

Supporting information

Safety of 3' -sialyllactose sodium salt (3'-SL) as a novel food pursuant to Regulation (EU) 2015/2283

EFSA-Q-2018-00204

**Summary results of the 90-day repeated dose toxicity study in the rat with
the NF**

Summary results of parameters with statistically significant differences in the 90-day repeated dose toxicity study in the rat with the NF (unpublished study report, 2019d)

Parameters	Exposure (day)	Sex	Control	Oligofructose control (5000 mg/kg bw)	3'-SL sodium salt		
					Low dose (1000 mg/kg bw)	Mid dose (3000 mg/kg bw)	High dose (5000 mg/kg bw)
Body weight (g)	57	F	219 ± 15.2	223 ± 14.2	234 ± 17.8 *	232 ± 6.1*	234 ± 20.2*
	60	M	397 ± 20.8	370 ± 27.4 **	381 ± 31.1	389 ± 21.7	375 ± 33.3*
		F	227 ± 12.6	232 ± 12.9	244 ± 15.4*	237 ± 7.6*	242 ± 21.6*
	64	M	417 ± 22.0	387 ± 29.9**	399 ± 31.7	411 ± 25.4	391 ± 36.3*
		F	234 ± 14.1	238 ± 14.1	250 ± 16.9*	246 ± 8.8*	250 ± 22.7**
	67	M	433 ± 24.0	399 ± 30.7**	414 ± 33.8	427 ± 26.2	404 ± 38.1*
		F	242 ± 15.5	243 ± 13.9	261 ± 16.3*	252 ± 7.1*	256 ± 22.0*
	71	M	450 ± 25.9	415 ± 33.8**	431 ± 36.1	443 ± 26.2	420 ± 42.3 *
		F	249 ± 17.1	250 ± 13.0	266 ± 17.2	256 ± 6.9	262 ± 22.7*
	74	M	462 ± 28.4	423 ± 36.6**	441 ± 38.2	455 ± 30.8	430 ± 41.9*
		F	249 ± 13.8	253 ± 13.9	267 ± 18.7*	260 ± 9.8*	265 ± 22.6*
	78	M	475 ± 29.8	439 ± 37.8	458 ± 39.7	470 ± 30.1	442 ± 44.8*
		F	256 ± 12.6	258 ± 11.5	273 ± 18.6	264 ± 9.5	270 ± 24.3*
	81	M	487 ± 27.6	446 ± 39.1**	470 ± 42.3	478 ± 30.8	449 ± 45.6*
	85	M	491 ± 28.3	452 ± 41.0 **	478 ± 41.9	487 ± 32.9	455 ± 45.6*
		F	260 ± 17.6	265 ± 12.4	280 ± 23.8	273 ± 11.9*	276 ± 24.9*
	88	M	498 ± 29.6	460 ± 42**	479 ± 43.4	490 ± 32.8	462 ± 46.8*
		F	263 ± 17.4	265 ± 13.9	277 ± 22.5	272 ± 11.6	278 ± 22.7*
91	M	502 ± 30.0	464 ± 40.2*	481 ± 44.6	496 ± 31.2	467 ± 48.4*	
	F	265 ± 14.8	267 ± 12.6	282 ± 21.2	272 ± 10.6	280 ± 23.6*	
Ulna length (mm)	8	M	19.7 ± 0.69	18.6 ± 0.40**	18.9 ± 0.36**	19.4 ± 0.33	19.2 ± 0.35*
		F	19.1 ± 0.52	18.3 ± 0.48**	19 ± 0.36	19.2 ± 0.41	18.7 ± 0.37*
	22	F	25.7 ± 0.39	25.4 ± 0.38	26.2 ± 0.34**	26.2 ± 0.35**	25.4 ± 0.44
	50	M	35.6 ± 0.71	34.0 ± 0.79**	35.2 ± 0.68	34.7 ± 0.89**	34.6 ± 0.60**

		F	32.7 ± 0.53	32.7 ± 0.56	33.4 ± 0.20*	33.1 ± 0.81	32.7 ± 0.54**
	64	M	38 ± 0.76	37.4 ± 0.70*	37.7 ± 0.69	37.6 ± 0.72	37.0 ± 0.67**
	78	F	35.2 ± 0.54	35.7 ± 0.56**	36.0 ± 0.44*	35.9 ± 0.47*	35.5 ± 0.73**
Haematology							
Haemoglobin (g/dL)	90	M	15.7 ± 0.40	15.1 ± 0.50*	15.1 ± 0.26*	15.7 ± 0.44	14.5 ± 0.551 *
		F	15.0 ± 0.31	14.4 ± 0.56**	14.5 ± 0.63	15.1 ± 0.48	14.4 ± 0.35**
Erythrocytes (x10 ¹² /L)	90	F	7.54 ± 0.33	7.03 ± 0.45*	7.09 ± 0.72	7.37 ± 0.54	6.99 ± 0.54*
Neutrophils (X10 ⁹ /L)	90	F	0.08 ± 0.02	0.09 ± 0.04	0.10 ± 0.04 *	0.07 ± 0.03	0.12 ± 0.05 *
PT (sec)	90	M	25.0 ± 2.42	23.0 ± 1.63*	20.8 ± 2.40**	22.2 ± 2.04**	21.5 ± 2.18**
		F	27.4 ± 2.27	22.7 ± 2.41**	24.0 ± 2.19*	25.3 ± 3.04*	22.0 ± 1.60*
Clinical chemistry parameters							
ALP (U/L)	week 4 rec	F	41 ± 7.2	72 ± 60.7	--	--	103 ± 36.2**
ALT (U/L)	week 4 rec	F	25 ± 3.4	24 ± 2.8	--	--	43 ± 12.2**
Glucose (mmol/L)	week 4 rec	F	8.9 ± 0.97	8.1 ± 0.97	--	--	7.1 ± 0.63**
Urea (mmol/L)	90	M	5.70 ± 0.59	4.75 ± 0.76**	5.19 ± 0.68	6.20 ± 0.92*	6.77 ± 1.08**
	90	F	5.70 ± 0.65	5.98 ± 1.16	5.94 ± 0.74	6.56 ± 0.71	7.37 ± 1.34**
Creatinine (µmol/L)	90	M	21 ± 2.3	22 ± 2.3	22 ± 1.6	23 ± 3.3*	23 ± 3.1*
Triglycerides (mmol/L)	90	M	0.41 ± 0.15	0.71 ± 0.10	0.42 ± 0.12	0.44 ± 0.23	0.61 ± 0.17*
	90	F	0.32 ± 0.08	0.30 ± 0.05	0.36 ± 0.12	0.34 ± 0.11	0.48 ± 0.20*
Sodium (mmol/L)	90	M	143 ± 1.2	141 ± 1.3**	142 ± 1.3*	140 ± 1.3**	140 ± 2.0**
	90	F	140 ± 1.0	140 ± 1.8	141 ± 1.3	140 ± 1.2	139 ± 1.6*
Potassium (mmol/L)	week 4 rec	M	5.1 ± 0.09	4.8 ± 0.31	--	--	4.5 ± 0.59*
	week 4 rec	F	4.4 ± 0.11	4.5 ± 0.21	--	--	5.0 ± 0.34**
Chloride (mmol/L)	90	M	101 ± 1.0	99 ± 1.5**	100 ± 0.9	98 ± 1.7**	94 ± 1.3**
	90	F	100 ± 1.4	99 ± 1.7	101 ± 1.1	99 ± 1.4	97 ± 2.0**
Inorganic phosphorus (mmol/L)	week 4 rec	M	1.73 ± 0.09	1.83 ± 0.09	--	--	1.29 ± 0.28**
	week 4 rec	F	1.29 ± 0.22	1.37 ± 0.12	--	--	1.79 ± 0.20**
Total protein (g/L)	90	M	64 ± 3.8	61 ± 2.9**	63 ± 2.2	64 ± 2.9	60 ± 1.6**
Albumin (g/L)	week 4 rec	M	35 ± 1.2	35 ± 0.9	--	--	33 ± 0.8*
	week 4 rec	F	39 ± 2.2	38 ± 1.8	--	--	36 ± 1.7*
A/G (Ratio)	week 4 rec	M	1.16 ± 0.08	1.20 ± 0.09	--	--	1.35 ± 0.06**

	week 4 rec	F	1.32 ± 0.08	1.28 ± 0.07	--	--	1.22 ± 0.05*
Urinalysis							
Volume (mL)	90	M	6.6 ± 1.57	7.0 ± 2.81	8.0 ± 3.31	8.3 ± 3.55	3.8 ± 1.06**
pH	90	M	7.0 ± 0.33	6.9 ± 0.55	7.6 ± 0.28**	8.0 ± 0.31**	8.0 ± 0.57**
	90	F	6.6 ± 0.29	7.0 ± 1.16	7.1 ± 0.36*	7.5 ± 0.31**	7.7 ± 0.37**
Specific gravity (g/L)	90	M	1036 ± 4.5	1032 ± 12.2	1030 ± 4.0	1036 ± 10.2	1051 ± 7.9 *
Total proteins (mg)	90	M	6.88 ± 1.322	5.48 ± 1.58	6.87 ± 2.62	6.06 ± 1.90	2.98 ± 0.99**
Total creatinin (µmol)	90	M	72.04 ± 8.14	66.50 ± 10.64	72.47 ± 25.09	73.13 ± 12.40	51.70 ± 15.04**
Organ weight (adjusted mean values)							
Kidneys (g)	90	F	1.85	1.82	2.00*	1.95*	1.93*
Brain (g)	90	M	2.34	2.24**	2.29	2.32	2.26**
Salivary glands (g)	90	M	0.77	0.73	0.73	0.71	0.68**
Testes (g)	90	M	3.51	3.60	3.35	3.57	3.73*
Prostate (g)	90	M	1.03	1.06	1.01	0.88	1.20*

Doses expressed in mg/kg bw/day of 3'-SL sodium salt; results expressed as mean ± standard deviation

MCH = mean cell haemoglobin; MCHC = mean cell haemoglobin concentration; MCV = mean cell volume; RDW = red cell distribution width; LUC = large unstained cells; ALT = alanine aminotransferase; AST = aspartate aminotransferase; A/G = albumin/globulin ratio

* Significantly different from control (p<0.05) (Control vs 3'-SL-treated groups or reference control); ** Significantly different from control (p<0.01) (Control vs 3'-SL-treated groups or reference control)