



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

### 1. Baboon

**Q5859:** P. B. Higgins, *et al.* Central GIP signaling stimulates peripheral GIP release and promotes insulin and pancreatic polypeptide secretion in nonhuman primates. *Am J Physiol Endocrinol Metab* 2016;311(4):E661-E670

**ALZET Comments:** CSF, artificial; CSF/CNS (ventricle); Monkey (baboon); 14 days, 2 weeks; Controls received mp w/ vehicle; animal info (all animals were housed in social groups in outdoor enclosures) ; ALZET pumps used to maintain the patency of the ventricular infusion line and cannula before connection to the syringe pump infusion system.

**Q1517:** N. S. Sunderland, *et al.* Tumor necrosis factor alpha induces a model of preeclampsia in pregnant baboons (*Papio hamadryas*). *Cytokine* 2011;56(2):192-199

**ALZET Comments:** Tumor necrosis factor-alpha; PBS; IV (femoral); Monkey (pregnant, baboon); 2ML4; Controls received mp w/ vehicle; animal info (female, baboon, *Papio hamadryas*).

**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

**ALZET Comments:** Chorionic gonadotropin hormone, human recomb.; Saline; SC; intrauterine; Monkey (baboon); 2ML1; Animal info (30 mo old, spontaneous endometriosis); tissue perfusion (oviductal lumen).

**Q0042:** Y. Fujimura, *et al.* Quantification of peripheral benzodiazepine receptors in human brain with 18F-PBR06. *Journal of Cerebral Blood Flow and Metabolism* 2010;29(S360-S375)

**ALZET Comments:** Nicotine; Monkey (baboon); 6 months; Long-term study; animal info (*Papio anubis*); functionality of mp verified by plasma nicotine concentration; pumps replaced at 15 days, 2, 3, 4 and 5 months.

**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

**ALZET Comments:** Chorionic gonadotropin hormone, human recomb.; Oviductal; Monkey (baboon); 5 days; 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

**ALZET Comments:** Gonadotrophin, human chorionic; Oviductal; Monkey (baboon); 5 days; Animal info (*papio anubis*).

**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

**ALZET Comments:** Gonadotrophin, human chorionic; Oviductal; Monkey (baboon); 5 days; Animal info (female, adult).

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

**ALZET Comments:** Gonadotrophin, chorionic; Oviductal lumen; Monkey (baboon); 2ML1; 7 days;

**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

**ALZET Comments:** Gonadotrophin, human chorionic, recomb.; interleukin-1, beta, recomb. human; interleukin-1 receptor antagonist, recomb. human; Oviductal; Monkey (baboon); 10 days; Controls received no treatment; pumps replaced at day 5; animal info (female, adult).

**P5475:** R. E. Shade, *et al.* Synergy between angiotensin and aldosterone in evoking sodium appetite in baboons. *American Journal of Physiology-Regulatory Integrative and Comparative Physiology* 2002;283(5):R1070-R1078



**ALZET Comments:** Angiotensin II; aldosterone; Saline; ethanol; SC; CSF/CNS; Monkey (baboon); 49 days; Controls received mp w/ vehicle; long-term study, pumps replaced every 7 days (6 times); angiotensin II diluted in saline and infused ICV; aldosterone diluted in 10% ethanol in saline and infused SC; some animals implanted w/ 2 pumps.

**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

**ALZET Comments:** Chorionic gonadotropin hormone, human; follicle stimulating hormone; Monkey (baboon); 5 days; animal info (normally cycling adult female baboon);

**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). *Biol. Reprod* 2000;63(3):820-825

**ALZET Comments:** Gonadotrophin, human chorionic; Intraovarian; Monkey (baboon); 4 days; Animal info (ovariectomized).

**P5297:** C. E. Hart, *et al.* PDGFbeta receptor blockade inhibits intimal hyperplasia in the baboon. *Circulation* 1999;99(4):564-569

**ALZET Comments:** Heparin, porcine; Saline; IV (femoral); Monkey (baboon); 4, 28, 56 days; Controls received mp w/ vehicle; pumps replaced after 28 days; cardiovascular; multiple pumps per animal (2); long-term study.

**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(25):2543-2548

**ALZET Comments:** Gonadotrophin, recomb. human chorionic; Intraovarian (corpus luteum); Monkey (baboon); 2ML1; 7 days; tissue perfusion (corpus luteum).

**P4060:** J. R. Blair-West, *et al.* Evidence that brain angiotensin II is involved in both thirst and sodium appetite in baboons. *Am. J. Physiol. (Regulatory Integrative Comp. Physiol. 44)* 1998;275(R1639-R1646)

**ALZET Comments:** Angiotensin II; Losartan potassium; ZD-7155; Ethanol; CSF, artificial;; SC; CSF/CNS;; Monkey (baboon); 2ML1; 2ML2; 2ML4; no duration posted; controls received mp w/vehicle; amoxicillin and buprenorphine given post-operatively; good methods; aCSF delivered during 1-2 week surgical recovery period; vehicle and compound-filled pumps were alternated; some pumps were filled with peptide and antagonist; ZD-7155 is an AT1 receptor antagonist; peptides; antihypertensive.

**P1880:** I. S. Kang, *et al.* Effect of treatment with gonadotropin-releasing hormone analogues on pregnancy outcome in the baboon. *Fertil. Steril* 1989;52(5):846-853

**ALZET Comments:** Luteinizing HRH antagonist; Water; SC; Monkey (baboon, pregnant); 7 days; no comment posted.

**P1465:** S. Brailowsky, *et al.* Effects of localized, chronic GABA infusions into different cortical areas of the photosensitive baboon, *Papio papio*. *Electroencephalogr. Clin. Neurophysiol* 1989;72(1):147-156

**ALZET Comments:** Aminobutyric acid, Y-; Saline; CSF/CNS; Monkey (baboon); 2ML1; 7 days; functionality of mp verified by removing and opening; pumps replaced once w/ saline-filled mp.

**P1023:** S. Brailowsky, *et al.* Epileptogenic  $\gamma$ -aminobutyric acid-withdrawal syndrome after chronic, intracortical infusion in baboons. *Neurosci. Lett* 1987;74(75-80)

**ALZET Comments:** Aminobutyric acid, Y-; Saline; CSF/CNS (frontal cortex); Monkey (baboon); 2ML1; no duration posted; controls received mp w/vehicle; mp connected to intracerebral cannula; agent filled mp replaced after 7 days with saline filled mp; tissue perfusion (frontal cortex).

**P0035:** N. Hagino, *et al.* Effect of D-Trp6-LH-RH on the pituitary-gonadal axis during the luteal phase in the baboon. *Acta Endocrinol* 1979;91(2):217-223

**ALZET Comments:** Luteinizing HRH agonist; Saline; SC; Monkey (baboon); 7 days; peptides.

## 2. Marmoset



**Q2105:** K. Kitamura, *et al.* Human Hepatocyte Growth Factor Promotes Functional Recovery in Primates after Spinal Cord Injury. PLoS One 2011;6(11):U83-U95

**ALZET Comments:** Hepatocyte growth factor, recomb. human; PBS; CSF/CNS (intrathecal); Monkey (marmoset); 2004; 4 weeks; Controls received mp w/ vehicle; animal info (adult, female, common, 295-350 g); ALZET rat intrathecal catheter used.

**Q0075:** K. A. Stockwell, *et al.* Continuous rotigotine administration reduces dyskinesia resulting from pulsatile treatment with rotigotine or L-DOPA in MPTP-treated common marmosets. Experimental Neurology 2010;221(1):79-85

**ALZET Comments:** Rotigotine hydrochloride; DMSO; water, sterile; SC; Marmoset; 2004; 28 days; Comparison of SC injections or PO administration vs. SC mp; animal info (adult, common, male, female, 2-7 years old, 350-500); 50% DMSO used; "These data suggest that dyskinesia induced by pulsatile drug treatment may be improved by switching to continuous rotigotine delivery." pg. 79; "...this study highlights the potential benefits of continuous drug delivery." pg 84.

**Q0515:** T. E. Ziegler, *et al.* Prolactin's mediative role in male parenting in parentally experienced marmosets (*Callithrix jacchus*). Hormones and Behavior 2009;56(4):436-443

**ALZET Comments:** Prolactin, human, recomb.; Glycerol; NaHCO<sub>3</sub>; NaCl; SC; Monkey (marmoset); 2004; Controls received mp w/ saline; animal info (2.5-9 yrs old, male, parentally experienced); "... these pellets (from Innovative Research of America) did not raise the level of prolactin in the blood over the level of our control parentally experienced fathers... Therefore, we chose to use the osmotic minipump (Alzet, CA) for our test males." pg 439; "The position of the pumps on the lower area of a male's back precluded any interference with infant carrying since infant carrying occurs nearer the neck" pg 439; comparison of pellets vs mp.

**Q0449:** K. A. Stockwell, *et al.* Continuous administration of rotigotine to MPTP-treated common marmosets enhances anti-parkinsonian activity and reduces dyskinesia induction. Experimental Neurology 2009;219(2):533-542

**ALZET Comments:** Rotigotine; Saline, sterile; SC; Monkey (marmoset); 2004; 58 days; Controls received mp w/ vehicle; animal info (adult common, male, female, 354 g); comparison of sc injections vs. mp; neurodegenerative (Parkinson's disease); post op. care (Rimadyl, Synulox); "pumps were removed... and replaced with new minipumps implanted into the opposite flank." pg 534; "These results demonstrate that the anti-parkinsonian benefits associated with a continuous infusion of rotigotine were more sustained compared to pulsatile rotigotine or L-DOPA treatment..." pg 541; long-term study.

**P8082:** R. J. Hornby, *et al.* Multiple vaccine and pyridostigmine bromide interactions in the common marmoset *Callithrix jacchus*: Immunological and endocrinological effects. INTERNATIONAL IMMUNOPHARMACOLOGY 2006;6(12):1765-1779

**ALZET Comments:** Pyridostigmine bromide; Saline, sterile isotonic; SC; Marmoset; 2004; 28 days; Controls received mp w/ vehicle; no stress (see p.1776); immunology; animal info (female, vasectomized male, 331-565g. 2-5.5 yrs. old); mp primed 40 hours.

**P8143:** G. D. Griffiths, *et al.* Development of methods to measure humoral immune responses against selected antigens in the common marmoset (*Callithrix jacchus*) and the effect of pyridostigmine bromide administration. INTERNATIONAL IMMUNOPHARMACOLOGY 2006;6(12):1755-1764

**ALZET Comments:** Pyridostigmine bromide; Saline, sterile isotonic; SC; Marmoset; 28 days; Controls received mp w/ vehicle; no stress (see p.1759,1762); immunology; animal info (male, female, 300-500g.); mp primed 40 hours; "delivery by pump ensured the animals would receive an appropriate dose of the drug over the desired time period.", oral delivery "would introduce unacceptable stress into the experiment and presentation in food was discounted because of difficulties in estimating the dose administered." (p.1757).

**P6741:** H. P. M. Van Helden, *et al.* Low levels of Sarin affect the EEG in marmoset monkeys: a pilot study. Journal of Applied Toxicology 2004;24(6):475-483

**ALZET Comments:** Pyridostigmine bromide; Propylene glycol: ethanol; acidic acid, glacial; water, distilled; SC; Marmoset; 2002; Controls received mp w/ vehicle; toxicology; sarin vapor.



- P6551:** H. P. M. Van Helden, *et al.* Low-level exposure of guinea pigs and marmosets to sarin vapour in air: Lowest-observable-adverse-effect level (LOAEL) for miosis. *Journal of Applied Toxicology* 2004;24(1):59-68  
**ALZET Comments:** Pyridostigmine bromide; Propylene glycol; ethanol; water; acetic acid, glacial; SC; Guinea pig; marmoset; 2002; 4 days; Controls received mp w/ vehicle; toxicology.
- P5707:** N. G. Muggleton, *et al.* Assessment of a combination of physostigmine and scopolamine as pretreatment against the behavioral effects of organophosphates in the common marmoset (*Callithrix jacchus*). *Psychopharmacology* 2003;166(3):212-220  
**ALZET Comments:** Physostigmine salicylate; scopolamine hydrobromide; Saline; SC; Monkey (marmoset); 2002; 14 days; Controls received mp w/ vehicle; behavioral testing; agents infused via same pumps; toxicology.
- P6348:** J. W. B. Marshall, *et al.* Assessment of cognitive and motor deficits in a marmoset model of stroke. *ILAR JOURNAL* 2003;44(2):153-160  
**ALZET Comments:** Clomethiazole; AR-R15896AR; NXY-059; Saline; SC; Monkey (marmoset); 2001D; 48 hours; Controls received mp w/ vehicle; pumps replaced every 24 hours; ischemia (cerebral); neuroprotective; post op. care (incubator); behavioral study.
- P6150:** J. W. B. Marshall, *et al.* Functional and histological evidence for the protective effect of NXY-059 in a primate model of stroke when given 4 hours after occlusion. *Stroke* 2003;34(9):2228-2233  
**ALZET Comments:** NXY-059; Saline; IV; Monkey (marmoset); 2001D; 48 hours; Controls received mp w/ vehicle; NXY-059 plasma levels taken; pumps replaced every 24 hours; post op. care (flunixin meglumine); behavior study; neuroprotective; ischemia (cerebral).
- P4851:** J. W. B. Marshall, *et al.* NXY-059, a free radical-trapping agent, substantially lessens the functional disability resulting from cerebral ischemia in a primate species. *Stroke* 2001;32(190-198)  
**ALZET Comments:** NXY-059; Saline; SC; monkey (marmoset); 2001D; 48 hours; controls received mp w/ vehicle; functionality of mp verified by plasma drug levels; pumps replaced after 24 hours; NXY-059 is a novel free-radical trapping agent; multiple pumps per animal (2) used simultaneously; ischemia (cerebral).
- P8576:** P. Villoslada, *et al.* Human Nerve Growth Factor Protects Common Marmosets against Autoimmune Encephalomyelitis by Switching the Balance of T Helper Cell Type 1 and 2 Cytokines within the Central Nervous System. *Journal of Experimental Medicine* 2000;191(10):1799-1806  
**ALZET Comments:** Saline; nerve growth factor, recomb. human; cytochrome C; CSF/CNS; Marmoset; 2004; 35-42 days; Controls received mp w/ cytochrome C; functionality of mp verified by CSF levels of rhNGF; pumps replaced after 7-14 days of saline; immunology; ALZET brain infusion kit used; peptides; animal info (*callithrix jacchus*); "we chose to use an intracranial route to ensure accurate delivery of the drug into the CNS. This resulted in sustained elevated concentrations of rhNGF in the CSF of all rhNGF-treated animals." (p. 1801).
- P4292:** J. W. B. Marshall, *et al.* Functional benefit from clomethiazole treatment after focal cerebral ischemia in a nonhuman primate species. *Experimental Neurology* 1999;156(121-129)  
**ALZET Comments:** Clomethiazole;; IP;; monkey (marmoset);; 2001D;; 24 hours;; clomethiazole is neuroprotective in rodents following ischemia; ischemia (cerebral).
- P1622:** J. M. Wood, *et al.* Biochemical effects of prolonged renin inhibition in marmosets. *J. Hypertens* 1989;7(8):615-618  
**ALZET Comments:** CGP-29287; Methylcellulose; Saline; IP; monkey (marmoset); 2002; 7 days; dose-response; CGP-29287 is a renin inhibitor.
- P1292:** J. M. Wood, *et al.* Sustained reduction in blood pressure during chronic administration of a renin inhibitor to normotensive marmosets. *J. Cardiovasc. Pharmacol* 1987;10(7):S96-S98  
**ALZET Comments:** CGP-29287; IP; monkey (marmoset); 2002; 14 days; dose-response; only high dose affected bp; mp removed after delivery.



### 3. Monkey

**Q8626:** C. Lecours, *et al.* Levodopa partially rescues microglial numerical, morphological, and phagolysosomal alterations in a monkey model of Parkinson's disease. *Brain Behav Immun* 2020;90(81-96

**Agents:** 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine **Vehicle:** Saline; **Route:** SC; **Species:** Monkey; **Pump:** Not stated;

**Duration:** 2 weeks;

**ALZET Comments:** Dose (0.5 mg/day); animal info (adult female monkeys, 4 to 11 years old, 2.4 to 4.6 kg);

1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine aka MPTP; neurodegenerative (Parkinson's Disease);

**Q8477:** R. P. Gale, *et al.* Use of molecularly-cloned haematopoietic growth factors in persons exposed to acute high-dose, high-dose rate whole-body ionizing radiations. *Blood Rev* 2020;100690

**Agents:** Granulocyte Macrophage Colony-Stimulating Factor, Recombinant Human **Vehicle:** Not stated; **Route:** SC; **Species:** Monkey; **Pump:** Not stated; **Duration:** 7 days;

**ALZET Comments:** Recombinant Human Granulocyte Macrophage Colony-Stimulating Factor aka rhG/M-CSF; dependence;

**Q8292:** H. Nakagawa, *et al.* Treatment With the Neutralizing Antibody Against Repulsive Guidance Molecule-a Promotes Recovery From Impaired Manual Dexterity in a Primate Model of Spinal Cord Injury. *Cereb Cortex* 2019;29(2):561-572

**Agents:** Angti-RGMA antibody **Vehicle:** Saline; **Route:** CNS/CSF; **Species:** Monkey; **Pump:** 2ML4; **Duration:** 4 weeks;

**ALZET Comments:** Dose (50 ug/kg/day); animal info (Rhesus, 3-5 years old, 2.8-5.4 kg); spinal cord injury;

**R0391:** T. Coutant, *et al.* Advances in Therapeutics and Delayed Drug Release. *Vet Clin North Am Exot Anim Pract* 2019;22(3):501-520

**Agents:** Florfenicol voriconazole; fentanyl; amikacin **Vehicle:** Not Stated; **Route:** SC; in vitro; **Species:** Rat; Snake (corn, rattle); Iguana; Cat; Hamster; Gelada; Pudu; Wallaby; Monkey; Quail; Hen; **Pump:** Not Stated; **Duration:** Not Stated;

**ALZET Comments:** "animal info (Eastern massasauga rattlesnakes (*Sistrurus catenatus*); timber rattlesnake (*Crotalus horridus*); pudu (*Pudu pudu*); wallaby (*Macropus rufogriseus*); iguanas (*Iguana iguana*); Mojave rattlesnakes (*Crotalus scutulatus*); corn snakes (*Elaphe guttata guttata*); Japanese quails (*Coturnix coturnix japonica*); hens (*Gallus domesticus*)); " Finally, the use of intracoelomic osmotic pumps was reported in iguanas (*Iguana iguana*) in a study of reproductive behavior.<sup>26</sup> No complication due

to the pump placement was reported in that study." pg. 508; Advantages: Can be extracted in case of drug overdose or toxicity, Is not altered by its biological environment, Release the drug at a constant rate, Low cost, Commercially available, Release rate and operation time can be chosen; Drawbacks: Necessitate 2 light surgical procedures under anesthesia to be

implanted and explanted, Can sometimes migrate in unwanted location (especially if implanted accidentally in air sacs during intracoelomic implantation) "

**Q7031:** M. Fregosi, *et al.* Changes of motor corticobulbar projections following different lesion types affecting the central nervous system in adult macaque monkeys. *European Journal of Neuroscience* 2018;48(4):2050-2070

**Agents:** Antibody, anti-Nogo-A **Vehicle:** Not Stated; **Route:** CSF/CNS (Intrathecal), SC; **Species:** Monkey (*Macaca fascicularis*); **Pump:** 2ML2; **Duration:** 4 weeks;

**ALZET Comments:** Dose (3 mg/ml); One pump administered the treatment intrathecally to the cervical spinal cord, whereas the other pump delivered the antibody close to the lesioned site in M1 below the dura; Multiple pumps per animal (2);