



**Studies With Information Regarding Stability of Agents
ALZET® Osmotic Pumps**

This bibliography does not include references prior to 2010. To obtain the bibliographic list of earlier references, please contact ALZET Technical Services at (800) 692-2990 or email to alzet@durect.com.

<u>Agent</u>	<u>Stability Verified Through</u>	<u>References</u>
6E10	5 weeks	P9867
A-127722		P6953
Acetylcholine HCl	13 days 15 days	P0439 P1926
ACTH	7 days 3 days 7 days 81-120 days	P0449 P0446 S1087 P2344
Adrenomedullin	21 days	P4131
Aldosterone	3 days	P0612
Aminoxyacetic acid	14 days	P0886
Aminolevulinic acid, 5-	12 hrs	P3750
Aminopyrine	7 days	P3395
Amitriptyline	7 days	P2779
Amyloid protein, beta	2,4 weeks	P7068
Angiostatin	7 days	P5052
Angiotensin II	6 days 6 days 6 days 10-12 days 14 days 7 days	P0480 P1008 P3530 P1992 P3064 P4590
Angiotensinogen	7 days 7 days 6 days	P1047 P0699 P1008
Antibody/Immunoglobulin	15 days	P8266, P1136
Antichymotripsin, alpha-1	28 days	Q0562
Apomorphine	20 days 14 days	P5291 P1291



Argatroban	4 weeks	Q2300
Arginine, N(omega)-hydroxy-nor-I Atrial Natriuretic Factor	10 days	Q4902
	14 days	P1724
	14 days	P1521
	13 days	P0911
	7-14 days	P1653
	6 days	P0871
	6 days	P1564
	7 days	P0990
	3 days	P1032
Atriopeptin III	7 days	P0990
Atropine, Methyl-	5 weeks	P0683
Azidothymidine	7 days	P1644
Bacteria, vibrio cholerae	7 days	P1380
Bafilomycin A1	2 weeks	P2976
BDNF, recombinant human	28 days	P5186
	2 weeks	P3290
	2 weeks	P3031
	2 weeks	P2933
	2 weeks	P2562
	30 days	P3430
	14 days	P9237
BE16627B	18 days	P2788
Benazeprilat	2 weeks	P3939
Benzylamine	2 weeks	P4873
	2 weeks	P5688
Benzylguanine, O6-	14 days	P7702
Bromodeoxyuridine	1 week (80%)	P3208
Buserelin	2 weeks	P0457
Buspirone HCl	2 weeks	P0813
C-reactive protein	2 weeks	P9632
C3	>40 days	Q3859
Calcitonin	7 days	P1087
Calcitonin-Gene Related Peptide (8-37)	14 days	P5575



Captopril	4 weeks	P0910
	2 weeks	P1036
Carbachol	6 days	P0628
Carboplatin	7 days	P5476
	4 weeks	Q0707
Carboxyfullerine Catalase	>40 days	Q3959
	7 days	P2520
	20 days	P1741
CCX662	16 days	Q3365
CART (42-89)	10 days	P4764
Celecoxib CGS-16949A	28 days	Q0379
	4, 12 weeks	P2209
	6 weeks	P2208
CGS-22652	2 weeks	P2678
CHF-1024	1 month	P7942
Chlordiazepoxide	"Half-time 8.8 days"	P9959
Chlorpromazine	2 weeks	P0385
Cholecystokinin 8	5 days	P0879
Chondroitinase ABC	7 days	P7563
Clozapine	2 weeks	P0385
CNP-22	7 days	P4017
Cocaine HCl	14 days	P2218
Collagenase	7 days	P1957
Cortisol, 21-hemisuccinate	18 days	P2997
Cytochrome C	14 days	P2256
	1 week	P4031
DADLE (enkephalin analog)	7 days	P2630
Dexamethasone	12-26 days	P3120
	26 days	Q2064
	7 days	Q4838



Dopamine HCl	14 days	P1291
	13 days	P0439
	13 days	P0959
	10 days	P1733
	7 days	P0592
	7 days	P1313
Dopamine, 6-hydroxy	8 days	P2562
	7 days	P3514
	7 days	P0495
	7 days	P0606
	7 days	S0317
	7 days	P3932
Doxorubicin	18 days	P2788
DNA	28 days	P6539
DPAT, 7-hydroxy-U-99194A maleate	14 days	P7137
Dynorphin A (1-13)	7 days	P1261
Echistatin	14 days	P5567
Edaravone	24 hours	P7529
Endomorphine Analog	>1 year	Q5105
Endostatin	32 days	P5030
Endothelin	3 days	P3586
	6 days	P1810
	6 days	P1803
Endothelin-1	4 weeks	P3039
	2 weeks	P4492
	2 weeks	P5690
Endothelin-3	3 days	P3586
Endotoxin	1 week	P1828
	1 week	P0425
Epinephrine	6 days	P3530
Estradiol, 17A-	7 days	P0763
Estradiol, 17B-	7 days	P0763
Estradiol, 2-hydroxy-	7 days	P0763



Estrone, 2-hydroxy-	7 days	P0763
Fadrozole	4 weeks 2 weeks	P2209 P2208
Fibroblast Growth Factor	4 days	P2490
Fibroblast Growth Factor, basic	Up to 4 weeks	P2901
Ficoll, 3H-carboxymethyl	7 days	P6599
Flurbiprofen	14 days	Q0222
Formoterol fumarate	20 hrs	P5817
Forskolin	7 days	P3932
Fluorodeoxy Cytidine	45 days	Q5174
Fluvoxamine	21 days	P2641
Furosemide	28 days	P5336
FMRFamide		P6115
GABA	14 days 13 days	P0886 P0439
Gabapentin	14 days	P5337
Gastrin-17	7 days	P7077
Gene, HSV-Tk + liposome	3 days	P3860
Gene, LacZ + Liposome	3 days	P3860
Gentamicin	7 days	Q2064
Glibenclamide	48 hours	Q2174
Glycine	13 days	P0959
Gonadotropin-releasing hormone	2 weeks	Q3663
GP120	2 weeks	P3880
Growth Hormone	7 days 4 days 2 weeks (rat)	P1478 P3289 Q0258
H7	24 hours	P2981
H89 (Protein kinase A inhibitor)	7 days	P5269



Haloperidol	2 weeks	P0813
	4 weeks	P0385
	2 weeks	P0556
Heregulin	7 days	P3717
Hexamethylphosphoramide	4 weeks	P3737
Horseradish Peroxidase	48 hours	P0389
HS024	4 weeks	P6559
HU210	6 weeks	Q2667
Human Placental Lactogen	6 days	P2220
Hydroxytryptamine Antagonist	1,2,3 weeks	P1735
Idazoxan	7 days	P1270
Imipramine	14 days	P5337
Insulin	4 weeks	S0774
	10 days	P1402
	10 days	P1442
	>11 days	P5850
Insulin-like Growth Factor I and II	6 days	P0599
	14 days	P4150
Insulin-like growth factor I, receptor antagonist	4 weeks	P7467
Interferon, alpha	8 weeks	Q1983
Interferon-gamma	7 days	Q1983
	8 weeks	
Interleukin 1	14 days	P2542
	7 days	P2140
	7 days	P1957
	14 days	P4586
Interleukin 2	7 days	P0550
	7 days	P2749
	6 days	P1837
Interleukin 3	7 days	P3567
Interleukin 6-PE	7 days	P1913
IL13-PE38QQR	7 days	P6373



Interleukin B, recomb. human	7 days	P2177
	7 days	P2639
Iododeoxyuridine	1 week (80%)	P3229
		P3165
JNJ-31020028	28 days	Q2631
Ketamine	14 days	P5337
Kisspeptin-54	14 days	P7900
KYP-2047	1 month	Q3622
Leptin	14 days	P5391
Lisuride	14 days	P1320
L-NAME	4 or 8 days	P2585
		P6953
Marinobufagenin	4 weeks	P7519
Melanin Concentrating Hormone	7+ days	P0985
Melatonin	14 days	P1111
Methotrexate	7 days	P0592
Methylene Blue	-----	P1906
MMP-2	28 days	P5819
MK-771 (thyroxine analog)	7 days	P0638
MPP ⁺	28 days	P8284
MTII (non-specific melanocortin agonist)	28 days	P5207
Morpine sulfate	7 days	P2630
	14 days	P5337
Nerve Growth Factor	15 days	P2348
	1 month	P1927
	1 month	P1658
	14 days	P3260
	14 days	P2933
	14 days	P2256
	14 days	P0923



	14 days	P0933
	14 days	S0632
	7 days	P0473
	14 days	P2758
	----	P2775
	14 days	P3877
Neuropeptide Y	14 days	P1983
Neurotensin	8 days	P0572
Neurotrophin-4/5	14 days	P7844
Neurotrophin-3	14 days	P8606
Nicotine Bitartrate	16 days	P0976
Nogo receptor, soluble fragment	1 month	P9513
Norepinephrine	14 days	P0632
	13 days	P0423
	13 days	P0439
	5 days	P0152
NT-3	14 days	P3290
	14 days	P2562
	28 days	P3913
NXY-059	3 days	P4957
Olanzapine	4 weeks	P9790
Oligodeoxynucleotide, antisense	14 days	P3934
Oligodeoxyn-, phosphorothioate	14 days	P3809
Osteogenic progein-1	14 days	P4902
	14 days	P6921
Oxtremorine	5 weeks	P0683
Oxytocin	10 days	P1976
	10 days	P2766
	10 days (44% destruction)	P3050
P110-TAT	28 days	Q3188
Parathyroid Hormone	13 days	P0415
	5 days	P1449
Parathyroid Hormone-like Protein	5 days	P1449
Peptide T	14 days	P2074



Peptide YY (3-36)	28 days 14 days	P8015 Q1576
Phenylarsonous acid	2 weeks	Q0586
Phosphonovaleric acid	7 days	P1597
Physostigmine	7 days	P1508
Pioglitazone	21 days 21 days	P8145 Q3340
Platelet-activating factor	12 days	P1926
Plasminogen activator inhibitor-1		P6129
Platelet factor-4	28 days	P5819
PR-21	14 days	Q0450
Prolactin	2 days	P1758
Propranolol	28 days 11 days 9 days -----	P1693 P5559 P0011 P2894
Proline, L-	7 days	P3740
Proline, nitric acid	7 days	P3740
Propionamide ditri-fluoroacetate	>2 hours	Q5308
Prostaglandin (A ₂ ,D ₂ ,E ₂ ,F _{2A} ,I ₁)	7 days	P3077
Prostaglandin E1	7 days ----- 1 week (70%)	P1917 P1092 P3028
Quinpirole	7 days 7 days	P2115 P1466
Rapamycin	14 days	P3013
Reelin, recomb.	2 weeks	P9766
RG108	20 days	Q4616
Rilmenidine	30 days	P6378
Rosiglitazone Maleate	24-48 hours	Q5322



Serotonin	13 days	P0439
	7 days	P0671
SHU-9119	21 days	Q2499
Small Interfering RNA (LNA modified)	>48 hours	P8305
	28 days	P8852
Somatostatin	7 days	P0967
Strychnine	13 days	P0959
Substance P	8 days	P0572
	14 days	P2259
Sulpiride	7 days	P2115
Superoxide Dismutase	20 days	P1741
	7 days	P2520
TAT-peptide	2 weeks	Q1165
Theophylline	7 days	P0823
THIP	14 days	P0886
Thymidine,5' amino5' deoxy-	6 days	P3380
Thyroid stimulating hormone	7 days	P1126
Thyrotropin Releasing Hormone	8 days	P0572
	7 days	P0967
	7 days	P1126
Thyroxine	14 days	P1306
	7 days	P1331
Tiagabine	7 days	P3415
Toxin, TGF- α chimeric-	7 days (80-100%)	P3210
Transforming Growth Factor	7 days	P2590
	7 days	P2583
	21 days	P4770
	2,4 weeks	P7068
TGF-B20 soluble receptor	14 days	P5046
Thrombospondin-1, three type 1 repeats	7 days	P8302
TLQP-21, synthetic	14 days	P7973
Triazolam	7 days	P2115
Triiodothyronine	7 days	P1331



Tryptophan, L-5-hydroxy-	1 week	P1882
TT-232	3 weeks	P8928
	3 weeks	P6497
	>3 weeks	P6894
Tumor Necrosis Factor	14 days	P4672
Urease		7 days
Uridine, Bromodeoxy-	7 days	P3208
	3-11 days	P7105
Uridine, 5-fluoro-2'-deoxy-	7 days	P3208
	7 days	P1917
Uridine, iododeoxy-	7 days	P2917
Valproic Acid	14 days	P0886
Valsartan	2 weeks	P3939
Vasoactive Intestinal Peptide	17 days	P2858
Vasopressin, arginine	7 days	P3109
Vasopressin, 1-desamino- 8-D-arginine	3 days	P0668
	7 days	P1556
VEGF	2 weeks	P5670
Verapamil	2 weeks	P5832
Vitamin D3, 1,25-dihydroxy-	4 weeks	P8289
VX	1 week	P9487
Y27632	4 weeks	P9438
	13 days	P7559



Recent References (2010-2019) on the Stability of Agents Administered Using ALZET® Osmotic Pumps

Q7293: A. T. Larsen, *et al.* The Dual Amylin and Calcitonin Receptor Agonist KBP-088 Induces Weight Loss and Improves Insulin Sensitivity Superior to Chronic Amylin Therapy. *J Pharmacol Exp Ther* 2019;370(1):35-43

Agents: Amylin, KBP-088 **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 4 weeks;

ALZET Comments: Dose: KBP-088 (5 µg/kg/day), rat amylin (100, 300, 1000 µg/kg/day); Controls received mp w/ vehicle; animal info (Long Evans rats (10 weeks old); stability verified (a stability test of amylin in the concentrations used in the osmotic pumps shows that the peptide remains stable throughout the study); KBP-088 is a potent dual amylin and calcitonin receptor agonist (DACRA); obesity;

Q6978: R. D. Cole, *et al.* Adolescent and adult nicotine exposure differentially impacts oral nicotine and oral saccharin self-administration in mice. *Behav Brain Res* 2019;359(836-844

ALZET Comments: nicotine hydrogen tartrate; Saline; SC; Mice; 1002; 2 weeks; Dose (3.0 mg/kg/d - adolescent, 6.3 mg/kg/d-adult); Controls received mp w/ vehicle; animal info (adolescent, adult); stability verified by (measuring the residual volume following surgical removal at the end of the exposure period for each time point); half-life 10 min (p.841); dependence;

Q7043: J. Yang, *et al.* Inhibition of the CD36 receptor reduces visceral fat accumulation and improves insulin resistance in obese mice carrying the BDNF-Val66Met variant. *J Biol Chem* 2018;293(34):13338-13348

ALZET Comments: Salvianolic acid B, neutralized; Saline; SC; Mice; 2004; 8 weeks; Dose (50 mg/kg/day); Controls received mp w/ vehicle; pumps replaced every 4 weeks; 4-week stability verified at 37 degree at pH 7.0 (Fig. 1C); salvianolic acid B is a polyphenol compound extracted from the roots of *Salvia miltiorrhiza* Bunge. It is also a CD36 antagonist; Obesity;

Q7046: M. Shimamura, *et al.* Therapeutic Effects of Systemic Administration of the Novel RANKL-Modified Peptide, MHP1, for Ischemic Stroke in Mice. *Biomed Res Int* 2018;2018(4637084

ALZET Comments: Microglial healing peptide 1; Saline; SC; Mice; 2001D; 24 hours; Dose (2 mg/mL); Controls received mp w/ vehicle; 24 hour stability verified by in vitro inhibitory activity of TLR4-induced inflammation. (); MHP1 is a Novel RANKL-Modified Peptide; Therapeutic indication (ischemic stroke);

Q5938: S. Zhu, *et al.* Recombinant Immunotoxin Therapy of Glioblastoma: Smart Design, Key Findings, and Specific Challenges. *Biomed Res Int* 2017;2017(7929286

ALZET Comments: NZ-1-(scdsFv)-PE38KDEL; Mice (SNG); 3 days; cancer (glioblastoma);no stress (see pg. 10);stability verified by (33-98% of activity 3 days at 37C; verified via incubation);

Q6186: E. Tarasco, *et al.* Effect of AP102, a subtype 2 and 5 specific somatostatin analog, on glucose metabolism in rats. *Endocrine* 2017;58(1):124-133

ALZET Comments: AP102, Pasireotide; Saline; SC; Rat; 2ML2; 4 weeks; Dose: AP102 (3 or 10 µg/kg/h); pasireotide (3 or 10 µg/kg/h); Controls received mp w/ vehicle; animal info (male Sprague-Dawley rats); post op. care: antibiotic (Enrofloxacin; 5.7 mg/kg), and analgesics (Flunixin; 1 mg/kg s.c.); pumps replaced every 2 weeks; 13-days stability verified by pump incubation at 37 degrees and liquid chromatography-mass spectrometry analysis; AP102 is a subtype 2 and 5 specific somatostatin analog;.

Q6119: Y. C. Shi, *et al.* Y5 receptor signalling counteracts the anorectic effects of PYY3-36 in diet-induced obese mice. *J Neuroendocrinol* 2017;29(10):

ALZET Comments: Peptide YY (3-36); Disodium hydrogen phosphate, NaCl, Tween 80; SC; Mice; 2004; 21 days; animal info (diet-induced obese wild-type, Y5R knockout); stability verified by (Peptide YY “was stable and functional over the period of the experiment”); Obesity and diabetes;.

Q5842: M. Kano. AMH/MIS as a contraceptive that protects the ovarian reserve during chemotherapy. *Proceedings of the National Academy of Sciences* 2017;114(9):E1688-E1697



ALZET Comments: Mullerian inhibiting substance, recombinant human; Saline; IP; Mice; 1007D; 15 days; Controls received mp w/ vehicle/animal info (6-7 weeks old) ; functionality of mp verified by rhMIS activity; pumps replaced every 5 or 7 days; cancer; half-life is ~ 4 hours (p. E1689); post op. care (carprofen analgesic (2.5 mg/mL) by oral gavage (100 µL)); stability verified by bioassay (“rhMIS activity was remarkably stable, with the material recovered from pumps that had been implanted in mice for 1 wk conserving full biological activity in the rat urogenital ridge bioassay”); “To test the efficacy of rhMIS protein for the preservation of ovarian reserve, we elected to use osmotic pumps implanted i.p. in C57BL/6N female mice to allow very precise delivery of MIS” pg. E1691; Therapeutic indication (Oncofertility, cancer); Dose (1200 ug/mL);.

Q5105: J. E. Zadina, *et al.* Endomorphin analog analgesics with reduced abuse liability, respiratory depression, motor impairment, tolerance, and glial activation relative to morphine. *Neuropharmacology* 2016;105(215-27

ALZET Comments: Morphine; endomorphine analog; Saline; CSF/CNS (intrathecal); Rat; 2001; 7 days; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 250-400g); half-life (p. 219); behavioral testing (tail flick test; rotarod testing); stability verified by (internal testing; stability >1 year at 37C); pumps primed in 37C saline for 16 hours; used PE-8 IT catheter; Dose (2 ug/hr morphine; 0.056-0.075 ug/hr analog);.

Q4902: C. Weber, *et al.* Macrophage Infiltration and Alternative Activation during Wound Healing Promote

MEK1-Induced Skin Carcinogenesis. *Cancer Res* 2016;76(4):805-817

ALZET Comments: arginine, N(omega)-hydroxy-nor-I; SC; Mice; 1004; 33 days; animal info (InvEE); functionality of mp verified by plasma levels; stress/adverse reaction: (see pg. 811); stability verified by (10 days see pg 811); immunology; “Continuous dosing at a rate of 0.25 mL per hour ensured constant compound levels. Successful ARG1 inhibition was confirmed in blood plasma and wounded skin samples taken 5 days after implantation” pg 811; nor-NOHA aka N(omega)-hydroxy-nor-I-arginine;.

Q5174: Y. Pan, *et al.* Inhibition of DNA Methyltransferases Blocks Mutant Huntingtin-Induced Neurotoxicity. *Sci Rep* 2016;6(31022

ALZET Comments: Cytidine, fluorodeoxy-; Saline; CSF/CNS; Mice; 2001; 1 week; ALZET brain infusion kit 3 used; neurodegenerative (Huntington’s disease); stability verified by (“...FdCyd fully maintained its neuroprotective activity after 45 days of pre-incubation” see supplement 2); “...decitabine and FdCyd, are known to be degraded rapidly by cytidine deaminase in the liver (in vivo half life of decitabine <20 min)62, indicating that systemic administration may not be an effective strategy for drug delivery to the brain. We therefore chose intracerebroventricular (icv) administration using an Alzet osmotic pump, which provides continuous infusion of drug at a consistent rate from a subcutaneous pump” pg 8; FdCyd aka Cytidine, fluorodeoxy-; decitabine and FdCyd are similar in structure.

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 neurotrophic 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);.

Q6165: C. K. Kandathil, *et al.* Effects of brain-derived neurotrophic factor (BDNF) on the cochlear nucleus in cats deafened as neonates. *Hear Res* 2016;342(134-143

ALZET Comments: Brain-derived neurotrophic factor, recomb. human; Perilymph, artificial; Ear (cochlea); Cat; 1002, 2004; 10 weeks; Dose (94 mg/ml; 0.25 ml/hr); pumps replaced after 2 and 4 weeks; BDNF stability verified by neuronal cell culture survival assay (28 days);.

Q4838: H. JIA, *et al.* PREVENTION OF TRAUMA-INDUCED COCHLEAR FIBROSIS USING INTRACOCHELEAR APPLICATION OF ANTI-INFLAMMATORY AND ANTIPROLIFERATIVE DRUGS. *neuroscience* 2016;316(261-278



ALZET Comments: Dexamethasone; Ara-C; Perilymph, artificial; Ear (cochlea); Rat; 2001; 7 days; Controls received mp w/ vehicle; animal info (Wistar, adult); animal info (Wistar, adult); stability verified by (incubation in 37C saline for 7 days see pg 268); one cochlea received vehicle only, while other received drug;.

Q4894: J. P. V. a. R. A. Gonzales. Chronic Intracerebroventricular Infusion of Monocyte Chemoattractant Protein-1 Leads to a Persistent Increase in Sweetened Ethanol Consumption During Operant Self-Administration But Does Not Influence Sucrose Consumption in Long-Evans Rats. *ALCOHOLISM-CLINICAL AND EXPERIMENTAL RESEARCH* 2016;40(1):

ALZET Comments: Monocyte chemoattractant protein-1, recombinant rat; CSF, artificial; water, distilled; albumin, rat serum; CSF/CNS; Rat; 1004; 5 weeks; Controls received mp w/ vehicle; animal info (male, Long Evans, 350g); functionality of mp verified by ELISA and manufacturers instructions see pg189; ALZET brain infusion kit 2 used; dose-response (pg.190); post op. care (bupivacaine intradermally; bupivacaine and gentamicin dripped into wound); behavioral testing (alcohol self administration); stability verified by (ELISA pg 192); cyanoacrylate adhesive; "We chose the ICV method to simulate the presence of brain-induced MCP-1 and the method's ability to target the whole brain with molecules that do not readily cross the BBB" pg 188-189; pumps primed at 37C sterile saline; Dose (0.2, 20, 2000 ng/day);.

Q5308: A. Clermont, *et al.* Plasma Kallikrein Mediates Vascular Endothelial Growth Factor-Induced Retinal Dysfunction and Thickening. *Invest Ophthalmol Vis Sci* 2016;57(6):2390-9

ALZET Comments: Fluoroacetate, Propionamide ditri-; PEG 400, PBS; SC; Rat, mice; 1003D, 1007D; 1 day, 2 days; Controls received mp w/ vehicle; animal info (Male Sprague-Dawley (SD) rats 10 wks, plasma prekallikrein gene-deficient mice (KLKB1-/-)); functionality of mp verified by enzyme activity assays; 10% PEG 400 used; dose-response (pg 2394, 2398); stability verified by (single bolus subcutaneous injection); Fluoroacetate, Propionamide ditri- aka VA999272; enzyme inhibitor (PKal inhibitor); enzyme inhibitor (PKal inhibitor); Resultant plasma level (pg 2394);.

Q5322: M. Bazargan, *et al.* Limited fetal metabolism of rosiglitazone: Elimination via the maternal compartment in the pregnant ewe. *Reprod Toxicol* 2016;61(162-8

ALZET Comments: Rosiglitazone Maleate; Water, Ethanol; SC; Sheep (pregnant); 2ML1; 16 days; animal info (Singleton pregnant sheep); functionality of mp verified by plasma level, amniotic fluid samples; 15% ethanol used; Multiple pumps per animal (4); stability verified by regular plasma level measurements (reached after day 5, tested through day 16; half life of 24-48 hours in sheep); Catheters flushed with heparinized saline; Dose (2.7 mg/fetus/d);.

Q7246: X. Bao, *et al.* Preclinical toxicity evaluation of a novel immunotoxin, D2C7-(scdsFv)-PE38KDEL, administered via intracerebral convection-enhanced delivery in rats. *Invest New Drugs* 2016;34(2):149-58

ALZET Comments: Immunotoxin, D2C7-(scdsFv)-PE38KDEL; CSF/CNS (right caudate nucleus); Rat; 2ML1, 2001; 72 hours; Dose (0, 0.05, 0.1, 0.35, 0.4 µg/rat/72 hrs); animal info (Sprague-Dawley; 13-17 weeks old; 360-460 g for males and 210-290 g for females); stability verified by (cytotoxicity assay); stability verified by (cytotoxicity assay); Brain coordinates (1 mm anterior to the bregma, 3 mm to the right of the cranium midline, and 5 mm into the caudate nucleus); cyanoacrylate adhesive (3 M Vetbond Tissue Adhesive); cancer (Glioblastoma); toxicology;.

Q4646: B. A. Williams, *et al.* Multimodal Perineural Analgesia with Combined Bupivacaine-Clonidine-Buprenorphine-Dexamethasone: Safe In Vivo and Chemically Compatible in Solution. *PAIN MEDICINE* 2015;16(186-198

ALZET Comments: Bupivacaine; clonidine; dexamethasone; Saline; CSF/CNS (sciatic nerve); Rat; 2ML1; 7 days; Controls received mp w/ vehicle; animal info (male, albino, CD[SD]); no stress (see pg. 192); post op. care (IM butorphanol tartrate 0.05 mg/kg, ceftiofur sodium 5 mg/kg); stability verified by (pg. 195); used polyurethane catheter 0.5mm ID 0.9 mmOD; pumps removed after 1 week; dose (66.6 µg/mL).

Q4616: P. Tognini, *et al.* Experience-dependent DNA methylation regulates plasticity in the developing visual cortex. *NATURE NEUROSCIENCE* 2015;18(956-+

ALZET Comments: RG108; Cyclodextrin, 2-hydroxypropyl-b-; CSF/CNS; Mice; 1007D; 3 days; Controls received mp w/ vehicle; animal info (C57BL6J, P25); 5% cyclodextrin used; stability verified by (37C t_{1/2} of 20 days); enzyme inhibitor;.



Q5007: C. Lahmann, *et al.* Systemic Administration of Glibenclamide Fails to Achieve Therapeutic Levels in the Brain and Cerebrospinal Fluid of Rodents. *PLoS One* 2015;10(7):e0134476

ALZET Comments: Glibenclamide; CSF, artificial; DMSO; BSA; CSF/CNS; Rat; Mice; 2ML4; 2004; Controls received mp w/ vehicle; animal info (mice nV57M, 11-14 weeks old, 25-30g; rats male Lister-hooded, young adults, 200-300g); functionality of mp verified by plasma levels; rats ALZET brain infusion kit 2 used; mice ALZET brain infusion kit 3 used; 0.1% DMSO used; stability verified by (in vitro experimentation see pg 9); Cannula placement verified via histological analysis;

Q5406: J. K. Hu, *et al.* Murine Antibody Responses to Cleaved Soluble HIV-1 Envelope Trimers Are Highly Restricted in Specificity. *J Virol* 2015;89(20):10383-98

ALZET Comments: BG505 SOSIP/664 trimer; Iscomatrix; SC; Mice; 1007D; 2001; 1002; 2002; 7 days; 14 days; animal info (129/SvJ); Multiple pumps per animal (2); stability verified by (incubation and imaging; 14 day stability. See figure 7 of supplement); immunology; Dose (various, see supplement table 6);

Q3365: M. J. Walters, *et al.* Inhibition of CXCR7 extends survival following irradiation of brain tumours in mice and rats. *British Journal of Cancer* 2014;110(5):1179-1188

ALZET Comments: CCX662; SC; Rat (pregnant); 2004; 2 weeks; 4 weeks;; Controls received mp w/ vehicle; animal info (Sprague Dawley, 115 days old); functionality of mp verified by plasma levels sampled at 9 and 16 days post implantation; pumps replaced every 7 days; cancer (glioblastoma); stability verified by (IC90 value after 16 days); CCX662 is a CXCR7 inhibitor.

Q3663: T. Takeda, *et al.* Maternal Exposure to Dioxin Imprints Sexual Immaturity of the Pups through Fixing the Status of the Reduced Expression of Hypothalamic Gonadotropin-Releasing Hormone. *MOLECULAR PHARMACOLOGY* 2014;85(1):74-82

ALZET Comments: Gonadotropin-releasing hormone; Saline; HCl; CSF/CNS; Rat; 2002; Controls received mp w/ vehicle; animal info (male, Wistar, PND63); ALZET brain infusion kit 2 used; behavioral testing (sexual behavior); stability verified by (incubation of GnRH at 37C for 2 weeks - half of GnRH remains in unchanged form pg.78); teratology; Cannula placement verified via 0.1% infusion of bromophenol blue; 0.1 M HCl.

Q3622: M. H. Savolainen, *et al.* The beneficial effect of a prolyl oligopeptidase inhibitor, KYP-2047, on alpha-synuclein clearance and autophagy in A30P transgenic mouse. *NEUROBIOLOGY OF DISEASE* 2014;68(1-15

ALZET Comments: KYP-2047; DMSO; saline; IP; Mice (transgenic); 28 days; Controls received mp w/ vehicle; animal info (Snca tm(A30P) or WT, 12-13 months old); functionality of mp verified by decrease in PREP activity; 50% DMSO used; neurodegenerative (Parkinson's disease; Lewy body dementia); post op. care (buprenorphine); stability verified by (stability experiment one month); pumps primed overnight in 37C saline; KYP-2047 is a enzyme inhibitor (PREP);

Q3616: C. W. Roman, *et al.* PAC1 receptor antagonism in the bed nucleus of the stria terminalis (BNST) attenuates the endocrine and behavioral consequences of chronic stress. *Psychoneuroendocrinology* 2014;47(151-165

ALZET Comments: Pituitary adenylate cyclase activating polypeptide; Saline; BSA; CSF/CNS; Rat; 2002; 14 days; Animal info (male, adult); behavioral testing (novel object recognition, open field, elevated plus maze); stability verified by (radioimmunoassays; 4% loss per day); cardiovascular; Cannula placement verified via crestyl violet staining and visual inspection; pituitary adenylate cyclase activating polypeptide aka PACP (6-38); delayed delivery; catheters filled with vehicle; pumps primed; PACAP (6-38) is a PAC1 receptor antagonist; stress; y-connector; PACAP (6-38)75uM;

Q3232: J. T. Ke, *et al.* Gliquidone decreases urinary protein by promoting tubular reabsorption in diabetic Goto-Kakizaki rats. *Journal of Endocrinology* 2014;220(2):129-141

ALZET Comments: Gliquidone; Dimethylformamide; IP; Rat; 7 days; Animal info (male, SPF-grade, Goto-Kakizaki, 8 weeks old, 250-300g); functionality of mp verified by blood drug levels; 99.8% dimethylformamide used; comparison of intragastric administration vs mp (pg.133); stability verified by (plasma serum); diabetes;

Q3859: L. L. Dugan, *et al.* Carboxyfullerene Neuroprotection Postinjury in Parkinsonian Nonhuman Primates. *Annals of Neurology* 2014;76(393-402



ALZET Comments: C3; SC; IP; Monkey (macaque); 2ML4; 30 days; Controls received mp w/ placebo; animal info (Macaca fascicularis); Multiple pumps per animal (2); neurodegenerative (Parkinson's disease); behavioral testing (locomotor activity); stability verified by (testing at 37C, C3 is stable for >40 days); Carboxyfullerine aka C3;

Q3426: F. Calcagnoli, *et al.* Chronic enhancement of brain oxytocin levels causes enduring anti-aggressive and pro-social explorative behavioral effects in male rats. *Hormones and Behavior* 2014;65(427-433

ALZET Comments: Oxytocin, synthetic; antagonist, peptidergic oxytocin; Saline, sterile, pyrogen-free; CSF/CNS; Rat; 1007D; 7 days; Controls received mp w/ vehicle; animal info (male, Groningen, adult); ALZET brain infusion kit 2 used; behavioral testing (resident intruder test); stability verified by (pilot study; 44% destruction of OVT over 10 day period in vivo); peptides; Cannula placement verified via dye injection after sacrifice; Plastics One guide cannula; dental acrylic cement and two stainless steel screws; pumps and catheters incubated in room temperature saline overnight;

Q3417: O. Ben Menachem-Zidon, *et al.* Intra-Hippocampal Transplantation of Neural Precursor Cells with Transgenic Over-Expression of IL-1 Receptor Antagonist Rescues Memory and Neurogenesis Impairments in an Alzheimer's Disease Model. *Neuropsychopharmacology* 2014;39(2):401-414

ALZET Comments: Interleukin-1 receptor antagonist; CSF/CNS; Mice (transgenic); 28 days; Controls received mp w/ vehicle; animal info (WT and Tg2576, 11 months old); pumps replaced every 2 weeks; ALZET brain infusion kit 3 used; neurodegenerative (Alzheimer's disease); behavioral testing (fear conditioning; morris water maze); stability verified by (IL-1-ra remains effective for 2 weeks in pumps); Used three anchoring screws;

Q2522: K. Yo, *et al.* Brown adipose tissue and its modulation by a mitochondria-targeted peptide in rat burn injury-induced hypermetabolism. *AMERICAN JOURNAL OF PHYSIOLOGY-ENDOCRINOLOGY AND METABOLISM* 2013;304(4):E331-E341

ALZET Comments: SS31; Saline; IV (jugular); Rat; 7 days; Control animals received mp w/ vehicle; animal info (Sprague Dawley, male, 16-19 wks old, 400-500 g); peptides; stability verified via stable isotope dilution method ("more than 7 days").

Q3188: X. Guo, *et al.* Inhibition of mitochondrial fragmentation diminishes Huntington's disease-associated neurodegeneration. *Journal of Clinical Investigation* 2013;123(12):5371-5388

ALZET Comments: P110-TAT; SC; Mice (transgenic); 8 weeks; Controls received mp w/TAT control peptide; animal info (R6/2 HD model, 5 weeks old); functionality of mp verified by FITC positive signal in neurons pg 5379; pumps replaced every 28 days; neurodegenerative (Huntington's disease); no stress (see pg.5381, 5383); behavioral testing (motor function and behaviors); stability verified by (HPLC with UV detection for 28 days); peptides; P110-TAT is a Drp1-selective peptide inhibitor.

Q3340: C. Grommes, *et al.* The PPARgamma agonist pioglitazone crosses the blood-brain barrier and reduces tumor growth in a human xenograft model. *Cancer Chemotherapy and Pharmacology* 2013;71(4):929-936

ALZET Comments: Pioglitazone; Dulbecco's modified eagle medium; CSF/CNS; Mice (SCID); 2004; 21 days; Controls received mp w/ vehicle; animal info (Balb/CJHanHsd-Prkdc-SCID, 6 weeks old); ALZET brain infusion kit used; comparison of oral dosing vs mp; cancer (tumors); dose-response (CNS); stability verified by (p.934 - incubation at 37C for 21 days); "Intracerebral treatment with 1 IM pio prolonged survival significantly from 49 to 68 days... This defines the minimal effective dose for oral pio treatment at 240 PPM (20.2 mg/kg) and for intracerebral pio treatment at 1 IM (0.11 ug/kg)." pg 932;

Q2667: L. Geurts, *et al.* Chronic Endocannabinoid System Stimulation Induces Muscle Macrophage and Lipid Accumulation in Type 2 Diabetic Mice Independently of Metabolic Endotoxaemia. *PLoS One* 2013;8(2):U622-U631

ALZET Comments: HU210; Tween; saline; SC; Mice; 2006; 6 weeks; Control animals received mp w/ vehicle; animal info (C57BL/6J, male, 9 wks old); HU210 is a potent agonist, a synthetic cannabinoid; functionality of mp verified via HPLC-HRMS in the brain tissue; stability verified (6 weeks, pg e55963);

Q2499: X. X. Zhu, *et al.* Hypothalamic signaling in anorexia induced by indispensable amino acid deficiency. *AMERICAN JOURNAL OF PHYSIOLOGY-ENDOCRINOLOGY AND METABOLISM* 2012;303(12):E1446-E1458



ALZET Comments: SHU-9119; CSF/CNS; Rat; 2004; Control animals received mp w/ artificial CSF; animal info (Sprague Dawley, 7-8 wks old); ; brain infusion kit 2 used; stability verified (21 days, pg E1450).

Q1983: Y. Yuan, *et al.* Role of microRNA-15a in autoantibody production in interferon-augmented murine model of lupus. MOLECULAR IMMUNOLOGY 2012;52(2):61-70

ALZET Comments: Interferon, alpha; interferon, gamma; PBS; BSA; SC; Mice; 2006; 16 weeks; Animal info (13 wks old, female, B/W); pumps replaced after 8 weeks; long-term study; stability verified after 8 weeks; "residue IFNs from the pumps at the end of treatment were tested on IFN and IFN responsive cell lines and demonstrated that the in vivo conditions in the pump did not affect bioactivity of both IFNs (data not shown)" pg 63.

Q2174: J. M. Simard, *et al.* Glibenclamide-10-h Treatment Window in a Clinically Relevant Model of Stroke. TRANSLATIONAL STROKE RESEARCH 2012;3(2):286-295

ALZET Comments: Glibenclamide; DMSO; saline; NaOH; SC; Rat; 2001; 48 hours; Controls received mp w/ vehicle; animal info (Wistar, male, 250-275 g); 5.5 hour delayed delivery accomplished by connecting 5.5 ul volume PE60; functionality of mp verified by residual volume; 8% DMSO used; stability verified via spectrophotometry; ischemia (cerebral).

Q2631: J. C. Morales-Medina, *et al.* Chronic administration of the Y(2) receptor antagonist, JNJ-31020028, induced anti-depressant like-behaviors in olfactory bulbectomized rat. Neuropeptides 2012;46(6):329-334

ALZET Comments: JNJ-31020028; DMSO; saline; CSF/CNS; Rat; 2002; 14 days; Control animals received mp w/ saline; animal info (Sprague Dawley, male, 150-170 g, OBX); 1% DMSO used; stability verified (28 days) pg 330; JNJ-31020028 is a Y2 receptor antagonist.

Q2300: K. M. Kassel, *et al.* Therapeutic Administration of the Direct Thrombin Inhibitor Argatroban Reduces Hepatic Inflammation in Mice with Established Fatty Liver Disease. American Journal of Pathology 2012;181(4):1287-1295

ALZET Comments: Argatroban; Acetic acid, glacial; sodium acetate; PEG 400; SC; Mice; 2004; 4 weeks; Control animals received mp w/ vehicle; animal info (LDLr -/-, male, 6 wks old); 20% PEG 400 used; stability verified (4 weeks); post op. care (buprenorphine HCl).

Q2064: E. Bas, *et al.* Efficacy of three drugs for protecting against gentamicin-induced hair cell and hearing losses. British Journal of Pharmacology 2012;166(6):1888-1904

ALZET Comments: Gentamicin; dexamethasone; melatonin; Ear (round window); Rat; 2001; 7 days; Controls received mp w/ saline; animal info (Wistar, male, 220-250 g); stability verified after 7 days (data not shown).

Q1165: J. Kim, *et al.* Sustained inhibition of PKC alpha; reduces intravasation and lung seeding during mammary tumor metastasis in an in vivo mouse model. ONCOGENE 2011;30(3):323-333

ALZET Comments: Peptide, TAT; peptide, alpha V5-3; pyrrolidine dithiocarbamate; antibody, anti-CXCR4; Saline; SC; Mice; 1002; 4 weeks; Animal info (BALB/c, 6 wks old, female); pumps replaced every 2 weeks; stability verified (2 weeks, pg 331); incorrectly listed using Model 2001; "Pumps were replaced every 2 weeks, which corresponds to the stability of the peptides in the pump." pg 331; bioluminescence IVIS100.

Q1576: S. L. Pedersen, *et al.* Peptide hormone isoforms: N-terminally branched PYY3-36 isoforms give improved lipid and fat-cell metabolism in diet-induced obese mice. JOURNAL OF PEPTIDE SCIENCE 2010;16(11):664-673

ALZET Comments: Peptide YY (3-36); peptide YY (3-36), isoform 2; peptide YY (3-36), isoform 3; Saline; SC; Mice; 1003D; 2002; 3 days; Controls received mp w/ vehicle; animal info (male, DIO C57BL/6J, NMRI, 8-9 wks old); incorrectly listed Model 1003 pumps used; stability verified pg 667 (2, 7, 14 days via HPLC); wound clips used.

Q1430: Y. L. Liu, *et al.* Subcutaneous oxyntomodulin analogue administration reduces body weight in lean and obese rodents. International Journal of Obesity 2010;34(12):1715-1725

ALZET Comments: OXM6421; oxyntomodulin; Saline; SC; Rat; mice; 2001; 7 days; Controls received mp w/ vehicle; animal info (Wistar, male, 250-300 g; DIO, male); peptides; stability verified by HPLC (7 days); OXM6421 is a long-acting oxyntomodulin (OXM) analogue; obesity.



Q0109: K. L. Chambliss, *et al.* Non-nuclear estrogen receptor-alpha signaling promotes cardiovascular protection but not uterine or breast cancer growth in mice. *Journal of Clinical Investigation* 2010;120(7):2319-2330

ALZET Comments: Estradiol; estrogen-dendrimer conjugate; DMSO; IP; Mice (SCID); 1004; 72 hours; 28 days; Controls received mp w/ empty dendrimer; cardiovascular; cancer (breast); animal info (female, ERE-Luc reporter, 10-13 weeks old; Ex3aERKO, 8-9 weeks old; C57BL/6 Apoe^{-/-}, 6 weeks old; SCID, 8 weeks old); functionality of mp verified by serum agent levels; Estradiol Dose (6 ug/d); replacement therapy (ovariectomy; pumps replaced after 28 days); half-life (p.2321); half life of EDC = 28 hours; stability verified by (Serum evaluation of experimental and control mice); photon recording with light emission tomography (LET) system with a CCD camera; Research Diets D10001.