References on the Administration of Anticonvulsive Agents Using ALZET® Osmotic Pumps

Carbamazepine

Q8475: K. Fukuyama, *et al.* Effects of Carbamazepine, Lacosamide and Zonisamide on Gliotransmitter Release Associated with Activated Astroglial Hemichannels. Pharmaceuticals (Basel) 2020;13(6):
Agents: Carbamazepine; Lacosamide; Zonisamide **Vehicle:** DMSO; Ethanol; **Route:** CSF/CNS (orbitofrontal cortex); **Species:** Rat; **Pump:** 2ML1; **Duration:** 7 days;
ALZET Comments: Dose (25 mg/kg/day); 0.2% DMSO, 1% Ethanol used; animal info (Sprague-Dawley rats); Carbamazepine aka CBZ, Lacosamide aka LCM, Zonisamide aka ZNS; dependence;

Q8473: K. Fukuyama, *et al.* Upregulated and Hyperactivated Thalamic Connexin 43 Plays Important Roles in Pathomechanisms of Cognitive Impairment and Seizure of Autosomal Dominant Sleep-Related Hypermotor Epilepsy with S284L-Mutant alpha4 Subunit of Nicotinic ACh Receptor. Pharmaceuticals (Basel) 2020;13(5):
Agents: Zonisamide; Carbamazepine **Vehicle:** Not stated; **Route:** CSF/CNS (orbitofrontal cortex); **Species:** Rat; **Pump:** 2ML1; **Duration:** 7 days;
ALZET Comments: Dose (25 mg/kg/day); animal info (male S286L-TG [21–23] and wild-type littermates); Zonisamide aka ZNS, Carbamazepine aka CBZ; neurodegenerative (Epilepsy);

Q5784: K. Deseure, *et al.* Differential drug effects on spontaneous and evoked pain behavior in a model of trigeminal neuropathic pain. J Pain Res 2017;10(279-286
Agents: Carbamazepine, baclofen, clomipramine **Vehicle:** DMSO, PEG, EtOH, Acetone; **Route:** SC; **Species:** Rat; **Pump:** 2ML1;
ALZET Comments: Controls received mp w/ vehicle; animal info (7 weeks old); dimethyl sulfoxide, propylene glycol, ethyl alcohol, and acetone at a ratio of 42:42:15:1; post op. care (morphine 5 mg/day); behavioral testing (Facial grooming); Therapeutic indication (Trigeminal neuralgia, neuropathic pain); Dose (30 mg/day carbamazepine (the first-line drug treatment for trigeminal neuralgia), 1.06 mg/day baclofen, 4.18 mg/day clomipramine, and 5 mg/day morphine);

Q0269: S. M. Cain, *et al.* High resolution micro-SPECT scanning in rats using ^{125}I beta-CIT: Effects of chronic treatment with carbamazepine. Epilepsia 2009;50(8):1962-1970
Agents: Carbamazepine **Vehicle:** DMSO; Propylene glycol; Ethyl alcohol; Acetone; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (adult, male, Sprague-Dawley, 160-270 g); functionality of mp verified by serum drug levels; 42% DMSO used; identified 3 mg/kg/day as the highest dose that could be reliably administered via minipumps over a 14-day period at 37 degrees Celsius, pg. 1969

P5195: H. C. Doheny, *et al.* A comparison of the efficacy of carbamazepine and the novel anti-epileptic drug levetiracetam in the tetanus toxin model of focal complex partial epilepsy. British Journal of Pharmacology 2002;135(6):1425-1434
Agents: Carbamazepine; levetiracetam **Vehicle:** DMSO; Propylene glycol; ethanol, saline; **Route:** IP; **Species:** Rat; **Pump:** Not Stated; **Duration:** 7 days;
ALZET Comments: Controls received mp/ vehicle; functionality of mp verified by drug serum levels; dose-response (text p.1428); carbamazepine was dissolved in 42.5% DMSO/42% Propylene glycol/15% ethanol. Levitiracetam was dissolved in saline; 2-day recovery period given using coiled PE-40 tubing; epilepsy; anticonvulsant

Deprenyl

P9373: F. Chenu, *et al.* Long-term administration of monoamine oxidase inhibitors alters the firing rate and pattern of dopamine neurons in the ventral tegmental area. International Journal of Neuropsychopharmacology 2009;12(4):475-485
Agents: Clorgyline; Phenelzine; Deprenyl **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Duration:** 2, 21 days;
ALZET Comments: Controls received mp w/ saline; enzyme inhibitor (MAO, monoamine oxidase); animal info (male, Sprague Dawley, 250-300 g.)

P5438: J. M. Mejia*, et al.* Monoamine oxidase inhibition during brain development induces pathological aggressive behavior in mice. Biological Psychiatry 2002;52(8):811-822
Agents: Chlorgyline; Deprenyl **Vehicle:** Saline; **Route:** SC; **Species:** Mice (pregnant); **Pump:** 2002; 2004; **Duration:** 6 weeks;
ALZET Comments: Controls received mp w/ vehicle; teratology; enzyme inhibitors (monoamine oxidase inhibitors); 2002 pumps were replaced w/ 2004 pumps after 2 weeks to complete a 6 week infusion; agents infused singly or concommitant in the same pump

P4227: W. Loscher*, et al.* Anticonvulsant efficacy of L-deprenyl (selegiline) during chronic treatment in mice: continuous versus discontinuous administration. Neuropharmacology 1998;37(1587-1593
Agents: Deprenyl, L- **Vehicle:** Water, distilled; **Route:** SC; **Species:** Mice; **Pump:** 2002; 2004; **Duration:** 2,4 weeks;
ALZET Comments: Controls received mp w/saline; functionality of mp verified by residual volume; comparison of daily i.p. injections vs. mp; good methods (p. 1588); anticonvulsant; also called selegiline

P2971: R. L. Sherry-McKenna*, et al.* Monoamine oxidase inhibitors: effects on tryptophan concentrations in the rat brain. J. Neural Transm 1994;41(155-163
Agents: Phenelzine; Tranylcypromine, 4-methoxy-; Acetylphenelzine, N2-; Tranylcypromine, 4-fluoro-; Tranylcypromine; Deprenyl **Vehicle:** Not Stated; **Route:** SC; IP; **Species:** Rat; **Pump:** Not Stated; **Duration:** 28 days;
ALZET Comments: antidepressant; controls received mp with vehicle; comparison of TCP and PLZ ip injections vs. mp

P2496: P. R. Paetsch*, et al.* Down-regulation of b-adrenergic and dopaminergic receptors induced by 2-phenylethylamine. Cellular and Molecular Neurobiology 1993;13(3):203-215
Agents: Phenylethylamine HCl, 2-; Deprenyl HCl; **Route:** SC; **Species:** Rat; **Pump:** 2002; 2ML2; **Duration:** 28 days;
ALZET Comments: Pumps replaced after 14 days; multiple pumps per animal (2); antidepressant

P2407: P. R. Paetsch*, et al.* Induction of functional down-regulation of beta-adrenoceptors in rats by 2-phenylethylamine. J. Pharm. Pharmacol 1993;82(1):22-24
Agents: Phenelzine sulfate; Phenylethylamine HCl, 2-; Deprenyl HCl **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2002; 2ML2; **Duration:** 21, 22 days;
ALZET Comments: Antidepressant; controls received mp w/ vehicle; multiple pumps per animal (2)

P3067: D. D. Mousseau*, et al.* Effects of age and chronic antidepressant treatment on [3H]tryptamine and [3H]dihydroalprenolol binding to rat cortical membranes. Cellular and Molecular Neurobiology 1993;13(1):3-13
Agents: Imipramine HCl; Desipramine HCl; Clomipramine HCl; Tranylcypromine HCl; Phenelzine sulfate; Clorgyline HCl; Deprenyl HCl **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2002; 2ML4; **Duration:** 14,28 days;
ALZET Comments: antidepressant; controls received mp with vehicle; drug concentrations determined from Greenshaw program

P3400: M. C. Carrillo*, et al.* The optimal dosage of (-) deprenyl for increasing superoxide dismutase activities in several brain regions decreases with age in male Fischer 344 rats. Life Sci 1993;52(1925-1934
Agents: Deprenyl **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 3 weeks;
ALZET Comments: controls received mp w/saline; dose-response

P1313: J. G. de Yebenes*, et al.* Continuous intracerebroventricular infusion of dopamine and dopamine agonists through a totally implanted drug delivery system in animal models of Parkinson's disease. J. Neural Transm 1988;27(141-160
Agents: Deprenyl; Dopamine; Lisuride; Pargyline; Pergolide **Vehicle:** HCl; Sodium metabisulfite; Water; **Route:** CSF/CNS;
Species: Rat; **Pump:** 2001; **Duration:** 6, 7 days;
ALZET Comments: mp connected to cannula; stability of DA verified in several vehicles, p 146; concomitant DA infusion with pargyline; DA infusion with deprenyl; replacement therapy (dopamine deficiency); stability verified in vitro; antihypertensive; neurodegenerative (Parkinson's disease)

P1096: D. O'Regan*, et al.* A behavioural and neurochemical analysis of chronic and selective monoamine oxidase inhibition. Psychopharmacology 1987;92(42-47
Agents: Deprenyl HCl; Clonidine HCl; Clorgyline HCl **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 13 days;
ALZET Comments: controls received mp w/vehicle; hypothalamic electrodes implanted for self-stimulation to further access agents effects; antihypertensive

P2709: J. G. de Yebenes*, et al.* Continuous intracerebroventricular infusion of dopamine and dopamine agonists through a totally implanted drug delivery system in animal models of Parkinson's disease. Movement Disorders 1987;2(3):143-158
Agents: Dopamine; Pargyline; Deprenyl; Lisuride; Pergolide **Vehicle:** HCl; Sodium metabisulfate; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2001; **Duration:** 6,7 days;
ALZET Comments: controls received mp with vehicles; replacement therapy (lesion in dopamine pathway); stability verified for 1 week by measuring dopamine concentrations and its metabolites at varying time intervals with HPLC; concomitant dopamine infusion w/ pargyline and w/ deprenyl; antihypertensive; neurodegenerative (Parkinson's disease)

P0211: R. M. Cohen*, et al.* Cardiovascular changes in response to selective monoamine oxidase inhibition in the rat. European Journal of Pharmacology 1982;80(155-160
Agents: Deprenyl, 1-; Clorgyline **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 21, 24 days;
ALZET Comments: mp model not stated; comparison of ip injection vs. infusion

Levetiracetam

Q10414: L. Bourhy*, et al.* Silencing of amygdala circuits during sepsis prevents the development of anxiety-related behaviours. Brain 2022;145(4):1391-1409
Agents: Levetiracetam **Vehicle:** Saline; **Route:** CSF/CNS (right lateral ventricle); **Species:** Mice; **Pump:** 1003D; **Duration:** 3 days;
ALZET Comments: Dose: (1 µl/h); Controls received mp w/ vehicle; animal info: Adult 2–5months old wild-type male C57Bl/6JRj mice and adult male and female FOS-CreERT2; post op. care: treated with (0.1 mg/kg) buprenorphine 30 mins. before surgery; behavioral testing (Morris water maze; novel object location/recognition; Open field test; Light/dark box test; olfactory habituation; fear conditioning); Levetiracetam aka (LEV); ALZET brain infusion kit 3 used; Brain coordinates (stereotaxic coordinates relative to bregma, antero-posterior: −0.5 mm; medial lateral: 1 mm; dorsoventral: 2.5 mm); dental cement used; liquid bonding resin; dental acrylic; neurodegenerative (anxiety; PTSD); immunology

Q9199: A. M. Costa*, et al.* Relationship between Delta Rhythm, Seizure Occurrence and Allopregnanolone Hippocampal Levels in Epileptic Rats Exposed to the Rebound Effect. Pharmaceuticals (Basel) 2021;14(2):
Agents: Levetiracetam **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 1 week;
ALZET Comments: Dose (); Controls received mp w/ vehicle; animal info (); Levetiracetam aka LEV; dependence;

Q8673: B. Miziak*, et al.* Anti-Epileptogenic Effects of Antiepileptic Drugs. International Journal of Molecular Sciences 2020;21(7):
Agents: Tiagabine; Valproate; Levetiracetam; **Route:** SC; CSF/CNS (intracerebral); IV; **Species:** Rat; **Duration:** 3, 21 days; 8 wks;
ALZET Comments: 50 mg/kg/day Tiagabine; 600 mg/kg/day Valproate; behavioral tests Morris Water Maze; Open Field Test);

Q8509: H. G. Gonzalez*, et al.* Levetiracetam Reduced the Basal Excitability of the Dentate Gyrus without Restoring Impaired Synaptic Plasticity in Rats with Temporal Lobe Epilepsy. Brain Sciences 2020;10(9):
Agents: Levetiracetam **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** Not stated; **Duration:** 1 week;
ALZET Comments: Dose (300 mg/kg/day); 0.9% Saline used; animal info (male Wistar rats, 250-300 g);

Q8471: C. H. Fu*, et al.* Early Seizure Activity Accelerates Depletion of Hippocampal Neural Stem Cells and Impairs Spatial Discrimination in an Alzheimer's Disease Model. Cell Rep 2019;27(13):3741-3751 e4
Agents: Levetiracetam **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 28 days;
ALZET Comments: Dose (75 mg/kg/day); Controls received mp w/ vehicle; animal info (male and female mice, 3 weeks to 14 months old); neurodegenerative (Alzheimer's);

Q7955: P. M. Casillas-Espinosa*, et al.* Disease-modifying effects of a novel T-type calcium channel antagonist, Z944, in a model of temporal lobe epilepsy. Prog Neurobiol 2019;182(101677
Agents: Z944; levetiracetam **Vehicle:** saline, normal, PEG and DMSO buffered; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 1, 4 weeks;
ALZET Comments: "Dose ((Z944 60 mg/kg/day), (levetiracetam 200 mg/kg/day)); 40% propylene glycol, 40% DMSO, and 20% normal saline solution used; Controls received mp w/ vehicle; animal info (11 weeks, male, Wistar); behavioral testing (Sucrose preference, Elevated plus maze, Open field, Morris water maze, Forced swim test); Z944 is a highly potent and selective T-type Ca2+ channel antagonist; Therapeutic indication (continuous levetiracetam infusion significantly reduced the average number of seizures and the seizure severity in comparison to vehicle treated animals, but without affecting the latency to the first seizure. Z944 treatment after SE significantly prolonged the latency to develop the first spontaneous seizure and also reduced the average number of seizures in comparison to the vehicle treated counterparts); "

Q8805: L. A. Pichardo Macias*, et al.* Effect of levetiracetam on extracellular amino acid levels in the dorsal hippocampus of rats with temporal lobe epilepsy. Epilepsy Research 2018;140(111-119
Agents: Levetiracetam **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 1 week;
ALZET Comments: Dose (300 mg/kg/day); 0.9% Saline used; animal info (Male, Wistar, 250-350 g); Levetiracetam aka LEV ; Brain coordinates (AP: −3.3 mm, L: ± 1.5 mm, and V: −1.8 mm); dependence;

Q6467: R. P. Haberman*, et al.* Heightened cortical excitability in aged rodents with memory impairment. Neurobiol Aging 2017;54(144-151
Agents: Levetiracetam **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 28 days;
ALZET Comments: Dose (10 mg/kg/day); Controls received mp w/ vehicle; animal info (Aged, male Long-Evans rats);

Q4492: M. Levesque*, et al.* The anti-ictogenic effects of levetiracetam are mirrored by interictal spiking and high-frequency oscillation changes in a model of temporal lobe epilepsy. Seizure-European Journal of Epilepsy 2015;25(18-25
Agents: Levetiracetam **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 2 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 250-300g); cardiovascular; "These pumps deliver a continuous dosing over 2 weeks, circumventing the need for repetitive invasive blood sampling. " pg 19;

Q5035: A. R. Ko*, et al.* Blockade of endothelin B receptor improves the efficacy of levetiracetam in chronic epileptic rats. Seizure 2015;31(133-40
Agents: Levetiracetam; SB202190; BQ788 **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 1003D; **Duration:** 3 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 7 days); pumps replaced between trials;

Q4439: A. M. Hall*, et al.* Tau-Dependent Kv4.2 Depletion and Dendritic Hyperexcitability in a Mouse Model of Alzheimer's Disease. JOURNAL OF NEUROSCIENCE 2015;35(6221-6230
Agents: Levetiracetam **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 28 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (hAPPJ20 on C57BL6J background); neurodegenerative (Alzheimer's disease); pumps primed at 37C for 24 hours;

Q3146: E. Suberbielle*, et al.* Physiologic brain activity causes DNA double-strand breaks in neurons, with exacerbation by amyloid-beta. Nature Neuroscience 2013;16(5):613-U140
Agents: Levetiracetam **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 28 days;
ALZET Comments: Controls received mp w/ saline; animal info (4-5 months, heterozygous hAPP transgenic and wild-type, C57Nl/6J);

Q6777: A. M. Spiegel*, et al.* Hilar interneuron vulnerability distinguishes aged rats with memory impairment. J Comp Neurol 2013;521(15):3508-23
Agents: Levetiracetam **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 4 weeks;
ALZET Comments: Dose (10 mg/kg/day); Controls received mp w/ vehicle; animal info (Aged, male Long-Evans rats at 8–9 months of age);

Q2454: P. E. Sanchez, *et al.* Levetiracetam suppresses neuronal network dysfunction and reverses synaptic and cognitive deficits in an Alzheimer's disease model. PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA 2012;109(42):E2895-E2903
Agents: Levetiracetam **Vehicle:** Saline, sterile; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 28 days;
ALZET Comments: Control animals received mp w/ vehicle; animal info (hAPPJ20, 4-6 mo old); neurodegenerative (Alzheimer's disease)

Q1474: S. Sugata, *et al.* Neuroprotective effect of levetiracetam on hippocampal sclerosis-like change in spontaneously epileptic rats. Brain Research Bulletin 2011;86(1-2):36-41
Agents: Levetiracetam **Vehicle:** Saline, physiological; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 4 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (spontaneously epileptic (SER), 4 wks old); functionality of mp verified by serum levetiracetam levels

Q0813: Y. Sugaya, *et al.* Levetiracetam suppresses development of spontaneous EEG seizures and aberrant neurogenesis following kainate-induced status epilepticus. Brain Research 2010;1352(;):187-199
Agents: Levetiracetam **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2004; **Duration:** 28 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague-Dawley, 8 wks old); 15 ul saline allowed for 3-day delayed delivery followed by 25-day levetiracetam delivery; "A preliminary study in which a mini-pump was filled with bromophenol blue instead of levetiracetam, confirmed that the pumped drug solution was constantly separated from the predrug saline for 3 days at 37 °C." pg 196; delayed delivery;

Q1259: L. Paulson, *et al.* Effect of levetiracetam on hippocampal protein expression and cell proliferation in rats. Epilepsy Research 2010;90(1-2):110-120
Agents: Levetiracetam **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ saline; animal info (female, Sprague Dawley, 200-225 g)

P9736: E. A. Elzayat, *et al.* Effect of Antiepileptic Agent, Levetiracetam, on Urodynamic Parameters and Neurogenic Bladder Overactivity in Chronically Paraplegic Rats. UROLOGY 2009;73(4):922-927
Agents: Levetiracetam **Vehicle:** Saline, normal; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; 2ML2; **Duration:** 1, 2 weeks;
ALZET Comments: Controls received no spinal cord transection; dose-response (Fig 2A); animal info (female, Sprague Dawley, 225-275 g, spinal cord transection)

P9181: E. A. Van Vliet, *et al.* Development of tolerance to levetiracetam in rats with chronic epilepsy. Epilepsia 2008;49(7):1151-1159
Agents: Levetiracetam **Vehicle:** Water, distilled; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 2 weeks;
ALZET Comments: Functionality of mp verified; pumps replaced after 1 week; tolerance; animal info (male, Sprague Dawley, adult, 500-700 g.); "flow rate of each pump was verified after removal and corresponded to the range given by the manufacturer indicating that all minipumps functioned properly." pg. 1156

P8935: D. G. Margineanu, *et al.* Effects of chronic treatment with levetiracetam on hippocampal field responses after pilocarpine-induced status epilepticus in rats. Brain Research Bulletin 2008;77(5):282-285
Agents: Levetiracetam **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 3 weeks; 21 days;
ALZET Comments: Controls received mp w/ vehicle; functionality of mp verified by drug plasma levels; dose-response (table 1, pg. 283); animal info (male, Sprague Dawley, 220-250 g.); epilepsy; "chronic treatment with levetiracetam completely inhibits the development of hippocampal hyperexcitability following pilocarpine-induced (status epilepticus)"

R0242: W. Loescher. The pharmacokinetics of antiepileptic drugs in rats: Consequences for maintaining effective drug levels during prolonged drug administration in rat models of epilepsy. Epilepsia 2007;48(7):1245-1258
Agents: Levetiracetam; phenobarbital; phenytoin; valproic acid; vigabatrin **Vehicle:** Water, distilled; PEG 300; Glycerol; PEG 400; Propylene glycol; **Route:** SC; IP; **Species:** Rat; Mice; Gerbils; **Pump:** 2ML1; 2ML2; **Duration:** 1,4,2 weeks; 7 days;
ALZET Comments: Comparison of IV, IP injections vs. food or water delivery vs mp; pumps replaced (every week in one set of experiments); stress/adverse reaction: (see pg. 1255); peritoneal irritation, peritonitis in some of the IP experiments); half-life (p. 1247) table 1 (18 compounds); animal info (epileptic, Sprague-Dawley, Wistar);

R0168: W. Löscher. Animal models of epilepsy for the development of antiepileptogenic and disease-modifying drugs. A comparison of the pharmacology of kindling and post-status epilepticus models of temporal lobe epilepsy. Epilepsy Research 2002;50(1-2):105-123
Agents: Levetiracetam **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Rat; **Pump:** Not Stated; **Duration:** 2 weeks;
ALZET Comments: ALZET pumps mentioned on pg. 113

P5195: H. C. Doheny, *et al.* A comparison of the efficacy of carbamazepine and the novel anti-epileptic drug levetiracetam in the tetanus toxin model of focal complex partial epilepsy. British Journal of Pharmacology 2002;135(6):1425-1434
Agents: Carbamazepine; levetiracetam **Vehicle:** DMSO; Propylene glycol; ethanol, saline; **Route:** IP; **Species:** Rat; **Pump:** Not Stated; **Duration:** 7 days;
ALZET Comments: Controls received mp/ vehicle; functionality of mp verified by drug serum levels; dose-response (text p.1428); carbamazepine was dissolved in 42.5% DMSO/42% Propylene glycol/15% ethanol. Levitiracetam was dissolved in saline; 2-day recovery period given using coiled PE-40 tubing; epilepsy; anticonvulsant

P5035: Diabetes. Effects of the novel antiepileptic drug levetiracetam on spontaneous recurrent seizures in the rat pilocarpine model of temporal lobe epilepsy. Epilepsia 2002;43(4):350-357
Agents: Levetiracetam **Vehicle:** Water, distilled; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 6 weeks;
ALZET Comments: Anticonvulsant; controls received mp w/ vehicle; functionality of mp verified by residual aspiration, plasma levels; pumps replaced every week; good methods (priming, filling p. 352-53); rats received 2-week saline infusion (pre-drug control period) then 2 week levetiracetam infusion then another 2-week saline infusion

Phenobarbital

R0242: W. Loescher. The pharmacokinetics of antiepileptic drugs in rats: Consequences for maintaining effective drug levels during prolonged drug administration in rat models of epilepsy. Epilepsia 2007;48(7):1245-1258
Agents: Levetiracetam; phenobarbital; phenytoin; valproic acid; vigabatrin **Vehicle:** Water, distilled; PEG 300; Glycerol; PEG 400; Propylene glycol; **Route:** SC; IP; **Species:** Rat; Mice; Gerbils; **Pump:** 2ML1; 2ML2; **Duration:** 1,4,2 weeks; 7 days;
ALZET Comments: Comparison of IV, IP injections vs. food or water delivery vs mp; pumps replaced (every week in one set of experiments); stress/adverse reaction: (see pg. 1255); peritoneal irritation, peritonitis in some of the IP experiments); half-life (p. 1247) table 1 (18 compounds); animal info (epileptic, Sprague-Dawley, Wistar); review; see p. 1254-1255; see table 4 for advantages + disadvantages of different application routes

P0494: F. J. Hock, *et al.* A novel method for the administration of the enzyme inducer phenobarbital to rats via an osmotic minipump. IRSC Med. Sci. : Biochem 1984;12(8):661
Agents: Phenobarbital **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 8 days;
ALZET Comments: Comparison of phenobarb. consumed po in drinking water vs. mp infusion;

P0447: T. P. Davis, *et al.* Centrally acting drugs alter in vitro B-endorphin processing in the rat. European Journal of Pharmacology 1984;100(249-251
Agents: Chlorpromazine; haloperidol; phenobarbital; promethazine; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 8 days;
ALZET Comments: Comparison of agents effects

P0401: W. Kuhnz, *et al.* A new method for kinetic studies of drug interactions in experimental animals during steady state: controlled-rate application of valproic acid, phenobarbital and their combinations via implanted osmotic minipumps in the mouse. Drug Research 1983;33(11):1579-1582
Agents: Phenobarbital, sodium; Valproate, sodium **Vehicle:** Water; **Route:** SC; **Species:** Mice (pregnant); **Pump:** 2001; 2002; **Duration:** 1, 2 weeks;
ALZET Comments: No stress see p. 1580, 1582; 1-2 pumps/animal; VPA and PB used singly and in combination in mp

P0311: I. M. Kapetanovic, *et al.* Phenobarbital pharmacokinetics in rat as a function of age. Drug Metabolism and Disposition 1982;10(6):586-589
Agents: Phenobarbital **Vehicle:** Water; **Route:** IP; **Species:** Rat; **Pump:** Not Stated; **Duration:** 5 days;
ALZET Comments: bolus injec. vs. mp infusion

P0036: B. Tabakoff, *et al.* The effect of selective lesions of brain noradrenergic systems on the development of barbiturate tolerance in rats. Brain Pathology 1979;176(327-336
Agents: Phenobarbital, sodium **Vehicle:** Propylene glycol; Water; **Route:** CSF/CNS; **Species:** Rat; **Duration:** 3 days;
ALZET Comments: Some groups given 6-OHDA or vehicle of ascorbic acid in Artificial CSF prior to infusion

Promethazine

P0447: T. P. Davis, *et al.* Centrally acting drugs alter in vitro B-endorphin processing in the rat. Eur. J. Pharmacol 1984;100(249-251
ALZET Comments: Chlorpromazine; haloperidol; phenobarbital; promethazine; SC; Rat; 2001; 8 days;

Tiagabine

Q8673: B. Miziak, *et al.* Anti-Epileptogenic Effects of Antiepileptic Drugs. International Journal of Molecular Sciences 2020;21(7):
Agents: Tiagabine; Valproate; Levetiracetam **Route:** SC; CSF/CNS (intracerebral); IV; **Species:** Rat;; **Duration:** 3; 21 days; 8 weeks;
ALZET Comments: Dose (50 mg/kg/day Tiagabine; 600 mg/kg/day Valproate); behavioral testing (Morris Water Maze; Open Field Test); neurodegenerative (Epilepsy);

R0177: A. Pitkanen. Efficacy of current antiepileptics neurodegeneration in epilepsy to prevent models. Epilepsy Research 2002;50(1-2):141-160
ALZET Comments: Vigabatrin; Tiagabine; SC; Rat; 2 months; Neuroprotection; long-term study.

P4724: A. Cleton, *et al.* Pharmacokinetic-pharmacodynamic modelling of tiagabine CNS effects upon chronic treatment in rats: lack of change in concentration-EEG effect relationship. European Journal of Pharmacology 2000;12(141-150
ALZET Comments: Tiagabine;; Saline;; IV (jugular);; Rat;; 2ML2;; 14 days;; Controls received mp w/ vehicle; functionality of mp verified by plasma levels; dose-response (graph p. 145); comparison of IV injections vs. mp; Tiagabine is a GABA uptake inhibitor; seizure prevention; Epilepsy;.

P3415: T. Halonen, *et al.* Tiagabine prevents seizures, neuronal damage and memory impairment in experimental status epilepticus. Eur. J. Pharmacol 1996;299(69-81
ALZET Comments: Tiagabine; Propylene glycol; SC; Rat; 2ML1; 7 days; functionality of mp verified by in vitro testing and residual volumes; dose-response; half-life (p. 70); compound stable for one week (see p. 78); stability.

Valproic Acid

Q10967: Y. S. Nam, *et al.* Valproic Acid Inhibits Progressive Hereditary Hearing Loss in a KCNQ4 Variant Model through HDAC1 Suppression. International Journal of Moelcular Sciences 2023;24(6):
Agents: Valproic acid **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Strain:** W276S; **Pump:** Not Stated; **Duration:** 4 weeks;
ALZET Comments: Dose (200 mg/kg/day); animal info: C57BL/6N background; genetic hearing loss

Q6273: Z. Wang, *et al.* Infusion of Valproic Acid Into the Renal Medulla Activates Stem Cell Population and Attenuates Salt-Sensitive Hypertension in Dahl S Rats. Cellular Physiology and Biochemistry 2017;42(3):1264-1273
Agents: Valproic acid **Vehicle:** Not Stated; **Route:** IR (intra-renal); **Species:** Rat; **Pump:** 2ML2; **Duration:** 10 days;
ALZET Comments: Dose (50mg/Kg/d); Controls received mp w/ vehicle; animal info (male Dahl salt-sensitive rats, SS-13BN);

Q6267: P. Farzanehfar, *et al.* Can Valproic Acid Regulate Neurogenesis from Nestin+ Cells in the Adult Midbrain? Neurochem Res 2017;42(8):2127-2134
Agents: Valproic acid **Vehicle:** Saline; **Route:** CSF/CNS (left midbrain); **Species:** Mice (transgenic); **Pump:** 1002; **Duration:** 2 weeks; 4 weeks;
ALZET Comments: Dose (0.25 mg/µl); Controls received mp w/ vehicle; animal info (NestinCreERT2 C57BL/6 mice); ALZET brain infusion kit 1 used; Brain coordinates (3.0 mm posterior to Bregma, 1.5 mm lateral to the midline, and 4.0 mm below the surface of the brain); neurodegenerative (Parkinson's disease);

Q4357: C. Z. Chang, *et al.* Valproic acid attenuates intercellular adhesion molecule-1 and E-selectin through a chemokine ligand 5 dependent mechanism and subarachnoid hemorrhage induced vasospasm in a rat model. Journal of Inflammation-London 2015;12(U1-U11
Agents: Valproic acid **Vehicle:** PBS; **Route:** Not Stated; **Species:** Rat; **Pump:** Not Stated; **Duration:** 5 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 300-400g); ischemia (cerebral); dose-response (pg 4-6); behavioral testing (modified limb-placing test); cardiovascular; bp measured using tail cuff;

Q4323: R. C. Bates, *et al.* Increasing pro-survival factors within whole brain tissue of Sprague Dawley rats via intracerebral administration of modified valproic acid. JOURNAL OF PHARMACOLOGICAL SCIENCES 2015;128(193-201
Agents: Valproic acid-PEG **Vehicle:** Not Stated; **Route:** CSF/CNS caudate putamen; sagittal fissure; **Species:** Rat; **Pump:** 2004; **Duration:** 25 days;
ALZET Comments: Animal info (male, Sprague Dawley, 275-300g); ALZET brain infusion kit 1 used; behavioral testing (elevated plus maze, open field test); wound clips used;

Q6725: W. H. Lu, *et al.* Valproic acid attenuates microgliosis in injured spinal cord and purinergic P2X4 receptor expression in activated microglia. J Neurosci Res 2013;91(5):694-705
Agents: Valproic acid **Vehicle:** PBS; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 1003D; **Duration:** 3 days;
ALZET Comments: Dose (1.5 µg VPA); Controls received mp w/ vehicle; animal info (Female adult Sprague-Dawley rats (n =41; 250 +/-30 g)); post op. care (sodium ampicillin); behavioral testing (locomotor function); enzyme inhibitor (histone deacetylase (HDAC) inhibitor); ALZET brain infusion kit 3 used; spinal cord injury;

Q3024: R. C. Bates, *et al.* Chronic central administration of valproic acid: increased pro-survival phospho-proteins and growth cone associated proteins with no behavioral pathology. Pharmacology Biochemistry and Behavior 2012;103(237-244
Agents: Valproic Acid **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2004; **Duration:** 28 days;
ALZET Comments: Controls received mp w/ saline; animal info (Sprague-Dawley, adult male, 250-280g); ALZET brain infusion kit (1) used; behavioral testing (elevated plus maze, and open field maze)

P9619: K. Kitazoe, *et al.* Valproic acid exerts anti-tumor as well as anti-angiogenic effects on myeloma. International Journal of Hematology 2009;89(1):45-57
Agents: Valproic acid **Vehicle:** PBS; **Route:** SC; **Species:** Mice (SCID); **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: Controls received mp w/vehicle; cancer (myeloma); animal info (8-10 wks old, female)

R0242: W. Loescher. The pharmacokinetics of antiepileptic drugs in rats: Consequences for maintaining effective drug levels during prolonged drug administration in rat models of epilepsy. Epilepsia 2007;48(7):1245-1258
Agents: Levetiracetam; phenobarbital; phenytoin; valproic acid; vigabatrin **Vehicle:** Water, distilled; PEG 300; Glycerol; PEG 400; Propylene glycol; **Route:** SC; IP; **Species:** Rat; Mice; Gerbils; **Pump:** 2ML1; 2ML2; **Duration:** 1,4,2 weeks; 7 days;
ALZET Comments: Comparison of IV, IP injections vs. food or water delivery vs mp; pumps replaced (every week in one set of experiments); stress/adverse reaction: (see pg. 1255); peritoneal irritation, peritonitis in some of the IP experiments);

P9073: Q. Shu, *et al.* Valproic Acid prolongs survival time of severe combined immunodeficient mice bearing intracerebellar orthotopic medulloblastoma xenografts. Clinical Cancer Research 2006;12(15):4687-4694
Agents: Valproic acid **Vehicle:** Sodium chloride; **Route:** SC; **Species:** Mice (SCID); **Pump:** 2001; **Duration:** 14 days;
ALZET Comments: Controls received no treatment; pumps replaced after 7 days; animal info (6-10 wks old, Rag 2)

P8386: A. Serralta*, et al.* Effect of intracerebroventricular continuous infusion of valproic acid versus single i.p. and i.c.v. injections in the amygdala kindling epilepsy model. Epilepsy Research 2006;70(1):15-26
Agents: Valproic acid **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2001; 2002; **Duration:** 7 days;
ALZET Comments: Controls received no treatment; dose-response (fig. 1); comparison of icv, IP injections vs. mp; no stress (see pg. 22); toxicology; multiple pumps per animal (2); animal info (male, Wistar, amygdala-kindled epilepsy, 380-420g.); mp primed 1 hr. in 37.5 celsius saline; evans blue dye used to confirm cannula placement, "

P3616: S. Ohdo*, et al.* Influence of feeding schedule on the chrono pharmacological aspects of sodium valproate in mice. J. Pharmacol. Exp. Ther 1996;278(1):74-81
Agents: Valproic acid **Vehicle:** Saline, sterile physiological; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** Not Stated;
ALZET Comments: Functionality of mp verified by plasma levels; half-life of less than 1 hour (p. 76); 2 mps implanted concomitantly

P2820: J.-G. Song. Chronopharmacokinetices of valproic acid in mice following constant-rate administration by osmotic minipump. Chinese Pharmacological Bulletin 1995;11(2):135-136
Agents: Valproic acid **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** Not Stated;
ALZET Comments: Comparison of iv injections vs. mp; article in Chinese w/ abstract in English

P1335: R. Paulson*, et al.* Effects of sodium valproate and oxygen on the CD-1 mouse fetus. J. Craniofac. Genet. Dev. Biol 1988;8(35-42
Agents: Valproic acid **Vehicle:** Sodium carbonate; Water; **Route:** SC; **Species:** Mice (pregnant); **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Dose-response (text, graph); half-life; 2 pumps implanted simultaneously; functionality of mp verified by plasma levels; no stress; toxicology/teratology

R0077: N. Ray*, et al.* Implantable osmotically powered drug delivery systems. In 'Drug Delivery Systems: Fundamentals and Techniques,' P. Johnson and J. G. Lloyd-Jones (eds.), Ellis Horwood Ltd. , Chichester, England and VCH Verlasgesellschaft mbH, Weinheim, Federal Republic of Germany 1987;Ch. 7):120-138
Agents: Antipyrine; bleomycin; dopamine HCl; melatonin; methotrexate, sodium; nicotine; prednisolone; radio-isotopes; valproic acid **Vehicle:** ^{14}C tracer; ^{3}H tracer; **Route:** IA; IP; SC; **Species:** Mice; Rabbit; Rat; **Pump:** Not Stated;
ALZET Comments: synoptic review of mp; post op. care; comparison of sc injections vs. mp infusion; pulsed delivery

P0848: H. Nau. Valproic acid teratogenicity in mice after various administration and phenobarbital-pretreatment regimens: the parent drug and not one of the metabolites assayed is implicated as teratogen. Fundam. Appl. Toxicol 1986;6(4):662-668
Agents: Valproic acid **Vehicle:** Water; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 1 day;
ALZET Comments: Teratology; states pump rate at 8 ul/hr; 2 doses of vpa infused;

P0886: W. Loscher. Development of tolerance to the anticonvulsant effect of GABAmimetic drugs in genetically epilepsy-prone gerbils. Pharmacol. Biochem. Behav 1986;24(1007-1013
Agents: Aminobutyric acid, Y-acetylenic Y-; Aminooxyacetic acid; Diazepam; THIP; Valproic acid **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 2 weeks;
ALZET Comments: controls received mp w/saline; diazepam too unstable to be used in mp; epilepsy; functionality of mp verified after 14 day exper. period - all 50 mps worked accurately; stability of VPA, THIP, GAG and AOAA

R0079: H. Nau*, et al.* Controlled-rate drug administration in testing for toxicity, in particular teratogenicity toward interspecies bioequivalence. In 'Topics in Pharmaceutical Sciences,' D. D. Breimer and P. Speiser (eds.), Elsevier Science Publishers B. V. , 1985 1985;143-157
Agents: Cyclophosphamide; Valproic acid **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated;
ALZET Comments: Pump model not stated; review; dose-response (graph); half-life; comparison of injections vs. mp infusion;

R0061: H. Nau. Improvement of testing for teratogenicity by pharmacokinetics. Concepts Toxicol 1985;3(130-137
Agents: Valproic acid **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Not Stated; **Pump:** Not Stated; **Duration:** Not Stated;
ALZET Comments: Teratology; injection-infusion comparison protocol w/ VPA discussed

P0366: W. Loscher, *et al.* Distribution of valproic acid and its metabolites in various brain areas of dogs and rats after acute and prolonged treatment. J. Pharmacol. Exp. Ther 1983;226(3):845-854
Agents: Valproic acid **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 1, 3, 14 days;
ALZET Comments: no comment posted

P0274: H. Nau, *et al.* Pharmacokinetics of valproic acid and metabolites in mouse plasma and brain following constant-rate application of the drug and its unsaturated metabolite with an osmotic delivery system. Bioorganic & Medicinal Chemistry Letters 1982;3(317-328
Agents: Valproic acid **Vehicle:** Sodium bicarbonate; Water; **Route:** SC; **Species:** Mice; **Pump:** 2001; 2002; **Duration:** 1 week;
ALZET Comments: Intermittent sc. injec. vs. mp infusion; 1 or 2 pumps/animal;

P0175: H. Nau, *et al.* A new model for embryotoxicity testing: teratogenicity and pharmacokinetics of valproic acid following constant-rate administration in the mouse using human therapeutic drug and metabolite concentrations. Life Sci 1981;29(26):2803-2813
Agents: Valproic acid **Vehicle:** Water; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: 1 or 2 pumps/mouse; comparison of injection vs. infusion and human vs. animal pharmacokinetics

Vigabatrin

Q11074: K. Fukuyama, *et al.* Opposing effects of clozapine and brexpiprazole on beta-aminoisobutyric acid: Pathophysiology of antipsychotics-induced weight gain. Schizophrenia 2023;9(1):8
Agents: Vigabatrin **Vehicle:** Clozapine; brexpiprazole; vigabatrin; **Route:** SC; **Species:** Rat; **Strain:** Sprague-Dawley; **Pump:** 2ML1; **Duration:** 14 days;
ALZET Comments: Dose: (clozapine 5 mg/kg/day, brexpiprazole 10 mg/kg/day, vigabatrin 75 mg/kg/day); Controls received mp w/ vehicle; animal info (Male; 6-7 weeks old); functionality of mp verified by plasma concentration p. 4 fig. 1; schizophrenia

Q9523: D. Walters, *et al.* Transcriptome analysis in mice treated with vigabatrin identifies dysregulation of genes associated with retinal signaling circuitry. Epilepsy Research 2020;166(106395
Agents: Vigabatrin **Vehicle:** PBS; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 12 days;
ALZET Comments: Dose (140 mg/kg/day); Controls received mp w/ vehicle; animal info (C57Bl/6 J mice, 8-10 weeks of age, 20.8–26.1 g in weight); Vigabatrin aka VGB; dependence;

Q6994: D. C. Walters, *et al.* Preclinical tissue distribution and metabolic correlations of vigabatrin, an antiepileptic drug associated with potential use-limiting visual field defects. Pharmacol Res Perspect 2019;7(1):e00456
Agents: Vigabatrin **Vehicle:** PBS; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 12 days;
ALZET Comments: Dose (35, 70, and 140 mg/kg/d); Controls received mp w/ vehicle; animal info (Male C57BL/6J mice, 8-10 weeks old, 20.8-26.1 g); post op. care (Carprofen); dependence;

Q7675: D. C. Walters, *et al.* Metabolomic analyses of vigabatrin (VGB)-treated mice: GABA-transaminase inhibition significantly alters amino acid profiles in murine neural and non-neural tissues. Neurochem Int 2019;125(151-162
Agents: Vigabatrin **Vehicle:** PBS; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: Dose (35, 70 and 140 mg/kg/d); dose-response (dose escalation); animal info (8–10 weeks of age and 20.8–26.1 g); Bigabatrin aka VGB; enzyme inhibitor (Vigabatrin inhibits GABA transaminase);

Q5697: K. R. Vogel, *et al.* mTOR Inhibition Mitigates Molecular and Biochemical Alterations of Vigabatrin-Induced Visual Field Toxicity in Mice. Pediatr Neurol 2017;66(44-52 e1
Agents: Vigabatrin **Vehicle:** PBS; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (C57BL6, 8 weeks old);

R0242: W. Loescher. The pharmacokinetics of antiepileptic drugs in rats: Consequences for maintaining effective drug levels during prolonged drug administration in rat models of epilepsy. Epilepsia 2007;48(7):1245-1258
Agents: Levetiracetam; phenobarbital; phenytoin; valproic acid; vigabatrin **Vehicle:** Water, distilled; PEG 300; Glycerol; PEG 400; Propylene glycol; **Route:** SC; IP; **Species:** Rat; Mice; Gerbils; **Pump:** 2ML1; 2ML2; **Duration:** 1,4,2 weeks; 7 days;
ALZET Comments: Comparison of IV, IP injections vs. food or water delivery vs mp; pumps replaced (every week in one set of experiments); stress/adverse reaction: (see pg. 1255); peritoneal irritation, peritonitis in some of the IP experiments); half-life (p. 1247) table 1 (18 compounds); animal info (epileptic, Sprague-Dawley, Wistar); review; see p. 1254-1255; see table 4 for advantages + disadvantages of different application routes

R0177: A. Pitkanen. Efficacy of current antiepileptics neurodegeneration in epilepsy to prevent models. Epilepsy Research 2002;50(1-2):141-160
Agents: Vigabatrin; Tiagabine **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 2 months;
ALZET Comments: Neuroprotection; pump use mentioned on p. 147 and 155; long-term study

P4904: T. Halonen*, et al.* Chronic elevation of brain GABA levels beginning two days after status epilepticus does not prevent epileptogenesis in rats. Neuropharmacology 2001;40(536-550
Agents: Vigabatrin **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 10 weeks;
ALZET Comments: controls received mp w/ vehicle; long-term study, pumps replaced every 2 weeks for 10 weeks; epilepsy; seizures.

P4343: A. Pitkanen*, et al.* Effects of vigabatrin treatment on status epilepticus-induced neuronal damage and mossy fiber sprouting in the rat hippocampus. Epilepsy Research 1999;33(67-85
Agents: Vigabatrin **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 2 months;
ALZET Comments: Controls received mp with vehicle; functionality of mp verified by plasma levels and residual volume; long-term study, pumps replaced every 2 weeks; enzyme inhibitor

P4249: D. A. Golombek*, et al.* Inhibition of GABA transaminase enhances light-induced circadian phase delays but not advances. J. Biol. Rhythms 1994;9(3-4):251-261
Agents: Vigabatrin **Vehicle:** Saline; **Route:** IP; **Species:** Hamster; **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: Controls received mp w/saline or no treatment; comparison of injections vs. mp; GABA transaminase inhibitor