



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

### 1. Cattle

**Q4384:** H. M. Crawford, *et al.* Evidence for a Role of Prolactin in Mediating Effects of Photoperiod during the Dry Period. *ANIMALS* 2015;5(803-820)

**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;

**Q4316:** J. H. Bae, *et al.* Continuous ophthalmic treatment using an osmotic pump in a bull calf following surgical removal of an ocular dermoid: a case report. *VETERINARNI MEDICINA* 2015;60(282-287)

**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 37C saline; pumps removed after 4 weeks;

**Q3560:** C. A. Martel, *et al.* Continuous low-dose infusion of tumor necrosis factor alpha in adipose tissue elevates adipose tissue interleukin 10 abundance and fails to alter metabolism in lactating dairy cows. *Journal of Dairy Science* 2014;97(4897-4906)

**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;

**Q2176:** A. Contri, *et al.* Successful use of a gonadotropin-releasing hormone (GnRH) analog for the treatment of tertiary hypogonadism (GnRH deficiency) in a 5-year-old Belgian Blue bull. *VETERINARY QUARTERLY* 2012;32(1):51-54

**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.

**P9771:** J. R. Roche, *et al.* Long-Term Infusions of Ghrelin and Obestatin in Early Lactation Dairy Cows. *Journal of Dairy Science* 2008;91(12):4728-4740

**ALZET Comments:** Ghrelin, Dap<sup>3</sup>; 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.

**P6946:** J. H. Hampton, *et al.* Gonadotropin requirements for dominant follicle selection in GnRH agonist-treated cows. *REPRODUCTION* 2004;127(6):695-703

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

**P7044:** T. L. Auchtung, *et al.* Prolactin mediates photoperiodic immune enhancement: Effects of administration of exogenous prolactin on circulating concentrations, receptor expression, and immune function in steers. *Biology of Reproduction* 2004;71(6):1913-1918

**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.

**P5812:** H. Jimenez-Severiano, *et al.* Effect of chronic treatment with the gonadotrophin-releasing hormone agonist azagly-nafarelin on basal concentrations of LH in prepubertal bulls. *REPRODUCTION* 2003;125(2):225-232



**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.

**P6227:** T. L. Davis, *et al.* Chronic treatment with an agonist of gonadotropin-releasing hormone enhances luteal function in cattle. *Biology of Reproduction* 2003;69(2):398-403

**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).

**P4752:** G. E. Mann, *et al.* Effect of continuous infusion of a GnRH agonist (Buserelin™) on ovarian hormone secretion and estrous cycle length in cows. *Theriogenology* 2000;54(219-227

**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).

**P4160:** N. D. Turner, *et al.* Plasma kinetics of zeranol in steers receiving variable doses in implant or mini-osmotic pump form. *Unknown* 1999;71-75

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

**P3546:** S.-G. Roh, *et al.* Characteristics of growth hormone secretion responsiveness to growth hormone-releasing peptide-2 (GHRP-2 or KP102) in calves. *Endocrine J* 1996;43(3):291-298

**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.

**P3692:** J. G. Gong, *et al.* Suppression in the secretion of follicle-stimulating hormone and luteinizing hormone, and ovarian follicle development in heifers continuously infused with a gonadotropin-releasing hormone agonist. *Biol. Reprod* 1996;55(68-74

**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).

**P3799:** N. D. Turner, *et al.* Metabolic and hormonal changes occurring in response to level and pattern of zeranol delivered to steers. *J. Anim. Sci* 1995;73(1):65-70

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

**P2910:** J. W. Oliver, *et al.* Evaluation of a dosing method for studying ergonovine effects in cattle. *Am. J. Vet. Res* 1994;55(1):173-176

**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.

**P2924:** E. Ronayne, *et al.* Effects of continuous administration of gonadotropin-releasing hormone (GnRH) or a potent GnRH analogue on blood luteinizing hormone and testosterone concentrations in prepubertal bulls. *Domest. Anim. Endocrinol* 1993;10(3):179-189



**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.

**P3186:** F. Grasselli, *et al.* Effects of a GnRH analogue (buserelin) infused via osmotic minipumps on pituitary and ovarian activity of prepubertal heifers. *Anim. Reprod. Sci* 1993;32(153-161

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

**P3000:** J. M. Dawson, *et al.* Effect of fish-meal supplementation and B-agonist administration on adipose tissue metabolism in steers given silage. *Anim. Prod* 1993;57(397-406

**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.

**P1763:** A. Wubishet, *et al.* Preovulatory LH profiles of superovulated cows and progesterone concentrations at embryo recovery. *Theriogenology* 1991;35(2):451-457

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

**P2354:** S. L. Lutz, *et al.* Effect of constant infusion of oxytocin on luteal lifespan and oxytocin-induced release of prostaglandin F<sub>2</sub>-a in heifers. *Domest. Anim. Endocrinol* 1991;8(4):573-585

**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.

**P1947:** G. R. Newton, *et al.* Effect of bovine interferon on acute changes in body temperature and serum progesterone concentration in heifers. *J. Dairy Sci* 1990;73(3439-3448

**ALZET Comments:** Interferon- $\alpha$ 1; cattle; 2ML1; 5 days; peptides; serum IFN- $\alpha$  levels (p. 3445).

**P1707:** B. F. Kimler, *et al.* Combination of radiation therapy and intracranial bleomycin in the 9L rat brain tumor model. *Int. J. Radiat. Oncol. Biol. Phys* 1990;18(1115-1121

**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.

**P4142:** S. E. Dodson, *et al.* Ovulatory responses to continuous administration of GnRH in nine-month-old prepubertal beef heifers. *Anim. Reprod. Sci* 1990;22(271-280

**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.

**P1621:** S. C. Nickerson, *et al.* Local immunostimulation of the bovine mammary gland with interleukin-2. *J. Dairy Sci* 1989;72(1764-1773

**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.

**P1576:** Y. Naito, *et al.* Effects of continuous administration of 1,25-dihydroxyvitamin D<sub>3</sub> on plasma minerals and unoccupied colon mucosal 1,25-dihydroxyvitamin D<sub>3</sub> receptor concentrations. *J. Dairy Sci* 1989;72(2936-2941

**ALZET Comments:** Vitamin D<sub>3</sub>, 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. D<sub>3</sub> therapy for preventing p.

**P1666:** W. R. McVey, *et al.* Effects of temporary calf removal and osmotic pump delivery of gonadotropin-releasing hormone on synchronized estrus, conception to a timed artificial insemination and gonadotropin secretion in norgestomet-estradiol valerate-treated cattle. *Theriogenology* 1989;32(6):969-978

**ALZET Comments:** Luteinizing HRH; Potassium phosphate; SC; cattle; 2001; 6, 7 days; pump placed s.c. in ear.



**P1189:** G. E. Lamming, *et al.* Continuous infusion of GnRH reduces the LH response to an intravenous GnRH injection but does not inhibit endogenous LH secretion in cows. *J. Reprod. Fertil* 1989;82(237-245

**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.

**P1501:** M. J. D'Occhio, *et al.* Pituitary and ovarian responses of post-partum acyclic beef cows to continuous long-term GnRH and GnRH agonist treatment. *J. Reprod. Fertil* 1989;85(495-502

**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.

**P1492:** J. E. Wheaton, *et al.* Use of osmotic pumps for subcutaneous infusion of growth hormone-releasing factors in steers and wethers. *J. Anim. Sci* 1988;66(2876-2895

**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.

**P1373:** M. Soll, *et al.* Control of induced infestations of adult *amblyomma hebraeum* with sustained release ivermectin. *Onderspoort J. Vet. Res* 1987;54(17-20

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

**P1064:** P. J. Battista, *et al.* Biogenic amine regulation of bovine luteal progesterone production in vivo. *J. Reprod. Fertil* 1987;80(2):517-522

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

**P0858:** A. Wubishet, *et al.* Continuous subcutaneous infusion of follicle stimulating hormone as a method of superovulating dairy cows. *Theriogenology* 1986;25(6):809-812

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

**P0831:** W. von Rechenberg, *et al.* Effect of long-term infusion of an LH-releasing hormone agonist on testicular function in bulls. *J. Endocrinol* 1986;109(R9-R11

**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.

**P0867:** C. L. Skaggs, *et al.* Pulsatile or continuous infusion of luteinizing hormone-releasing hormone and hormonal concentrations in prepubertal beef heifers. *J. Anim. Sci* 1986;62(1034-1048

**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.

**P0931:** J. R. Egerton, *et al.* Prophylaxis of nematode infections in cattle with an indwelling rumino-reticular ivermectin sustained release bolus. *Vet. Parasitol* 1986;22(67-75

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

## 2. Horse

**Q3671:** J. F. Thorson, *et al.* Hypothalamic Distribution, Adenohypophyseal Receptor Expression, and Ligand Functionality of RFamide-Related Peptide 3 in the Mare During the Breeding and Nonbreeding Seasons. *Biology of Reproduction* 2014;90(2):U75-U83



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

**Q3670:** J. F. Thorson, *et al.* Pharmacologic application of native GnRH in the winter anovulatory mare, II: Accelerating the timing of pregnancy. *Theriogenology* 2014;81(4):625-631

**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;.

**Q3669:** J. F. Thorson, *et al.* Pharmacologic application of native GnRH in the winter anovulatory mare, I: Frequency of reversion to the anovulatory state following ovulation induction and cessation of treatment. *Theriogenology* 2014;81(4):579-586

**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 37C saline; used contralateral location for next pump implantation;.

**P8916:** S. M. Collins, *et al.* Continuous administration of low-dose GnRH in mares II. Pituitary and ovarian responses to uninterrupted treatment beginning near the autumnal equinox and continuing throughout the anovulatory season. *Theriogenology* 2007;68(4):673-681

**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 years); 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.

**R0209:** A. Rothen-Weinhold, *et al.* Formulation and technology aspects of controlled drug delivery in animals. *PSTT* 2000;3(7):222-231

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

**P3967:** S. E. Wheeler, *et al.* Prolactin concentrations are not suppressed in mares administered constant exogenous melatonin. *J. Equine Vet. Sci* 1998;18(1):44-47

**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.

**P2503:** J. H. Hyland. Uses of gonadotrophin releasing hormone (GnRH) and its analogues for advancing the breeding season in the mare. *Anim. Reprod. Sci* 1993;33(195-207

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

**P3241:** S. E. Becker, *et al.* Effects of gonadotropin-releasing hormone infused in a pulsatile or continuous fashion on serum gonadotropin concentrations and ovulation in the mare. *J. Anim. Sci* 1992;70(1208-1215

**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.



**P2042:** T. C. Lowis, *et al.* The effect of an extended artificial photoperiod and gonadotrophin-releasing hormone infusions in inducing fertile oestrus in anoestrous mares. *Aust. Vet. J* 1991;68(12):400-402

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

**P2350:** T. V. Little, *et al.* Ovarian and hormonal responses in anoestrous mares to a GnRH agonist: a comparison of injections with osmotic minipump delivery. *J. Reprod. Fertil* 1991;44(680-682)

**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.

**P2223:** M. S. Boyle, *et al.* The effects of continuous treatment of stallions with high levels of a potent GnRH analogue. *J. Reprod. Fertil. , Suppl* 1991;44(169-182)

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

**P1984:** C. G. V. Ainsworth, *et al.* Continuous infusion of gonadotrophin-releasing hormone (GnRH) advances the onset of oestrous cycles in thoroughbred mares on Australian studfarms. *J. Reprod. Fertil* 1991;44(235-240)

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

**P1491:** D. J. Kesler, *et al.* The effect of constant delivery of GnRH on the episodic secretion of equine LH. *J. Controlled Release* 1988;8(55-61)

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

**P1322:** J. H. Hyland, *et al.* Control of transitional anestrus in mares by infusion of gonadotropin releasing hormone. *Theriogenology* 1988;29(6):1383-1391

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

**P1131:** D. J. Kesler, *et al.* Constant delivery of GnRH to infertile or subfertile females with hypothalamic-pituitary axes that release hormones in episodic bursts. *Proc. 14th Int'l Symp. on Controlled Release of Bioactive Materials* 1987;47-48

**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; progesterin silastic implants used concomitantly with GnRH; peptides.

**P1134:** J. H. Hyland, *et al.* Infusion of gonadotrophin-releasing hormone (GnRH) induces ovulation and fertile oestrus in mares during seasonal anoestrus. *J. Reprod. Fertil* 1987;35(211-220)

**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;.

**Q4908:** MingWu, *et al.* Placental growth factor 2 — A potential therapeutic strategy for chronic myocardial ischemia. *International Journal of Cardiology* 2016;203(534-542

**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);.

**Q5376:** N. J. Hunt, *et al.* Changes in orexinergic immunoreactivity of the piglet hypothalamus and pons after exposure to chronic postnatal nicotine and intermittent hypercapnic hypoxia. *Eur J Neurosci* 2016;43(12):1612-22

**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; toxicology; Chronic postnatal nicotine and intermittent hypercapnic hypoxia (IHH); Dose (2 mg/kg/day);.

**Q5358:** A. Garcia-Alvarez, *et al.* Beta-3 adrenergic agonists reduce pulmonary vascular resistance and improve right ventricular performance in a porcine model of chronic pulmonary hypertension. *Basic Res Cardiol* 2016;111(4):49

**ALZET Comments:** BRL37344; Saline; IV (right jugular vein); pigs; 2ML2; 14 days; Controls received mp w/ vehicle; 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);.

**Q5289:** A. Vivekanandarajah, *et al.* Postnatal nicotine effects on the expression of nicotinic acetylcholine receptors in the developing piglet hippocampus and brainstem. *Int J Dev Neurosci* 2015;47(Pt B):183-91

**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; toxicology; Dose (2 mg/kg/d); Resultant plasma level (20.3 ± 2.5 ng/mL);.

**Q4474:** K. D. Katleba, *et al.* Steroid regulation of early postnatal development in the corpus epididymidis of pigs. *JOURNAL OF ENDOCRINOLOGY* 2015;225(125-134

**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;.

**Q3348:** A. D. Lassaletta, *et al.* Microvascular Notch Signaling Is Upregulated in Response to Vascular Endothelial Growth Factor and Chronic Myocardial Ischemia. *CIRCULATION JOURNAL* 2014;78(3):743-751

**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;.

**Q2769:** N. J. Hunt, *et al.* Orexin receptors in the developing piglet hypothalamus, and effects of nicotine and intermittent hypercapnic hypoxia exposures. *Brain Research* 2013;1508(1):73-82

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

**Q2620:** T. Berger, *et al.* Increased testicular Sertoli cell population induced by an estrogen receptor antagonist. *MOLECULAR AND CELLULAR ENDOCRINOLOGY* 2013;366(1):53-58

**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.



**Q2846:** A. A. Al Dayeh, *et al.* Real-time monitoring of the growth of the nasal septal cartilage and the nasofrontal suture. American Journal of Orthodontics and Dentofacial Orthopedics 2013;143(6):773-783

**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.

**R0364:** R. Gatti, *et al.* Enhanced Cough, Animal Models. Methods in Pharmacology and Toxicology 2012;1(17):343-360

**ALZET Comments:** Enalaprilat; Lisinopril; Imidapril; Saline; IP; Guinea 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;

**Q1774:** A. Bienemann, *et al.* The development of an implantable catheter system for chronic or intermittent convection-enhanced delivery. Journal of Neuroscience Methods 2012;203(2):284-291

**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.

**Q1664:** L. M. Chu, *et al.* Resveratrol supplementation abrogates pro-arteriogenic effects of intramyocardial vascular endothelial growth factor in a hypercholesterolemic swine model of chronic ischemia. Surgery 2011;150(3):390-399

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

**Q1390:** W. K. Ward, *et al.* Controlled release of dexamethasone from subcutaneously-implanted biosensors in pigs: Localized anti-inflammatory benefit without systemic effects. JOURNAL OF BIOMEDICAL MATERIALS RESEARCH PART A 2010;94A(1):280-287

**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.

**Q0190:** C. Troidl, *et al.* Calcium-dependent signalling is essential during collateral growth in the pig hind limb-ischemia model. Journal of Molecular and Cellular Cardiology 2010;49(1):142-151

**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 (cefquinome, fentanyl); ischemia (hind limb); excellent color photograph of multiple mp placement (Fig. 1); multiple pumps per animal (2).

**Q1605:** M. P. Robich, *et al.* Effects of neuropeptide Y on collateral development in a swine model of chronic myocardial ischemia. Journal of Molecular and Cellular Cardiology 2010;49(6):1022-1030

**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).

**Q0076:** D. A. Massuto, *et al.* Intrauterine Infusion of Latency-Associated Peptide (LAP) During Early Porcine Pregnancy Affects Conceptus Elongation and Placental Size. Biology of Reproduction 2010;82(3):534-542

**ALZET Comments:** PBS; LAP-RGD; LAP-RGE; Intrauterine (uterine horn); Pig (pregnant); 5 days; Controls received mp w/ vehicle; peptides; animal info (gilt, ovariohysterectomy); 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.





**Q0968:** S. Authier, *et al.* Cardiovascular Effects of Oxytocin Infusion in a Porcine Model of Myocardial Infarct. *Journal of Cardiovascular Pharmacology* 2010;55(1):74-82

**ALZET Comments:** Oxytocin; Saline; SC; Pig; 2ML4; 21 days; Controls received mp w/ vehicle; animal info (domestic, Yorkshire-Landrace, castrated, male, 21-29 kg).

**P9115:** S. Tang, *et al.* Brain-derived neurotrophic factor (BDNF) and TrkB in the piglet brainstem after post-natal nicotine and intermittent hypercapnic hypoxia. *Brain Research* 2008;1232(1):195-205

**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).

**P8833:** M. Boodhwani, *et al.* Comparison of vascular endothelial growth factor and fibroblast growth factor-2 in a swine model of endothelial dysfunction. *European Journal of Cardio-thoracic Surgery* 2008;33(4):645-650

**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.).

**R0359:** A Review of the Foreign-body Response to Subcutaneously-implanted Devices: The Role of Macrophages and Cytokines in Biofouling and Fibrosis. *Journal of Diabetes Science and Technology* 2008;2(5):768-777

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

**P8496:** Z. Y. Sun, *et al.* Masticatory mechanics of a mandibular distraction osteogenesis site: Interfragmentary micromovement. *Bone* 2007;41(2):188-196

**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 serotonergic 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).

**P8836:** T. C. Nichols, *et al.* Protease-resistant insulin-like growth factor (IGF)-Binding protein-4 inhibits IGF-I actions and neointimal expansion in a porcine model of neointimal hyperplasia. *Endocrinology* 2007;148(10):5002-5010

**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.

**P8680:** M. M. Joyce, *et al.* Pig conceptuses secrete estrogen and interferons to differentially regulate uterine STAT1 in a temporal and cell type-specific manner. *Endocrinology* 2007;148(9):4420-4431

**ALZET Comments:** Conceptus secretory proteins, porcine; Intrauterine; 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).

**P8536:** M. M. Joyce, *et al.* Pig conceptuses increase uterine interferon-regulatory factor 1 (IRF1), but restrict expression to stroma through estrogen-induced IRF2 in luminal epithelium. *Biology of Reproduction* 2007;77(2):292-302

**ALZET Comments:** Conceptus secretory proteins, porcine; Albumin, porcine serum; dye, india ink; PBS; Intrauterine (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).



**P8579:** A. Eskild-Jensen, *et al.* AT1 receptor blockade prevents interstitial and glomerular apoptosis but not fibrosis in pigs with neonatal induced partial unilateral ureteral obstruction. *Am J Physiol Renal Physiol* 2007;292(6):F1771-F1781

**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.

**P8207:** R. Machaalani, *et al.* Postnatal nicotine and/or intermittent hypercapnic hypoxia effects on apoptotic markers in the developing piglet brainstem medulla. *Neuroscience* 2006;142(1):107-117

**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).

**P7813:** D. Heffernan, *et al.* Local arginine supplementation results in sustained wound nitric oxide production and reductions in vascular endothelial growth factor expression and granulation tissue formation. *Journal of Surgical Research* 2006;133(1):46-54

**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.

**P8182:** A. Eskild-Jensen, *et al.* Glomerular and tubular function during AT1 receptor blockade in pigs with neonatal induced partial ureteropelvic obstruction. *American Journal of Physiology-Renal Physiology* 2006;292(3):921-929

**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.

**P8163:** M. Boodhwani, *et al.* High-dose atorvastatin is associated with impaired myocardial angiogenesis in response to vascular endothelial growth factor in hypercholesterolemic swine. *Journal of Thoracic and Cardiovascular Surgery* 2006;132(6):1299-1306

**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).

**P7481:** A. C. Morton, *et al.* Interleukin-1 receptor antagonist alters the response to vessel wall injury in a porcine coronary artery model. *Cardiovascular Research* 2005;68(3):493-501

**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.

**P7198:** R. Machaalani, *et al.* Effects of postnatal nicotine exposure on apoptotic markers in the developing piglet brain. *Neuroscience* 2005;132(2):325-333

**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 (Fragmin®) 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 (Fragmin®) is a low molecular weight heparin derivative.

**R0231:** S. B. Freedman, *et al.* Therapeutic angiogenesis for coronary artery disease. *Ann. Intern. Med* 2002;136(1):54-71

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



**P5198:** F. R. Dunshea, *et al.* Insulin-like growth factor-I and analogues increase growth in artificially-reared neonatal pigs. *Br. J Nutr* 2002;87(6):587-593

**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;.

**R0222:** Y. S. Ng, *et al.* Therapeutic angiogenesis for cardiovascular disease. *Current Controlled Trials in Cardiovascular Medicine* 2001;2(6):278-285

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

**P4717:** G. J. Hausman, *et al.* Expression of insulin-like growth factor binding proteins (IGFBPs) before and during the hormone sensitive period of adipose tissue development in the fetal pig. *Growth, Development, and Aging* 2000;64(51-67)

**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

**Q6917:** K. J. McCarty, *et al.* Effect of chronic melatonin supplementation during mid to late gestation on maternal uterine artery blood flow and subsequent development of male offspring in beef cattle. *J Anim Sci* 2018;96(12):5100-5111

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

**Q7174:** M. Batailler, *et al.* Pineal-dependent increase of hypothalamic neurogenesis contributes to the timing of seasonal reproduction in sheep. *Sci Rep* 2018;8(1):6188

**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;.

**Q6226:** A. J. Turner, *et al.* Tubuloglomerular feedback responses in offspring of dexamethasone-treated ewes. *Am J Physiol Renal Physiol* 2017;313(4):F864-F873

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

**Q5322:** M. Bazargan, *et al.* Limited fetal metabolism of rosiglitazone: Elimination via the maternal compartment in the pregnant ewe. *Reprod Toxicol* 2016;61(162-8)

**ALZET Comments:** Rosiglitazone Maleate; Water, Ethanol; SC; Sheep (pregnant); 2ML1; 16 days; animal info (Singleton pregnant sheep); functionality of mp verified by plasma level, amniotic 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);.

**Q4800:** K. B. a. T. E. Spencer. Biological Roles of Interferon Tau (IFNT) and Type I IFN Receptors in Elongation of the Ovine Conceptus1. *Biology of Reproduction* 2015;92(2)(47):1-10

**ALZET Comments:** oligonucleotides, 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;.



**Q4521:** G. Maneenil, *et al.* Oral, Nasal and Pharyngeal Exposure to Lipopolysaccharide Causes a Fetal Inflammatory Response in Sheep. *PLoS One* 2015;10(U1091-U1101)

**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. Eifert, *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 overnight 37C saline with catheters;

**Q4336:** K. E. Brooks, *et al.* Peroxisome Proliferator Activator Receptor Gamma (PPARG) Regulates Conceptus Elongation in Sheep. *BIOLOGY OF REPRODUCTION* 2015;92(U102-U114)

**ALZET Comments:** Oligonucleotide, antisense morpholino PPARG; 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 mesosalpinx and sutures; pumps primed in 37C sterile PBS for 24 hours.

**Q4748:** T. G. A. M. Wolfs, *et al.* Chorioamnionitis-induced fetal gut injury is mediated by direct gut exposure of inflammatory mediators or by lung inflammation. *AMERICAN JOURNAL OF PHYSIOLOGY-GASTROINTESTINAL AND LIVER PHYSIOLOGY* 2014;306(5):G382-G393

**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;

**Q3963:** J. Lee, *et al.* Intrauterine Coadministration of ERK1/2 Inhibitor U0126 Inhibits Interferon TAU Action in the Endometrium and Restores Luteolytic PGF(2alpha) Pulses in Sheep. *Biology of Reproduction* 2014;91(U177-U185)

**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;

**Q3925:** M. L. Hyde, *et al.* In vivo measurement of the absorption of strontium in the rumen and small intestine of sheep as an index of calcium absorption capacity. *British Journal of Nutrition* 2014;112(718-724)



**ALZET Comments:** Hydroxyvitamin D3, 1a-; SC; Sheep (ewe); 2002; 6 days; Animal info (merino, mature); functionality of mp verified by plasma 1,25-dihydroxycholecalciferol levels;.

**Q3494:** B. Guo, *et al.* A gene expression estimator of intramuscular fat percentage for use in both cattle and sheep. JOURNAL OF ANIMAL SCIENCE AND BIOTECHNOLOGY 2014;5(U1-U12)

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

**Q2962:** T. E. Spencer, *et al.* Conceptus-derived prostaglandins regulate gene expression in the endometrium prior to pregnancy recognition in ruminants. REPRODUCTION 2013;146(4):377-387

**ALZET Comments:** IFNT; PGE2 251; PGF2a 409; PGI2; 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 PGI2 1483ng in vehicle); vehicle (2% ethanol in saline);.

**Q3013:** K. A. Raheem, *et al.* Regulation of the hyaluronan system in ovine endometrium by ovarian steroids. REPRODUCTION 2013;145(5):491-504

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

**Q2615:** F. R. Murdoch, *et al.* Intraperitoneal medetomidine: a novel analgesic strategy for postoperative pain management in pregnant sheep. Laboratory Animals 2013;47(1):66-70

**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.";

**Q2679:** J. Lopez-Saucedo, *et al.* Superovulation, in vivo embryo recovery and cryopreservation for Aoudad (*Ammotragus lervia*) females using osmotic pumps and vitrification: a preliminary experience and its implications for conservation. TROPICAL CONSERVATION SCIENCE 2013;6(1):149-157

**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.

**Q3106:** C. O. Lemley, *et al.* Uterine Infusion of Melatonin or Melatonin Receptor Antagonist Alters Ovine Feto-Placental Hemodynamics During Midgestation. Biology of Reproduction 2013;89(2):U24-U32

**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;.

**Q3071:** X. D. Feng, *et al.* Cortisol stimulates proliferation and apoptosis in the late gestation fetal heart: differential effects of mineralocorticoid and glucocorticoid receptors. American Journal of Physiology-Regulatory Integrative and Comparative Physiology 2013;305(4):R343-R350

**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.

**Q2583:** P. Dorniak, *et al.* Cortisol and Interferon Tau Regulation of Endometrial Function and Conceptus Development in Female Sheep. Endocrinology 2013;154(2):931-941

**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.

**Q2328:** M. B. Rabaglino, *et al.* Genomics of estradiol-3-sulfate action in the ovine fetal hypothalamus. *PHYSIOLOGICAL GENOMICS* 2012;44(13):669-677

**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.

**Q2166:** F. P. Ganchou, *et al.* EFFECT OF CHRONIC ADMINISTRATION OF ENDOTHELIN RECEPTOR TYPE A ANTAGONIST (BQ-610) ON FUNCTIONAL LIFESPAN OF THE CORPUS LUTEUM IN SHEEP. *REVISTA CIENTIFICA-FACULTAD DE CIENCIAS VETERINARIAS* 2012;22(4):321-331

**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.

**Q2056:** P. Dorniak, *et al.* Endometrial HSD11B1 and Cortisol Regeneration in the Ovine Uterus: Effects of Pregnancy, Interferon Tau, and Prostaglandins. *Biology of Reproduction* 2012;86(4):U106-U115

**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).

**Q2057:** P. Dorniak, *et al.* Conceptus-Derived Prostaglandins Regulate Endometrial Function in Sheep. *Biology of Reproduction* 2012;87(1):U80-U86

**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 d 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:  $MCR = \frac{\text{infusion rate}}{\text{change in plasma concentration at steady state}}$ ." pg 4968.

**Q1399:** J. Winikor, *et al.* Complex Actions of Estradiol-3-Sulfate in Late Gestation Fetal Brain. *REPRODUCTIVE SCIENCES* 2011;18(7):654-665

**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).

**Q1159:** M. W. Kemp, *et al.* Exposure to In Utero Lipopolysaccharide Induces Inflammation in the Fetal Ovine Skin. *REPRODUCTIVE SCIENCES* 2011;18(1):88-98

**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.

**Q1040:** P. Dorniak, *et al.* Prostaglandins Regulate Conceptus Elongation and Mediate Effects of Interferon Tau on the Ovine Uterine Endometrium. *Biology of Reproduction* 2011;84(6):1119-1127

**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.

**P4397:** G. R. Polglase, *et al.* Pulmonary vascular and alveolar development in preterm lambs chronically colonized with *Ureaplasma parvum*. *Am J Physiol Lung Cell Mol Physiol* 2010;299(2):L232-41

**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);.

**Q0020:** B. W. Kramer, *et al.* Modulation of fetal inflammatory response on exposure to lipopolysaccharide by chorioamnion, lung, or gut in sheep. *American Journal of Obstetrics and Gynecology* 2010;202(1):U177-U185

**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).

**Q1175:** N. Knutson, *et al.* Interaction of PGHS-2 and glutamatergic mechanisms controlling the ovine fetal hypothalamus-pituitary-adrenal axis. *American Journal of Physiology-Regulatory Integrative and Comparative Physiology* 2010;299(1):R365-R370

**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.

**P9920:** R. C. Bott, *et al.* Uterine Vein Infusion of Interferon Tau (IFNT) Extends Luteal Life Span in Ewes. *Biology of Reproduction* 2010;82(4):725-735

**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.

**P9464:** C. E. Wood, *et al.* Blockade of PGHS-2 inhibits the hypothalamus-pituitary-adrenal axis response to cerebral hypoperfusion in the sheep fetus. *American Journal of Physiology-Regulatory Integrative and Comparative Physiology* 2009;296(6):R1813-R1819

**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).

**Q0525:** C. E. Schaub, *et al.* Blockade of Estrogen Action Upregulates Estrogen Receptor-alpha mRNA in the Fetal Brain. *Neonatology* 2009;96(2):115-119

**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.

**Q0435:** B. S. Muhlhausler, *et al.* Rosiglitazone Increases the Expression of Peroxisome Proliferator-Activated Receptor-gamma Target Genes in Adipose Tissue, Liver, and Skeletal Muscle in the Sheep Fetus in Late Gestation. *Endocrinology* 2009;150(9):4287-4294



**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.

**P9267:** S. A. Reini, *et al.* Cardiac corticosteroid receptors mediate the enlargement of the ovine fetal heart induced by chronic increases in maternal cortisol. *Journal of Endocrinology* 2008;198(2):419-427

**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.

**P9200:** M. D. Doerr, *et al.* Effects of endothelin receptor type-A and type-B antagonists on prostaglandin F<sub>2alpha</sub>-induced luteolysis of the sheep corpus luteum. *Biology of Reproduction* 2008;78(4):688-696

**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).

**P8297:** I. Nitsos, *et al.* Chronic exposure to intra-amniotic lipopolysaccharide affects the ovine fetal brain. *JOURNAL OF THE SOCIETY FOR GYNECOLOGIC INVESTIGATION* 2006;13(4):239-247

**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).

**P8191:** B. W. Kramer, *et al.* The clever fetus: Responding to inflammation to minimize lung injury. *Biology of the Neonate* 2005;88(3):202-207

**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).





**P7193:** S. G. Kallapur, *et al.* Chronic endotoxin exposure does not cause sustained structural abnormalities in the fetal sheep lungs. AMERICAN JOURNAL OF PHYSIOLOGY-LUNG CELLULAR AND MOLECULAR PHYSIOLOGY 2005;288(5):L966-L974

**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.

**P7533:** O. Hafstrom, *et al.* Cardiorespiratory effects of nicotine exposure during development. RESPIRATORY PHYSIOLOGY & NEUROBIOLOGY 2005;149(1-3):325-341

**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).

**P6473:** O. Hafstroem, *et al.* Postnatal nicotine exposure does not further compromise hypoxia defense mechanisms in prenatally nicotine-exposed lambs. Acta Paediatrica 2004;93(4):545-551

**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.

**P5622:** H. W. Sundell, *et al.* Impaired cardiorespiratory recovery after laryngeal stimulation in nicotine-exposed young lambs. PEDIATRIC RESEARCH 2003;53(1):104-112

**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).

**P5984:** Y. Kitano, *et al.* Epinephrine inhibits tracheal occlusion induced lung growth in fetal sheep. Fetal Diagnosis and Therapy 2003;18(5):333-337

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

**R0165:** M. Pecina, *et al.* Articular cartilage repair: the role of bone morphogenetic proteins. International Orthopaedics 2002;26(3):131-136

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

**P5209:** J. P. Newnham, *et al.* The fetal maturational and inflammatory responses to different routes of endotoxin infusion in sheep. Am. J. Obstet. Gynecol 2002;186(5):1062-1068

**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.

**P5440:** T. J. M. Moss, *et al.* Intra-amniotic endotoxin induces lung maturation by direct effects on the developing respiratory tract in preterm sheep. American Journal of Obstetrics and Gynecology 2002;187(4):1059-1065

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

**P5061:** T. J. M. Moss, *et al.* Early gestational intra-amniotic endotoxin - Lung function, surfactant, and morphometry. AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE 2002;165(805-811

**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.

**R0171:** S. Lofthouse. Immunological aspects of controlled antigen delivery. Advanced Drug Delivery Reviews 2002;54(6):863-870



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

**R0220:** G. Huszenicza, *et al.* Clinical endocrinology of thyroid gland function in ruminants. *Vet. Med-Czech* 2002;47(7):199-210

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

**P5886:** O. Hafstrom, *et al.* Prenatal nicotine exposure blunts the cardiorespiratory response to hypoxia in lambs. *AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE* 2002;166(12):1544-1549

**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.

**P4902:** M. Jelic, *et al.* Regeneration of articular cartilage chondral defects by osteogenic protein-1 (bone morphogenetic protein-7) in sheep. *Growth Factors* 2001;19(101-113)

**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;.

**P4771:** A. Perez-Romero, *et al.* Growth hormone response to long-term GH-RH administration in lambs. *Journal of Physiology and Biochemistry* 2000;56(2):107-115

**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;.