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

Q5012: J. K. a. M.-S. Kim. The Evaluation of Osmotic Pump as Glaucoma Drug Delivery System in Normal Dogs. Pakistan Veterinary Journal 2015;35(2):239-241
ALZET Comments: Dorzolamide; timolol; SC (Eye); Dog; 2004; 24 days; Controls received no mp; Controls received no mp; "Osmotic pump, as one of the constant drug delivery systems, can be placed in the subcutaneous pocket with minimal surgical skills, and continuously
administer the wanted drugs into the target regions" pg 241; picture of implantation pg 240; Interesting (use of pump in veterinary application);.

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;.

Q0959: Z. Aktas*, et al.* Matrix metalloproteinase-9 expression in retinal ganglion cell layer and effect of topically applied brimonidine tartrate 0.2% therapy on this expression in an endothelin-1-induced optic nerve ischemia model. International Ophthalmology 2010;30(3):253-259
ALZET Comments: Endothelin-1, human, porcine; Eye (optic nerve); Rabbit; 2002; 2 weeks; Animal info (New Zealand, albino); vinyl tubing used; image of pump and tubing through the upper eyelid (Fig.1, Fig 2b);.

P7650: K. Okabe*, et al.* Effect of benzalkonium chloride on transscleral drug delivery. INVESTIGATIVE OPHTHALMOLOGY & VISUAL SCIENCE 2005;46(703-708
ALZET Comments: Betamethasone, phosphate 21-; benzalkonium chloride; Eye (intrasclera); Rabbit; 1002; 1 week; Animal info (albino, 2.0-2.5 kg); diagram of pump position and cannulation (p.704); silicone tube used to connect mp.

P6277: C. A. Leamey*, et al.* Disruption of Retinogeniculate Pattern Formation by Inhibition of Soluble Guanylyl Cyclase. The Journal of Neuroscience 2004;21(11):3871-3880
ALZET Comments: KT5823; Oxadiazolo quinoxalin-1-one, 1H-[1,2,4], [4,3-a]; DMSO; saline; Eye; Ferret; 1-2 weeks; Controls received mp w/ vehicle; dose-response (p.3875); enzyme inhibitor (guanylyl cyclase; protein Kinase G); DMSO at 50%; OD1; KT5832 added to vehicle control.

P6550: B. C. Chauhan*, et al.* Model of endothelin-1 - Induced chronic optic neuropathy in rat. INVESTIGATIVE OPHTHALMOLOGY & VISUAL SCIENCE 2004;45(1):144-152
ALZET Comments: Endothelin-1; Balanced salt solution; Eye (retrobulbar optic nerve); Rat; 2004; 21,42,84 days; Controls received mp w/ vehicle and fellow eye w/ no treatment; dose-response (fig.5); long-term study; pumps replaced every 28 days; peptides; post op. care (rentamicin, buprenex).

P7940: J. Ambati*, et al.* Transscleral delivery of bioactive protein to the choroid and retina. Invest Ophthalmol. Vis. Sci 2000;41(5):1186-1191
ALZET Comments: Immunoglobulin G, FITC-, rabbit; antibody, monoclonal mouse anti-ICAM-1; immunoglobulin, mouse IgG2a; Eye (superotemporal scleral surface, transscleral); Rabbit; 2001D; 2ML4; 3,5,13,20,28 days; 24 hours; Controls received mp w/ control Ab; functionality of mp verified by fluorescence in occular tissues and plasma mAb levels; stability verified by efficacy experiments, FITC linkage timing; half-life (p. 1188), 3 days; ALZET brain infusion kit used; animal info (dutch-belted, pigmented); "We have developed a minimally invasive transscleral drug delivery modality that can deliver

therapeutic concentrations of bioactive proteins to the choroid and retina without significant systemic absorption or tissue damage." (P. 1186-87).

P4259: D. B. Clarke*, et al.* Prolonged administration of NT-4/5 fails to rescue most axotomized retinal ganglion cells in adult rats. Vision Research 1998;38(1517-1524
ALZET Comments: NT-4/5; PBS; Eye (vitreous chamber); Rat; 2002; 14,28 days; controls received mp w/vehicle; comparison of injections vs. mp; peptides.

P3483: H. Sawai*, et al.* Brain-derived neurotrophic factor and neurotrophin-4/5 stimulate growth of axonal branches from regenerating retinal ganglion cells. J. Neurosci 1996;16(12):3887-3894
ALZET Comments: NT-4/5; PBS; Eye (vitreous chamber); Rat; 2002; 14 days; comparison of intraocular injections vs. mp.

P2852: T. Sakamoto*, et al.* Effect of intravitreal administration of indomethacin on experimental subretinal neovascularization in the subhuman primate. Arch Ophthalmol 1995;113(222-226
ALZET Comments: Indomethacin; GBR buffer; Cyclodextrin, B-; Eye (vitreous); monkey; 2ML2; 14 days; control eyes received mp with vehicles; enzyme inhibitor; indomethacin is a cyclooxygenase (COX) inhibitor; detailed description of vitreal cannula implantation; empty pump implanted at time of cannula implantation to allow 1-month recovery period; beta-cyclodextrin used as a carrier molecule; some monkeys served both as control and drug treatment group (different treatment in each eye); a vitreous opacity appeared in some eyes during infusion but disappeared after the pump was disconnected.

P2490: G. Soubrane*, et al.* Basic fibroblast growth factor experimentally induced choroidal angiogenesis in the minipig. Curr. Eye Res 1994;13(183-195
ALZET Comments: Fibroblast growth factor; PBS; Eye (suprachoroidal space); Pig (mini); 2001; no duration posted; stability verified by biological activity assay (p 185-6) after 4 days; peptides; spatial distribution of exogenous FGF examined (p 188); basic FGF used.

R0095: D. C. Metrikin*, et al.* Intravitreal drug administration with depot devices. Curr. Opin. Ophthalm 1994;5(111):21-29
ALZET Comments: Eye; no duration posted; comparison of drug delivery systems vs. mp; tissue perfusion (p. 26).

P1978: S. Lerman*, et al.* Miniosmotic pumps for liposomal drug delivery. Liposome Technol 1993;1(429-438
ALZET Comments: Liposomes; Eye (lens); rabbit; 2ML1; no duration posted; pulsed delivery described; detailed surgical methods.

P2491: B. K. Colasanti. A comparison of the ocular and central effects of delta-9 tetrahydrocannabinol and cannabigerol. J. Ocular Pharmacol 1990;6(4):259-269
ALZET Comments: Cannabinol, delta-9-tetrahydro-; Cannabigerol; PEG 400; Eye (cornea); cat; 9 days; controls received mp w/ vehicle; dose-response (p.262); unilateral delivery.

P1552: P. J. Linser*, et al.* A role for carbonic anhydrase in early eye morphogenesis. Invest. Ophthalmol. Vis. Sci 1989;30(4):783-785
ALZET Comments: Methazolamide; Tyrode's solution; Eye; in vitro (egg, eye); Bird (chicken embryo); 2001; 3 days; comparison of topical dosing vs. mp infusion; tissue perfusion.

P1722: S. Lerman. Test models to determine potential ocular drug induced side effects. Lens Eye Toxic. Res 1989;6(1/2):1-36
ALZET Comments: 8-MOP; Chromophore; Sorbinil; Liposomes; Radio-isotopes; Eye (lens); rabbit; 2ML1; 7 days; tissue perfusion (ocular lens); liposome-encapsulated agents.

P4548: D. W. Sretavan*, et al.* Modification of retinal ganglion cell axon morphology by prenatal infusion of tetrodotoxin. Nature 1988;336(1):468-471
ALZET Comments: Tetrodotoxin;; Citrate buffer;; Eye;; cat (fetus);; 2002;; 16 days;; teratology;.

P1112: J. M. Megaw*, et al.* Application of miniosmotic pumps for liposomal drug delivery to the ocular lens. Invest. Ophthalmol. Vis. Sci 1987;28(1429-1433
ALZET Comments: Methoxypsoralen, 8-; Radio-isotopes; Sorbinil; 3H tracer; Eye; rabbit; 2ML1; 7 days; mp connected to PE 60 tubing in eye; tissue perfusion.

P0665: K. Miki*, et al.* An indwelling cannula system for the primate eye. J. Neurosci. Methods 1985;13(3/4):267-279
ALZET Comments: Leucine; Radio-isotopes; 3H tracer; Balanced salt solution; Eye (vitreous); monkey; 2001; 1 week; comparison of 3H-Leucine injec vs. mp infusion; stress/no stress p. 276; surgical methods; tissue perfusion.

P0644: K. Miki*, et al.* Intraocular cannula for continuous, chronic drug delivery: histopathologic observations and function. Arch. Ophthalmol 1985;103(5):712-717
ALZET Comments: Fluorescein sodium; Leucine; Radio-isotopes; 3H tracer; Eye (vitreous); rabbit; 2001; 1 week; agents admin. in combination; tissue perfusion.

P0691: D. M. Maurice*, et al.* The absence of corneal toxicity with low-level topical anesthesia. Am. J. Ophthalmol 1985;93(6):691-696
ALZET Comments: Proparacaine; Eye (corneal stroma); rabbit; 1701; no duration posted; tissue perfusion (central stroma of cornea); comparison of intermittent admin of eye drops vs. mp infusion - analagous to injection/ infusion comparison; mp primed overnight in saline.

P1511: B. K. Colasanti. Intraocular pressure, ocular toxicity and neurotoxicity in response to 11-hydroxy-delta9-tetrahydrocannabinol and 1-nantradol. J. Ocular Pharmacol 1985;1(2):123-135
ALZET Comments: Cannabinol, tetrahydro-; Nantradol, 1-; PEG 400; Eye; cat; 2001; 9 days; topical application; tissue perfusion.

P0561: K. Miki*, et al.* A method for chronic drug infusion into the eye. Jpn. J. Ophthalmol 1984;28(2):140-146
ALZET Comments: Fluorescein sodium; Saline; Eye; rabbit; 2001; 2002; no duration posted; detailed account of materials, surgical procedures & complications; stress/adverse reaction (infection at implantation site) see p. 144-145; tissue perfusion.

P0466: B. K. Colasanti*, et al.* Intraocular pressure, ocular toxicity and neurotoxicity after administration of delta9-tetrahydrocannabinol or cannabichromene. Exp. Eye Res 1984;38(63-71
ALZET Comments: Cannabichromene; Cannabinol, delta-9-tetrahydro-; PEG 400; Eye (cornea); cat; 2001; 9 days; comparison of agents effects; pump implanted sc and connected via sc tubing to cornea; tissue perfusion.

P0577: B. K. Colasanti*, et al.* Intraocular pressure, ocular toxicity and neurotoxicity after administration of cannabinol or cannabigerol. Exp. Eye Res 1984;39(3):251-259
ALZET Comments: Cannabigerol; Cannabinol; PEG 400; Eye; cat; 9 days; mp model not stated; comparison of agents effects; intermittent eye drop admin. vs. mp infusion; tissue perfusion.

P0652: B. K. Colasanti*, et al.* Ocular hypotension, ocular toxicity, and neurotoxicity in response to marihuana extract and cannabidiol. Gen. Pharmacol 1984;15(6):479-484
ALZET Comments: Cannabidiol; Marihuana extract; Cannabinol, delta-9-tetrahydro-; PEG; Eye (cornea); cat; 9 days; mp model not stated; comparison of acute topical admin/ injec vs. mp infusion; comparison of agents effects; agents admin. topically to cat corneas; tissue perfusion.

P0044: J. A. Eliason*, et al.* An ocular perfusion system. Invest. Ophthalmol. Vis. Sci 1980;19(1):102-105
ALZET Comments: Fluorescein sodium; Saline; Eye (cornea); rabbit; 12 days; tissue perfusion (cornea).

P0032: J. B. Michelson*, et al.* Experimental endophthalmitis treated with an implantable osmotic minipump. Arch. Ophthalmol 1979;97(7):1345-1346

ALZET Comments: Gentamicin sulfate; Eye (vitreous); rabbit; 4.5 days; mp model not stated; comparison of intravitreal injection vs. infusion; antibiotic; tissue perfusion.

P0004: M. G. Falcon*, et al.* Antivirals for the therapy of herpetic eye disease. Trans. Ophthal. Soc. UK 1977;97(330-332
ALZET Comments: Ara-AMP; Eye; Rabbit; 45 hours; Ara-AMP (Adenine arabinoside 5'monophospate) is an antiviral.