Stability Summary

Product group: Biopharma

Brand name: BioHale® Trehalose Dihydrate

Product description: Trehalose Dihydrate
low endotoxin grade

1. Stability Statement

DFE Pharma has defined a shelf life for all of its products based on a stability testing program conforming to IPEC Excipient Stability Program Guide 2022.
DFE Pharma guarantees that its products comply with all specifications up until the end of their shelf life period (the expiry date), when stored in the original unopened packaging. For BioHale® Trehalose Dihydrate the established shelf life is 48 months, based on ongoing stability studies.
There is no special controlled storage condition required. Our recommendation is to store the product in its original unopened pack at room temperature (normal warehouse conditions) and allowing temporary excursions from these conditions. This recommendation is supported by our stability studies under controlled ICH conditions covering both physical/chemical and microbiological attributes.
Our experience of many years as supplier of excipients to customers all over the world including humid and hot regions confirms that our products are stable during storage and transport.

2. Materials and Methods

DFE-Pharma conducts a stability program conforming IPEC Excipients Stability Program Guide 2022 for supporting the stability of its products. Three validation batches of BioHale® Trehalose Dihydrate, produced in The Netherlands, have been stability tested under ICH long term and accelerated conditions (Table 1).

Table 1: Overview of batches BioHale® Trehalose (small packs)

Batch	Prod. date	Stability start	Duration of data (months) at	
			25/60	40/75
2107009.2076	Jul 21	Jul 21	36 (ongoing)	6
2107020.2076	Jul 21	Jul 21	36 (ongoing)	6
2107047.2076	Jul 21	Jul 21	36 (ongoing)	6

3. Packaging and storage

The stability batches were packed into low density polyethylene (LDPE) bags each containing ca 100 g of Trehalose Dihydrate. The bags were then packaged into a 300 ml HDPE drum, which is of same material and wall thickness as commercial drums. The closed drums were stored at 25°C/60%RH (25/60) and 40°C/75%RH (40/75).

At each scheduled time point the batches were analyzed for selected tests from the product specification using the specified analytical methods. The selected tests are those deemed relevant to potential chemical, functional and microbiological product acceptability

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4. Results and Discussion

The 36 months data of the 25/60 and the 6 months data of the 40/75 condition show that all Trehalose Dihydrate tests are within specification. A 48 months shelf life can be assigned based on these data.
The chosen methodology is deemed to be acceptable based on the fact that Trehalose Dihydrate is a stable non-active excipients without formation of toxic by-products during storage. The approach is in compliance with IPEC stability guide.
The possible shelf limiting parameters are change of colour and absorption of water during storage. Trehalose Dihydrate is a non-reducing sugar, which will minimize colour changes. Trehalose Dihydrate is stored in a highly protective drum, mitigating the risk of water uptake and microbial growth.

To exemplify the results of the batches are shown in the addendum.

5. Conclusion

For BioHale® Trehalose Dihydrate, based on 36 months stability data, the product shelf life is extended to 48 months.

Retest Date
The expiry date as documented on the product and the corresponding Certificate of Analysis is generated as follows:

Retest date = (Production date) + (shelf life in months) – (one month).

The retest date in the ERP system and CoA has been adapted with the extended shelf life and will be printed on newly produced batches. It is not possible to adapt the retest/ expiry date printed on the CoA and packaging label of batches produced before this shelf life extension. Batches produced before the shelf life extension fulfil the product specification parameters till the revised shelf life and DFE Pharma confirms with this document that the customer can use batches produced prior to the shelf life extension until the extended shelf life of 48 months.

We trust this information which is made up to the best of our knowledge will be helpful to you.

Name : Peter Ebben
Job title : Global Quality Control Manager
Signature :

This document is controlled by a validated, electronic system and is valid without signature.
The above facsimile signature is only for display.

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Addendum: Stability Data Tables

Product	Batch	Prod date	Start stab		Packaging					
Biohale® Trehalose Dihydrate	2107009.2076	Jul-21	Jul-21		small pack					
			months at 25/60							at 40/75
Test	**Specification**	0	3	6	9	12	18	24	36	3	6
Appearance of solution	clear, colorless	pass	pass	pass	pass	pass	pass	pass	pass	pass	pass
Color of solution (Abs 10cm)	complies	pass	pass	pass	pass	pass	pass	pass	pass	pass	pass
Reducing sugars	max 0,1%	pass	pass	pass	pass	pass	pass	pass	pass	pass	pass
pH	4,5 - 6,5	5,4	5,4	5,4	5,5	5,5	5,7	5,9	5,4	5,6	5,4
Specific optical rotation	197 - 201°	199	201	199	199	199	199	200	199	199	199
Chlorides	≤ 125 ppm	<125	--	--	--	--	--	--	--	<125	<125
Sulfates	≤ 200 ppm	<200	--	--	--	--	--	--	--	<200	<200
Soluble starch	complies	pass	--	--	--	--	--	--	--	pass	pass
Water content (KF)	9,0 - 11,0%	9,6	9,5	9,6	9,6	9,7	9,6	9,9	9,5	9,6	9,6
Sulfated ash	max 0,1%	0,0	--	--	--	--	--	--	--	0,0	0,0
Heavy metals	max 5 ppm	pass	--	--	--	--	--	--	--	pass	pass
Iron	max 5 ppm	pass	--	--	--	--	--	--	--	pass	pass
Total Nitrogen	max 0,005%	0,001	--	--	--	--	--	--	--	<0,001	0,001
Residual solvents Acetone	max 900 ppm	97	--	--	--	--	--	--	--	<90	<90
Impuritiy A (Glucose)	max 0,5%	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1
Impuritiy B (Oligosaccharides	max 0,5%	0,2	0,2	0,2	0,2	0,2	0,2	0,2	0,2	0,2	0,2
Each unspecified impurity	max 0,2%	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1
Total impurities	max 1,0%	0,2	0,2	0,2	0,2	0,2	0,2	0,2	0,2	0,2	0,2
Total impurites RRT < 1,0	max 0,5%	0,2	0,2	0,2	0,2	0,2	0,2	0,2	0,2	0,2	0,2
Total impurites RRT > 1,0	max 0,5%	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1
Assay (anhydrous basis)	98.0-101.0%	99,5	99,5	99,3	99,6	99,9	101,0	100,2	99,7	99,6	99,7
Bacterial endotoxins	max 0,3 EU/g	pass	--	--	--	--	--	--	--	pass	pass
TAMC	max 50 CFU/g	<10	--	--	--	30	--	<10	<10	<10	<10
TYMC	max 10 CFU/g	<10	--	--	--	<10	--	<10	<10	<10	<10
S. aureus	absent in 10g	pass	--	--	--	pass	--	pass	pass	pass	pass
Salmonella spp.	absent in 10g	pass	--	--	--	pass	--	pass	pass	pass	pass
E. coli	absent in 10g	pass	--	--	--	pass	--	pass	pass	pass	pass
P. Aeruginosa	absent in 10g	pass	--	--	--	pass	--	pass	pass	pass	pass

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Addendum: Stability Data Tables

Product	Batch	Prod date	Start stab		Packaging						
Biohale® Trehalose Dihydrate	2107020.2076	Jul-21	Jul-21		small pack						
			months at 25/60							at 40/75	
Test	**Specification**	0	3	6	9	12	18	24	36	3	6
Appearance of solution	clear, colorless	pass	pass	pass	pass	pass	pass	pass	pass	pass	pass
Color of solution (Abs 10cm)	complies	pass	pass	pass	pass	pass	pass	pass	pass	pass	pass
Reducing sugars	max 0,1%	pass	pass	pass	pass	pass	pass	pass	pass	pass	pass
pH	4,5 - 6,5	5,4	5,5	5,3	5,7	5,5	5,6	5,5	5,5	5,4	5,3
Specific optical rotation	197 - 201°	200	200	199	200	200	199	199	200	199	199
Chlorides	≤ 125 ppm	<125	--	--	--	--	--	--	--	<125	<125
Sulfates	≤ 200 ppm	<200	--	--	--	--	--	--	--	<200	<200
Soluble starch	complies	pass	--	--	--	--	--	--	--	pass	pass
Water content (KF)	9,0 - 11,0%	9,6	9,6	9,5	9,6	10,0	9,6	9,5	9,6	9,7	9,5
Sulfated ash	max 0,1%	0,0	--	--	--	--	--	--	--	0,0	0,0
Heavy metals	max 5 ppm	pass	--	--	--	--	--	--	--	pass	pass
Iron	max 5 ppm	pass	--	--	--	--	--	--	--	pass	pass
Total Nitrogen	max 0,005%	0,001	--	--	--	--	--	--	--	<0,001	0,001
Residual solvents Acetone	max 900 ppm	<90	--	--	--	--	--	--	--	<90	<90
Impuritiy A (Glucose)	max 0,5%	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1
Impuritiy B (Oligosaccharides	max 0,5%	0,2	0,2	0,2	0,2	0,2	0,2	0,2	0,2	0,2	0,2
Each unspecified impurity	max 0,2%	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1
Total impurities	max 1,0%	0,2	0,2	0,2	0,2	0,2	0,2	0,2	0,2	0,2	0,2
Total impurites RRT < 1,0	max 0,5%	0,2	0,2	0,2	0,2	0,2	0,2	0,2	0,2	0,2	0,2
Total impurites RRT > 1,0	max 0,5%	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1
Assay (anhydrous basis)	98.0-101.0%	99,9	99,7	99,3	99,6	100,4	100,3	99,4	98,6	98,9	99,3
Bacterial endotoxins	max 0,3 EU/g	pass	--	--	--	--	--	--	--	pass	pass
TAMC	max 50 CFU/g	<10	--	--	--	<10	--	<10	<10	<10	<10
TYMC	max 10 CFU/g	<10	--	--	--	<10	--	<10	<10	<10	<10
S. aureus	absent in 10g	pass	--	--	--	pass	--	pass	pass	pass	pass
Salmonella spp.	absent in 10g	pass	--	--	--	pass	--	pass	pass	pass	pass
E. coli	absent in 10g	pass	--	--	--	pass	--	pass	pass	pass	pass
P. Aeruginosa	absent in 10g	pass	--	--	--	pass	--	pass	pass	pass	pass

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Addendum: Stability Data Tables

Product	Batch	Prod date	Start stab		Packaging						
Biohale® Trehalose Dihydrate	2107047.2076	Jul-21	Jul-21		small pack						
			months at 25/60							at 40/75	
Test	**Specification**	0	3	6	9	12	18	24	36	3	6
Appearance of solution	clear, colorless	pass	pass	pass	pass	pass	pass	pass	pass	pass	pass
Color of solution (Abs 10cm)	complies	pass	pass	pass	pass	pass	pass	pass	pass	pass	pass
Reducing sugars	max 0,1%	pass	pass	pass	pass	pass	pass	pass	pass	pass	pass
pH	4,5 - 6,5	5,4	5,5	5,3	5,6	5,5	5,6	5,7	5,2	5,5	5,3
Specific optical rotation	197 - 201°	199	199	199	200	200	200	199	200	200	199
Chlorides	≤ 125 ppm	<125	--	--	--	--	--	--	--	<125	<125
Sulfates	≤ 200 ppm	<200	--	--	--	--	--	--	--	<200	<200
Soluble starch	complies	pass	--	--	--	--	--	--	--	pass	pass
Water content (KF)	9,0 - 11,0%	9,1	9,6	9,5	9,6	10,1	9,6	9,5	9,6	9,6	9,5
Sulfated ash	max 0,1%	0,0	--	--	--	--	--	--	--	0,0	0,0
Heavy metals	max 5 ppm	pass	--	--	--	--	--	--	--	pass	pass
Iron	max 5 ppm	pass	--	--	--	--	--	--	--	pass	pass
Total Nitrogen	max 0,005%	0,001	--	--	--	--	--	--	--	<0,001	0,001
Residual solvents Acetone	max 900 ppm	<90	--	--	--	--	--	--	--	<90	<90
Impuritiy A (Glucose)	max 0,5%	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1
Impuritiy B (Oligosaccharides	max 0,5%	0,2	0,2	0,2	0,2	0,2	0,2	0,2	0,2	0,2	0,2
Each unspecified impurity	max 0,2%	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1
Total impurities	max 1,0%	0,2	0,2	0,2	0,2	0,2	0,2	0,2	0,2	0,2	0,2
Total impurites RRT < 1,0	max 0,5%	0,2	0,2	0,2	0,2	0,2	0,2	0,2	0,2	0,2	0,2
Total impurites RRT > 1,0	max 0,5%	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1	<0,1
Assay (anhydrous basis)	98.0-101.0%	100,0	99,9	99,4	100,4	100,4	99,9	99,0	99,6	100,0	99,4
Bacterial endotoxins	max 0,3 EU/g	pass	--	--	--	--	--	--	--	pass	pass
TAMC	max 50 CFU/g	<10	--	--	--	<10	--	<10	<10	<10	<10
TYMC	max 10 CFU/g	<10	--	--	--	<10	--	<10	<10	<10	<10
S. aureus	absent in 10g	pass	--	--	--	pass	--	pass	pass	pass	pass
Salmonella spp.	absent in 10g	pass	--	--	--	pass	--	pass	pass	pass	pass
E. coli	absent in 10g	pass	--	--	--	pass	--	pass	pass	pass	pass
P. Aeruginosa	absent in 10g	pass	--	--	--	pass	--	pass	pass	pass	pass

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