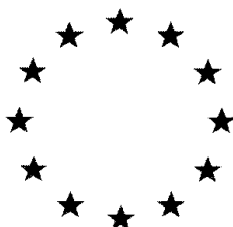


European Commission



VOLUME 3 – Annex B (AS)

Laminarin

B.2 Physical and chemical properties

Rapporteur Member State: The Netherlands

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**Draft Re-Assessment Report and Proposed decision of the Netherlands
prepared in the context of the possible renewal of laminarin under Regulation
(EC) 1107/2009**

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TABLE OF CONTENTS – VOLUME 3 B.2

B.2	Physical and chemical properties of the active substance	4
B.2.1	References relied on	9

B.2 Physical and chemical properties of the active substance

The entries refer to the data requirements as defined in Regulation (EU) No 283/2013. No new studies were submitted. The data presented in the table below was evaluated previously and considered adequate for the inclusion of the active substance in Annex I of Directive 91/414/EEC.

Note on test items used: Some of the test should be performed on the technical active ingredient (e.g. safety relevant data). For some endpoints the freeze dried substance was used for testing rather than the technical concentrate (TK). Assuming the only difference is that the substance is dispersed in water, negative outcome of studies performed with the freeze dried material should also result in a negative test result for the TK.

Test or Study & Data point	Guideline and Method	Test material purity and specification	Findings	GLP Y/N	Reference *	Acceptability/ comments
B.2.1 Melting point, boiling point	Method A.1 (Annex of Regulation (EC) No.440/2008) OECD Test Guideline 102	Laminarin 98% Batch No.S210300	No melting point could be determined (decomposition of test substance above 200°C)	Y	Licata-Messana L., 2000a	
	Method A.2 (Annex of Regulation (EC) No.440/2008) OECD Test Guideline 103	-	Not possible to determine experimentally a boiling point (substance decomposes before melting).	Y	Licata-Messana L., 2000b	
B.2.2 Vapour pressure, volatility	Method A.4 (Annex of Regulation (EC) No.440/2008)	Laminarin 98% Batch No.S210300	Vapour pressure: $< 2.6 \cdot 10^{-5}$ Pa at 25°C	Y	Tremain S.P., 2001	
	Calculation	-	Henry's law constant: $< 3.45 \cdot 10^{-7}$ Pa.m ³ .mol ⁻¹ at 23-25°C	-		
B.2.3 Appearance	Visual inspection	Laminarin 98% Batch	White to off-white crystals	Y	Licata-Messana L., 2000a	

Test or Study & Data point	Guideline and Method	Test material purity and specification	Findings	GLP Y/N	Reference *	Acceptability/ comments
(Physical state, colour)		No.S210300				
B.2.4 Spectra (UV/VIS, IR, NMR, MS), molar extinction at relevant wavelengths, optical purity	OECD Test Guideline 101	Laminarin 98% Batch No.S210300	<p>UV/VIS:</p> <p>At pH 1.9: $\lambda_{\max} = 264 \text{ nm}$; $\epsilon = 245 \text{ to } 294 \text{ L.mol}^{-1}.\text{cm}^{-1}$</p> <p>At pH 7.0: $\lambda_{\max} = 260 \text{ nm}$; $\epsilon = 242 \text{ to } 290 \text{ L.mol}^{-1}.\text{cm}^{-1}$</p> <p>At pH 11.8: $\lambda_{\max} = 258 \text{ nm}$; $\epsilon = 264 \text{ to } 317 \text{ L.mol}^{-1}.\text{cm}^{-1}$</p> <p>MS (ES - FAB): No useable spectra could be acquired.</p> <p>IR: IR spectrum is consistent with proposed chemical structure</p> <p>NMR: NMR spectra are consistent with proposed chemical structure.</p> <p>Optical purity: laminarin does not present resolved optical isomers (long chain of D-glucose with β-linkage); hence the optical purity was not studied.</p>	Y	Cuthbert J.E., 2001	
	MS (MALDI-TOF)	Laminarin	<p>MS (MALDI-TOF):</p> <p>Large distribution of MNa^+ ions with oligomers separated by 162 Da (glucose linkage leading to a loss of 18 Da). Double distribution separated by two mass units: one polysaccharide formed by glucose monomers only, one polysaccharide formed by glucose monomers and ending by a D-mannitol end-group (182 g/mol).</p>	N	Delolme F., 2000	
B.2.5 Solubility in water	Method A.6 (Annex of Regulation (EC) No.440/2008)	Laminarin 98% Batch No.S210300	301.5 g/L at 23°C	Y	Anding C., 2002	
B.2.6 Solubility	Method A.6	Laminarin 98%	n-heptane : < 10 mg/L expressed as glucose	Y	Licata-Messana L., 2001a	

Test or Study & Data point	Guideline and Method	Test material purity and specification	Findings	GLP Y/N	Reference *	Acceptability/ comments
in organic solvents	(Annex of Regulation (EC) No.440/2008) OECD Test Guideline 105	Batch No.S210300	xylene : < 10 mg/L expressed as glucose 1,2-dichloroethane : < 10 mg/L expressed as glucose methanol : 60 mg/L expressed as glucose acetone : 21 mg/L expressed as glucose ethylacetate : < 10 mg/L expressed as glucose		Licata-Messana L., 2001b Licata-Messana L., 2001c Licata-Messana L., 2001d Licata-Messana L., 2001e Licata-Messana L., 2001f	
B.2.7 Partition co-efficient n-octanol/water	Method A.8 (Annex of Regulation (EC) No.440/2008)	Laminarin 98% Batch No.S210300	$\log P_{ow} = -1.6$ at 20°C	Y	Quintelas G., 2001a	
B.2.8 Dissociation in water dissociation constant(s) (pKa values) identity of dissociated species dissociation constant(s) (pKa values) of the active principle	Method C.7 (Annex of Regulation (EC) No.440/2008)	Laminarin 98% Batch No.S210300	No dissociation in water (at pH = 4, 7 and 9).	Y	Quintelas G., 2001b	
	Method C.7 (Annex of Regulation (EC) No.440/2008) OECD Test Guideline 111	Laminarin 98% Batch No.S210300	Laminarin is hydrolytically stable at the full range of environmental pH values (pH 4 to 9).	Y	Comb A.L., 2003	
B.2.9 Flammability and self-heating	Method A.10 (Annex of Regulation (EC) No.440/2008)	Laminarin 90% Batch No.S01/2000	Not highly flammable.	Y	Licata-Messana L., 2000c	The outcome of this study can still be used to classify according to

Test or Study & Data point	Guideline and Method	Test material purity and specification	Findings	GLP Y/N	Reference *	Acceptability/ comments
						Regulation (EC) 1272/2008. Laminarin does not classify as a flammable substance.
	Method A.12 (Annex of Regulation (EC) No.440/2008)	Laminarin 90% Batch No.S01/2000	Neither development nor ignition of gas observed.	Y	Licata-Messana L., 2000d	The outcome of this study can still be used to classify according to Regulation (EC) 1272/2008. Laminarin does not react violently in contact with water.
	Method A.16 (Annex of Regulation (EC) No.440/2008)	Laminarin 90% Batch No.S01/2000	No self-ignition observed up to 420°C.	Y	Licata-Messana L., 2000e	The outcome of this study can still be used to classify according to Regulation (EC) 1272/2008. Laminarin does not classify as a self-heating

Test or Study & Data point	Guideline and Method	Test material purity and specification	Findings	GLP Y/N	Reference *	Acceptability/ comments
						substance.
B.10 Flash point	Not applicable (solid).					
B.2.11 Explosive properties	Method A.14 (Annex of Regulation (EC) No 440/2008)	Laminarin 90% Batch No.S01/2000	Not explosive (no heat sensitivity, no shock sensitivity, no friction sensitivity).	Y	Licata-Messana L., 2000f	Based on the criteria defined in appendix 6 of the UN manual for tests and criteria, laminarin is not expected to be explosive.
B.2.12 Surface tension	Method A.5 (Annex of Regulation (EC) No 440/2008) OECD Test Guideline 115	Laminarin 98% Batch No.S210300	At 1 g/L in water: 72.2 ± 0.9 mN/m (at 20.2°C)	Y	Licata-Messana L., 2000g	
B.2.13 Oxidising properties	Method A.17 (Annex of Regulation (EC) No 440/2008)	Laminarin 90% Batch No.S01/2000	Not oxidising.	Y	Licata-Messana L., 2000h	Based on the criteria defined in appendix 6 of the UN manual for tests and criteria, laminarin is not expected to be oxidising.
B.2.14 Other studies			-			

B.2.1 References relied on

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
CA 2.1/01	Licata-Messana L.	2000a	Laminarin – Melting point SEPC Report No.00-907005-003 GLP, unpublished	N	N		Laboratoires Goëmar SAS
CA 2.1/02	Licata-Messana L.	2000b	Laminarin – Boiling point SEPC Report No.00-907005-004 GLP, unpublished	N	N		Laboratoires Goëmar SAS
CA 2.2/01	Tremain S.P.	2001	Laminarin: Determination of Vapour Pressure SafePharm Laboratories Limited Report No.1303/005 GLP, unpublished	N	N		Laboratoires Goëmar SAS
CA 2.4/01	Cuthbert J.E.	2001	Laminarin - Determination of Spectra SafePharm Laboratories Limited Report No.1476/001 GLP, unpublished	N	N		Laboratoires Goëmar SAS
CA 2.4/02	Delolme F.	2000	Analysis by MALDI-TOF Mass Spectrometry CNRS Report No.FC000828 Non-GLP, unpublished	N	N		Laboratoires Goëmar SAS
CA 2.5/01	Anding C.	2002	Hydrosolubility of laminarin Défitraces Report No.DEF/01-069 GLP, unpublished	N	N		Laboratoires Goëmar SAS
CA 2.6/01	Licata-Messana L.	2001a	Laminarin – Solubility in n-Heptane	N	N		Laboratoires Goëmar SAS

			SEPC Report No.00-907005-009 GLP, unpublished				
CA 2.6/02	Licata-Messana L.	2001b	Laminarin – Solubility in Xylene SEPC Report No.00-907005-010 GLP, unpublished	N	N		Laboratoires Goëmar SAS
CA 2.6/03	Licata-Messana L.	2001c	Laminarin – Solubility in 1,2 Dichloroethane SEPC Report No.00-907005-011 GLP, unpublished	N	N		Laboratoires Goëmar SAS
CA 2.6/04	Licata-Messana L.	2001d	Laminarin – Solubility in Methanol SEPC Report No.00-907005-012 GLP, unpublished	N	N		Laboratoires Goëmar SAS
CA 2.6/05	Licata-Messana L.	2001e	Laminarin – Solubility in Acetone SEPC Report No.00-907005-013 GLP, unpublished	N	N		Laboratoires Goëmar SAS
CA 2.6/06	Licata-Messana L.	2001f	Laminarin – Solubility in Ethyl acetate SEPC Report No.00-907005-014 GLP, unpublished	N	N		Laboratoires Goëmar SAS
CA 2.7/01	Quintelas G.	2001a	Laminarin – Determination of the partition coefficient of Laminarin Defitraces Report No.SEP/00-074 GLP, unpublished	N	N		Laboratoires Goëmar SAS
CA 2.8/01	Quintelas G.	2001b	Laminarin –Abiotic degradation of Laminarin pH dependent hydrolysis (Test C7) Defitraces Report No.SEP/00-075 GLP, unpublished	N	N		Laboratoires Goëmar SAS
CA	Comb A.I.	2003	Laminarin – Abiotic	N	N		Laboratoires

2.8/02			degradation : hydrolysis as a function of pH Huntingdon Life Sciences Report No.GOM/004 GLP, unpublished				Goëmar SAS
CA 2.9/01	Licata- messana I.	2000c	Laminarin – Flammability of solids SEPC Report No.00- 907005-016 GLP, unpublished	N	N		Laboratoires Goëmar SAS
CA 2.9/02	Licata- messana I.	2000d	Laminarin – Flammability in contact with water SEPC Report No.00- 907005-017 GLP, unpublished	N	N		Laboratoires Goëmar SAS
CA 2.9/03	Licata- messana I.	2000e	Laminarin – Self ignition temperature of solids SEPC Report No.00- 907005-019 GLP, unpublished	N	N		Laboratoires Goëmar SAS
CA 2.11/01	Licata- messana I.	2000f	Laminarin – Explosive properties SEPC Report No.00- 907005-018 GLP,unpublished	N	N		Laboratoires Goëmar SAS
CA 2.12/01	Licata- messana I.	2000g	Laminarin – Surface tension SEPC Report No.00- 907005-007 GLP, unpublished	N	N		Laboratoires Goëmar SAS
CA 2.13/01	Licata- messana I.	2000h	Laminarin – Oxidizing properties SEPC Report No.00- 907005-020 GLP, unpublished	N	N		Laboratoires Goëmar SAS