

REFERENCE DATA OF CLINICAL CHEMISTRY AND HEMATOLOGY IN JUVENILE GÖTTINGEN MINIPIGS

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Introduction: Juvenile animal toxicity studies are conducted prior to clinical trials in children. Generally, the rat is the preferred species for juvenile safety testing, but for some drugs, rodent species may not be an appropriate model and larger species are used. Moreover, the regulatory authority may request juvenile studies in both rodent and non-rodent species. The large litter size (5-8 piglets), short pre-weaning period (4 weeks), and early onset of sexual maturity (within 6 months) confer a considerable advantage of the Minipig in juvenile toxicity testing. Moreover, Minipigs are ideal for cross-fostering and show less interference between off-spring and mother than i.e. the dog. Reference data on clinical chemistry and hematology parameters of juvenile animals are important for the evaluation of findings in juvenile toxicity studies, and in present investigation these parameters were analyzed in juvenile Göttingen Minipigs.



2-2.5 mL blood was collected with the Minipig in dorsal recumbency.

Results: The results on clinical chemistry and hematology in piglets of different ages are reported in table 1-3. Reference values on clinical chemistry and hematology are also available from www.minipigs.dk

Materials and Methods: Blood samples were obtained from 7 male and 7 female Göttingen Minipigs before weaning at 2 and 4 weeks of age and after weaning at 5 weeks of age. The Minipigs were born and housed at Ellegaard Göttingen Minipigs A/S, Denmark. Iron is routinely administered within 48 hours of birth to prevent anemia in Minipigs, and in this examination, blood samples were obtained from Minipigs aged 2 days and 1 week to which 1) no iron was administered 2) an iron supplement was given less than 24 hours after birth or 3) iron was administered immediately after the first blood sampling at PND 2. Twenty-four markers of clinical serum chemistry and 20 markers of hematology were analyzed.

Table 1: Clinical chemistry parameters in piglets of different ages.

Abbrv.	Unit	Male 2 days	Female 2 days	Male 1 week	Female 1 week	Male 2 weeks	Female 2 weeks	Male 4 weeks	Female 4 weeks	Male 5 weeks	Female 5 weeks
ALAT	µKat/L	ND	ND	0.34 (0.03)	0.39 (0.08)	0.44 (0.16)	0.42 (0.11)	0.33 (0.10)	0.40 (0.02)	0.57 (0.15)	0.60 (0.10)
ASAT	µKat/L	0.97 (0.08)	0.99 (0)	0.46 (0.09)	0.43 (0.01)	0.75 (0.33)	0.88 (0.44)	0.51 (0.20)	0.46 (0.06)	0.56 (0.22)	0.61 (0.32)
ALKPH	µKat/L	39.68 (13.3)	28.62 (8.66)	17.59 (4.24)	17.97 (3.88)	18.79 (3.24)	18.49 (10.6)	10.61 (2.47)	7.39 (1.11)	3.43 (0.93)	2.77 (0.33)
GGT	µKat/L	2.09 (0.78)	2.28 (0.34)	1.03 (0.25)	1.01 (0.19)	1.40 (0.24)	1.33 (0.34)	1.22 (0.18)	1.24 (0.18)	1.82 (0.64)	1.67 (0.75)
BILI	mmol/L	3.55 (1.37)	2.72 (0.65)	1.71 (0.45)	1.57 (0.65)	1.75 (0.28)	1.62 (0.50)	1.56 (0.53)	1.35 (0.31)	2.61 (1.35)	4.67 (2.19)
CHOL	mmol/L	1.90 (0.25)	2.52 (0.86)	3.15 (0.69)	3.54 (0.61)	3.05 (0.47)	3.64 (0.90)	4.78 (1.26)	6.80 (2.33)	3.94 (1.85)	3.74 (1.44)
TRIG	mmol/L	4.37 (2.62)	3.70 (1.67)	1.91 (1.05)	1.95 (0.46)	1.39 (0.24)	1.33 (0.62)	1.34 (0.65)	1.63 (0.88)	0.74 (0.24)	1.22 (0.81)
UREA	mmol/L	6.35 (1.45)	6.20 (1.90)	4.75 (2.05)	3.76 (1.27)	3.35 (0.92)	3.76 (1.48)	2.43 (0.75)	1.93 (0.50)	4.39 (2.86)	4.61 (1.89)
CREAT	µmol/L	36.43 (2.30)	38 (5.80)	46.0 (3.97)	48.14 (6.72)	47.29 (6.37)	45.71 (7.54)	43.71 (8.79)	43.14 (4.41)	60.43 (8.75)	57.29 (7.61)
GLUC	mmol/L	6.92 (1.06)	7.02 (1.24)	7.49 (1.02)	7.84 (1.02)	7.00 (0.93)	7.01 (0.53)	7.67 (1.19)	7.02 (0.66)	4.99 (0.63)	4.83 (1.34)
Ca	mmol/L	136.6 (2.29)	140.1 (1.57)	3.06 (0.18)	2.93 (0.21)	2.95 (0.15)	2.94 (0.22)	139.8 (2.18)	141.2 (1.96)	2.59 (0.13)	143.9 (3.21)
Mg	mmol/L	4.93 (0.69)	4.41 (0.81)	1.14 (0.13)	1.04 (0.12)	1.20 (0.14)	1.18 (0.19)	4.64 (0.46)	4.94 (0.53)	0.97 (0.03)	6.38 (1.22)
P	mmol/L	3.40 (0.31)	3.56 (0.49)	3.14 (0.22)	2.86 (0.31)	3.50 (0.45)	3.45 (0.40)	2.84 (0.10)	2.96 (0.05)	2.73 (0.35)	2.56 (0.15)
Na	mmol/L	0.79 (0.09)	0.80 (0.05)	140.1 (1.92)	139.5 (1.23)	140.8 (2.3)	143.3 (2.30)	1.03 (0.03)	1.00 (0.07)	144.2 (1.61)	1.15 (0.17)
K	mmol/L	1.78 (0.39)	1.77 (0.35)	5.23 (0.46)	5.10 (0.53)	5.37 (1.11)	6.49 (1.55)	3.22 (0.21)	3.23 (0.07)	5.31 (0.31)	2.37 (0.22)
Cl	mmol/L	90.31 (1.85)	93.01 (3.10)	94.98 (1.60)	96.34 (1.57)	95.01 (1.33)	96.67 (2.96)	95.79 (1.64)	97.67 (1.70)	100.1 (1.73)	99.34 (2.62)
PROT	g/L	58.59 (14.2)	54.33 (9.58)	49.63 (4.93)	47.26 (4.20)	51.39 (2.12)	52.64 (8.06)	54.63 (2.71)	54.67 (3.14)	59.53 (3.07)	59.00 (4.78)
ALB	g/L	17.62 (3.36)	18.48 (2.64)	31.31 (2.93)	30.67 (3.43)	36.14 (2.70)	37.54 (4.30)	43.79 (1.21)	43.17 (1.68)	47.46 (2.62)	45.01 (2.09)
GLO	g/L	0.41 (0.09)	0.51 (0.07)	18.32 (4.94)	16.59 (1.82)	15.24 (3.60)	15.1 (5.42)	4.17 (0.87)	3.90 (0.83)	12.07 (2.89)	3.37 (0.80)
AL/G	ratio	44.76 (13.4)	36.96 (8.05)	1.83 (0.58)	1.86 (0.27)	2.57 (1.03)	2.76 (1.00)	10.84 (2.05)	11.5 (2.62)	4.27 (1.66)	13.99 (3.30)
AMYL	µKat/L	9.61 (13.95)	4.75 (2.55)	36.31 (8.77)	37.69 (11.3)	37.12 (12.0)	38.64 (12.7)	13.76 (10.5)	13.06 (6.45)	32.69 (5.13)	8.21 (8.39)
CK	µKat/L	10.27 (1.88)	8.57 (0.84)	5.28 (4.62)	4.81 (1.05)	16.22 (11.9)	14.29 (11.5)	11.22 (0.79)	11.73 (0.95)	11.16 (8.56)	12.14 (2.41)
LDH	µKat/L	ND	ND	8.74 (2.03)	7.78 (0.58)	11.86 (3.21)	10.21 (1.95)	ND	ND	9.6 (1.06)	0.09 (0.06)
SDH	µKat/L	31.15 (4.49)	28.89 (7.11)	ND	ND	ND	ND	49.32 (4.20)	45.83 (3.24)	0.08 (0.02)	25.34 (3.62)

(Standard deviation). ND = not determined.

Table 2: Hematology parameters for piglets on different iron dosage regimen.

Abbrv.	Unit	2 days, Iron 24 h PP.	2 days, iron 48 h PP	2 days, iron 9 days PP	1 week, iron 24 h PP	1 week, iron 48 h PP	1 week, iron 9 days PP
HB	mmol/L	6.00 (1.16)	7.09 (0.95)	6.73 (0.76)	4.74 (0.58)	6.13 (0.62)	4.72 (0.40)
RBC	10 ¹² /L	4.67 (0.91)	5.47 (0.76)	5.44 (0.63)	3.76 (0.60)	4.64 (0.54)	4.14 (0.43)
HT	L/L	0.28 (0.06)	0.33 (0.04)	0.32 (0.03)	0.25 (0.03)	0.30 (0.03)	0.24 (0.02)
RETIC	% (UD)	7.53 (1.52)	6.30 (1.15)	6.66 (0.96)	ND	ND	ND
RETIC	10 ¹² /L	0.35 (0.10)	0.34 (0.03)	0.36 (0.05)	0.08 (0.04)	0.08 (0.04)	0.08 (0.05)
MCV	fL	59.85 (3.93)	61.1 (3.00)	59.11 (2.62)	19.2 (0.28)	20.17 (0.26)	19.68 (0.22)
MCH	fmol	1.29 (0.10)	1.30 (0.05)	1.24 (0.07)	66.33 (5.13)	65.6 (4.17)	58.00 (2.58)
MCHC	mmol/L	21.58 (1.15)	21.2 (0.39)	20.89 (0.36)	1.27 (0.09)	1.33 (0.09)	1.14 (0.07)
WBC	10 ⁹ /L	11.93 (2.74)	9.86 (2.77)	12.78 (2.60)	20.93 (9.35)	19.21 (4.42)	20.6 (8.87)
NEUTRO	% (UD)	50.46 (10.2)	51.5 (6.10)	48.78 (9.59)	1.00 (0)	0.9 (0.32)	1.25 (0.50)
NEUTRO	10 ⁹ /L	6.08 (2.15)	5.03 (1.45)	6.18 (1.47)	15.03 (7.73)	10.66 (2.91)	12.98 (5.39)
LYMPHO	% (UD)	46.15 (10.9)	45.5 (5.48)	48.11 (8.68)	70.5 (6.35)	55.8 (8.94)	63.5 (5.74)
LYMPHO	10 ⁹ /L	5.65 (1.71)	4.53 (1.41)	6.21 (1.94)	ND	ND	ND
EOS	% (UD)	2.00 (1.68)	2.19 (1.01)	2.22 (2.05)	0.17 (0.41)	0.30 (0.48)	ND
EOS	10 ⁹ /L	0.26 (0.26)	0.20 (0.13)	0.29 (0.27)	0.28 (0.12)	0.62 (0.53)	0.38 (0.36)
BASO	% (UD)	0.23 (0.44)	0.10 (0.32)	0.22 (0.44)	1.67 (0.82)	3.40 (2.32)	1.75 (0.96)
BASO	10 ⁹ /L	0.02 (0.04)	0.02 (0.04)	0.03 (0.05)	5.40 (2.08)	7.72 (2.62)	6.90 (2.97)
MONO	% (UD)	1.23 (0.44)	0.80 (0.42)	0.78 (0.44)	26.83 (6.05)	39.9 (7.95)	33.25 (4.57)
MONO	10 ⁹ /L	0.15 (0.08)	0.08 (0.06)	0.11 (0.08)	0.17 (0.08)	0.15 (0.08)	0.30 (0.22)
THROMB	10 ⁹ /L	369.7 (71.1)	203.0 (94.4)	525.7 (86.0)	30.23 (3.21)	26.43 (4.08)	29.6 (2.49)

Table 3: Hematology parameters for piglets aged 2, 4 and 5 weeks.

Abbrv.	Unit	Male 2 weeks	Female 2 weeks	Male 4 weeks	Female 4 weeks	Male 5 weeks	Female 5 weeks
HB	mmol/L	6.50 (0.79)	6.42 (1.10)	5.59 (1.17)	7.10 (0.86)	6.13 (1.45)	6.87 (0.81)
RBC	10 ¹² /L	4.86 (0.51)	5.23 (0.64)	5.69 (0.62)	6.44 (0.55)	6.74 (0.99)	7.25 (0.60)
HT	mmol/L	0.33 (0.04)	0.32 (0.06)	0.28 (0.05)	0.34 (0.04)	0.30 (0.07)	0.33 (0.03)
RETIC	% (UD)	ND	ND	6.21 (1.20)	4.64 (1.20)	ND	2.58 (1.02)
RETIC	10 ¹² /L	0.06 (0.05)	0.07 (0.05)	0.35 (0.05)	0.30 (0.08)	0.03 (0.05)	0.18 (0.07)
MCV	fL	19.99 (0.34)	19.87 (0.31)	48.00 (5.00)	52.71 (4.54)	20.23 (0.66)	45.57 (1.81)
MCH	fmol	67.00 (4.20)	62.29 (9.89)	0.97 (0.12)	1.10 (0.11)	44.50 (4.14)	0.95 (0.07)
MCHC	mmol/L	1.34 (0.08)	1.24 (0.19)	20.20 (0.61)	20.93 (0.47)	0.90 (0.11)	20.70 (0.81)
WBC	10 ⁹ /L	17.37 (6.53)	16.65 (4.15)	16.39 (5.24)	17.31 (4.34)	17.02 (5.89)	16.06 (5.35)
NEUTRO	% (UD)	0.71 (0.49)	1.00 (0.00)	23.57 (4.72)	26.43 (7.83)	1.33 (0.52)	36.00 (12.2)
NEUTRO	10 ⁹ /L	11.70 (4.02)	10.02 (3.26)	3.74 (1.07)	4.31 (0.65)	10.82 (3.03)	6.20 (4.55)
LYMPHO	% (UD)	69.29 (8.54)	61.71 (11.2)	74.43 (5.00)	70.71 (7.87)	64.50 (5.54)	60.00 (11.9)
LYMPHO	10 ⁹ /L	ND	ND	12.26 (4.35)	12.49 (4.63)	606.7 (105)	9.24 (1.75)
EOS	% (UD)	0.29 (0.49)	0.43 (0.79)	1.57 (0.79)	2.43 (1.62)	0.17 (0.41)	2.86 (1.07)
EOS	10 ⁹ /L	0.34 (0.21)	0.45 (0.37)	0.27 (0.14)	0.40 (0.22)	0.22 (0.15)	0.41 (0.12)
BASO	% (UD)	1.71 (1.11)	2.86 (1.95)	ND	0.14 (0.38)	1.33 (0.52)	0.14 (0.38)
BASO	10 ⁹ /L	5.21 (2.54)	5.98 (2.88)	ND	0.04 (0.08)	5.80 (2.73)	0.04 (0.05)
MONO	% (UD)	28.00 (7.70)	34.43 (10.7)	0.71 (0.49)	0.29 (0.49)	33.00 (5.59)	1.00 (0.58)
MONO	10 ⁹ /L	0.10 (0.06)	0.13 (0.05)	0.11 (0.04)	0.07 (0.08)	0.18 (0.16)	0.17 (0.05)
THROMB	10 ⁹ /L	25.53 (2.60)	26.36 (3.95)	507.8 (156)	493.0 (96.1)	32.22 (4.94)	323.6 (134)