References on the Administration of Naloxone and Naltrexone Using ALZET® Osmotic Pumps

Naloxone

Q9368: F. Meng, *et al.* Naloxone Facilitates Contextual Learning and Memory in a Receptor-Independent and Tet1-Dependent Manner. Cellular and Molecular Neurobiology 2021;41(5):1031-1038
Agents: Naloxone; Morphine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Dose (); animal info (Male mice, 2-3 months old); behavioral testing (Morris Water Maze Test); dependence;

Q8526: K. Hamamura, *et al.* Behavioral Effects of Continuously Administered Bergamot Essential Oil on Mice With Partial Sciatic Nerve Ligation. Frontiers in Pharmacology 2020;11(1310
Agents: Naloxone HCl **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** 1 week;
ALZET Comments: Dose (1 mg/100 uL); 0.9% NaCl used; animal info (four-week-old male ddY-strain mice, 24 g); behavioral testing (double activity monitoring system; Von Frey Test); spinal cord injury;

Q7026: P. M. Grace, *et al.* Protraction of neuropathic pain by morphine is mediated by spinal damage associated molecular patterns (DAMPs) in male rats. Brain, Behavior, and Immunity 2018;72(45-50
Agents: naloxone; A438079; YVAD-cmk, Ac- **Vehicle:** Not Stated; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 2001;
ALZET Comments: Dose (naloxone: 60 ug/h; A438079: 30 ng/h; ac-YVAD-cmk: 1 ug/h); animal info (10-12 week old male Fischer 344 rats); enzyme inhibitor (caspase-1);

Q7170: J. E. Anttila, *et al.* Post-stroke Intranasal (+)-Naloxone Delivery Reduces Microglial Activation and Improves Behavioral Recovery from Ischemic Injury. eNeuro 2018;5(2):
Agents: Naloxone **Vehicle:** Water, ultrapure; **Route:** CSF/CNS (left ventricle); **Species:** Rat; **Pump:** 2002; **Duration:** 12 days;
ALZET Comments: Dose (96 mg/ml, 0.5 ul/h); Controls received mp w/ vehicle; animal info (Adult male Sprague-Dawley rats, 200–250 g); behavioral testing (locomotor activity); half-life (1.57 +/- 0.784 h); ischemia (ischemia stroke);

Q6219: L. V. Lima, *et al.* Short-duration physical activity prevents the development of activity-induced hyperalgesia through opioid and serotoninergic mechanisms. Pain 2017;158(9):1697-1710
Agents: Naloxone **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 5 days;
ALZET Comments: Dose (3 mg/kg/d); Controls received mp w/ vehicle;

Q6094: L. Deng, *et al.* Prophylactic treatment with the tricyclic antidepressant desipramine prevents development of paclitaxel-induced neuropathic pain through activation of endogenous analgesic systems. Pharmacol Res 2016;114(75-89
Agents: Desipramine, naloxone, AM251, AM630 **Vehicle:** Water, saline, PEG 400, DMSO; **Route:** SC; **Species:** Rat; **Pump:** 2ML4;
Duration: 28 days;
ALZET Comments: Dose: Desipramine (10 mg/kg/d), Naloxone (12 mg/kg/d), AM251 (3 mg/kg/d), AM630 (3 mg/kg/day); Desipramine dissolved distilled water, naloxone dissolved in saline, AM251 and AM630 dissolved in 50% PEG400 and 50% DMSO; Controls received mp w/ vehicle; animal info (Sprague-Dawley rats weighing 275–350 g); Multiple pumps per animal (2 when given the treatment of 2 different agents), Desipramine,vehicle, all antagonists delivered in separate osmotic pumps;

Q5226: S. H. Lockie, *et al.* Combination cannabinoid and opioid receptor antagonists improves metabolic outcomes in obese mice. Mol Cell Endocrinol 2015;417(10-19
Agents: Naloxone **Vehicle:** Saline, normal; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ vehicle; animal info: obesity induced, C57black/6J male mice, 6 wks old; functionality of mp verified by behavioral test; dose-response (pg 13, 14); dose-response (pg 13, 14); behavioral testing (Porsolt forced swim, Elevated Plus Maze, Dowel Gnawing); delayed delivery (24 hours via a 1.5 cm vinyl catheter); Isoflurane anesthesia used; minipump combined with a dose of 1 mg/kg/day of rimonabant (rim nal) injected IP; Dose: 0.5 mg/mouse/day

Q3949: P. R. Kramer, *et al.* Attenuation of myogenic orofacial nociception and mechanical hypersensitivity by viral mediated enkephalin overproduction in male and female rats. BMC Neuroscience 2015;15(U1-U12
Agents: Naloxone methiodide; naloxone **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 10 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (SD, 280-300g); behavioral testing (von Frey filament);

Q2587: K. L. Sato, *et al.* Spinal cord stimulation reduces hypersensitivity through activation of opioid receptors in a frequency-dependent manner. European Journal of Pain 2013;17(4):551-561
Agents: Naloxone; Naltrindole **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 1007D; **Duration:** Not Stated;
ALZET Comments: Control animals received mp w/ vehicle; animal info (Sprague Dawley, 250-350 g)

Q3440: K. Y. Chou, *et al.* Ultra-low dose (+)-naloxone restores the thermal threshold of morphine tolerant rats. Journal of the Formosan Medical Association 2013;112(12):795-800
Agents: Morphone; naloxone **Vehicle:** Saline; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** Not Stated; **Duration:** 5 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Wistar, 350-400g); behavioral testing (tail-flick); dependence; IT catheter created from PE tube joined with silastic tube with epoxy resin and silicon rubber;

Q1824: G. J. Hathway, *et al.* A critical period in the supraspinal control of pain: Opioid-dependent changes in brainstem rostroventral medulla function in preadolescence. Pain 2012;153(4):775-783
Agents: Naloxone hydrochloride; naloxone methiodide; morphine sulfate **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ saline; animal info (Sprague Dawley, 200-250 g, P7, P14, P21, P28)

Q1441: J. N. Peart, *et al.* Sustained Ligand-Activated Preconditioning via delta-Opioid Receptors. The Journal of Pharmacology and Experimental Therapeutics 2011;336(1):274-281
Agents: Naloxone; BW373U86; U50,488H; morphine-6-glucuronide; morphine-3-glucuronide; wortmannin; PKI-(14-22)-amide
Vehicle: Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** 5 days;
ALZET Comments: Animal info (7-12 wks old, C57/BL6, male);BW373U86 also known as ()-4-[(*R*)--[(2*S*,5*R*)-4-allyl-2,5-dimethyl-1-piperazinyl]-3-hydroxy-hydroxybenzyl]-*N*,*N*-diethylbenzamide is a delta opioid receptor selective agonist; U50,488H also known as *trans*-()-3,4-dichloro-*N*-methyl-*N*-(2-(1-pyrrolidin)cyclohexyl)-benzeneacetamide methane sulfonate hydrate is a kappa opioid selective receptor agonist

Q1488: S. H. Lockie, *et al.* CNS Opioid Signaling Separates Cannabinoid Receptor 1-Mediated Effects on Body Weight and Mood-Related Behavior in Mice. Endocrinology 2011;152(10):3661-3667
Agents: Naloxone; binaltorphimine, nor **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;
ALZET Comments: Animal info (129/SvEv, lacking MOR, KOR, DOR); ALZET brain infusion kit 3 used; cyanoacrylate adhesive used; post op. care (meloxiocam); cannula placement verified at end of experiment by methylene blue staining; half-life "Naloxone... has a short half-life in vivo"; "NorBNI has... an extremely long half-life" pg 3662

P9908: S. L. Lin, *et al.* Ultra-low dose naloxone upregulates interleukin-10 expression and suppresses neuroinflammation in morphine-tolerant rat spinal cords. Behavioural Brain Research 2010;207(1):30-36
Agents: Naloxone; morphine **Vehicle:** Not Stated; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Duration:** 5 days;
ALZET Comments: Controls received mp w/saline; animal info (male, Wistar, 350-400 g); pumps contained morphine alone or morphine and naloxone; two intrathecal catheters implanted

Q1210: S. L. Lin, *et al.* Co-administration of ultra-low dose naloxone attenuates morphine tolerance in rats via attenuation of NMDA receptor neurotransmission and suppression of neuroinflammation in the spinal cords. Pharmacology Biochemistry and Behavior 2010;96(2):236-245
Agents: Morphine; Naloxone **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Duration:** 5 days;
ALZET Comments: Controls received mp w/ saline; animal info (pathogen-free, male, Wistar, 350-400 g); infusion rate of 1 ul/hr; two catheters inserted intrathecally

Q0909: M. R. Hutchinson, *et al.* Evidence that opioids may have toll-like receptor 4 and MD-2 effects. Brain, Behavior, and Immunity 2010;24(1):83-95
Agents: Morphine; Naloxone **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** Not Stated;
ALZET Comments: Controls received mp w/ saline; animal info (adult, male, Sprague Dawley, 300-375 g); multiple pumps per animal (2)

Q0746: R. J. Horvath, *et al.* Inhibition of microglial P2X(4) receptors attenuates morphine tolerance, Iba1, GFAP and μ opioid receptor protein expression while enhancing perivascular microglial ED2. Pain 2010;150(3):401-413
Agents: Morphine sulfate; naloxone **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 1, 4, 7 days;
ALZET Comments: Controls received mp w/ saline; animal info (male, Sprague-Dawley, 175-200 g); one pump contained morphine plus naloxone; "All morphine pumps were filled with 0.833 mg/kg/hr morphine to deliver the equivalent of twice daily 10 mg/kg injections over the course of 24 h" pg 402; tolerance

P9163: M. R. Hutchinson, *et al.* Non-stereoselective reversal of neuropathic pain by naloxone and naltrexone: involvement of toll-like receptor 4 (TLR4). European Journal of Neuroscience 2008;28(1):20-29
Agents: Naloxone **Vehicle:** Saline, sterile; **Route:** SC; CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 2001; **Duration:** 4 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 300-375 g.); sciatic nerve injury

P8708: S. Sirohi, *et al.* mu-opioid receptor up-regulation and functional supersensitivity are independent of antagonist efficacy. The Journal of Pharmacology and Experimental Therapeutics 2007;323(2):701-707
Agents: Naltrexol HCl, 6B-; Naloxone HCl **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Controls received placebo pellets; dose-response (fig 3, 5); comparison of pellets, SC injections vs. mp; animal info (male, Swiss-Webster, 22-30g)

P8677: T. King, *et al.* Morphine treatment accelerates sarcoma-induced bone pain, bone loss, and spontaneous fracture in a murine model of bone cancer. Pain 2007;132(1-2):154-168
Agents: Morphine; Naloxone **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ vehicle; dose-response (p. 157, 159); no stress (see pg. 155); cancer (bone); multiple pumps per animal (2); animal info (20-25g, male, adult, C3H/HeJ); pain

P9065: S. A. Dunbar, *et al.* Ketorolac prevents recurrent withdrawal induced hyperalgesia but does not inhibit tolerance to spinal morphine in the rat. European Journal of Pain 2007;11(1):1-6
Agents: Morphine sulfate; Naloxone hydrochloride; Ketorlac **Route:** SC; CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 2001; **Duration:** 4, 7 days;
ALZET Comments: Controls received mp w/ saline; tolerance; animal info (adult, male, Sprague Dawley, 350 g.)

P7749: A. Meunier, *et al.* Attenuation of pain-related behavior in a rat model of trigeminal neuropathic pain by viral-driven enkephalin overproduction in trigeminal ganglion neurons. Molecular Therapy 2005;11(4):608-616
Agents: Naloxone; Naloxone methiodide **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 1007D; **Duration:** 3 days;
ALZET Comments: Controls received mp w/ saline; animal info (male, Sprague-Dawley, 175-200g.);chronic constrictive injury of the left infraorbital nerve

P7012: B. C. Yoburn, *et al.* Opioid agonist and antagonist treatment differentially regulates immunoreactive mu-opioid receptors and dynamin-2 in vivo. European Journal of Pharmacology 2004;498(1-3):87-96
Agents: Naloxone; Etorphine hcl; Morphine sulfate **Vehicle:** Saline, normal; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Controls received inert, placebo pellets or saline injections; comparison of SC injections vs. pellets vs. mp; tolerance; "Intermittent naloxone and etorphine treatment did not regulate u-opioid receptor or dynamin-2, despite the fact that the total amount of drug administered was the same as continuous treatment." (pg. 94); animal info (m, 22-30 grams)

P6850: Y. N. Hou, *et al.* Differential effects of gestational buprenorphine, naloxone, and methadone on mesolimbic mu opioid and ORL1 receptor G protein coupling. Brain Research 2004;151(1-2):149-157
Agents: Buprenorphine; naloxone; methadone **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat (pregnant); **Pump:** 2ML4;
ALZET Comments: Controls received mp w/ water; dose-response (fig. 3); teratology

P6702: V. Rajashekara, *et al.* Chronic opioid antagonist treatment dose-dependently regulates mu-opioid receptors and trafficking proteins in vivo. Pharmacology Biochemistry and Behavior 2003;75(4):909-913
Agents: Naloxone HCL **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Controls received placebo pellets; dose-response (fig.2)

P7207: A. Ogawa, *et al.* Hard-food mastication suppresses complete Freund's adjuvant-induced nociception. Neuroscience 2003;120(4):1081-1092
Agents: Naloxone **Vehicle:** Not Stated; **Route:** IV (jugular); **Species:** Rat; **Pump:** Not Stated; **Duration:** 3, 6 days;
ALZET Comments: Controls received mp w/ saline; functionality of mp verified by measuring residual volume

R0195: B. Liu, *et al.* Role of microglia in inflammation-mediated neurodegenerative diseases: Mechanisms and strategies for therapeutic intervention. The Journal of Pharmacology and Experimental Therapeutics 2003;304(1):1-7
Agents: Naloxone **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Rat; **Pump:** Not Stated; **Duration:** Not Stated;
ALZET Comments: Neurodegenerative; Pg. 5

P6250: J. Froehlich, *et al.* Preclinical and clinical studies on naltrexone: What have they taught each other? Alcoholism Clinical and Experimental Research 2003;27(3):533-539
Agents: Naloxone **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Rat; **Pump:** Not Stated; **Duration:** 7 days;
ALZET Comments: Dose-response (p.5); dependence

Q1495: R. T. Rahim, *et al.* Administration of mu-, kappa- or delta -receptor agonists via 2 osmotic minipumps suppresses murine splenic antibody responses. INTERNATIONAL IMMUNOPHARMACOLOGY 2001;1(2001-2009
Agents: Morphine sulfate; U50,488H; DPDPE; naltriben methanesulfonate; deltorphin II; naloxone **Vehicle:** Sodium chloride; DMSO; saline, sterile; **Route:** SC; **Species:** Mice; **Pump:** 1003D; **Duration:** 48 hours;
ALZET Comments: Controls received mp w/ saline; animal info (6 wks old, pathogen free, C3HeBrFeJ); comparison of pellets vs. mp; multiple pumps per animal (2); "Minipumps have two advantages, (1) a variety of agonists and antagonists can be used that are not available in slow-release pellet form, and (2) full dose-response curves can be generated." pg 2002; "Minipumps have an advantage over slow-release pellets in that they do not result in splenic atrophy. Thus, drugs administered by the minipumps appear to be less potent, but also to have fewer side effects, than morphine given by slow-release pellets." pg 2007; "The use of osmotic minipumps should permit more extensive and definitive testing of the pharmacokinetics and pharmacodynamic action of a variety of opioids for their effects on immune cell function." pg 2008; 10% DMSO used

P4800: X. Li, *et al.* Opioid-induced hyperalgesia and incisional pain. Anesthesia & Analgesia 2001;93(204-209
Agents: Morphine sulfate; Naloxone **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 6 days;
ALZET Comments: Controls received mp w/ vehicle; tolerance; dependence

Q6819: J. Braz, *et al.* Therapeutic Efficacy in Experimental Polyarthritis of Viral-Driven Enkephalin Overproduction in Sensory Neurons. The Journal of Neuroscience 2001;21(20):7881–7888
Agents: Naloxone; Naloxone methiodide **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 3 dayss;
ALZET Comments: Dose (3 mg/kg/day); Controls received mp w/ vehicle; animal info (polyarthritic male sprawg dawley rats, 6 weeks old); behavioral testing (foot withdrawal (pain)); Therapeutic indication (Rheumatoid arthritis);

P4965: Z. Vertes, *et al.* Epidermal growth factor influenced by opioid peptides in immature rat uterus. Journal of Endocrinological Investigation 2000;23(502-508
Agents: Enkephalin analog; Naloxone **Vehicle:** Saline; **Route:** IP; **Species:** Rat; **Pump:** 1003D; **Duration:** 1,3 days;
ALZET Comments: Controls received mp w/ vehicle; functionality of mp verified by aspirating remaining contents; peptides; Enkephalin analog ENK was (D-Met2-Pro5)enkephalinamide, inhibits epidermal growth factor.

P5212: X. Lu, *et al.* Naloxone prevents microglia-induced degeneration of dopaminergic substantia nigra neurons in adult rats. Neuroscience 2000;97(2):285-291
Agents: Naloxone **Vehicle:** PBS; ethanol; **Route:** SC; CSF/CNS (substantia nigra); **Species:** Rat; **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: Controls received mp w/ vehicle;CNS infusion using PBS; SC infusion in 60% ethanol vehicle to enhance solubility (p.286); SC infusion compared to CNS administration; neurodegenerative (Parkinson's disease)

P4560: M. Mavridis, *et al.* Dopamine-opiate interaction in the regulation of neostriatal and pallidal neuronal activity as assessed by opioid precursor peptides and glutamate decarboxylase messenger RNA expression. Neuroscience 1999;92(3):945-966
Agents: Naloxone **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 8 days;
ALZET Comments: ontrols received mp w/vehicle; functionality of mp verified by residual volume

P4155: R. Spanagel, *et al.* Forced opiate withdrawal under anaesthesia augments and prolongs the occurrence of withdrawal signs in rats. Drug and Alcohol Dependence 1998;52(251-256
Agents: Naloxone **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: controls received mp w/saline; dependence

P3768: I. H. Jonsdottir, *et al.* Duration and mechanisms of the increased natural cytotoxicity seen after chronic voluntary exercise in rats. Acta Physiologica Scandinavica 1997;160(333-339
Agents: Naloxone HCl **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 7 days;
ALZET Comments: controls received mp w/saline; no stress (see pg. 337)

P3323: C. Alcaraz, *et al.* Chronic naloxone-induced supersensitivity affects neither tolerance to nor physical dependence on morphine at hypothalamus-pituitary-adrenocortical axis. Neuropeptides 1996;30(1):29-36
Agents: Naloxone **Vehicle:** Water, distilled; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: controls received mp w/vehicle; tolerance; dependence

P3058: B. C. Yoburn, *et al.* Opioid antagonist-induced receptor upregulation: effects of concurrent agonist administration. Brain Research Bulletin 1994;33(2):237-240
Agents: Naloxone; Fentanyl citrate; Etorphine HCl **Vehicle:** NaCl; **Route:** SC; **Species:** Mice; **Pump:** 2001; 2002; **Duration:** 7,8 days;
ALZET Comments: Controls received placebo pellets

P2878: L. Rocha, *et al.* Chronic pretreatment with naloxone modifies benzodiazepine receptor binding in amygdaloid kindled rats. Epilepsy Research 1994;17(135-142
Agents: Naloxone HCl **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: controls received mp with saline; functionality of pump verified with pump emptying

P3555: C. A. Paronis, *et al.* Sensitization and tolerance to the discriminative stimulus effects of mu-opioid agonists. Psychopharmacology 1994;114(601-610
Agents: Naloxone HCl; Morphine sulfate; Meperidine HCl; Fentanyl citrate **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 7 days;
ALZET Comments: controls received sham pumps; tolerance

P3204: I. Jimenez, *et al.* Subchronic naloxone inhibits hypertension induced by stress in the rat. Pharmacol. Comm 1994;4(3):207-213
Agents: Naloxone **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: controls received mp with saline

P2940: J. R. Earl, *et al.* Proinflammatory effects of morphine in the rat adjuvant arthritis model. Int. J. Tiss. Reac 1994;XVI(4):163-170
Agents: Morphine sulfate; Naloxone HCl **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** Not Stated;
ALZET Comments: Controls received mp with saline or were naive

P3060: B. C. Yoburn, *et al.* Opioid receptor regulation in mice. J. Pharmacol. Exp. Ther 1993;265(1):314-320
Agents: Etorphine HCl; Fentanyl citrate; Naloxone HCl **Vehicle:** NaCl; **Route:** SC; **Species:** Mice; **Pump:** 2001; 2002; **Duration:** 7,8 Days;
ALZET Comments: Controls received placebo pellets; dose-response; comparison of sc fentanyl injections vs. mp; good methods; tolerance

P2877: L. Rocha*, et al.* Characterization of mu opioid receptor binding during amygdala kindling in rats and effects of chronic naloxone pretreatment: an autoradiographic study. Epilepsy Research 1993;14(195-208
Agents: Naloxone HCl **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: controls received mp with saline; functionality of pump verified with pump emptying

P3247: D. Levesque*, et al.* The potentiating effcets of restraint stress and continuous naloxone infusion on the analgesic potency of morphine are additive. Brain Research 1993;617(176-180
Agents: Naloxone HCl **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 7 days;
ALZET Comments: controls received empty mp; stress/adverse reaction (pg. 179); possible surgical stress of pump removal may have affected results

P3292: C. Gouarderes*, et al.* Opioid and substance p receptor adaptations in the rat spinal cord following sub-chronic intrathecal treatment with morphine and naloxone. Neuroscience 1993;54(3):799-807
Agents: Morphine; Naloxone **Vehicle:** Saline; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: controls received mp w/saline; tolerance; medical category:pain/analgesia;skc

P2178: C. Alcaraz*, et al.* Chronic naloxone treatment induces supersensitivity to a mu but not to a kappa agonist at the hypothalamus-pituitary-adrenocortical axis level. J. Pharmacol. Exp. Ther 1993;266(3):1602-1606
Agents: Naloxone **Vehicle:** Water; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: controls received mp w/water

P1405: C. Alcaraz*, et al.* Chronic kappa opioid receptor antagonism produces supersensitivity to U-50,488H at the hypothalamo-pituitary-adrenocortical (HPA) axis level. Journal of Pharmacology and Experimental Therapeutics 1993;266(3):1385-1389
Agents: Naloxone **Vehicle:** Water, distilled; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 7 days;
ALZET Comments: controls received mp w/water

P2047: C. A. Paronis*, et al.* Apparent pA2 value of naltrexone is not changed in rats following continuous exposure to morphine or naloxone. Life Sci 1992;50(1407-1416
Agents: Morphine sulfate; Naloxone HCl **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 7 days;
ALZET Comments: controls received empty pumps previously used, which is not recommended by the manufacturer

P2327: M. D. Johnson*, et al.* Effect of naloxone on hypertension in dahl salt-sensitive rats. Heart Circ. Physiol 1992;31(H162-H167
Agents: Naloxone **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 28 days;
ALZET Comments: controls received sham operation; pumps replaced at 2 weeks

P2314: P. D. Henion*, et al.* Developmental regulation of leucine-enkephalin expression in adrenal chromaffin cells by glucocorticoids and innervation. J. Neurosci 1992;12(10):3818-3827
Agents: Naloxone **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 4 days;
ALZET Comments: neuroscience; multiple pumps per animal (2)

P2033: C. A. Paronis*, et al.* Increased analgesic potency of Mu agonists after continuous naloxone infusion in rats. J. Pharmacol. Exp. Ther 1991;259(2):582-589
Agents: Naloxone **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 7 days;
ALZET Comments: no comment posted

P3174: M. J. Millan*, et al.* Opioid systems in the response to inflammatory pain: sustained blockade suggests role of kappa- but not mu-opioid receptors in the modulation of nociception, behaviour and pathology. Neuroscience 1991;42(2):541-553
Agents: Naloxone **Vehicle:** Water, sterile; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 7 days;
ALZET Comments: controls received mp with vehicle; mp placed on flank

P1847: M. J. Millan, *et al.* The influence of sustained opioid receptor blockade in a model of long-term, localized inflammatory pain in rats. Neurosci. Lett 1990;113(50-55
Agents: Naloxone HCl **Vehicle:** Water; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 6 days;
ALZET Comments: no comment posted

P1638: D. S. Bruce, *et al.* Is the polar bear (Ursus maritimus) a hibernator?: continued studies on opioids and hibernation. Pharmacology Biochemistry & Behavior 1990;35(705-711
Agents: Naloxone **Vehicle:** Saline; **Route:** SC; **Species:** Squirrel; **Pump:** 2ML4; **Duration:** 35 days;
ALZET Comments: no comment posted

P1321: T. S. Shippenberg, *et al.* Involvement of B-endorphin and u-opioid receptors in mediating the aversive effect of lithium in the rat. European Journal of Pharmacology 1988;154(135-144
Agents: Naloxone **Vehicle:** Water; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: no comment posted

P1409: M. J. Millan, *et al.* Antagonist-induced opioid receptor up-regulation 1: characterization of supersensitivity to selective mu and kappa agonists. Journal of Pharmacology and Experimental Therapeutics 1988;247(2):721-728
Agents: Naloxone **Vehicle:** Water; **Route:** SC; **Species:** Rat; **Pump:** 2001; 2ML1; **Duration:** 1 week;
ALZET Comments: no comment posted

P1299: M. J. Millan, *et al.* Long-term blockade of u-opioid receptors suggests a role in control of ingestive behaviour, body weight and core temperature in the rat. Brain Research 1988;450(247-258
Agents: Bremazocine; MR-2266; MR-2267; Naloxone; Sufentanil **Vehicle:** DMSO; HCl; Sodium hydroxide; Propylene glycol; Water; **Route:** SC; **Species:** Rat; **Pump:** 2001; 2ML1; **Duration:** 3, 6, 7 days;
ALZET Comments: mp malfunction -- pump plugged at 4 days due to propylene glycol; water was vehicle for naloxone; propylene glycol, HCl, NaOH was vehicle for MR-2200; pump replaced at 3 days

P1439: M. Chen, *et al.* Naloxone attenuates development of hypertension in two-kidney one-clip goldblatt rats. American Journal of Physiology Endocrinology and Metabolism 1988;255(E839-E842
Agents: Naloxone **Vehicle:** Saline; **Route:** Abdomen; **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days;
ALZET Comments: Mp connected to catheter; tissue perfusion

P1267: O. F. X. Almeida, *et al.* Evidence for the involvement of endogenous opioids in the inhibition of luteinizing hormone by corticotropin-releasing factor. Endocrine Society 1988;122(3):1034-1041
Agents: Naloxone **Vehicle:** Water; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 6 hours;
ALZET Comments: controls received mp w/water; concomitant CRF ICV infusion; 3 exp., only 1 used mp

P1164: C. W. Stevens, *et al.* Chronic antagonist infusion does not increase morphine antinociception in rat spinal cord. Brain Research 1987;425(2):388-390
Agents: Naloxone HCl; Naltrexone HCl **Vehicle:** Saline; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: mp connected to a 'Y' catheter; half-life; morphine administered intrathecally via the external arm of the 'Y' catheter; concomitant infusion of agents; comparison of bolus injections vs. mp infusion

P1165: M. J. Millan, *et al.* Evidence that mu-opioid receptors mediate midbrain 'stimulation-produced analgesia' in the freely moving rat. Neuroscience 1987;22(3):885-896
Agents: Naloxone **Vehicle:** Water; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: controls received mp w/ vehicle; concomitant administration of morphine; stimulation of midbrain

P1181: S. L. Lightman, *et al.* Changes in hypothalamic preproenkephalin A mRNA following stress and opiate withdrawal. Nature 1987;328(13):643-645
Agents: Morphine; Naloxone **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 12 days;
ALZET Comments: controls received spent mp; agents infused separately

P0595: S. George, *et al.* Met-enkephalin concentrations in straitum respond reciprocally to alterations in dopamine neurotransmission. Peptides 1987;8(3):487-492
Agents: Apomorphine; FK-33824; Haloperidol; Naloxone **Vehicle:** Ethanol; Tartaric acid; Water; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 5, 9 days;
ALZET Comments: mp model not stated; controls received mp w/unspecified vehicle or were sham-operated; agents infused separately w/appropriate vehicle; comparison of sc inject. vs. mp infusion

P1156: D. S. Bruce, *et al.* Opioids and hibernation. I. effects of naloxone on bear hit's depression of guinea pig ileum contractility and on induction of summer hibernation in the ground squirrel. Life Sciences 1987;41(18):2107-2113
Agents: Naloxone **Vehicle:** Saline; **Route:** SC; **Species:** Squirrel; **Pump:** 2ML4; **Duration:** 28 days;
ALZET Comments: Controls received mp w/ saline; concomitant administration of winter bear plasma or its albumin fraction

P0898: M. Sugimoto, *et al.* Involvement of medullary opioid-peptidergic and spinal noradrenergic systems in the regulation of formalin-induced persistent pain. Neuropharmacology 1986;25(5):481-485
Agents: Naloxone HCl **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 3 days;
ALZET Comments: controls received mp w/saline or no treatment; comparison of single icv injection vs. mp infusion

P0894: D. H. Malin, *et al.* Clonidine reverses the behavioral and respiratory effects of continuous naloxone infusion. Pharmacology Biochemistry and Behavior 1986;25(5):989-993
Agents: Naloxone **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 28, 52 hours;
ALZET Comments: Controls received mp w/saline; 2 separate experiments using mps

P0953: S. J. Hollenbach, *et al.* Early administration of methylprednisolone promotes survival in rats with intra-abdominal sepsis. Circulatory Shock 1986;20(2):161-168
Agents: Clindamycin; Methylprednisolone; Gentamicin; Naloxone **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: controls received mp w/saline; toxicology; multiple pumps per animal (3); comparison of bolus injections vs. mp infusion; antibiotic

P0742: D. S. Baskin, *et al.* Treatment of experimental stroke with opiate antagonists, effects on neurological function, infarct size, and survival. Journal of Neurosurgery 1986;64(99-103
Agents: Diprenorphine; Naloxone; Naltrexone **Vehicle:** Saline; **Route:** SC; **Species:** Cat; **Pump:** 2ML1; **Duration:** 7 days;
ALZET Comments: mp functionality and accuracy of delivery verified; acute ip adminis. of agents w/mp infusion; ischemia

P0619: D. H. Malin, *et al.* Continuous infusion of naloxone: effects on behavior and oxygen consumption. Pharmacology Biochemistry and Behavior 1985;22(5):791-795
Agents: Naloxone **Vehicle:** Water; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 52 hours;
ALZET Comments: comparison of injec of 3 naloxone doses vs. mp infusion; multiple pumps per animal (2)

P0741: G. Leng, *et al.* Central opoids: a possible role in parturition? Journal of Endocrinology 1985;106(2):219-224
Agents: Naloxone HCl **Vehicle:** Saline; **Route:** SC; **Species:** Rat (pregnant); **Pump:** 2002; **Duration:** Not Stated;
ALZET Comments: Controls received mps w/ saline

P1072: R. D. Huffman, *et al.* An intraventricular infusion model for inducing morphine dependence in rats: Quantitative assessment of precipitated withdrawal. Behavioral Neuroscience 1985;99(5):861-880
Agents: Morphine; Naloxone **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 1701; **Duration:** 14 days;
ALZET Comments: controls received mp w/Naloxone; mp connected to cannula; water infused for 6 days before being replaced w/agent filled mp; 2 pumps/animal; comparison of 3 morphine pellets vs. mp infusion; pump replaced

P0610: A. L. Beckman, *et al.* Antagonism of brain opioid peptide action reduces hibernation bout duration. Brain Research 1985;328(201-205
Agents: Naloxone HCl **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Squirrel; **Pump:** 2001; **Duration:** 2, 7 days;
ALZET Comments: Dose-response data

P0509: L. C. Saland, *et al.* Chronic infusion of opiate peptides to rat cerebrospinal fluid with osmotic minipumps. Anatomical Record 1984;210(115-123
Agents: Endorphin, a-; Endorphin, ovine B-; Enkephalin, methionine-; Naloxone HCl **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2001; **Duration:** 1, 2 days;
ALZET Comments: Comparison of agents effects; peptides

P0421: R. M. Quock, *et al.* Influence of chronic naloxone treatment on development of hypertension in the spontaneously hypertensive rat. Naunyn-Schmiedeberg's Archives of Pharmacology 1984;325(88-90
Agents: Naloxone HCl **Vehicle:** Water; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 8 weeks;
ALZET Comments: pump replaced weekly; long-term study; 1-2 pumps of naloxone/test animal; controls got 1 pump w/ water

P0904: A. Pfeiffer, *et al.* An increase in opiate receptor-sites is associated with enhanced cardiovascular depressant, but not respiratory depressant action of morphine. Brain Research 1984;296(305-311
Agents: Naloxone **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 4 weeks;
ALZET Comments: controls received mp w/ saline; pumps replaced after 2 weeks

P0349: Z. Wiesenfeld, *et al.* Continuous naloxone administration via osmotic minipump decreases autotomy but has no effect on nociceptive threshold in the rat. Pain 1983;16(2):145-153
Agents: Naloxone HCl **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; 2ML1; **Duration:** 2, 5 weeks;
ALZET Comments: Pumps replaced weekly; stress/adverse reaction (fibrous tissue growth, mp malfunction)

P0240: L. F. Tseng. Tolerance and cross tolerance to morphine after chronic spinal D-Ala2-D-Leu5-enkephalin infusion. Life Sciences 1982;31(987-992
Agents: Enkephalin agonist DADL; Naloxone **Vehicle:** Saline; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 2001; **Duration:** 5 days;
ALZET Comments: agents infused alone and/or concomitantly; peptides

P0171: J. E. Jalowiec, *et al.* Opioid modulation of ingestive behavior. Pharmacology Biochemistry and Behavior 1981;15(3):477-484
Agents: Naloxone HCl **Vehicle:** Water; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 8 days;
ALZET Comments: Exp. 1-2) morphine or naloxone injections 3) 2001, 8 days naloxone; morphine injec. on last day, 4) naloxone injec; comparison of injec vs. mp infusion

P0109: J. Hetta, *et al.* Prenatal naloxone affects survival and morphine sensitivity of rat offspring. Neuroscieince Letters 1980;16(3):323-327
Agents: Naloxone **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 7 days;
ALZET Comments: no comment posted

Naltrexone

Q10530: E. Gondoh, *et al.* Possible mechanism for improving the endogenous immune system through the blockade of peripheral mu-opioid receptors by treatment with naldemedine. British Journal of Cancer 2022;127(8):1565-1574
Agents: Methylnaltrexone **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 21 days;
ALZET Comments: "Dose: (0.1 ml/10g)Controls received mp w/ vehicle; animal info: Male ICR mice (20–25 g)behavioral testing: Hot-plate test; methylnaltrexone is a peripheral MOR antagonist; immunology

Q9209: L. Dehe, *et al.* Chronic Naltrexone Therapy Is Associated with Improved Cardiac Function in Volume Overloaded Rats. Cardiovascular Drugs and Therapy 2021;35(4):733-743
Agents: Naltrexone **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 28 days;
ALZET Comments: Dose (10 mg/kg/h); Controls received mp w/ vehicle; animal info (male Wistar rats, 280–300 g); 163 mmHg - 142 mmHg;cardiovascular;

Q9503: E. A. Townsend*, et al.* Evaluation of a Dual Fentanyl/Heroin Vaccine on the Antinociceptive and Reinforcing Effects of a Fentanyl/Heroin Mixture in Male and Female Rats. ACS Chemical Neuroscience 2020;11(9):1300-1310
Agents: Naltrexone **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 2 weeks;
ALZET Comments: Dose (0.032 mg/kg/h); animal info (SDawley, 10 weeks); behavioral testing (tail withdrawal test);

Q9088: E. A. Townsend*, et al.* Conjugate vaccine produces long-lasting attenuation of fentanyl vs. food choice and blocks expression of opioid withdrawal-induced increases in fentanyl choice in rats. Neuropsychopharmacology 2019;44(10):1681-1689
Agents: Naltrexone; Clonidine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 1 week;
ALZET Comments: Dose (Naltrexone- 0.01, 0.032, or 0.1 mg/kg/hr or 3.2, 10 ug/kg/hr); Controls received mp w/ vehicle; animal info (19 Sprague Dawley, 10 weeks old); behavioral testing (Tail Withdrawal Test); dependence;

Q8792: S. K. Panigrahi*, et al.* Effects of Naltrexone on Energy Balance and Hypothalamic Melanocortin Peptides in Male Mice Fed a High-Fat Diet. Journal of the Endocrine Society 2019;3(3):590-601
Agents: Naltrexone Hydrochloride **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;
ALZET Comments: Dose (20 mg/kg/day); Controls received mp w/ vehicle; animal info (Male, C57BL/6J, 3 months old);

Q7421: bioRxiv. Effectiveness and selectivity of a heroin conjugate vaccine to attenuate heroin, 6-acetylmorphine, and morphine antinociception in rats: Comparison with naltrexone. bioRxiv 2019;577494
Agents: Naltrexone **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days;
ALZET Comments: Dose (0.01 mg/kg/h); Controls received mp w/ vehicle; animal info (Adult male and female Sprague Dawley rats); pumps were aseptically removed on day 15; Therapeutic indication (opiod use disorder treament);

Q7076: A. Levy*, et al.* Bupropion and naltrexone combination alters high fructose corn syrup self-administration and gene expression in rats. Neuropharmacology 2018;135(547-554
Agents: Bupropion hydrochloride, naltrexone hydrochloride **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 12 days;
ALZET Comments: Dose (40 mg/kg/day BUP, 4 mg/kg/day NTX); Controls received sham surgery; animal info (Adult male Sprague-Dawley rats weighing 200-250 g); behavioral testing (locomotion tests); Drugs administered together or in separate pumps; Contrave® is an adjunct pharmacotherapy for obesity that contains bupropion and naltrexone.; Therapeutic indication (Obesity);

Q4836: L. S. Hwa*, et al.* Dissociation of u-opioid receptor and CRF-R1 antagonist effects on escalated ethanol consumption and mPFC serotonin in C57BL/6J mice. Addiction Biology 2016;21(111-124
Agents: CP154526; naltrexone **Vehicle:** DMSO; CSF, artificial; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 1002; **Duration:** 14 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, C58BL/6J, 8 weeks old); functionality of mp verified by IAA drinking test or morphine-sensitive tail withdrawal; ALZET brain infusion kit 3 used; 4% DMSO used; Cannula placement verified via Nissl staining;

Q2540: F. R. Theberge*, et al.* Effect of Chronic. Delivery of the Toll-like Receptor 4 Antagonist (+)-Naltrexone on Incubation of Heroin Craving. Biological Psychiatry 2013;73(8):729-737
Agents: Naltrexone **Vehicle:** Water, sterile; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 14 days;
ALZET Comments: Control animals received mp w/ vehicle; 14-day pump used

Q3077: C. R. Gibbons*, et al.* Involvement of brain opioid receptors in the anti-allodynic effect of hyperbaric oxygen in rats with sciatic nerve crush-induced neuropathic pain. Brain Research 2013;1537(;):111-116
Agents: Naltrexone HCl **Vehicle:** Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 1007D; **Duration:** 7 days;
ALZET Comments: Animal info (male, Sprague Dawley, albino, 160-180g); ALZET brain infusion kit used; post op. care (ampicillin 100 mg/kg IM; meloxicam 2.0 mg/kg IM); behavioral testing (flexion reflex, flinch response, mechanical threshold pressure); Incision closed with wound clip

Q1813: E. M. Vadizan, *et al.* Chronic treatment with the opioid antagonist naltrexone favours the coupling of spinal cord mu-opioid receptors to G-alpha$_z$ protein subunits. Neuropharmacology 2012;62(2):757-764
Agents: Naltrexone **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ saline; animal info (Sprague Dawley, male, 250-300 g)

Q0724: N. J. Stagg, *et al.* Regular Exercise Reverses Sensory Hypersensitivity in a Rat Neuropathic Pain Model Role of Endogenous Opioids. Anesthesiology 2011;114(4):940-948
Agents: Naltrexone **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2006; **Duration:** 5 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 250-380 g); wound clips used; neuropathic pain

Q0697: B. Mathew, *et al.* The Novel Role of the Mu Opioid Receptor in Lung Cancer Progression: A Laboratory Investigation. Anesthesia & Analgesia 2011;112(3):558-567
Agents: Naltrexone, methyl **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 12 days;
ALZET Comments: Controls received mp w/ PBS; animal info (MOR KO, C57BL/6 wt); cancer (lung); Methylnaltrexone (also known as MNTX) is a mu opioid receptor inhibitor

Q0016: K. G. Hill, *et al.* Chronic Naltrexone Treatment and Ethanol Responsivity in Outbred Rats. Alcoholism Clinical and Experimental Research 2010;34(2):272-279
Agents: Naltrexone HCl **Vehicle:** Saline, physiological; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 2 weeks;
ALZET Comments: Controls received mp w/vehicle; Dependence; Animal info (male, Long-Evans, 250 g); Dose-response (fig .1)

Q1544: S. Fitting, *et al.* Interactive Comorbidity between Opioid Drug Abuse and HIV-1 Tat Chronic Exposure Augments Spine Loss and Sublethal Dendritic Pathology in Striatal Neurons. American Journal of Pathology 2010;177(3):1397-1410
Agents: Naltrexone **Vehicle:** DMSO; saline, sterile; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (HIV-1, TAT, adult, 2-6 mo old); 50% DMSO used

Q1577: E. Chung, *et al.* Hyperbaric Oxygen Treatment Induces a 2-Phase Antinociceptive Response of Unusually Long Duration in Mice. JOURNAL OF PAIN 2010;11(9):847-853
Agents: L-NAME; naltrexone **Vehicle:** Saline, physiological; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 2001; **Duration:** Not Stated;
ALZET Comments: Controls received mp w/ vehicle; animal info (NIH, Swiss, 18-22 g); ALZET brain infusion kit used; hyperbaric oxygen

P9480: K. F. Hauser, *et al.* HIV-1 Tat and Morphine Have Interactive Effects on Oligodendrocyte Survival and Morphology. Glia 2009;57(2):194-206
Agents: Naltrexone **Vehicle:** DMSO; saline, sterile; **Route:** SC; **Species:** Mice (transgenic); **Pump:** 1007D; **Duration:** 7 days;
ALZET Comments: Animal info (TAT); 50% DMSO used

P9245: A. J. Bruce-Keller, *et al.* Morphine causes rapid increases in glial activation and neuronal injury in the striatum of inducible HIV-1 tat transgenic mice. Glia 2008;56(13):1414-1427
Agents: Naltrexone **Vehicle:** DMSO; Saline, sterile; **Route:** SC; **Species:** Mice (transgenic); **Pump:** 1007D; **Duration:** 2, 5,10 days;
ALZET Comments: Controls received mp w/ vehicle; pumps replaced after 5 days; animal info (male, female, C3H x C57BL/6, Tat (+), Tat (-), 2-6 months old); 50% DMSO used

P6432: M. Hummel, *et al.* Genetic and pharmacological manipulation of mu opioid receptors in mice reveals a differential effect on behavioral sensitization to cocaine. Neuroscience 2004;125(1):211-220
Agents: Naltrexone **Vehicle:** Saline; **Route:** SC; **Species:** Mice (knockout); **Pump:** 1002; **Duration:** 21 days;
ALZET Comments: Pumps replaced at day 13; behavioral study

P5891: J. E. Jones, *et al.* Effect of naltrexone on food intake and body weight in Syrian hamsters depends on metabolic status. PHYSIOLOGY & BEHAVIOR 2003;78(1):67-72
Agents: Naltrexone **Vehicle:** Water; sterile; **Route:** SC; **Species:** Hamster; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ vehicle; comparison of acute injections vs. chronic mp; naltrexone is a nonselective opiod antagonist; behavorial study

P6029: A. Bailey, *et al.* Quantitative autoradiography of adenosine receptors in brains of chronic naltrexone-treated mice. British Journal of Pharmacology 2003;139(6):1187-1195
Agents: Naltrexone **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ vehicle

P6162: A. S. Levine, *et al.* Naltrexone infusion inhibits the development of preference for a high- sucrose diet. American Journal of Physiology Regulatory, Integrative, and Comparable Physiology 2002;283(5):R1149-R1154
Agents: Naltrexone **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 20 days;
ALZET Comments: Pumps replaced once; post op. care (topical antibiotic)

P5172: M. J. Glass, *et al.* Opioid receptor blockade in rat nucleus tractus solitarius alters amygdala dynorphin gene expression. American Journal of Physiology Regulatory, Integrative, and Comparable Physiology 2002;283(1):R161-R167
Agents: Naltrexone **Vehicle:** CSF, artificial; **Route:** CSF/CNS (nucleus of solitary tract); **Species:** Rat; **Pump:** 1007D; **Duration:** 13 days;
ALZET Comments: Controls received mp w/ vehicle; ALZET brain infusion kit used; 7-day recovery period; cannula placement verifyed by histological examination

P5242: J. E. Jones, *et al.* Effects of naltrexone and CCK on estrous behavior and food intake in Syrian hamsters. Peptides 2001;22(4):601-606
Agents: Naltrexone **Vehicle:** Saline; **Route:** SC; **Species:** Hamster; **Pump:** 1003D; **Duration:** 48 hours;
ALZET Comments: Controls received mp w/ vehicle

P4920: M. S. Cowen, *et al.* Alterations in central preproenkephalin mRNA expression after chronic free-choice ethanol consumption by fawn-hooded rats. Alcoholism Clinical and Experimental Research 2001;25(1126-1133
Agents: Naltrexone **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 4 weeks;
ALZET Comments: controls received mp w/ vehicle; tolerance; dependence

Q6818: N. Boyadjieva, *et al.* Chronic Ethanol Inhibits NK Cell Cytolytic Activity: Role of Opioid Peptide -Endorphin. The Journal of Immunology 2001;167(10):5645-5652
Agents: β-endorphin; naltrexone **Vehicle:** CSF, artificial; **Route:** CSF/CNS (bilateral paraventricular nuclei); **Species:** Rat; **Pump:** 2002; **Duration:** 4 hours; 16 hours;
ALZET Comments: Dose (100 ng of β-EP/0.5 µl/h); Controls received mp w/ vehicle; animal info (Male Fischer-344 rats of 150–175 g body weight); naltrexone is an opiate antagonist; Brain coordinates (1.8 mm behind bregma, 1.5 mm lateral to the midline, and 7.7 mm below the skull surface); bilateral cannula used: The osmotic pump was implanted was connected with two infusion cannulae (bilateral guide cannula) using a Y-connector;

P5752: N. Boyadjieva, *et al.* Chronic ethanol inhibits NK cell cytolytic activity: role of opioid peptide beta-endorphin. J Immunol 2001;167(10):5645-5652
Agents: Endorphin, B-; Naltrexone **Vehicle:** CSF, artificial; **Route:** CSF/CNS (paraventricular nucleus); **Species:** Rat; **Pump:** 2002; **Duration:** 4,16 hours;
ALZET Comments: Controls received mp w/ vehicle; naltrexone is an opiate antagonist; used a Y-connector to connect pump with a bilateral cannula; bilateral infusion;

P4753: L. D. Middaugh, *et al.* Naltrexone effects on ethanol consumption and response to ethanol conditioned cues in C57BL/6 mice. Psychopharmacology 2000;151(321-327
Agents: Naltrexone **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ vehicle; dose-response (graph p. 324); comparison of SC injections vs. mp; good methods priming p. 322; tolerance; Naltrexone is an opioid antagonist; injected naltrexone reduced drinking behavior, infused naltrexone did not; repeated injections and infusion increased ethanol consumption; recovery period

P4602: M. S. Cowen, *et al.* Ethanol consumption by Fawn-Hooded rats following abstinence: effect of naltrexone and changes in m-opioid receptor density. Alcoholism Clinical and Experimental Research 1999;23(6):1008-1014
Agents: Naltrexone **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 4 weeks;
ALZET Comments: Controls received mp w/vehicle; tolerance; dependence

P4307: E. M. Unterwald, *et al.* Quantitative immunolocalization of mu opioid receptors: regulation by naltrexone. Neuroscience 1998;85(3):897-905
Agents: Naltrexone HCl **Vehicle:** Saline, sterile; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Controls received mp with vehicle

P4179: P. M. Kunko, *et al.* Alterations in locomotor activity during chronic cocaine administration: effect of dopamine receptors and interaction with opioids. J. Pharmacol. Exp. Ther 1998;285(1):277-284
Agents: Cocaine; Naltrexone HCl; Morphine sulfate **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: controls received mp w/vehicle; functionality of mp verified by plasma levels; dose-response (p. 279-280); tolerance

P3840: C. M. Kotz, *et al.* Effect of naltrexone on feeding, neuropeptide Y and uncoupling protein gene expression during lactation. Neuroendocrinology 1997;65(259-264
Agents: Naltrexone **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 1003D; **Duration:** Not Stated;
ALZET Comments: Controls received mp w/saline; functionality of mp verified by residual volume; no stress (see pg. 260)

P3183: H. B. Weems, *et al.* Solubilization of high-affinity, guanine nucleotide-sensitive mu-opioid receptors from rat brain membranes. J. Neurochem 1996;66(1042-1050
Agents: Naltrexone **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: no comment posted

P3517: C. M. Kotz, *et al.* Naltrexone induces arcuate nucleus neuropeptide Y gene expression in the rat. American Journal of Physiology Regulatory, Integrative, and Comparable Physiology 1996;271(R289-R294
Agents: Naltrexone **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 1003D; **Duration:** 48 hours;
ALZET Comments: controls received vehicle infusion; functionality of mp verified by measuring residual volume

P3316: E. M. Unterwald, *et al.* Chronic opioid antagonist administration upregulates mu opioid receptor binding without altering mu opioid receptor mRNA levels. Mol. Brain Research 1995;33(351-355
Agents: Naltrexone **Vehicle:** Saline, sterile; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: controls received mp w/saline

P3476: D. P. Menard, *et al.* Alteration of calcitonin gene related peptide and its receptor binding sites during the development of tolerance to mu and delta opioids. Canadian Journal of Physiology and Pharmacology 1995;73(1089-1095
Agents: Morphine sulfate; Naltrexone; Enkephalin; U-50,488H **Vehicle:** Saline; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: tolerance

P2797: G. I. Keshet, *et al.* Maternal naltrexone prevents morphological and behavioral alterations induced in rats by prenatal stress. Pharmacol. Biochem. Behav 1995;50(3):413-419
Agents: Ascorbic acid; Naltrexone **Vehicle:** Saline; **Route:** SC; **Species:** Rat (pregnant); Rat; **Pump:** Not Stated; **Duration:** 7 days;
ALZET Comments: controls received mp w/ vehicle

P2919: T. Rubino, *et al.* Effect of chronic exposure to naltrexone and opioid selective agonists on G protein mRNA levels in the rat nervous system. Mol. Brain Research 1994;23(333-337
Agents: Naltrexone; DAGO; Enkephalin analog DADLE; DPDPE; U-50,488H **Vehicle:** Not Stated; **Route:** SC; CSF/CNS; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: DAGO is a mu-opioid agonist; DPDPE is a delta-opioid agonist

P2869: S. B. Jaffe, *et al.* Effect of opioid antagonism on B-endorphin processing and proopiomelanocortin-peptide release in the hypothalamus. Brain Research 1994;648(24-31
Agents: Naltrexone HCl **Vehicle:** Lactic acid; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 7 days;
ALZET Comments: controls received empty silastic implants

P2569: O. J. Igwe. Modulation of substance P-ergic system in the rat spinal cord by an opioid antagonist. Mol. Brain Research 1994;21(263-273
Agents: Naltrexone HCl **Vehicle:** Water, distilled; Cyclodextrin; **Route:** SC; **Species:** Rat; **Pump:** 2001; 2002; **Duration:** 8,15 days;
ALZET Comments: Controls received mp w/ vehicle

P2306: D. O. Freier, *et al.* Morphine-induced alterations in thymocyte subpopulations of B6C3F1 mice. J. Pharmacol. Exp. Ther 1993;265(1):81-88
Agents: Naltrexone **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** Not Stated;
ALZET Comments: Immunology; dependence; pumps used to evaluate naltrexone's ability administered via Alzet mini-osmotic pumps to block morphine actions on the thymocytes; main study used morphine pellets

P3240: T. E. Cote, *et al.* Naltrexone-induced upregulation of mu opioid receptors on 7315c cell and brain membranes: enhancement of opioid efficacy in inhibiting adenylyl cyclase. J. Pharmacol. Exp. Ther 1993;267(1):238-244
Agents: Naltrexone **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: controls received mp with saline

P2653: D. M. Bronstein, *et al.* Pre- and posttranslational regulation of B-endorphin biosynthesis in the CNS: effects of chronic naltrexone treatment. J. Neurosci 1993;60(40-49
Agents: Naltrexone **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 8 days;
ALZET Comments: controls received mp w/ water; comparison of ip injections, NIDA pellets and mp

P2371: C. E. Markowitz, *et al.* Effect of opioid receptor antagonism on proopiomelanocortin peptide levels and gene expression in the hypothalamus. Mol. and Cellular Neurosciences 1992;3(184-190
Agents: Naltrexone **Vehicle:** Lactic acid; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 1, 3 weeks;
ALZET Comments: Controls received empty silastic implants; comparison of sc injections vs. mp

P2036: F. J. Ayesta, *et al.* Paradoxical effect of chronic fentanyl treatment on naltrexone-induced supersensitivity and upregulation. J. Pharmacol. Exp. Ther 1992;260(168-174
Agents: Naltrexone **Vehicle:** Water, distilled; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: no comment posted

P3055: A. M. Young, *et al.* Increased sensitivity to rate-altering and discriminative stimulus effects of morphine following continuous exposure to naltrexone. Psychopharmacology 1991;103(67-73
Agents: Naltrexone HCl **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 8 days;
ALZET Comments: controls received mp with saline; dose-response

P2440: G. C. Teskey, *et al.* Modifications of social conflict-induced analgesic and activity responses in male mice receiving chronic opioid agonist and antagonist treatments. Pharmacol. Biochem. Behav 1991;38(485-493
Agents: Levorphanol tartrate; Naltrexone HCl; U-50,488H; ICI-154,129 **Vehicle:** Saline; **Route:** IP; **Species:** Mice; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Functionality of mp verified by measuring residual pump volume; tolerance

P1719: L. C. Saland, *et al.* Chronic naltrexone infusion: effects on innervation of rat neurointermediate lobe. Brain Research Bulletin 1990;24(6):779-786
Agents: Naltrexone HCl **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: no comment posted

P1665: L. Ahtee, *et al.* Augmentation of morphine-induced changes in brain monoamine metabolism after chronic naltrexone treatment. Journal of Pharmacology and Experimental Therapeutics 1990;255(2):803-808
Agents: Naltrexone HCl **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: controls received a smooth, hollow glass capsule of the same size and weight as pumps

P1164: C. W. Stevens, *et al.* Chronic antagonist infusion does not increase morphine antinociception in rat spinal cord. Brain Research 1987;425(2):388-390
Agents: Naloxone HCl; Naltrexone HCl **Vehicle:** Saline; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: mp connected to a 'Y' catheter; half-life; morphine administered intrathecally via the external arm of the 'Y' catheter; concomitant infusion of agents; comparison of bolus injections vs. mp infusion

P1205: L. Steinberg, *et al.* The influence of chronic naltrexone infusions on energy metabolism in pregnant rats. Nutr. Rep. Int 1986;33(1):89-98
Agents: Naltrexone HCl **Vehicle:** Saline; **Route:** SC; **Species:** Rat; Rat (pregnant); **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: controls received mp w/ saline; mp implanted in pregnant rats on day 3 of exp. (7 days sperm positive)

P0742: D. S. Baskin, *et al.* Treatment of experimental stroke with opiate antagonists, effects on neurological function, infarct size, and survival. Journal of Neurosurgery 1986;64(99-103
Agents: Diprenorphine; Naloxone; Naltrexone **Vehicle:** Saline; **Route:** SC; **Species:** Cat; **Pump:** 2ML1; **Duration:** 7 days;
ALZET Comments: mp functionality and accuracy of delivery verified; acute ip adminis. of agents w/mp infusion; ischemia (cerebral)

P0564: A. Tempel, *et al.* Neurochemical and functional correlates of naltrexone-induced opiate receptor up-regulation. The Journal of Pharmacology and Experimental Therapeutics 1985;232(2):439-444
Agents: Naltrexone HCl **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 8 days;
ALZET Comments: comparison of ip injec vs. mp infusion vs. pellets

P0749: A. M. Moudy, *et al.* Differential up-regulation of microsomal and synaptic membrane mu opoid receptors. Biochemical and Biophysical Research Communications 1985;132(2):735-741
Agents: Naltrexone HCl **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: controls received mp w/ saline

P0528: R. Marks-Kaufman, *et al.* Modifications in food intake and energy metabolism in rats as a function of chronic naltrexone infusions. Pharmacology Biochemistry & Behavior 1984;20(6):911-916
Agents: Naltrexone HCl **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2002; **Duration:** 2 weeks;
ALZET Comments: no comment posted

P0239: R. S. Zukin, *et al.* Naltrexone-induced opiate receptor supersensitivity. Brain Research 1982;245(285-292
Agents: Naltrexone HCl **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 1 week;
ALZET Comments: comparison of pellets vs. mp infusion

P0242: G. L. Nieder, *et al.* Effects of opiate antagonists on early pregnancy and pseudopregnancy in mice. Journals of Reproduction Fertility 1982;65(341-346
Agents: Naltrexone **Vehicle:** Saline; **Route:** SC; **Species:** Mice (pregnant); **Pump:** 2001; **Duration:** 9 days;
ALZET Comments: Comparison of agents