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Downsized Sinclair™ vs. Göttingen™ Minipigs Similarities and Differences of Toxicological Reference Range Data in Preclinical Safety Studies

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BACKGROUND

Minipigs (MP) are recognized as offering advantages over other established non-rodent models, such as beagle dogs, based upon substantial evidence of similarities to humans with regard to anatomy, physiology, and biochemistry. Currently, MPs are used increasingly in nonclinical contract research organizations (CRO) and the biopharmaceutical industry to support investigational new drugs (IND)-enabling toxicology studies. However, similarities and differences in toxicological reference data between the commonly used Göttingen™ MP and Sinclair™ breeds have not been reported.

OBJECTIVE

To provide scientific justification for the selection of the most appropriate breed of MP for clients' drug development program, and as part of the Altasciences Historical Control Database initiative, this study was performed to compare reference baseline/background data for a battery of standard toxicological parameters obtained from Sinclair™ and Göttingen™ MP studies conducted at Altasciences Columbia site.

STUDY DESIGN AND METHODS

Data for Göttingen™ MPs (3-7 months old; Marshall) was extracted from an electronic data capture system (Pristima®) and compared with the reference data of downsized Sinclair™ MPs (2-4 months old; Book of Normals 2021; Sinclair BioResources), including body weight, clinical pathology (hematology, serum chemistry, coagulation, urinalysis), organ weights and histopathology background lesions of a panel of tissues from 10 physiological organ systems. Multiple statistical analyses, including mean and standard deviation (SD), range (min, max), fold difference of mean, quartile, interquartile range (IQR), and Tukey fence (upper and lower limit), were used for data comparison.

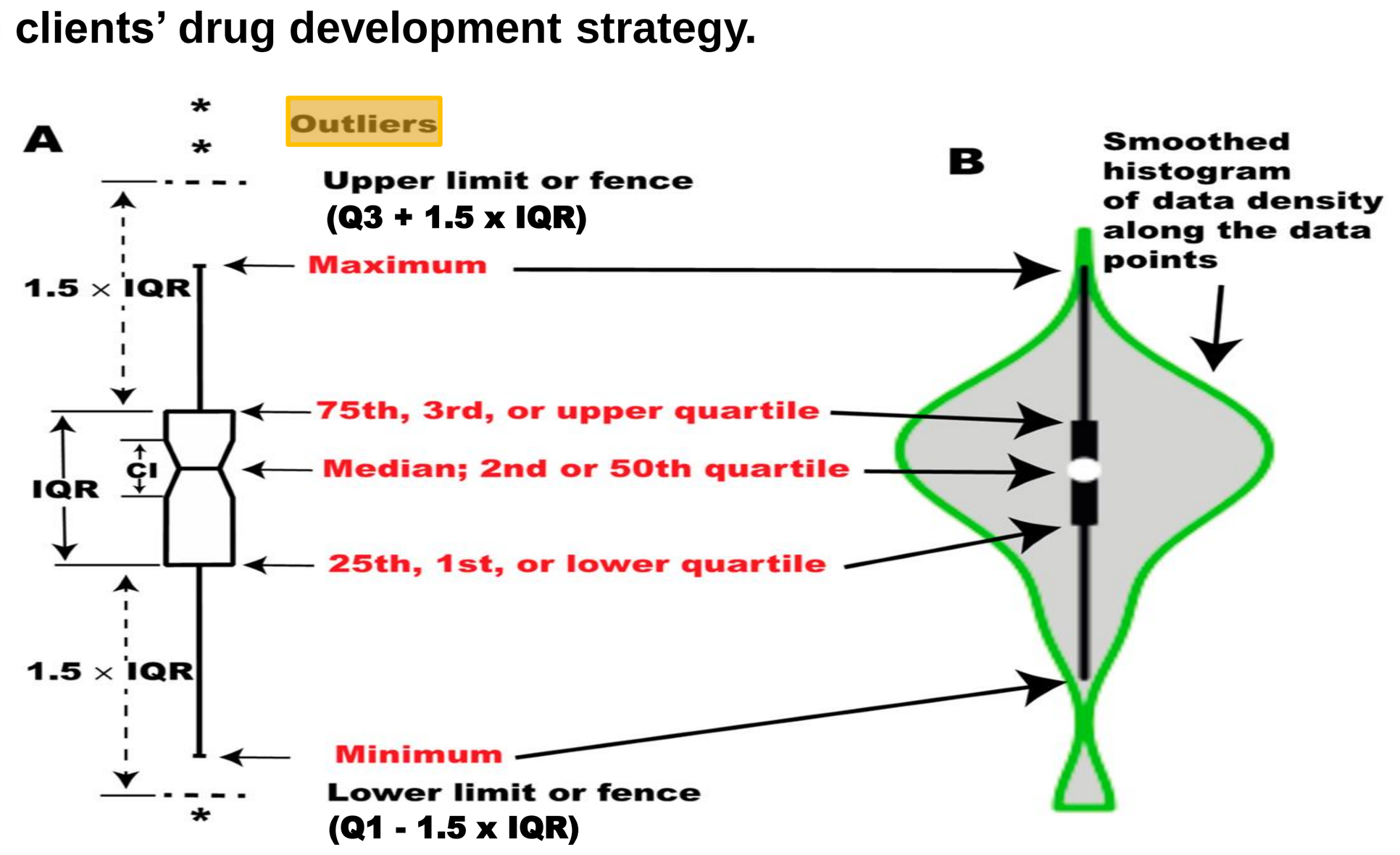
RESULTS

Body weights were similar between these two MP breeds up to approximately three months of age. There was considerable overlap of mean and statistical clinical pathology values between Sinclair™ vs. Göttingen™ MPs, except that **basophil, lymphocyte, monocyte, white blood cells (WBC), globulin, and total bilirubin** values were significantly higher (2-5—fold) in Sinclair™ MPs as compared to Göttingen™ MPs. In addition, **brain and thymus weights** for Sinclair™ MPs were higher than Göttingen™ MPs in both males (1.4—fold and 2.5—fold, respectively) and females (1.3—fold and 1.4—fold, respectively). The sex differences in organ weight to brain or body weight ratio were also observed, as the **heart and adrenal weights to brain ratio** were lower, while **thymus weight to body weight ratio** was higher in male (only) Sinclair™ MPs as compared to Göttingen™ MPs. The relatively higher blood basophil, lymphocyte, monocyte, WBC, globulin values, and thymus weight in Sinclair™ MPs may indicate a potential difference in immune system function (further validation study is warranted).

The most common microscopic finding noted in Sinclair™ MPs was **multifocal lymphohistiocytic infiltration** in various tissues at low levels of severity and incidence. Detailed descriptions of similarities and differences of background, histopathological findings and incidence (Sinclair™ vs. Göttingen™) are discussed.

CONCLUSIONS

Based on data comparison in this study, all apparent differences among clinical pathology, organ weight and background microscopic findings between Sinclair™ vs Göttingen™ MPs were considered minor in magnitude and biological significance. This study, for the first time, provides assessment criteria for minipig breed selection, data quality control and interpretation of results in preclinical toxicity studies using **downsized Sinclair™ MPs, which have similar toxicological reference data vs. Göttingen™, are more cost effective, and readily available at different ages ensuring customized study design for each clients' drug development strategy.**



KEY PATHOLOGY DATA COMPARISON (DOWNSIZED SINCLAIR™ VS. GÖTTINGEN™ MINIPIGS; MOST WITHIN 3-6 MONTHS OF AGE OR YOUNG ADULT)

Outliers (parameter or value) | Mean or Tukey Fences

Table 1. Hematology and Coagulation

Analyte	Abbrev.	Units	N	Mean	SD	Range		Tukey Fence	IQR			Tukey Fence	N	Mean	SD	Range		Mean Fold Change
			Göttingen™ Male			Min	Max	LL	Q1	Median	Q3	UL	Sinclair™ Male			Min	Max	Sinclair™/ Göttingen™
Basophil (Absolute)	BAS	(10^{3} /µL)	108	**0.02**	0.02	0.00	0.13	**-0.01**	0.01	0.01	0.02	**0.04**	47	**0.10**	0.08	0.00	0.30	**5.1**
Basophil Percent	BAS %	(%)	108	**0.22**	0.23	0.00	1.40	**-0.09**	0.10	0.10	0.23	**0.41**	47	**0.50**	0.40	0.00	1.30	**2.3**
Eosinophil (Absolute)	EOS	(10^{3} /µL)	108	0.21	0.14	0.03	0.80	-0.09	0.12	0.18	0.25	0.46	47	0.28	0.27	0.00	1.47	1.3
Eosinophil Percent	EOS %	(%)	108	2.37	1.52	0.70	10.00	-0.85	1.40	2.00	2.90	5.15	47	1.40	1.30	0.00	6.00	0.6
Hemoglobin	Hb	(g/dL)	108	13.34	1.21	5.90	15.40	10.81	12.80	13.40	14.13	16.11	47	13.40	1.30	11.20	16.40	1.0
Hematocrit	HCT	(%)	108	39.51	3.80	18.50	47.10	30.78	37.45	39.60	41.90	48.58	47	42.40	3.80	35.30	51.30	1.1
Lymphocyte (Absolute)	LYM	(10^{3} /µL)	108	**4.79**	1.26	2.20	8.60	**1.03**	3.84	4.83	5.72	**8.53**	47	**11.62**	3.83	4.95	20.46	**2.4**
Lymphocyte Percent	LYM %	(%)	108	53.71	8.95	25.70	73.30	25.40	46.48	54.45	60.53	81.60	47	60.80	12.90	22.10	78.60	1.1
Mean Corpuscular Hemoglobin	MCH	(pg)	108	16.47	1.73	13.50	21.70	11.86	15.20	16.15	17.43	20.76	47	17.90	1.10	15.00	19.40	1.1
Mean Corpuscular Hemoglobin Conc.	MCHC	(g/dL)	108	33.78	1.12	29.70	36.90	32.01	33.40	33.90	34.33	35.71	47	31.70	0.90	30.10	33.90	0.9
Mean Corpuscular Volume	MCV	(fL)	108	48.76	4.90	39.80	62.70	36.70	45.70	47.75	51.70	60.70	47	56.40	3.30	49.40	62.00	1.2
Monocyte (Absolute)	MONO	(10^{3} /µL)	108	**0.29**	0.13	0.07	0.65	**-0.02**	0.21	0.28	0.36	**0.59**	47	**0.98**	0.51	0.31	2.69	**3.3**
Monocyte Percent	MONO %	(%)	108	3.28	1.19	0.90	6.60	0.34	2.48	3.10	3.90	6.04	47	5.20	2.50	2.00	14.00	1.6
Neutrophil (Absolute)	NEU	(10^{3} /µL)	108	3.60	1.57	1.26	14.05	-0.02	2.70	3.22	4.51	7.22	47	6.03	3.64	2.07	20.03	1.7
Neutrophil Percent	NEU %	(%)	108	39.37	9.28	17.10	70.00	10.09	31.58	39.30	45.90	67.39	47	30.50	12.50	12.90	73.70	0.8
Platelet Count	PLT	(10^{3} /µL)	108	505.17	181.27	7.00	951.00	119.13	417.25	533.00	616.00	914.13	47	459.00	123.00	149.00	669.00	0.9
Red Blood Cell Count	RBC	(10^{6} /µL)	108	8.17	0.98	3.35	10.30	6.01	7.67	8.25	8.78	10.44	47	7.54	0.75	6.00	9.79	0.9
Reticulocyte Count (Absolute)	RET	(10^{9} /L)	103	167.55	100.08	24.10	521.90	-77.50	95.75	141.40	211.25	384.50	47	130.45	61.77	37.30	276.30	0.8
Reticulocyte Count Percent	RET %	(%)	103	2.08	1.30	0.32	7.71	-1.23	1.18	1.63	2.78	5.19	47	1.76	0.90	0.46	3.77	0.8
White Blood Cell Count	WBC	(10^{3} /µL)	108	**9.01**	2.33	4.02	20.06	**2.48**	7.27	9.31	10.46	**15.26**	45	**18.81**	4.70	9.21	28.29	**2.1**
Coagulation																		
Activated Partial Thromboplastin Time	APTT	(sec)	86	15.22	4.08	9.30	29.10	4.49	12.18	14.55	17.30	24.99	51	16.30	2.00	12.10	21.80	1.1
Prothrombin Time	PT	(sec)	88	12.92	1.09	11.20	15.00	9.10	12.10	12.45	14.10	17.10	51	14.40	1.60	10.90	18.40	1.1

Table 3a. Organ Weight (Male)

Organ	Units	N	Mean	SD	Range		Tukey Fence	IQR			Tukey Fence	N	Mean	SD	Range		Mean Fold Change
		Göttingen™ Male			Min	Max	LL	Q1	Median	Q3	UL	Sinclair™ Male			Min	Max	Sinclair™/ Göttingen™
Adrenal (2)																	
Absolute Weight	G	29	1.843	0.373	1.210	2.610	0.635	1.490	1.896	2.060	2.915	12	1.390	0.197	1.040	1.710	0.8
% Body Weight	%	29	0.015	0.003	0.011	0.025	0.010	0.014	0.015	0.017	0.021	12	0.011	0.002	0.009	0.015	0.7
% Brain Weight	%	29	**3.367**	0.510	2.527	4.611	**2.542**	3.165	3.304	3.580	**4.202**	12	**1.810**	0.260	1.320	2.300	**0.5**
Brain																	
Absolute Weight	G	29	**54.634**	6.419	40.750	64.230	**39.965**	51.080	54.966	58.490	**69.605**	12	**76.700**	4.780	67.700	85.200	**1.4**
% Body Weight	%	29	0.464	0.089	0.316	0.668	0.221	0.407	0.444	0.531	0.717	12	0.610	0.086	0.510	0.770	1.3
% Brain Weight	%	29	100.000	0.000	100.000	100.000	100.000	100.000	100.000	100.000	100.000	12	100.000		100.000	100.000	1.0
Heart																	
Absolute Weight	G	29	65.295	14.608	39.360	92.966	25.630	53.590	65.300	72.230	100.190	12	59.400	8.750	43.400	73.100	0.9
% Body Weight	%	29	0.544	0.074	0.355	0.697	0.344	0.496	0.526	0.597	0.749	12	0.470	0.033	0.390	0.520	0.9
% Brain Weight	%	29	**118.824**	18.915	92.342	162.241	**79.841**	107.258	114.766	125.536	**152.954**	12	**77.300**	9.670	62.000	89.200	**0.7**
Kidney (2)																	
Absolute Weight	G	29	65.794	20.871	17.470	125.420	26.338	56.120	63.970	75.975	105.758	12	58.900	6.920	48.300	72.600	0.9
% Body Weight	%	29	0.550	0.245	0.210	1.718	0.322	0.466	0.502	0.562	0.707	12	0.470	0.100	0.340	0.710	0.9
% Brain Weight	%	29	121.356	43.766	34.196	299.632	51.583	103.270	115.271	137.727	189.414	12	77.100	9.980	66.100	93.800	0.6
Liver / Gall Bladder																	
Absolute Weight	g	29	263.012	63.520	170.000	379.500	43.650	200.700	279.700	305.400	462.450	12	324.000	44.500	246.000	394.000	1.2
% Body Weight	%	29	2.173	0.346	1.700	3.647	1.730	2.022	2.147	2.217	2.509	12	2.590	0.520	1.760	3.670	1.2
% Brain Weight	%	29	480.508	100.386	322.269	692.789	205.011	396.731	482.927	524.544	716.264	12	423.000	56.100	332.000	516.000	0.9
Pituitary Gland																	
Absolute Weight	g	29	0.091	0.038	0.026	0.225	0.012	0.067	0.083	0.104	0.160	12	0.103	0.034	0.072	0.191	1.1
% Body Weight	%	29	0.001	0.000	0.000	0.002	0.000	0.001	0.001	0.001	0.001	12	0.001	0.000	0.001	0.001	1.3
% Brain Weight	%	29	0.168	0.075	0.053	0.401	0.075	0.135	0.157	0.175	0.235	12	0.130	0.047	0.090	0.260	0.8
Spleen																	
Absolute Weight	g	29	48.726	34.069	14.760	139.300	-58.405	21.020	35.282	73.970	153.395	12	44.600	19.700	12.500	86.100	0.9
% Body Weight	%	29	0.372	0.222	0.112	0.801	-0.354	0.200	0.269	0.569	1.123	12	0.340	0.130	0.140	0.580	0.9
% Brain Weight	%	29	89.231	62.361	27.484	253.429	-113.761	39.026	60.782	140.884	293.672	12	57.400	23.600	18.400	105.000	0.6
Thyroid (2)																	
Absolute Weight	g	29	1.422	0.570	0.630	2.381	0.084	1.160	1.380	1.877	2.953	12	1.220	0.274	0.744	1.730	0.9
% Body Weight	%	29	0.010	0.002	0.008	0.014	0.006	0.009	0.010	0.011	0.014	12	0.010	0.002	0.007	0.014	1.0
% Brain Weight	%	29	2.598	0.950	1.500	4.155	-0.274	1.958	2.338	3.446	5.677	12	1.580	0.310	1.100	2.150	0.6
Testis (2)																	
Absolute Weight	g	29	36.472	9.811	21.680	56.120	12.350	30.530	37.146	42.650	60.830	12	49.900	19.600	21.200	78.500	1.4
% Body Weight	%	29	0.312	0.105	0.131	0.529	0.015	0.237	0.323	0.386	0.609	12	0.380	0.110	0.210	0.520	1.2
% Brain Weight	%	29	67.039	16.615	37.145	88.825	13.253	54.855	72.586	82.589	124.191	12	64.600	24.300	31.400	95.800	1.0
Thymus																	
Absolute Weight	g	29	**10.563**	5.483	3.720	28.895	**-1.378**	6.425	10.100	11.627	**19.431**	12	**26.400**	12.000	9.850	48.600	**2.5**
% Body Weight	%	29	**0.085**	0.034	0.027	0.166	**0.016**	0.066	0.081	0.099	**0.149**	12	**0.200**	0.089	0.110	0.410	**2.4**
% Brain Weight	%	29	19.467	9.819	6.404	52.569	-3.734	13.202	18.752	24.494	41.430	12	34.400	16.200	14.500	65.200	1.8

Table 4. Histopathology (Most Common Background Lesion Incidence in Downsized Sinclair™ Minipigs)

SYSTEMS / Organs / Tissues	Sinclair™ Male (N=11)	Sinclair™ Female (N=11)
CARDIOVASCULAR SYSTEM		
Heart		
Inflammation (lymphohistiocytic, multifocal) (minimal)	1 (9.1%)	0
DIGESTIVE SYSTEM		
Salivary glands		
Inflammation (lymphohistiocytic, multifocal) (mild)	1 (9.1%)	0
Esophagus		
Inflammation (lymphohistiocytic, multifocal) (minimal)	0	1 (9.1%)
Stomach		
Inflammation (lymphohistiocytic, muscularis, multifocal)	2 (18.2%)	0
Erosion (focal)	1 (9.1%)	0
Small Intestine		
Mononuclear infiltrates (ileum) (slight)	0	1 (9.1%)
Large Intestine		
Hemorrhage (multifocal) (minimal)	0	1 (9.1%)
Liver		
Inflammation (lymphohistiocytic, multifocal) (minimal)	1 (9.1%)	2 (18.2%)
ENDOCRINE SYSTEM		
Adrenal glands		
Congestion (medullary, focal) (minimal)	0	1 (9.1%)
Hemorrhage (capsular, focal) (minimal)	0	1 (9.1%)
Inflammation (lymphohistiocytic, multifocal) (minimal)	0	1 (9.1%)
Mammary glands		
Inflammation (lymphohistiocytic, focal) (minimal)	0	1 (9.1%)
Thyroid		
Cyst (focal) (mild)	1 (9.1%)	0
Cyst (follicular, focal) (mild)	0	1 (9.1%)
Inflammation (lymphohistiocytic, multifocal) (minimal)	1 (9.1%)	0
Atrophy (follicular) (minimal to slight)	1 (9.1%)	1 (9.1%)
Ectasia (follicular) (slight)	0	1 (9.1%)
HEMATOPOIETIC AND LYMPHATIC SYSTEMS		
Cervical lymph node		
Hemorrhage (slight to moderate)	1 (9.1%)	1 (9.1%)
Inflammation (moderate)	1 (9.1%)	0
Mineralization (slight)	1 (9.1%)	0
Granuloma (moderate)	1 (9.1%)	0
Spleen		
Congestion (diffuse) (moderate)	3 (27.3%)	3 (27.3%)

SYSTEMS / Organs / Tissues	Sinclair™ Male (N=11)	Sinclair™ Female (N=11)
INTEGUMENTARY SYSTEM		
Skin		
Inflammation (lymphohistiocytic, focal) (minimal)	0	1 (9.1%)
MUSCULOSKELETAL SYSTEM		
Skeletal muscle		
Inflammation (lymphohistiocytic, focal) (minimal)	1 (9.1%)	0
NERVOUS SYSTEM		
Brain		
Inflammation (lymphocytic, ventricular, focal) (minimal)	2 (18.2%)	0
Glial nodule (multifocal) (minimal)	1 (9.1%)	1 (9.1%)
Lacrimal Gland		
Inflammation (lymphohistiocytic, multifocal) (minimal to mild)	3 (27.3%)	3 (27.3%)
Duct inflammation (suppurative, multifocal) (moderate)	0	1 (9.1%)
Atrophy (diffuse) (mild)	0	1 (9.1%)
Hypertrophy (multifocal) (mild)	0	1 (9.1%)
MALE REPRODUCTIVE SYSTEM		
Testes		
Hypoplasia/atrophy (tubular) (slight)	1 (9.1%)	NA
RESPIRATORY SYSTEM		
Lung		
Hemorrhage (minimal)	1 (9.1%)	0
Microgranuloma (minimal)	1 (9.1%)	0
Interstitial inflammation (lymphohistiocytic, multifocal) (minimal to mild)	3 (27.3%)	1 (9.1%)
Broncho interstitial pneumonia (suppurative, focal to multifocal) (mild to marked)	1 (9.1%)	4 (36.4%)
URINARY SYSTEM		
Kidneys		
Mononuclear infiltrate (minimal to moderate)	2 (18.2%)	3 (27.3%)
Tubular basophilia (focal to multifocal) (minimal to slight)	3 (27.3%)	3 (27.3%)
Inflammation (lymphohistiocytic, multifocal) (minimal to mild)	4 (36.4%)	3 (27.3%)
Glomerulosclerosis (slight)	1 (9.1%)	0

- Eleven clinically healthy and sexually mature downsized Sinclair™ Minipigs were microscopically examined consistent with international guidelines and/or criteria for toxicological research.
- Although this data should be regarded as a sample only, the most common microscopical lesion was **inflammation with multifocal lymphohistiocytic infiltration in various tissues at low levels of severity (minimal to mild)**, suggestive of a traumatic or non-specific infectious etiology; **Spleen, Lacrimal gland, Lung and Kidneys** most commonly had increased incidence and severity scores.
- Few cases of hemorrhage and congestion may be an artifact of euthanasia[1]. Other occasional findings in both sexes are generally of a mild and focal nature.

Table 2. Blood Chemistry and Urinalysis

Analyte	Abbrev.	Units	N	Mean	SD	Range		Tukey Fence	IQR			Tukey Fence	N	Mean	SD	Range		Mean Fold Change
			Göttingen™ Male			Min	Max	LL	Q1	Median	Q3	UL	Sinclair™ Male			Min	Max	Sinclair™/ Göttingen™
A\G Ratio	A\G	N/A	107	2.8	0.7	1.6	5.5	1.1	2.3	2.7	3.1	4.3	51	1.3	0.3	0.6	1.9	0.5
Albumin	ALB	(g/dL)	107	4.2	0.3	2.9	4.8	3.5	4.0	4.2	4.4	5.0	51	3.4	0.4	2.3	4.3	0.8
Alkaline Phosphatase	ALP	(IU/L)	107	149.3	46.0	91.0	381.0	59.8	122.0	142.0	163.5	225.8	51	102.0	26.0	51.0	168.0	0.7
Alanine Aminotransferase	ALT	(IU/L)	107	35.4	15.8	21.0	171.0	15.5	29.0	33.0	38.0	51.5	51	32.0	8.0	20.0	55.0	0.9
Aspartate Aminotransferase	AST	(IU/L)	107	34.8	24.5	14.0	181.0	0.0	22.0	27.0	39.5	65.8	51	37.0	17.0	18.0	91.0	1.1
Blood Urea Nitrogen	BUN	(mg/dL)	107	6.4	2.4	2.0	15.0	0.5	5.0	6.0	8.0	12.5	51	8.0	3.0	5.0	17.0	1.3
Calcium	CA	(mg/dL)	107	10.7	0.5	8.5	11.8	9.7	10.4	10.7	10.9	11.7	51	10.6	0.4	9.8	11.4	1.0
Cholesterol	CHOL	(mg/dL)	107	70.8	17.0	32.0	120.0	26.0	59.0	68.0	81.0	114.0	51	79.0	14.0	47.0	110.0	1.1
Chloride	CL	(mmol/L)	107	100.3	2.3	94.0	110.0	94.5	99.0	100.0	102.0	106.5	51	103.0	3.0	96.0	110.0	1.0
Creatinine	CREA	(mg/dL)	107	0.7	0.1	0.4	1.0	0.4	0.7	0.7	0.8	1.0	51	0.9	0.2	0.6	1.4	1.2
Globulin	GLOB	(g/dL)	107	**1.6**	0.3	0.9	2.7	**0.8**	1.4	1.6	1.8	**2.4**	51	**2.8**	0.5	2.0	4.2	**1.8**
Glucose	GLU	(mg/dL)	107	92.8	20.1	52.0	207.0	58.5	82.5	88.0	98.5	122.5	51	86.0	12.0	58.0	112.0	0.9
Bicarbonate	HCO3	(mmol/L)	18	18.8	2.9	13.0	23.0	12.0	17.3	20.0	20.8	26.0	51	24.0	4.0	16.0	31.0	1.3
Potassium	K	(mmol/L)	107	5.1	0.9	3.4	7.2	2.7	4.5	5.1	5.7	7.5	51	5.8	0.9	4.1	8.0	1.1
Lactate Dehydrogenase	LDH	(IU/L)	102	449.6	131.0	253.0	980.0	151.9	363.0	423.0	503.8	714.9	51	538.0	172.0	338.0	1198.0	1.2
Sodium	Na	(mmol/L)	107	142.6	2.6	136.0	153.0	136.5	141.0	143.0	144.0	148.5	51	144.0	3.0	137.0	151.0	1.0
Phosphorus	Phos	(mg/dL)	107	7.8	1.1	4.2	11.1	5.9	7.4	7.8	8.4	9.9	51	9.5	0.8	7.3	10.6	1.2
Total Bilirubin	TBIL	(mg/dL)	107	**0.1**	0.1	0.1	0.6	**0.1**	0.1	0.1	0.1	**0.1**	51	**0.2**	0.1	0.1	0.6	**1.7**
Total Protein	TPRO	(g/dL)	107	5.8	0.4	4.1	7.0	5.0	5.6	5.8	6.0	6.6	51	6.2	0.5	5.1	7.2	1.1
Triglyceride	TRIG	(mg/dL)	107	29.0	11.4	12.0	73.0	1.5	21.0	27.0	34.0	53.5	51	50.0	27.0	18.0	139.0	1.7
Urinalysis																		
pH	pH	N/A	76	7.63	0.86	6.00	9.00	4.75	7.00	7.50	8.50	10.75	51	6.91	1.01	5.00	9.00	0.9
Specific Gravity	SG	N/A	77	1.0	0.011	1.002	1.050	0.993	1.015	1.024	1.030	1.053	51	1.020	0.008	1.008	1.038	1.0
Urobilinogen	UBG	(mg/dL)	77	0.22	0.13	0.20	1.00	0.20	0.20	0.20	0.20	0.20	51	0.22	0.11	0.20	1.00	1.0

Table 3b. Organ Weight (Female)

Organ	Units	N	Mean	SD	Range		Tukey Fence	IQR			Tukey Fence	N	Mean	SD	Range		Mean Fold Change
		Göttingen™ Female			Min	Max	LL	Q1	Median	Q3	UL	Sinclair™ Female			Min	Max	Sinclair™/ Göttingen™
Adrenal (2)																	
Absolute Weight	g	29	1.842	0.390	0.950	2.440	0.680	1.550	1.970	2.130	3.000	12	1.230	0.150	1.040	1.480	0.7
% Body Weight	%	29	0.015	0.003	0.011	0.023	0.007	0.013	0.014	0.017	0.023	12	0.010	0.002	0.008	0.015	0.7
% Brain Weight	%	29	3.187	0.794	0.402	4.320	1.537	2.824	3.297	3.682	4.968	12	1.710	0.220	1.420	2.060	0.5
Brain																	
Absolute Weight	g	29	**55.505**	5.576	42.530	64.098	**41.565**	52.650	55.930	60.040	**71.125**	12	**72.200**	3.160	64.900	77.900	**1.3**
% Body Weight	%	29	0.591	0.714	0.295	4.265	0.156	0.394	0.443	0.553	0.790	12	0.590	0.068	0.470	0.710	1.0
% Brain Weight	%	29	100.000		100.000	100.000	100.000	100.000	100.000	100.000	100.000	12	100.000		100.000	100.000	1.0
Heart																	
Absolute Weight	g	29	62.303	11.762	37.330	85.741	33.825	55.440	62.110	69.850	91.465	12	53.300	7.310	39.200	64.800	0.9
% Body Weight	%	29	0.501	0.063	0.389	0.654	0.340	0.461	0.494	0.542	0.664	12	0.430	0.029	0.390	0.500	0.9
% Brain Weight	%	29	107.974	23.516	12.326	147.306	63.139	97.864	111.142	121.015	155.740	12	73.800	9.640	60.400	88.400	0.7
Kidney (2)																	
Absolute Weight	g	29	62.985	17.156	33.940	104.700	6.620	48.740	61.790	76.820	118.940	12	53.200	4.100	46.200	59.300	0.8
% Body Weight	%	29	0.502	0.100	0.359	0.761	0.243	0.426	0.488	0.548	0.732	12	0.430	0.050	0.360	0.520	0.9
% Brain Weight	%	29	109.923	33.872	10.978	185.783	31.510	90.883	114.582	130.466	189.840	12	73.800	5.560	63.000	80.700	0.7
Liver/Gall Bladder																	
Absolute Weight	g	29	261.017	72.042	166.500	424.300	73.870	204.640	264.400	291.820	422.590	12	312.000	29.100	268.000	363.000	1.2
% Body Weight	%	29	2.061	0.265	1.773	2.899	1.475	1.901	1.954	2.185	2.611	12	2.530	0.310	2.090	3.130	1.2
% Brain Weight	%	29	452.211	130.930	48.633	752.892	199.190	390.083	447.526	517.345	708.239	12	433.000	42.600	365.000	513.000	1.0
Ovary																	
Absolute Weight	g	29	2.045	1.068	0.530	3.820	-2.016	0.980	1.846	2.977	5.973	12	NA	NA	NA	NA	NA
% Body Weight	%	29	0.022	0.035	0.007	0.199	-0.011	0.010	0.012	0.024	0.045	12	NA	NA	NA	NA	NA
% Brain Weight	%	29	3.640	1.837	1.217	6.891	-3.200	1.970	3.273	5.417	10.587	12	NA	NA	NA	NA	NA
Pituitary Gland																	
Absolute Weight	g	29	0.113	0.131	0.045	0.780	0.025	0.073	0.088	0.105	0.153	12	0.081	0.019	0.057	0.118	0.7
% Body Weight	%	29	0.001	0.001	0.000	0.006	0.000	0.001	0.001	0.001	0.001	12	0.001	0.000	0.000	0.001	1.1
% Brain Weight	%	29	0.161	0.045	0.077	0.279	0.043	0.131	0.151	0.190	0.279	12	0.110	0.028	0.082	0.170	0.7
Spleen																	
Absolute Weight	g	29	57.490	78.860	14.040	443.640	-34.980	25.080	34.860	65.120	125.180	12	48.600	17.200	22.200	72.500	0.8
% Body Weight	%	29	0.461	0.579	0.127	3.153	-0.297	0.178	0.237	0.494	0.969	12	0.400	0.150	0.170	0.620	0.9
% Brain Weight	%	29	80.023	50.707	25.741	207.617	-62.526	42.847	64.454	113.095	218.468	12	67.600	24.400	30.200	104.000	0.8
Thyroid (2)																	
Absolute Weight	g	29	1.420	0.799	0.420	2.796	-0.615	0.960	1.200	2.010	3.585	12	1.040	0.282	0.653	1.510	0.7
% Body Weight	%	29	0.009	0.003	0.007	0.015	0.003	0.008	0.009	0.010	0.015	12	0.008	0.002	0.006	0.012	0.9
% Brain Weight	%	29	2.489	1.257	0.990	4.961	-0.382	1.729	2.200	3.136	5.247	12	1.440	0.380	1.000	2.060	0.6
Thymus																	
Absolute Weight	g	29	16.587	16.649	4.580	79.790	-5.585	8.560	11.240	17.990	32.135	12	22.500	8.580	13.100	44.100	1.4
% Body Weight	%	29	0.130	0.122	0.032	0.606	-0.008	0.071	0.092	0.124	0.203	12	0.180	0.061	0.100	0.300	1.4
% Brain Weight	%	29	26.075	24.187	8.918	138.829	-9.943	13.747	20.749	29.540	53.230	12	31.300	12.300	18.300	62.200	1.2
Uterus																	
Absolute Weight	g	29	76.197	68.999	3.540	206.000	-185.400	7.800	63.000	136.600	329.800	12	NA	NA	NA	NA	NA
% Body Weight	%	29	0.528	0.468	0.039	1.564	-1.180	0.084	0.480	0.927	2.190	12	NA	NA	NA	NA	NA
% Brain Weight	%	29	124.279	116.629	7.273	358.448	-311.484	16.106	58.351	234.499	562.089	12	NA	NA	NA	NA	NA

Comparison of the Sinclair™ vs. Göttingen™ MPs (N=1,390; most 2-6 months of age; 2004-2015 US) background pathology reference data (incidence/severity) obtained from the Society of Toxicologic Pathology (STP) publication[1] revealed noteworthy similarities and differences:

- The most common organs with background findings
  - Göttingen™: **kidneys, lymph nodes, testes, and cardiovascular system, and integument lesions**
  - Downsized Sinclair™: **kidneys, spleen, lacrimal gland, and lung**
- The most common background lesions for all organ systems (most present only at low levels of severity in nature)
  - Göttingen™: **inflammatory cell infiltrates, foci of inflammation, and hemorrhage (minimal to mild)**
  - Downsized Sinclair™: **inflammation with multifocal lymphohistiocytic infiltration (minimal to mild)**
- The most common organs with increased severity scores
  - Göttingen™: **lymph nodes and male reproductive organs**
  - Downsized Sinclair™: **lymph node and lung**

In comparison, varying background pathology data of Göttingen™ MPs (N=835; 1995-2007 EU) reported in another STP publication included[2]:

- Spontaneous histopathological findings in the **gallbladder (cholecystitis and hypoplasia/aplasia), skeletal muscle (myositis/myofiber necrosis), and adipose tissue (serous atrophy) in the bone marrow,** with **low incidence** and in general **focal and mild**.

Downsized Sinclair™ MPs have a lower incidence of background pathology findings in all organ systems (at similar low severity), which are consistent with current INHAND criteria for swine. Sinclair™ MP, are readily available from the Sinclair Bioresources for use at Altasciences Columbia reducing variability in background pathology findings arising from different study site or geographic cohorts (United States vs. Europe). Going forward, Altasciences will continue to expand our minipig Historical Control Data (HCD) system.

Reference
1. Helke et al, 2016. Toxicologic Pathology 44(3) 325-337.
2. Jeppesen et al, 2015. Toxicologic Pathology, 43: 257-266.