

Batch No. PH12084024 Date of initial test: Aug 10, 2012 40±2 ℃, 75±5%RH

Test	Specification, Ph. Eur.	Duration, month				
		0	1	2	3	6
Identification	Meet the requirements	Positive	N/A	N/A	N/A	N/A
Appearance	White or almost white, crystalline powder.	White crystalline powder.				
Color of solution	Clear and not more intense than Y_7	Comply	Comply	Comply	Comply	Comply
pH	2.4 ~ 3.0	2.7	2.6	2.7	2.7	2.7
Related substances	Impurity B: NMT 0.15%	0.00%	0.00%	0.00%	0.00%	0.00%
	Any unspecified impurity: NMT 0.10%	0.01%	0.01%	0.01%	0.00%	0.00%
	Total impurities: NMT 0.2%	0.01%	0.02%	0.01%	0.00%	0.00%
Loss on drying	NMT 0.5%	0.01%	0.02%	0.02%	0.01%	0.01%
Assay	99.0 ~ 101.0%	99.7%	99.6%	100.1%	99.8%	99.9%

Tabulated Accelerated Study Data for Pyridoxine HCl (VB_6) -2

Batch No. PH12084025 Date of initial test: Aug 10, 2012 40±2 ℃, 75±5%RH

Test	Specification, Ph. Eur.	Duration, month				
		0	1	2	3	6
Identification	Meet the requirements	Positive	N/A	N/A	N/A	N/A
Appearance	White or almost white, crystalline powder.	White crystalline powder.				
Color of solution	Clear and not more intense than Y_7	Comply	Comply	Comply	Comply	Comply
pH	2.4 ~ 3.0	2.7	2.6	2.7	2.7	2.7
Related substances	Impurity B: NMT 0.15%	0.00%	0.00%	0.00%	0.00%	0.00%
	Any unspecified impurity: NMT 0.10%	0.01%	0.01%	0.00%	0.00%	0.00%
	Total impurities: NMT 0.2%	0.02%	0.02%	0.00%	0.00%	0.00%
Loss on drying	NMT 0.5%	0.01%	0.03%	0.01%	0.01%	0.01%
Assay	99.0 ~ 101.0%	99.7%	99.7%	99.9%	99.8%	99.7%

Tabulated Accelerated Study Data for Pyridoxine HCl (VB_6) -3

Batch No. PH12084026 Date of initial test: Aug 11, 2012 40±2 ℃, 75±5%RH

Test	Specification, Ph. Eur.	Duration, month				
		0	1	2	3	6
Identification	Meet the requirements	Positive	N/A	N/A	N/A	N/A
Appearance	White or almost white, crystalline powder.	White crystalline powder.				
Color of solution	Clear and not more intense than Y_7	Comply	Comply	Comply	Comply	Comply
pH	2.4 ~ 3.0	2.7	2.6	2.7	2.7	2.7
Related substances	Impurity B: NMT 0.15%	0.00%	0.00%	0.00%	0.00%	0.00%
	Any unspecified impurity: NMT 0.10%	0.00%	0.01%	0.01%	0.00%	0.00%
	Total impurities: NMT 0.2%	0.00%	0.02%	0.01%	0.00%	0.00%
Loss on drying	NMT 0.5%	0.01%	0.01%	0.01%	0.01%	0.01%
Assay	99.0 ~ 101.0%	99.7%	100.1%	99.9%	99.8%	99.8%

3.2 Data from long-term stability study

Batch number	Manufacturing date
PH12084024	Aug. 8, 2012
PH12084025	Aug. 8, 2012
PH12084026	Aug. 9, 2012

CANAVIT
Canadian Feed Additives Inc.
additifs d'alimentation canadiens inc.

Tabulated Long Term Study Data for Pyridoxine HCl (VB_6) -1

Batch No. PH12084024 | Date of initial test: Aug 10, 2012 | 25±2 ℃, 60±5%RH

Test	Specification, Ph. Eur.	Duration, month								
		0	3	6	9	12	18	24	36	48
Identification	Meet the requirements	Positive	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Appearance	White or almost white, crystalline powder.	White crystalline powder.								
Color of solution	Clear and not more intense than Y_7	Comply	Comply	Comply	Comply	Comply	Comply	Comply	Comply	Comply
pH	2.4 ~ 3.0	2.7	2.7	2.7	2.7	2.7	2.7	2.7	2.7	2.7
Related substances	Any unspecified impurity: NMT 0.10% Impurity B: NMT 0.15% Total impurities: NMT 0.2%	0.01% N. D.* 0.01%	N. D. N. D. N. D.	N. D. N. D. N. D.	0.01% N. D. 0.01%	N. D. N. D. N. D.	0.04% N. D. 0.06%	0.03% N. D. 0.07%	0.03% N. D 0.08%	<0.05% N. D <0.05%
Loss on drying	NMT 0.5%	0.01%	0.01%	0.03%	0.01%	0.01%	0.03%	0.03%	0.02%	0.01%
Assay	99.0 ~ 101.0%	99.7%	99.8%	99.8%	99.9%	99.9%	100.0%	100.1%	100.1%	100.0%

* Remark: N. D. = Not Detected

Tabulated Long Term Study Data for Pyridoxine HCl (VB_6) -2

Batch No. PH12084025 | Date of initial test: Aug 10, 2012 | 25±2 ℃, 60±5%RH

Test	Specification, Ph. Eur.	Duration, month								
		0	3	6	9	12	18	24	36	48
Identification	Meet the requirements	Positive	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Appearance	White or almost white, crystalline powder.	White crystalline powder.								
Color of solution	Clear and not more intense than Y_7	Comply	Comply	Comply	Comply	Comply	Comply	Comply	Comply	Comply
pH	2.4 ~ 3.0	2.7	2.7	2.7	2.7	2.7	2.7	2.6	2.7	2.7
Related substances	Any unspecified impurity: NMT 0.10% Impurity B: NMT 0.15% Total impurities: NMT 0.2%	0.01% N. D.* 0.01%	N. D. N. D. N. D.	N. D. N. D. N. D.	0.01% N. D. 0.01%	N. D. N. D. N. D.	0.05% N. D. 0.06%	0.04% N. D. 0.07%	0.03% N. D 0.07%	<0.05% N. D <0.05%
Loss on drying	NMT 0.5%	0.01%	0.01%	0.03%	0.01%	0.01%	0.02%	0.03%	0.02%	0.01%
Assay	99.0 ~ 101.0%	99.7%	99.6%	99.8%	100.1%	100.0%	100.3%	100.1%	100.1%	100.1%

* Remark: N. D. = Not Detected

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Tabulated Long Term Study Data for Pyridoxine HCl (VB_6) -3

Batch No. PH12084026 Date of initial test: Aug 11, 2012 25±2 ℃, 60±5%RH

Test	Specification, Ph. Eur.	Duration, month								
		0	3	6	9	12	18	24	36	48
Identification	Meet the requirements	Positive	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Appearance	White or almost white, crystalline powder.	White crystalline powder.								
Color of solution	Clear and not more intense than Y7	Comply	Comply	Comply	Comply	Comply	Comply	Comply	Comply	Comply
pH	2.4 ~ 3.0	2.7	2.7	2.7	2.7	2.7	2.7	2.6	2.7	2.7
Related substances	Any unspecified impurity: NMT 0.10% Impurity B: NMT 0.15% Total impurities: NMT 0.2%	0.01% N. D.* 0.01%	N. D. N. D. N. D.	N. D. N. D. N. D.	0.01% N. D. 0.01%	N. D. N. D. N. D.	0.05% N. D. 0.06%	0.04% N. D. 0.06%	0.04% N. D 0.07%	<0.05% N. D <0.05%
Loss on drying	NMT 0.5%	0.01%	0.01%	0.01%	0.01%	0.01%	0.01%	0.01%	0.02%	0.01%
Assay	99.0 ~ 101.0%	99.7%	99.7%	99.7%	99.9%	99.7%	99.8%	100.1%	100.2%	100.2%

* Remark: N. D. = Not Detected

n. Physical-chemical interactions (incompatibilities) with other substances.

No incompatibilities with other substances