### Table 2 – Effects of maternal GH or IGF treatment on placental growth and function

<table>
<thead>
<tr>
<th>Species and strain/breed</th>
<th>Hormone administered</th>
<th>Maternal nutrition</th>
<th>Placental outcomes</th>
<th>Weight/size</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Type</td>
<td>Dose</td>
<td>Route</td>
<td>Frequency</td>
<td>Timing in pregnancy</td>
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<td></td>
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<td>Type</td>
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<td>Early</td>
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</tbody>
</table>

**GH administration – rat (term ~GD21-23)**

<table>
<thead>
<tr>
<th></th>
<th>Purified</th>
<th>1 mg/d</th>
<th>s.c.</th>
<th>Twice daily</th>
<th>GD10 to GD19</th>
<th>Purina rat chow, 60% of ad libitum controls</th>
<th>Plac Wt ↓22% at GD20</th>
<th>NR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat, Fisher 344</td>
<td>oGH</td>
<td>(maternal weight NR)</td>
<td>injection</td>
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<tr>
<td>(Chiang and Nicoll 1991)</td>
<td>(NIDDK-15)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Purified</th>
<th>5 mg/d</th>
<th>s.c.</th>
<th>Twice daily</th>
<th>GD10 to GD19</th>
<th>Purina rat chow, 60% of ad libitum controls</th>
<th>Plac Wt ↓75% at GD20 (all pups resorbing)</th>
<th>NR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat, Fisher 344</td>
<td>bGH</td>
<td>(maternal weight NR)</td>
<td>injection</td>
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<tr>
<td>(Chiang and Nicoll 1991)</td>
<td>(USDA-B-1)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>rh GH</th>
<th>2.4 mg/kg daily</th>
<th>s.c.</th>
<th>Continuous</th>
<th>GD11 to GD21</th>
<th>Standard rat chow ad libitum</th>
<th>Plac Wt at GD20 =</th>
<th>Fetal:placental weight =</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat, Sprague-Dawley (Gargosky, et al. 1991)</td>
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<tr>
<td>Species, Strain</td>
<td>Treatment</td>
<td>Dose</td>
<td>Route</td>
<td>Frequency</td>
<td>Duration</td>
<td>Weight at GD20</td>
<td>Note</td>
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<tr>
<td>Rat, Wistar</td>
<td>rh GH</td>
<td>2.0 mg/kg daily</td>
<td>s.c. injection</td>
<td>Once daily</td>
<td>GD1 until delivery</td>
<td>NR</td>
<td>Plac Wt at GD20 = NR</td>
<td></td>
</tr>
<tr>
<td>Rat, Sprague-Dawley</td>
<td>Purified pGH</td>
<td>1.0 IU/kg daily</td>
<td>s.c. injection</td>
<td>Twice daily</td>
<td>GD1 until term</td>
<td>ad libitum</td>
<td>Plac Wt at GD21 = NR</td>
<td></td>
</tr>
<tr>
<td>Rat, Sprague-Dawley</td>
<td>Purified pGH</td>
<td>5.0 IU/kg daily</td>
<td>s.c. injection</td>
<td>Twice daily</td>
<td>GD1 until term</td>
<td>ad libitum</td>
<td>Plac Wt at GD21 = NR</td>
<td></td>
</tr>
<tr>
<td>Rat (Woodall, et al. 1999)</td>
<td>rb GH</td>
<td>6 mg/kg daily</td>
<td>s.c. injection</td>
<td>3 per day</td>
<td>GD10 to GD20</td>
<td>ad libitum or 30% ad libitum rat chow</td>
<td>Plac Wt at GD20 = in both maternal nutrition groups</td>
<td></td>
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</tbody>
</table>

**GH administration – mouse (term ~GD19-GD21)**

<table>
<thead>
<tr>
<th>Species, Strain</th>
<th>Treatment</th>
<th>Dose</th>
<th>Route</th>
<th>Frequency</th>
<th>Duration</th>
<th>Weight at GD20</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mouse, C57BL/6J (B6)</td>
<td>rh placental</td>
<td>0.25 mg/kg</td>
<td>s.c. infusion</td>
<td>Continuous</td>
<td>GD12.5 to</td>
<td>ad libitum</td>
<td>Plac Wt at GD18.5 = Fetal:placental weight =</td>
</tr>
<tr>
<td>Study</td>
<td>Treatment</td>
<td>Daily</td>
<td>Route</td>
<td>Timing</td>
<td>Duration</td>
<td>Endpoint</td>
<td>Effect</td>
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<tr>
<td>(Liao, et al. 2016) Mouse, C57BL/6J (B6)</td>
<td>rh placental GH (GH-V)</td>
<td>1 mg/kg</td>
<td>s.c. infusion</td>
<td>Continuous</td>
<td>GD12.5 to GD18.5</td>
<td>ad libitum</td>
<td>Plac Wt at GD18.5 = Fetal:placental weight =</td>
</tr>
<tr>
<td>(Liao et al. 2016) Mouse, C57BL/6J (B6)</td>
<td>rh placental GH (GH-V)</td>
<td>2 mg/kg</td>
<td>s.c. infusion</td>
<td>Continuous</td>
<td>GD12.5 to GD18.5</td>
<td>ad libitum</td>
<td>Plac Wt at GD18.5 = Fetal:placental weight =</td>
</tr>
<tr>
<td>(Liao et al. 2016) Mouse, C57BL/6J (B6)</td>
<td>rh placental GH (GH-V)</td>
<td>5 mg/kg</td>
<td>s.c. infusion</td>
<td>Continuous</td>
<td>GD12.5 to GD18.5</td>
<td>ad libitum</td>
<td>Plac Wt at GD18.5 = Fetal:placental weight =</td>
</tr>
</tbody>
</table>

**GH administration – pig (term ~GD115)**

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment</th>
<th>Daily</th>
<th>Route</th>
<th>Timing</th>
<th>Duration</th>
<th>Endpoint</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pig, Yorkshire x Landrace gilts (Sterle, et al.)</td>
<td>rp GH</td>
<td>5 mg/d</td>
<td>i.m. injection</td>
<td>Once daily</td>
<td>GD30 to GD43</td>
<td>NR</td>
<td>Plac Wt at GD44 ↑22% Placental implantation length ↑,</td>
</tr>
<tr>
<td>1995)</td>
<td>μg/kg daily</td>
<td>6 mg/d (40 μg/kg daily)</td>
<td>Once daily</td>
<td>GD10 until GD27</td>
<td>2.6 kg/d of barley-commercial diet mix (16.6% protein)</td>
<td>Placental chorion weight = at GD28, GD37 &amp; GD62 Plac wt tend ↑22% at term Placental protein % ↑32%</td>
<td>NR</td>
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<tr>
<td>Pig, Large White × Landrace gilts (Rehfeldt, et al. 2001)</td>
<td>rp GH</td>
<td>5 mg/d (maternal)</td>
<td>i.m. injection</td>
<td>GD0 to GD30</td>
<td>2.5 – 3.0 kg/d of corn-</td>
<td>At GD65: Plac wt &amp;</td>
<td>NR</td>
</tr>
<tr>
<td>Treatment</td>
<td>Hormone</td>
<td>Dose</td>
<td>Route</td>
<td>Time Period</td>
<td>Soybean Diet</td>
<td>Implantation Length</td>
<td>Placental Protein %</td>
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<tr>
<td>Pig, unilaterally hysterectomised &amp; ovariectomised gilts (breed not stated) (Sterle et al. 2003)</td>
<td>rp GH</td>
<td>5 mg/d</td>
<td>i.m. injection</td>
<td>GD30 to GD64</td>
<td>2.5 – 3.0 kg/d of corn-soybean diet meeting NRC requirements (14% protein)</td>
<td>At GD65: Plac wt &amp; implantation length = Placental protein % ↑5.5% and uterine-placental contact area ↑49%</td>
<td>NR</td>
</tr>
<tr>
<td>Pig, Large White x Landrace gilts</td>
<td>rp GH</td>
<td>6 mg/d (\sim 35 \mu g/kg daily)</td>
<td>i.m. injection</td>
<td>Once daily</td>
<td>GD80 to GD114</td>
<td>2.5 – 3.0 kg/d of corn-soybean diet meeting NRC requirements (14% protein)</td>
<td>Plac wt ↑24% at birth</td>
</tr>
<tr>
<td>Pig, Large White x Landrace gilts and sows</td>
<td>rp GH</td>
<td>2 mg/d in gilts, 3.5 mg/d in sows (both \sim 15 \mu g/kg daily)</td>
<td>i.m. injection</td>
<td>GD25 to GD50</td>
<td>2.2 kg/day (gilts) or 2.5 kg/d (sows) of diet containing 13.0 MJ DE/kg and 15.2% CP</td>
<td>Plac Wt and area at GD50 =</td>
<td>Fetal:placental weight = Placental trophoblast thickness, folding and vascularisation = SLC2A1 (GLUT1) protein in trophoblast ↑35% and basal trophoblast membrane ↑44%</td>
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<tr>
<td>GH administration – sheep (term ~GD149-GD151)</td>
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<tr>
<td>Sheep, primigravid Arcott ewes (Stelwagen, et al. 1994)</td>
<td>rb GH</td>
<td>0.1 mg/kg daily</td>
<td>i.m. injection</td>
<td>Once daily</td>
<td>GD97 to GD124</td>
<td>Mixed ration meeting NRC requirements, fed to allow &gt;10% refusals (ad libitum)</td>
<td>Plac wt = at GD124 and birth</td>
</tr>
<tr>
<td>Sheep, Coopworth-Border cross</td>
<td>rb GH</td>
<td>0.2 mg/kg daily</td>
<td>s.c. injection</td>
<td>Twice daily</td>
<td>GD125 to GD134</td>
<td>Ad libitum concentrates (sheep nuts)</td>
<td>Plac wt =</td>
</tr>
<tr>
<td>Study</td>
<td>Treatment Details</td>
<td>Utero-placentaluptakes of oxygen, glucose &amp; lactate =</td>
<td>Placental simple diffusion ↑50%</td>
<td>Placental facilitated diffusion (glucose) trend ↑</td>
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<tr>
<td>Harding, et al. 1997</td>
<td>plus barley straw</td>
<td>Utero-placentaluptakes of oxygen, glucose &amp; lactate =</td>
<td>Placental simple diffusion ↑50%</td>
<td>Placental facilitated diffusion (glucose) trend ↑</td>
<td></td>
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<tr>
<td>Sheep, Border Leicester x Romney (Jenkinson, et al. 1999)</td>
<td>rb GH 0.15 mg/kg daily s.c. injection Twice daily GD101-GD107</td>
<td>Caruncle wt = Fetal fluid wt ↑74%</td>
<td>Caruncle no. trend ↑10%</td>
<td>NR</td>
<td></td>
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<tr>
<td>Sheep, Romney</td>
<td>rb GH 0.15 s.c. Twice daily GD70 Ad libitum concentrates (sheep nuts) plus lucerne chaff</td>
<td>Plac wt =</td>
<td></td>
<td>NR</td>
<td></td>
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<tr>
<td>Study</td>
<td>Treatment</td>
<td>Dose (mg/kg)</td>
<td>Route</td>
<td>Duration</td>
<td>Concentrates Used</td>
<td>Fetal Membrane &amp; Bladder Fluid Weight</td>
<td>Ad Libitum (maximises)</td>
</tr>
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<tr>
<td>Sheep, Romney (Jenkinson et al. 1999)</td>
<td>rb GH</td>
<td>0.15</td>
<td>s.c. injection</td>
<td>Twice daily</td>
<td>GD98-GD111 concentrates</td>
<td>Caruncle no. = Fetal membrane &amp; amniotic fluid wt = Allantoic fluid wt ↑74%</td>
<td>Placenta wt = Caruncle no. = Fetal membrane wt = Allantoic &amp; amniotic fluid wt</td>
</tr>
<tr>
<td>Sheep, embryo transfer to</td>
<td>rb GH</td>
<td>0.14</td>
<td>s.c. injection</td>
<td>Twice daily</td>
<td>GD35-GD80</td>
<td>Ad libitum maximises Placenta wt ↑38.5%</td>
<td>Placenta wt</td>
</tr>
<tr>
<td>Breed</td>
<td>Treatment Details</td>
<td>Maternal Growth &amp; Induces IUGR or Moderate Intake (Maximises Fetal-Placental Growth) of Diet Containing 10.2 MJ DE/kg and 13.7% CP</td>
<td>Placentome No. = Fetal Membrane Wt ↑&gt;4-fold</td>
<td>Fetal Fluid Volume ↑&gt;4-fold</td>
<td>No Effects in Moderately-Fed Group</td>
<td>Fetal Plasma Lactate ↑54%</td>
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<tr>
<td>Sheep, mixed breeds (Costine, et al. 2005)</td>
<td>rb GH, sustained release formula 500 mg s.c. injection Single dose Given at estrus (breeding)</td>
<td>Plac Wt, placental length, no. of cotyledons, cotyledonary weight = at Fetal:chorioallantoic weight tend ↑ at GD80 = at GD25 and GD140</td>
<td>Maternal growth &amp; induces IUGR or moderate intake (maximises fetal-placental growth) of diet containing 10.2 MJ DE/kg and 13.7% CP</td>
<td>Placentome no. = Fetal membrane wt ↑&gt;4-fold</td>
<td>Fetal fluid volume ↑&gt;4-fold</td>
<td>No effects in moderately-fed group</td>
<td></td>
</tr>
<tr>
<td>Sheep, embryo transfer to Dorset Horn x Mule ewe lambs (prepubertal) (Wallace, et al. 2006)</td>
<td>rb GH</td>
<td>0.14 mg/kg daily</td>
<td>s.c. injection</td>
<td>Twice daily</td>
<td>GD35-GD65</td>
<td>Ad libitum (maximises maternal growth &amp; induces IUGR) of diet containing 12.0 MJ DE/kg and 14% CP</td>
<td>Plac wt = Placentome no. = Fetal fluid volume =</td>
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</tr>
<tr>
<td>Sheep, embryo</td>
<td>rb GH</td>
<td>0.14</td>
<td>s.c.</td>
<td>Twice daily</td>
<td>GD95-GD125</td>
<td>Ad libitum</td>
<td>Plac wt =</td>
</tr>
<tr>
<td>Transfer to Dorset Horn x Mule ewe lambs (prepubertal) (Wallace et al. 2006)</td>
<td>mg/kg daily injection</td>
<td>(maximises maternal growth &amp; induces IUGR) or moderate intake (maximises fetal-placental growth) of diet containing 12.0 MJ DE/kg and 14% CP</td>
<td>Placentome no. = Fetal fluid volume ↑118%</td>
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<tr>
<td>Sheep, Romney ewes, following placental embolization (IUGR model)</td>
<td>rb GH 0.2 mg/kg daily i.m. injection Twice daily GD100-GD128 Ad libitum pelleted diet Plac wt = at GD128-131</td>
<td>Fetal:placental wt = Fetal plasma glucose and lactate =</td>
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</tbody>
</table>
Sheep, whiteface crossbred ewes, all twin pregnancies (Wright, et al. 2008) | rb GH | 0.2 mg/kg daily | s.c. injection | Twice daily | GD35-GD55 | At GD55 and GD133-138: Plac wt = NR

**IGF1 administration – rat (term ~GD21-23)**

Rat, Sprague-Dawley (Gargosky et al. 1991) | rh IGF1 | 1.4 mg/kg daily | s.c. infusion | Continuous | GD11 to GD21 | Standard rat chow *ad libitum* | Plac wt = at GD21 | Fetal:placental weight =

Rat (Woodall et al. 1999) | rh IGF1 | 6 mg/kg daily | s.c. injection | 3 per day | GD10 to GD20 | *ad libitum* or 30% *ad libitum* rat chow | Plac Wt at GD20 = in both maternal nutrition | NR
<table>
<thead>
<tr>
<th>IGF1 administration – sheep (term ~GD149-GD151)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep (Liu, et al. 1994)</td>
</tr>
<tr>
<td>rh IGF1</td>
</tr>
<tr>
<td>30 µg/kg per hour i.v. infusion Continuous for 4 h</td>
</tr>
<tr>
<td>GD129-GD133 standard laboratory diet</td>
</tr>
<tr>
<td>Placental blood flow = Placental transfer by simple &amp; facilitated diffusion = Placental lactate production ↑56%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>IGF1 administration – guinea pig (term ~GD69-70)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guinea pig, Dunkin-Hartley, nulliparous (Sohlström, et al. 2001)</td>
</tr>
<tr>
<td>rh IGF1</td>
</tr>
<tr>
<td>565 µg/daily (~0.8-1.1 mg/kg) s.c. infusion continuous GD20-GD37</td>
</tr>
<tr>
<td>ad libitum or 70% ad libitum commercial guinea pig</td>
</tr>
<tr>
<td>At GD40: Plac wt ↑10% in ad libitum-fed Plac wt ↑13% in 70% ad</td>
</tr>
<tr>
<td>NR</td>
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<tr>
<td>Guinea pig, IMVS coloured (Sferruzzi-Perri, et al. 2006)</td>
</tr>
<tr>
<td>Guinea pig (Sferruzzi-Perri, et al. 2007b)</td>
</tr>
<tr>
<td>Species</td>
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<tr>
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<tr>
<td>Guinea pig (Sferruzzi-Perri, et al. 2007a)</td>
</tr>
<tr>
<td>Guinea pig, Dunkin-Hartley, nulliparous (Sohlström et al.)</td>
</tr>
<tr>
<td>Guinea pig, IMVS coloured (Sferruzzi-Perri et al. 2006)</td>
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<tr>
<td>Guinea pig</td>
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<tr>
<td>Guinea pig</td>
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</tbody>
</table>

At GD35: Plac wt = Plac methyl-D-glucose total uptake and uptake/g = Plac amino-isobutyric acid total uptake and uptake/g = Placental gene expression of SLC2A1 (GLUT1) and SLC38A2 (system A amino acid transporter) =
<table>
<thead>
<tr>
<th>(Sferruzzi-Perri et al. 2007a)</th>
<th>daily infusion</th>
<th>Plac wt =</th>
<th>Placental methyl-D-glucose total uptake and uptake/g = and ↑ fetal tissue uptake</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placental amino-isobutyric acid total uptake and uptake/g and fetal tissue uptake =</td>
<td></td>
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</tbody>
</table>

- = unchanged; ↑ increased; ↓ decreased; Abdom circ, abdominal circumference; b, bovine; BWt, birth weight; CP, crude protein; CRL, crown-rump length; DE, digestible energy; Fetal Wt, fetal weight; FFA, free fatty acid; GD, gestation day (days after mating); GH, growth hormone; h, human; IGF, insulin-like growth factor; i.m. intramuscular; No., number; NR, not reported; o, ovine; p, porcine; Plac Wt, placental weight; r, recombinant; s.c. subcutaneous;


Stelwagen K, Grieve DG, Walton JS, Ball JL & McBride BW 1994 Effect of bovine somatotropin administration during the last trimester of gestation on maternal growth,


