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);


**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);


**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


**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.)
**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 concomitant in the same pump

**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

**Agents:** Phenelzine; Tranylcypromine, 4-methoxy-; Acetylphenelzine, N2-; Tranylcypromine, 4-fluoro-; 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

**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)

**Agents:** Phenelzine sulfate; Phenylethylamine HCl, 2-; Deprenyl HCl  **Vehicle:** Saline;  **Route:** SC;  **Species:** Rat;  **Pump:** 2002; 2ML2;  **Duration:** 28 days;
**ALZET Comments:** Antidepressant; controls received mp w/ vehicle; multiple pumps per animal (2)

**Agents:** Imipramine HCl; Desipramine HCl; Clomipramine HCl; Tranylcypromine HCl; Phenelzine sulfate; Chlorgyline 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

**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)

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; hypothalmic electrodes implanted for self-stimulation to further access agents effects; antihypertensive


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)


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

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;


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);


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);


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);


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); "

Q8460: "

**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;


**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;


**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;


**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;


**Agents:** Levetiracetam  **Vehicle:** Saline;  **Route:** SC;  **Species:** Mice;  **Pump:** Not Stated;  **Duration:** 28 days;

**ALZET Comments:** Controls received mp w/ vehicle; animal info (4-5 months, heterozygous hAPP transgenic and wild-type, C57N1/6J);


**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);


**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)


**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

**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;


**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)


**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)


**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


**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);


**Agents:** Levetiracetam  
**Vehicle:** Not Stated;  
**Route:** Not Stated;  
**Species:** Rat;  
**Pump:** Not Stated;  
**Duration:** 2 weeks;  

**ALZET Comments:** ALZET pumps mentioned on pg. 113

**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


**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


**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;


**Agents:** Chlorpromazine; haloperidol; phenobarbital; promethazine  
**Route:** SC  
**Species:** Rat  
**Pump:** 2002  
**Duration:** 8 days  
**ALZET Comments:** Comparison of agents effects


**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


**Agents:** Phenobarbital  
**Vehicle:** Water  
**Route:** IP  
**Species:** Rat  
**Pump:** Not Stated  
**Duration:** 5 days  
**ALZET Comments:** bolus injec. vs. mp infusion


**Agents:** Phenobarbital, sodium  
**Vehicle:** Propylene glycol  
**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


ALZET Comments: Chlorpromazine; haloperidol; phenobarbital; promethazine; SC; Rat; 2001; 8 days; Comparison of agents effects.

Tiagabine

Agents: Tiagabine; Valproate; Levetiracetam Vehicle: Not Stated; Route: SC, CSF/CNS (intracerebral); IV; Species: Rat; Pump: Not stated; Duration: 3 days; 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);


ALZET Comments: Vigabatrin; Tiagabine; SC; Rat; 2 months; Neuroprotection; pump use mentioned on p. 147 and 155; long-term study.


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.


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


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);


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);


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;
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;

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;

Agents: Valproic Acid Vehicle: Not Stated; Route: SC; Species: Rat; Pump: 2004; Duration: 28 days;
ALZET Comments: Controls received mp w/ saline; cancer (myeloma); animal info (Sprague-Dawley, adult male, 250-280g); ALZET brain infusion kit (1) used; behavioral testing (elevated plus maze, and open field maze)

Agents: Valproic acid Vehicle: PBS; Route: SC; Species: Mice (SCID); Pump: 2001; Duration: 14 days;
ALZET Comments: Controls received mp with vehicle; 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; 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);

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)

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); toxicity; 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, ”

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

**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


**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


**Agents:** Antipyrine; bleomycin; dopamine HCl; melatonin; methotrexate, sodium; nicotine; prednisolone; radio-isotopes; valproic acid  
**Vehicle:** 14C tracer; 3H tracer  
**Route:** IA; IP; SC  
**Species:** Mice; Rabbit; Rat  
**Pump:** Not Stated  
**Duration:** 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;

**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**

**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;


**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;


**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:** Not Stated;  
**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


**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.
**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

**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