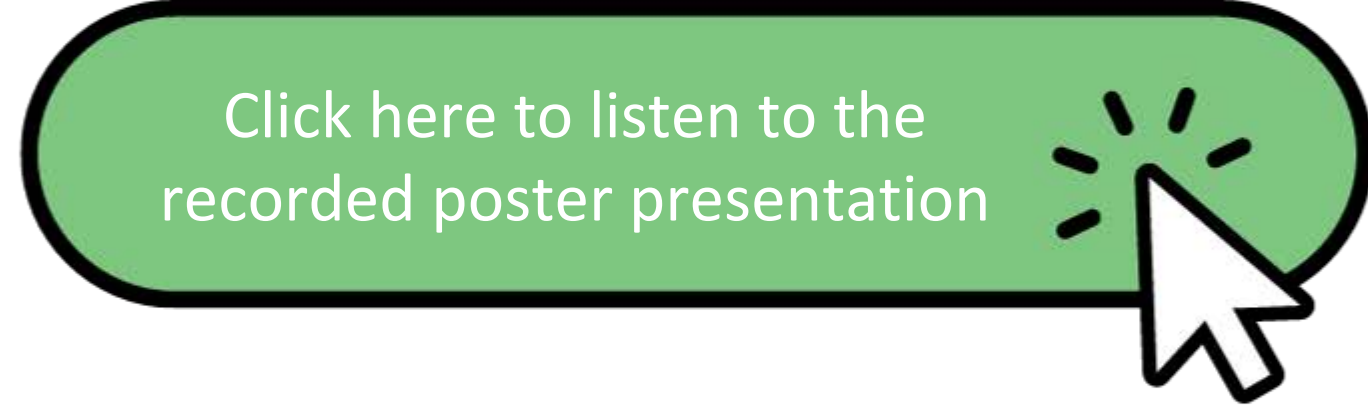


# Comparison of Cardiovascular and Respiratory Parameters in Three Strains of Research Pigs; Sinclair Nanopig™, Göttingen Minipig®, and Yucatan™ Miniature Swine

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## ABSTRACT

Minipigs are growing in popularity for nonclinical safety assessment studies, including safety pharmacology. The Sinclair Nanopig™ is a redefined, smaller version of the original Sinclair minipig. This strain was developed by selective breeding and diet management. Sexual maturity is reached at approximately 4.5 months (6 to 8 kg). The cardiovascular and respiratory parameters from Sinclair Nanopigs™ were compared to Göttingen® and Yucatan™ minipigs (total of 62 pigs). The average weight of all pigs was 19±6 kg (10 to 28 kg), with an average age of 6.5 mon. Minipigs were instrumented with DSI L11R implants placed preperitoneal, using the jugular vein for electrocardiographic measurements and the femoral artery for blood pressure measurements. Ponemah® software was used for data capture and analysis. Average baseline values obtained from 13 Sinclair Nanopigs™ were SBP=121±9 mmHg, DBP=87±15 mmHg, HR=88±18 bpm, PR=100±43 ms, QRS=60±20 ms, QT=296±27 ms, QTcH=282±13 ms, BT=37.7±0.7 °C, respiratory rate=23±4 Rf, tidal volume=185±90 ml, and minute volume=4084±1854 ml/min (mean±SD). On average, values were within 11% of the average values obtained from Göttingen® and Yucatan™ minipigs except for blood pressure which was approximately 22% lower than the other strains. To confirm the Sinclair Nanopig™ sensitivity to a cardiovascular compound, dofetilide was administered to a group of five pigs. Dofetilide produced the expected prolongation of QTcH; 56 ms at 0.1 mg/kg and 77 ms at 0.3 mg/kg with an MDD=11.5 ms. In conclusion, the cardiovascular and respiratory parameters from the redefined Sinclair Nanopig™ were comparable to those of the Göttingen® and Yucatan™ minipigs.

## METHODS

Minipigs were instrumented with Data Sciences International L11R implants with the body of the implants placed preperitoneally on the abdominal wall to lessen rejection. A solid tip ECG lead was placed in the jugular vein and the femoral artery was used for the blood pressure catheter. Impedance leads provided respiratory values. Data Sciences International Ponemah® software was used for data acquisition and data analysis.

Table 1. Telemetry value comparisons

Parameter	Mean ± SD		
	Sinclair Nanopig™	Göttingen®	Yucatan™
Systolic Blood Pressure (mmHg)	121 ± 9	149 ± 10	141 ± 25
Diastolic Blood Pressure (mmHg)	87 ± 15	105 ± 11	97 ± 16
Mean Arterial Pressure (mmHg)	103 ± 12	127 ± 11	117 ± 25
Pulse Pressure (mmHg)	35 ± 9	44 ± 4	47 ± 10
Heart Rate (bpm)	88 ± 18	85 ± 6	83 ± 15
PR Interval (ms)	100 ± 43	117 ± 15	110 ± 15
QRS Duration (ms)	60 ± 20	52 ± 4	49 ± 7
QT Interval (ms)	296 ± 27	309 ± 15	315 ± 30
QTcH (ms)	282 ± 14	314 ± 11	301 ± 41
Body Temperature (°C)	37.7 ± 0.7	37.8 ± 0.4	38.2 ± 0.4
Respiratory Rate (Rf)	23 ± 4	22 ± 5	21 ± 9
Tidal Volume (mL)	185 ± 90	223 ± 51	226 ± 96
Minute Volume (mL/min)	4084 ± 1854	4558 ± 90	4158 ± 1361

Table 2. Effects of Dofetilide (60 min post-dose) in Sinclair Nanopigs™

Parameter	Mean ± SD		
	Baseline	0.1 mg/kg PO	0.3 mg/kg PO
Systolic Blood Pressure (mmHg)	124 ± 9	125 ± 10	128 ± 12
Diastolic Blood Pressure (mmHg)	85 ± 15	88 ± 20	91 ± 21
Mean Arterial Pressure (mmHg)	103 ± 14	106 ± 16	109 ± 17
Pulse Pressure (mmHg)	39 ± 10	36 ± 12	37 ± 13
Heart Rate (bpm)	81 ± 7	83 ± 10	85 ± 9
PR Interval (ms)	125 ± 20	125 ± 22	123 ± 19
QRS Duration (ms)	46 ± 4	46 ± 3	46 ± 4
QT Interval (ms)	308 ± 7	369 ± 18	396 ± 15
QTcH (ms)	282 ± 10	338 ± 20	359 ± 22
Body Temperature (°C)	37.4 ± 0.4	37.4 ± 0.7	37.3 ± 0.9
Respiratory Rate (Rf)	25 ± 3	24 ± 0	24 ± 5
Tidal Volume (mL)	245 ± 41	243 ± 80	242 ± 59
Minute Volume (mL/min)	5929 ± 629	5845 ± 1870	5933 ± 2150

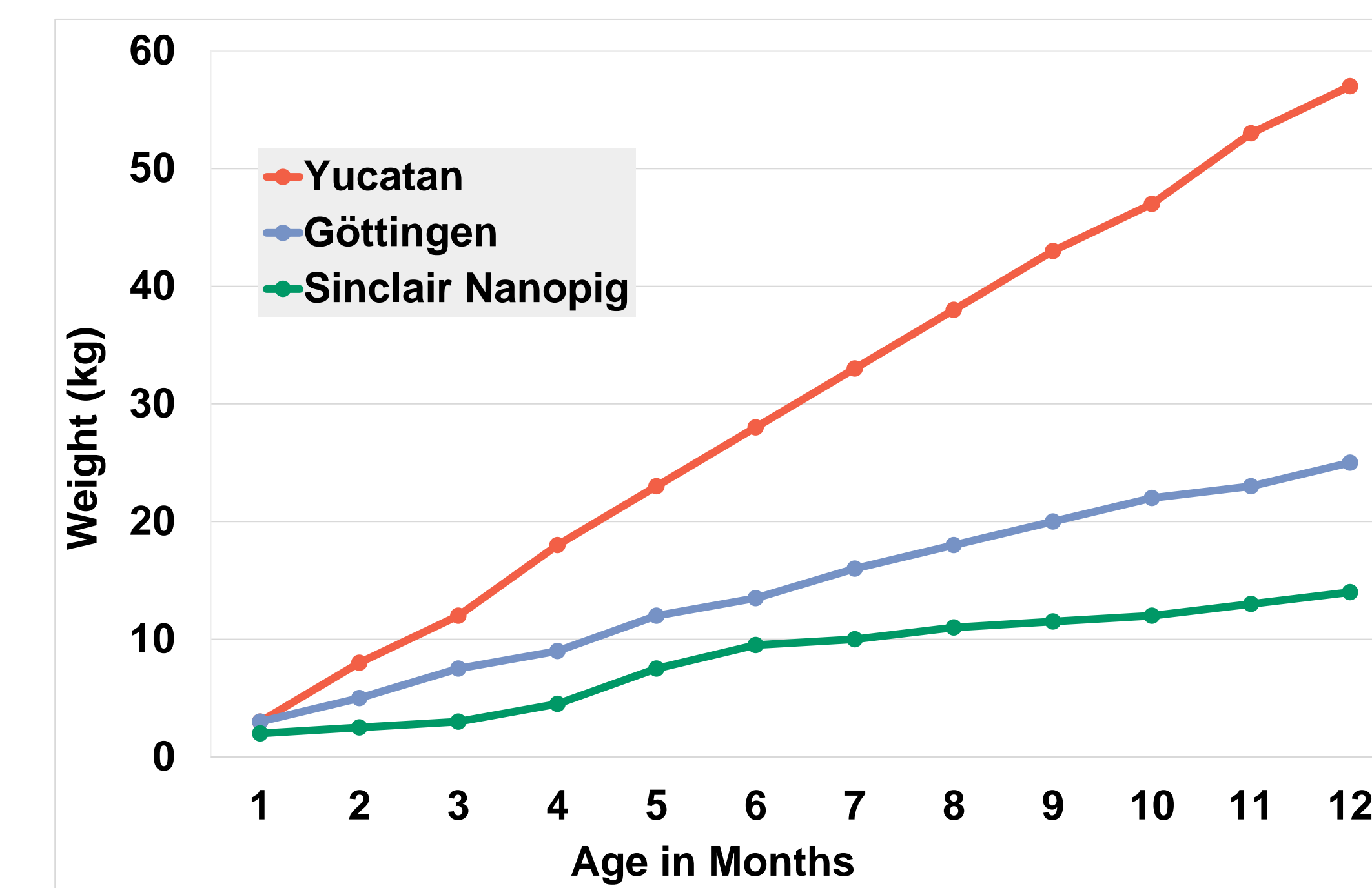


Figure 2. Average weight by age (kg)

## RESULTS

All values from the Sinclair Nanopigs™ were within 11% of the average values obtained from the Göttingen® and Yucatan™ minipigs except for blood pressure which was approximately 22% lower than the other two strains (Table 1).

Dofetilide produced the expected prolongation of the QT interval; 56 ms at 0.1 mg/kg dofetilide and 77 ms at 0.3 mg/kg dofetilide with a minimum detectable difference (MDD) of 11.5 ms, 4.1% change from vehicle control (Table 2, Figure 1).

## CONCLUSION

- The cardiovascular and respiratory parameters from the redefined and smaller Sinclair Nanopig™ were comparable to those of the Göttingen® and Yucatan™ miniature swine.
- At 6-8 kg at maturity and a slower growth rate, implant longevity is improved, thereby allowing longer use and lowering test article requirements.
- The Sinclair Nanopig™ offers a good research model for safety pharmacology assessments.

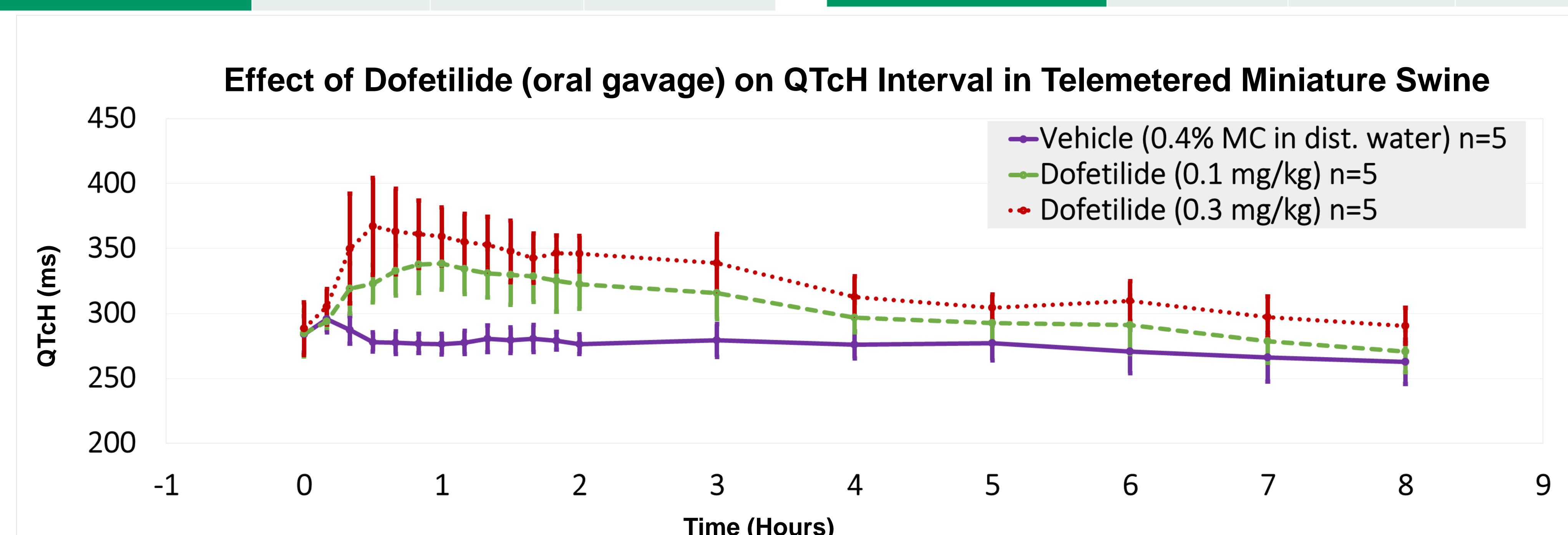


Figure 1. Study 757-2101