

Toxicological Reference Data for 6- to 9-Month Male and Female Sinclair Nanopigs®

Kaileigh McGinley¹, Derek Brocksmitth², Scott E. Boley¹, Lisa Biegel¹, Guy Bouchard²
¹Altasciences Preclinical Columbia, LLC., Columbia, MO, USA; ²Sinclair Bio Resources, LLC., Auxvasse, MO, USA

Click here to listen to the recorded poster presentation

ABSTRACT

The use of miniature swine in safety assessment studies has grown in popularity over the past decade as the industry aims to minimize the use of canines and primates in support of the 3Rs initiatives. While there is considerable data for several breeds of miniature swine widely available to the research community, much of the data obtained from the Sinclair Nanopig® is proprietary to the organizations utilizing the model. The Sinclair Nanopig® is comparable to the well-established breeds, such as Yucatan and Göttingen minipigs®, in terms of physiology and metabolism, but is more similar in body weight to a beagle dog when maintained on a high-fiber, low-fat diet. This provides an advantage in using the Sinclair Nanopig® in that less test article is required for IND-enabling studies compared to the beagle dog or the Göttingen minipig®. The current poster presents reference data (body weight, hematology, serum chemistry, electrocardiography (ECG), ophthalmology, macroscopic tissue observations, and microscopic pathology) for the Sinclair Nanopig® at ages that correlate to the most common ages used in safety assessment studies. These data are critical for toxicologists and pharmacologists as a reference for normal variation among animal models used in nonclinical drug development. The goal of this poster is to expand upon the standard reference data for the Sinclair Nanopig® available to the entire research community.

INTRODUCTION

Miniature swine is a viable option as a non-rodent test system for studies to evaluate the safety and efficacy of new (bio)pharmaceuticals. It has long been recognized that pigs share many anatomical, physiological, and functional similarities with humans, and miniature swine are easily managed in a laboratory setting. There are several lineages of miniature swine that are purpose-bred for biomedical research. The Hormel Institute developed the Sinclair Miniature Swine in 1949. This lineage is also known as the “Minnesota Minipig” or “Hormel Minipig” and is one of the background lineages used to develop the Göttingen minipigs®. The Sinclair Nanopig® was created from the Sinclair miniature swine (Sinclair S-1) through a concerted effort that involved selective breeding for smaller size and controlled feeding of a high-fiber, low-fat minipig diet. This resulted in a miniature swine model comparable in body weight to a beagle dog, which mitigates previous challenges associated with utilizing swine models for standard pre-clinical studies, namely the amount of test articles needed for IND-enabling studies. Downsizing of the Sinclair S-1 did not involve any genetic manipulations to the lineage. Thus, the background data established in the Sinclair S-1 miniature swine remains highly relevant for the downsized Sinclair Nanopig®. However, as the request for the Sinclair Nanopig® in nonclinical drug development continues to increase, it remains ever important to continue to generate a robust database of background data in the Sinclair Nanopig® itself.

METHODS

Venous blood samples were obtained from both male and female Sinclair Nanopigs® from the following age groups: 2-3, 4-5, 6-7, 8-9, 10-11, and >12 months. Standard panels for hematology and serum chemistry, consistent with those performed for toxicology studies, were generated using GLP-validated equipment. Electrocardiography (ECG) and ophthalmology examinations were conducted for male and female Sinclair Nanopigs® at 3, 4-5, 6-7, and over 9 months of age. A board-certified veterinary ophthalmologist performed the ophthalmology examinations using a portable slit-lamp biomicroscope and a binocular indirect ophthalmoscope for the posterior segment. ECG leads I, II, III, aVR, aVF, and aVL were collected, and the following variables were derived: heart rate, PR-interval, QT-interval, QRS-interval, ST-interval, P-wave, and T-wave durations. The rhythm was also carefully reviewed for irregularities and arrhythmia. The pathology data were generated from a group of 25 young adult male Sinclair Nanopigs®.

Table 1. Hematology Data

Hematology Parameters	Male 2-3 Months (n=54)				Female 2-3 Months (n=46)				Male 4-5 Months (n=42)				Female 4-5 Months (n=40)				Male 6-7 Months (n=50)				Female 6-7 Months (n=50)				Male 8-9 Months (n=50)				Female 8-9 Months (n=51)			
	Mean	SD	95% Reference Range		Mean	SD	95% Reference Range		Mean	SD	95% Reference Range		Mean	SD	95% Reference Range		Mean	SD	95% Reference Range		Mean	SD	95% Reference Range		Mean	SD	95% Reference Range		Mean	SD	95% Reference Range	
WBC (10 ³ /µL)	14.5	2.9	9	19.8	14.2	2.4	10.2	18.3	13.7	2.7	9.5	19.9	13.77	2.5	9.3	18.8	14.3	4.1	6.2	22.4	11.4	2.5	6.3	16.4	13.9	3.0	7.9	20.0	11.6	2.5	6.6	16.5
RBC (10 ⁶ /µL)	7.7	0.8	6.2	9.1	7.9	0.7	6.5	9.2	7.7	0.9	6.7	9.8	7.57	0.5	6.8	8.5	7.5	0.6	6.3	8.7	7.7	0.6	6.5	8.9	7.8	0.9	6.0	9.5	7.4	0.5	6.5	8.4
Hgb (g/dL)	14.3	1.3	11.8	16.6	14.5	1	12.5	16	14.7	1.9	11.4	17.9	14.54	0.9	12.9	16.2	14.4	1.2	12.0	16.8	15.2	1.1	12.9	17.4	14.6	1.3	12.0	17.3	14.9	0.8	13.2	16.6
HCT (%)	43.3	3.8	36.2	50.7	43.3	3.2	37.1	48.9	43.2	4.4	35.1	50.3	41.25	3.2	35.8	47.7	43.2	3.6	36.1	50.4	45.5	2.7	40.1	50.9	45.1	4.3	36.5	53.8	45.0	2.7	39.7	50.3
MCV (fL)	56.4	3.4	49.9	62.1	55.5	1.9	52.3	59.3	56.7	3.1	51.5	62.3	55.01	3.7	49	61.2	57.6	1.8	54.1	61.2	59.6	3.2	53.3	66.0	58.4	3.3	51.9	65.0	60.7	3.7	53.4	68.1
MCH (pg)	18.5	1	16.4	20.1	18.5	0.8	16.8	19.9	19.3	1.4	16.8	22.1	19.2	1	17.6	20.8	19.2	0.7	17.8	20.6	19.9	1.0	18.0	21.8	19.0	1.1	16.8	21.1	20.0	0.8	18.4	21.7
MCHC (g/dL)	32.9	0.8	31.4	34.4	33.3	0.8	31.8	34.6	33.8	1.7	30.7	36.8	34.94	1.2	32.4	36.5	33.4	1.2	30.9	35.8	33.4	1.4	30.6	36.1	32.5	1.1	30.2	34.7	33.0	1.2	30.6	35.5
PLT (10 ³ /µL)	564.4	128.3	351.4	826.5	562.6	113.4	335.4	771.5	470.6	101.9	324.3	634.2	441.12	80.3	259.7	588.7	460.7	155.7	149.3	772.2	395.8	131.7	132.3	659.3	465.2	138.9	187.4	742.9	386.0	122.1	141.8	630.1
NEU (10 ³ /µL)	3.4	1.5	0.5	6.2	2.8	1.3	0.1	5.3	3.7	1.5	1.6	6.4	3.19	1	1.4	5.1	5.2	3.6	0.0	12.3	2.5	1.3	0.0	5.1	4.7	2.6	0.0	9.9	2.7	1.7	0.0	6.1
NEU (%)	24.2	9.8	3.9	42.7	21.3	6.8	10.9	36	28.6	10.4	11.9	47.8	22.68	6	11.2	36.3	32.9	15.9	1.0	64.7	21.9	8.6	4.8	39.0	33.8	13.5	6.8	60.7	23.3	9.5	4.4	42.3
LYM (10 ³ /µL)	9.4	2.5	4.1	13.9	10.1	2	7	13	8.8	1.7	5.7	11.3	9.85	2.3	5.8	14.4	7.7	2.4	2.8	12.6	8.1	1.9	4.3	11.8	7.9	2.0	3.9	11.8	7.4	1.8	3.9	11.0
LYM (%)	65.7	10.8	39.8	80.2	72.3	5.1	61.9	80.1	64.8	9.5	46.6	79.4	71.65	4.8	64.8	79.8	54.3	10.7	33.0	75.7	71.2	9.0	53.2	89.2	57.1	12.0	33.1	81.0	65.6	10.6	44.5	86.7
MONO (10 ³ /µL)	0.63	0.18	0.37	1.13	0.85	0.38	0.25	1.7	0.49	0.15	0.28	0.75	0.53	0.17	0.31	0.88	1.0	0.9	0.0	2.9	0.4	0.3	0.0	0.9	0.6	0.5	0.0	1.5	0.5	0.3	0.0	1.2
MONO (%)	4.69	1.53	2.42	7.7	5.45	1.99	2.8	10.09	3.68	1.19	1.69	6.3	3.9	0.98	2.59	5.75	7.5	8.4	0.0	24.4	3.7	2.3	0.0	8.4	4.1	2.8	0.0	9.8	4.5	2.1	0.4	8.6
EOS (10 ³ /µL)	0.19	0.13	0.03	0.45	0.15	0.07	0.04	0.3	0.14	0.07	0.05	0.29	0.18	0.07	0.09	0.3	0.2	0.1	0.0	0.4	0.2	0.1	0.0	0.5	0.2	0.1	0.0	0.4	0.3	0.2	0.0	0.7
EOS (%)	1.4	0.92	0.27	3.44	1.07	0.58	0.41	2.49	0.95	0.41	0.39	1.91	1.26	0.45	0.59	2.31	1.3	0.9	0.0	3.0	1.8	1.0	0.0	3.9	1.2	0.6	0.0	2.5	2.2	1.7	0.0	5.6
BAS (10 ³ /µL)	0.06	0.05	0.01	0.15	0.04	0.01	0.02	0.07	0.05	0.04	0.01	0.12	0.03	0.01	0.01	0.06	0.1	0.1	0.0	0.2	0.0	0.0	0.0	0.1	0.1	0.1	0.0	0.2	0.0	0.0	0.0	0.1
BAS (%)	0.38	0.27	0.1	1	0.28	0.08	0.2	0.4	0.35	0.22	0.1	0.7	0.22	0.07	0.1	0.31	0.4	0.2	0.0	0.9	0.4	0.2	0.0	0.7	0.5	0.4	0.0	1.3	0.4	0.1	0.1	0.6
LUC (10 ³ /µL)	0.16	0.09	0.03	0.34	0.13	0.09	0.03	0.37	0.11	0.08	0	0.29	0.13	0.03	0.09	0.17	0.5	1.0	0.0	2.4	0.1	0.1	0.0	0.4	0.3	1.2	0.0	2.7	0.4	0.9	0.0	2.2
LUC (%)	1.05	0.57	0.3	2.3	0.98	0.75	0.2	2.82	0.74	0.46	0	1.66	1.09	0.38	0.7	1.8	3.5	7.3	0.0	18.1	1.0	0.9	0.0	2.8	2.3	7.4	0.0	17.1	3.7	6.5	0.0	16.7
RET (10 ³ /L)	84.1	43.8	19	177	95.2	45.5	28.6	177.2	77.4	25.1	38.1	128.2	65.63	27.2	25.2	124.1	91.5	43.5	4.5	178.5	90.0	30.9	28.2	151.8	90.4	39.3	11.8	169.0	82.7	44.8	0.0	172.4
RET (%)	1.1	0.6	0.3	2.5	1.2	0.6	0.4	2.7	1	0.3	0.5	1.7	0.86	0.3	0.3	1.6	1.2	0.6	0.1	2.3	1.2	0.4	0.3	2.0	1.2	0.5	0.1	2.2	1.1	0.6	0.0	2.3

Table 2. Serum Chemistry Data

Serum Chemistry Parameters	Male 2-3 Months (n=54)				Female 2-3 Months (n=46)				Male 4-5 Months (n=42)				Female 4-5 Months (n=40)				Male 6-7 Months (n=50)				Female 6-7 Months (n=50)				Male 8-9 Months (n=51)				Female 8-9 Months (n=50)			
	Mean	SD	95% Reference Range		Mean	SD	95% Reference Range		Mean	SD	95% Reference Range		Mean	SD	95% Reference Range		Mean	SD	95% Reference Range		Mean	SD	95% Reference Range		Mean	SD	95% Reference Range		Mean	SD	95% Reference Range	
BUN (mg/dL)	15.2	5.3	6.1	22.9	18.2	3.2	13	25	13.9	3.9	8	22	14.8	2.7	9.9	19	13.6	3.3	6.9	20.2	14.3	3.4	7.5	21.1	13.7	4.9	3.9	23.4	16.1	2.4	11.3	20.9
CRE (mg/dL)	0.9	0.2	0.5	1.3	0.9	0.2	0.5	1.3	1.1	0.2	0.8	1.5	1.1	0.1	0.9	1.3	1.1	0.1	0.8	1.4	1.1	0.2	0.6	1.5	1.1	0.2	0.6	1.6	1.3	0.2	0.9	1.6
GLU (mg/dL)	97.8	16.5	71.4	137.6	88.3	10.2	70.5	108.8	84.5	12.5	65.9	108.5	76.9	15.6	56	102.2	102.0	29.0	43.9	160.1	78.5	16.3	46.0	111.1	96.0	23.5	49.1	142.9	78.7	16.4	45.8	111.6
Na (mEq/L)	144.3	2.7	139	149.1	143.6	4.3	136.1	151	143.4	3.1	138.9	150	144	1.9	141	147.1	143.7	9.7	124.2	163.2	138.6	13.8	111.0	166.2	141.2	5.4	130.3	152.0	144.1	3.1	138.0	150.2
K (mEq/L)	5.9	0.7	4.6	7.1	6.4	0.7	5	7.8	5.8	0.8	4.3	7.1	6	0.8	4.8	7.3	5.6	0.8	4.1	7.2	5.7	0.7	4.4	7.1	5.5	1.0	3.6	7.5	6.1	0.6	4.8	7.4
Cl (mEq/L)	102.3	1.8	99	106	102.9	2.7	98	107.9	101.1	2.3	96	104	103.5	2.3	100	107	101.4	6.5	88.4	114.5	99.4	8.1	83.1	115.6	99.6	4.4	90.8	108.5	101.9	2.1	97.6	108.2
ALP (U/L)	96.4	22.6	63.1	135.8	85.3	19.5	55.1	121.6	68.3	18.9	39	106.2	66.9	16.5	32.9	98.2	99.2	37.3	24.6	173.9	65.3	18.4	28.5	102.0	90.6	60.7	0.0	212.1	56.8	15.9	25.0	88.6
ALT (U/L)	39.4	6.4	28.9	55.2	41.7	8.9	25.1	59	37.8	7.8	25.6	50.4	42.8	5.6	34.9	53.2	40.1	10.9	18.4	61.9	41.9	10.3	21.4	62.5	45.8	15.8	14.2	77.5	45.2	9.8	25.6	64.8
AST (U/L)	32.1	7.7	21	47	30.9	8.7	19	51.8	27.7	7.5	18	43.2	28.1	5.7	17.6	38	54.4	57.6	0.0	169.6	29.9	13.8	2.4	57.4	45.0	42.7	0.0	130.5	35.7	32.0	0.0	99.7
TBIL (mg/dL)	0.15	0.06	0.1	0.29	0.13	0.05	0.1	0.2	0.13	0.05	0.1	0.2	0.1	0	0.1	0.1	0.2	0.1	0.0	0.3	0.1	0.0	0.0	0.2	0.2	0.1	0.1	0.3	0.2	0.1	0.0	0.0
DBIL (mg/dL)	0.03	0.02	0	0.05	0.03	0.01	0.01	0.04	0.03	0.01	0.02	0.05	0.03	0.04	0	0.1	0.1	0.1	0.0	0.3	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0
Cr (U/L)	370	193.7	113	718	390.8	213.6	165	828.8	454.7	274.8	175.3	1246.1	283.8	116	156	541.3	486.0	550.1	0	1568.2	505.1	733.7	0	1972.6	499.3	617.7	0	1734.7	612.3	727.8	0	2067.9
GGT (U/L)	44.3	9	27.2	58.9	46.1	11.5	26.4	70.8	44.5	9.5	29	63.1	48.3	10.5	29.9	66.3	192.9	347.8	0	888.5	40.1	13.5	31.1	67.2	131.1	178.8	0	488.6	49.4	17.4	14.6	84.2
TP (g/dL)	6.2	0.6	5.1	7.1	6.1	0.4	5.4	6.8	6.6	0.4	5.9	7.3	6.2	0.2	5.8	6.7	6.6	0.5	5.5	7.7	6.2	0.8	4.6	7.9	7.0	0.6	5.7	8.2	6.8	0.5	5.8	7.7
ALB (g/dL)	4.1	0.4	3.1	4.8	3.9	0.3	3.5	4.4	4.2	0.3	3.8	4.7	4	0.2	3.5	4.3	4.0	0.5	3.0	5.1	3.7	0.9	1.9	5.4	5.1	0.8	4.0	22.0	3.7	0.8	2.1	5.3
GLOB (g/dL)	2.2	0.4	1.5	3	2.2	0.3	1.7	2.8	2.6	0.4	1.8	3.2	2.3	0.3	1.8	2.8	2.6	0.6	1.4	3.7	2.6	0.5	1.7	3.5	3.1	0.7	1.6	4.5	14.0	61.4	0.0	136.8
A/G ratio	1.8	0.2	1.2	2.7	1.8	0.4	1.4	2.1	1.7	0.4	1.4	2.4	1.8	0.3	1.2	2.2	1.7	0.5	0.7	2.6	1.5	0.5	0.7	2.6	1.5	0.5	0.7	2.5	2.3	1.9	0.4	1.9
Ca (mg/dL)	1044.3	60.5	878	1155.5	930.2	21.1	591	1423.3	1013	286	586.8	1511.7	977.2	164.4	843.8	1349.3	1075.1	53.3	24.7	181.9	293.7	32.8	15.8	255.5	959.2	289.2	42.2	1417.6	97.1	267	487.3	1458.2
Ca (mg/dL)	11.3	0.6	10.5	12.5	11.3	0.5	10.3	12.3	11.1	0.5	10.4	12.3	10.8	0.5	10.1	11.7	11.8	0.8	9.6	12.9	10.5	1.2	7.2	13.9	11.6	0.6	10.0	12.4	11.6	0.8	9.8	12.4
CHOL (mg/dL)	8.1	0.8	6.3	9.3	8.1	0.6	7	9.3	8.1	0.9	6.8	9.7	7.5	0.5	6.5	8.3	7.8	0.9	6.0	9.7	7.1	1.0	5.1	9.0	7.4	0.9	5.7	9.2	7.3	0.4	6.4	8.1
PHOS (mg/dL)	94.9	24.8	51.1	129.7	105.5	29.8	62.3	160.9	103.2	19.8	67	138.2	92.4	12.9	68.5	113.2	94.9	24.7	45.4	144.3	100.2	24.8	50.6	149.9	82.3	14.4	53.5	111.1	127.6	28.2	71.2	164.0
LDH (mg/dL)	43.8	15	23.7	79.4	42.5	15.8	22.1	81.8	34.1	11.7	18	59.2	33.2	9.3	18.9	51.4	43.3	17.9	7.5	79.1	43.3	17.8	7.7	78.9	17.8	11.9	63.1	46.7	20.1	6.5	86.9	
TRIG (U/L)	513.5	126.7	287.7	753	526.6	63.8	427	666	397.4	68.2	263	489.3	497.2	66.2	319.1	636.6	400.4	117.9	164.6	636.1	424.4	99.2	226.1	622.7	454.2	252.1	0	958.3	496.2	286.3	0	1068.8