



References on the Administration of Analgesics  
Using the ALZET® Osmotic Pumps

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## Narcotic

### 1. Alfentanil

**P1206:** M. Fujinaga, R. I. Mazze, E. C. Jackson and J. M. Baden. Reproductive and teratogenic effects of sufentanil and alfentanil in sprague-dawley rats. *Anesth. Analg* 1988;67(166-169)

**ALZET Comments:** Alfentanil; Sufentanil; Saline; SC; Rat (pregnant); 2ML2; 14 days; controls received mp w/ saline; dose-response (text); 3 doses of sufentanil infused; agents infused separately; author states 'in terms of experimental design, the cost of using sc implanted osmotic minipumps is small'; teratology.

### 2. Buprenorphine

**Q6540:** S. L. Withey, R. Hill, A. Lyndon, W. L. Dewey, E. Kelly and G. Henderson. Effect of Tamoxifen and Brain-Penetrant Protein Kinase C and c-Jun N-Terminal Kinase Inhibitors on Tolerance to Opioid-Induced Respiratory Depression in Mice. *J Pharmacol Exp Ther* 2017;361(1):51-59

**ALZET Comments:** Morphine; buprenorphine; methadone; Saline; SC; Mice; 6 days; Dose (45 mg/kg/d; 5 mg/kg/day; 60 mg/kg/day); Controls received mp w/ vehicle; animal info (Male CD-1 mice, approximately 30g); comparison of morphine alkaloid pellet vs mp;

**Q4834:** R. Hill, A. Lyndon, S. Withey, J. Roberts, Y. Kershaw, J. MacLachlan, A. Lingford-Hughes, E. Kelly, C. Bailey, M. Hickman and G. Henderson. Ethanol Reversal of Tolerance to the Respiratory Depressant Effects of Morphine. *Neuropsychopharmacology* 2016;41(762-773)

**ALZET Comments:** Buprenorphine; methadone; Saline; SC; Mice; 6 days; Controls received mp w/ vehicle; animal info (male, CD-1, 30g); behavioral testing (tail flick latencies, mouse locomotion); dependence; Dose (Buprenorphine 5 mg/kg/day; methadone 60 mg/kg/day);.

**Q4987:** S. Mundt, M. Groettrup and a. M. Basler. Analgesia in mice with experimental meningitis reduces pain without altering immune parameters. *Altx* 2015;32(3):183-189

**ALZET Comments:** Buprenorphine; SC; Mice; 1007D; 7 days; Controls received mp w/ PBS; animal info (female, C57BL6, 8 weeks old); behavioral testing (pain score); "we used subcutaneously implanted ALZET® osmotic pumps to apply the analgesic buprenorphine. We observed strongly reduced pain scores in diseased mice receiving analgesics, whereas the immune response was not altered in these mice. Hence, our study offers a new treatment option to improve wellbeing of mice used to study LCMV-induced meningitis without grossly altering immune parameters " pg 184; "In this study, we subcutaneously implanted ALZET® osmotic pumps releasing the analgesic agent buprenorphine. Continuous delivery with osmotic pumps ensures constant compound levels for maximized therapeutic efficacy and reduced adverse effects. Additionally, unnecessary stressful animal handling due to repeated injection is not required. " pg 188; Dose (0.15 mg/kg/day);.

**Q0846:** R. S. Yamdeu, M. Shaqura, S. A. Mousa, M. Schaefer and J. Droese. p38 Mitogen-activated Protein Kinase Activation by Nerve Growth Factor in Primary Sensory Neurons Upregulates  $\mu$ -Opioid Receptors to Enhance Opioid Responsiveness Toward Better Pain Control. *Anesthesiology* 2011;114(1):150-161

**ALZET Comments:** Fentanyl propionanilide; buprenorphine hydrochloride; Saline, isotonic; CSF/CNS (intrathecal); Rat; 96 hours; Controls received mp w/ vehicle; animal info (male Wistar, 200-250 g); pain.

**P9868:** M. S. Virk, S. Arttamangkul, W. T. Birdsong and J. T. Williams. Buprenorphine Is a Weak Partial Agonist That Inhibits Opioid Receptor Desensitization. *Journal of Neuroscience* 2009;29(22):7341-7348

**ALZET Comments:** Buprenorphine; DMSO; water; Rat; 2ML1; Controls received mp w/ vehicle; functionality of mp verified by plasma drug levels; animal info (male, Sprague Dawley, 150-200 g.); 40% DMSO used; "the osmotic minipump delivered buprenorphine efficiently and predictably" pg. 7342.

**P9326:** F. M. Placenza, H. Rajabi and J. Stewart. Effects of chronic buprenorphine treatment on levels of nucleus accumbens glutamate and on the expression of cocaine-induced behavioral sensitization in rats. *Psychopharmacology* 2008;200(3):347-355

**ALZET Comments:** Buprenorphine; SC; Rat; 2ML2; Controls received sham surgery; animal info (male, Long-Evans, 350-375 g.).



**P8265:** R. E. Sorge and J. Stewart. The effects of long-term chronic buprenorphine treatment on the locomotor and nucleus accumbens dopamine response to acute heroin and cocaine in rats. *Pharmacology Biochemistry and Behavior* 2006;84(2):300-305

**ALZET Comments:** Buprenorphine HCL; SC; Rat; 2ML2; 14, 28 days; Controls received sham surgery; dose-response (fig. 2); pumps replaced after 14 days; half-life (pg. 300) long half-life; tolerance; animal info (male, Long-Evans, 325-350g.).

**P8264:** R. E. Sorge and J. Stewart. The effects of chronic buprenorphine on intake of heroin and cocaine in rats and its effects on nucleus accumbens dopamine levels during self-administration. *Psychopharmacology* 2006;188(1):28-41

**ALZET Comments:** Buprenorphine; SC; Rat; 2ML2; 28 days; Controls received sham surgery; functionality of mp verified by plasma buprenorphine levels; dose-response (fig. 1); pumps replaced after 14 days; no stress (see pg. 29); dependence; animal info (male, Long-Evans, 300-350g.).

**P7423:** R. E. Sorge, H. Rajabi and J. Stewart. Rats maintained chronically on buprenorphine show reduced heroin and cocaine seeking in tests of extinction and drug-induced reinstatement. *Neuropsychopharmacology* 2005;30(9):1681-1692

**ALZET Comments:** Buprenorphine; CSF/CNS (nucleus accumbens); Rat; 2ML2; Controls received incision and pocket, no pump; dependence; post op. care (antibiotic injection); animal info (male, long-evans, 350-375 g); Plastics One 20G cannula used.

**P6955:** J. Patenaude, M. D'Elia, C. Hamelin, D. Garrel and J. Bernier. Burn injury induces a change in T cell homeostasis affecting preferentially CD4<sup>+</sup> T cells. *Journal of Leukocyte Biology* 2005;77(2):141-150

**ALZET Comments:** Buprenorphine; Mice; 1,5,10 days;

**P7403:** M. D'Elia, J. Patenaude, C. Hamelin, D. R. Garrel and J. Bernier. Corticosterone binding globulin regulation and thymus changes after thermal injury in mice. *AMERICAN JOURNAL OF PHYSIOLOGY-ENDOCRINOLOGY AND METABOLISM* 2005;288(5):E852-E860

**ALZET Comments:** Buprenorphine; SC; Mice; 12 hours; Pain treatment.

### 3. Butorphanol [Back to top](#)

**Q5136:** M. Meredith M. Clancy DVM, P. Butch KuKanich DVM and J. M. S. I. DVM. Pharmacokinetics of butorphanol delivered with an osmotic pump during a seven-day period in common peafowl (*Pavo cristatus*). *American Journal of Veterinary Research* 2015;76(12):1070-1076

**ALZET Comments:** Butorphanol; SC; Bird (peafowl); 2ML1; 7 days; animal info: 14 healthy adult male common peafowl; functionality of mp verified by plasma levels; good methods (pg. 1071-1072); "Use of these osmotic pumps may provide options for avian analgesia." pg 1070; analgesic administration to avian species; Pharmacokinetics; Dose: 247 ug/kg/h; Resultant plasma level ((mean, 106.4 ug/L; range, 61.8 to 133.0 ug/L)); Industry authored (Wildlife Conservation Society); Interesting (Plasma concentrations of butorphanol in common peafowl were maintained at or above reported efficacious analgesic concentrations; Use of these osmotic pumps may provide options for avian analgesia) pg. 1070.

**Q1826:** A. Mitra, C. M. Kotz, E. M. Kim, M. K. Grace, M. A. Kuskowski, C. J. Billington and A. S. Levine. Effects of butorphanol on feeding and neuropeptide Y in the rat. *Pharmacology Biochemistry and Behavior* 2012;100(3):575-580

**ALZET Comments:** Butorphanol tartrate; SC; Rat; 2ML1; 48 hours; Controls received mp w/ saline; animal info (Sprague Dawley, male, 302 g); "Implantation of the pumps took less than 1 min per rat, and the length of the anesthesia was approximately 5 min per rat." pg 576; functionality of mp verified via residual volume.

**P9327:** Y. H. Tian, K. W. Lee, I. J. You, S. Y. Lee and C. G. Jang. 7-nitroindazole, nitric oxide synthase inhibitor, attenuates physical dependence on Butorphanol in rat. *Synapse* 2008;62(8):582-589

**ALZET Comments:** Butorphanol tartrate; nitroindazole, 7-; Saline; DMSO; CSF/CNS; Rat; 2001; 72 hours; Enzyme inhibitor (nitric oxide synthase, NOS); animal info (male, Sprague Dawley, 250-275 g.); pump connected to catheter after 1 week recovery period; 10% DMSO used; PE60 tubing used.



**P7624:** S. Tanaka, L. W. Fan, L. T. Tien, Y. Park, L. Y. Liu-Chen, R. W. Rockhold and I. K. Ho. Butorphanol dependence increases hippocampal kappa-opioid receptor gene expression. *Journal of Neuroscience Research* 2005;82(2):255-263

**ALZET Comments:** Butorphanol tartrate; Saline, physiological; CSF/CNS; Rat; 2001; 3 days; Controls received mp w/ vehicle; dependence; post op. care (procaine penicillin G; animal info (male, Sprague-Dawley, 250-275 g).

**P7657:** S. Y. Lee and C. G. Jang. Increases in 3H-alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid AMPA receptor binding and mRNA expression of AMPA-sensitive glutamate receptor A GluR-A subunits in rats withdrawn from butorphanol. *JOURNAL OF TOXICOLOGY AND ENVIRONMENTAL HEALTH-PART A-CURRENT ISSUES* 2005;68(23-24):2163-2174

**ALZET Comments:** Butorphanol tartrate; CSF/CNS; Rat; 2001; 3 days; Controls received mp w/ saline; dependence; animal info (male, Sprague-Dawley 230-250 g).

**P7059:** S. Y. Kim, N. Chudapongse, S. M. Lee, M. C. Levin, J. T. Oh, H. J. Park and I. K. Ho. Proteomic analysis of phosphotyrosyl proteins in the rat brain: Effect of butorphanol dependence. *Journal of Neuroscience Research* 2004;77(6):867-877

**ALZET Comments:** Butorphanol tartrate; CSF/CNS; Rat; 2001; 72 hours; Controls received mp w/ saline; functionality of mp verified by residual drug volume; dependence; post op. care (procaine penicillin G); stadol; mp primed overnight at 35 degree C in sterile saline.

**P6118:** D. S. Kim, H. K. Lim, S. Y. Jang and S. Oh. Changes of the level of G protein alpha-subunit mRNA by tolerance to and withdrawal from butorphanol. *Neurochemical Research* 2003;28(12):1771-1778

**ALZET Comments:** Butorphanol; Saline; CSF/CNS; Rat; 2001; 3 days; Controls received mp w/ vehicle; tolerance; guide cannula used (10mm); solution was filter sterilized.

**P5962:** L. W. Fan, L. T. Tien, S. Tanaka, T. Ma, N. Chudapongse, S. Sinchaisuk, R. W. Rockhold and I. K. Ho. Changes in the brain kappa-opioid receptor levels of rats in withdrawal from physical dependence upon butorphanol. *Neuroscience* 2003;121(4):1063-1074

**ALZET Comments:** Butorphanol; morphine; Saline, sterile; CSF/CNS; Rat; 2001; 72 hours; Controls received mp w/ vehicle; dependence; post op. care (penicillin, 0.5% sensorcaine in wound site); guide cannula with stylet was used; dental cement used to adhere cannula to skull; protective aluminum cap was placed around the cannula; tygon tubing was used; solutions were filter sterilized during filling of the pumps; brain diagram (p. 1066).

**P5479:** S. Sinchaisuk, I. K. Ho and R. W. Rockhold. Focal kappa-opioid receptor-mediated dependence and withdrawal in the nucleus paragigantocellularis. *Pharmacology Biochemistry and Behavior* 2002;74(1):241-252

**ALZET Comments:** Morphine sulfate; butorphanol tartrate; CSF/CNS; Rat; 2001; 3 days; Controls received mp w/ saline; dependence; minipumps were inserted 6-10 days after guide cannula implantation; stylet used.

**P5743:** S. Y. Jang, Y. Kim and S. Oh. The bindings of [3H]muscimol and [3H]flunitrazepam are elevated in discrete brain regions of butorphanol-withdrawal rats. *Neurochem Res* 2002;27(9):939-946

**ALZET Comments:** Butorphanol; CSF/CNS; Rat; 2001; 3 days; Controls received mp w/ saline; tolerance; dependence.

**P6208:** L. W. Fan, S. Tanaka, L. T. Tien, T. G. Ma, R. W. Rockhold and I. K. Ho. Withdrawal from dependence upon butorphanol uniquely increases kappa1-opioid receptor binding in the rat brain. *Brain Research Bulletin* 2002;58(2):149-160

**ALZET Comments:** Butorphanol tartrate; morphine; Saline, sterile physiological; CSF/CNS; Rat; 2001; 72 hours; Controls received mp w/ vehicle; functionality of mp verified by residual drug volume; good methods (p. 150); dependence; post op. care (sensorcaine, procaine penicillin G); guide cannula & stylet used; dental cement secured cannula.

**P6207:** L. W. Fan, S. Tanaka, Y. Park, K. Sasaki, T. G. Ma, L. T. Tien, R. W. Rockhold and I. K. Ho. Butorphanol dependence and withdrawal decrease hippocampal K-2-opioid receptor binding. *Brain Research* 2002;958(2):277-290

**ALZET Comments:** Butorphanol tartrate; Saline, sterile physiological; CSF/CNS; Rat; 2001; 72 hours; Controls received mp w/ vehicle; functionality of mp verified by residual volume; good methods (p. 279); dependence; post op. care (sensorcaine, procaine penicillin).

#### 4. Codeine [Back to top](#)



**P4917:** M. Chew, J. M. White, A. A. Somogyi, F. Bochner and R. J. Irvine. Precipitated withdrawal following codeine administration is dependent on CYP genotype. *European Journal of Pharmacology* 2001;425(159-164)

**ALZET Comments:** Morphine tartrate; Codeine phosphate; Saline; SC; Rat; 2ML1; 7 days; functionality of mp verified by plasma drug levels; dose response (graphs p. 161); dependence.

## 5. Fentanyl [Back to top](#)

**Q6131:** A. Kliewer, F. Schmiedel, S. Sianati, A. Bailey, J. T. Bateman, E. S. Levitt, J. T. Williams, M. J. Christie and S. Schulz. Phosphorylation-deficient G-protein-biased mu-opioid receptors improve analgesia and diminish tolerance but worsen opioid side effects. *Nat Commun* 2019;10(1):367

**ALZET Comments:** Fentanyl citrate; morphine sulphate salt pentahydrate; PBS; water, sterile; SC; Mice (transgenic); 1007D; 7 days; Dose (Fentanyl (2mg/kg/day); Morphine (17 mg/kg/day)); animal info (knock-in mice with 11S/T-A mutations (Oprm1tm3.1Shlz, MGI:6117673, 11S/T-A)); behavioral testing (hot plate test; open field locomotion test); dependence; "...we used subcutaneously implanted osmotic pumps to deliver opioids at a constant rate. This approach is a powerful means of assessing both tolerance and dependence in rodents" (p.5).

**Q5277:** J. P. Anand, B. T. Boyer, H. I. Mosberg and E. M. Jutkiewicz. The behavioral effects of a mixed efficacy antinociceptive peptide, VRP26, following chronic administration in mice. *Psychopharmacology (Berl)* 2016;233(13):2479-87

**ALZET Comments:** VRP26, Fentanyl; Saline; SC; mice; 1007D; 7 days; Controls received mp w/ vehicle; animal info (Male, female C57BL/6 wild-type, homozygous MOR knockout; 20-30 g, 8-16 wks); functionality of mp verified by in vitro testing (pg. 2481); dose-response (pg 2481); good methods (pg 2481); behavioral testing (tail suspension test, conditioned place preference and locomotor activities); behavioral testing (tail suspension test, conditioned place preference and locomotor activities); peptides; Primed for 4 hours, 37 degree Saline; antinociceptive peptide; Dose (0.3 mg/kg/day fentanyl or 10 mg/kg/day VRP26);

**Q3568:** J. D. Mitzelfelt, C. S. Carter and D. Morgan. Thermal sensitivity across ages and during chronic fentanyl administration in rats. *Psychopharmacology* 2014;231(1):75-84

**ALZET Comments:** Fentanyl; Saline; SC; Rat; 2ML4; 28 days; Controls received mp w/ vehicle; animal info (male, Fischer 344 x Brown Norway, 16, 20 and 24 months old); behavioral testing (temperature preference/heat and cold sensitivity, locomotor activity); Pumps removed after 4 weeks;.

**Q0846:** R. S. Yamdeu, M. Shaqura, S. A. Mousa, M. Schaefer and J. Droese. p38 Mitogen-activated Protein Kinase Activation by Nerve Growth Factor in Primary Sensory Neurons Upregulates  $\mu$ -Opioid Receptors to Enhance Opioid Responsiveness Toward Better Pain Control. *Anesthesiology* 2011;114(1):150-161

**ALZET Comments:** Fentanyl propionanilide; buprenorphine hydrochloride; Saline, isotonic; CSF/CNS (intrathecal); Rat; 96 hours; Controls received mp w/ vehicle; animal info (male Wistar, 200-250 g); pain.

**Q0735:** K. M. Raehal and L. M. Bohn. The role of beta-arrestin2 in the severity of antinociceptive tolerance and physical dependence induced by different opioid pain therapeutics. *Neuropharmacology* 2011;60(1):58-65

**ALZET Comments:** Morphine; methadone; fentanyl; oxycodone; Water, sterile, distilled; SC; Mice; 7 days; Animal info (male, WT, barr2-KO); dependence; wound clips used.

**Q0785:** J. D. Mitzelfelt, J. P. DuPree, D. O. Seo, C. S. Carter and D. Morgan. Effects of chronic fentanyl administration on physical performance of aged rats. *Experimental Gerontology* 2011;46(1):65-72

**ALZET Comments:** Fentanyl; SC; Rat; 2ML4; 4 weeks; Controls received mp w/ saline; animal info (male, Fisher 344 x Brown Norway, 12, 24, 30 mo old); behavioral testing (open field activity, grip strength, rotarod).

**Q0820:** H. Zheng, Y. Zeng, X. X. Zhang, J. Chu, H. H. Loh and P. Y. Law.  $\mu$ -Opioid Receptor Agonists Differentially Regulate the Expression of miR-190 and NeuroD. *MOLECULAR PHARMACOLOGY* 2010;77(1):102-109

**ALZET Comments:** Morphine; fentanyl; Mice; 1003D; 3 days; Controls received mp w/ saline; animal info (CD1 (ICR), 6-8 wks old).



**Q0727:** A. R. Waxman, C. Arout, M. Caldwell, A. Dahan and B. Kest. Acute and chronic fentanyl administration causes hyperalgesia independently of opioid receptor activity in mice. *Neuroscience Letters* 2009;462(1):68-72

**ALZET Comments:** Fentanyl; Saline; SC; Mice; 2001; 6 days; Controls received mp w/ vehicle; animal info (adult, male, CD-1); comparison of SC injections vs. mp; "Although acute fentanyl injection (0.25 mg/kg) caused hyperalgesia within 15 min, hyperalgesia was not similarly evident on infusion Day 1 even though pumps were filled with a fentanyl dose (10mg/kg/24 h) that dispenses ~0.42 mg/kg/h, almost double the dose given by bolus injection." pg 71.

**Q0264:** J. M. Sykes, S. Cox and E. C. Ramsay. Evaluation of an osmotic pump for fentanyl administration in cats as a model for nondomestic felids. *American Journal of Veterinary Research* 2009;70(8):950-955

**ALZET Comments:** Fentanyl; Saline, sterile; SC; Cat (felid); 2ML1; 96 hours; Animal info (spayed, female, 56 months old, 4.5 kg); functionality of mp verified by residual volume; comparison of transdermal patch vs. SC mp; no stress see pg 952; "if fentanyl is "to be used for nondomestic cats, then the faster elimination of fentanyl after removal of a delivery device is an important advantage of the osmotic pump versus the transdermal patch" pg 953; "Compared with a transdermal patch, an osmotic pump provides several pharmacokinetic advantages for fentanyl administration in cats." pg 954.

**P9594:** S. Sirohi, S. V. Dighe, P. A. Madia and B. C. Yoburn. The Relative Potency of Inverse Opioid Agonists and a Neutral Opioid Antagonist in Precipitated Withdrawal and Antagonism of Analgesia and Toxicity. *Journal of Pharmacology and Experimental Therapeutics* 2009;330(2):513-519

**ALZET Comments:** Fentanyl; SC; Mice; 2001; 72 hours; Dependence; animal info (Swiss-Webster, 25-33g).

## 6. Hydromorphone [Back to top](#)

**Q3537:** A. Koesters, K. L. Engisch, M. M. Rich and M. M. Rich. Decreased cardiac excitability secondary to reduction of sodium current may be a significant contributor to reduced contractility in a rat model of sepsis. *CRITICAL CARE* 2014;18(U351-U357)

**ALZET Comments:** Hydromorphone; IP; Rat; 24 hours; Animal info (female, Wistar, adult, 250-300g); post op. care (buprenorphine 0.12 mg/kg SC injection); used 2ML size pump; pain relief;

**P9162:** P. Kumar, S. Sunkaraneni, S. Sirohi, S. V. Dighe, E. A. Walker and B. C. Yoburn. Hydromorphone efficacy and treatment protocol impact on tolerance and mu-opioid receptor regulation. *European Journal of Pharmacology* 2008;597(1-3):39-45

**ALZET Comments:** Hydromorphone; Saline; SC; Mice; 2001; 7 days; Controls received inert placebo pellet; tolerance; animal info (male, Swiss Webster, 22-30 g.); "There was substantially more tolerance with infusion treatment compared to injection treatment." pg. 43.

**P3843:** G. J. Lesser, S. A. Grossman, K. W. Leong, H. Lo and S. Eller. In vitro and in vivo studies of subcutaneous hydromorphone implants designed for the treatment of cancer pain. *Pain* 1996;65(265-272)

**ALZET Comments:** Hydromorphone; SC;; rabbit;; 2ML4;; 4 weeks;; functionality of mp verified by blood sample assays; comparison of IV bolus administration vs. EVA polymer drug delivery vs. mp; pain; cancer;.

**P2556:** W. Kowalski, R. T. Chatterton, R. R. Kazer and A. C. Wentz. The impact of subchronic hypercortisolemia on progesterone metabolism and the luteinizing hormone-progesterone axis in the cynomolgus monkey. *J. Clin. Endocrinol. Metab* 1993;77(6):1597-1604

**ALZET Comments:** Hydrocortisone phosphate; Hydromorphone; Saline; SC; monkey; 2 months; monkeys received both a mp w/ HP and a mp w/ saline on alternating menstrual cycles; long-term study.

**P0770:** M. C. Behm, M. V. Stout-Caputi, M. P. Mahalik and R. F. Gautieri. Evaluation of the teratogenic potential of hydromorphone administered via a miniature implantable pump in mice. *Res. Commun. Substance Abuse* 1985;6(3):165-177

**ALZET Comments:** Hydromorphone; Saline; Water; SC; mice (pregnant); 2001; 4 days; no stress or complications (see pg. 170-71); describes mp as 'valuable tool...' and discusses advantages of this type of delivery system (see pgs. 165, 176); toxicology.



## 7. Levorphanol [Back to top](#)

**P2440:** G. C. Teskey and M. Kavaliers. 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)

**ALZET Comments:** Levorphanol tartrate; Naltrexone HCl; U-50,488H; ICI-154,129; Saline; IP; mice; 2001; 7 days; functionality of mp verified by measuring residual pump volume; tolerance.

## 8. Meperidine [Back to top](#)

**P3555:** C. A. Paronis and S. G. Holtzman. Sensitization and tolerance to the discriminative stimulus effects of mu-opioid agonists. *Psychopharmacology* 1994;114(601-610)

**ALZET Comments:** Naloxone HCl; Morphine sulfate; Meperidine HCl; Fentanyl citrate; Saline; SC; Rat; 2ML1; 7 days; controls received sham pumps; tolerance.

**P2408:** C. A. Paronis and S. G. Holtzman. Development of tolerance to the analgesic activity of mu agonists after continuous infusion of morphine, meperidine or fentanyl in rats. *J. Pharmacol. Exp. Ther* 1992;262(1):1-9

**ALZET Comments:** Morphine; Meperidine; Fentanyl; Saline; SC; Rat; 2ML1; 1 week; tolerance.

**P0588:** W. K. Schmidt, S. W. Tam, G. S. Sholtzberger, D. H. Smith Jr, R. Clark and V. G. Vernier. Nalbuphine. *Drug Alcohol Depend* 1985;14(339-362)

**ALZET Comments:** Ethylketocyclazocine; Heroin; Meperidine; Oxymorphone; Pentazocine; Propoxyphene; Bremazocine; Buprenorphine; Butorphanol; Methadone; Morphine; Nalbuphine; U-50,488H; SC; mice; 3 days; comparison of sc morphine pellets vs. mp infusion; comparison of agents effects; controls received unspecified placebo infusion.

## 9. Methadone [Back to top](#)

**Q6540:** S. L. Withey, R. Hill, A. Lyndon, W. L. Dewey, E. Kelly and G. Henderson. Effect of Tamoxifen and Brain-Penetrant Protein Kinase C and c-Jun N-Terminal Kinase Inhibitors on Tolerance to Opioid-Induced Respiratory Depression in Mice. *J Pharmacol Exp Ther* 2017;361(1):51-59

**ALZET Comments:** Morphine; buprenorphine; methadone; Saline; SC; Mice; 6 days; Dose (45 mg/kg/d; 5 mg/kg/day; 60 mg/kg/day); Controls received mp w/ vehicle; animal info (Male CD-1 mice, approximately 30g); comparison of morphine alkaloid pellet vs mp;.

**Q6771:** S. Schreiber, M. Bader, V. Rubovitch and C. G. Pick. Interaction between methylphenidate, methadone and different antidepressant drugs on antinociception in mice, and possible clinical implications. *World J Biol Psychiatry* 2017;18(4):300-307

**ALZET Comments:** methadone; escitalopram; venlafaxine; desipramine; clomipramine; SC; Mice; 2002; 14 days; Dose: methadone (0.5 mg/kg) venlafaxine (2.5 mg/kg); escitalopram (20mg/kg); desipramine (1mg/kg); clomipramine (0.5 mg/kg); animal info (Male ICR mice, 25-35g); dependence.

**Q4834:** R. Hill, A. Lyndon, S. Withey, J. Roberts, Y. Kershaw, J. MacLachlan, A. Lingford-Hughes, E. Kelly, C. Bailey, M. Hickman and G. Henderson. Ethanol Reversal of Tolerance to the Respiratory Depressant Effects of Morphine. *Neuropsychopharmacology* 2016;41(762-773)

**ALZET Comments:** Buprenorphine; methadone; Saline; SC; Mice; 6 days; Controls received mp w/ vehicle; animal info (male, CD-1, 30g); behavioral testing (tail flick latencies, mouse locomotion); dependence; Dose (Buprenorphine 5 mg/kg/day; methadone 60 mg/kg/day);.

**Q4151:** A. A. Vestal-Laborde, A. C. Eschenroeder, J. W. Bigbee, S. E. Robinson, C. Sato-Bigbee and C. Sato-Bigbee. The Opioid System and Brain Development: Effects of Methadone on the Oligodendrocyte Lineage and the Early Stages of Myelination. *Developmental Neuroscience* 2014;36(409-421)

**ALZET Comments:** Methadone; Saline; SC; Rat (pregnant); 2ML4; 28 days; Controls received mp w/ vehicle; animal info (female, Pregnant, Sprague Dawley, GD7); teratology; dependence;.



**Q3624:** S. Schreiber, Y. Barak, A. Hostovsky, R. Baratz-Goldstein, I. Volis, V. Rubovitch and C. G. Pick. Interaction of Different Antidepressants with Acute and Chronic Methadone in Mice, and Possible Clinical Implications. *Journal of Molecular Neuroscience* 2014;52(4):598-604

**ALZET Comments:** Methadone; SC; Mice; 1007D; 14 days; Animal info (male, ICR, 25-35g); behavioral testing (hot plate); dependence;

**Q0735:** K. M. Raehal and L. M. Bohn. The role of beta-arrestin2 in the severity of antinociceptive tolerance and physical dependence induced by different opioid pain therapeutics. *Neuropharmacology* 2011;60(1):58-65

**ALZET Comments:** Morphine; methadone; fentanyl; oxycodone; Water, sterile, distilled; SC; Mice; 7 days; Animal info (male, WT, barr2-KO); dependence; wound clips used.

**Q0694:** N. Quillinan, E. K. Lau, M. Virk, M. von Zastrow and J. T. Williams. Recovery from mu-Opioid Receptor Desensitization after Chronic Treatment with Morphine and Methadone. *Journal of Neuroscience* 2011;31(12):4434-4443

**ALZET Comments:** Morphine; methadone; Water; SC; Rat; 2ML1; 2001; 6 days; Controls received mp w/ vehicle; tolerance; animal info (adult (150-250 g, male, Sprague Dawley).

**Q1116:** J. L. Hay, J. Kaboutari, J. M. White, A. Salem and R. Irvine. Model of methadone-induced hyperalgesia in rats and effect of memantine. *European Journal of Pharmacology* 2010;626(2-3):229-233

**ALZET Comments:** Methadone; SC; Rat; 2002; 14 days; Controls received mp w/ saline; animal info (adult, male, Sprague Dawley); post op. care (Topical antibiotic powder); wound clips used.

**Q0665:** P. A. Madia, S. V. Dighe, S. Sirohi, E. A. Walker and B. C. Yoburn. Dosing protocol and analgesic efficacy determine opioid tolerance in the mouse. *Psychopharmacology* 2009;207(3):413-422

**ALZET Comments:** Etorphine; oxycodone; hydrocodone; methadone; Saline; DMSO; SC; Mice; 2001; 7 days; Controls received placebo pellets wrapped in nylon mesh; animal info (Male, Swiss Webster, 23-30 g); tolerance; comparison of SC injections vs mp; "Higher doses of hydrocodone, oxycodone, and methadone could not be infused due to solubility issues." pg 415; 20% DMSO used; "infusion with hydrocodone or methadone produced greater tolerance than acute or intermittent treatment" pg 417.

**Q0910:** F. Leri, Y. Zhou, B. Goddard, A. Levy, D. Jacklin and M. J. Kreek. Steady-state methadone blocks cocaine seeking and cocaine-induced gene expression alterations in the rat brain. *European Neuropsychopharmacology* 2009;19(4):238-249

**ALZET Comments:** Methadone; SC; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; animal info (Sprague Dawley, male, 225-250 g); wound clips used.

**P9213:** N. Devidze, Y. Zhou, A. Ho, Q. Zhang, D. W. Pfaff and A. J. Kreek. Steady-State Methadone Effect on Generalized Arousal in Male and Female Mice. *Behavioral Neuroscience* 2008;122(6):1248-1256

**ALZET Comments:** Methadone; Saline; SC; Mice; 2002; 14 days; Controls received mp w/ vehicle; dose-response (fig. 1, 2, 3); half-life (p. 1249) "short"; animal info (male, female, C57BL/6, 12 wks old, 25-27 g.); "because of methadone's short half-life in rodents, methadone was delivered through osmotic pumps to mimic SSM maintenance in humans." p. 1249; incorrectly stated 2ML2 pumps used; behavioral (home cage motor activity, sensory testing, contextual fear conditioning).

**P8673:** F. Leri, R. E. Sorge, E. Cummins, D. Woehrling, J. G. Pfaus and J. Stewart. High-dose methadone maintenance in rats: Effects on cocaine self-administration and behavioral side effects. *Neuropsychopharmacology* 2007;32(11):2290-2300

**ALZET Comments:** Methadone HCl; SC; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; good methods p. 2291; dependence; animal info (male, Sprague-Dawley, Long Evans).

## 10. Morphine [Back to top](#)

**Q7004:** S. Moon, S. Kang, H. Shin, T. Yayeh, B. Sur and S. Oh. Morphine Dependence is Attenuated by Treatment of 3,4,5-Trimethoxy Cinnamic Acid in Mice and Rats. *Neurochem Res* 2019;





**ALZET Comments:** Morphine; Trimethoxy cinnamic acid, 3, 4, 5-; Saline; CSF/CNS (lateral ventricle); Rat; 2ML1; 7 days; Dose (26 nmol/10µ l/hr); Controls received mp w/ vehicle; animal info (male Sprague–Dawley rats, 220–240 g)); behavioral testing (Conditioned Place Preference Test); dependence;

**Q6131:** A. Kliewer, F. Schmiedel, S. Sianati, A. Bailey, J. T. Bateman, E. S. Levitt, J. T. Williams, M. J. Christie and S. Schulz. Phosphorylation-deficient G-protein-biased mu-opioid receptors improve analgesia and diminish tolerance but worsen opioid side effects. *Nat Commun* 2019;10(1):367

**ALZET Comments:** Fentanyl citrate; morphine sulphate salt pentahydrate; PBS; water, sterile; SC; Mice (transgenic); 1007D; 7 days; Dose (Fentanyl (2mg/kg/day); Morphine (17 mg/kg/day)); animal info (knock-in mice with 11S/T-A mutations (Oprm1tm3.1Shlz, MGI:6117673, 11S/T-A)); behavioral testing (hot plate test; open field locomotion test); dependence; "...we used subcutaneously implanted osmotic pumps to deliver opioids at a constant rate. This approach is a powerful means of assessing both tolerance and dependence in rodents" (p.5).

**Q6963:** D. H. Malin, M. M. Henceroth, J. Elayoubi, J. R. Campbell, A. Anderson, P. Goyarzu, J. Izygon, C. A. Madison, C. P. Ward and E. S. Burstein. A subtype-specific neuropeptide FF receptor antagonist attenuates morphine and nicotine withdrawal syndrome in the rat. *Neurosci Lett* 2018;684(98-103

**ALZET Comments:** Morphine sulfate, Nicotine bitartrate; Saline, isotonic; SC; Rat; 2ML1; 7 days; Dose (morphine at 0.3 and 0.6 mg/kg/hr, nicotine at 9 mg/kg/day); Controls received mp w/ vehicle; animal info (male Sprague-Dawley rats averaging 234 g); dependence;

**Q7153:** T. Lilius, E. Kangas, M. Niemi, P. Rauhala and E. Kalso. Ketamine and norketamine attenuate oxycodone tolerance markedly less than that of morphine: from behaviour to drug availability. *Br J Anaesth* 2018;120(4):818-826

**ALZET Comments:** Morphine, oxycodone; Sterile water; SC; Rats; 2ML1; 7 days; Dose (oxycodone 3.6 mg day<sup>-1</sup>); (morphine 40 mg ml<sup>-1</sup>); animal info (Male Sprague–Dawley rats); behavioral testing (tail-flick, hot-plate tests); Toxicology (tolerance);

**Q3539:** Y. C. Cheng, R. Y. Tsai, Y. T. Sung, I. J. Chen, T. Y. Tu, Y. Y. Mao and C. S. Wong. Melatonin regulation of transcription in the reversal of morphine tolerance: Microarray analysis of differential gene expression. *Int J Mol Med* 2018;

**ALZET Comments:** Morphine; Saline; CSF/CNS (intrathecal); Rat; 7 days; Dose (15 µg/h); Controls received mp w/ vehicle; animal info (27 Male Wistar rats (350 400 g), each rat (with 12 weeks of age)); neurodegenerative ();

**Q7171:** S. Arttamangkul, D. A. Heinz, J. R. Bunzow, X. Song and J. T. Williams. Cellular tolerance at the micro-opioid receptor is phosphorylation dependent. *Elife* 2018;7(**ALZET Comments:** Morphine sulfate; Water; SC; Rat; 2ML1; 7 days; Dose (80mg/kg/day); animal info (5-6 Weeks); tolerance;

**Q6540:** S. L. Withey, R. Hill, A. Lyndon, W. L. Dewey, E. Kelly and G. Henderson. Effect of Tamoxifen and Brain-Penetrant Protein Kinase C and c-Jun N-Terminal Kinase Inhibitors on Tolerance to Opioid-Induced Respiratory Depression in Mice. *J Pharmacol Exp Ther* 2017;361(1):51-59

**ALZET Comments:** Morphine; buprenorphine; methadone; Saline; SC; Mice; 6 days; Dose (45 mg/kg/d; 5 mg/kg/day; 60 mg/kg/day); Controls received mp w/ vehicle; animal info (Male CD-1 mice, approximately 30g); comparison of morphine alkaloid pellet vs mp;

**Q5887:** A. Rivera, B. Gago, D. Suarez-Boomgaard, T. Yoshitake, R. Roales-Bujan, A. Valderrama-Carvajal, A. Bilbao, J. Medina-Luque, Z. Diaz-Cabiale, K. V. Craenenbroeck, D. O. Borroto-Escuela, J. Kehr, F. Rodriguez de Fonseca, L. Santin, A. de la Calle and K. Fuxe. Dopamine D4 receptor stimulation prevents nigrostriatal dopamine pathway activation by morphine: relevance for drug addiction. *Addict Biol* 2017;22(5):1232-1245

**ALZET Comments:** Morphine; PD168,077; DMSO; NaCl; SC; Rat; 2ML1; 6 days; animal info (male, Sprague Dawley, 225-250g); 2% DMSO used; behavioral testing (withdrawal behavior; tail-flick test); dependence; Dose (Morphine 20 mg/kg/day; PD168,077 1 or 3 mg/kg/day);

**Q6065:** V. D. McLane, I. Bergquist, J. Cormier, D. J. Barlow, K. L. Houseknecht, E. J. Bilsky and L. Cao. Long-term morphine delivery via slow release morphine pellets or osmotic pumps: Plasma concentration, analgesia, and naloxone-precipitated withdrawal. *Life Sci* 2017;185(1-7



**ALZET Comments:** Morphine; Saline; SC; Mice; 2001; 7 days; Dose (64 mg/mL); animal info (8 week old C57BL/6NCr mice); comparison of pellets vs mp; Resultant plasma level (Fig. 1, Pg 3); dependence;.

**Q6212:** A. Lyndon, S. Audrey, C. Wells, E. S. Burnell, S. Ingle, R. Hill, M. Hickman and G. Henderson. Risk to heroin users of polydrug use of pregabalin or gabapentin. *Addiction* 2017;112(9):1580-1589

**ALZET Comments:** Morphine; SC; Mice; 6 days; Dose (45 mg/kg/day); animal info (Male CD-1 mice weighing 30 g); comparison of sc pellet vs mp; tolerance;.

**Q6304:** A. Kaneguchi, J. Ozawa, H. Moriyama and K. Yamaoka. Nociception contributes to the formation of myogenic contracture in the early phase of adjuvant-induced arthritis in a rat knee. *J Orthop Res* 2017;35(7):1404-1413

**ALZET Comments:** Morphine hydrochloride; SC; Rat; 2ML1; 5 days; Dose (41–48 mg/kg/day); animal info (8-week-old male Wistar rats weighing 200–240 g); Therapeutic indication (Knee arthritis);.

**Q5745:** K. Gong and L. Jasmin. Sustained Morphine Administration Induces TRPM8-Dependent Cold Hyperalgesia. *J Pain* 2017;18(2):212-221

**ALZET Comments:** Morphine; Saline; SC; Rat, Mice; 2ML1, 1007D; 7 days; Controls received mp w/ vehicle; animal info (180-200 g) ; functionality of mp verified by residual volume; behavioral testing (Cold plate assay); Therapeutic indication (Analgesic, Opioid); Dose (15 mg/mL);.

**Q5812:** M. Flinspach, Q. Xu, A. D. Piekarz, R. Fellows, R. Hagan, A. Gibbs, Y. Liu, R. A. Neff, J. Freedman, W. A. Eckert, M. Zhou, R. Bonesteel, M. W. Pennington, K. A. Eddinger, T. L. Yaksh, M. Hunter, R. V. Swanson and A. D. Wickenden. Insensitivity to pain induced by a potent selective closed-state Nav1.7 inhibitor. *Sci Rep* 2017;7(39662)

**ALZET Comments:** JNJ63955918, Morphine; Saline; CSF/CNS (intrathecal); Rat; 2002, 2001; 14 days, 2 weeks; Controls received mp w/ vehicle; animal info (250-300g) behavioral testing (Hargreaves test, hotplate test, tail-flick test, formalin flinching); JNJ63955918 is a tarantula venom-derived peptide (a potent, highly selective, closed-state Nav1.7 blocking peptide) ; Therapeutic indication (Pain, analgesia, electrophysiology);.

**Q5511:** J. Zhao, H. Wang, T. Song, Y. Yang, K. Gu, P. Ma, Z. Zhang, L. Shen, J. Liu and W. Wang. Thalidomide Promotes Morphine Efficacy and Prevents Morphine-Induced Tolerance in Rats with Diabetic Neuropathy. *Neurochem Res* 2016;41(12):3171-3180

**ALZET Comments:** Morphine; Saline; SC; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 180-200g);behavioral testing (von Frey testing; hind paw withdrawal); dependence; Dose (2 mg/kg/day);.

**Q5105:** J. E. Zadina, M. R. Nilges, J. Morgenweck, X. Zhang, L. Hackler and M. B. Fasold. 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);.

**Q5502:** T. Yayeh, K. Yun, S. Jang and S. Oh. Morphine dependence is attenuated by red ginseng extract and ginsenosides Rh2, Rg3, and compound K. *J Ginseng Res* 2016;40(4):445-452

**ALZET Comments:** Ginsenoside, Rg3; ginsenoside, Rh; compound K; morphine; Saline; CSF/CNS; Rat; 2ML1; 7 days; Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 220-240g); behavioral testing (conditioned place preference; escaping behavior); dependence; cyanoacrylate wound closure; Dose (morphine 26nmol/10ul/hr, ginsenoside 10 ug/ul/h); Brain coordinates (L: 1.3 mm; AeP: e0.5 mm; and DeV: e4.3 mm);.

**Q5076:** R. Y. Tsai, J. C. Wang, K. Y. Chou, C. S. Wong and C. H. Cherng. Resveratrol reverses morphine-induced neuroinflammation in morphine-tolerant rats by reversal HDAC1 expression. *J Formos Med Assoc* 2016;115(6):445-54

**ALZET Comments:** Morphine; CSF/CNS (intrathecal); Rat; 120 hours; Controls received mp w/ saline; animal info (male, Wistar); behavioral testing (tail-flick); Dose (15 ug/h);.



**Q5165:** P. Nardelli, J. A. Vincent, R. Powers, T. C. Cope and M. M. Rich. Reduced motor neuron excitability is an important contributor to weakness in a rat model of sepsis. *Exp Neurol* 2016;282(1-8)

**ALZET Comments:** Oxymorphone; IP; Rat; 5 days; post op. care (buprenorphine SC 0.12 mg/kg; 5 ml SC saline; Baytril SC 10 mg/kg Q12H); used 2ML size; pumps used for continuous pain relief in rat sepsis model; Dose (30 ug/kg/h);.

**Q6574:** J. S. Kim, C. H. Brown and G. M. Anderson. Anti-opioid Effects of RFRP-3 on Magnocellular Neuron Activity in Morphine-naïve and Morphinetreated Female Rats. *Endocrinology* 2016;157(10):4003-4011

**ALZET Comments:** Morphine; Saline; Rat; 2002; 10.1210/en.2016-1374; Dose (10 mg/kg/day); Controls received mp w/ vehicle; animal info (Female adult freely-cycling Sprague-Dawley rats wehing ~280 g); dependence.

**Q5359:** K. Gong, A. Bhargava and L. Jasmin. GluN2B N-methyl-D-aspartate receptor and excitatory amino acid transporter 3 are upregulated in primary sensory neurons after 7 days of morphine administration in rats: implication for opiate-induced hyperalgesia. *Pain* 2016;157(1):147-58

**ALZET Comments:** Morphine; Ro 25-6981; Saline; SC; Rat; 2ML1; 1 week; Controls received mp w/ vehicle; animal info (Male Sprague-dawley rats, 220-250 g); functionality of mp verified by behavioral tests; good methods (pg. 148); post op. care (opiate administration using pumps); behavioral testing (Hargreaves plantar test); Dependence/tolerance induced; Opiate use; Dose ( 15 mg/ml Morphine, 5 mg/kg Ro 25-6981);.

**Q5804:** K. A. Eddinger, E. S. Rondon, V. I. Shubayev, M. R. Grafe, M. Scadeng, K. R. Hildebrand, L. M. Page, S. A. Malkmus, J. J. Steinauer and T. L. Yaksh. Intrathecal Catheterization and Drug Delivery in Guinea Pigs: A Small-animal Model for Morphine-evoked Granuloma Formation. *Anesthesiology* 2016;125(2):378-94

**ALZET Comments:** Morphine; Saline; SC; Guinea pig; 2002; 14 days, 2 weeks; Controls received mp w/ vehicle; good methods (catheter construction pg. 379); stress/adverse reaction: Note that these animals were receiving infusion through in-house/Non-Alzet catheters (see pg. 385 Therapeutic indication (Granuloma); Dose (0.25, 2.5, 8, or 25 mg/ml);.

## 11. Nalbuphine [Back to top](#)

**P8971:** S. Jang, H. Kim, D. Kim, M. W. Jeong, T. Ma, S. Kim, I. K. Ho and S. Oh. Attenuation of morphine tolerance and withdrawal syndrome by coadministration of nalbuphine. *ARCHIVES OF PHARMACAL RESEARCH* 2006;29(8):677-684

**ALZET Comments:** Morphine chloride; nalbuphine HCl; Saline; CSF/CNS; Rat; 2001; 3 days; Controls received mp w/ vehicle; comparison of IP injections vs. mp; tolerance; dependence; animal info (male, Sprague Dawley, 220-240 g).

**P0588:** W. K. Schmidt, S. W. Tam, G. S. Sholtzberger, D. H. Smith Jr, R. Clark and V. G. Vernier. Nalbuphine. *Drug Alcohol Depend* 1985;14(339-362)

**ALZET Comments:** Ethylketocyclazocine; Heroin; Meperidine; Oxymorphone; Pentazocine; Propoxyphene; Bremazocine; Buprenorphine; Butorphanol; Methadone; Morphine; Nalbuphine; U-50,488H; SC; mice; 3 days; comparison of sc morphine pellets vs. mp infusion; comparison of agents effects; controls received unspecified placebo infusion.

## 12. Normorphine [Back to top](#)

**P0170:** R. Schulz, M. Wuster, P. Rubini and A. Herz. Functional opiate receptors in the guinea-pig ileum: their differentiation by means of selective tolerance development. *J. Pharmacol. Exp. Ther* 1981;219(2):547-550

**ALZET Comments:** DsThr; Enkephalin agonist DADL; Fentanyl; FK-33824; MR-2034; MRZ; Normorphine; Water; SC; Guinea pig; 2001; 6 days; peptides.

**P0173:** R. Schulz and M. Wuster. Are there sybtypes (isoreceptors) of multiple opiate receptors in the mouse vas deferens. *Eur. J. Pharmacol* 1981;76(61-66)



**ALZET Comments:** Endorphin, a-neo-; DsThr; Dynorphin; Enkephalin analog DADLE; FK-33824; MR-2034; MRZ; Normorphine; Sufentanil; Water; SC; mice; 2001; 6 days; peptides; MRZ is 5,9-dimethyl,2'S-5,9-dimethyl-2'-hydroxy-2-(2-methoxy-propyl)-6,7-benzomorphan, a kappa opioid agonist.

### 13. Oxymorphone [Back to top](#)

**P9615:** K. R. Novak, P. Nardelli, T. C. Cope, G. Filatov, J. D. Glass, J. Khan and M. M. Rich. Inactivation of sodium channels underlies reversible neuropathy during critical illness in rats. *Journal of Clinical Investigation* 2009;119(5):1150-1158

**ALZET Comments:** Oxymorphone; Intramuscular (abdominal); Rat; Post op. care (buprenorphine); animal info (female, Wistar, 250-300g).

**P4892:** M. B. Gillingham, M. D. Clark, E. M. Dahly, L. A. Krugner-Higby and D. M. Ney. A comparison of two opioid analgesics for relief of visceral pain induced by intestinal resection in rats. *CONTEMPORARY TOPICS IN LABORATORY ANIMAL SCIENCE* 2001;40(1):21-26

**ALZET Comments:** Oxymorphone HCl; IP; Rat; 32 hours; functionality of mp verified by pain relief indicators - posture, physical condition, behavior; comparison of iv infusions vs mp; compared bolus iv infusion, continuous iv infusion, osmotic pump.

**P0588:** W. K. Schmidt, S. W. Tam, G. S. Sholtzberger, D. H. Smith Jr, R. Clark and V. G. Vernier. Nalbuphine. *Drug Alcohol Depend* 1985;14(339-362)

**ALZET Comments:** Ethylketocyclazocine; Heroin; Meperidine; Oxymorphone; Pentazocine; Propoxyphene; Bremazocine; Buprenorphine; Butorphanol; Methadone; Morphine; Nalbuphine; U-50,488H; SC; mice; 3 days; comparison of sc morphine pellets vs. mp infusion; comparison of agents effects; controls received unspecified placebo infusion.

### 14. Pentazocine [Back to top](#)

**P3459:** R. Bergeron, C. de Montigny and G. Debonnel. Effect of short-term and long-term treatments with sigma ligands on the N-methyl-D-aspartate response in the CA(3) region of the rat dorsal hippocampus. *Br. J. Pharmacol* 1997;120(1351-1359)

**ALZET Comments:** Haloperidol; JO-1784; Pentazocine; DTG; SC; Rat; 2-21 days; controls received mp w/saline; DTG is di(2-tolyl)guanidin.

**P1911:** A. D. Weissman and E. B. De Souza. Chronic treatment of rats with the specific sigma ligand D-pentazocine fails to modulate dopamine D2 and sigma binding in brain. *Eur. J. Pharmacol* 1991;195(163-165)

**ALZET Comments:** Pentazocine, d-; Saline; SC; Rat; 2ML4; 4 weeks; no comment posted.

**P0588:** W. K. Schmidt, S. W. Tam, G. S. Sholtzberger, D. H. Smith Jr, R. Clark and V. G. Vernier. Nalbuphine. *Drug Alcohol Depend* 1985;14(339-362)

**ALZET Comments:** Ethylketocyclazocine; Heroin; Meperidine; Oxymorphone; Pentazocine; Propoxyphene; Bremazocine; Buprenorphine; Butorphanol; Methadone; Morphine; Nalbuphine; U-50,488H; SC; mice; 3 days; comparison of sc morphine pellets vs. mp infusion; comparison of agents effects; controls received unspecified placebo infusion.

### 15. Propoxyphene [Back to top](#)

**P0588:** W. K. Schmidt, S. W. Tam, G. S. Sholtzberger, D. H. Smith Jr, R. Clark and V. G. Vernier. Nalbuphine. *Drug Alcohol Depend* 1985;14(339-362)

**ALZET Comments:** Ethylketocyclazocine; Heroin; Meperidine; Oxymorphone; Pentazocine; Propoxyphene; Bremazocine; Buprenorphine; Butorphanol; Methadone; Morphine; Nalbuphine; U-50,488H; SC; mice; 3 days; comparison of sc morphine pellets vs. mp infusion; comparison of agents effects; controls received unspecified placebo infusion.



16. Sufentanil [Back to top](#)

**P4727:** A. Diaz, A. Pazos, J. Florez and M. A. Hurlle. Autoradiographic mapping of m-opioid receptors during opiate tolerance and supersensitivity in the rat central nervous system. *Naunyn-Schmiedeberg's Arch Pharmacol* 2000;362(101-109)

**ALZET Comments:** Sufentanil citrate; Nimodipine;; Saline; Ethanol; Propylene glycol; Water;; SC;; Rat;; 2001;; 7 days;; Controls received mp w/ vehicle; tolerance; Group 1 received sufentanil, Group 2 received sufentanil & nimodipine, Group 3 received nimodipine, Group 4 received vehicle; Nimodipine is a Ca channel blocker; sufentanil was diluted in saline; nimodipine was diluted in 10% ethanol / 20% propylene glycol / 70% water;.

**P4728:** A. Diaz, J. Florez, A. Pazos and M. A. Hurlle. Opioid tolerance and supersensitivity induce regional changes in the autoradiographic density of dihydropyridine-sensitive calcium channels in the rat central nervous system. *Pain* 2000;86(227-235)

**ALZET Comments:** Sufentanil citrate; Nimodipine;; Saline; Ethanol; Propylene glycol; Water;; SC;; Rat;; 2001;; 7 days;; Controls received mp w/ vehicle; tolerance; Group 1 received vehicle alone, Group 2 received chronic sufentanil, Group 3 received sufentanil & nimodipine, Group 4 received nimodipine alone; Nimodipine is a CA<sup>2+</sup> antagonist opioid; sufentanil citrate was diluted in saline; nimodipine was diluted in 10% ethanol / 20% propylene glycol / 70% water.

**P3361:** J. V. Garaulet, M. L. Laorden and M. V. Milanes. Effect of chronic administration of dihydropyridine Ca<sup>2+</sup> channel ligands on sufentanil-induced tolerance to u- and k- opioid agonists in the guinea pig ileum myenteric plexus. *Regul. Pept* 1996;63(1-8)

**ALZET Comments:** Sufentanil; Nimodipine; Bay K 8644; Saline; SC; Guinea pig; 2001; 7 days; controls received mp w/saline; tolerance.

**R0117:** C. W. Stevens. Perspectives on opioid tolerance from basic research: behavioural studies after spinal administration in rodents. *Cancer Surveys* 1994;21(25-47)

**ALZET Comments:** Morphine; DADLE; ST-91; Sufentanil; DAMGO; CSF/CNS (intrathecal); Rat; 7 days; controls received mp w/ saline; cancer; peptides; tolerance; comprehensive review of mp infusion methods using y-catheter.

**P4187:** J. V. Garaulet, M. L. Laorden and M. V. Milanes. Cross-tolerance between mu- and kappa-opioid agonists in the guinea pig ileum myenteric plexus. *J. Pharmacol. Exp. Ther* 1994;269(3):993-999

**ALZET Comments:** Sufentanil; Saline, sterile; SC; Guinea pig; 2001; 7 days; controls received mp w/vehicle; tolerance.

**R0132:** T. L. Yaksh. Tolerance: factors involved in changes in the dose-effect relationship with chronic drug exposure. In 'Towards a new pharmacotherapy of pain', A. I. Basbaum & J. -M. Besson (eds), John Wiley & Sons Ltd 1991;

**ALZET Comments:** Morphine; Sufentanil; Enkephalin; Saline; IV; CSF/CNS (intrathecal); CSF/CNS; Rat; 7 days; controls received mp w/vehicle; dose-response (p. 163); tolerance; pain; reference of mp pump study on pp. 162-164.

**P2081:** M. Sosnowski and T. L. Yaksh. Differential cross-tolerance between intrathecal morphine and sufentanil in the rat. *Anesthesiology* 1990;73(1141-1147)

**ALZET Comments:** Morphine sulfate; Sufentanil citrate; Saline; CSF/CNS (intrathecal); Rat; 2001; 7 days; dose-response; tolerance; PE10 heat fused to PE60; externalized loop of catheter permitted cessation of infusion without pump removal.

Non-Narcotic

17. Acetylsalicylic Acid [Back to top](#)

**Q0421:** C. Rivat, C. Becker, A. Blugeot, B. Zeau, A. Mauborgne, M. Pohl and J. J. Benoliel. Chronic stress induces transient spinal neuroinflammation, triggering sensory hypersensitivity and long-lasting anxiety-induced hyperalgesia. *Pain* 2010;150(2):358-368

**ALZET Comments:** CI-988; chlordiazepoxide; Acetylsalicylic acid; DMSO; saline; SC; CSF/CNS (intrathecal); Rat; 2ML1; 2001; 2002; 14 days; Controls received mp w/ vehicle; animal info (Male, Sprague-Dawley, 300-325 g, 8 wks old; ALZET intrathecal catheter used (0007740); behavioral testing (elevated plus-maze).



**P8555:** A. Adamek, K. Hu, B. Bayer, H. Wagner, G. Ertl, J. Bauersachs and S. Frantz. High dose aspirin and left ventricular remodeling after myocardial infarction. *Basic Research In Cardiology* 2007;102(4):334-340

**ALZET Comments:** Acetylsalicylic acid, lysine; Saline; SC; Mice; 2002; 4 weeks; Controls received mp w/ placebo; functionality of mp verified by serum salicylate concentrations; pumps replaced after 2 weeks; cardiovascular; ischemia (cardiac); animal info (female, C57BL/6, 8-12 weeks old, 20-25 grams); MI induced by coronary artery ligation.

**P4829:** M. Yuan, N. Konstantopoulos, J. Lee, L. Hansen, Z.-W. Li, M. Karin and S. E. Shoelson. Reversal of obesity- and diet-induced insulin resistance with salicylates or targeted disruption of *Ikkb*. *Science* 2001;293(1673-1677)

**ALZET Comments:** Acetylsalicylic acid; salicylate, sodium; SC; Rat; mice; 2002; 2ML2; 3-4 weeks; Controls received mp w/ vehicle; 2ML2 used in rats, 2002 used in mice; acetylsalicylic acid also called aspirin: dose was 120 mg/kg/day; diabetes (type II).

**P0455:** T. Oshima, E. R. McCluskey, A. Honda and P. Needleman. Pharmacological manipulation of canine cyclooxygenase and thromboxane synthetase in vivo: differential renal and platelet recovery rates. *J. Pharmacol. Exp. Ther* 1984;229(2):598-602

**ALZET Comments:** Acetylsalicylic acid; DMSO; Saline; IV (superficial cervical vein); dog; 2ML1; 3 days; pumps primed for 4 hrs. before implant; used prefilled catheter in vein; greater solubility of ASA in DMSO allowed greater concentration in smaller total volume.

#### 18. Aminopyrine [Back to top](#)

**P3395:** S. K. Kuwahara, T. J. Shinn, B. D. Schreider, M. L. Phan and A. N. Kotake. Aminopyrine infusion breath test for the determination of changes in P450 metabolism in vivo. *Xenobiotica* 1995;25(9):973-980

**ALZET Comments:** Aminopyrine; Formate, sodium; radio-isotopes; <sup>14</sup>C tracer; water, acidified; NaOH; SC; Rat; 2001; no duration posted; stability of [N-dimethyl-<sup>14</sup>C] aminopyrine verified by radiochromatographic analysis- no decomposition observed.

**P1268:** S. Azri and K. W. Renton. Depression of murine hepatic mixed function oxidase during infection with listeria monocytogenes. *J. Pharmacol. Exp. Ther* 1987;234(3):1089-1093

**ALZET Comments:** Aminopyrine; Radio-isotopes; <sup>14</sup>C tracer; Saline; SC; mice; 2002; 7 days; animals infected with listeria monocytogenes.

#### 19. Antipyrine [Back to top](#)

**R0077:** N. Ray and F. Theeuwes. Implantable osmotically powered drug delivery systems. In 'Drug Delivery Systems: Fundamentals and Techniques,' P. Johnson and J. G. Lloyd-Jones (eds. ), Ellis Horwood Ltd. , Chichester, England and VCH Verlagsgesellschaft mbH, Weinheim, Federal Republic of Germany 1987;Ch. 7):120-138

**ALZET Comments:** Antipyrine; bleomycin; dopamine HCl; melatonin; methotrexate, sodium; nicotine; prednisolone; radio-isotopes; valproic acid; <sup>14</sup>C tracer; <sup>3</sup>H tracer; IA; IP; SC; Mice, rabbit, Rat; no duration posted; ALZA-authored; synoptic review of mp; post op. care (antibiotic); comparison of sc injections vs. mp infusion; pulsed delivery.

**P0592:** S. L. Sendelbeck and J. Urquhart. Spatial distribution of dopamine, methotrexate and antipyrine during continuous intracerebral microperfusion. *Brain Research* 1985;328(251-258)

**ALZET Comments:** Antipyrine; Dopamine HCl; Methotrexate, sodium; Radio-isotopes; <sup>14</sup>C tracer; <sup>3</sup>H tracer; CSF, artificial; Sodium fluorescein; CSF/CNS (diencephalon); rabbit; 2001; 6 days; comparison of agents effects; mp primed in saline 16 hr. prior to implant; stability of labelled & unlabelled Dop. & MTX tested by paper chromat. after 7 days at 37C; brain tissue distribution;.

#### 20. Indomethacin [Back to top](#)

**Q4542:** Y. R. Na, Y. N. Yoon, D. Son, D. Jung, G. J. Gu, S. H. Seok and S. H. Seok. Consistent Inhibition of Cyclooxygenase Drives Macrophages towards the Inflammatory Phenotype. *PLoS One* 2015;10(U1730-U1742)



**ALZET Comments:** NA-398; SC-560; indomethacin; DMSO; SC; Mice; 30 days; Controls received mp w/ vehicle; animal info (female, BALB/c); immunology;.

**P4819:** M. C. Babin, K. Ricketts, J. P. Skvorak, M. Gazaway, L. W. Mitcheltree and R. P. Casillas. Systemic administration of candidate antivesicants to protect against topically applied suitor mustard in the mouse ear vesicant model (MEVM ). Journal of Applied Toxicology 2000;20(S141-S144

**ALZET Comments:** Hydrocortisone; indomethacin; olvanil; PEG 200; SC; mice; 2 days; Controls received mp w/ vehicle; toxicology.

**P4475:** M. G. Zlatnik, I. Buhimschi, K. Chwalisz, Q.-P. Liao, G. R. Saade and R. E. Garfield. The effect of indomethacin and prostacyclin agonists on blood pressure in a rat model of preeclampsia. Am. J. Obstet. Gynecol 1999;180(5):1191-1195

**ALZET Comments:** Iloprost; Cicaprost; L-NAME; Indomethacin; Saline;; SC;; Rat (pregnant);; 2ML2;; 2 weeks;; controls received mp w/vehicle; comparison of SC injections vs. mp; cardiovascular; L-NAME is a synthase inhibitor;.

**P3986:** P. K. Henke, T. M. Bergamini, A. L. Watson, K. R. Brittan, D. W. Powell and J. C. Peyton. Bacterial products primarily mediate fibroblast inhibition in biomaterial infection. J. Surg. Res 1998;74(17-22

**ALZET Comments:** Antibody, anti-interferon gamma; Antibody, indomethacin; Antibody, anti-TNFa; Antibody, interleukin 1 alpha; PBS, sterile; ETHANOL; Indomethacin; SC; mice; 1007D; 7 days; immunology; pump implanted next to Dacron graft; peptides.

**P3918:** P. K. Henke, T. M. Bergamini, K. R. Brittan and H. C. Polk Jr. Prostaglandin E2 modulates monocyte MHC-II (Ia) suppression in biomaterial infection. J. Surg. Res 1997;69(372-378

**ALZET Comments:** Indomethacin; Antibody, anti-IL-1a; Antibody, anti-TNFa; PBS; ETHANOL; SC; Mice; 7 days; Controls received mp w/ vehicle; immunology.

**P4207:** K. Shimoda, M. Nomura and M. Kato. Effect of antioxidants, anti-inflammatory drugs, and histamine antagonists on Sparfloxacin-induced phototoxicity in mice. Fundam. Appl. Toxicol 1996;31(133-140

**ALZET Comments:** Catalase; Dimethyl sulfoxide; Dexamethasone; Indomethacin; Pyrilamine maleate; AA-861; Cimetidine; Phenidone; Ethanol; Saline; SC; mice; 1007D; 72 hours; all agents infused concomitantly in the same pump; preliminary study conducted to test solubility and toxicity for 5 days; enzyme inhibitors; toxicology.

**P3614:** M. Fernandez, J. C. Garcia-Pagan, M. Casadevall, M. I. Mourelle, J. M. Pique, J. Bosch and J. Rodes. Acute and chronic cyclooxygenase blockade in portal-hypertensive rats: influence on nitric oxide biosynthesis. Gastroenterol 1996;110(1529-1535

**ALZET Comments:** Indomethacin; Sodium carbonate; SC; Rat; 2ML2; 7 days; sonication used to suspend indomethacin.

**P2852:** T. Sakamoto, D. Soriano, J. Nassaralla, T. L. Murphy, A. Oganessian, C. Spec, D. R. Hinton and S. J. Ryan. Effect of intravitreal administration of indomethacin on experimental subretinal neovascularization in the subhuman primate. Arch Ophthalmol 1995;113(222-226

**ALZET Comments:** Indomethacin; GBR buffer; Cyclodextrin, B-; Eye (vitreous); monkey; 2ML2; 14 days; control eyes received mp with vehicles; enzyme inhibitor; indomethacin is a cyclooxygenase (COX) inhibitor; detailed description of vitreal cannula implantation; empty pump implanted at time of cannula implantation to allow 1-month recovery period; beta-cyclodextrin used as a carrier molecule; some monkeys served both as control and drug treatment group (different treatment in each eye); a vitreous opacity appeared in some eyes during infusion but disappeared after the pump was disconnected.

## 21. Ketorolac [Back to top](#)

**P8822:** J. M. Scarlett, E. E. Jobst, P. J. Enriori, D. D. Bowie, A. K. Batra, W. F. Grant, M. A. Cowley and D. L. Marks. Regulation of central melanocortin signaling by interleukin-1beta. Endocrinology 2007;148(9):4217-4225

**ALZET Comments:** Ketorolac; Saline, sterile; SC; Mice; 1007D; 2 days; Controls received mp w/ vehicle; animal info (male, C57BL/6J, 4-5 wks old).



**P5091:** M. D. Southall, L. A. Bolyard and M. R. Vasko. Twenty-four hour exposure to prostaglandin downregulates prostanoid receptor binding but does not alter PGE(2)-mediated sensitization of rat sensory neurons. *Pain* 2002;96(285-296

**ALZET Comments:** Ketorolac tromethamine; Saline; CSF/CNS (intrathecal); Rat; 2001; 48 hours; controls received mp w/ vehicle; ketorolac is an NSAID sold as Toradol; cannula patency verified by saline injection.

**P4204:** J. V. Shufflebarger, J. Doyle, T. Roth, K. Maguire and D. M. Rothkopf. The effect of ketorolac on microvascular thrombosis in an experimental rabbit model. *Plast. Reconstr. Surg* 1996;98(140-145

**ALZET Comments:** Ketorolac; IV (jugular); rabbit; 2ML1; 7 days; controls received mp w/saline; functionality of mp verified by residual volume; comparison of i.m. injections vs. mp; ketorolac also called Toradol; NSAID.

## 22. Naproxen [Back to top](#)

**Q3710:** A. C. Rosa, A. Pini, L. Lucarini, C. Lanzi, E. Veglia, R. L. Thurmond, H. Stark, E. Masini and E. Masini. Prevention of Bleomycin-Induced Lung Inflammation and Fibrosis in Mice by Naproxen and JNJ7777120 Treatment. *Journal of Pharmacology and Experimental Therapeutics* 2014;351(308-316

**ALZET Comments:** JNJ7777120; naproxen; SC; Mice; 1004; Control animals received mp w/ vehicle; animal info (male, C57BL/6, ~2 mo old, 25-30 g); infusion rate listed as 0.11 ul/hr; JNJ7777120 also known as (1-[(5-chloro-1H-indol-2-yl)carbonyl]-4-methylpiperazine), is a selective H4R antagonist; one group received combination of JNJ7777120 and naproxen.

**P8571:** C. Baj-Rossi, T. Rezzonico Jost, A. Cavallini, F. Grassi, G. De Micheli and S. Carrara. Continuous monitoring of Naproxen by a cytochrome P450-based electrochemical sensor. *Biosens Bioelectron* 2014;53(283-7

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

**Q4700:** C. Baj-Rossi, T. R. Jost, A. Cavallini, F. Grassi, G. De Micheli and S. Carrara. Continuous monitoring of Naproxen by a cytochrome P450-based electrochemical sensor. *BIOSENSORS & BIOELECTRONICS* 2014;53(;):283-287

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

**P9697:** X. X. Wang, S. Budel, K. Baughman, G. Gould, K. H. Song and S. M. Strittmatter. Ibuprofen Enhances Recovery from Spinal Cord Injury by Limiting Tissue Loss and Stimulating Axonal Growth. *Journal of Neurotrauma* 2009;26(1):81-95

**ALZET Comments:** Ibuprofen; naproxen; PBS; SC; Rat; mice; 2004; 2ML4; 4 weeks; Controls received mp w/ vehicle; animal info (female, Sprague Dawley, 11-12 wks old, 250-270 g., female, C57BL/6, 8-9 wks old, 20 g.); spinal cord injury; behavioral testing (BBB locomotor scale, Basso mouse scale).

## 23. Sodium Salicylate [Back to top](#)

**P4829:** M. Yuan, N. Konstantopoulos, J. Lee, L. Hansen, Z.-W. Li, M. Karin and S. E. Shoelson. Reversal of obesity- and diet-induced insulin resistance with salicylates or targeted disruption of *Ikkb*. *Science* 2001;293(1673-1677

**ALZET Comments:** Acetylsalicylic acid; salicylate, sodium; SC; Rat; mice; 2002; 2ML2; 3-4 weeks; Controls received mp w/ vehicle; 2ML2 used in rats, 2002 used in mice; acetylsalicylic acid also called aspirin; dose was 120 mg/kg/day; diabetes (type II).

**P3550:** C. J. Gordon. Pharmacological analysis of diisopropyl fluorophosphate: effects on core temperature, heart rate, and motor activity in the unrestrained rat. *Pharmacol. Biochem. Behav* 1996;55(2):185-194

**ALZET Comments:** Scopolamine; Methyloscopolamine nitrate; Salicylate, sodium; SC; Rat; 2002; 10 days; temperatures were taken with radiotelemetry.

**P1664:** K. Bergman, E. Cekan, P. Slanina, J. Gabrielsson and K.-E. Hellenas. Effects of dietary sodium selenite supplementation on salicylate-induced embryo- and fetotoxicity in the rat. *Toxicology* 1990;61(135-146

**ALZET Comments:** Salicylate, sodium; Water; IV; Rat; 2ML1; no duration posted; teratology.





**24. Tramadol** [Back to top](#)

**P4849:** Y. C. Tsai and S. J. Won. Effects of tramadol on T lymphocyte proliferation and natural killer cell activity in rats with sciatic constriction injury. *Pain* 2001;92(63-69)

**ALZET Comments:** Tramadol; Saline; SC; Rat; 2ML1; 7 days; Controls received mp w/ vehicle; comparison of sc injections vs. mp; immunology; multiple pumps per animal (2) used in high-dose groups; nociception; tramadol is a centrally acting analgesic.

**P4947:** Y. C. Tsai, Y. H. Sung, P. J. Chang, F. C. Kang and K. S. Chu. Tramadol relieves thermal hyperalgesia in rats with chronic constriction injury of the sciatic nerve. *FUNDAMENTAL & CLINICAL PHARMACOLOGY* 2000;14(335-340)

**ALZET Comments:** Tramadol; Saline; SC; Rat; 2ML1; 7 days; controls received mp w/ vehicle; functionality of mp verified by paw withdrawal latency (analgesia index); dose-response (graph p. 337); comparison of sc injection vs. mp; analgesia.

**25. F13640** [Back to top](#)

**P8923:** K. Deseure, S. Breand and F. C. Colpaert. Curative-like analgesia in a neuropathic pain model: Parametric analysis of the dose and the duration of treatment with a high-efficacy 5-HT<sub>1A</sub> receptor agonist. *European Journal of Pharmacology* 2007;568(1-3):134-141

**ALZET Comments:** F13640; Acetate buffer; water, sterile; SC; Rat; 2ML1; 2ML2; 2ML4; 2, 4, 8 weeks; 1, 2, 4, 7 days; Controls received mp w/ vehicle; dose-response (fig. 2); long-term study; pumps replaced; half-life (p. 139) 2.5 hrs. in rat plasma; multiple pumps per animal (2); post op. care (Na ampicillin); animal info (male, Sprague Dawley, 220-240 g., intraorbital nerve ligation).

**P7681:** F. C. Colpaert, K. Deseure, L. Stinus and H. Adriaensen. High-efficacy 5-hydroxytryptamine 1A receptor activation counteracts opioid hyperalldynia and affective conditioning. *Journal of Pharmacology and Experimental Therapeutics* 2006;316(2):892-899

**ALZET Comments:** F13640; morphine, HCl; Saline; SC; Rat; 2ML2; 6 weeks; Controls received mp w/ vehicle; long-term study; pumps replaced every two weeks; multiple pumps per animal (2); animal info (male, Sprague-Dawley, 220-240 g); during pump replacement a new incision was made about 1 cm away from the previous incision.

**P6803:** F. C. Colpaert, W. P. Wu, J. X. Hao, I. Royer, F. Sautel, Z. Wiesenfeld-Hallin and X. J. Xu. High-efficacy 5-HT<sub>1A</sub> receptor activation causes a curative-like action on allodynia in rats with spinal cord injury. *European Journal of Pharmacology* 2004;497(1):29-33

**ALZET Comments:** F13640; SC; Rat; 2ML4; 56 days; Controls received mp w/ saline; functionality of mp verified by plasma levels; long-term study; pumps replaced at day 28; 5-HT<sub>1A</sub> receptor agonist; spinal cord injury; pain.

**P6234:** W. P. Wu, J. X. Hao, X. J. Xu, Z. Wiesenfeld-Hallin, W. Koek and F. C. Colpaert. The very-high-efficacy 5-HT<sub>1A</sub> receptor agonist, F 13640, preempts the development of allodynia-like behaviors in rats with spinal cord injury. *European Journal of Pharmacology* 2003;478(2-3):131-137

**ALZET Comments:** F13640; SC; Rat; 2ML4; 56 days; Controls received mp w/ saline; functionality of mp verified by F13640 plasma levels; long-term study; pumps replaced (after 28 days).

**P5716:** L. A. B. Slot, W. Koek, J. P. Tarayre and F. C. Colpaert. Tolerance and inverse tolerance to the hyperalgesic and analgesic actions, respectively, of the novel analgesic, F 13640. *European Journal of Pharmacology* 2003;466(3):271-279

**ALZET Comments:** F13640; Water, distilled; SC; Rat; 2ML2; 5 weeks; Controls received mp w/ saline; dose-response (Fig.2; p.275); pumps replaced every week, F13640 is a novel analgesic; serotonin receptor agonist; post op. care (the site of pump emplacement was massaged daily to avoid tissue adherence).

**P5902:** K. Deseure, W. Koek, H. Adriaensen and F. C. Colpaert. Continuous administration of the 5-hydroxytryptamine 1A agonist (3-ch loro-4-fluoro-phenyl)-[4-fluoro-4-[(5-methyl-pyridin-2-ylmethyl)-amino]-methyl]piperidin-1-yl]-methadone (F



13640) attenuates allodynia-like behavior in a rat model of trigeminal neuropathic pain. *Journal of Pharmacology and Experimental Therapeutics* 2003;306(2):505-514

**ALZET Comments:** F13640; F13714; morphine; baclofen; Saline; SC; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; Post Op. Care (aerosol bandage applied to protect against bacterial contamination); F13640 is a novel analgesic & 5-HT<sub>1A</sub> receptor agonist; behavioral study; F13640, F13714 & morphine were infused in one pump; baclofen infused in two pumps due to limited solubility.

**P6585:** F. C. Colpaert, J. P. Tarayre, W. Koek, P. J. Pauwels, L. Bardin, X. J. Xu, Z. Wiesenfeld-Hallin, C. Cosi, E. Carilla-Durand, M. B. Assie and B. Vacher. Large-amplitude 5-HT<sub>1A</sub> receptor activation: a new mechanism of profound, central analgesia. *Neuropharmacology* 2002;43(6):945-958

**ALZET Comments:** F13640; morphine HCL; imipramine HCL; ketamine HCL; gabapentin; Water, double distilled; SC; Rat; 2ML2; 14 days; Controls received mp w/ saline; dose-response (fig. 3); comparison of IP & SC injections vs. mp; tolerance; dependence; "Continuous F 13640 infusion uniquely produced profound analgesia in this model of severe, chronic pain." (p. 955).