

**CYCLOLAB**

Cyclodextrin Research & Development Laboratory Ltd.
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VAT No.: HU 10678970

**CERTIFICATE OF ANALYSIS****Product: Sulfobutyl-ether- β -cyclodextrin sodium salt (SBECD)****K-No:**

Quality: pharma grade (USP and EP)

Site of manufacture: H-1097 Illatos út 7 Budapest, Hungary

Batch No: **47K260919**

Date of manufacture: September 2, 2019

Date of qualification: October 15, 2019

Supplied amount:

Expiry date: *August, 2022*

Test and method	Specification	Result
Appearance / <i>visual</i>	white or off-white powder	white powder
Identification A / <i>IR</i> ; <i>USP <197>, EP 2.2.24</i>	complies with SBECD reference	complies
Identification B (Assay method) <i>HPLC; USP <621>, EP 2.2.29</i>	t_R of major peak complies with SBECD reference	complies
Identification C / <i>CE</i> ; <i>USP <1053></i> <i>NMR; USP <761> EP 2.2.33</i>	meets the requirements of average degree of substitution	complies
Identification D / <i>USP <191>, EP 2.3.1</i>	positive test for sodium	complies
Assay / <i>HPLC; USP <621>, EP 2.2.29</i>	95.0-105.0% on the anhydrous basis	101.4 %
Heavy metals <i>ICP-MS, USP <232, 233></i>	Cadmium NMT 0.2 $\mu\text{g/g}$ Lead NMT 0.5 $\mu\text{g/g}$ Arsenic NMT 1.5 $\mu\text{g/g}$ Mercury NMT 0.3 $\mu\text{g/g}$ Cromium NMT 110 $\mu\text{g/g}$ Nickel NMT 2 $\mu\text{g/g}$ Molybdenum NMT 150 $\mu\text{g/g}$ Vanadium NMT 1 $\mu\text{g/g}$	< 0.02 $\mu\text{g/g}$ < 0.2 $\mu\text{g/g}$ < 0.2 $\mu\text{g/g}$ < 0.02 $\mu\text{g/g}$ < 0.2 $\mu\text{g/g}$ < 0.2 $\mu\text{g/g}$ < 0.2 $\mu\text{g/g}$ < 0.2 $\mu\text{g/g}$
Limit of Beta Cyclodextrin (Betadex) / <i>HPLC; USP <621></i>	NMT 0.1% on the anhydrous basis	0.06%
Limit of 1,4-Butane Sultone / <i>GC; USP <621>, EP 2.2.28</i>	NMT 0.5 ppm	<0.5 ppm
Limit of Sodium Chloride / <i>USP <221></i>	NMT 0.2 %	<0.03%
Limit of 4-Hydroxybutane-1-sulfonic Acid / <i>CE; USP <1053></i>	NMT 0.09%	< LOD (0.02%)
Limit of Bis(4-sulfobutyl) Ether Disodium / <i>CE; USP <1053></i>	NMT 0.05%	<LOD (0.02%)
Bacterial Endotoxin Test / <i>USP <85>, EP 2.6.12</i>	≤ 24 IU/g	< 6 IU/g
Microbial Enumeration Tests / <i>USP <61>, EP 2.6.12</i>	TAMC ≤ 100 CFU/g; TYMC ≤ 50 CFU/g	< 10 CFU/g; < 10 CFU/g
Test for Specified Microorganism / <i>USP <62>, EP 2.6.13</i>	absence of Escherichia Coli /1 g absence of Salmonella /10 g	negative negative

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Expiry date: August, 2022

Test and method	Specification	Results
Clarity of solution (30%, w/v) / visual; see details in the USP Monograph, EP 2.2.1	the solution is clear, and essentially free from particles of foreign matter	complies
Clarity of solution (15%, w/v) / visual; EP 2.2.1	the solution is clear and colorless	complies
Phosphate content / UV-VIS USP <857>, EP 2.2.25	525-700 $\mu\text{g/g}$	655 $\mu\text{g/g}$
Average Degree of Substitution [DS] / NMR; EP 2.2.33	5.9 – 6.6	6.0
Average Degree of Substitution [DS] / CE; USP <1053>	6.2 - 6.9	6.4
Peak distribution / CE; USP <1053>	Each SBECD peak (I-X) meets the limit range (peak area %) of the Monograph	
	SBECD sodium peaks	Limit range (peak area %)
	I (DS-1)	0-0.3
	II (DS-2)	0-0.9
	III (DS-3)	0.5-5.0
	IV (DS-4)	2.0-10.0
	V (DS-5)	10.0-20.0
	VI (DS-6)	15.0-25.0
	VII (DS-7)	20.0-30.0
	VIII (DS-8)	10.0-25.0
	IX (DS-9)	2.0-12.0
	X (DS-10)	0-4.0
Residual solvents: ethanol / GC; USP <621>, EP 2.2.28	NMT 2500 ppm	210 ppm
pH (30%, w/v) / USP <791>	4.0 – 6.8	6.3
pH (15%, w/v) / EP 2.2.3	5.0 – 7.5	6.2
Water Content / USP <921> Method I, EP 2.5.12	NMT 10.0%	5.9 %
Impurities / HPLC, EP 2.2.29		
IMP A (BCD)	NMT 0.1%	< 0.1%
IMP C (HOBSA)	NMT 0.1%	< 0.1%
IMP D (DIBSA)	NMT 0.05%	< 0.05%
IMP B (1,4-BS)	NMT 0.5 ppm	<0.5 ppm
Reducing sugar / UV VIS EP 2.2.25	NMT 0.05%	<0.05%

Packaging and Storage: Preserve in well-closed containers, store at room temperature. Protect from moisture.

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Batch No: **47K260919**

Expiry date: *August, 2022*

Date: *October 15, 2019*

[Signature]
Quality Control

Qualification: meets the requirements of USP and EP.

Released: yes no

Date: *October 15, 2019*

[Signature]
Quality Assurance