References on the Administration of Agents to Livestock Using ALZET® Osmotic Pumps

1. Cattle

ALZET Comments: Prolactin; Saline; SC; Cattle (pregnant); 28 days; Controls received no mp; animal info (female, Holstein, multiparous); functionality of mp verified by blood samples; pumps removed after 28 days.;

ALZET Comments: Ciprofloxacin; Eye; Cattle (bull); 4 weeks; Animal info (male, Hanwoo bull calf, 6 months old); functionality of mp verified by drug levels in aqueous humor and residual volume; good methods (pg. 284); no stress (see pg. 285); “As the owner could not apply topical medications regularly, a drug-filled osmotic pump (Alzet; Alza, Palo Alto, CA) was implanted subconjunctivally under the upper eyelid and connected to a catheter at the lateral limbus.” pg 282; “... it is clear that the osmotic infusion pump maintained the aqueous concentration of ciprofloxacin at a reasonable steady state until its removal four weeks after implantation. The amount of drug remaining in the pump was about 17 μg/ml after four weeks. This also demonstrates the reliability of the pump.” pg. 286; picture of pump pg 283; pumps primed for 40 hours in 37°C saline; pumps removed after 4 weeks.;

ALZET Comments: Tumor necrosis factor alpha; Saline; SC; Cattle (lactating); 2ML1; 7 days; Controls received mp w/ vehicle; animal info (female, Holstein, late lactation); Multiple pumps per animal (2); immunology.;

ALZET Comments: Buserelin acetate; NaCl; SC; Cattle (bull); 2ML4; 9 weeks; Animal info (Belgian, blue, beef, 5 years old); pumps replaced every 28 days; long-term study; buserelin acetate is a gonadotrophin releasing hormone analog.

ALZET Comments: Ghrelin, Dap³ ; obestatin; DMSO; SC; Cattle (cow); 2ML4; 8 weeks; Controls were untreated; functionality of mp verified by residual volume; long-term study; pumps replaced after 28 days; animal info (multiparous); 50% DMSO used; wound clips used; peptides.

ALZET Comments: Buserelin; SC; Cattle; 2ML4; 2 months; Long-term study.

ALZET Comments: Prolactin, recomb. bovine; Saline; SC; Cattle; 2ML2; 10 days; Comparison of IV injections vs mp; no stress (see pg. 1914); immunology; peptides; post op. care (prodine, excenel); each animal received 4 rounds of 10 day prolactin treatment (2 w/ mp, 2 IV injection) with 11 days of non treatment between each round; wound clips used.

ALZET Comments: Azagly-Nafarelin; Gonadotrophin-releasing hormone agonist; Mannitol; water, distilled; SC; Cattle (bull); 2ML4; 50 weeks; Controls received mp w/ vehicle; functionality of mp verified by blood samples taken; dose-response (p.227); Azagly-Nafarelin (GnRH agonist) was dissolved in 5% mannitol in water.

ALZET Comments: Azagly-NaFarelin; Sodium Chloride; SC; Cattle; 2ML2; 2ML4; 9, 18 days; Controls received no treatment; replacement therapy (ovariectomy); agent is a gonadotrophin-releasing hormone agonist.

P5097: H. A. Garverick, et al. Regulation of expression of ovarian mRNA encoding steroidogenic enzymes and gonadotrophin receptors by FSH and GH in hypogonadotrophic cattle. REPRODUCTION 2002;123(651 -661
ALZET Comments: Buserelin; SC; cattle; 2ML4; 7.5 weeks; long-term study, pmps replaced after 28 days; buserelin is a gonadotrophin-releasing hormone (GnRH) agonist; multiple pumps per animal (2).

ALZET Comments: Buserelin; SC; cattle (lactating); 2ML2; 30 days; Functionality of mp verified by residual volume; pumps replaced at Day 16; multiple pumps per animal (2) used at once; Buserelin is a GnRH (gonadotropin releasing hormone).

ALZET Comments: Zeranol; Water; cattle (steer); 56 days; comparison of pellets vs. mp; long-term study, pumps replaced after 28 days.

ALZET Comments: Growth hormone-rel. factor-2; DMSO; PEG 400; Tween 80; Saline; SC; cattle; 2ML2; 14 days; controls received mp w/ vehicle; peptides; agent also called KP102; multiple pumps per animal (3 or 4); comparison between injections vs. mp.

ALZET Comments: Buserelin; SC; cattle; 2ML4; 48 days; controls received no treatment; long-term study, pumps replaced after 28 days; agent is a GnRH agonist; pumps replaced in opposite shoulder than original placement; researchers compare mp w/ injections from previous study (p. 72).

ALZET Comments: Zeranol; cattle; 1,2,4,8 days; no comment posted.

ALZET Comments: Ergonovine, maleate; SC; cattle; 2ML2; 12 days; controls received mp with saline; functionality of mp verified by serum levels; dose-response (graph pg. 174); toxicology; "The results confirm use of this animal dosing method to study biological effects...without bioavailability concerns"; multiple pumps per animal (2-3)for dosing; ergovine is an ergot alkaloid.

ALZET Comments: Luteinizing HRH; Leuprolide acetate; Saline; SC; cattle; 2ML4; 28,56 days; controls received mp with vehicle; functionality of mp verified by plasma levels; long-term study, pumps replaced at 28 days; peptides.

ALZET Comments: Buserelin; SC; cattle; 2ML2; 12 days; no comment posted.

ALZET Comments: Cimaterol; SC; cattle; 2ML4; 6 weeks; controls received mp w/ buffer; long-term study, pumps replaced every 24 days; cimaterol is a B-adrenergic agonist.

ALZET Comments: Follicle stimulating hormone; SC; cattle; 7 days; no comment posted.

ALZET Comments: Oxytocin; Saline; SC; cattle; 2ML2; no duration posted; controls received mp w/ saline; functionality of mp verified by RIA analysis of plasma levels; comparison of jugular infusion by computer-controlled pump; peptides.

ALZET Comments: Interferon-a1; cattle; 2ML1; 5 days; peptides; serum IFN-a levels (p. 3445).

ALZET Comments: Bleomycin; CSF/CNS (intratumoral); cattle; Rat; 2001; 2002; 7, 14 days; Antibiotic; controls received pumps with saline only; tissue perfusion (tumor); dose-response (graph, p. 1117); comparison of ip injections vs. mp.

ALZET Comments: Gonadotrophin-releasing hormone; Saline, sterile; SC; cattle; 2ML2; no duration posted; comparison of pellets vs. mp; "the consistent ovulatory response recorded in heifers treated with osmotic minipumps demonstrates the importance of administering GnRH at a constant and controlled rate" (p. 271); peptides.

ALZET Comments: Interleukin-2; Water; mammary gland; cattle; 2 weeks; tissue perfusion; stress/adverse reaction some local mechanical damage (see pg. 1772); peptides; bovine IL-2 used.

ALZET Comments: Vitamin D3, 1,25-dihydroxy-; Propylene glycol; SC; cattle; 2ML1; 7 days; functionality of mp verified by measuring plasma vit. D levels; discusses comparison of IM injections vs. mp; states pump effectively maintained plasma conc. throughout (p. 2939), states conc. achieved via pump may improve vit. D3 therapy for preventing p.

ALZET Comments: Luteinizing HRH; Potassium phosphate; SC; cattle; 2001; 6, 7 days; pump placed s.c. in ear.
ALZET Comments: Luteinizing HRH; Saline; SC; cattle; 2ML2; 14 days; pump primed 10 hours before implant; bolus iv injections given the day before and 14th day of GnRH infusion; functionality of mp verified by incubation in vitro for 15 hours after removal; peptides.

ALZET Comments: Buserelin; Luteinizing HRH; SC; cattle; 2ML4; 4, 8, 12, 16, 28 days; dose-response; multiple pumps per animal (1 or 2) depending upon dose; functionality of mp verified indirectly by plasma levels; peptides.

ALZET Comments: 4SG-29; RO-23-7863; Growth hormone-rel. factor; DMSO; Water; SC; cattle; sheep; 2002; 2ML1; 7 days; functionality of mp verified by plasma levels; peptides.

ALZET Comments: Ivermectin; PO (intraruminal); cattle; 2ML4; no duration posted; veterinary application.

ALZET Comments: Epinephrine, l-; Norepinephrine, l-; Serotonin; Saline; SC; cattle; 72 hours; Pump model not stated; concomitant infusion of agents; comparison of agents effects.

ALZET Comments: Follicle stimulating hormone; Saline; SC; cattle; 2ML1; 7 days; comparison of im injections vs. mp infusion; peptides.

ALZET Comments: Buserelin; SC; cattle; 2ML4; 21-22 days; mp replaced after 21 days; mps primed in saline 18 hours prior to implant; multiple pumps per animal (2); functionality (pump rates) calculated upon removal; peptides.

ALZET Comments: Luteinizing HRH; Saline; SC; cattle; 2ML1; 4 days; controls were untreated; dose-response; half-life data for FSH; comparison of ip injections vs. mp infusion; peptides.

ALZET Comments: Ivermectin; PO (intraruminal); cattle; 2ML4; no duration posted; controls received mp w/vehicle; RUTS prototype; micellar vehicle; mp cont. within a stainless steel bolus with AM radio transmitter; functionality of mp verified.

2. Horse

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Bibliography

ALZET Comments: Gonadotropin-releasing hormone; Horse; 7 days; 12-18 days; Animal info (female, Quarter horse and mixed breed, 5-10 years old);

ALZET Comments: Gonadotropin-releasing hormone; Saline; SC; Horse (mare); 2ML2; 2ML4; 8 weeks; Controls received mp w/vehicle; animal info (female, Quarter Horse grade); pumps replaced every 14 days (2ML2) or 28 days (2ML4); Multiple pumps per animal (4 2ML2 or 2 2ML4); used contralateral side for next pump implantation; pumps removed at end of study;

ALZET Comments: Gonadotropin-releasing hormone; Saline, sterile; SC; Horse (mare); 2ML2; 28 days; Controls received sham pumps (silastic tubing); animal info (female, American Quarter Horses, 409-522 kg); pumps replaced every 14 days; post op. care (wound cleaned, disinfected with povidone iodine, antibacterial ointment - PO); pumps primed for 16 hours in 37°C saline; used contralateral location for next pump implantation;

ALZET Comments: Gonadotropin-releasing hormone; Saline, physiological; SC; Horse; 2004; 120 days; Controls received sham pumps; long-term study; pumps replaced every 30 days; animal info (mare, 18 mo to 24 yrs); pumps were disinfected using chlorhexidine gluconate, sham pumps were made from silicon tubing filled with medical grade silicone adhesive to approximate the size of the ALZET pumps, then cold-sterilized (similar to pumps) before surgical insertion.

ALZET Comments: Gonadotrophin-releasing hormone; Cat; horse;

ALZET Comments: Melatonin; Saline; DMSO; SC; horse; 12 weeks; controls received mp w/vehicle; functionality of mp verified by serum assays on days 5, 26 and 59; long-term study, pumps replaced every 28 days.

P3029: D. K. Vanderwall, et al. Corpus luteal function in nonpregnant mares following intrauterine administration of prostaglandin E2 or estradiol-17B. Theriogenology 1994;42(1069-1083
ALZET Comments: Prostaglandin E2; Estradiol, 17B-; Ethanol; PBS; intrauterine; horse; 2001; 7 days; controls received no treatment or mp with vehicle; tissue perfusion (uterine horn lumen); no stress (see pg. 1078); benzathine penicillin-G given prophylactically.

ALZET Comments: Luteinizing HRH; SC; horse; 2ML2; 2ML4; 14 or 28 days; comprehensive review of other GnRH induced estrous studies (pp. 198-199).

ALZET Comments: Luteinizing HRH; IV (jugular); horse; 2ML1; 7-16 days; controls received no treatment; functionality of mp verified by LH plasma levels; comparison of iv pulsatile infusion vs. mp; peptides.
**ALZET Comments:** Luteinizing HRH; Saline; SC; horse; 28 days; peptides.

**ALZET Comments:** Wy-40972; Saline; SC; horse; 2002; 14 days; controls received saline injections; functionality of mp verified by LH RIA; comparison of i.m. injections vs mp; pumps inserted via trochar; Wy-40972 is lutrelin.

**ALZET Comments:** Buserelin; SC; horse; 28 days; functionality of mp verified by dissection; animals received 1-2 pumps.

**ALZET Comments:** Luteinizing HRH; Saline; SC; horse; 2ML4; 28 days; peptides.

**ALZET Comments:** Luteinizing HRH; SC; horse; 2001; 6 days; functionality of mp verified in vitro; peptides.

**ALZET Comments:** Luteinizing HRH; Saline; SC; horse; 2ML4; 28 days; peptides.

**ALZET Comments:** Luteinizing HRH; Potassium phosphate; SC; horse; 2001; 7 days; controls receive mp w/ vehicle; dose-response; mp primed 4 hours before implant; 2 experiments using mp; progestrin silastic implants used concomitantly with GnRH; peptides.

**ALZET Comments:** Luteinizing HRH; Saline; SC; horse; 2ML4; 28 days; controls remained untreated; dose-response; infusion of GnRH via mp did not produce linear plasma increases, possibly because of stability of GnRH in solution or pooling at implant site; peptides.

### 3. Pig

Q6526: A. Vivekanandarajah, et al. Intermittent hypercapnic hypoxia effects on the nicotinic acetylcholine receptors in the developing piglet hippocampus and brainstem. Neurotoxicology 2017;60(23-33
**ALZET Comments:** Nicotine Hydrogen Tartate Salt; Water (sterile); IP; Pig (neonate); 2ML2; 14 days; Dose (2.0 mg/kg/day); animal info (mixed-breed miniature piglets); comparison of patch vs mp; Resultant plasma level (serum cotinine: 23.1 +17.3 ng/mL); “The use of an osmotic minipump as opposed to a skin patch was chosen as the method of nicotine delivery given it provides a steady state, same dose, infusion over our 14 day study whereas patches result in sudden spikes in plasma levels and require replacement of patches every 1-2 days dependent on chosen patch ” pg. 2 ;.

Q6137: J. Huang, et al. Hypoxia and nicotine effects on Pituitary adenylate cyclase activating polypeptide (PACAP) and its receptor 1 (PAC1) in the developing piglet brainstem. Neurotoxicology 2017;62(30-38
ALZET Comments: Nicotine; Water; IP; Pig; 2ML2; 14 days; Dose (2 mg/kg/day); Controls received mp w/ vehicle; “The delivery of nicotine via the minipump provides a steady state infusion over our 14 day study whereas other methods result in sudden spikes in plasma levels (reviewed by Shiffman et al., 2005) and require more animal handling and stress.” pg. 31.


ALZET Comments: Placental growth factor-2, recombinant human; PBS; IV; Pig; 2ML2; 14 days; Controls received mp w/ vehicle; animal info (Sus Scrofa, 20-25kg); functionality of mp verified by plasma levels; ischemia (myocardial); cardiovascular; Dose (15 ug/kg/day);


ALZET Comments: Nicotine hydrogen tartrate salt; Water; SC; Pig (mini); 2ML2; 14 days; Controls received mp w/ vehicle; animal info (male mixed breed miniature piglets, postnatal day 2, 1.27 kg); functionality of mp verified by brain analysis; toxicity; chronic postnatal nicotine and intermittent hypercapnic hypoxia (IHH); Dose (2 mg/kg/day);


ALZET Comments: BRL37344; Saline; IV (right jugular vein); pigs; 2ML2; 14 days; Animal info (pig, 4 months old, 45 kg); functionality of mp verified by plasma levels; cardiovascular; antihypertensive; PE-60 catheter used for IV application; BRL37344 is a B3AR agonist; Dose (10 ug/kg/day BRL37344);


ALZET Comments: Nicotine Hydrogen Tartrate; water; IP; Pig (mini); 2ML2; 14 days; Controls received mp w/ vehicle; animal info (piglets); functionality of mp verified by blood and urine samples; toxicity; Dose (2 mg/kg/d); Resultant plasma level (20.3 ± 2.5 ng/mL);


ALZET Comments: Fulvestrant; DMSO; PBS; Pig; 2ML2; 2ML4; 4 weeks; Controls received mp w/ vehicle; animal info (boar, 6-6.5 weeks old); 50% DMSO used; Fulvestrant is a nuclear estrogen receptor antagonist and G protein-coupled receptor agonist;


ALZET Comments: Vascular endothelial growth factor, recombinant human; Heparin; Saline; Intrapericardial; Pig; 2ML4; 4 weeks; Animal info (male, Yorkshire miniswine, 13-22kg); ischemia (cardiac, chronic); stress/adverse reaction: (see pg. 746); post op. care (Enrofloxacin 68mg PO daily for 5 days; aspirin 325 mg/day for 5 days; buprenorphine HCL 0.3 mg/kg, transdermal fentanyl patch 4mcg/kg for 72h); cardiovascular;


ALZET Comments: Nicotine; Water, sterile; IP; Pig; 2ML2; 14 days; Control animals received mp w/ vehicle; animal info (piglet, mixed bred).


ALZET Comments: ICI 182,780; Saline; DMSO; SC; Pig; 2ML2; 2ML4; Control animals received mp w/ vehicle; animal info (1 wk old, Sygen); 50% DMSO used; pumps replaced after 4 weeks.
ALZET Comments: Amikacin; gentamicin; SC; Pig (mini); Animal info (female, 3.5-4.5 mo old, 12-27 kg); 2ML sized pumps used; pump implanted in the back of the neck.

ALZET Comments: Enalaprilat; Lisinopril; Imidapril; Saline; IP; Guniea pig; 2ML1; Dose (enalaprilat (0.1, 0.5, 1, 5, 10, 20 mg/ml), lisinopril (0.1, 0.5, 1, 5, 10, 20 mg/ml), imidapril (1, 5, 10, 20, 30 mg/ml)); Controls received mp w/ vehicle; enzyme inhibitor (angiotensin-converting-enzyme); cardiovascular.;

ALZET Comments: CSF, artificial (agent); CSF/CNS (patumen); Pig; 2ML4; 1 month; Animal info (Large White/Landrace); "due to concerns regarding the risk of blockage, catheters were modified to be connected to Alzet osmotic minipumps" pg 288.

ALZET Comments: Vascular endothelial growth factor, recomb. human; Intrapericardial; Pig; Animal info (intact, male, Yorkshire); stress/adverse effects "sudden cardiac death", pg 393.

ALZET Comments: Dexamethasone; Cyclodextrin, 2-hydroxypropyl-b-; SC; Pig (mini); 2004; 2ML4; 28 days; Controls received mp w/ normal saline; animal info (Yucatan, adult, 60-70 kg); functionality of mp verified by opening and inspecting the pump; dose-response; multiple pumps per animal (2); Fig 1, image of biosensor array with ALZET pump.

ALZET Comments: Phorbol didecanoate, 4-alpha;-IA (femoral); Pig; 2ML1; 7 days; Controls received mp w/ saline or sham operation; cardiovascular; animal info (male, juvenile, crossbred, 38kg, femoral artery occlusion); post op. care (cefoxinone, fentanyl); ischemia (hind limb); excellent color photograph of multiple mp placement (Fig. 1); multiple pumps per animal (2).

ALZET Comments: Neuropeptide Y (3-36); Heparin; BSA; PBS; Intramyocardial; Pig (miniswine); 4 weeks; Controls received mp w/ placebo; animal info (Intact, adult, male, Yorkshire, miniswine); 2ML sized pump used; tissue perfusion (myocardium).

ALZET Comments: PBS; LAP-RGD; LAP-RGE; Intratrauterine (uterine horn); Pig (pregnant); 5 days; Controls received mp w/ vehicle; peptides; animal info (gilt, ovariohystorectomy); polyethylene catheter used; fig. 1, image of pump implantation.

Q0847: C. R. Barb, et al. Luteinizing hormone secretion as influenced by age and estradiol in the prepubertal gilt. ANIMAL REPRODUCTION SCIENCE 2010;122(3-4):324-327
ALZET Comments: Estradiol benzoate; Propylene glycol; SC; Pig; 2ML2; 10 days; Controls received mp w/ vehicle; animal info (gilt, OVX, 90, 150, 210 day old); functionality of mp verified by serum estradiol levels; replacement therapy (ovariectomized); pump implanted SC behind the ear.
**ALZET Comments:** Oxytocin; Saline; SC; Pig; 2ML4; 21 days; Controls received mp w/ vehicle; animal info (domestic, Yorkshire-Landrace, castrated, male, 21-29 kg).

**ALZET Comments:** Nicotine hydrogen tartrate salt; Water, sterile; IP; Pig; 2ML2; 13 days; Controls received mp w/ vehicle; animal info (male, female, piglet, mixed breed).

**ALZET Comments:** Vascular endothelial growth factor 165, recomb. human; Heparin; Intramyocardial; Pig (miniswine); 2ML4; 4 weeks; Tissue perfusion (myocardial); half-life (p. 649) "short"; cardiovascular; peptides; ischemia (cardiac); animal info (Yucatan mini-swine, 20-30 kg.).

**ALZET Comments:** Antibody, TGF beta neutralizing; Vascular endothelial growth factor; SC; Pig (mini); 28 days; animal info (Yucatan mini pigs); enzyme inhibitor (pSmad2).

**ALZET Comments:** Amikacin; Sub-masseteric tunnel; Pig; 2ML2; 14 days; Bone healing; x-ray image showing pump adjacent to mandible bone (p. 189); pump positioned near mandible bone to deliver antibiotics for infection control; tissue perfusion (sub-masseteric tunnel).

P8483: M. Say, et al. Changes in serotoninergic receptors 1A and 2A in the piglet brainstem after intermittent hypercapnic hypoxia (IHH) and nicotine. Brain Res 2007;1152(17-26
**ALZET Comments:** Nicotine; Water, sterile; IP; Pig (neonate); 2ML2; 2 weeks; Controls received mp w/ vehicle; SIDS; animal info (mini-piglet; 0-2 days old).

**ALZET Comments:** Insulin-like growth factor-binding protein-4; Insulin-like growth factor-binding protein-4, mutated; Insulin-like growth factor-1, recomb. human; PBS; IA (carotid); IA (femoral); Pig; 21 days; Controls received mp w/ vehicle; cardiovascular; peptides; animal info (male, female, spotted Poland/China, 12 months old); protease resistant mutant form of IGFBP-4.

**ALZET Comments:** Conceptus secretory proteins, porcine; Intruterine; Pig; 2ML1; Controls received mp w/ albumin, porcine serum; tissue perfusion (uterus); good methods p. 4421; peptides; multiple pumps per animal (2); animal info (female).

**ALZET Comments:** Conceptus secretory proteins, porcine; Albumin, porcine serum; dye, india ink; PBS; Intruterine (uterine horn); Pig; 2ML1; 4 days; Controls received mp w/ PSA; peptides; multiple pumps per animal (2); animal info (female, pseudopregnant); india ink used to confirm agent distribution in uterus; tissue perfusion (uterine horn).

ALZET Comments: Candesartan; Saline, physiological; Na2CO3; SC; Pig; 2ML1; 7 days; Controls received mp w/ isotonic saline; no stress (see pg. F1774); animal info (female, Danish Landrace, 23 days old, partial left ureter obstruction); renal physiology.


ALZET Comments: Nicotine hydrogen tartrate salt; Water, sterile; IP; Pig (neonate); 2ML2; 11-13 days; Controls received mp w/ vehicle; functionality of mp verified by serum cotinine; no stress (see p.109); animal info (mixed-breed miniature piglet, 2 days old, male, female, 1.2 kg).


ALZET Comments: Arginine, L-; Saline; Wound site; Pig; 2ML2; 14 days; Controls received mp w/ vehicle; functionality of mp verified by residual volume; animal info (female, domestic, Landrace, 15-20kg., hernia defect); tubing was looped and contained multiple side holes to ensure uniform delivery within the aqueous wound compartment; ultrasonography.


ALZET Comments: Candesartan; Saline, physiological; SC; Pig (neonate); 7 days; Controls received mp w/ vehicle; no stress (see pg. F923); animal info (female, Danish Landrace; 2, 23 days old); congenital urinary tract obstruction model.


ALZET Comments: Vascular endothelial growth factor 165, recomb. human; Heparin; Perivascular (circumflex coronary artery); Pig (mini); 2ML4; 4 weeks; Cardiovascular; peptides; ischemia (cardiac); animal info (male, female, yucatan, 20-30 kg, 23 weeks old).


ALZET Comments: Interleukin -1 receptor antagonist, recomb. human; Saline, normal; SC; Pig; 2ML2; 14-18, 28 days; Controls received mp w/ vehicle; functionality of mp verified by agent plasma levels; pumps replaced at day 14; no stress (see pg. 495); cardiovascular; multiple pumps per animal (3); animal info (Yorkshire white); mp primed; mp implanted sc in groin crease.


ALZET Comments: Nicotine hydrogen tartrate salt; water, sterile; IP; Pig (neonate); 2ML2; 2 weeks; Controls received mp w/ vehicle; functionality of mp verified by cotinine levels in serum and urine; no stress (see pg. 326); post op. care (cephalexin).

P5861: M. Scheinowitz, et al. Dalteparin sodium (Fragminâ) administration following acute infarction does not affect myocardial perfusion and function in swine. Cardiovascular Drugs and Therapy 2002;16(4):303-309

ALZET Comments: Dalteparin sodium; albumin; IP; Pig; 2ML1; 1 week; Controls received mp w/ albumin; functionality of mp verified by blood samples taken; multiple pumps per animal (2); Dalteparin sodium (Fragminâ) is a low molecular weight heparin derivative.


ALZET Comments: Vascular endothelial growth factor; Periadventitial; Pig; 3,4 weeks; Replacement therapy (coronary ligation); cardiovascular; ischemia (cardiac); review, pg. 59.

ALZET Comments: Insulin-like growth factor I; Insulin-like growth factor I, LR3-; Acetic acid; SC; Pig (neonate); 2001; 8, 9 or 18 days; Controls received mp w/ vehicle; functionality of mp verified by plasma levels; pumps replaced after 8 or 9 days; peptides.

Q6866: L. VO, et al. LOWERING OF BLOOD GLUCOSE TO NONDIABETIC LEVELS IN A HYPERGLYCEMIC PIG BY ALLOGRAFTING OF FETAL PIG ISLETLIKE CELL CLUSTERS. Transplantation 2001;71(11):1671–1677

ALZET Comments: Insulin; SC; Pig; 2ML4; 28 days; Dose (200 U/pump); animal info (Large White Landrace pigs); diabetes.


ALZET Comments: Vascular endothelial growth factor; Pig; Cardiovascular; peptides; MRI; ALZET pumps mentioned on pg. 279.


ALZET Comments: Growth hormone, recomb. porcine;; pig (fetus); Functionality of mp verified by plasma levels; replacement therapy (hypophysectomy); teratology; peptides; pellets used for thyroxine administration.

4. Sheep


ALZET Comments: Melatonin; Intrauterine; Sheep (pregnant);


ALZET Comments: Ara-C; CNS/CSF (third ventricle); Sheep; 2ML4; 4 Weeks; Dose (500ug/day); animal info (Ewes, 58.8 ± 4.5 kg, 59.4 ± 4 kg)); Ara-C aka cytosine-b-D-arabinofuranoside; Ara-C aka cytosine-b-D-arabinofuranoside;


ALZET Comments: Dexamethasone 21-phosphate disodium salt; IV (lateral saphenous vein); Sheep (pregnant); 2ML1; 48 hours; Dose (0.48 mg/h);


ALZET Comments: Rosiglitazone Maleate; Water, Ethanol; SC; Sheep (pregnant); 2ML1; 16 days; animal info (Singleton pregnant sheep); functionality of mp verified by plasma level, amniotix fluid samples; 15% ethanol used; Multiple pumps per animal (4); stability verified by regular plasma level measurements (reached after day 5, tested through day 16; half life of 24-48 hours in sheep); Catheters flushed with heparinized saline; Dose (2.7 mg/fetus/d);


ALZET Comments: oligonucleotdies, antisense morpholino; PBS; Intrauterine; Sheep (ewe, pregnant); 2ML1; 7 days; Controls received mp w/ control oligonucleotides; animal info (female, Columbia Rambouillet); teratology; cyanoacrylate adhesive; used vinyl catheter tubing (0007760) to cannulate uterine lumen; pump affixed to mesosalpinx using cyanoacrylate glue;
ALZET Comments: Endotoxin, LPS; Oral cavity; Sheep (ewe); 1 day; 6 days; Controls received mp w/ saline; animal info (Merino); teratology; immunology;.

Q3870: A. W. Efert, et al. Effect of melatonin or maternal nutrient restriction on vascularity and cell proliferation in the ovine placenta. ANIMAL REPRODUCTION SCIENCE 2015;153(13-21
ALZET Comments: Melatonin; luzindole; DMSO; water; Intrauterine; Sheep (ewe; pregnant); 2ML4; 28 days; Controls received mp w/ vehicle; animal info (female, Western white face, GD62); functionality of mp verified by serum levels; 45% DMSO used; good methods (pg 15); no stress (see pg. 15); post op. care (BID IM injection flunixin meglumine; QD IP injection Penicillin G Procaine); teratology; cardiovascular; used 20 cm of PE 60 tubing; pumps primed in 37C saline with catheters;.

ALZET Comments: Oligonucleotide, antisense morpholino PPARD; oligonucleotide, antisense morpholino PPARG; PBS; Intrauterine (uterine horn); Sheep (ewe); 2ML1; 7 days; Controls received mp w/ control morpholino; animal info (Ovis aries, 7 days after mating); cyanoacrylate adhesive; used vinyl catheter tubing; pump glued to mesosalpinyx and sutures; pumps primed in 37C sterile PBS for 24 hours.

ALZET Comments: Endotoxin, LPS; Intra-amniotic; Sheep (fetus); 24 hours; Controls received mp w/ saline; animal info (124 gestation day); immunology;.

Q3583: I. Nitsos, et al. The Impact of Chronic Intrauterine Inflammation on the Physiologic and Neurodevelopmental Consequences of Intermittent Umbilical Cord Occlusion in Fetal Sheep. REPRODUCTIVE SCIENCES 2014;21(658-670
ALZET Comments: Endotoxin, LPS; Amniotic sac; Sheep (fetus); 2ML4; 4 weeks; Controls received mp w/ saline; animal info (female, pregnant, GD80); post op. care (benacillin); teratology; immunology; E.coli LPS 055:B5, 18 mg/ml;.

Q3577: G. C. Musk, et al. Thermal and mechanical nociceptive threshold testing in pregnant sheep. VETERINARY ANAESTHESIA AND ANALGESIA 2014;41(305-311
ALZET Comments: Medetomidine; Saline; IP; Sheep (pregnant); 2ML1; 7 days; Animal info (female, Merino singleton, pregnant at GD118-121); functionality of mp verified by plasma levels; comparison of transdermal patch vs mp; behavioral testing (mechanical nociceptive threshold; thermal nociceptive threshold); pumps primed at 37C overnight;.

Q4730: S. Lie, et al. Exposure to rosiglitazone, a PPAR-gamma agonist, in late gestation reduces the abundance of factors regulating cardiac metabolism and cardiomyocyte size in the sheep fetus. AMERICAN JOURNAL OF PHYSIOLOGY-REGULATORY INTEGRATIVE AND COMPARATIVE PHYSIOLOGY 2014;306(6):R429-R437
ALZET Comments: Rosiglitazone; Ethanol; SC; Sheep (fetus); 2ML4; 14 days; Controls received mp w/ vehicle; animal info (fetus, 123-126 days gestation); 15% ethanol used; cardiovascular;.

ALZET Comments: U0126; serum protein, ovine; interferon tau, recombinant ovine; DMSO; Intrauterine (uterine horn); Sheep (ewe); 2ML1; 6 days; Controls received mp w/ vehicle; animal info (female, Suffolk Ovis aries); 3% DMSO used; tissue perfusion (uterine horn); cyanoacrylate adhesive; used cyanoacrylate glue to anchor pump; interferon tau aka IFNT;.

ALZET Comments: Hydroxyvitamin D3, 1a-; SC; Sheep (ewe); 2002; 6 days; Animal info (merino, mature); functionality of mp verified by plasma 1,125-dihydroxycholecalciferol levels.

ALZET Comments: Oxytocin; Sheep; 90 days; Pumps replaced every 30 days; long-term study.

ALZET Comments: IFNT; PGE2 251; PGF2a 409; PGF2; Ethanol; saline; SC; Sheep; 2ML1; Animal info (mature Rambouillet ewes (Ovaris)); multiple pumps per animal (2); paper does not mention pumps much; recombinant ovine (rO) IFNT (101ug in vehicle), a PG mixture (PGE2 251ng, PGF2a 409ng, and PGF 1483ng in vehicle); vehicle (2% ethanol in saline).

ALZET Comments: Buserelin acetate; Saline; SC; Sheep (ewe); 28 days; Animal info (ovariectomized, ewes).

ALZET Comments: Medetomidine; Saline, sterile; IP; Sheep (pregnant); 2ML1; Control animals received mp w/ vehicle; animal info (adult, merino, ewe, pregnant, 128 GD); no stress, pg 70 "In the authors' experience, leaving pumps in situ for up to six days is not associated with any complications."

ALZET Comments: Follicle stimulating hormone, porcine; SC; Sheep; 1003D; Animal info (aoudad, aka Barbary, female); multiple pumps used (2); "the traditional procedures for superovulation in domestic ruminants are complicated and difficult to perform in wild females because the procedure requires many physical contact and repetitive procedures, i.e., the administration of FSH two times per day. Thus, we choose to deliver FSH using osmotic pumps to minimize such manipulations... and we considered that it was the best approach for wild ruminant females and most likely represents a more "physiological" delivery method, with the continuous administration of FSH rather than blood level spikes." pg 152-153.

ALZET Comments: Melatonin; Luzindole; DMSO; water; Intrauterine (uterine horn); Sheep (ewe); 2ML4; 28 days; Controls received mp w/ vehicle; functionality of mp verified by serum levels of melatonin taken; 45% DMSO used; stress/adverse reaction: (see pg.2); post op. care (For two days: flunixin meglumine 50 mg/ml IM twice a day; Penicillin G procain 300,000 u/ml once per day); tissue perfusion (uterus mesometrium); cardiovascular.

ALZET Comments: Cortisol; potassium canrenoate; mifepristone; Saline; SC; Sheep (ewe); 2ML2; 10 days; Controls received mp w/ vehicle; animal info (female, singleton pregnancies); teratology; cardiovascular; impact of maternal stress during late gestation.

ALZET Comments: Cortisol; PF915275; meloxicam; interferon, tau, recomb. ovine; Ethanol; Intrauterine (uterine horn); Sheep (ewe); 2ML1; Control animals received mp w/ vehicle; animal info (mature, rambouillet, female, ewe); 2% ethanol
used; vinyl catheter used (0007760); "Our previous studies found that infusion of that amount of IFNT in the uterine lumen each day mimics effects of the conceptus on endometrial expression of hormone receptors and IFNT-stimulated genes during early pregnancy in ewes" pg 932.

ALZET Comments: Estradiol-3-sulfate; Water; CSF/CNS; Sheep (fetus); 2ML2; 7-12 days; Animal info (twin fetuses, 120-127 days of gestation); good methods, pg 669; functionality of mp verified via visual inspection at the time of death and tissue collection.

ALZET Comments: BQ610; Methanol; saline; Intraovarian (corpus luteum); Sheep (ewe); 2002; 14 days; Controls received mp w/ vehicle; animal info (nonpregnant, Suffolk); tissue perfusion (corpus luteum); BQ-610 is an endothelin receptor type A antagonist.

ALZET Comments: Interferon, tau, recomb. ovine; meloxicam; PGE2, ovine serum; PGF2a, ovine serum; PGI2, ovine serum; Ethanol; saline; Intrauterine (uterine horn); Sheep (ewe); 2ML1; 7 days; Controls received mp w/ vehicle; animal info (Mature Rambouillet); good methods (pg 2); vinyl tubing used (0007760); 2% ethanol used; enzyme inhibitor (prostaglandin synthase two); tissue perfusion (intrauterine).

ALZET Comments: Interferon, tau, recomb. ovine; meloxicam; PGE2, ovine serum; PGF2a, ovine serum; PGI2, ovine serum; Ethanol; saline; Intrauterine (uterine horn); Sheep (ewe); 2ML1; 5 days; Controls received mp w/ vehicle; animal info (Mature Rambouillet); tissue perfusion (intrauterine); multiple pumps used (2); enzyme inhibitor (prostaglandin synthase two).

Q2715: A. Atik, et al. Long-Term Pulmonary Effects of Intrauterine Exposure to Endotoxin Following Preterm Birth in Sheep. REPRODUCTIVE SCIENCES 2012;19(12):1352-1364
ALZET Comments: Endotoxin, LPS; Saline; Intrauterine; Sheep (ewe); 2ML4; 28 days; Control animals received mp w/ saline; multiple pumps used (2).

Q1487: C. E. Wood. Fetal Hypothalamus-Pituitary-Adrenal Responses to Estradiol Sulfate. Endocrinology 2011;152(12):4966-4973
ALZET Comments: Estradiol-3-sulfate; CSF/CNS; IV (femoral, saphenous); Sheep (ewe); 2ML4; Animal info (120-125 days of gestation); post op. care (ampicillin); "metabolic clearance rates (MCR) were calculated for each hormone using infusion rates and changes in plasma concentration from this (for E2SO4) and one previous (for E2) study from this laboratory using the following formula: MCR (infusion rate)/(change in plasma concentration at steady state)." pg 4968.

ALZET Comments: Estradiol-3-sulfate; Water; CSF/CNS; Sheep (pregnant); 2ML2; 7, 12 days; Controls received mp w/ vehicle; animal info (ewe); post op. care (ampicillin).

ALZET Comments: Endotoxin, LPS; Lung (intratracheal); Sheep (fetus); 2001D; 24 hours; Controls received mp w/ saline; animal info (ewe); catheter was placed in the trachea and sealed in place with surgical adhesive; good methods."To
effectively separate the fetal lung from the amniotic cavity and to allow fetal lung fluid to collect (preventing lung distention), a catheter with sealed bag (sited in the uterine space) was tightly sutured to the trachea." pg 89.


ALZET Comments: Meloxicam; interferon, recomb. ovina, tau; Ethanol; saline; Intrauterine (uterine horn); Sheep (ewe); 2ML1; 7 days; Controls received mp w/ vehicle; animal info (ewe, mature, Rambouillet); cyanoacrylate adhesive; enzyme inhibitor (prostaglandin synthase (PTGS)); vinyl catheter used (0007760); "The Alzet pump was then affixed to the mesometrial ligament between the uterine horn and oviduct by using cyanoacrylate glue... and then secured by sewing the oviduct to the perimetrium of the uterine horn, using 0 coated polyglactin suture." pg 1120; 2% ethanol used; photo of pump and catheter placement, fig. 1; "Intrauterine infusion of that amount of IFNT mimics effects of the conceptus on endometrial expression of hormone receptors and IFNT-stimulated genes during early pregnancy in ewes." pg 1120.


ALZET Comments: Endotoxin, LPS; Intrauterine; Sheep (fetus); 28 days; Teratology (preterm fetus exposed to proinflammatory stimuli in utero have a self-limiting lung injury response); Therapeutic indication (bronchopulmonary dysplasia and pulmonary hypertension).


ALZET Comments: Endotoxin, LPS; Saline; Lung (trachea); uterus (amniotic fluid); Sheep (pregnant); 2ML1; 2, 7 days; Controls received mp w/ vehicle; teratology; no stress (see pg. 77e2, 77e4); multiple pumps per animal (2); animal info (female, time-mated pregnant).


ALZET Comments: Nimesulide; DMSO; CSF/CNS; Sheep (ewe, pregnant); 2ML2; 5-7 days; Controls received mp w/ vehicle; animal info (pregnant, with singleton or twin fetuses, 127 GD); 50% DMSO used.


ALZET Comments: Interferon-tau, recomb. ovine; IV (uterine vein); Sheep (ewe); 2001D; 2ML1; 7 days; 24 hours; Controls received mp w/BSA or sham surgeries; animal info (white-faced, western range ewe); cyanoacrylate adhesive.


ALZET Comments: Nimesulide; DMSO; water; CSF/CNS; Sheep (fetus); 2ML2; 10 days; Controls received mp w/ vehicle; enzyme inhibitor (prostaglandin endoperoxide synthase-2); teratology; post op. care (ampicillin); animal info (fetal sheep, GD 126-136); 50% DMSO used; "chronic infusion of the drug intracerebroventricularly, for days, has a dramatic effect of reducing fetal HPA axis activity." (p. R1818).


ALZET Comments: Nimesulide; DMSO; water; CSF/CNS; Sheep (fetus); 2ML2; 10 days; Controls received mp w/ vehicle; enzyme inhibitor (prostaglandin endoperoxide synthase-2); teratology; post op. care (ampicillin); animal info (fetal sheep, GD 126-136); 50% DMSO used; "chronic infusion of the drug intracerebroventricularly, for days, has a dramatic effect of reducing fetal HPA axis activity." (p. R1818).


ALZET Comments: ICI 182,780; DMSO; water; CSF/CNS; Sheep (ewe); 2ML4; 6-14 days; Twin fetus control received mp w/ vehicle; animal info (fetus, twins); post op. care (ampicillin); 50% DMSO used; ICV catheter placement verified post mortem.

ALZET Comments: Rosiglitazone; Ethanol; water; SC; Sheep (ewe); 2ML4; Controls received mp w/ vehicle; animal info (adult, Merino, 123-126 days old); multiple pumps per animal (4); 7% ethanol used; endocrinology.

ALZET Comments: Canrenoate, potassium; RU 486; Saline; ethanol; Intrapericardial; Sheep (fetus); 2ML2; 10 days; Controls received mp w/ vehicle or sham surgery; no stress (see pg. 422); cardiovascular; post op. care (flunixin); animal info (female, male, Ovis aries, gd 118-123); mifepristone dissolved in 47.5% EtOH, entire quantity for delivery loaded into catheter with saline in mp (similar to the Lynch coil method); endocrinology.

P9189: J. Gersting, et al. Inhibition of brain prostaglandin endoperoxide synthase-2 prevents the preparturient increase in fetal adrenocorticotropin secretion in the sheep fetus. Endocrinology 2008;149(8):4128-4136
ALZET Comments: Nimesulide; DMSO; water; CSF/CNS; Sheep; 2ML2; 2ML4; Controls received mp w/ vehicle; post op. care (ampicillin); animal info (ewe, fetus, 119-125 d gestation); nimesulide is a COX-2 selective NSAID; incisions were sutured; 50% DMSO used.

ALZET Comments: BQ123; BQ610; BQ788; Methanol; saline; Intraovarian (corpus luteum); Sheep; 2002; 14 days; Controls received mp w/ vehicle; tissue perfusion (corpus luteum); good methods (pg. 689); post op. care (penicillin); animal info (female); pumps were primed overnight prior to surgery; vinyl catheter tubing (0007760) used; catheter stabilized to connective tissue capsule and ovarian tunica albuginea using nylon monofilament; all compounds are EDNRA type-A endothelin antagonists.

P7971: I. R. S. Sosenko, et al. IL-1 alpha causes lung inflammation and maturation by direct effects on preterm fetal lamb lungs. PEDIATRIC RESEARCH 2006;60(3):294-298
ALZET Comments: Interleukin-1, alpha, recomb. ovine; Intratracheal; Sheep (fetus); 2001D; Controls received mp w/ saline; animal info (merino, ewes + fetuses); silicone tubing used to collect lung fluid; vinyl tubing for intratracheal infusion; tissue perfusion (trachea).

ALZET Comments: Endotoxin, LPS; Intra-amniotic; Sheep (pregnant); 2ML4; 28 days; Controls received mp w/ saline; no stress (see pg. 240,242); teratology; post op. care (Penicillin); animal info (female, gestation days 80-108); mp attached to fetal forelimb using 3/0 braided silk ligature to ensure mp remained in amniotic fluid; "Intra-amniotic LPS infusion caused histological chorioamnionitis...but did not cause fetal death, preterm birth or abortion." (p. 242).

P7558: M. O. Kelleher, et al. The use of ciliary neurotrophic factor to promote recovery after peripheral nerve injury by delivering it at the site of the cell body. Acta Neurochirurgica 2006;148(1):55-61
ALZET Comments: Ciliary neurotrophic factor; CSF/CNS (intrathecal, subarachnoid space); Sheep; 2ML4; 28 days; Controls received mp w/ physiological saline; no stress (see pg. 57); half-life (pg. 59) 3 minutes in serum; peptides; post op. care (cefuroxime); median nerve transected and repaired; "The adverse cytokine-like side-effects associated with systemic administration of CNTF, namely cough, asthenia, nausea, anorexia and weight loss, aphthous stomatitis and fever were not observed in any of our animals". (pg. 57).

ALZET Comments: Endotoxin, LPS; Intra-amniotic; Sheep (pregnant); 28 days; Controls received mp w/ saline; comparison of intra-amniotic injections vs. mp; half-life (p. 204) 35 hours in amniotic fluid; teratology; animal info (gestational day 80-108, female).
ALZET Comments: Endotoxin; Saline; Intra-amniotic; Sheep (pregnant); 2ML4; 28 days; Controls received mp w/ vehicle; functionality of mp verified by amniotic fluid endotoxin levels; comparison of intra-amniotic injections vs. mp; no stress (see pg. L969); teratology.

ALZET Comments: Nicotine bitartrate; SC; Rat (pregnant); monkey (pregnant); mice (pregnant); sheep (pregnant); Rat, mice, monkey, sheep (lamb); 28 days; Half-life (p. 327) 54 min in rats, 2-2.5 hours in humans, 5-7 min. in mice; teratology; "Most studies of prenatal nicotine exposure have been performed in rats using maternal continuous subcutaneous infusions by osmotic minipumps (ALZET) of nicotine bitartrate". (p. 326).

ALZET Comments: Nicotine bitartrate; SC; Sheep (lamb); sheep (pregnant); 2ML4; 21,50 days; Pumps replaced after 28 days in pregnant sheep, after approx. 10 days in lambs; teratology.

ALZET Comments: Nicotine tartrate; Saline; SC; Sheep (lamb, neonate); 2ML4; 4 weeks; Controls received mp w/ vehicle; functionality of mp verified by nicotine plasma levels (HPLC method); cardiovascular; teratology; postnatal lambs (1 day old).

ALZET Comments: Epinephrine; Saline; Ascorbic acid; SC; Sheep (fetus); 2ML1; 4 days; Teratology.

ALZET Comments: Osteogenic protein-1; Acetate buffer; Knee (articular cavity); Sheep; Controls received mp w/ vehicle; OP-I also called BMP-7.

ALZET Comments: Endotoxin, E. coli; Saline; IP; Intratracheal; intragastric, intra-amniotic; Sheep (lamb); Sheep (fetus); 2001D; 24 hours; Controls received mp w/ vehicle; comparison of intra-amniotic injections vs. mp; immunology; teratology; description of fetal surgery (p.1063); correct pump placement confirmed by examining newborn lambs.

ALZET Comments: Endotoxin; Saline; Intra-amniotic; intratracheal; Sheep (lamb, pregnant); sheep (fetus); 2001D; 24 hours; Controls received mp w/ vehicle; teratology.

ALZET Comments: Endotoxin, E. coli; Saline; Amniotic sac; sheep (lamb, fetus); 2ML4; 4 weeks; controls received mp w/ vehicle; tissue perfusion (amniotic sac); comparison of intra-amniotic injections vs. mp; immunology; teratology; pre-natal lung development.

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Bibliography

ALZET Comments: Antigens; Mice; sheep; Immunology; ALZET pumps mentioned on pgs. 865, 866.

ALZET Comments: Thyrotropin-rel. factor; SC; Sheep; 11 days; ALZET pumps mentioned on pg. 203.

ALZET Comments: Nicotine bitartrate; SC; Sheep (pregnant); 2ML4; 49 days; Functionality of mp verified by plasma levels taken; pumps replaced once; teratology; cardiovascular; sudden infant death syndrome.

ALZET Comments: Osteogenic protein-1; Acetate buffer; knee (articular cavity); sheep; 2002; 14 days; controls received mp w/ vehicle; tissue perfusion (knee joint defect); functionality of mp verified by aspiration of residual volume after explant; stability verified by in vitro compatibility tests, ELISA, HPLC; good methods (in vitro bio-compatibility table 1 p. 106); OP-1 is also known as BMP-7. Pump was stapled to femoral shaft, PE-60 catheter tubing perfused knee joint; "Results of this study suggest that a recombinant BMP delivered via a mini-osmotic pump into the joint fluid stimulate the repair of articular cartilage defects in sheep." p. 106;

ALZET Comments: Growth hormone-rel. hormone;; Saline;; SC;; sheep (lambs);; 4 weeks;; Controls received mp w/ vehicle; comparison of various methods of administration; stability verified by plasma growth hormone & insulin-like growth factor levels; peptides;.