



References on the In Vitro or In Situ
Use of ALZET® Osmotic Pumps

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.²⁶ 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) "

Q5395: T. H. Lin, *et al.* NF-kappaB decoy oligodeoxynucleotide mitigates wear particle-associated bone loss in the murine continuous infusion model. Acta Biomater 2016;41(273-81

ALZET Comments: Ultra-high molecular weight polyethylene particles; oligodeoxynucleotide, decoy; oligodeoxynucleotide, scrambled; Endotoxin, LPS; Brain-derived neurotropic factor;; Saline; In Vitro (cell culture); Bone (Femur); Mice (nude); 2006; 4 weeks; Controls received mp w/ vehicle; animal info (Male athymic nude mice, 10-15 weeks old); stability verified by (in vitro experiment); dose-response (pg. 277); good methods (pg. 276); tissue perfusion (bone); Dose (15 mg/ml UHMWPE, 50uM decoy, 1 ug/ml LPS); Therapeutic indication (Bone loss, chronic inflammation);

Q4037: J. Pajarinen, *et al.* Modulation of mouse macrophage polarization in vitro using IL-4 delivery by osmotic pumps. JOURNAL OF BIOMEDICAL MATERIALS RESEARCH PART A 2015;103(1339-1345

ALZET Comments: Interleukin-4, mouse recombinant; BSA; PBS; In vitro (cell culture); Cell culture; 2006; 4 weeks; 1% BSA used; immunology; "Osmotic pumps delivered IL-4 at a rate that closely followed the expected delivery rate." pg 1343; used vinyl tubing; pumps lead into mouse bone marrow macrophage augmented media; incubated at 37C.

Q4514: M. T. Jones, *et al.* Monitoring of jokulhlaups and element fluxes in proglacial Icelandic rivers using osmotic samplers. JOURNAL OF VOLCANOLOGY AND GEOTHERMAL RESEARCH 2015;291(112-124

ALZET Comments: In situ (marine environment); 2ML1 (osmosampler); 9 months; "This technique allows for continued and unsupervised deployment of a sampler for weeks to months, representing a cost-efficient formof chemical monitoring." pg 112;.

Q3922: E. R. Horn, *et al.* Gender- Related Sensitivity of Development and Growth to Real Microgravity in *Xenopus laevis*. Journal of Experimental Zoology Part A-Ecological Genetics and Physiology 2014;321(1-12

ALZET Comments: Nettle powder; Water, spring; In vitro; Toad (tadpole); 2ML2; 12 days; Animal info (*Xenopus laevis*); teratology; spaceflight;.

P8571: C. Baj-Rossi, *et al.* Continuous monitoring of Naproxen by a cytochrome P450-based electrochemical sensor. Biosens Bioelectron 2014;53(283-7

ALZET Comments: Naproxen; PBS; In vitro; 1002; Naproxen is anon- steroidal anti-inflammatory agent; This paper reports the characterization of an electrochemical biosensor for the continuous monitoring of Naproxen delivered by alzet pumps.

Q4700: C. Baj-Rossi, *et al.* Continuous monitoring of Naproxen by a cytochrome P450-based electrochemical sensor. BIOSENSORS & BIOELECTRONICS 2014;53(:):283-287



ALZET Comments: Naproxen; Methanol; In Vitro; 1002; 16 hours; Functionality of mp verified by naproxen levels measured with sensors;.

Q2848: D. Sabater, *et al.* The use of Transwells(TM) improves the rates of differentiation and growth of cultured 3T3L1 cells. ANALYTICAL AND BIOANALYTICAL CHEMISTRY 2013;405(16):5605-5610

ALZET Comments: Spermine nitric oxide complex; DMEM-GlutaMAX-I; In vitro (cell culture); 1003D; 3 days; Spermine nitric oxide complex is a nitric oxide donor; polyethylene capillary tube used; image of ALZET pump inside Transwells(TM); pumps were placed in wells containing sterile water.

Q3602: E. T. Polymeropoulos, *et al.* Respirometry: Correcting for Diffusion and Validating the Use of Plastic Multiwell Plates with Integrated Optodes. PHYSIOLOGICAL AND BIOCHEMICAL ZOOLOGY 2013;86(5):588-592

ALZET Comments: Sodium sulfite; In Vitro; 1003D;

Q6717: L. Lapham, *et al.* Temporal variability of in situ methane concentrations in gas hydrate-bearing sediments near Bullseye Vent, Northern Cascadia Margin. Geochemistry, Geophysics, Geosystems 2013;14(7):2445-2459

ALZET Comments: In situ (marine environment); 2ML1 (osmosampler); In situ CH₄ concentrations were measured on water samples collected with a Mini-Pore Fluid Array (mPFA), which is a modified version of an existing sample collection tool that collects and maintains samples at in situ pressure. The mPFA is a polyvinyl chloride box that contains three OsmoSamplers, a high-pressure valve submerged in oil to reduce corrosion, and three 300 m long coils of copper tubing (Figure 3). Each OsmoSampler has eight 2ML1 semipermeable membranes that separate a saturated salt solution from deionized water, creating an osmotic potential, which creates the pump. Sampler pumping rates were calibrated in the laboratory prior to deployment and found to be ~0.5 mL/d at 4°C.

Q2744: A. Hill, *et al.* In vitro-in vivo evaluation of nanosuspension release from subcutaneously implantable osmotic pumps. International Journal of Pharmaceutics 2013;451(1-2):57-66

ALZET Comments: Compound A, nanosuspension; Acetonitrile; water; SC; in vitro; Mice; 1007D; 7 days; Animal info (Crl NMRI, 27-32.5 g, female); comparison of SC mp versus bolus injections; "Subcutaneously implanted osmotic pumps prove to be a valuable delivery system for nanosuspensions in pharmacokinetic studies by consideration of the key parameter viscosity in release kinetics."; good methods.

Q5534: C. M. Buffinton, *et al.* Stress and strain adaptation in load-dependent remodeling of the embryonic left ventricle. Biomech Model Mechanobiol 2013;12(5):1037-51

ALZET Comments: Verapamil; Saline; In vitro (egg); Bird (chicken embryo); 2001; Controls received mp w/ (saline); Dose (1 ng/μl);

Q2714: C. J. Xu, *et al.* A Portable Chemotaxis Platform for Short and Long Term Analysis. PLoS One 2012;7(9):U279-U285

ALZET Comments: FITC; In vitro (cell migration); 2ML2; 24, 72 hours; Controls received mp w/ PBS; "we show that by powering our chemotaxis platform with two ALZET osmotic pumps, our chemotaxis platform can achieve both exquisite control and long-term stability over the gradient." pg 2.

Q2112: A. Hill, *et al.* Controlled delivery of nanosuspensions from osmotic pumps: Zero order and non-zero order kinetics. JOURNAL OF CONTROLLED RELEASE 2012;158(3):403-412

ALZET Comments: Fenofibrate nanosuspension; captopril; methylene blue; Hydroxypropylmethylcellulose; dioctyl sulfosuccinate sodium salt; hydroxyethylcellulose; In vitro; 1007D; 7 days; Functionality of mp verified; effect of different osmolalities, viscosities, particle size, and pump orientation on release rate kinetics.

Q2083: A. Gkritzalis-Papadopoulos, *et al.* Adaptation of an Osmotically Pumped Continuous in Situ Water Sampler for Application in Riverine Environments. ENVIRONMENTAL SCIENCE & TECHNOLOGY 2012;46(13):7293-7300

ALZET Comments: In situ (marine environment); 2ML1 (osmosampler); 1 month; Comparison of osmotic pump in situ water osmosampler versus manual sampling; 12 Model 2ML1 pumps; maximum depth of 180 cm; "The Alzet pump specification states that there is a ±10% uncertainty in flow rate for each pump element in the absence of any calibration. By comparison, the maximum error in the laboratory determination of flow rate was ±5%, and the error using the dye marker



was ± 1 cm and does not change with sample age." pg 7297; "The key modification that we have made to osmosampler technology to enable use and evaluation in dynamic environments is implementation of time stamping using a tracer/dye. This enables comparison of performance with laboratory characterization of flow rate as a function of temperature." pg 7298.

Q1960: G. Remington, *et al.* Modeling chronic olanzapine exposure using Pharmacological limitations. *Pharmacology Biochemistry and Behavior* 2011;100(1):86-89

ALZET Comments: Olanzapine; Acetic acid, glacial; water, sterile; In vitro; 2ML4; Controls received vehicle; drug levels verified using a liquid-liquid extraction and liquid chromatography; "We suggest that olanzapine administration via (ALZET pumps) represents a viable option for (sub)chronic exposure with the caveats that a) duration be confined to 2 weeks..., and b) consideration be given to strategies in dissolving olanzapine that diminish the risk of oxidation." pg 89; "we strongly agree with van der Zwaal and colleagues (2008) that the issue of drug degradation is not specific to olanzapine, and that it is imperative to establish whether compounds being considered for minipump administration are capable of remaining stable in solution at body temperature."

Q0754: V. N. Ivanenko, *et al.* Description, distribution and microhabitats of a new species of Tisbe (Copepoda: Harpacticoida: Tisbidae) from a deep-sea hydrothermal vent field at the Mid-Atlantic Ridge (37degreesN, Lucky Strike). *CAHIERS DE BIOLOGIE MARINE* 2011;52(1):89-106

ALZET Comments: Sodium sulfide; In situ (marine environment); "A new species, Tisbe dahmsi, sp. nov., is described from the Eiffel Tower edifice located in the Lucky Strike vent field"; pump at depth of 1698 m.

P9959: C. H. Vinkers, *et al.* The rapid hydrolysis of chlordiazepoxide to demoxepam may affect the outcome of chronic osmotic minipump studies. *Psychopharmacology* 2010;208(4):555-562

ALZET Comments: Chlordiazepoxide; In vitro; "When the cumulative CDP concentration over time was corrected for its hydrolysis, drug release from the minipumps followed the theoretical release profile over time (white symbols), suggesting that CDP hydrolysis completely accounted for the declined CDP release over time." pg 558; "In general, the use of osmotic minipumps presents a valid and attractive alternative to the labor-intensive daily injections. However, the issue of drug stability and release should always be carefully investigated before initiating chronic minipump experiments." pg 562.

Q0254: Y. P. Yan, *et al.* Monocyte chemoattractant protein-1 plays a critical role in neuroblast migration after focal cerebral ischemia. *Journal of Cerebral Blood Flow and Metabolism* 2007;27(6):1213-1224

ALZET Comments: Monocyte chemoattractant protein-1; CSF, artificial; BSA; CSF/CNS (striatum); in vitro (cell culture); Rat; 1003D; 2001; 3, 7 days; Controls received sham operation; peptidies; cardiovascular; animal info (SHR, 270-300g); ischemia (cerebral); dose-response (fig. 5); in vitro MCP-1 administration to neurospheres in a culture plate was performed by submerging mp in normal saline in an adjacent well in the culture plate, connected via catheter (see fig. 5D).

P7395: H. W. Jannasch, *et al.* Continuous chemical monitoring with osmotically pumped water samplers: OsmoSampler design and applications. *LIMNOLOGY AND OCEANOGRAPHY-METHODS* 2004;2(102-113

ALZET Comments: In situ (marine environment); 2ML1 (osmosampler); >3 years; Novel use of ALZET Osmotic Pumps to sample seawater (osmosampler); "the inherent simplicity of osmotic pumps makes them an excellent replacement for electromechanical pumps, especially for extended sampling periods in harsh aquatic environments." p. 103; device diagram, p. 103, fig 1; flow rate is 4 ul/hr at 20 Celsius; membranes have successfully been used for more than 3 years; pumps have operated at depths up to 4,000 m.

P6591: G. Paasche, *et al.* Technical report: Modification of a cochlear implant electrode for drug delivery to the inner ear. *OTOLOGY & NEUROTOLOGY* 2003;24(2):222-227

ALZET Comments: Dye, methylene blue; in vitro; 2002; 3 days;

P4692: B. Bittner, *et al.* The impact of co-solvents and the composition of experimental formulations on the pump rate of the ALZET® osmotic pump. *International Journal of Pharmaceutics* 2000;205(195-198



ALZET Comments: Mannitol; Radio-isotopes; Pyrrolidone, N-methyl-2-; Propylene glycol; PEG; 14C tracer; Water; Dimethylacetamide; in vitro; 2ML1; 8 days; Functionality of mp verified by in vitro testing; ALZAIT chemical compatibility kit used; various solvents employed to find compatibility with drug reservoir.

P9100: S. Froidevaux, *et al.* Differential regulation of somatostatin receptor type 2 (sst 2) expression in AR4-2J tumor cells implanted into mice during octreotide treatment. *Cancer Res* 1999;59(15):3652-3657

ALZET Comments: Octreotide; NaCl; SC; in vitro (cell culture); Mice (SCID); 1002; 7 days; Cancer; animal info (AR4-2J tumor-bearing, CB17).

P4075: D. Sedmera, *et al.* A quantitative study of the ventricular myoarchitecture in the stage 21-29 chick embryo following decreased loading. *Eur. J. Morphology* 1998;36(2):105-119

ALZET Comments: Verapamil; Saline; In vitro (egg); extraembryonic vascular bed; Bird (chicken embryo); 2001; 24, 48, 72 hours; controls received mp w/vehicle; pump immersed in saline; teratology; cardiovascular.

P3556: M. I. Arnot, *et al.* Dimethyl sulfoxide/propylene glycol is a suitable solvent for the delivery of diazepam from osmotic minipumps. *J. Pharm. & Tox. Meth* 1996;36(29-31)

ALZET Comments: Diazepam; Clonazepam; flumazenil; DMSO; Propylene glycol; Tetraglycol; ³H tracer; Radio-isotopes; in vitro (egg); 2ML4; no duration posted; no comment posted.

P2537: H. W. Jannasch, *et al.* Submersible, osmotically pumped analyzers for continuous determination of nitrate in situ. *Anal. Chem* 1994;66(3352-3361)

ALZET Comments: In vitro; 2ML1; 2ML4; no duration posted; "Our sample pumps, therefore, usually contain at least four 2ML1 membranes for a total flow rate of at least 12 ul/h at 20C."

P3604: G. Lorenzi, *et al.* Cultivation of hamster kidney cells in a dynamic cell culture system in space (spacelab IML-1 mission). *Microgravity Sci. Technol* 1993;VI/1(34-38)

ALZET Comments: NaHCO₃; Glucose; HEPES; DMEM; Serum, fetal calf; Gentamicin; in vitro (cell culture); 2001; no duration posted; mp connected to cell culture chamber; "...the osmotic pump delivered sufficient fresh medium to support cell growth in the perfusion chambers." p. 37; spaceflight.

P3217: R. S. Janzer, *et al.* Astrocytes secrete a factor inducing the expression of HT7-protein and neurothelin in endothelial cells of chorioallantoic vessels. *Adv. Exp. Med. Biol* 1993;331(217-221)

ALZET Comments: Medium, astrocyte conditioned-; In vitro (egg); chorioallantoic membrane; Bird (chicken embryo); 2002; 5 days; controls received mp with PBS; gelfoam placed on chorioallantoic membrane; mp connected to gelfoam with PE tubing; mp kept in saline.

P3013: J. F. Di Joseph, *et al.* Osmotic pump delivery of rapamycin. *Transplantation* 1993;55(2):450-452

ALZET Comments: Rapamycin; Dimethylacetamide; Tween 80; PEG 400; in vitro; 2002; 2 weeks; stability verified by in vitro testing and HPLC for 14 days; in vitro validation of functionality and rapamycin stability.

Q0611: J. A. Lobrinus, *et al.* Induction of the blood-brain barrier specific HT7 and neurothelin epitopes in endothelial cells of the chick chorioallantoic vessels by a soluble factor derived from astrocytes. *DEVELOPMENTAL BRAIN RESEARCH* 1992;70(207-211)

ALZET Comments: Medium, astrocyte conditioned-; In vitro (egg); chorioallantoic membrane; Bird (chicken embryo); 2004; 5 days; Schematic diagram of the experiment with ALZET pump, fig. 1; mp connected to gelfoam with PE tubing; mp kept in saline.

P1954: E. B. Clark, *et al.* Effect of chronic verapamil treatment on ventricular function and growth in chick embryos. *Am. J. Physiol* 1991;261(H166-H171)

ALZET Comments: Verapamil; In vitro (egg); Bird (chicken embryo, extraembryonic vascular bed); no duration posted; en ovo, schematic p. H167.



P4504: O. Rasmussen, *et al.* Plant protoplast development on "Biokosmos 9". ESA 1990;307(527-530

ALZET Comments: Growth medium; In vitro (cell culture); 14 days; mp used to deliver growth medium to protoplasts during spaceflight.

P2765: H. L. Vahlsing, *et al.* An improved device for continuous intraventricular infusions prevents the introduction of pump-derived toxins and increases the effectiveness of ngf treatments. Exp. Neurol 1989;105(3):233-243

ALZET Comments: Nerve growth factor; CSF, artificial; in vitro; CSF/CNS; Rat; 2002; 3, 7, or 14 days; no stress-see page 236; stress/adverse reaction: pages 233,236; previous experiments by investigators brought about evidence that mp were introducing cytotoxic substances into infusion fluid. This paper documents creation of coiled (Lynch coil) tubing method w/air/oil spacer whereby the fluid infused is insulated from mp while still propelled by its advance; paraffin dipping of pump utilized to reduce release rate; residual flow rate was slower in in vivo pumps than in in vitro pumps; with the modified pump fewer than 10% of rats had infusion-induced lesions; tracing air-oil space movement allows a precise measurement of volume of infusate.

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.

P3948: F. K. Gmunder, *et al.* Mammalian cell cultivation in space. Adv. Space Res 1989;9(11):119-127

ALZET Comments: Culture media; Glucose; Fetal calf serum; HEPES buffer; Gentamycin;; in vitro (cell culture); 2001; 2002; diagram of dynamic cell culture system on page 123; in vitro; spaceflight.

P1301: G. F. Seran, *et al.* Metabolism of methadone by chicken embryos prevents induction of chronic opioid-type dependence after a single injection: use of osmotic pumps for continuous infusion. Pharmacol. Biochem. Behav 1988;30(2):357-363

ALZET Comments: Methadol, N-desmethyl-1-acetyl; Methadone; Radio-isotopes; 3H tracer; Propylene glycol; Saline; Water; In vitro (egg); Bird (chicken embryo); 2001; 7 days; pump delivered to chicken egg via catheter; pump extracorporeal; comparison of a single injection vs. mp infusion.

P1382: F. K. Gmunder, *et al.* Dynamic cell culture system: a new cell cultivation instrument for biological experiments in space. J. Biotechnol 1988;7(217-228

ALZET Comments: Culture media, DMEM; HEPES; Serum, fetal calf; Gentamicin; Glucose; in vitro (cell culture); 2001; 7 days; Mp connected to cell culture chamber; cytotoxicity described; spaceflight.

P1389: T. A. Carpenter, *et al.* Magnetic resonance imaging of the delivery of a paramagnetic contrast agent by an osmotic pump. Drug Design Delivery 1988;3(263-266

ALZET Comments: GdDTPA; Water; in vitro; 2ML1; 220 hours; GdDTPA is gadolinium diethylenetriamine pentaacetic acid; MRI.

P0773: M. D. Lifschitz. Prostaglandins may mediate chloride concentration gradient across domes formed by MDCK1 cells. Am. J. Physiol 1986;250(F525-F531

ALZET Comments: Prostaglandin E2; Glycine; in vitro (cell culture); 2002; 5 hours; mp infusion in culture dish to continually add PGE2 to MDCK cell culture.

P0218: J. E. Neely, *et al.* Using miniature osmotic infusion pumps to maintain tritiated thymidine exposure to cells in culture. J. Histochem. Cytochem 1982;30(6):536-537

ALZET Comments: Radio-isotopes; Thymidine; 3H tracer; Saline; in vitro (cell culture); 2001; no duration posted; pumps immersed in tissue culture dish for thymidine experiments.

P0241: J. M. Hock, *et al.* Use of osmotic minipumps for delivery of parathyroid hormone. Calcif. Tissue Int 1982;34(270-272



ALZET Comments: Parathyroid hormone, bovine 1-84; Culture medium, BGJ; Cysteine; HCl; Saline; Serum, rat; bone (parietal); in vitro; Rat; no duration posted; in vitro: pump immersed in Ringer's solution 2-6 days; in vivo: tubing from mp wired to supraorbital ridges w/outlet cut in tubing overlying parietal bone for 2 days; peptides; tissue perfusion.

P1240: P. R. Waggoner, *et al.* Method for long term delivery of soluble agents to the chick chorioallantoic membrane. *Experientia* 1981;37(3):321-322

ALZET Comments: Thyroxine, I-; In vitro (egg); chorioallantoic membrane; Bird (chicken embryo); 2001; 7 days; mp placed in small test tube filled w/ water and then sealed w/ parafilm; mp connected to catheter that bathed the chorioallantoic membrane.