

APPENDIX M: ANIMAL NUMBERS, DOSE GROUPS, AND FATES

PRODUCT IDENTIFICATION

L. reuteri 3630 & *L. reuteri* 3632

Individual Animal Numbers, Dose Groups, and Fates
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Group	Dose Level	Sex	Animal	Cage	Removal Day	Removal Week	Removal Date	Removal Time	Time Slot	Removal Symptom	Pathology Reason
1	0 CFU/kg bw/day	Male	3801	1	30	5	12/05/21	9:09	First	Term	Term
			3802	1	30	5	12/05/21	9:37	First	Term	Term
			3803	2	30	5	12/05/21	10:02	First	Term	Term
			3804	2	30	5	12/05/21	10:28	First	Term	Term
			3805	3	30	5	12/05/21	11:02	First	Term	Term
			3806	3	31	5	13/05/21	10:18	First	Term	Term
			3807	4	31	5	13/05/21	10:45	First	Term	Term
			3808	4	31	5	13/05/21	11:12	First	Term	Term
			3809	5	31	5	13/05/21	11:46	First	Term	Term
			3810	5	31	5	13/05/21	12:19	First	Term	Term
1	0 CFU/kg bw/day	Female	3811	6	30	5	12/05/21	11:20	First	Term	Term
			3812	6	30	5	12/05/21	12:18	First	Term	Term
			3813	7	30	5	12/05/21	13:42	First	Term	Term
			3814	7	30	5	12/05/21	14:07	First	Term	Term
			3815	8	30	5	12/05/21	14:24	First	Term	Term
			3816	8	31	5	13/05/21	14:40	First	Term	Term
			3817	9	31	5	13/05/21	14:54	First	Term	Term
			3818	9	31	5	13/05/21	15:26	First	Term	Term
			3819	10	31	5	13/05/21	16:06	First	Term	Term
			3820	10	31	5	13/05/21	16:35	First	Term	Term
2	low CFU/kg bw/day	Male	3821	11	30	5	12/05/21	9:13	First	Term	Term
			3822	11	30	5	12/05/21	9:43	First	Term	Term
			3823	12	30	5	12/05/21	10:07	First	Term	Term
			3824	12	30	5	12/05/21	10:32	First	Term	Term
			3825	13	31	5	13/05/21	10:19	First	Term	Term
			3826	13	31	5	13/05/21	10:46	First	Term	Term
			3827	14	31	5	13/05/21	11:19	First	Term	Term
			3828	14	31	5	13/05/21	11:56	First	Term	Term
			3829	15	19	3	01/05/21	9:28	.	HSac	HSac
			3830	15	31	5	13/05/21	12:39	First	Term	Term
2	low CFU/kg bw/day	Female	3831	16	30	5	12/05/21	11:24	First	Term	Term
			3832	16	30	5	12/05/21	12:19	First	Term	Term
			3833	17	30	5	12/05/21	13:43	First	Term	Term
			3834	17	30	5	12/05/21	14:07	First	Term	Term
			3835	18	30	5	12/05/21	14:33	First	Term	Term
			3836	18	31	5	13/05/21	14:40	First	Term	Term

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Numbers, Dose Groups, and Fates
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Group	Dose Level	Sex	Animal	Cage	Removal Day	Removal Week	Removal Date	Removal Time	Time Slot	Removal Symptom	Pathology Reason
2	low CFU/kg bw/day	Female	3837	19	31	5	13/05/21	15:00	First	Term	Term
			3838	19	31	5	13/05/21	15:43	First	Term	Term
			3839	20	31	5	13/05/21	16:06	First	Term	Term
			3840	20	31	5	13/05/21	16:44	First	Term	Term
3	mid CFU/kg bw/day	Male	3841	21	30	5	12/05/21	9:22	First	Term	Term
			3842	21	30	5	12/05/21	9:52	First	Term	Term
			3843	22	30	5	12/05/21	10:09	First	Term	Term
			3844	22	30	5	12/05/21	10:51	First	Term	Term
			3845	23	30	5	12/05/21	11:04	First	Term	Term
			3846	23	31	5	13/05/21	10:19	First	Term	Term
			3847	24	31	5	13/05/21	10:50	First	Term	Term
			3848	24	31	5	13/05/21	11:30	First	Term	Term
			3849	25	31	5	13/05/21	12:05	First	Term	Term
			3850	25	31	5	13/05/21	12:43	First	Term	Term
3	mid CFU/kg bw/day	Female	3851	26	30	5	12/05/21	12:16	First	Term	Term
			3852	26	30	5	12/05/21	13:40	First	Term	Term
			3853	27	30	5	12/05/21	13:44	First	Term	Term
			3854	27	30	5	12/05/21	14:19	First	Term	Term
			3855	28	30	5	12/05/21	14:40	First	Term	Term
			3856	28	31	5	13/05/21	14:41	First	Term	Term
			3857	29	31	5	13/05/21	15:11	First	Term	Term
			3858	29	31	5	13/05/21	15:44	First	Term	Term
			3859	30	31	5	13/05/21	16:14	First	Term	Term
			3860	30	31	5	13/05/21	17:13	First	Term	Term
4	high CFU/kg bw/day	Male	3861	31	30	5	12/05/21	9:29	First	Term	Term
			3862	31	30	5	12/05/21	9:56	First	Term	Term
			3863	32	30	5	12/05/21	10:19	First	Term	Term
			3864	32	30	5	12/05/21	10:52	First	Term	Term
			3865	33	30	5	12/05/21	11:19	First	Term	Term
			3866	33	31	5	13/05/21	10:20	First	Term	Term
			3867	34	31	5	13/05/21	10:59	First	Term	Term
			3868	34	31	5	13/05/21	11:39	First	Term	Term
			3869	35	31	5	13/05/21	12:11	First	Term	Term
			3870	35	31	5	13/05/21	14:39	First	Term	Term
4	high CFU/kg bw/day	Female	3871	36	30	5	12/05/21	12:16	First	Term	Term

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Numbers, Dose Groups, and Fates
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Group	Dose Level	Sex	Animal	Cage	Removal Day	Removal Week	Removal Date	Removal Time	Time Slot	Removal Symptom	Pathology Reason
4	high CFU/kg bw/day	Female	3872	36	30	5	12/05/21	13:41	First	Term	Term
			3873	37	30	5	12/05/21	14:06	First	Term	Term
			3874	37	30	5	12/05/21	14:19	First	Term	Term
			3875	38	30	5	12/05/21	14:45	First	Term	Term
			3876	38	31	5	13/05/21	14:54	First	Term	Term
			3877	39	31	5	13/05/21	15:17	First	Term	Term
			3878	39	31	5	13/05/21	15:55	First	Term	Term
			3879	40	31	5	13/05/21	16:35	First	Term	Term
			3880	40	31	5	13/05/21	16:55	First	Term	Term

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

APPENDIX N: INDIVIDUAL ANIMAL NECROPSY OBSERVATIONS

PRODUCT IDENTIFICATION

L. reuteri 3630 & *L. reuteri* 3632

Individual Animal Necropsy Observations
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Animal:	3801	Group:	1	Sex:	Male
		Dose:	0 CFU		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3802	Group:	1	Sex:	Male
		Dose:	0 CFU		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3803	Group:	1	Sex:	Male
		Dose:	0 CFU		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

Last Clinical Observations:

Hypersalivation, Slight

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3804	Group:	1	Sex:	Male
		Dose:	0 CFU		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3805	Group:	1	Sex:	Male
		Dose:	0 CFU		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

Last Clinical Observations:

Hypersalivation, Slight

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3806	Group:	1	Sex:	Male
		Dose:	0 CFU		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Necropsy Observations
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Animal:	3806 (Continued)	Group:	1	Sex:	Male
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Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3807	Group:	1	Sex:	Male
		Dose:	0 CFU		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3808	Group:	1	Sex:	Male
		Dose:	0 CFU		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3809	Group:	1	Sex:	Male
		Dose:	0 CFU		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3810	Group:	1	Sex:	Male
		Dose:	0 CFU		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3811	Group:	1	Sex:	Female
		Dose:	0 CFU		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3812	Group:	1	Sex:	Female
		Dose:	0 CFU		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Necropsy Observations
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Animal:	3812 (Continued)	Group:	1	Sex:	Female
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Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3813	Group:	1	Sex:	Female
		Dose:	0 CFU		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3814	Group:	1	Sex:	Female
		Dose:	0 CFU		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3815	Group:	1	Sex:	Female
		Dose:	0 CFU		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3816	Group:	1	Sex:	Female
		Dose:	0 CFU		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3817	Group:	1	Sex:	Female
		Dose:	0 CFU		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3818	Group:	1	Sex:	Female
		Dose:	0 CFU		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Necropsy Observations
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Animal:	3818 (Continued)	Group:	1	Sex:	Female
Gross Pathology Observations [Correlation]:					
No observations found					
Any remaining protocol required tissues, which have been examined, have no visible lesions					
Animal:	3819	Group:	1	Sex:	Female
		Dose:	0 CFU		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		
Gross Pathology Observations [Correlation]:					
uterus : fluid filled					
Any remaining protocol required tissues, which have been examined, have no visible lesions					
Animal:	3820	Group:	1	Sex:	Female
		Dose:	0 CFU		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		
Gross Pathology Observations [Correlation]:					
No observations found					
Any remaining protocol required tissues, which have been examined, have no visible lesions					
Animal:	3821	Group:	2	Sex:	Male
		Dose:	1.668E+10		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		
Gross Pathology Observations [Correlation]:					
No observations found					
Any remaining protocol required tissues, which have been examined, have no visible lesions					
Animal:	3822	Group:	2	Sex:	Male
		Dose:	1.668E+10		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		
Gross Pathology Observations [Correlation]:					
No observations found					
Any remaining protocol required tissues, which have been examined, have no visible lesions					
Animal:	3823	Group:	2	Sex:	Male
		Dose:	1.668E+10		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		
Gross Pathology Observations [Correlation]:					
No observations found					
Any remaining protocol required tissues, which have been examined, have no visible lesions					
Animal:	3824	Group:	2	Sex:	Male
		Dose:	1.668E+10		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Necropsy Observations
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Animal:	3824 (Continued)	Group:	2	Sex:	Male
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Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3825	Group:	2	Sex:	Male
		Dose:	1.668E+10		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3826	Group:	2	Sex:	Male
		Dose:	1.668E+10		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3827	Group:	2	Sex:	Male
		Dose:	1.668E+10		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3828	Group:	2	Sex:	Male
		Dose:	1.668E+10		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

testes-combined : (Comment) R-11mm x 6mm, L-16mm x 4mm

testes-combined : bilateral; small

epididymides-combined : (Comment) R-32mmx3mm, L-42mmx3mm

epididymides-combined : bilateral; small

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3829	Group:	2	Sex:	Male
		Dose:	1.668E+10		
Necropsy Date:	5/1/2021	Study Day (Week) of Death:	19 (3)		

Last Clinical Observations:

Irregular Respiration

Gross Pathology Observations [Correlation]:

esophagus : (Comment) has a small tear with food particles near opening

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Necropsy Observations
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Animal:	3829 (Continued)	Group:	2	Sex:	Male
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Gross Pathology Observations [Correlation] (Continued):

esophagus : hole
lungs : (Comment) clear colorless fluid present
lungs : enlarged; red
all gross lesions : (Comment) clear colorless fluid in thoracic cavity
all gross lesions : fluid filled; clear

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3830	Group:	2	Sex:	Male
		Dose:	1.668E+10		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3831	Group:	2	Sex:	Female
		Dose:	1.668E+10		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3832	Group:	2	Sex:	Female
		Dose:	1.668E+10		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3833	Group:	2	Sex:	Female
		Dose:	1.668E+10		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3834	Group:	2	Sex:	Female
		Dose:	1.668E+10		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Necropsy Observations
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Animal:	3835	Group:	2	Sex:	Female
		Dose:	1.668E+10		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3836	Group:	2	Sex:	Female
		Dose:	1.668E+10		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3837	Group:	2	Sex:	Female
		Dose:	1.668E+10		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3838	Group:	2	Sex:	Female
		Dose:	1.668E+10		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3839	Group:	2	Sex:	Female
		Dose:	1.668E+10		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3840	Group:	2	Sex:	Female
		Dose:	1.668E+10		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3841	Group:	3	Sex:	Male
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* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Necropsy Observations
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Animal:	3841 (Continued)	Group:	3	Sex:	Male
		Dose:	3.337E+10		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3842	Group:	3	Sex:	Male
		Dose:	3.337E+10		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3843	Group:	3	Sex:	Male
		Dose:	3.337E+10		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3844	Group:	3	Sex:	Male
		Dose:	3.337E+10		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3845	Group:	3	Sex:	Male
		Dose:	3.337E+10		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3846	Group:	3	Sex:	Male
		Dose:	3.337E+10		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3847	Group:	3	Sex:	Male
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* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Necropsy Observations
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Animal:	3847 (Continued)	Group:	3	Sex:	Male
		Dose:	3.337E+10		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3848	Group:	3	Sex:	Male
		Dose:	3.337E+10		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3849	Group:	3	Sex:	Male
		Dose:	3.337E+10		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3850	Group:	3	Sex:	Male
		Dose:	3.337E+10		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

testes-combined : (Comment) R-1.8 cm x 1.2 cm
testes-combined : right; small

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3851	Group:	3	Sex:	Female
		Dose:	3.337E+10		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3852	Group:	3	Sex:	Female
		Dose:	3.337E+10		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Necropsy Observations
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Animal:	3853	Group:	3	Sex:	Female
		Dose:	3.337E+10		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3854	Group:	3	Sex:	Female
		Dose:	3.337E+10		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

Gross Pathology Observations [Correlation]:

uterus : fluid filled

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3855	Group:	3	Sex:	Female
		Dose:	3.337E+10		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3856	Group:	3	Sex:	Female
		Dose:	3.337E+10		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3857	Group:	3	Sex:	Female
		Dose:	3.337E+10		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3858	Group:	3	Sex:	Female
		Dose:	3.337E+10		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3859	Group:	3	Sex:	Female
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* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Necropsy Observations
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Animal:	3859 (Continued)	Group:	3	Sex:	Female
		Dose:	3.337E+10		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3860	Group:	3	Sex:	Female
		Dose:	3.337E+10		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3861	Group:	4	Sex:	Male
		Dose:	1.001E+11		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3862	Group:	4	Sex:	Male
		Dose:	1.001E+11		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3863	Group:	4	Sex:	Male
		Dose:	1.001E+11		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3864	Group:	4	Sex:	Male
		Dose:	1.001E+11		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3865	Group:	4	Sex:	Male
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* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Necropsy Observations
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Animal:	3865 (Continued)	Group:	4	Sex:	Male
		Dose:	1.001E+11		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3866	Group:	4	Sex:	Male
		Dose:	1.001E+11		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3867	Group:	4	Sex:	Male
		Dose:	1.001E+11		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3868	Group:	4	Sex:	Male
		Dose:	1.001E+11		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3869	Group:	4	Sex:	Male
		Dose:	1.001E+11		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3870	Group:	4	Sex:	Male
		Dose:	1.001E+11		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3871	Group:	4	Sex:	Female
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* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Necropsy Observations
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Animal:	3871 (Continued)	Group:	4	Sex:	Female
		Dose:	1.001E+11		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3872	Group:	4	Sex:	Female
		Dose:	1.001E+11		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3873	Group:	4	Sex:	Female
		Dose:	1.001E+11		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3874	Group:	4	Sex:	Female
		Dose:	1.001E+11		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3875	Group:	4	Sex:	Female
		Dose:	1.001E+11		
Necropsy Date:	5/12/2021	Study Day (Week) of Death:	30 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3876	Group:	4	Sex:	Female
		Dose:	1.001E+11		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3877	Group:	4	Sex:	Female
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* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Necropsy Observations
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Animal:	3877 (Continued)	Group:	4	Sex:	Female
		Dose:	1.001E+11		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3878	Group:	4	Sex:	Female
		Dose:	1.001E+11		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3879	Group:	4	Sex:	Female
		Dose:	1.001E+11		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	3880	Group:	4	Sex:	Female
		Dose:	1.001E+11		
Necropsy Date:	5/13/2021	Study Day (Week) of Death:	31 (5)		

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

APPENDIX O: INDIVIDUAL ANIMAL TERMINAL BODY AND ORGAN WEIGHTS

PRODUCT IDENTIFICATION

L. reuteri 3630 & *L. reuteri* 3632

Individual Animal Terminal Body and Organ Weights
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

0 CFU Group 1	Terminal BW (g)	Adrenal Glands Wt (g)	Brain Wt (g)	Epididymides Wt (g)	Heart Wt (g)	Kidneys Wt (g)	Liver Wt (g)
	Day 30/31	Day 30/31	Day 30/31	Day 30/31	Day 30/31	Day 30/31	Day 30/31
	3801	432	0.088	2.13	0.964	1.32	3.29
3802	412	0.082	2.07	1.184	1.21	2.85	12.03
3803	461	0.076	2.22	1.383	1.44	2.94	12.79
3804	480	0.069	2.20	1.391	1.46	3.43	13.34
3805	463	0.080	2.29	1.225	1.41	3.38	11.83
3806	396	0.059	2.07	1.244	1.08	2.84	9.89
3807	461	0.082	2.21	1.706	1.38	3.60	13.44
3808	402	0.055	2.28	1.424	1.42	2.83	10.44
3809	498	0.098	2.25	1.335	1.63	3.92	16.54
3810	403	0.029 E	2.18	1.346	1.38	2.81	11.80
Mean	440.8	0.0766	2.190	1.3202	1.373	3.189	12.381
SD	36.5	0.0137	0.079	0.1914	0.148	0.391	1.847
N	10	9	10	10	10	10	10

E = Exclude

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Terminal Body and Organ Weights
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

0 CFU Group 1	Spleen	Testes	Thymus
	Wt (g)	Wt (g)	Wt (g)
	Day 30/31	Day 30/31	Day 30/31
3801	0.82	2.90	0.371
3802	0.80	2.94	0.452
3803	0.72	3.61	0.319
3804	0.77	3.88	0.257
3805	0.80	3.54	0.399
3806	0.55	3.29	0.388
3807	0.62	3.70	0.487
3808	0.88	3.71	0.235
3809	0.93	3.29	0.400
3810	0.79	3.88	0.336
Mean	0.768	3.474	0.3644
SD	0.113	0.356	0.0795
N	10	10	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Terminal Body and Organ Weights
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

1.668E+10 CFU Group 2	Terminal	Adrenal	Brain	Epididymides	Heart	Kidneys	Liver
	BW	Glands Wt	Wt	Wt	Wt	Wt	Wt
	(g)	(g)	(g)	(g)	(g)	(g)	(g)
	Day 30/31	Day 30/31	Day 30/31	Day 30/31	Day 30/31	Day 30/31	Day 30/31
3821	455	0.089	2.04	1.441	1.48	3.51	12.18
3822	399	0.050	2.29	1.200	1.26	3.09	12.08
3823	410	0.072	2.31	1.424	1.22	3.07	11.18
3824	370	0.068	2.17	1.375	1.35	2.93	10.77
3825	443	0.064	2.16	1.455	1.47	3.18	14.20
3826	482	0.043 E	2.22	1.440	1.63	3.57	14.34
3827	447	0.078	2.34	1.535	1.52	3.72	17.31
3828	454	0.063	2.07	0.573	1.37	3.24	12.85
3829	-	NT	NT	NT	NT	NT	NT
3830	418	0.087	2.29	1.188	1.45	2.94	12.17
Mean	430.9	0.0714	2.210	1.2923	1.417	3.250	13.009
SD	34.4	0.0130	0.107	0.2937	0.129	0.286	2.010
N	9	8	9	9	9	9	9

E = Exclude

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Terminal Body and Organ Weights
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

1.668E+10 CFU Group 2	Spleen	Testes	Thymus
	Wt	Wt	Wt
	(g)	(g)	(g)
	Day 30/31	Day 30/31	Day 30/31
3821	1.00	3.41	0.476
3822	1.10	2.86	0.564
3823	1.00	3.23	0.303
3824	0.68	3.68	0.297
3825	0.84	3.90	0.375
3826	0.89	3.77	0.593
3827	0.93	3.25	0.367
3828	0.90	0.90	0.609
3829	NT	NT	NT
3830	0.72	3.59	0.387
Mean	0.896	3.177	0.4412
SD	0.135	0.911	0.1226
N	9	9	9

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Terminal Body and Organ Weights
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

3.337E+10 CFU Group 3	Terminal	Adrenal	Brain	Epididymides	Heart	Kidneys	Liver
	BW	Glands Wt	Wt	Wt	Wt	Wt	Wt
	(g)	(g)	(g)	(g)	(g)	(g)	(g)
	Day 30/31	Day 30/31	Day 30/31	Day 30/31	Day 30/31	Day 30/31	Day 30/31
3841	397	0.069	2.02	1.432	1.24	2.60	11.03
3842	475	0.053	2.37	1.308	1.39	3.20	13.37
3843	438	0.081	2.19	1.369	1.44	3.78	12.68
3844	409	0.046	2.22	1.277	1.38	3.32	11.86
3845	447	0.063	2.26	1.291	1.30	2.93	14.44
3846	478	0.080	2.26	1.181	1.38	3.28	14.37
3847	405	0.065	2.23	1.208	1.14	2.80	11.70
3848	481	0.091	2.26	1.432	1.54	3.72	13.25
3849	418	0.071	2.19	1.244	1.32	2.90	11.12
3850	480	0.046	2.18	1.377	1.40	3.59	14.25
Mean	442.8	0.0665	2.218	1.3119	1.353	3.212	12.807
SD	34.1	0.0151	0.089	0.0885	0.110	0.403	1.327
N	10	10	10	10	10	10	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Terminal Body and Organ Weights
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

3.337E+10 CFU Group 3	Spleen	Testes	Thymus
	Wt (g)	Wt (g)	Wt (g)
	Day 30/31	Day 30/31	Day 30/31
3841	0.67	3.52	0.321
3842	0.82	3.53	0.246
3843	0.78	3.82	0.317
3844	0.88	3.39	0.252
3845	1.02	3.57	0.306
3846	1.12	3.02	0.548
3847	0.72	3.07	0.333
3848	1.07	4.03	0.377
3849	0.90	3.13	0.434
3850	0.92	2.76	0.471
Mean	0.890	3.384	0.3605
SD	0.148	0.390	0.0972
N	10	10	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Terminal Body and Organ Weights
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

1.001E+11 CFU Group 4	Terminal	Adrenal	Brain	Epididymides	Heart	Kidneys	Liver
	BW	Glands Wt	Wt	Wt	Wt	Wt	Wt
	(g)	(g)	(g)	(g)	(g)	(g)	(g)
	Day 30/31	Day 30/31	Day 30/31	Day 30/31	Day 30/31	Day 30/31	Day 30/31
3861	465	0.079	2.24	1.295	1.35	3.19	14.14
3862	376	0.081	1.80	1.541	1.32	3.21	10.97
3863	398	0.065	2.16	1.521	1.24	3.16	10.78
3864	430	0.050	2.10	1.493	1.42	3.27	13.74
3865	483	0.076	2.32	1.572	1.61	3.61	15.30
3866	462	0.078	2.16	1.314	1.45	3.01	12.25
3867	473	0.056	2.30	1.368	1.50	3.59	20.78
3868	448	0.059	2.25	1.367	1.49	2.96	11.68
3869	421	0.070	2.17	1.380	1.32	3.07	10.03
3870	506	0.079	2.35	1.018 E	1.52	3.80	14.39
Mean	446.2	0.0693	2.185	1.4279	1.422	3.287	13.406
SD	40.0	0.0112	0.157	0.1041	0.113	0.283	3.129
N	10	10	10	9	10	10	10

E = Exclude

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Terminal Body and Organ Weights
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

1.001E+11 CFU Group 4	Spleen	Testes	Thymus
	Wt (g)	Wt (g)	Wt (g)
	Day 30/31	Day 30/31	Day 30/31
3861	0.81	3.51	0.254
3862	0.67	2.89	0.254
3863	0.76	3.43	0.366
3864	0.71	3.58	0.485
3865	0.95	3.89	0.377
3866	0.90	3.62	0.543
3867	0.98	3.36	0.418
3868	0.87	3.67	0.432
3869	0.74	3.19	0.308
3870	1.14	3.53	0.298
Mean	0.853	3.467	0.3735
SD	0.144	0.276	0.0973
N	10	10	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Terminal Body and Organ Weights
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

0 CFU Group 1	Terminal BW (g)	Adrenal Glands Wt (g)	Brain Wt (g)	Heart Wt (g)	Kidneys Wt (g)	Liver Wt (g)	Ovaries with Oviducts Wt (g)
	Day 30/31	Day 30/31	Day 30/31	Day 30/31	Day 30/31	Day 30/31	Day 30/31
	3811	270	0.065	2.07	0.88	1.98	7.83
3812	253	0.072	1.87	0.99	2.08	9.56	0.127
3813	245	0.062	1.91	0.87	1.64	6.85	0.135
3814	251	0.066	2.03	0.92	1.76	7.28	0.106
3815	273	0.090	1.92	0.92	1.96	7.61	0.129
3816	209	0.080	1.84	0.77	1.60	6.19	0.128
3817	254	0.082	2.00	0.84	1.93	7.10	0.125
3818	273	0.050	1.95	0.91	1.76	7.77	0.119
3819	250	0.088	1.86	0.85	1.86	6.38	0.100
3820	271	0.072	1.97	0.84	1.88	7.67	0.141
Mean	254.9	0.0727	1.942	0.879	1.845	7.424	0.1250
SD	19.4	0.0125	0.076	0.060	0.153	0.943	0.0135
N	10	10	10	10	10	10	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Terminal Body and Organ Weights
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

0 CFU Group 1	Spleen Wt (g)	Thymus Wt (g)	Uterus Wt (g)
	Day 30/31	Day 30/31	Day 30/31
	3811	0.68	0.484
3812	0.90	0.287	0.57
3813	0.54	0.365	0.96
3814	0.57	0.465	0.44
3815	0.49	0.308	0.51
3816	0.44	0.299	0.37
3817	0.58	0.432	0.54
3818	0.51	0.375	0.65
3819	0.40	0.312	1.10
3820	0.52	0.261	0.43
Mean	0.563	0.3588	0.647
SD	0.141	0.0787	0.252
N	10	10	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Terminal Body and Organ Weights
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

1.668E+10 CFU Group 2	Terminal	Adrenal	Brain	Heart	Kidneys	Liver	Ovaries with
	BW	Glands Wt	Wt	Wt	Wt	Wt	Oviducts Wt
	(g)						
	Day 30/31						
3831	249	0.056	1.93	0.92	1.80	7.36	0.125
3832	273	0.042	1.93	1.03	1.86	8.07	0.114
3833	272	0.067	1.97	1.02	2.12	8.14	0.135
3834	252	0.075	1.93	1.01	1.70	7.84	0.123
3835	237	0.107	1.88	0.95	1.92	7.37	0.122
3836	245	0.083	1.81	0.79	1.68	6.98	0.107
3837	261	0.072	1.88	0.87	1.84	6.59	0.120
3838	260	0.066	2.06	0.96	1.87	7.25	0.114
3839	280	0.092	2.06	0.93	1.98	9.29	0.108
3840	245	0.073	2.03	0.85	1.59	5.90	0.134
Mean	257.4	0.0733	1.948	0.933	1.836	7.479	0.1202
SD	14.2	0.0181	0.083	0.078	0.155	0.931	0.0097
N	10	10	10	10	10	10	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Terminal Body and Organ Weights
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

1.668E+10 CFU Group 2	Spleen	Thymus	Uterus
	Wt (g)	Wt (g)	Wt (g)
	Day 30/31	Day 30/31	Day 30/31
3831	0.47	0.340	0.49
3832	0.45	0.358	0.45
3833	0.48	0.367	0.55
3834	0.43	0.341	0.46
3835	0.47	0.278	0.55
3836	0.46	0.232	0.48
3837	0.56	0.534	0.47
3838	0.51	0.278	0.48
3839	0.53	0.368	0.42
3840	0.50	0.287	0.60
Mean	0.486	0.3383	0.495
SD	0.039	0.0827	0.055
N	10	10	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Terminal Body and Organ Weights
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

3.337E+10 CFU Group 3	Terminal	Adrenal	Brain	Heart	Kidneys	Liver	Ovaries with
	BW	Glands Wt	Wt	Wt	Wt	Wt	Oviducts Wt
	(g)						
	Day 30/31						
3851	274	0.088	1.89	0.99	1.95	7.91	0.162
3852	260	0.080	1.99	0.93	1.86	7.68	0.108
3853	251	0.075	1.89	0.86	1.78	7.47	0.099
3854	253	0.079	1.92	0.83	1.81	7.69	0.147
3855	261	0.092	1.91	0.88	1.83	8.08	0.133
3856	262	0.085	2.10	0.84	1.89	7.27	0.130
3857	255	0.065	1.99	0.81	1.64	6.65	0.107
3858	241	0.061	1.87	0.82	1.65	6.78	0.103
3859	259	0.067	2.12	0.96	1.84	7.06	0.132
3860	272	0.066	1.95	0.84	1.65	7.91	0.156
Mean	258.8	0.0758	1.963	0.876	1.790	7.450	0.1277
SD	9.7	0.0107	0.088	0.063	0.109	0.495	0.0227
N	10	10	10	10	10	10	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Terminal Body and Organ Weights
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

3.337E+10 CFU Group 3	Spleen	Thymus	Uterus
	Wt (g)	Wt (g)	Wt (g)
	Day 30/31	Day 30/31	Day 30/31
3851	0.62	0.300	0.45
3852	0.67	0.347	0.54
3853	0.55	0.397	0.41
3854	0.61	0.443	0.91
3855	0.56	0.333	0.57
3856	0.65	0.502	0.56
3857	0.47	0.318	0.48
3858	0.49	0.324	0.33
3859	0.53	0.413	0.42
3860	0.58	0.235	0.68
Mean	0.573	0.3612	0.535
SD	0.066	0.0777	0.165
N	10	10	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Terminal Body and Organ Weights
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

1.001E+11 CFU Group 4	Terminal BW (g)	Adrenal Glands Wt (g)	Brain Wt (g)	Heart Wt (g)	Kidneys Wt (g)	Liver Wt (g)	Ovaries with Oviducts Wt (g)
	Day 30/31	Day 30/31	Day 30/31	Day 30/31	Day 30/31	Day 30/31	Day 30/31
	3871	230	0.091	1.98	0.83	1.72	6.89
3872	252	0.085	2.02	0.87	1.92	7.05	0.126
3873	217	0.061	1.94	0.71	1.75	7.57	0.126
3874	259	0.066	1.89	0.86	1.97	9.24	0.142
3875	264	0.068	2.06	0.90	2.13	9.85	0.164
3876	288	0.082	2.14	0.94	1.78	8.09	0.161
3877	294	0.042	2.09	0.87	1.83	7.63	0.135
3878	237	0.062	1.95	0.80	1.60	6.80	0.149
3879	249	0.061	1.99	0.80	1.69	6.87	0.097
3880	252	0.058	1.94	0.83	1.84	6.18	0.115
Mean	254.2	0.0676	2.000	0.841	1.823	7.617	0.1366
SD	23.9	0.0146	0.077	0.063	0.153	1.154	0.0211
N	10	10	10	10	10	10	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Terminal Body and Organ Weights
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

1.001E+11 CFU Group 4	Spleen	Thymus	Uterus
	Wt (g)	Wt (g)	Wt (g)
	Day 30/31	Day 30/31	Day 30/31
3871	0.47	0.294	0.46
3872	0.45	0.300	1.01
3873	0.50	0.210	0.39
3874	0.52	0.173	1.38
3875	0.47	0.425	0.46
3876	0.58	0.376	0.31
3877	0.58	0.441	0.45
3878	0.56	0.295	0.41
3879	0.48	0.274	0.38
3880	0.51	0.205	0.42
Mean	0.512	0.2993	0.567
SD	0.047	0.0915	0.345
N	10	10	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

APPENDIX P: INDIVIDUAL ANIMAL ORGAN-TO-BODY WEIGHT RATIOS

PRODUCT IDENTIFICATION

L. reuteri 3630 & *L. reuteri* 3632

Individual Animal Organ-To-Body Weight Ratios
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

0 CFU Group 1	Adrenal	Brain	Epididymides	Heart	Kidneys	Liver	Spleen
	/TBW (Ratio)						
	Day 30/31						
3801	0.204	4.93	2.231	3.06	7.62	27.11	1.90
3802	0.199	5.02	2.874	2.94	6.92	29.20	1.94
3803	0.165	4.82	3.000	3.12	6.38	27.74	1.56
3804	0.144	4.58	2.898	3.04	7.15	27.79	1.60
3805	0.173	4.95	2.646	3.05	7.30	25.55	1.73
3806	0.149	5.23	3.141	2.73	7.17	24.97	1.39
3807	0.178	4.79	3.701	2.99	7.81	29.15	1.34
3808	0.137	5.67	3.542	3.53	7.04	25.97	2.19
3809	0.197	4.52	2.681	3.27	7.87	33.21	1.87
3810	.	5.41	3.340	3.42	6.97	29.28	1.96
Mean	0.1716	4.992	3.0054	3.115	7.222	27.998	1.748
SD	0.0250	0.359	0.4428	0.237	0.452	2.398	0.271
N	9	10	10	10	10	10	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Organ-To-Body Weight Ratios
 PSL Study Number 55164: Limosilactobacillus Reuteri:
 28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

0 CFU Group 1	Testes /TBW (Ratio)	Thymus /TBW (Ratio)
	Day 30/31	Day 30/31
	3801	6.71
3802	7.14	1.097
3803	7.83	0.692
3804	8.08	0.535
3805	7.65	0.862
3806	8.31	0.980
3807	8.03	1.056
3808	9.23	0.585
3809	6.61	0.803
3810	9.63	0.834
Mean	7.921	0.8303
SD	0.983	0.1867
N	10	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Organ-To-Body Weight Ratios
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

1.668E+10 CFU Group 2	Adrenal	Brain	Epididymides	Heart	Kidneys	Liver	Spleen
	/TBW	/TBW	/TBW	/TBW	/TBW	/TBW	/TBW
	(Ratio)	(Ratio)	(Ratio)	(Ratio)	(Ratio)	(Ratio)	(Ratio)
	Day 30/31	Day 30/31	Day 30/31	Day 30/31	Day 30/31	Day 30/31	Day 30/31
3821	0.196	4.48	3.167	3.25	7.71	26.77	2.20
3822	0.125	5.74	3.008	3.16	7.74	30.28	2.76
3823	0.176	5.63	3.473	2.98	7.49	27.27	2.44
3824	0.184	5.86	3.716	3.65	7.92	29.11	1.84
3825	0.144	4.88	3.284	3.32	7.18	32.05	1.90
3826	.	4.61	2.988	3.38	7.41	29.75	1.85
3827	0.174	5.23	3.434	3.40	8.32	38.72	2.08
3828	0.139	4.56	1.262	3.02	7.14	28.30	1.98
3830	0.208	5.48	2.842	3.47	7.03	29.11	1.72
Mean	0.1683	5.164	3.0193	3.291	7.549	30.152	2.084
SD	0.0292	0.544	0.7138	0.216	0.418	3.582	0.333
N	8	9	9	9	9	9	9

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Organ-To-Body Weight Ratios
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

1.668E+10 CFU Group 2	Testes	Thymus
	/TBW (Ratio)	/TBW (Ratio)
	Day 30/31	Day 30/31
3821	7.49	1.046
3822	7.17	1.414
3823	7.88	0.739
3824	9.95	0.803
3825	8.80	0.847
3826	7.82	1.230
3827	7.27	0.821
3828	1.98	1.341
3830	8.59	0.926
Mean	7.439	1.0185
SD	2.227	0.2519
N	9	9

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Organ-To-Body Weight Ratios
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

3.337E+10 CFU Group 3	Adrenal	Brain	Epididymides	Heart	Kidneys	Liver	Spleen
	/TBW (Ratio)						
	Day 30/31						
3841	0.174	5.09	3.607	3.12	6.55	27.78	1.69
3842	0.112	4.99	2.754	2.93	6.74	28.15	1.73
3843	0.185	5.00	3.126	3.29	8.63	28.95	1.78
3844	0.112	5.43	3.122	3.37	8.12	29.00	2.15
3845	0.141	5.06	2.888	2.91	6.55	32.30	2.28
3846	0.167	4.73	2.471	2.89	6.86	30.06	2.34
3847	0.160	5.51	2.983	2.81	6.91	28.89	1.78
3848	0.189	4.70	2.977	3.20	7.73	27.55	2.22
3849	0.170	5.24	2.976	3.16	6.94	26.60	2.15
3850	0.096	4.54	2.869	2.92	7.48	29.69	1.92
Mean	0.1506	5.028	2.9772	3.060	7.251	28.897	2.004
SD	0.0334	0.312	0.2917	0.193	0.710	1.581	0.252
N	10	10	10	10	10	10	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Organ-To-Body Weight Ratios
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

3.337E+10 CFU Group 3	Testes	Thymus
	/TBW (Ratio)	/TBW (Ratio)
	Day 30/31	Day 30/31
3841	8.87	0.809
3842	7.43	0.518
3843	8.72	0.724
3844	8.29	0.616
3845	7.99	0.685
3846	6.32	1.146
3847	7.58	0.822
3848	8.38	0.784
3849	7.49	1.038
3850	5.75	0.981
Mean	7.681	0.8123
SD	1.007	0.1948
N	10	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Organ-To-Body Weight Ratios
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

1.001E+11 CFU Group 4	Adrenal	Brain	Epididymides	Heart	Kidneys	Liver	Spleen
	/TBW (Ratio)						
	Day 30/31						
3861	0.170	4.82	2.785	2.90	6.86	30.41	1.74
3862	0.215	4.79	4.098	3.51	8.54	29.18	1.78
3863	0.163	5.43	3.822	3.12	7.94	27.09	1.91
3864	0.116	4.88	3.472	3.30	7.60	31.95	1.65
3865	0.157	4.80	3.255	3.33	7.47	31.68	1.97
3866	0.169	4.68	2.844	3.14	6.52	26.52	1.95
3867	0.118	4.86	2.892	3.17	7.59	43.93	2.07
3868	0.132	5.02	3.051	3.33	6.61	26.07	1.94
3869	0.166	5.15	3.278	3.14	7.29	23.82	1.76
3870	0.156	4.64	.	3.00	7.51	28.44	2.25
Mean	0.1564	4.908	3.2775	3.194	7.393	29.908	1.902
SD	0.0291	0.237	0.4525	0.177	0.614	5.559	0.178
N	10	10	9	10	10	10	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Organ-To-Body Weight Ratios
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

1.001E+11 CFU Group 4	Testes	Thymus
	/TBW	/TBW
	(Ratio)	(Ratio)
	Day 30/31	Day 30/31
3861	7.55	0.546
3862	7.69	0.676
3863	8.62	0.920
3864	8.33	1.128
3865	8.05	0.781
3866	7.84	1.175
3867	7.10	0.884
3868	8.19	0.964
3869	7.58	0.732
3870	6.98	0.589
Mean	7.792	0.8394
SD	0.522	0.2136
N	10	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Organ-To-Body Weight Ratios
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

0 CFU Group 1	Adrenal	Brain	Heart	Kidneys	Liver	Ovaries with	Spleen
	/TBW (Ratio)	/TBW (Ratio)	/TBW (Ratio)	/TBW (Ratio)	/TBW (Ratio)	oviducts/TBW (Ratio)	/TBW (Ratio)
	Day 30/31	Day 30/31					
3811	0.241	7.67	3.26	7.33	29.00	0.519	2.52
3812	0.285	7.39	3.91	8.22	37.79	0.502	3.56
3813	0.253	7.80	3.55	6.69	27.96	0.551	2.20
3814	0.263	8.09	3.67	7.01	29.00	0.422	2.27
3815	0.330	7.03	3.37	7.18	27.88	0.473	1.79
3816	0.383	8.80	3.68	7.66	29.62	0.612	2.11
3817	0.323	7.87	3.31	7.60	27.95	0.492	2.28
3818	0.183	7.14	3.33	6.45	28.46	0.436	1.87
3819	0.352	7.44	3.40	7.44	25.52	0.400	1.60
3820	0.266	7.27	3.10	6.94	28.30	0.520	1.92
Mean	0.2877	7.650	3.458	7.252	29.148	0.4927	2.212
SD	0.0593	0.526	0.242	0.515	3.227	0.0636	0.545
N	10	10	10	10	10	10	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Organ-To-Body Weight Ratios
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

0 CFU Group 1	Thymus /TBW (Ratio)	Uterus /TBW (Ratio)
	Day 30/31	Day 30/31
	3811	1.793
3812	1.134	2.25
3813	1.490	3.92
3814	1.853	1.75
3815	1.128	1.87
3816	1.431	1.77
3817	1.701	2.13
3818	1.374	2.38
3819	1.248	4.40
3820	0.963	1.59
Mean	1.4114	2.539
SD	0.3012	0.991
N	10	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Organ-To-Body Weight Ratios
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

1.668E+10 CFU Group 2	Adrenal	Brain	Heart	Kidneys	Liver	Ovaries with	Spleen
	/TBW	/TBW	/TBW	/TBW	/TBW	oviducts/TBW	/TBW
	(Ratio)	(Ratio)	(Ratio)	(Ratio)	(Ratio)	(Ratio)	(Ratio)
	Day 30/31	Day 30/31					
3831	0.225	7.75	3.69	7.23	29.56	0.502	1.89
3832	0.154	7.07	3.77	6.81	29.56	0.418	1.65
3833	0.246	7.24	3.75	7.79	29.93	0.496	1.76
3834	0.298	7.66	4.01	6.75	31.11	0.488	1.71
3835	0.451	7.93	4.01	8.10	31.10	0.515	1.98
3836	0.339	7.39	3.22	6.86	28.49	0.437	1.88
3837	0.276	7.20	3.33	7.05	25.25	0.460	2.15
3838	0.254	7.92	3.69	7.19	27.88	0.438	1.96
3839	0.329	7.36	3.32	7.07	33.18	0.386	1.89
3840	0.298	8.29	3.47	6.49	24.08	0.547	2.04
Mean	0.2869	7.581	3.627	7.134	29.014	0.4686	1.891
SD	0.0790	0.391	0.279	0.488	2.740	0.0494	0.153
N	10	10	10	10	10	10	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Organ-To-Body Weight Ratios
 PSL Study Number 55164: Limosilactobacillus Reuteri:
 28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

1.668E+10 CFU Group 2	Thymus	Uterus
	/TBW	/TBW
	(Ratio)	(Ratio)
	Day 30/31	Day 30/31
3831	1.365	1.97
3832	1.311	1.65
3833	1.349	2.02
3834	1.353	1.83
3835	1.173	2.32
3836	0.947	1.96
3837	2.046	1.80
3838	1.069	1.85
3839	1.314	1.50
3840	1.171	2.45
Mean	1.3100	1.934
SD	0.2936	0.285
N	10	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Organ-To-Body Weight Ratios
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

3.337E+10 CFU Group 3	Adrenal	Brain	Heart	Kidneys	Liver	Ovaries with	Spleen
	/TBW	/TBW	/TBW	/TBW	/TBW	oviducts/TBW	/TBW
	(Ratio)	(Ratio)	(Ratio)	(Ratio)	(Ratio)	(Ratio)	(Ratio)
	Day 30/31	Day 30/31					
3851	0.321	6.90	3.61	7.12	28.87	0.591	2.26
3852	0.308	7.65	3.58	7.15	29.54	0.415	2.58
3853	0.299	7.53	3.43	7.09	29.76	0.394	2.19
3854	0.312	7.59	3.28	7.15	30.40	0.581	2.41
3855	0.352	7.32	3.37	7.01	30.96	0.510	2.15
3856	0.324	8.02	3.21	7.21	27.75	0.496	2.48
3857	0.255	7.80	3.18	6.43	26.08	0.420	1.84
3858	0.253	7.76	3.40	6.85	28.13	0.427	2.03
3859	0.259	8.19	3.71	7.10	27.26	0.510	2.05
3860	0.243	7.17	3.09	6.07	29.08	0.574	2.13
Mean	0.2926	7.592	3.385	6.919	28.782	0.4918	2.212
SD	0.0376	0.387	0.202	0.377	1.494	0.0744	0.225
N	10	10	10	10	10	10	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Organ-To-Body Weight Ratios
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

3.337E+10 CFU Group 3	Thymus	Uterus
	/TBW (Ratio)	/TBW (Ratio)
	Day 30/31	Day 30/31
3851	1.095	1.64
3852	1.335	2.08
3853	1.582	1.63
3854	1.751	3.60
3855	1.276	2.18
3856	1.916	2.14
3857	1.247	1.88
3858	1.344	1.37
3859	1.595	1.62
3860	0.864	2.50
Mean	1.4004	2.064
SD	0.3139	0.635
N	10	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Organ-To-Body Weight Ratios
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

1.001E+11 CFU Group 4	Adrenal	Brain	Heart	Kidneys	Liver	Ovaries with	Spleen
	/TBW	/TBW	/TBW	/TBW	/TBW	oviducts/TBW	/TBW
	(Ratio)	(Ratio)	(Ratio)	(Ratio)	(Ratio)	(Ratio)	(Ratio)
	Day 30/31	Day 30/31					
3871	0.396	8.61	3.61	7.48	29.96	0.657	2.04
3872	0.337	8.02	3.45	7.62	27.98	0.500	1.79
3873	0.281	8.94	3.27	8.06	34.88	0.581	2.30
3874	0.255	7.30	3.32	7.61	35.68	0.548	2.01
3875	0.258	7.80	3.41	8.07	37.31	0.621	1.78
3876	0.285	7.43	3.26	6.18	28.09	0.559	2.01
3877	0.143	7.11	2.96	6.22	25.95	0.459	1.97
3878	0.262	8.23	3.38	6.75	28.69	0.629	2.36
3879	0.245	7.99	3.21	6.79	27.59	0.390	1.93
3880	0.230	7.70	3.29	7.30	24.52	0.456	2.02
Mean	0.2691	7.912	3.317	7.208	30.065	0.5399	2.022
SD	0.0662	0.575	0.170	0.691	4.360	0.0868	0.189
N	10	10	10	10	10	10	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Organ-To-Body Weight Ratios
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

1.001E+11 CFU Group 4	Thymus	Uterus
	/TBW (Ratio)	/TBW (Ratio)
	Day 30/31	Day 30/31
3871	1.278	2.00
3872	1.190	4.01
3873	0.968	1.80
3874	0.668	5.33
3875	1.610	1.74
3876	1.306	1.08
3877	1.500	1.53
3878	1.245	1.73
3879	1.100	1.53
3880	0.813	1.67
Mean	1.1678	2.241
SD	0.2912	1.338
N	10	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

APPENDIX Q: INDIVIDUAL ANIMAL ORGAN-TO-BRAIN WEIGHT RATIOS

PRODUCT IDENTIFICATION

L. reuteri 3630 & *L. reuteri* 3632

Individual Animal Organ-To-Brain Weight Ratios
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

0 CFU Group 1	Adrenal	Epididymides	Heart	Kidneys	Liver	Spleen	Testes
	/BrW (Ratio)						
	Day 30/31						
3801	0.041	0.453	0.62	1.54	5.50	0.38	1.36
3802	0.040	0.572	0.58	1.38	5.81	0.39	1.42
3803	0.034	0.623	0.65	1.32	5.76	0.32	1.63
3804	0.031	0.632	0.66	1.56	6.06	0.35	1.76
3805	0.035	0.535	0.62	1.48	5.17	0.35	1.55
3806	0.029	0.601	0.52	1.37	4.78	0.27	1.59
3807	0.037	0.772	0.62	1.63	6.08	0.28	1.67
3808	0.024	0.625	0.62	1.24	4.58	0.39	1.63
3809	0.044	0.593	0.72	1.74	7.35	0.41	1.46
3810	.	0.617	0.63	1.29	5.41	0.36	1.78
Mean	0.0350	0.6023	0.626	1.455	5.650	0.350	1.585
SD	0.0063	0.0808	0.052	0.162	0.783	0.048	0.139
N	9	10	10	10	10	10	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Organ-To-Brain Weight Ratios
 PSL Study Number 55164: Limosilactobacillus Reuteri:
 28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

0 CFU Group 1	Thymus /BrW (Ratio)
	Day 30/31
3801	0.174
3802	0.218
3803	0.144
3804	0.117
3805	0.174
3806	0.187
3807	0.220
3808	0.103
3809	0.178
3810	0.154
Mean	0.1670
SD	0.0386
N	10

* The doses listed are the nominal values for each dose group

Individual Animal Organ-To-Brain Weight Ratios
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

1.668E+10 CFU Group 2	Adrenal /BrW (Ratio)	Epididymides /BrW (Ratio)	Heart /BrW (Ratio)	Kidneys /BrW (Ratio)	Liver /BrW (Ratio)	Spleen /BrW (Ratio)	Testes /BrW (Ratio)
	Day 30/31	Day 30/31	Day 30/31	Day 30/31	Day 30/31	Day 30/31	Day 30/31
	3821	0.044	0.706	0.73	1.72	5.97	0.49
3822	0.022	0.524	0.55	1.35	5.28	0.48	1.25
3823	0.031	0.616	0.53	1.33	4.84	0.43	1.40
3824	0.031	0.634	0.62	1.35	4.96	0.31	1.70
3825	0.030	0.674	0.68	1.47	6.57	0.39	1.81
3826	.	0.649	0.73	1.61	6.46	0.40	1.70
3827	0.033	0.656	0.65	1.59	7.40	0.40	1.39
3828	0.030	0.277	0.66	1.57	6.21	0.43	0.43
3830	0.038	0.519	0.63	1.28	5.31	0.31	1.57
Mean	0.0324	0.5838	0.643	1.474	5.889	0.406	1.434
SD	0.0064	0.1314	0.070	0.154	0.855	0.063	0.416
N	8	9	9	9	9	9	9

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Organ-To-Brain Weight Ratios
 PSL Study Number 55164: Limosilactobacillus Reuteri:
 28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

1.668E+10 CFU Group 2	Thymus /BrW (Ratio)
	Day 30/31
3821	0.233
3822	0.246
3823	0.131
3824	0.137
3825	0.174
3826	0.267
3827	0.157
3828	0.294
3830	0.169
Mean	0.2009
SD	0.0601
N	9

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Organ-To-Brain Weight Ratios
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

3.337E+10 CFU Group 3	Adrenal	Epididymides	Heart	Kidneys	Liver	Spleen	Testes
	/BrW (Ratio)						
	Day 30/31						
3841	0.034	0.709	0.61	1.29	5.46	0.33	1.74
3842	0.022	0.552	0.59	1.35	5.64	0.35	1.49
3843	0.037	0.625	0.66	1.73	5.79	0.36	1.74
3844	0.021	0.575	0.62	1.50	5.34	0.40	1.53
3845	0.028	0.571	0.58	1.30	6.39	0.45	1.58
3846	0.035	0.523	0.61	1.45	6.36	0.50	1.34
3847	0.029	0.542	0.51	1.26	5.25	0.32	1.38
3848	0.040	0.634	0.68	1.65	5.86	0.47	1.78
3849	0.032	0.568	0.60	1.32	5.08	0.41	1.43
3850	0.021	0.632	0.64	1.65	6.54	0.42	1.27
Mean	0.0300	0.5930	0.610	1.448	5.771	0.401	1.527
SD	0.0070	0.0561	0.047	0.173	0.514	0.061	0.183
N	10	10	10	10	10	10	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Organ-To-Brain Weight Ratios
 PSL Study Number 55164: Limosilactobacillus Reuteri:
 28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

3.337E+10 CFU Group 3	Thymus /BrW (Ratio)
	Day 30/31
3841	0.159
3842	0.104
3843	0.145
3844	0.114
3845	0.135
3846	0.242
3847	0.149
3848	0.167
3849	0.198
3850	0.216
Mean	0.1629
SD	0.0443
N	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Organ-To-Brain Weight Ratios
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

1.001E+11 CFU Group 4	Adrenal	Epididymides	Heart	Kidneys	Liver	Spleen	Testes
	/BrW (Ratio)						
	Day 30/31						
3861	0.035	0.578	0.60	1.42	6.31	0.36	1.57
3862	0.045	0.856	0.73	1.78	6.09	0.37	1.61
3863	0.030	0.704	0.57	1.46	4.99	0.35	1.59
3864	0.024	0.711	0.68	1.56	6.54	0.34	1.70
3865	0.033	0.678	0.69	1.56	6.59	0.41	1.68
3866	0.036	0.608	0.67	1.39	5.67	0.42	1.68
3867	0.024	0.595	0.65	1.56	9.03	0.43	1.46
3868	0.026	0.608	0.66	1.32	5.19	0.39	1.63
3869	0.032	0.636	0.61	1.41	4.62	0.34	1.47
3870	0.034	.	0.65	1.62	6.12	0.49	1.50
Mean	0.0319	0.6637	0.652	1.509	6.118	0.389	1.588
SD	0.0063	0.0867	0.047	0.135	1.226	0.046	0.088
N	10	9	10	10	10	10	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Organ-To-Brain Weight Ratios
 PSL Study Number 55164: Limosilactobacillus Reuteri:
 28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

1.001E+11 CFU Group 4	Thymus /BrW (Ratio)
	Day 30/31
3861	0.113
3862	0.141
3863	0.169
3864	0.231
3865	0.163
3866	0.251
3867	0.182
3868	0.192
3869	0.142
3870	0.127
Mean	0.1711
SD	0.0443
N	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Organ-To-Brain Weight Ratios
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

0 CFU Group 1	Adrenal	Heart	Kidneys	Liver	Ovaries with	Spleen	Thymus
	/BrW (Ratio)	/BrW (Ratio)	/BrW (Ratio)	/BrW (Ratio)	oviducts/BrW (Ratio)	/BrW (Ratio)	/BrW (Ratio)
	Day 30/31	Day 30/31	Day 30/31				
3811	0.031	0.43	0.96	3.78	0.068	0.33	0.234
3812	0.039	0.53	1.11	5.11	0.068	0.48	0.153
3813	0.032	0.46	0.86	3.59	0.071	0.28	0.191
3814	0.033	0.45	0.87	3.59	0.052	0.28	0.229
3815	0.047	0.48	1.02	3.96	0.067	0.26	0.160
3816	0.043	0.42	0.87	3.36	0.070	0.24	0.163
3817	0.041	0.42	0.97	3.55	0.063	0.29	0.216
3818	0.026	0.47	0.90	3.98	0.061	0.26	0.192
3819	0.047	0.46	1.00	3.43	0.054	0.22	0.168
3820	0.037	0.43	0.95	3.89	0.072	0.26	0.132
Mean	0.0376	0.453	0.951	3.825	0.0644	0.290	0.1839
SD	0.0072	0.034	0.080	0.502	0.0069	0.074	0.0342
N	10	10	10	10	10	10	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Organ-To-Brain Weight Ratios
 PSL Study Number 55164: Limosilactobacillus Reuteri:
 28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

0 CFU Group 1	Uterus /BrW (Ratio)
	Day 30/31
3811	0.43
3812	0.30
3813	0.50
3814	0.22
3815	0.27
3816	0.20
3817	0.27
3818	0.33
3819	0.59
3820	0.22
Mean	0.334
SD	0.133
N	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Organ-To-Brain Weight Ratios
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

1.668E+10 CFU Group 2	Adrenal	Heart	Kidneys	Liver	Ovaries with	Spleen	Thymus
	/BrW	/BrW	/BrW	/BrW	oviducts/BrW	/BrW	/BrW
	(Ratio)	(Ratio)	(Ratio)	(Ratio)	(Ratio)	(Ratio)	(Ratio)
	Day 30/31	Day 30/31	Day 30/31				
3831	0.029	0.48	0.93	3.81	0.065	0.24	0.176
3832	0.022	0.53	0.96	4.18	0.059	0.23	0.185
3833	0.034	0.52	1.08	4.13	0.069	0.24	0.186
3834	0.039	0.52	0.88	4.06	0.064	0.22	0.177
3835	0.057	0.51	1.02	3.92	0.065	0.25	0.148
3836	0.046	0.44	0.93	3.86	0.059	0.25	0.128
3837	0.038	0.46	0.98	3.51	0.064	0.30	0.284
3838	0.032	0.47	0.91	3.52	0.055	0.25	0.135
3839	0.045	0.45	0.96	4.51	0.052	0.26	0.179
3840	0.036	0.42	0.78	2.91	0.066	0.25	0.141
Mean	0.0377	0.479	0.943	3.841	0.0618	0.250	0.1740
SD	0.0098	0.039	0.079	0.446	0.0051	0.020	0.0445
N	10	10	10	10	10	10	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Organ-To-Brain Weight Ratios
 PSL Study Number 55164: Limosilactobacillus Reuteri:
 28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

1.668E+10 CFU Group 2	Uterus /BrW (Ratio)
	Day 30/31
3831	0.25
3832	0.23
3833	0.28
3834	0.24
3835	0.29
3836	0.27
3837	0.25
3838	0.23
3839	0.20
3840	0.30
Mean	0.254
SD	0.029
N	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Organ-To-Brain Weight Ratios
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

3.337E+10 CFU Group 3	Adrenal /BrW (Ratio)	Heart /BrW (Ratio)	Kidneys /BrW (Ratio)	Liver /BrW (Ratio)	Ovaries with oviducts/BrW (Ratio)	Spleen /BrW (Ratio)	Thymus /BrW (Ratio)
	Day 30/31	Day 30/31	Day 30/31	Day 30/31	Day 30/31	Day 30/31	Day 30/31
	3851	0.047	0.52	1.03	4.19	0.086	0.33
3852	0.040	0.47	0.93	3.86	0.054	0.34	0.174
3853	0.040	0.46	0.94	3.95	0.052	0.29	0.210
3854	0.041	0.43	0.94	4.01	0.077	0.32	0.231
3855	0.048	0.46	0.96	4.23	0.070	0.29	0.174
3856	0.040	0.40	0.90	3.46	0.062	0.31	0.239
3857	0.033	0.41	0.82	3.34	0.054	0.24	0.160
3858	0.033	0.44	0.88	3.63	0.055	0.26	0.173
3859	0.032	0.45	0.87	3.33	0.062	0.25	0.195
3860	0.034	0.43	0.85	4.06	0.080	0.30	0.121
Mean	0.0387	0.447	0.913	3.805	0.0652	0.292	0.1836
SD	0.0059	0.035	0.061	0.340	0.0121	0.033	0.0358
N	10	10	10	10	10	10	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Organ-To-Brain Weight Ratios
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

3.337E+10 CFU Group 3	Uterus /BrW (Ratio)
	Day 30/31
3851	0.24
3852	0.27
3853	0.22
3854	0.47
3855	0.30
3856	0.27
3857	0.24
3858	0.18
3859	0.20
3860	0.35
Mean	0.273
SD	0.086
N	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Organ-To-Brain Weight Ratios
PSL Study Number 55164: Limosilactobacillus Reuteri:
28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

1.001E+11 CFU Group 4	Adrenal	Heart	Kidneys	Liver	Ovaries with	Spleen	Thymus
	/BrW	/BrW	/BrW	/BrW	oviducts/BrW	/BrW	/BrW
	(Ratio)	(Ratio)	(Ratio)	(Ratio)	(Ratio)	(Ratio)	(Ratio)
	Day 30/31	Day 30/31	Day 30/31				
3871	0.046	0.42	0.87	3.48	0.076	0.24	0.148
3872	0.042	0.43	0.95	3.49	0.062	0.22	0.149
3873	0.031	0.37	0.90	3.90	0.065	0.26	0.108
3874	0.035	0.46	1.04	4.89	0.075	0.28	0.092
3875	0.033	0.44	1.03	4.78	0.080	0.23	0.206
3876	0.038	0.44	0.83	3.78	0.075	0.27	0.176
3877	0.020	0.42	0.88	3.65	0.065	0.28	0.211
3878	0.032	0.41	0.82	3.49	0.076	0.29	0.151
3879	0.031	0.40	0.85	3.45	0.049	0.24	0.138
3880	0.030	0.43	0.95	3.19	0.059	0.26	0.106
Mean	0.0338	0.420	0.912	3.810	0.0683	0.256	0.1484
SD	0.0072	0.025	0.079	0.575	0.0099	0.022	0.0406
N	10	10	10	10	10	10	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

Individual Animal Organ-To-Brain Weight Ratios
 PSL Study Number 55164: Limosilactobacillus Reuteri:
 28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

1.001E+11 CFU Group 4	Uterus /BrW (Ratio)
	Day 30/31
3871	0.23
3872	0.50
3873	0.20
3874	0.73
3875	0.22
3876	0.14
3877	0.22
3878	0.21
3879	0.19
3880	0.22
Mean	0.286
SD	0.183
N	10

* The doses listed are the nominal values for each dose group in terms of CFU/kg bw/day.

APPENDIX R: HISTOPATHOLOGY

PRODUCT IDENTIFICATION

L. reuteri 3630 & *L. reuteri* 3632

Submitted By:

StageBio
5930 Main Street
Mount Jackson, VA 22842



PATHOLOGY REPORT

***Limosilactobacillus reuteri*: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS**

Product Safety Labs (PSL) Study Number 55164

Prepared by

StageBio
5930 Main Street
Mount Jackson, VA 22842

Testing Facility

Product Safety Labs
2394 US Highway 130
Dayton, New Jersey 08810

Sponsor

Elanco Animal Health Incorporated
2500 Innovation Way
Greenfield, Indiana, 46140

September 7, 2021

Final Pathology Report
Elanco Animal Health Incorporated
PSL Study Number 55164

TABLE OF CONTENTS

1.0	GLP Compliance Statement- Histopathology Slide Preparation	3
2.0	GLP Compliance Statement- Histopathology Evaluation	4
3.0	Executive Summary	5
4.0	Introduction	6
4.1	Protocol	6
4.2	Objective	6
5.0	Methods	6
5.1	Compliance Statement	6
5.2	Study Design	6
	Table 1. Dose Levels	6
5.3	Necropsy	7
5.4	Histological Processing	7
6.0	Results	8
6.1	Animal Mortality	8
6.2	Macroscopic Observations	8
6.3	Microscopic Observations	8
7.0	Conclusion	9
	REFERENCE	9
	Appendix A. Histopathology Incidence Tables (Expanded Summary Report of Histopathology)	10
	Appendix B. Histopathology Incidence Tables (Individual Data Listing of Gross to Microscopic Correlation)	31
	Appendix C. Histopathology Incidence Tables (Individual Gross and Microscopic Observations)	33
	Appendix D. Tissue Accountability	124
	Appendix E. Quality Assurance Statement	126

Final Pathology Report
Elanco Animal Health Incorporated
PSL Study Number 55164

1.0 GLP Compliance Statement- Histopathology Slide Preparation

The histological slide preparation portion of Product Safety Labs Study Number 55164, which was performed at StageBio, 5930 Main Street, Mount Jackson, VA 22842, was conducted in compliance with U.S. FDA GLP: 21 CFR Part 58, 1987.

[Redacted Signature]

Erin Galati, HT (ASCP)
Principal Investigator
StageBio

9/7/21

Date

Final Pathology Report
Elanco Animal Health Incorporated
PSL Study Number 55164

2.0 GLP Compliance Statement- Histopathology Evaluation

The histopathological slide evaluation portion of Product Safety Labs Study Number 55164, which was performed at StageBio, 5930 Main Street, Mount Jackson, VA 22842, was conducted in compliance with U.S. FDA GLP: 21 CFR Part 58, 1987.


Allen W. Singer, DVM, DACVP, DABT
Principal Investigator
StageBio

9-7-21
Date

3.0 Executive Summary

The objective of this study was to evaluate the potential toxicity of *Limosilactobacillus reuteri* (*L. reuteri*) ATCC PTA-126787 (*L. reuteri* 3630) and ATCC PTA-126788 (*L. reuteri* 3632) in male and female rats likely to arise from daily exposure via oral gavage over a test period of 28 days. A no-observed-adverse-effect-level (NOAEL) was also sought for each sex.

Methods: According to the protocol, 80 rats (40 male and 40 female) were assigned to four treatment groups in this study. Following the in-life procedures, all surviving animals were euthanized on Day 30/31 and subjected to a full necropsy. One Group 2 male rat did not survive to Day 30/31; it also was subjected to a full necropsy. Protocol-required tissues were collected at necropsy and forwarded to StageBio where protocol-specified tissues from all animals in Group 1 and Group 4, the unscheduled death animal, and gross lesions from all animals, were processed, embedded in paraffin, sectioned and stained with hematoxylin and eosin (H&E). The resulting microscopic slides were evaluated by Allen W. Singer, DVM, DACVP, DABT of StageBio. This pathology report by StageBio presents the results of the microscopic evaluation of protocol-required tissues from all animals in Group 1 and Group 4, the unscheduled death animal, and gross lesions from all animals.

Conclusion: The objective of this study was to evaluate the potential toxicity of *Limosilactobacillus reuteri* (*L. reuteri*) ATCC PTA-126787 (*L. reuteri* 3630) and ATCC PTA-126788 (*L. reuteri* 3632) in male and female rats likely to arise from daily exposure via oral gavage at doses up to 760 mg/kg bw/day *L. reuteri* 3630 plus 455 mg/kg bw/day *L. reuteri* 3632 over a test period of 28 days. A no-observed-adverse-effect-level (NOAEL) was also sought for each sex.

There were no gross or microscopic findings attributed to administration with the test articles, ATCC PTA-126787 (*L. reuteri* 3630) and ATCC PTA-126788 (*L. reuteri* 3632). Thus, based solely on the microscopic examinations, the no-observed adverse effect level (NOAEL) was the high-dose group, *L. reuteri* 3630 (760 mg/kg bw/day) plus *L. reuteri* 3632 (455 mg/kg bw/day).

4.0 Introduction

4.1 Protocol

This report presents the histopathology results of a study to evaluate the potential toxicity of *Limosilactobacillus reuteri* (*L. reuteri*) ATCC PTA-126787 (*L. reuteri* 3630) and ATCC PTA-126788 (*L. reuteri* 3632) in male and female rats likely to arise from daily exposure via oral gavage over a test period of 28 days, PSL Study Number 55164, Elanco Animal Health Incorporated, Greenfield, Indiana, 46140. All in-life procedures and tissue harvests were performed at Product Safety Labs under the direction of Raghavendra Gowda, PhD. As per Protocol Amendment No.: 7 dated 17Aug21, the Study Director was revised to Mark Bauter, BS. Histology was performed at StageBio and microscopic evaluation was completed by Allen W. Singer, DVM, DACVP, DABT at StageBio.

4.2 Objective

The objective of this study was to evaluate the potential toxicity of *Limosilactobacillus reuteri* (*L. reuteri*) ATCC PTA-126787 (*L. reuteri* 3630) and ATCC PTA-126788 (*L. reuteri* 3632) in male and female rats likely to arise from daily exposure via oral gavage over a test period of 28 days. A no-observed-adverse-effect-level (NOAEL) was also sought for each sex.

5.0 Methods

5.1 Compliance Statement

The portions of this study conducted at StageBio were conducted in compliance with the U.S. FDA GLP: 21 CFR Part 58, 1987. An electronic copy of this report in portable document format (PDF) will be provided to PSL in addition to the hard copy. The PDF is a representation of the pathology report hard copy. However, only the signed hard copy of the pathology report is considered raw data.

5.2 Study Design

Forty male (M) and 40 female (F) animals were enrolled in this study, as shown in Table 1, below:

Table 1. Dose Levels

Group	Number of Animals (Male/Female)	Test Article (mg/kg bw/day)	Targeted Dose Level (CFU/kg/day)	Calculated ^b Dose (CFU/kg/day)	Dose Volume (mL/kg/day)	Test Article Concentration (mg/mL ^a)
1	10/10	0 Vehicle Only	0	0	5	0
2	10/10	<i>L. reuteri</i> 3630 (126.5) +	1.668E+10 +	3.1E+09 +		<i>L. reuteri</i> 3630 (25.3) +
		<i>L. reuteri</i> 3632 (75.8)	1.668E+10	7.5E+09		<i>L. reuteri</i> 3632 (15.2)
3	10/10	<i>L. reuteri</i> 3630 (253.3) +	3.337E+10 +	4.5E+09 +		<i>L. reuteri</i> 3630 (50.7) +
		<i>L. reuteri</i> 3632 (151.6)	3.337E+10	1.4E+10	<i>L. reuteri</i> 3632 (30.3)	
4	10/10	<i>L. reuteri</i> 3630 (760) + <i>L. reuteri</i> 3632 (455)	1.001E+11 + 1.001E+11	1.6E+10 + 5.7E+10	<i>L. reuteri</i> 3630 (152) + <i>L. reuteri</i> 3632 (91)	

^a LR3630 = 132 000 000 000 CFU/g (1.32E+11) and LR3632 = 220 000 000 000 CFU/g (2.2E+11)

^b Calculated using the geometric mean

5.3 Necropsy

At terminal sacrifice on Day 30/31, all surviving animals were euthanized and subjected to a full necropsy. The single unscheduled death was also subjected to a full necropsy. Necropsies included examination of the external surface of the body, all orifices, musculoskeletal system and the thoracic, abdominal, pelvic and cranial cavities and their contents. At scheduled termination, the following organs were weighed: adrenals (combined), brain, epididymides (combined, males only), heart, kidneys (combined), liver, ovaries with oviducts (combined, females only), testes (combined, males only), spleen, thymus, and uterus (females only). The following organs and tissues from all animals were preserved in 10% neutral buffered formalin:

accessory genital organs (prostate and seminal vesicles)	nasal turbinates
adrenals	nose
all gross lesions	ovaries
aorta	oviducts
bone (femur)	pancreas
bone marrow (from femur and sternum)	parathyroid
brain - sections including medulla/pons, cerebellar and cerebral cortex	peripheral nerve (sciatic)
cecum	pharynx
cervix	pituitary gland
colon	rectum
duodenum	salivary glands (sublingual, submandibular, and parotid)
esophagus	skeletal muscle
Harderian gland	skin
heart	spinal cord - 3 levels: cervical, mid-thoracic, and lumbar
ileum with Peyer's patches	spleen
jejunum	sternum
kidneys	stomach
larynx	thymus
liver	thyroid
lungs	trachea
lymph node mandibular	urinary bladder
lymph node mesenteric	uterus
mammary gland	vagina

The epididymides, eyes, optic nerve, and testes from all animals were preserved in modified Davidson's fixative and then stored in ethanol. The gross lesions for testes and epididymides were required for histopathological evaluation.

5.4 Histological Processing

Collected tissues from all animals were forwarded to StageBio where the protocol-required tissues from all surviving animals in Group 1 and Group 4, the unscheduled death animal, and gross lesions from all animals were processed, embedded in paraffin, sectioned and stained with hematoxylin and eosin (H&E). Animal information from PSL's Gross Pathology Results was entered into Pristima[®] at StageBio. All microscopic slides were evaluated, and microscopic findings were entered directly into Pristima[®] by Allen W. Singer, DVM, DACVP, DABT of StageBio. Gross to microscopic correlations and the incidence of microscopic findings are presented in the Histopathology Incidence Tables portion of this report.

Pristima[®] allows data entry for one test article only, so the test article is identified as "Various" in the header of pages in the Histopathology Incidence Tables. The term "Various" refers to all of the test articles used in this study and as described in Table 1.

Within the Histopathology Incidence Tables, the following abbreviations apply:

L=Left
R=Right
M=Male
F=Female
1>=Minimal
2>=Mild
3>=Moderate
4>=Marked
5>=Severe

Within the Tissue Accountability Appendix, the following abbreviation applies:

SOPs=Standard Operating Procedures

6.0 Results

6.1 Animal Mortality

There was one unscheduled death, Group 2 male 3829, on Day 19, among the animals submitted for histopathological evaluation. At necropsy, this animal had a visible tear of the esophagus, with fluid/edema noted in the thoracic cavity and around the lungs; these changes were attributed to inadvertent esophageal dosing trauma and served as the cause of death. No evidence of ATCC PTA-126787 (*L. reuteri* 3630) and ATCC PTA-126788 (*L. reuteri* 3632) toxicity was observed in this animal.

Unscheduled death male Animal 3829 had several gross findings, including small esophageal tear with food particles near the opening; lungs red and swollen with clear, colorless fluid; and clear colorless fluid in the thoracic cavity. Although the physical esophageal perforation was not present on the microscopic slide presented, there was significant chronic-active inflammation surrounding the esophagus, trachea, pharynx and into mediastinal tissues, consistent with a trauma-induced tear. The lungs also had significant inflammation of the pleural surfaces, related to spread of the mediastinal infection caused by the tear. Similar inflammation was found microscopically around the epicardial surfaces of the heart and surrounding the thymic tissue.

6.2 Macroscopic Observations

All animals other than Animal 3829, as discussed above, survived to the scheduled in-life termination necropsy. Among these, only a few necropsy findings were noted as follows (with *microscopic correlates* in parentheses): Group 1 female Animal 3819 had a fluid filled uterus (*dilatation*); Group 2 male Animal 3828 had small, bilateral testes (right – 11mm x 6mm, and left – 16mm x 4mm) (*atrophy*), and small, bilateral epidymides (right – 32mm x 3mm, and left – 42mm x 3mm) (*hypospermia*); Group 3 male Animal 3850 had a small, right testis (1.8cm x 1.2cm) (*atrophy*); and Group 3 female Animal 3854 had a fluid filled uterus (*dilatation*).

All these were common incidental macroscopic findings in control rats of this age and strain, and were unrelated to the ATCC PTA-126787 (*L. reuteri* 3630) and ATCC PTA-126788 (*L. reuteri* 3632) administration.

6.3 Microscopic Observations

There were no microscopic changes noted that were related to administration of the test articles. Findings, morphologies, severities observed, and incidences of changes seen, including that of early-stage "chronic progressive renal nephropathy", a very common spontaneous change in rats, were consistent with those expected in untreated rats of this age, sex, and strain (McInnes, 2012; Palm, 1998). Most of these were simple cellular infiltrates of various organs.

Final Pathology Report
Elanco Animal Health Incorporated
PSL Study Number 55164

7.0 Conclusion

The objective of this study was to evaluate the potential toxicity of *Limosilactobacillus reuteri* (*L. reuteri*) ATCC PTA-126787 (*L. reuteri* 3630) and ATCC PTA-126788 (*L. reuteri* 3632) in male and female rats likely to arise from daily exposure via oral gavage at doses up to 760 mg/kg bw/day *L. reuteri* 3630 plus 455 mg/kg bw/day *L. reuteri* 3632 over a test period of 28 days. A no-observed-adverse-effect-level (NOAEL) was also sought for each sex.

There were no gross or microscopic findings attributed to administration with the test articles, ATCC PTA-126787 (*L. reuteri* 3630) and ATCC PTA-126788 (*L. reuteri* 3632). Thus, based solely on the microscopic examinations, the no-observed adverse effect level (NOAEL) was the high-dose group, *L. reuteri* 3630 (760 mg/kg bw/day) plus *L. reuteri* 3632 (455 mg/kg bw/day).

Signature:



Allen W. Singer, DVM, DACVP, DABT
Study Pathologist

9-7-21
Date

REFERENCE

Palm M. *The incidence of chronic progressive nephrosis in young Sprague-Dawley rats from two different breeders*. Lab Anim, 1998 Oct;32(4):477-82. doi: 10.1258/002367798780599785.PMID:9807762.

McInnes EF. *Background Lesions in Laboratory Animals, A Color Atlas*. Edinburgh: Saunders Elsevier, 2012.

Final Pathology Report
Elanco Animal Health Incorporated
PSL Study Number 55164

Appendix A. Histopathology Incidence Tables (Expanded Summary Report of Histopathology)

Expanded Summary Report of Histopathology

Study: 55164

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Rat/Sprague-Dawley	Repeat Dose Toxicity/Oral Gavage				
	Males				
	Dosage Group: Control	2	3	4	
	Number of Animals:	10	1	1	10
	Number Examined:	10	1	1	10
	Number Unremarkable:	0	0	0	0
Artery, Aorta	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Bone Marrow	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Bone, Femur	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Bone, Sternum	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Brain	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Epididymis	Number examined:	10	1	0	10
	Number unremarkable:	10	0	0	9
Hypospermia	5>	0	1	0	0
	Total Finding Incidence	0	1	0	0
Infiltrate	1>	0	0	0	1

Expanded Summary Report of Histopathology

Study: 55164

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Rat/Sprague-Dawley	Repeat Dose Toxicity/Oral Gavage				
	Males				
	Dosage Group: Control	2	3	4	
	Number of Animals:	10	1	1	10
	Number Examined:	10	1	1	10
	Number Unremarkable:	0	0	0	0
Epididymis	Number examined:	10	1	0	10
	Number unremarkable:	10	0	0	9
Infiltrate	Total Finding Incidence	0	0	0	1
Esophagus	Number examined:	10	0	0	10
	Number unremarkable:	7	0	0	10
Degeneration	1>	1	0	0	0
	2>	2	0	0	0
	Total Finding Incidence	3	0	0	0
Eye	Number examined:	10	0	0	9
	Number unremarkable:	10	0	0	9
Gland, Adrenal	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Gland, Harderian	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Gland, Mammary	Number examined:	9	0	0	8
	Number unremarkable:	9	0	0	8

Expanded Summary Report of Histopathology

Study: 55164

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Rat/Sprague-Dawley	Males	Repeat Dose Toxicity/Oral Gavage			
	Dosage Group:	Control	2	3	4
	Number of Animals:	10	1	1	10
	Number Examined:	10	1	1	10
	Number Unremarkable:	0	0	0	0
Gland, Parathyroid	Number examined:	8	0	0	10
	Number unremarkable:	8	0	0	10
Gland, Pituitary	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Gland, Prostate	Number examined:	10	0	0	10
	Number unremarkable:	6	0	0	8
Infiltrate	1>	3	0	0	2
	2>	1	0	0	0
	Total Finding Incidence	4	0	0	2
Gland, Salivary, Parotid	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Gland, Salivary, Sublingual	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Gland, Salivary, Submandibular	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10

Expanded Summary Report of Histopathology

Study: 55164

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Test Article: Various

Rat/Sprague-Dawley	Repeat Dose Toxicity/Oral Gavage				
	Males				
	Dosage Group:	Control	2	3	4
	Number of Animals:	10	1	1	10
	Number Examined:	10	1	1	10
	Number Unremarkable:	0	0	0	0
Gland, Seminal Vesicle	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Gland, Thyroid	Number examined:	9	0	0	10
	Number unremarkable:	9	0	0	10
Heart	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Kidney	Number examined:	10	0	0	10
	Number unremarkable:	4	0	0	3
Chronic Progressive Nephropathy	1>	3	0	0	6
	Total Finding Incidence	3	0	0	6
Cyst	1>	1	0	0	0
	Total Finding Incidence	1	0	0	0
Infiltrate, mononuclear cell	1>	3	0	0	5
	Total Finding Incidence	3	0	0	5
Large Intestine, Cecum	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10

Expanded Summary Report of Histopathology

Study: 55164

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Rat/Sprague-Dawley	Repeat Dose Toxicity/Oral Gavage				
	Males				
	Dosage Group: Control	2	3	4	
	Number of Animals:	10	1	1	10
	Number Examined:	10	1	1	10
	Number Unremarkable:	0	0	0	0
Large Intestine, Colon	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Large Intestine, Rectum	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Larynx	Number examined:	9	0	0	10
	Number unremarkable:	9	0	0	10
Liver	Number examined:	10	0	0	10
	Number unremarkable:	0	0	0	0
Infiltrate, mononuclear cell	1>	10	0	0	10
	Total Finding Incidence	10	0	0	10
Necrosis	1>	0	0	0	1
	Total Finding Incidence	0	0	0	1
Vacuolation, cytoplasmic	2>	0	0	0	1
	Total Finding Incidence	0	0	0	1
Lungs	Number examined:	10	0	0	10
	Number unremarkable:	7	0	0	8

Expanded Summary Report of Histopathology

Study: 55164

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Rat/Sprague-Dawley		Repeat Dose Toxicity/Oral Gavage				
		Males				
		Dosage Group: Control	2	3	4	
Number of Animals:		10	1	1	10	
Number Examined:		10	1	1	10	
Number Unremarkable:		0	0	0	0	
Lungs		Number examined:	10	0	0	10
		Number unremarkable:	7	0	0	8
Aggregate, alveolar macrophage		1>	1	0	0	1
		Total Finding Incidence	1	0	0	1
Infiltrate, perivascular, eosinophil		1>	2	0	0	0
		2>	0	0	0	1
		Total Finding Incidence	2	0	0	1
Inflammation		1>	2	0	0	0
		Total Finding Incidence	2	0	0	0
Lymph Node, Mandibular		Number examined:	10	0	0	10
		Number unremarkable:	10	0	0	10
Lymph Node, Mesenteric		Number examined:	10	0	0	9
		Number unremarkable:	10	0	0	9
Muscle, Skeletal		Number examined:	10	0	0	10
		Number unremarkable:	9	0	0	10
Infiltrate		1>	1	0	0	0
		Total Finding Incidence	1	0	0	0

Expanded Summary Report of Histopathology

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StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Rat/Sprague-Dawley	Repeat Dose Toxicity/Oral Gavage				
	Males				
	Dosage Group:	Control	2	3	4
	Number of Animals:	10	1	1	10
	Number Examined:	10	1	1	10
	Number Unremarkable:	0	0	0	0
Nasal Turbinate	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Nerve, Optic	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Nose	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Pancreas	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Peripheral nerve (sciatic)	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Peyer's Patch	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10

Expanded Summary Report of Histopathology

Study: 55164

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Rat/Sprague-Dawley	Repeat Dose Toxicity/Oral Gavage				
	Males				
	Dosage Group: Control	2	3	4	
	Number of Animals:	10	1	1	10
	Number Examined:	10	1	1	10
	Number Unremarkable:	0	0	0	0
Pharynx	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	9
Degeneration	2>	0	0	0	1
	Total Finding Incidence	0	0	0	1
Skin	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Small Intestine, Duodenum	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Small Intestine, Ileum	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Small Intestine, Jejunum	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Spinal Cord, Cervical	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10

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Test Article: Various

Rat/Sprague-Dawley	Repeat Dose Toxicity/Oral Gavage				
	Males				
	Dosage Group:	Control	2	3	4
	Number of Animals:	10	1	1	10
	Number Examined:	10	1	1	10
	Number Unremarkable:	0	0	0	0
Spinal Cord, Lumbar	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Spinal Cord, Midthoracic	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Spleen	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Stomach	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Testes	Number examined:	10	1	1	10
	Number unremarkable:	10	0	0	10
Atrophy	4>	0	0	1	0
	5>	0	1	0	0
	Total Finding Incidence	0	1	1	0
Thoracic Cavity	Number examined:	0	0	0	0
	Number unremarkable:	0	0	0	0

Expanded Summary Report of Histopathology

Study: 55164

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Rat/Sprague-Dawley		Repeat Dose Toxicity/Oral Gavage			
	Males				
	Dosage Group:	Control	2	3	4
	Number of Animals:	10	1	1	10
	Number Examined:	10	1	1	10
	Number Unremarkable:	0	0	0	0
Thymus	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Trachea	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Urinary Bladder	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10

Expanded Summary Report of Histopathology

Study: 55164

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Rat/Sprague-Dawley

Repeat Dose Toxicity/Oral Gavage

		Females			
		Dosage Group: Control	3	4	
		Number of Animals:	10	1	10
		Number Examined:	10	1	10
		Number Unremarkable:	0	0	0
Artery, Aorta	Number examined:	10	0	10	
	Number unremarkable:	10	0	10	
Bone Marrow	Number examined:	10	0	10	
	Number unremarkable:	10	0	10	
Bone, Femur	Number examined:	10	0	10	
	Number unremarkable:	10	0	10	
Bone, Sternum	Number examined:	10	0	10	
	Number unremarkable:	10	0	10	
Brain	Number examined:	10	0	10	
	Number unremarkable:	10	0	10	
Cervix	Number examined:	10	0	10	
	Number unremarkable:	10	0	10	

Expanded Summary Report of Histopathology

Study: 55164

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Rat/Sprague-Dawley

Repeat Dose Toxicity/Oral Gavage

Females

	Dosage Group:	Control	3	4
	Number of Animals:	10	1	10
	Number Examined:	10	1	10
	Number Unremarkable:	0	0	0
Esophagus	Number examined:	10	0	10
	Number unremarkable:	10	0	10
Eye	Number examined:	10	0	10
	Number unremarkable:	10	0	10
Gland, Adrenal	Number examined:	10	0	10
	Number unremarkable:	10	0	10
Gland, Harderian	Number examined:	10	0	8
	Number unremarkable:	10	0	8
Gland, Mammary	Number examined:	7	0	8
	Number unremarkable:	7	0	8
Gland, Parathyroid	Number examined:	9	0	9
	Number unremarkable:	9	0	9

Expanded Summary Report of Histopathology

Study: 55164

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Rat/Sprague-Dawley

Repeat Dose Toxicity/Oral Gavage

Females

	Dosage Group:	Control	3	4
	Number of Animals:	10	1	10
	Number Examined:	10	1	10
	Number Unremarkable:	0	0	0
Gland, Pituitary	Number examined:	10	0	10
	Number unremarkable:	10	0	10
Gland, Salivary, Parotid	Number examined:	7	0	7
	Number unremarkable:	7	0	7
Gland, Salivary, Sublingual	Number examined:	10	0	10
	Number unremarkable:	10	0	10
Gland, Salivary, Submandibular	Number examined:	10	0	10
	Number unremarkable:	10	0	10
Gland, Thyroid	Number examined:	10	0	10
	Number unremarkable:	10	0	10
Heart	Number examined:	10	0	10
	Number unremarkable:	10	0	10

Expanded Summary Report of Histopathology

Page 14 of 20

Printed: 09/07/2021 10:12:47 AM

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Study: 55164

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Rat/Sprague-Dawley	Females			Repeat Dose Toxicity/Oral Gavage
	Dosage Group:	Control	3	4
	Number of Animals:	10	1	10
	Number Examined:	10	1	10
	Number Unremarkable:	0	0	0
Kidney	Number examined:	10	0	10
	Number unremarkable:	6	0	6
Chronic Progressive Nephropathy	1>	0	0	1
	Total Finding Incidence	0	0	1
Cyst	1>	1	0	1
	Total Finding Incidence	1	0	1
Infiltrate, mononuclear cell	1>	2	0	3
	Total Finding Incidence	2	0	3
Mineralization	1>	1	0	0
	Total Finding Incidence	1	0	0
Large Intestine, Cecum	Number examined:	10	0	10
	Number unremarkable:	10	0	10
Large Intestine, Colon	Number examined:	10	0	10
	Number unremarkable:	10	0	10
Large Intestine, Rectum	Number examined:	10	0	10
	Number unremarkable:	10	0	10

Expanded Summary Report of Histopathology

Study: 55164

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Rat/Sprague-Dawley	Females			Repeat Dose Toxicity/Oral Gavage
	Dosage Group:	Control	3	4
	Number of Animals:	10	1	10
	Number Examined:	10	1	10
	Number Unremarkable:	0	0	0
Larynx	Number examined:	10	0	10
	Number unremarkable:	9	0	9
Infiltrate	2>	1	0	1
	Total Finding Incidence	1	0	1
Liver	Number examined:	10	0	10
	Number unremarkable:	0	0	0
Infiltrate, mononuclear cell	1>	10	0	10
	Total Finding Incidence	10	0	10
Necrosis	1>	1	0	0
	Total Finding Incidence	1	0	0
Lungs	Number examined:	10	0	10
	Number unremarkable:	10	0	9
Inflammation	1>	0	0	1
	Total Finding Incidence	0	0	1
Lymph Node, Mandibular	Number examined:	10	0	10
	Number unremarkable:	10	0	10

Expanded Summary Report of Histopathology

Study: 55164

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Rat/Sprague-Dawley

Repeat Dose Toxicity/Oral Gavage

		Females			
		Dosage Group:	Control	3	4
		Number of Animals:	10	1	10
		Number Examined:	10	1	10
		Number Unremarkable:	0	0	0
Lymph Node, Mesenteric	Number examined:	9	0	10	
	Number unremarkable:	9	0	10	
Muscle, Skeletal	Number examined:	10	0	10	
	Number unremarkable:	10	0	10	
Nasal Turbinate	Number examined:	10	0	10	
	Number unremarkable:	10	0	10	
Nerve, Optic	Number examined:	10	0	10	
	Number unremarkable:	10	0	10	
Nose	Number examined:	10	0	10	
	Number unremarkable:	10	0	10	
Ovary	Number examined:	10	0	10	
	Number unremarkable:	10	0	10	

Expanded Summary Report of Histopathology

Study: 55164

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Rat/Sprague-Dawley	Females			Repeat Dose Toxicity/Oral Gavage
	Dosage Group:	Control	3	4
	Number of Animals:	10	1	10
	Number Examined:	10	1	10
	Number Unremarkable:	0	0	0
Oviduct	Number examined:	10	0	10
	Number unremarkable:	10	0	10
Pancreas	Number examined:	10	0	10
	Number unremarkable:	9	0	9
Atrophy	1>	1	0	0
	2>	0	0	1
	Total Finding Incidence	1	0	1
Peripheral nerve (sciatic)	Number examined:	9	0	10
	Number unremarkable:	9	0	10
Peyer's Patch	Number examined:	10	0	10
	Number unremarkable:	10	0	10
Pharynx	Number examined:	10	0	10
	Number unremarkable:	10	0	9
Degeneration	2>	0	0	1
	Total Finding Incidence	0	0	1

Expanded Summary Report of Histopathology

Study: 55164

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Rat/Sprague-Dawley Repeat Dose Toxicity/Oral Gavage

		Females		
		Dosage Group: Control	3	4
		Number of Animals:	10	10
		Number Examined:	10	10
		Number Unremarkable:	0	0
Skin		Number examined:	9	10
		Number unremarkable:	9	10
Small Intestine, Duodenum		Number examined:	10	10
		Number unremarkable:	10	10
Small Intestine, Ileum		Number examined:	10	10
		Number unremarkable:	10	10
Small Intestine, Jejunum		Number examined:	10	10
		Number unremarkable:	10	10
Spinal Cord, Cervical		Number examined:	10	10
		Number unremarkable:	10	10
Spinal Cord, Lumbar		Number examined:	10	10
		Number unremarkable:	10	10

Expanded Summary Report of Histopathology

Study: 55164

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Rat/Sprague-Dawley	Repeat Dose Toxicity/Oral Gavage			
	Females			
	Dosage Group:	Control	3	4
	Number of Animals:	10	1	10
	Number Examined:	10	1	10
	Number Unremarkable:	0	0	0
Spinal Cord, Midthoracic	Number examined:	10	0	10
	Number unremarkable:	10	0	10
Spleen	Number examined:	10	0	10
	Number unremarkable:	10	0	10
Stomach	Number examined:	10	0	10
	Number unremarkable:	10	0	10
Thoracic Cavity	Number examined:	0	0	0
	Number unremarkable:	0	0	0
Thymus	Number examined:	10	0	10
	Number unremarkable:	10	0	10
Trachea	Number examined:	10	0	10
	Number unremarkable:	10	0	10

Expanded Summary Report of Histopathology

Study: 55164

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Rat/Sprague-Dawley	Females				Repeat Dose Toxicity/Oral Gavage
	Dosage Group:	Control	3	4	
	Number of Animals:	10	1	10	
	Number Examined:	10	1	10	
	Number Unremarkable:	0	0	0	
Urinary Bladder	Number examined:	10	0	9	
	Number unremarkable:	10	0	9	
Uterus	Number examined:	10	1	10	
	Number unremarkable:	9	0	8	
Dilatation	1>	1	0	1	
	2>	0	1	1	
	Total Finding Incidence	1	1	2	
Vagina	Number examined:	10	0	8	
	Number unremarkable:	10	0	8	

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Elanco Animal Health Incorporated
PSL Study Number 55164

Appendix B. Histopathology Incidence Tables (Individual Data Listing of Gross to Microscopic Correlation)

Individual Data Listing of Gross to Microscopic Correlation

Page 1 of 1

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Study: 55164

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Rat/Sprague-Dawley			Repeat Dose Toxicity/Oral Gavage	
Animal #	Gross Observations		Status	Microscopic Observations
	Sex	Group		
3828	M	2		
	Epididymis, Small, bilateral, R-32mm x 3mm,L-42mm x 3mm		Correlated	Epididymis, Hypospermia, severe, bilateral
	Testes, Small, bilateral, R-11mm x 6mm, L-16mm x 4mm		Correlated	Testes, Atrophy, severe, bilateral
3829	M	2		
	Esophagus, Tear, with food particles near opening, small		Not Correlated	
	Lungs, Fluid, colorless, clear		Correlated	Lungs, Pleural Inflammation, marked
	Lungs, Red, Noted		Not Correlated	
	Lungs, Swollen, Noted		Correlated	Lungs, Pleural Inflammation, marked
	Thoracic Cavity, Fluid, colorless, clear		Not Applicable	
3850	M	3		
	Testes, Small, right, R-1.8cm x 1.2cm		Correlated	Testes, Atrophy, marked, unilateral
3819	F	1		
	Uterus, Fluid filled, Noted		Correlated	Uterus, Dilatation, minimal
3854	F	3		
	Uterus, Fluid filled, Noted		Correlated	Uterus, Dilatation, mild

Final Pathology Report
Elanco Animal Health Incorporated
PSL Study Number 55164

Appendix C. Histopathology Incidence Tables (Individual Gross and Microscopic Observations)

Individual Gross and Microscopic Observations

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Study: 55164

Pristima® Version 7.2.0 Build 31

Study Title: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3801

Group: 1

Day Of Death: Dosing Phase, Day 30

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Gland, Prostate	Within Normal Limits		Infiltrate, minimal	
Kidney	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Lungs	Within Normal Limits		Infiltrate, perivascular, eosinophil, minimal	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary, Parotid
Gland, Salivary, Sublingual	Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid	Heart
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum	Larynx
Liver	Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal
Nasal Turbinate	Nerve, Optic	Nose	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen
Stomach	Testes	Thymus	Trachea	Urinary Bladder

Individual Gross and Microscopic Observations

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Study: 55164

Pristima® Version 7.2.0 Build 31

Study Title: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3801

Group: 1

Day Of Death: Dosing Phase, Day 30

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments
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Continued from previous page ...

Required tissues not microscopically examined:

None

Tissues microscopically examined and within normal limits:

Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid	Heart	Large Intestine, Cecum
Large Intestine, Colon	Large Intestine, Rectum	Larynx	Lymph Node, Mandibular	Lymph Node, Mesenteric
Muscle, Skeletal	Nasal Turbinate	Nerve, Optic	Nose	Pancreas
Peripheral nerve (sciatic)	Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum
Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic
Spleen	Stomach	Testes	Thymus	Trachea
Urinary Bladder				

Individual Gross and Microscopic Observations

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Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3802

Group: 1

Day Of Death: Dosing Phase, Day 30

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Epididymis	Within Normal Limits		Tissue Comment: Extra (normal) epididymis present on slide. No Abnormalities Detected	
Esophagus	Within Normal Limits		Degeneration, mild, muscularis	
Gland, Parathyroid	Within Normal Limits		Both Missing	
Gland, Prostate	Within Normal Limits		Infiltrate, minimal	
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary, Parotid
Gland, Salivary, Sublingual	Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid	Heart
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum	Larynx
Liver	Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal
Nasal Turbinate	Nerve, Optic	Nose	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum

Individual Gross and Microscopic Observations

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Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3802

Group: 1

Day Of Death: Dosing Phase, Day 30

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Continued from previous page ...				
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen
Stomach	Testes	Thymus	Trachea	Urinary Bladder
Required tissues not microscopically examined: Gland, Parathyroid				
Tissues microscopically examined and within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Eye	Gland, Adrenal	Gland, Harderian	Gland, Mammary
Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual	Gland, Salivary, Submandibular	Gland, Seminal Vesicle
Gland, Thyroid	Heart	Kidney	Large Intestine, Cecum	Large Intestine, Colon
Large Intestine, Rectum	Larynx	Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric
Muscle, Skeletal	Nasal Turbinate	Nerve, Optic	Nose	Pancreas
Peripheral nerve (sciatic)	Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum
Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic
Spleen	Stomach	Testes	Thymus	Trachea

Individual Gross and Microscopic Observations

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Study: 55164

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StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3802

Group: 1

Day Of Death: Dosing Phase, Day 30

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments
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Continued from previous page ...

Urinary Bladder

Individual Gross and Microscopic Observations

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Study: 55164

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StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3803

Group: 1

Day Of Death: Dosing Phase, Day 30

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Kidney	Within Normal Limits		Chronic Progressive Nephropathy, minimal Infiltrate, mononuclear cell, minimal	
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Lungs	Within Normal Limits		Inflammation, minimal, focal, alveolus	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary, Parotid
Gland, Salivary, Sublingual	Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid	Heart
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum	Larynx
Liver	Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal
Nasal Turbinate	Nerve, Optic	Nose	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen
Stomach	Testes	Thymus	Trachea	Urinary Bladder

Individual Gross and Microscopic Observations

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Study: 55164

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StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3803

Group: 1

Day Of Death: Dosing Phase, Day 30

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Continued from previous page ...				
Required tissues not microscopically examined:				
None				
Tissues microscopically examined and within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary, Parotid
Gland, Salivary, Sublingual	Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid	Heart
Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum	Larynx	Lymph Node, Mandibular
Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic	Nose
Pancreas	Peripheral nerve (sciatic)	Peyer's Patch	Pharynx	Skin
Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar
Spinal Cord, Midthoracic	Spleen	Stomach	Testes	Thymus
Trachea	Urinary Bladder			

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:15:28 AM

Study: 55164

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Study Title: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3804

Group: 1

Day Of Death: Dosing Phase, Day 30

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Kidney	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary, Parotid
Gland, Salivary, Sublingual	Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid	Heart
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum	Larynx
Liver	Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal
Nasal Turbinate	Nerve, Optic	Nose	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen
Stomach	Testes	Thymus	Trachea	Urinary Bladder

Required tissues not microscopically examined:

None

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:15:28 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3804

Group: 1

Day Of Death: Dosing Phase, Day 30

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Continued from previous page ...				
Tissues microscopically examined and within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary, Parotid
Gland, Salivary, Sublingual	Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid	Heart
Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum	Larynx	Lungs
Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic
Nose	Pancreas	Peripheral nerve (sciatic)	Peyer's Patch	Pharynx
Skin	Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord, Cervical
Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen	Stomach	Testes
Thymus	Trachea	Urinary Bladder		

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:15:28 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

Study Title: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3805

Group: 1

Day Of Death: Dosing Phase, Day 30

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Gland, Prostate	Within Normal Limits		Infiltrate, minimal	
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary, Parotid
Gland, Salivary, Sublingual	Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid	Heart
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum	Larynx
Liver	Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal
Nasal Turbinate	Nerve, Optic	Nose	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen
Stomach	Testes	Thymus	Trachea	Urinary Bladder

Required tissues not microscopically examined:

None

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:15:28 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3805

Group: 1

Day Of Death: Dosing Phase, Day 30

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Continued from previous page ...				
Tissues microscopically examined and within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid	Heart	Kidney
Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum	Larynx	Lungs
Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic
Nose	Pancreas	Peripheral nerve (sciatic)	Peyer's Patch	Pharynx
Skin	Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord, Cervical
Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen	Stomach	Testes
Thymus	Trachea	Urinary Bladder		

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:15:28 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3806

Group: 1

Day Of Death: Dosing Phase, Day 31

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Gland, Mammary	Within Normal Limits		Missing	
Kidney	Within Normal Limits		Cyst, minimal	
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary, Parotid
Gland, Salivary, Sublingual	Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid	Heart
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum	Larynx
Liver	Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal
Nasal Turbinate	Nerve, Optic	Nose	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen
Stomach	Testes	Thymus	Trachea	Urinary Bladder

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:15:28 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3806

Group: 1

Day Of Death: Dosing Phase, Day 31

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Continued from previous page ...				
Required tissues not microscopically examined:				
Gland, Mammary				
Tissues microscopically examined and within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid	Heart	Large Intestine, Cecum
Large Intestine, Colon	Large Intestine, Rectum	Larynx	Lungs	Lymph Node, Mandibular
Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic	Nose
Pancreas	Peripheral nerve (sciatic)	Peyer's Patch	Pharynx	Skin
Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar
Spinal Cord, Midthoracic	Spleen	Stomach	Testes	Thymus
Trachea	Urinary Bladder			

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:15:28 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3807

Group: 1

Day Of Death: Dosing Phase, Day 31

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments
Esophagus	Within Normal Limits		Degeneration, mild, muscularis
Gland, Prostate	Within Normal Limits		Infiltrate, mild
Kidney	Within Normal Limits		Chronic Progressive Nephropathy, minimal
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal
Lungs	Within Normal Limits		Aggregate, alveolar macrophage, minimal Infiltrate, perivascular, eosinophil, minimal Inflammation, minimal
Muscle, Skeletal	Within Normal Limits		Infiltrate, minimal
Tissues grossly within normal limits:			
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum Brain
Epididymis	Esophagus	Eye	Gland, Adrenal Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate Gland, Salivary, Parotid
Gland, Salivary, Sublingual	Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid Heart
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum Larynx
Liver	Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric Muscle, Skeletal

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:15:28 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

Study Title: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3807

Group: 1

Day Of Death: Dosing Phase, Day 31

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Continued from previous page ...				
Nasal Turbinate	Nerve, Optic	Nose	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen
Stomach	Testes	Thymus	Trachea	Urinary Bladder
Required tissues not microscopically examined: None				
Tissues microscopically examined and within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Eye	Gland, Adrenal	Gland, Harderian	Gland, Mammary
Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual	Gland, Salivary, Submandibular
Gland, Seminal Vesicle	Gland, Thyroid	Heart	Large Intestine, Cecum	Large Intestine, Colon
Large Intestine, Rectum	Larynx	Lymph Node, Mandibular	Lymph Node, Mesenteric	Nasal Turbinate
Nerve, Optic	Nose	Pancreas	Peripheral nerve (sciatic)	Peyer's Patch
Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum
Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen	Stomach

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:15:28 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3807

Group: 1

Day Of Death: Dosing Phase, Day 31

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments
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Continued from previous page ...

Testes

Thymus

Trachea

Urinary Bladder

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:15:28 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

Study Title: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3808

Group: 1

Day Of Death: Dosing Phase, Day 31

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Esophagus	Within Normal Limits		Degeneration, minimal, muscularis	
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary, Parotid
Gland, Salivary, Sublingual	Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid	Heart
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum	Larynx
Liver	Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal
Nasal Turbinate	Nerve, Optic	Nose	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen
Stomach	Testes	Thymus	Trachea	Urinary Bladder
Required tissues not microscopically examined:				
None				

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:15:28 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3808

Group: 1

Day Of Death: Dosing Phase, Day 31

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Continued from previous page ...				
Tissues microscopically examined and within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Eye	Gland, Adrenal	Gland, Harderian	Gland, Mammary
Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid	Heart	Kidney
Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum	Larynx	Lungs
Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic
Nose	Pancreas	Peripheral nerve (sciatic)	Peyer's Patch	Pharynx
Skin	Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord, Cervical
Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen	Stomach	Testes
Thymus	Trachea	Urinary Bladder		

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:15:28 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3809

Group: 1

Day Of Death: Dosing Phase, Day 31

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Gland, Parathyroid	Within Normal Limits		Both Missing	
Gland, Thyroid	Within Normal Limits		Both Missing	
Kidney	Within Normal Limits		Chronic Progressive Nephropathy, minimal	
Larynx	Within Normal Limits		Missing	
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary, Parotid
Gland, Salivary, Sublingual	Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid	Heart
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum	Larynx
Liver	Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal
Nasal Turbinate	Nerve, Optic	Nose	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:15:28 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3809

Group: 1

Day Of Death: Dosing Phase, Day 31

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Continued from previous page ...				
Stomach	Testes	Thymus	Trachea	Urinary Bladder
Required tissues not microscopically examined:				
Gland, Parathyroid	Gland, Thyroid	Larynx		
Tissues microscopically examined and within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Pituitary	Gland, Prostate	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Heart	Large Intestine, Cecum	Large Intestine, Colon
Large Intestine, Rectum	Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal
Nasal Turbinate	Nerve, Optic	Nose	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen
Stomach	Testes	Thymus	Trachea	Urinary Bladder

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:15:28 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3810

Group: 1

Day Of Death: Dosing Phase, Day 31

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Gland, Adrenal	Within Normal Limits		No Abnormalities Detected One of the pair is Missing	
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary, Parotid
Gland, Salivary, Sublingual	Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid	Heart
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum	Larynx
Liver	Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal
Nasal Turbinate	Nerve, Optic	Nose	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen
Stomach	Testes	Thymus	Trachea	Urinary Bladder
Required tissues not microscopically examined: None				

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:15:28 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3810

Group: 1

Day Of Death: Dosing Phase, Day 31

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments
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Continued from previous page ...

Tissues microscopically examined and within normal limits:

Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary, Parotid
Gland, Salivary, Sublingual	Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid	Heart
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum	Larynx
Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate
Nerve, Optic	Nose	Pancreas	Peripheral nerve (sciatic)	Peyer's Patch
Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum
Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen	Stomach
Testes	Thymus	Trachea	Urinary Bladder	

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:15:28 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

Study Title: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3811

Group: 1

Day Of Death: Dosing Phase, Day 30

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Kidney	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Thyroid	Heart	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Large Intestine, Rectum	Larynx	Liver	Lungs
Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic
Nose	Ovary	Oviduct	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen
Stomach	Thymus	Trachea	Urinary Bladder	Uterus
Vagina				

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:15:28 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3811

Group: 1

Day Of Death: Dosing Phase, Day 30

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Continued from previous page ...				
Required tissues not microscopically examined:				
None				
Tissues microscopically examined and within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Thyroid	Heart	Large Intestine, Cecum	Large Intestine, Colon
Large Intestine, Rectum	Larynx	Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric
Muscle, Skeletal	Nasal Turbinate	Nerve, Optic	Nose	Ovary
Oviduct	Pancreas	Peripheral nerve (sciatic)	Peyer's Patch	Pharynx
Skin	Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord, Cervical
Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen	Stomach	Thymus
Trachea	Urinary Bladder	Uterus	Vagina	

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:15:28 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3812

Group: 1

Day Of Death: Dosing Phase, Day 30

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Gland, Salivary, Parotid	Within Normal Limits		Both Missing	
Kidney	Within Normal Limits		Mineralization, minimal	
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal Necrosis, minimal, focal	
Peripheral nerve (sciatic)	Within Normal Limits		Missing	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Thyroid	Heart	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Large Intestine, Rectum	Larynx	Liver	Lungs
Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic
Nose	Ovary	Oviduct	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen

Individual Gross and Microscopic Observations

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Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3812

Group: 1

Day Of Death: Dosing Phase, Day 30

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Continued from previous page ...				
Stomach	Thymus	Trachea	Urinary Bladder	Uterus
Vagina				
Required tissues not microscopically examined:				
Gland, Salivary, Parotid	Peripheral nerve (sciatic)			
Tissues microscopically examined and within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Sublingual	Gland, Salivary, Submandibular
Gland, Thyroid	Heart	Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum
Larynx	Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal
Nasal Turbinate	Nerve, Optic	Nose	Ovary	Oviduct
Pancreas	Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum
Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic
Spleen	Stomach	Thymus	Trachea	Urinary Bladder
Uterus	Vagina			

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:15:28 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

Study Title: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3813

Group: 1

Day Of Death: Dosing Phase, Day 30

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments
Gland, Mammary	Within Normal Limits		Missing
Gland, Parathyroid	Within Normal Limits		Both Missing
Gland, Salivary, Parotid	Within Normal Limits		Both Missing
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal
Tissues grossly within normal limits:			
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum
			Brain
Cervix	Esophagus	Eye	Gland, Adrenal
			Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid
			Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Thyroid	Heart	Kidney
			Large Intestine, Cecum
Large Intestine, Colon	Large Intestine, Rectum	Larynx	Liver
			Lungs
Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate
			Nerve, Optic
Nose	Ovary	Oviduct	Pancreas
			Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum
			Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic
			Spleen
Stomach	Thymus	Trachea	Urinary Bladder
			Uterus

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:15:28 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

Study Title: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3813

Group: 1

Day Of Death: Dosing Phase, Day 30

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Continued from previous page ...				
Vagina				
Required tissues not microscopically examined:				
Gland, Mammary	Gland, Parathyroid	Gland, Salivary, Parotid		
Tissues microscopically examined and within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Pituitary	Gland, Salivary, Sublingual	Gland, Salivary, Submandibular	Gland, Thyroid	Heart
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum	Larynx
Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate
Nerve, Optic	Nose	Ovary	Oviduct	Pancreas
Peripheral nerve (sciatic)	Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum
Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic
Spleen	Stomach	Thymus	Trachea	Urinary Bladder
Uterus	Vagina			

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:15:28 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

Study Title: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3814

Group: 1

Day Of Death: Dosing Phase, Day 30

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Gland, Mammary	Within Normal Limits		Missing	
Gland, Salivary, Parotid	Within Normal Limits		Tissue Comment: Fragment of parotid present attached to submandibular gland; larger section of parotid also present. No Abnormalities Detected	
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Thyroid	Heart	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Large Intestine, Rectum	Larynx	Liver	Lungs
Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic
Nose	Ovary	Oviduct	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen
Stomach	Thymus	Trachea	Urinary Bladder	Uterus

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:15:28 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

Study Title: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3814

Group: 1

Day Of Death: Dosing Phase, Day 30

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments
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Continued from previous page ...

Vagina

Required tissues not microscopically examined:

Gland, Mammary

Tissues microscopically examined and within normal limits:

Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual	Gland, Salivary, Submandibular
Gland, Thyroid	Heart	Kidney	Large Intestine, Cecum	Large Intestine, Colon
Large Intestine, Rectum	Larynx	Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric
Muscle, Skeletal	Nasal Turbinate	Nerve, Optic	Nose	Ovary
Oviduct	Pancreas	Peripheral nerve (sciatic)	Peyer's Patch	Pharynx
Skin	Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord, Cervical
Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen	Stomach	Thymus
Trachea	Urinary Bladder	Uterus	Vagina	

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:15:28 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

Study Title: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3815

Group: 1

Day Of Death: Dosing Phase, Day 30

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Gland, Salivary, Parotid	Within Normal Limits		Both Missing	
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Thyroid	Heart	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Large Intestine, Rectum	Larynx	Liver	Lungs
Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic
Nose	Ovary	Oviduct	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen
Stomach	Thymus	Trachea	Urinary Bladder	Uterus
Vagina				

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:15:28 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

Study Title: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3815

Group: 1

Day Of Death: Dosing Phase, Day 30

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments
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Continued from previous page ...

Required tissues not microscopically examined:
Gland, Salivary, Parotid

Tissues microscopically examined and within normal limits:

Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Sublingual	Gland, Salivary, Submandibular
Gland, Thyroid	Heart	Kidney	Large Intestine, Cecum	Large Intestine, Colon
Large Intestine, Rectum	Larynx	Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric
Muscle, Skeletal	Nasal Turbinate	Nerve, Optic	Nose	Ovary
Oviduct	Pancreas	Peripheral nerve (sciatic)	Peyer's Patch	Pharynx
Skin	Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord, Cervical
Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen	Stomach	Thymus
Trachea	Urinary Bladder	Uterus	Vagina	

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:15:28 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

Study Title: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3816

Group: 1

Day Of Death: Dosing Phase, Day 31

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Thyroid	Heart	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Large Intestine, Rectum	Larynx	Liver	Lungs
Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic
Nose	Ovary	Oviduct	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen
Stomach	Thymus	Trachea	Urinary Bladder	Uterus
Vagina				
Required tissues not microscopically examined:				
None				

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:15:28 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3816

Group: 1

Day Of Death: Dosing Phase, Day 31

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Continued from previous page ...				
Tissues microscopically examined and within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Thyroid	Heart	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Large Intestine, Rectum	Larynx	Lungs	Lymph Node, Mandibular
Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic	Nose
Ovary	Oviduct	Pancreas	Peripheral nerve (sciatic)	Peyer's Patch
Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum
Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen	Stomach
Thymus	Trachea	Urinary Bladder	Uterus	Vagina

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:15:28 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

Study Title: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3817

Group: 1

Day Of Death: Dosing Phase, Day 31

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Larynx	Within Normal Limits		Infiltrate, mild	
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Thyroid	Heart	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Large Intestine, Rectum	Larynx	Liver	Lungs
Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic
Nose	Ovary	Oviduct	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen
Stomach	Thymus	Trachea	Urinary Bladder	Uterus
Vagina				

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:15:28 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3817

Group: 1

Day Of Death: Dosing Phase, Day 31

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Continued from previous page ...				
Required tissues not microscopically examined:				
None				
Tissues microscopically examined and within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Thyroid	Heart	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Large Intestine, Rectum	Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric
Muscle, Skeletal	Nasal Turbinate	Nerve, Optic	Nose	Ovary
Oviduct	Pancreas	Peripheral nerve (sciatic)	Peyer's Patch	Pharynx
Skin	Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord, Cervical
Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen	Stomach	Thymus
Trachea	Urinary Bladder	Uterus	Vagina	

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:15:28 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

Study Title: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3818

Group: 1

Day Of Death: Dosing Phase, Day 31

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments
Kidney	Within Normal Limits		Infiltrate, mononuclear cell, minimal
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal
Lymph Node, Mesenteric	Within Normal Limits		Missing
Pancreas	Within Normal Limits		Atrophy, minimal, focal
Tissues grossly within normal limits:			
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum
			Brain
Cervix	Esophagus	Eye	Gland, Adrenal
			Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid
			Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Thyroid	Heart	Kidney
			Large Intestine, Cecum
Large Intestine, Colon	Large Intestine, Rectum	Larynx	Liver
			Lungs
Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate
			Nerve, Optic
Nose	Ovary	Oviduct	Pancreas
			Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum
			Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic
			Spleen
Stomach	Thymus	Trachea	Urinary Bladder
			Uterus

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:15:28 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3818

Group: 1

Day Of Death: Dosing Phase, Day 31

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
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Continued from previous page ...

Vagina

Required tissues not microscopically examined:
Lymph Node, Mesenteric

Tissues microscopically examined and within normal limits:

Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Thyroid	Heart	Large Intestine, Cecum	Large Intestine, Colon
Large Intestine, Rectum	Larynx	Lungs	Lymph Node, Mandibular	Muscle, Skeletal
Nasal Turbinate	Nerve, Optic	Nose	Ovary	Oviduct
Peripheral nerve (sciatic)	Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum
Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic
Spleen	Stomach	Thymus	Trachea	Urinary Bladder
Uterus	Vagina			

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:15:28 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

Study Title: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3819

Group: 1

Day Of Death: Dosing Phase, Day 31

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Gland, Mammary	Within Normal Limits		Missing	
Kidney	Within Normal Limits		Cyst, minimal	
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Skin	Within Normal Limits		Missing	
Uterus	Fluid filled, Noted	Correlated	Dilatation, minimal	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Thyroid	Heart	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Large Intestine, Rectum	Larynx	Liver	Lungs
Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic
Nose	Ovary	Oviduct	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:15:28 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3819

Group: 1

Day Of Death: Dosing Phase, Day 31

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Continued from previous page ...				
Stomach	Thymus	Trachea	Urinary Bladder	Vagina
Required tissues not microscopically examined:				
Gland, Mammary	Skin			
Tissues microscopically examined and within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual	Gland, Salivary, Submandibular
Gland, Thyroid	Heart	Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum
Larynx	Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal
Nasal Turbinate	Nerve, Optic	Nose	Ovary	Oviduct
Pancreas	Peripheral nerve (sciatic)	Peyer's Patch	Pharynx	Small Intestine, Duodenum
Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic
Spleen	Stomach	Thymus	Trachea	Urinary Bladder
Vagina				

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:15:28 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

Study Title: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3820

Group: 1

Day Of Death: Dosing Phase, Day 31

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Thyroid	Heart	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Large Intestine, Rectum	Larynx	Liver	Lungs
Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic
Nose	Ovary	Oviduct	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen
Stomach	Thymus	Trachea	Urinary Bladder	Uterus
Vagina				
Required tissues not microscopically examined:				
None				

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:15:28 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3820

Group: 1

Day Of Death: Dosing Phase, Day 31

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Continued from previous page ...				
Tissues microscopically examined and within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Thyroid	Heart	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Large Intestine, Rectum	Larynx	Lungs	Lymph Node, Mandibular
Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic	Nose
Ovary	Oviduct	Pancreas	Peripheral nerve (sciatic)	Peyer's Patch
Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum
Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen	Stomach
Thymus	Trachea	Urinary Bladder	Uterus	Vagina

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:17:04 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

Study Title: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3828

Group: 2

Day Of Death: Dosing Phase, Day 31

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments
Epididymis	Small, bilateral, R-32mm x 3mm, L-42mm x 3mm	Correlated	Hypospermia, severe, bilateral
Testes	Small, bilateral, R-11mm x 6mm, L-16mm x 4mm	Correlated	Atrophy, severe, bilateral

Tissues grossly within normal limits:
There are no such tissues

Required tissues not microscopically examined:
None

Tissues microscopically examined and within normal limits:
There are no such tissues

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:17:04 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3829

Group: 2

Day Of Death: Dosing Phase, Day 19

Sex: M

Death Status: Humane Sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments
Esophagus			Tissue Comment: Although a clear tear was not present on the sections evaluated, massive chronic active inflammation with fibrinous material is present surrounding all esophageal sections. This inflammation spread to the adjacent tracheal, pharyngeal, and thyroid sections (not diagnosed separately). While the gross tear was not confirmed microscopically, the inflammation clearly was a sequella of that tear.
	Tear, with food particles near opening, small	Not Correlated	Inflammation, severe, chronic active
Gland, Mammary	Within Normal Limits		Missing
Heart	Within Normal Limits		Inflammation, marked, chronic active, epicardium
Kidney	Within Normal Limits		Chronic Progressive Nephropathy, minimal
Lungs			Tissue Comment: Marked suppurative inflammation of pleural surfaces present; inflammation is fibrinous and edematous with embedded bacterial colonies.
	Fluid, colorless, clear	Correlated	Pleural Inflammation, marked
	Red, Noted	Not Correlated	
	Swollen, Noted	Correlated	Pleural Inflammation, marked
Spleen	Within Normal Limits		Extramedullary Hematopoiesis, marked
Thymus	Within Normal Limits		Tissue Comment: As noted under organ THCA (thoracic cavity), severe edematous, fibrinous inflammation surrounds and divides the thymus tissue. Atrophy, marked

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:17:04 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

Study Title: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3829

Group: 2

Day Of Death: Dosing Phase, Day 19

Sex: M

Death Status: Humane Sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
			Continued from previous page ...	
Thoracic Cavity	Fluid, colorless, clear	Not Applicable	Tissue Comment: Although no section was submitted for "thoracic cavity, fluid", presumptive evidence was found for such a gross observation, consisting of fibrinous, suppurative inflammation of the lung pleura, thymus/mediastinal tissues, as well as heart epicardium, and peri-tracheal, pharynx, and esophageal tissues. All these were consistent with an antemortem esophageal perforation.	
			Missing	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Eye	Gland, Adrenal	Gland, Harderian	Gland, Mammary
Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid	Heart	Kidney
Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum	Larynx	Liver
Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic
Nose	Pancreas	Peripheral nerve (sciatic)	Peyer's Patch	Pharynx
Skin	Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord, Cervical
Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen	Stomach	Testes

Individual Gross and Microscopic Observations

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Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3829

Group: 2

Day Of Death: Dosing Phase, Day 19

Sex: M

Death Status: Humane Sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Continued from previous page ...				
Thymus	Trachea	Urinary Bladder		
Required tissues not microscopically examined:				
Gland, Mammary	Thoracic Cavity			
Tissues microscopically examined and within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Eye	Gland, Adrenal	Gland, Harderian	Gland, Parathyroid
Gland, Pituitary	Gland, Prostate	Gland, Salivary, Parotid	Gland, Salivary, Sublingual	Gland, Salivary, Submandibular
Gland, Seminal Vesicle	Gland, Thyroid	Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum
Larynx	Liver	Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal
Nasal Turbinate	Nerve, Optic	Nose	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Stomach
Testes	Trachea	Urinary Bladder		

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:18:42 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Rat/Sprague-Dawley

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Animal #: 3850

Group: 3

Day Of Death: Dosing Phase, Day 31

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments
Testes	Small, right, R-1.8cm x 1.2cm	Correlated	Atrophy, marked, unilateral

Tissues grossly within normal limits:
There are no such tissues

Required tissues not microscopically examined:
None

Tissues microscopically examined and within normal limits:
There are no such tissues

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:18:42 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Rat/Sprague-Dawley

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Animal #: 3854

Group: 3

Day Of Death: Dosing Phase, Day 30

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments
Uterus	Fluid filled, Noted	Correlated	Dilatation, mild

Tissues grossly within normal limits:
There are no such tissues

Required tissues not microscopically examined:
None

Tissues microscopically examined and within normal limits:
There are no such tissues

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3861

Group: 4

Day Of Death: Dosing Phase, Day 30

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments
Kidney	Within Normal Limits		Chronic Progressive Nephropathy, minimal
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal
Tissues grossly within normal limits:			
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum
Epididymis	Esophagus	Eye	Gland, Adrenal
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate
Gland, Salivary, Sublingual	Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum
Liver	Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric
Nasal Turbinate	Nerve, Optic	Nose	Pancreas
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic
Stomach	Testes	Thymus	Trachea
Required tissues not microscopically examined:			
None			

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3861

Group: 4

Day Of Death: Dosing Phase, Day 30

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Continued from previous page ...				
Tissues microscopically examined and within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary, Parotid
Gland, Salivary, Sublingual	Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid	Heart
Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum	Larynx	Lungs
Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic
Nose	Pancreas	Peripheral nerve (sciatic)	Peyer's Patch	Pharynx
Skin	Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord, Cervical
Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen	Stomach	Testes
Thymus	Trachea	Urinary Bladder		

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3862

Group: 4

Day Of Death: Dosing Phase, Day 30

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Epididymis	Within Normal Limits		Infiltrate, minimal	
Kidney	Within Normal Limits		Chronic Progressive Nephropathy, minimal	
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary, Parotid
Gland, Salivary, Sublingual	Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid	Heart
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum	Larynx
Liver	Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal
Nasal Turbinate	Nerve, Optic	Nose	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen
Stomach	Testes	Thymus	Trachea	Urinary Bladder

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3862

Group: 4

Day Of Death: Dosing Phase, Day 30

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Continued from previous page ...				
Required tissues not microscopically examined:				
None				
Tissues microscopically examined and within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Esophagus	Eye	Gland, Adrenal	Gland, Harderian	Gland, Mammary
Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid	Heart	Large Intestine, Cecum
Large Intestine, Colon	Large Intestine, Rectum	Larynx	Lungs	Lymph Node, Mandibular
Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic	Nose
Pancreas	Peripheral nerve (sciatic)	Peyer's Patch	Pharynx	Skin
Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar
Spinal Cord, Midthoracic	Spleen	Stomach	Testes	Thymus
Trachea	Urinary Bladder			

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3863

Group: 4

Day Of Death: Dosing Phase, Day 30

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary, Parotid
Gland, Salivary, Sublingual	Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid	Heart
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum	Larynx
Liver	Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal
Nasal Turbinate	Nerve, Optic	Nose	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen
Stomach	Testes	Thymus	Trachea	Urinary Bladder
Required tissues not microscopically examined:				
None				
Tissues microscopically examined and within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3863

Group: 4

Day Of Death: Dosing Phase, Day 30

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Continued from previous page ...				
Epididymis	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary, Parotid
Gland, Salivary, Sublingual	Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid	Heart
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum	Larynx
Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate
Nerve, Optic	Nose	Pancreas	Peripheral nerve (sciatic)	Peyer's Patch
Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum
Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen	Stomach
Testes	Thymus	Trachea	Urinary Bladder	

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3864

Group: 4

Day Of Death: Dosing Phase, Day 30

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Kidney	Within Normal Limits		Chronic Progressive Nephropathy, minimal Infiltrate, mononuclear cell, minimal	
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary, Parotid
Gland, Salivary, Sublingual	Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid	Heart
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum	Larynx
Liver	Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal
Nasal Turbinate	Nerve, Optic	Nose	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen
Stomach	Testes	Thymus	Trachea	Urinary Bladder
Required tissues not microscopically examined: None				

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3864

Group: 4

Day Of Death: Dosing Phase, Day 30

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments
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Continued from previous page ...

Tissues microscopically examined and within normal limits:

Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary, Parotid
Gland, Salivary, Sublingual	Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid	Heart
Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum	Larynx	Lungs
Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic
Nose	Pancreas	Peripheral nerve (sciatic)	Peyer's Patch	Pharynx
Skin	Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord, Cervical
Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen	Stomach	Testes
Thymus	Trachea	Urinary Bladder		

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3865

Group: 4

Day Of Death: Dosing Phase, Day 30

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Kidney	Within Normal Limits		Chronic Progressive Nephropathy, minimal Infiltrate, mononuclear cell, minimal	
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Lungs	Within Normal Limits		Aggregate, alveolar macrophage , minimal	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary, Parotid
Gland, Salivary, Sublingual	Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid	Heart
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum	Larynx
Liver	Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal
Nasal Turbinate	Nerve, Optic	Nose	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen
Stomach	Testes	Thymus	Trachea	Urinary Bladder

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

Study Title: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Rat/Sprague-Dawley

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Animal #: 3865

Group: 4

Day Of Death: Dosing Phase, Day 30

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments
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Continued from previous page ...

Required tissues not microscopically examined:

None

Tissues microscopically examined and within normal limits:

Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary, Parotid
Gland, Salivary, Sublingual	Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid	Heart
Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum	Larynx	Lymph Node, Mandibular
Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic	Nose
Pancreas	Peripheral nerve (sciatic)	Peyer's Patch	Pharynx	Skin
Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar
Spinal Cord, Midthoracic	Spleen	Stomach	Testes	Thymus
Trachea	Urinary Bladder			

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3866

Group: 4

Day Of Death: Dosing Phase, Day 31

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Gland, Prostate	Within Normal Limits		Infiltrate, minimal	
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Pharynx	Within Normal Limits		Degeneration, mild, submucosal muscle	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary, Parotid
Gland, Salivary, Sublingual	Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid	Heart
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum	Larynx
Liver	Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal
Nasal Turbinate	Nerve, Optic	Nose	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen
Stomach	Testes	Thymus	Trachea	Urinary Bladder

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3866

Group: 4

Day Of Death: Dosing Phase, Day 31

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Continued from previous page ...				
Required tissues not microscopically examined:				
None				
Tissues microscopically examined and within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid	Heart	Kidney
Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum	Larynx	Lungs
Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic
Nose	Pancreas	Peripheral nerve (sciatic)	Peyer's Patch	Skin
Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar
Spinal Cord, Midthoracic	Spleen	Stomach	Testes	Thymus
Trachea	Urinary Bladder			

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

Study Title: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3867

Group: 4

Day Of Death: Dosing Phase, Day 31

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments
Eye	Within Normal Limits		One of the pair is Inadequate
Gland, Mammary	Within Normal Limits		Missing
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal Necrosis, minimal, focal Vacuolation, cytoplasmic, mild, diffuse
Tissues grossly within normal limits:			
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum
Epididymis	Esophagus	Eye	Gland, Adrenal
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate
Gland, Salivary, Sublingual	Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum
Liver	Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric
Nasal Turbinate	Nerve, Optic	Nose	Pancreas
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic
Stomach	Testes	Thymus	Trachea

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3867

Group: 4

Day Of Death: Dosing Phase, Day 31

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments
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Continued from previous page ...

Required tissues not microscopically examined:

Eye Gland, Mammary

Tissues microscopically examined and within normal limits:

Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Esophagus	Gland, Adrenal	Gland, Harderian	Gland, Parathyroid
Gland, Pituitary	Gland, Prostate	Gland, Salivary, Parotid	Gland, Salivary, Sublingual	Gland, Salivary, Submandibular
Gland, Seminal Vesicle	Gland, Thyroid	Heart	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Large Intestine, Rectum	Larynx	Lungs	Lymph Node, Mandibular
Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic	Nose
Pancreas	Peripheral nerve (sciatic)	Peyer's Patch	Pharynx	Skin
Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar
Spinal Cord, Midthoracic	Spleen	Stomach	Testes	Thymus
Trachea	Urinary Bladder			

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3868

Group: 4

Day Of Death: Dosing Phase, Day 31

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Kidney	Within Normal Limits		Chronic Progressive Nephropathy, minimal Infiltrate, mononuclear cell, minimal	
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary, Parotid
Gland, Salivary, Sublingual	Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid	Heart
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum	Larynx
Liver	Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal
Nasal Turbinate	Nerve, Optic	Nose	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen
Stomach	Testes	Thymus	Trachea	Urinary Bladder

Required tissues not microscopically examined:

None

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3868

Group: 4

Day Of Death: Dosing Phase, Day 31

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments
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Continued from previous page ...

Tissues microscopically examined and within normal limits:

Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary, Parotid
Gland, Salivary, Sublingual	Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid	Heart
Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum	Larynx	Lungs
Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic
Nose	Pancreas	Peripheral nerve (sciatic)	Peyer's Patch	Pharynx
Skin	Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord, Cervical
Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen	Stomach	Testes
Thymus	Trachea	Urinary Bladder		

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3869

Group: 4

Day Of Death: Dosing Phase, Day 31

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Gland, Mammary	Within Normal Limits		Missing	
Gland, Prostate	Within Normal Limits		Infiltrate, minimal	
Kidney	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Lungs	Within Normal Limits		Infiltrate, perivascular, eosinophil, mild	
Lymph Node, Mesenteric	Within Normal Limits		Missing	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary, Parotid
Gland, Salivary, Sublingual	Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid	Heart
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum	Larynx
Liver	Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal
Nasal Turbinate	Nerve, Optic	Nose	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3869

Group: 4

Day Of Death: Dosing Phase, Day 31

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Continued from previous page ...				
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen
Stomach	Testes	Thymus	Trachea	Urinary Bladder
Required tissues not microscopically examined:				
Gland, Mammary	Lymph Node, Mesenteric			
Tissues microscopically examined and within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual	Gland, Salivary, Submandibular
Gland, Seminal Vesicle	Gland, Thyroid	Heart	Large Intestine, Cecum	Large Intestine, Colon
Large Intestine, Rectum	Larynx	Lymph Node, Mandibular	Muscle, Skeletal	Nasal Turbinate
Nerve, Optic	Nose	Pancreas	Peripheral nerve (sciatic)	Peyer's Patch
Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum
Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen	Stomach
Testes	Thymus	Trachea	Urinary Bladder	

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3870

Group: 4

Day Of Death: Dosing Phase, Day 31

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Kidney	Within Normal Limits		Chronic Progressive Nephropathy, minimal Infiltrate, mononuclear cell, minimal	
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary, Parotid
Gland, Salivary, Sublingual	Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid	Heart
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum	Larynx
Liver	Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal
Nasal Turbinate	Nerve, Optic	Nose	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen
Stomach	Testes	Thymus	Trachea	Urinary Bladder
Required tissues not microscopically examined:				
None				

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3870

Group: 4

Day Of Death: Dosing Phase, Day 31

Sex: M

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments
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Continued from previous page ...

Tissues microscopically examined and within normal limits:

Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Epididymis	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary, Parotid
Gland, Salivary, Sublingual	Gland, Salivary, Submandibular	Gland, Seminal Vesicle	Gland, Thyroid	Heart
Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum	Larynx	Lungs
Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic
Nose	Pancreas	Peripheral nerve (sciatic)	Peyer's Patch	Pharynx
Skin	Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord, Cervical
Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen	Stomach	Testes
Thymus	Trachea	Urinary Bladder		

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

Study Title: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3871

Group: 4

Day Of Death: Dosing Phase, Day 30

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Gland, Harderian	Within Normal Limits		Both Missing	
Gland, Mammary	Within Normal Limits		Missing	
Kidney	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Thyroid	Heart	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Large Intestine, Rectum	Larynx	Liver	Lungs
Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic
Nose	Ovary	Oviduct	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen
Stomach	Thymus	Trachea	Urinary Bladder	Uterus

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

Study Title: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3871

Group: 4

Day Of Death: Dosing Phase, Day 30

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Continued from previous page ...				
Vagina				
Required tissues not microscopically examined:				
Gland, Harderian	Gland, Mammary			
Tissues microscopically examined and within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Parathyroid
Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual	Gland, Salivary, Submandibular	Gland, Thyroid
Heart	Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum	Larynx
Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate
Nerve, Optic	Nose	Ovary	Oviduct	Pancreas
Peripheral nerve (sciatic)	Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum
Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic
Spleen	Stomach	Thymus	Trachea	Urinary Bladder
Uterus	Vagina			

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

Study Title: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3872

Group: 4

Day Of Death: Dosing Phase, Day 30

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Brain	Within Normal Limits		Tissue Comment: Olfactory bulb presentation insufficient. No Abnormalities Detected	
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Uterus	Within Normal Limits		Dilatation, minimal	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Thyroid	Heart	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Large Intestine, Rectum	Larynx	Liver	Lungs
Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic
Nose	Ovary	Oviduct	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen
Stomach	Thymus	Trachea	Urinary Bladder	Uterus

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3872

Group: 4

Day Of Death: Dosing Phase, Day 30

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
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Continued from previous page ...

Vagina

Required tissues not microscopically examined:

None

Tissues microscopically examined and within normal limits:

Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Thyroid	Heart	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Large Intestine, Rectum	Larynx	Lungs	Lymph Node, Mandibular
Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic	Nose
Ovary	Oviduct	Pancreas	Peripheral nerve (sciatic)	Peyer's Patch
Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum
Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen	Stomach
Thymus	Trachea	Urinary Bladder	Vagina	

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

Study Title: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3873

Group: 4

Day Of Death: Dosing Phase, Day 30

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Gland, Salivary, Parotid	Within Normal Limits		Both Missing	
Kidney	Within Normal Limits		Cyst, minimal	
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Urinary Bladder	Within Normal Limits		Missing	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Thyroid	Heart	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Large Intestine, Rectum	Larynx	Liver	Lungs
Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic
Nose	Ovary	Oviduct	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen
Stomach	Thymus	Trachea	Urinary Bladder	Uterus

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

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Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3873

Group: 4

Day Of Death: Dosing Phase, Day 30

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Continued from previous page ...				
Vagina				
Required tissues not microscopically examined:				
Gland, Salivary, Parotid	Urinary Bladder			
Tissues microscopically examined and within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Sublingual	Gland, Salivary, Submandibular
Gland, Thyroid	Heart	Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum
Larynx	Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal
Nasal Turbinate	Nerve, Optic	Nose	Ovary	Oviduct
Pancreas	Peripheral nerve (sciatic)	Peyer's Patch	Pharynx	Skin
Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar
Spinal Cord, Midthoracic	Spleen	Stomach	Thymus	Trachea
Uterus	Vagina			

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3874

Group: 4

Day Of Death: Dosing Phase, Day 30

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Gland, Harderian	Within Normal Limits		No Abnormalities Detected One of the pair is Missing	
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Uterus	Within Normal Limits		Dilatation, mild	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Thyroid	Heart	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Large Intestine, Rectum	Larynx	Liver	Lungs
Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic
Nose	Ovary	Oviduct	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen
Stomach	Thymus	Trachea	Urinary Bladder	Uterus

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3874

Group: 4

Day Of Death: Dosing Phase, Day 30

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments
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Continued from previous page ...

Vagina

Required tissues not microscopically examined:

None

Tissues microscopically examined and within normal limits:

Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Thyroid	Heart	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Large Intestine, Rectum	Larynx	Lungs	Lymph Node, Mandibular
Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic	Nose
Ovary	Oviduct	Pancreas	Peripheral nerve (sciatic)	Peyer's Patch
Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum
Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen	Stomach
Thymus	Trachea	Urinary Bladder	Vagina	

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3875

Group: 4

Day Of Death: Dosing Phase, Day 30

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Gland, Parathyroid	Within Normal Limits		Both Missing	
Gland, Salivary, Parotid	Within Normal Limits		Both Missing	
Larynx	Within Normal Limits		Infiltrate, mild	
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Lungs	Within Normal Limits		Inflammation, minimal, alveolus	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Thyroid	Heart	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Large Intestine, Rectum	Larynx	Liver	Lungs
Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic
Nose	Ovary	Oviduct	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3875

Group: 4

Day Of Death: Dosing Phase, Day 30

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Continued from previous page ...				
Stomach	Thymus	Trachea	Urinary Bladder	Uterus
Vagina				
Required tissues not microscopically examined:				
Gland, Parathyroid	Gland, Salivary, Parotid			
Tissues microscopically examined and within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Pituitary	Gland, Salivary, Sublingual	Gland, Salivary, Submandibular	Gland, Thyroid
Heart	Kidney	Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum
Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic
Nose	Ovary	Oviduct	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen
Stomach	Thymus	Trachea	Urinary Bladder	Uterus

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3875

Group: 4

Day Of Death: Dosing Phase, Day 30

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments
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Continued from previous page ...

Vagina

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3876

Group: 4

Day Of Death: Dosing Phase, Day 31

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Gland, Mammary	Within Normal Limits		Missing	
Kidney	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Thyroid	Heart	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Large Intestine, Rectum	Larynx	Liver	Lungs
Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic
Nose	Ovary	Oviduct	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen
Stomach	Thymus	Trachea	Urinary Bladder	Uterus
Vagina				

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3876

Group: 4

Day Of Death: Dosing Phase, Day 31

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments
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Continued from previous page ...

Required tissues not microscopically examined:

Gland, Mammary

Tissues microscopically examined and within normal limits:

Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual	Gland, Salivary, Submandibular
Gland, Thyroid	Heart	Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum
Larynx	Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal
Nasal Turbinate	Nerve, Optic	Nose	Ovary	Oviduct
Pancreas	Peripheral nerve (sciatic)	Peyer's Patch	Pharynx	Skin
Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar
Spinal Cord, Midthoracic	Spleen	Stomach	Thymus	Trachea
Urinary Bladder	Uterus	Vagina		

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3877

Group: 4

Day Of Death: Dosing Phase, Day 31

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Gland, Harderian	Within Normal Limits		No Abnormalities Detected One of the pair is Missing	
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Vagina	Within Normal Limits		Missing	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Thyroid	Heart	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Large Intestine, Rectum	Larynx	Liver	Lungs
Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic
Nose	Ovary	Oviduct	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen
Stomach	Thymus	Trachea	Urinary Bladder	Uterus

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3877

Group: 4

Day Of Death: Dosing Phase, Day 31

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments
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Continued from previous page ...

Vagina

Required tissues not microscopically examined:

Vagina

Tissues microscopically examined and within normal limits:

Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Thyroid	Heart	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Large Intestine, Rectum	Larynx	Lungs	Lymph Node, Mandibular
Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic	Nose
Ovary	Oviduct	Pancreas	Peripheral nerve (sciatic)	Peyer's Patch
Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum
Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen	Stomach
Thymus	Trachea	Urinary Bladder	Uterus	

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

Study Title: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3878

Group: 4

Day Of Death: Dosing Phase, Day 31

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Thyroid	Heart	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Large Intestine, Rectum	Larynx	Liver	Lungs
Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic
Nose	Ovary	Oviduct	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen
Stomach	Thymus	Trachea	Urinary Bladder	Uterus
Vagina				
Required tissues not microscopically examined:				
None				

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3878

Group: 4

Day Of Death: Dosing Phase, Day 31

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Continued from previous page ...				
Tissues microscopically examined and within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Thyroid	Heart	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Large Intestine, Rectum	Larynx	Lungs	Lymph Node, Mandibular
Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic	Nose
Ovary	Oviduct	Pancreas	Peripheral nerve (sciatic)	Peyer's Patch
Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum
Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen	Stomach
Thymus	Trachea	Urinary Bladder	Uterus	Vagina

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

Study Title: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3879

Group: 4

Day Of Death: Dosing Phase, Day 31

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Kidney	Within Normal Limits		Chronic Progressive Nephropathy, minimal Infiltrate, mononuclear cell, minimal	
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Pharynx	Within Normal Limits		Degeneration, mild, submucosal muscle	
Vagina	Within Normal Limits		Missing	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Thyroid	Heart	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Large Intestine, Rectum	Larynx	Liver	Lungs
Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic
Nose	Ovary	Oviduct	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3879

Group: 4

Day Of Death: Dosing Phase, Day 31

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Continued from previous page ...				
Stomach	Thymus	Trachea	Urinary Bladder	Uterus
Vagina				
Required tissues not microscopically examined:				
Vagina				
Tissues microscopically examined and within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Thyroid	Heart	Large Intestine, Cecum	Large Intestine, Colon
Large Intestine, Rectum	Larynx	Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric
Muscle, Skeletal	Nasal Turbinate	Nerve, Optic	Nose	Ovary
Oviduct	Pancreas	Peripheral nerve (sciatic)	Peyer's Patch	Skin
Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar
Spinal Cord, Midthoracic	Spleen	Stomach	Thymus	Trachea

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

StudyTitle: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3879

Group: 4

Day Of Death: Dosing Phase, Day 31

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments
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Continued from previous page ...

Urinary Bladder

Uterus

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

Study Title: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3880

Group: 4

Day Of Death: Dosing Phase, Day 31

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Gland, Harderian	Within Normal Limits		Both Missing	
Gland, Salivary, Parotid	Within Normal Limits		Both Missing	
Liver	Within Normal Limits		Infiltrate, mononuclear cell, minimal	
Pancreas	Within Normal Limits		Atrophy, mild	
Tissues grossly within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Harderian
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Parotid	Gland, Salivary, Sublingual
Gland, Salivary, Submandibular	Gland, Thyroid	Heart	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Large Intestine, Rectum	Larynx	Liver	Lungs
Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal	Nasal Turbinate	Nerve, Optic
Nose	Ovary	Oviduct	Pancreas	Peripheral nerve (sciatic)
Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic	Spleen
Stomach	Thymus	Trachea	Urinary Bladder	Uterus

Individual Gross and Microscopic Observations

Printed: 09/07/2021 10:19:34 AM

Study: 55164

Pristima® Version 7.2.0 Build 31

Study Title: Limosilactobacillus reuteri: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Various

Repeat Dose Toxicity/Oral Gavage

Rat/Sprague-Dawley

Animal #: 3880

Group: 4

Day Of Death: Dosing Phase, Day 31

Sex: F

Death Status: Terminal sacrifice

Tissue	Gross Observations/Comments	Status	Microscopic Observations/Comments	
Continued from previous page ...				
Vagina				
Required tissues not microscopically examined:				
Gland, Harderian	Gland, Salivary, Parotid			
Tissues microscopically examined and within normal limits:				
Artery, Aorta	Bone Marrow	Bone, Femur	Bone, Sternum	Brain
Cervix	Esophagus	Eye	Gland, Adrenal	Gland, Mammary
Gland, Parathyroid	Gland, Pituitary	Gland, Salivary, Sublingual	Gland, Salivary, Submandibular	Gland, Thyroid
Heart	Kidney	Large Intestine, Cecum	Large Intestine, Colon	Large Intestine, Rectum
Larynx	Lungs	Lymph Node, Mandibular	Lymph Node, Mesenteric	Muscle, Skeletal
Nasal Turbinate	Nerve, Optic	Nose	Ovary	Oviduct
Peripheral nerve (sciatic)	Peyer's Patch	Pharynx	Skin	Small Intestine, Duodenum
Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord, Cervical	Spinal Cord, Lumbar	Spinal Cord, Midthoracic
Spleen	Stomach	Thymus	Trachea	Urinary Bladder
Uterus	Vagina			

Final Pathology Report
Elanco Animal Health Incorporated
PSL Study Number 55164

Appendix D. Tissue Accountability

Animal	Tissue	Tissue Accountability Statement
3802	Gland, Parathyroid, Both	Recut and/or retrim slides are not required for this tissue since StageBio SOPs require step sections on the original slide.
3806	Gland, Mammary	Despite the retrim slide produced at StageBio, this tissue is not present on slides for assessment.
3809	Gland, Parathyroid, Both	Tissue verified as missing from the wet tissues received. A second technician verified the tissue as missing from wets at the time of trimming.
3809	Gland, Thyroid, Both	Tissue verified as missing from the wet tissues received. A second technician verified the tissue as missing from wets at the time of trimming.
3809	Larynx	Tissue verified as missing from the wet tissues received. A second technician verified the tissue as missing from wets at the time of trimming.
3810	Gland, Adrenal, One-of-Pair	Tissue verified as missing from the wet tissues received. A second technician verified the tissue as missing from wets at the time of trimming.
3829	Gland, Mammary	Despite the retrim slide produced at StageBio, this tissue is not present on slides for assessment.
3829	Thoracic Cavity	Despite the retrim slide produced at StageBio, this tissue is not present on slides for assessment.
3867	Gland, Mammary	Despite the retrim slide produced at StageBio, this tissue is not present on slides for assessment.
3869	Gland, Mammary	Despite the retrim slide produced at StageBio, this tissue is not present on slides for assessment.
3869	Lymph Node, Mesenteric	Tissue verified as missing from the wet tissues received. A second technician verified the tissue as missing from wets at the time of trimming.
3812	Gland, Salivary, Parotid, Both	Despite the retrim slide produced at StageBio, this tissue is not present on slides for assessment.
3812	Peripheral nerve (sciatic)	Despite the retrim slide produced at StageBio, this tissue is not present on slides for assessment.
3813	Gland, Mammary	Despite the retrim slide produced at StageBio, this tissue is not present on slides for assessment.
3813	Gland, Parathyroid, Both	Recut and/or retrim slides are not required for this tissue since StageBio SOPs require step sections on the original slide.
3813	Gland, Salivary, Parotid, Both	Despite the retrim slide produced at StageBio, this tissue is not present on slides for assessment.
3814	Gland, Mammary	Despite the retrim slide produced at StageBio, this tissue is not present on slides for assessment.
3815	Gland, Salivary, Parotid, Both	Despite the retrim slide produced at StageBio, this tissue is not present on slides for assessment.
3818	Lymph Node, Mesenteric	Despite the retrim slide produced at StageBio, this tissue is not present on slides for assessment.
3819	Gland, Mammary	Tissue verified as missing from the wet tissues received. A second technician verified the tissue as missing from wets at the time of trimming.
3819	Skin	Tissue verified as missing from the wet tissues received. A second technician verified the tissue as missing from wets at the time of trimming.
3871	Gland, Harderian, Both	Tissue verified as missing from the wet tissues received. A second technician verified the tissue as missing from wets at the time of trimming.
3871	Gland, Mammary	Despite the retrim slide produced at StageBio, this tissue is not present on slides for assessment.
3873	Gland, Salivary, Parotid, Both	Despite the retrim slide produced at StageBio, this tissue is not present on slides for assessment.
3873	Urinary Bladder	Despite the retrim slide produced at StageBio, this tissue is not present on slides for assessment.
3874	Gland, Harderian, One-of-Pair	Despite the retrim slide produced at StageBio, this tissue is not present on slides for assessment.
3875	Gland, Parathyroid, Both	Recut and/or retrim slides are not required for this tissue since StageBio SOPs require step sections on the original slide.
3875	Gland, Salivary, Parotid, Both	Despite the retrim slide produced at StageBio, this tissue is not present on slides for assessment.
3876	Gland, Mammary	Despite the retrim slide produced at StageBio, this tissue is not present on slides for assessment.
3877	Gland, Harderian, One-of-Pair	Despite the retrim slide produced at StageBio, this tissue is not present on slides for assessment.
3877	Vagina	Tissue verified as missing from the wet tissues received. A second technician verified the tissue as missing from wets at the time of trimming.
3879	Vagina	Despite the retrim slide produced at StageBio, this tissue is not present on slides for assessment.
3880	Gland, Harderian, Both	Despite the retrim slide produced at StageBio, this tissue is not present on slides for assessment.
3880	Gland, Salivary, Parotid, Both	Despite the retrim slide produced at StageBio, this tissue is not present on slides for assessment.

Final Pathology Report
Elanco Animal Health Incorporated
PSL Study Number 55164

Appendix E. Quality Assurance Statement



QUALITY ASSURANCE STATEMENT

Study Title: *Limosilactobacillus reuteri*: 28-Day Repeat-Dose Oral Gavage Toxicity Study in Rats

Study Number: 55164

StageBio Document Identification (ID): SBDOC000773

The following have been inspected by the StageBio Quality Assurance Unit (QAU) as required by the Good Laboratory Practice (GLP) regulations disseminated by the U.S. Food and Drug Administration (FDA, 21 CFR 58), as well as the study protocol and amendment, and applicable StageBio SOPs.

Area Inspected	Date(s) of Inspection	Date Inspection Reported to Principal Investigator and Test Site Management	Date Inspection Reported to Study Director, Test Facility Management, and Lead QAU (as applicable)
Critical Phase (Staining)	04JUN21	08JUN21	08JUN21
Data Review	22-23JUN21	29JUN21	29JUN21
Draft Report	30JUN21	01JUL21	01JUL21
Final Report	07SEP21	07SEP21	07SEP21

The report is an accurate reflection of the raw data.

Signature Page



SBDOC000773: 55164 QAS

Testing Facility: Product Safety Labs / 55164

StageBio Study ID: 00752-0046

Sponsor: Elanco Animal Health Incorporated /

Title: LIMOSILACTOBACILLUS REUTERI: 28-DAY REPEAT-DOSE ORAL GAVAGE TOXICITY STUDY IN RATS

Reason for Signing

Signature

I am the author of this Quality Assurance Statement

9B6FBD88-5B38-FA44-8893
-5B9927C38702

Kelly Koontz
Quality Assurance
9/7/2021 10:25:50 AM
