



References on the Administration of Human Chorionic Gonadotropin
Using ALZET® Osmotic Pumps

Q7612: M. M. O'Neil, *et al.* Differential Regulation of Gonadotropins in Response to Continuous Infusion of Native Gonadotropin-Releasing Hormone in the Winter Anovulatory Mare and Effects of Treatment With Estradiol-17beta. *J Equine Vet Sci* 2019;75(93-103

Agents: Gonadotropin-releasing Hormone **Vehicle:** Saline; **Route:** SC; **Species:** Horse; **Pump:** 2ML2; **Duration:** 14 days;
ALZET Comments: Dose (20 mg/mL); 0.9% Saline used; animal info (Female,); dependence;

Q7399: J. A. Blair, *et al.* CNS luteinizing hormone receptor activation rescues ovariectomy-related loss of spatial memory and neuronal plasticity. *Neurobiol Aging* 2019;78(111-120

Agents: Chorionic gonadotropin hormone, human **Vehicle:** CSF, artificial; **Route:** CSF/CNS (right lateral ventricle); **Species:** Mice; **Pump:** 1004; **Duration:** Not Stated;

ALZET Comments: Controls received mp w/ vehicle; animal info (Female, C57Bl/6J); behavioral testing (Morris water maze); hCG aka LHR agonist; enzyme inhibitor (Luteinizing hormone inhibitor); ALZET brain infusion kit 3 used; Brain coordinates (AP=-0.5, ML= -1.1, DV= -2.5); bilateral cannula used; Cannula placement verified via injecting fast green, observing cannula track by cryosectioning ; neurodegenerative (Spatial memory);

Q7077: C. Laldinsangi, *et al.* Expression profiling of c-kit and its impact after esiRNA silencing during gonadal development in catfish. *Gen Comp Endocrinol* 2018;266(38-51

Agents: Chorionic gonadotropin hormone, human **Vehicle:** Saline; **Route:** IP; **Species:** Fish (catfish); **Pump:** Not Stated;
ALZET Comments: Dose (5000 IU/100 ul); Controls received mp w/ vehicle;

Q5617: R. Muruganankumar, *et al.* In vivo induction of human chorionic gonadotropin by osmotic pump advances sexual maturation during pre-spawning phase in adult catfish. *Gen Comp Endocrinol* 2017;251(74-84

Agents: Gonadotrophin, human chorionic **Vehicle:** Saline; **Route:** IP; **Species:** Fish (catfish); **Pump:** 1002; **Duration:** 21 days;
ALZET Comments: Dose (5000 IU); Controls received mp w/ vehicle; animal info (21 month old); "...the sustained-release of hCG through osmotic pump has been shown to be a reliable method to induce vitellogenesis and ovulation in females" pg. 75;

Q6290: K. Kyritsi, *et al.* Knockdown of Hepatic Gonadotropin-Releasing Hormone by Vivo-Morpholino Decreases Liver Fibrosis in Multidrug Resistance Gene 2 Knockout Mice by Down-Regulation of miR-200b. *American Journal of Pathology* 2017;187(7):1551-1565

Agents: Gonadotropin-releasing hormone; cetrorelix **Vehicle:** Saline; **Route:** IP; **Species:** Mice; mice (knockout); **Duration:** 1wk
ALZET Comments: Dose (GRH: 250 ng/kg; cetrorelix: 10 mg/kg/day); animal info (12 week old FVB/NJ wild-type and Mdr2_/_ mice weighing 25-30g); Therapeutic indication (liver fibrosis);

Q4061: D. Ray, *et al.* Gonadotropin-Releasing Hormone Stimulates Biliary Proliferation by Paracrine/Autocrine Mechanisms. *American Journal of Pathology* 2015;185(1061-1072

Agents: Gonadotropin-releasing hormone **Vehicle:** Not Stated; **Route:** IP; **Species:** Rat; **Pump:** Not Stated; **Duration:** 1 week;
ALZET Comments: Controls received mp w/ saline; animal info (male, Fischer 344);

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

Agents: Gonadotropin-releasing hormone **Vehicle:** Not Stated; **Species:** Horse; **Duration:** 7 days; 12-18 days;
ALZET Comments: 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

Agents: Gonadotropin-releasing hormone **Vehicle:** Saline **Route:** SC **Species:** Horse (mare) **Pump:** 2ML2; 2ML4; **Duration:** 8w
ALZET Comments: 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

Agents: Gonadotropin-releasing hormone **Vehicle:** Saline, sterile; **Route:** SC; **Species:** Horse (mare); **Pump:** 2ML2; **Duration:** 28 days;

ALZET Comments: 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;

Q3663: T. Takeda, *et al.* Maternal Exposure to Dioxin Imprints Sexual Immaturity of the Pups through Fixing the Status of the Reduced Expression of Hypothalamic Gonadotropin-Releasing Hormone. *MOLECULAR PHARMACOLOGY* 2014;85(1):74-82

Agents: Gonadotropin-releasing hormone **Vehicle:** Saline; HCl; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2002;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, Wistar, PND63); ALZET brain infusion kit 2 used; behavioral testing (sexual behavior); stability verified by (incubation of GnRH at 37C for 2 weeks - half of GnRH remains in unchanged form pg.78); teratology; Cannula placement verified via 0.1% infusion of bromophenol blue; 0.1 M HCl

R0324: P. M. Gibbons. ADVANCES IN REPTILE CLINICAL THERAPEUTICS. *Journal of Exotic Pet Medicine* 2014;23(1):21-38

Agents: Amikacin; Florfenicol; Gonadotropin-releasing hormone **Vehicle:** Not Stated; **Species:** Snake; Iguana;

ALZET Comments: Animal info (Euttata corn snake, C scutulaus Mojave rattlesnake, green iguana); stress/adverse reaction: (see pg. 23);

Q3170: D. J. Piekarski, *et al.* Gonadotropin-inhibitory hormone reduces sexual motivation but not lordosis behavior in female Syrian hamsters (*Mesocricetus auratus*). *Hormones and Behavior* 2013;64(3):501-510

Agents: Gonadotropin-inhibitory hormone **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Hamster; **Pump:** 2002; **Duration:** 15 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (female, Syrian hamsters, adult); functionality of mp verified pg503; behavioral testing (partner preferences, vaginal scent marking, lordosis test); peptides; Cannula placement verified via angiotensin injection; GnIH aka RFamide related peptide-3; pumps primed overnight

Q5608: A. Miura, *et al.* Administration of 17 α -hydroxyprogesterone into mature male Japanese eel reduces sperm motility by decreasing potassium ion concentrations in the seminal plasma. *Aquaculture* 2013;414-415(217-223

Agents: Gonadotrophin, human chorionic **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Fish (Eel); **Pump:** 1002; **Duration:** 6 weeks;

ALZET Comments: animal info (male, 303g, freshwater) ; ""The osmotic pump releases 5 μ l of solution per day for approximately 45–50 days when the fish are maintained at a water temperature of 20 $^{\circ}$ C"" (pg 218); Therapeutic indication (sperm motility); Dose (330 IU/week);

Q2691: H. Kagawa, *et al.* Using osmotic pumps to deliver hormones to induce sexual maturation of female Japanese eels, *Anguilla japonica*. *Aquaculture* 2013;388(:):30-34

Agents: Salmon pituitary extract; gonadotrophin, human chorionic; gonadotropin-releasing hormone analogue **Vehicle:** Sodium chloride; **Route:** IP; **Species:** Fish (eel); **Pump:** 2002; **Duration:** Not Stated;

ALZET Comments: Control animals received mp w/ saline, vehicle; animal info (female, cultured); functionality of mp verified via residual volume; "osmotic pump was implanted into the peritoneal cavity of each eel after cutting an approximately 8-mm opening in the abdomen with a fine scalpel. The wound was not sutured, but healed naturally within 2 weeks." pg 31; "This study confirms the effectiveness of using osmotic pumps to induce the maturation of captive female eels..." pg 33; comparison of mp vs injections

R0333: H. Kagawa. Oogenesis in Teleost Fish. *Aquaculture* 2013;6(4):99-127

Agents: Gonadotropin releasing hormone **Vehicle:** BSA; Sodium chloride; **Route:** IP; **Species:** Fish (eel); **Pump:** 2002;

ALZET Comments: Controls received mp w/ vehicle; animal info (freshwater eels, *Anguilla* spp.); 0.1% BSA used; dose-response (pg 118); "implantation of these osmotic pumps loaded with protein hormones, instead of repeated injections of hormones, is a reliable sustained-release delivery system for inducing sexual maturation in fish." pg 119; picture of pump implantation pg 118; Dose (GnRH α 0.9, 1.8 or 3.6 μ g/day; hCG 50 IU/day; salmon pituitary extract 2.24 mg/day);



Q1551: J. R. A. Sherwin, *et al.* The Endometrial Response to Chorionic Gonadotropin Is Blunted in a Baboon Model of Endometriosis. *Endocrinology* 2010;151(10):4982-4993

Agents: Chorionic gonadotropin hormone, human recomb. **Vehicle:** Saline; **Route:** SC; intrauterine; **Species:** Monkey (baboon); **Pump:** 2ML1; **Duration:** Not Stated;

ALZET Comments: Animal info (30 mo old, spontaneous endometriosis); tissue perfusion (oviductal lumen)

Q1005: J. J. Brosens, *et al.* Proteomic analysis of endometrium from fertile and infertile patients suggests a role for apolipoprotein A-I in embryo implantation failure and endometriosis. *MOLECULAR HUMAN REPRODUCTION* 2010;16(4):273-285

Agents: Chorionic gonadotropin hormone, human recomb. **Route:** Oviductal; **Species:** Monkey (baboon); **Duration:** 5 days;

ALZET Comments: Animal info (cycling, female, 7-12 years old, 12-18 kg); tissue perfusion (oviduct)

Q0235: J. Evans, *et al.* Prokineticin 1 mediates fetal-maternal dialogue regulating endometrial leukemia inhibitory factor. *FASEB Journal* 2009;23(7):2165-2175

Agents: Gonadotrophin, human chorionic **Vehicle:** Not Stated; **Route:** Oviductal; **Species:** Monkey (baboon); **Pump:** Not Stated; **Duration:** 5 days;

ALZET Comments: Animal info (papio annubis)

P9567: G. A. Dissen, *et al.* Excessive Ovarian Production of Nerve Growth Factor Facilitates Development of Cystic Ovarian Morphology in Mice and Is a Feature of Polycystic Ovarian Syndrome in Humans. *Endocrinology* 2009;150(6):2906-2914

Agents: Gonadotrophin, human chorionic **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** 1 week;

ALZET Comments: Animal info (immature, 24-27d)

Q0835: Y. Kasuga, *et al.* Induction of sexual maturation of male Japanese eel (*Anguilla japonica*) by continuous administration of various hormones using osmotic pump. *Cybium* 2008;32(2):171-171

Agents: Chorionic gonadotropin hormone, human; salmon pituitary extract; gonadotropin-releasing hormone agonist **Vehicle:** Not Stated; **Route:** IP; **Species:** Fish (eel); **Pump:** 2006; **Duration:** 42 days;

ALZET Comments: Animal info (male, Japanese); long-term study; comparison of IP injections vs IP mp; incorrectly listed Model 2002; "HCG administration of 50 IU day⁻¹ by using OS was an efficient and reliable method for the artificial maturation of male Japanese eel, instead of the weekly injections method." pg 171

P8047: J. R. A. Sherwin, *et al.* Identification of novel genes regulated by chorionic gonadotropin in baboon endometrium during the window of implantation. *Endocrinology* 2007;148(2):618-626

Agents: Gonadotrophin, human chorionic **Vehicle:** Not Stated; **Route:** Oviductal; **Species:** Monkey (baboon); **Pump:** Not Stated; **Duration:** 5 days;

ALZET Comments: Animal info (female, adult)

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

Agents: Gonadotropin-releasing hormone **Vehicle:** Saline, physiological; **Route:** SC; **Species:** Horse; **Pump:** 2004; **Duration:** 120 days;

ALZET Comments: 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

R0259: J. M. Sykes. Techniques for drug delivery in reptiles and amphibians. *Journal of Exotic Pet Medicine* 2006;15(3):210-217

Agents: Amikacin; gonadotropin-releasing hormone **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Snake; Iguana; **Pump:** 1002; **Duration:** Not Stated;

ALZET Comments: Peptides; animal info (corn snake); review, see p. 211; ref #9; "Alzet osmotic pumps can deliver medications continuously without the need for periodic injections. They hold promise for future delivery options in reptiles." (p. 211)



P8309: T. M. Siler-Khodr, *et al.* Dose-related of GnRH II analog in the cycling rhesus monkey. *Contraception* 2006;74(2):157-164
Agents: Gonadotropin-releasing hormone II, analog **Vehicle:** PBS; **Route:** SC; **Species:** Monkey; **Pump:** Not Stated; **Duration:** 6 days;

ALZET Comments: Controls received mp w/ vehicle; dose-response (fig. 1); stress/adverse reaction: (see pg. 160) 1 control (of 13) and 1 treated (of 19) animals died of diarrhea; half-life (pg. 160) 4 hours; peptides; animal info (Rhesus, female, 5-7 yrs. old); mp primed 16 hours in PBS; Endocrinology

Q5660: A. T. Fazleabas. A Baboon Model for Simulating Pregnancy. *Methods in Molecular Medicine* 2006;121(101-110)

Agents: Gonadotrophin, chorionic **Vehicle:** Not Stated; **Route:** Oviductal lumen; **Species:** Monkey (baboon); **Pump:** 2ML1; **Duration:** 7 days;

ALZET Comments:

P7516: Z. Strakova, *et al.* In vivo infusion of interleukin-1 beta and chorionic gonadotropin induces endometrial changes that mimic early pregnancy events in the baboon. *Endocrinology* 2005;146(9):4097-4104

Agents: Gonadotrophin, human chorionic, recomb.; Interleukin-1, beta, recomb. human; Interleukin-1 receptor antagonist, recomb. human **Vehicle:** Not Stated; **Route:** Oviductal; **Species:** Monkey (baboon); **Pump:** Not Stated; **Duration:** 10 days;

ALZET Comments: Controls received no treatment; pumps replaced at day 5; animal info (female, adult)

P5846: R. V. Nemade, *et al.* Involvement of nitric oxide and the ovarian blood follicle barrier in murine follicular cyst development. *Fertility and Sterility* 2002;78(6):1301-1308

Agents: L-NAME; D-NAME; Gonadotrophin, human chorionic **Vehicle:** Water, sterile; **Route:** SC; **Species:** Mice; **Pump:** 1003D; 1007D; **Duration:** 3,4,7 days;

ALZET Comments: Functionality of mp verified by plasma levels taken; enzyme inhibitor (nitric oxide synthase) "L-NAME"; multiple pumps per animal in some groups; human choriogonadotropin is (hCG)

Q6839: C. J. P. Jones, *et al.* Ultrastructure of epithelial plaque formation and stromal cell transformation by post-ovulatory chorionic gonadotropin treatment in the baboon (*Papio anubis*). *Human Reproduction* 2001;16(12):2680-2690

Agents: Chorionic gonadotropin hormone, human; follicle stimulating hormone **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Monkey (baboon); **Pump:** Not Stated; **Duration:** 5 days;

ALZET Comments: animal info (normally cycling adult female baboon);

Q7694: C. J. Jones, *et al.* Ultrastructure of epithelial plaque formation and stromal cell transformation by post-ovulatory chorionic gonadotropin treatment in the baboon (*Papio anubis*). *Hum Reprod* 2001;16(12):2680-90

Agents: Gonadotrophin, human chorionic; Follicle stimulating hormone, recomb. **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Baboon; **Pump:** Not Stated; **Duration:** 4 days;

ALZET Comments: Controls received mp w/ FSH; animal info (adult, female); Bioactive vs heat-inactivated HCG were compared to FSH treatment. Pump usage described in other study "The HCG treatment protocol has previously been described (Christensen *et al.*, 1995; Fazleabas *et al.*, 1999) and involves infusion of HCG between days 6 and 10 post-ovulation via a cannula attached to an Alzet minipump." p.2680;

P9110: S. Banaszak, *et al.* Modulation of the action of chorionic gonadotropin in the baboon (*Papio anubis*) uterus by a progesterone receptor antagonist (ZK 137. 316). *Biology of Reproduction* 2000;63(3):820-825

Agents: Gonadotrophin, human chorionic **Vehicle:** Not Stated; **Route:** Intraovarian; **Species:** Monkey (baboon); **Pump:** Not Stated; **Duration:** 4 days;

ALZET Comments: Animal info (ovariectomized)

P4635: L. Zhang, *et al.* Estrogen mediates the protective effects of pregnancy and chorionic gonadotropin in a mouse model of vascular injury. *Arteriosclerosis, Thrombosis, and Vascular Biology* 1999;19(2059-2065)

Agents: Estradiol, 17B-; Progesterone; Gonadotrophin, human chorionic **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 14 days;

ALZET Comments: Controls received sham operation; functionality of mp verified by serum levels; replacement therapy (ovariectomy); vascular cuff injury; B human chorionic gonadotropin used;



- P4163:** A. T. Fazleabas, *et al.* Modulation of the baboon (*papio anubis*) uterine endometrium by chorionic gonadotrophin during the period of uterine receptivity. *Proc. Natl. Acad. Sci. USA* 1999;96(2543-2548
Agents: Gonadotrophin, recomb. human chorionic **Vehicle:** Not Stated; **Route:** Intraovarian (corpus luteum); **Species:** Monkey (baboon); **Pump:** 2ML1; **Duration:** 7 days;
ALZET Comments: tissue perfusion (corpus luteum)
- P1951:** G. S. Hamilton, *et al.* The superovulation of synchronous adult rats using follicle-stimulating hormone delivered by continuous infusion. *Biology of Reproduction* 1991;44(851-856
Agents: Follicle stimulating hormone; Gonadotrophin, human chorionic **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 3, 4, 7 days;
ALZET Comments: peptides
- P1859:** J. A. Carnegie. Immunolocalization of fibronectin and laminin within rat blastocysts cultured under serum-free conditions. *J. Reprod. Fertil* 1991;91(423-434
Agents: Follicle stimulating hormone; Gonadotrophin, human chorionic **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 1 day;
ALZET Comments: pumps removed and reimplanted into different animals
- P1745:** P. E. Patton, *et al.* The effect of intraluteal infusion of deglycosylated human chorionic gonadotropin on the corpus luteum in rhesus monkeys. *J. Clin. Endocrinol. Metab* 1990;70(4):1213-1218
Agents: Gonadotrophin, human chorionic **Vehicle:** Albumin, bovine serum; Saline; **Route:** Intraovarian (corpus luteum); **Species:** Monkey; **Pump:** 2ML1; **Duration:** 7 days;
ALZET Comments: Tissue perfusion (corpus luteum); functionality of mp verified by sectioning
- P3801:** M.-C. Leveille, *et al.* Preimplantation embryo development and serum steroid levels in immature rats induced to ovulate or superovulate with pregnant mares' serum gonadotropin injection of follicle-stimulating hormone infusions. *Gamete Res* 1989;23(127-138
Agents: Follicle stimulating hormone, porcine; Gonadotrophin, human chorionic **Vehicle:** Saline, sterile; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 72 hours;
ALZET Comments: comparison of sc PMSG injections vs. mp; peptides
- P0520:** F. Garza, *et al.* Luteinizing hormone increases the number of ova shed in the cyclic hamster and guinea-pig. *J. Endocrinol* 1984;101(289-298
Agents: Gonadotrophin, pregnant mare serum; Luteinizing hormone; Follicle stimulating hormone, ovine; Gonadotrophin, human chorionic **Vehicle:** Albumin, bovine serum; PBS; **Route:** SC; **Species:** Guinea pig; hamster; mice; Rat; **Pump:** 2001; **Duration:** 2, 5 days;
ALZET Comments: Comparison of agents effects; replacement therapy (hypophysectomy); agents admin. singly; peptides; bovine, ovine, & human LH used