



## References on the Administration of Benzodiazepines Using ALZET® Osmotic Pumps

### 1. Adinazolam

**P0433:** A. Turmel, *et al.* Sensitization of rat forebrain neurons to serotonin by adinazolam, an antidepressant triazolobenzodiazepine. *Eur. J. Pharmacol* 1984;99(241-244)

**ALZET Comments:** Adinazolam; Diazepam; Benzyl alcohol; Ethanol; Propylene glycol; Sodium benzoate; Water; IP; Rat; 2002; 5 and 14 days; comparison of adinazolam. iv injec vs. mp infusion; comparison of agents effects; adinazolam. used with water vehicle, Diaz. with combination vehicle.

### 2. Alprazolam

**Q5063:** N. Ito, *et al.* Contribution of protein binding, lipid partitioning, and asymmetrical transport to drug transfer into milk in mouse versus human. *Pharm Res* 2013;30(9):2410-22

**ALZET Comments:** acetaminophen, cephalothin sodium salt, clindamycin hydrochloride, disopyramide phosphate salt, labetalol hydrochloride, nitrofurantoin +-propranolol hydrochloride, terbutaline hemisulfate salt, verapamil hydrochloride, Acyclovir, alprazolam, atenolol, anhydrous caffeine, cefotaxime sodium salt, cephapirin sodium salt, diltiazem hydrochloride, metronidazole, nitrazepam, prednisolone, 6-propyl-2-thiouracil, trazadone hydrochloride, chloramphenicol, cimetidine, theophylline, fluconazole, metoprolol, mirtazapine, praziquantel, quetiapine fumarate, triprolidine hydrochloride, metformin, moclobemide.; DMSO; water; IP; mice; 1003D; animal info: lactating mice, postnatal age of 14 days; functionality of mp verified by measurement of drug concentration in milk and plasma; mp were used to infuse study lactational drug transfer.

**P3498:** V. A.-M. I. Tanay, *et al.* Chronic administration of antipanic drugs alters rat brainstem GABA-A receptor subunit mRNA levels. *Neuropharmacology* 1996;35(9/10):1475-1482

**ALZET Comments:** Phenelzine; alprazolam; imipramine; buspirone; Water, sterile; DMSO; propylene glycol; SC; Rat; 21 days; Antidepressant; controls received mp w/ vehicle; pumps were turned in subcutaneous pocket to avoid fibrous tissue outgrowth.

**P3673:** J. J. Byrnes, *et al.* Chronic benzodiazepine administration. *Psychopharmacology* 1993;111(91-95)

**ALZET Comments:** Alprazolam; Lorazepam; PEG 400; SC; mice; 2001; 2002; 7, 8, or 14 days; controls received vehicle; tolerance.

**P2332:** G. B. Kaplan, *et al.* Effects of benzodiazepine administration on A1 adenosine receptor binding in-vivo and ex-vivo. *J. Pharm. Pharmacol* 1992;44(700-703)

**ALZET Comments:** Alprazolam; Lorazepam; PEG 400; IP; mice; 2001; 6 days; controls received mp w/ vehicle.

**P3033:** J.-L. Moreau, *et al.* Physical dependence induced in DBA/2J mice by benzodiazepine receptor full agonists, but not by the partial agonist Ro 16-6028. *Eur. J. Pharmacol* 1990;190(269-273)

**ALZET Comments:** Triazolam; Alprazolam; Diazepam; Propylene glycol; SC; mice; 2001; 7 days; controls received mp with vehicle; functionality of mp verified by receptor binding study; comparison of oral alprazolam vs. mp; ". . .the use of implantable minipumps. . .permitted. . .development of behavioral tolerance associated with downregulation of benzodiazepine receptor binding and GABA receptor function. . ."; dependence.

**P1779:** L. G. Miller, *et al.* Chronic benzodiazepine administration. IV. Rapid development of tolerance and receptor downregulation associated with alprazolam administration. *Biochem. Pharmacol* 1989;38(21):3773-3777

**ALZET Comments:** Alprazolam; PEG 400; SC; mice; 2001; 2002; 14 days; functionality of mp verified by measuring plasma levels; tolerance.



**P1396:** J. Bell, *et al.* Increased central nonadrenergic activity during benzodiazepine withdrawal: an electrophysiological study. *Neuropharmacology* 1988;27(11):1187-1190

**ALZET Comments:** Alprazolam; Lorazepam; Ethanol; Propylene glycol; Saline; SC; Rat; 2ML2; 12 days; no comment posted.

### 3. Chlordiazepoxide

**Q5755:** C. Brouillard, *et al.* Long-lasting bradypnea induced by repeated social defeat. *Am J Physiol Regul Integr Comp Physiol* 2016;311(2):R352-64

**ALZET Comments:** Chlordiazepoxide; Saline; SC; Rat; 2ML1; 5 days; Controls received mp w/ vehicle; animal info (weight: 290-310g); behavioral testing (Social defeat); chlordiazepoxide is a benzodiazepine receptor agonist; Days infused (D5 – D+10) (Housing: individual cages post. Op.); Therapeutic indication (Anxiety); Dose (10 mg/kg\*day);

**Q2541:** C. Sevoz-Couche, *et al.* Involvement of the dorsomedial hypothalamus and the nucleus tractus solitarii in chronic cardiovascular changes associated with anxiety in rats. *JOURNAL OF PHYSIOLOGY-LONDON* 2013;591(7):1871-1887

**ALZET Comments:** Chlordiazepoxide; SC; Rat; 2ML1; 6 days; Control animals received mp w/ vehicle; animal info (Sprague Dawley, male, 250-300 g).

**R0297:** A. de Mooij-van Malsen, *et al.* Cross-species behavioural genetics: A starting point for unravelling the neurobiology of human psychiatric disorders. *PROGRESS IN NEURO-PSYCHOPHARMACOLOGY & BIOLOGICAL PSYCHIATRY* 2011;35(6):1383-1390

**ALZET Comments:** Chlordiazepoxide; SC; Mice; 1 week; Animal info (C57BL/6J).

**P9959:** C. H. Vinkers, *et al.* The rapid hydrolysis of chlordiazepoxide to demoxepam may affect the outcome of chronic osmotic minipump studies. *Psychopharmacology* 2010;208(4):555-562

**ALZET Comments:** Chlordiazepoxide; In vitro; "When the cumulative CDP concentration over time was corrected for its hydrolysis, drug release from the minipumps followed the theoretical release profile over time (white symbols), suggesting that CDP hydrolysis completely accounted for the declined CDP release over time." pg 558; "In general, the use of osmotic minipumps presents a valid and attractive alternative to the labor-intensive daily injections. However, the issue of drug stability and release should always be carefully investigated before initiating chronic minipump experiments." pg 562.

**Q0421:** C. Rivat, *et al.* 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).

**P9610:** C. H. K. West, *et al.* Antidepressant drugs with differing pharmacological actions decrease activity of locus coeruleus neurons. *INTERNATIONAL JOURNAL OF NEUROPSYCHOPHARMACOLOGY* 2009;12(5):627-641

**ALZET Comments:** Desipramine; mirtazapine; chlorpheniramine; Paroxetine; scopolamine; amphetamine; escitalopram; chlordiazepoxide; SC; IP; Rat; 2ML2; 14, 21 days; Controls received mp w/vehicle; dose-response (Fig 2-5); pumps replaced on day 14; good methods pg 629; animal info (male, Sprague Dawley, 5-7 mo old, 550-700g); "Importantly, use of minipumps also eliminates the need for repeated handling and injection of animals to administer the drug chronically." pg. 628; IP catheter used.

**P9061:** M. J. H. Kas, *et al.* Differential genetic regulation of motor activity and anxiety-related behaviors in mice using an automated home cage task. *Behavioral Neuroscience* 2008;122(4):769-776

**ALZET Comments:** Chlordiazepoxide; Saline; SC; Mice; 1007D; 7 days; Controls received mp w/ saline; animal info (C57BL/6J, male); chlordiazepoxide is an anxiolytic.

**P7318:** J. Andre, *et al.* Involvement of cholecystokinergic systems in anxiety-induced hyperalgesia in male rats: Behavioral and biochemical studies. *Journal of Neuroscience* 2005;25(35):7896-7904



**ALZET Comments:** Chlordiazepoxide; Water, distilled; SC; Rat; 2ML1; 4-7 days; Controls received mp w/ saline.

**P4378:** D. J. Cash, *et al.* Desensitization of a g-aminobutyric acid type A receptor in rat is increased by chronic treatment with chlordiazepoxide: a molecular mechanism of dependence. *Journal of Pharmacology and Experimental Therapeutics* 1997;283(2):704-711

**ALZET Comments:** Chlordiazepoxide;; SC;; Rat;; 15 days;; controls received mp with vehicle; tolerance; dependence; chlordiazepoxide is a tranquilizer; rats were 6-8 weeks old;

#### 4. Clonazepam

**P3556:** M. I. Arnot, *et al.* Dimethyl sulfoxide/propylene glycol is a suitable solvent for the delivery of diazepam from osmotic minipumps. *J. Pharm. & Tox. Meth* 1996;36(29-31

**ALZET Comments:** Diazepam; Clonazepam; flumazenil; DMSO; Propylene glycol; Tetraglycol; <sup>3</sup>H tracer; Radio-isotopes; in vitro (egg); 2ML4; no duration posted; no comment posted.

**P3305:** L. Lima, *et al.* Serotonin turnover rate, [3H] paroxetine binding sites, and 5-HT1A receptors in the hippocampus of rats subchronically treated with clonazepam. *Neuropharmacology* 1995;34(10):1327-1333

**ALZET Comments:** Clonazepam; PEG; CSF/CNS (dorsal raphe nucleus); Rat; 10 days; comparison of IP injections vs. mp.

**P2654:** K. Brodin, *et al.* Clomipramine and clonazepam increase cholecystokinin levels in rat ventral tegmental area and limbic regions. *Eur. J. Pharmacol* 1994;263(175-180

**ALZET Comments:** Nortriptyline; Amitriptyline; Clomipramine; Alaproclate; Clonazepam; Alcohol; Saline; SC; Rat; 2ML2; 14 days; antidepressant; controls received mp w/ vehicle; functionality of mp verified by plasma levels; dose-response (Table 1; pg. 177); enzyme inhibitor; clonazepam is a benzodiazepene; the others are monoamine uptake inhibitors.

**P1650:** L. G. Miller, *et al.* Chronic benzodiazepine administration. VI. a partial agonist produces behavioral effects without tolerance or receptor alterations. *J. Pharmacol. Exp. Ther* 1990;254(1):33-36

**ALZET Comments:** Clonazepam; RO-16-6028; PEG 400; SC; mice; 14 days; functionality of mp verified by tissue levels; dose-response (graph); tolerance/dependence.

#### 5. Diazepam

**Q2140:** C. H. Vinkers, *et al.* GABA-A Receptor alpha Subunits Differentially Contribute to Diazepam Tolerance after Chronic Treatment. *PLoS One* 2012;7(8):U614-U624

**ALZET Comments:** Diazepam; zolpidem; TPA023; bretazenil; PEG 400; alcohol; water, distilled; SC; Mice; 2004; 4 weeks; Controls received mp w/ vehicle; animal info (129 Sv/Ev Tac, 10-12 wks old); 95% PEG 400 used; 2.5% alcohol used; stress/adverse effects "severe hypothermia likely explains the death of seven animal's postsurgically..." pg 9; TPA023 is an alpha 2/3 selective GABA<sub>A</sub> receptor positive allosteric modulator.

**Q1966:** M. Spolidoro, *et al.* Food restriction enhances visual cortex plasticity in adulthood. *Nature Communications* 2011;2(;):U210-U217

**ALZET Comments:** Diazepam; mercaptopropionic acid; Propylene glycol; CSF/CNS (visual cortex); Rat; 2002; Animal info (Long Evans hooded, P60-P90, male, female); 50% propylene glycol used.

**P9449:** E. A. Stone, *et al.* Evaluation of the repeated open-space swim model of depression in the mouse. *Pharmacology Biochemistry and Behavior* 2008;91(1):190-195

**ALZET Comments:** Imipramine HCl, desmethyl; diazepam; fluoxetine; haloperidol; Saline; DMSO; water; SC; Mice; 1002; 14 days; Controls received mp w/either saline, 25, 50% or 100% DMSO; half-life (p. 191); animal info (male, Swiss Webster, 8-10 wks old); behavioral testing (swimming behavior, tail-suspension test, sucrose suspension test); "since drugs have relatively short half-lives in mice, to more closely mimic the human condition in which blood levels are maintained for



prolonged periods, all agents were administered by osmotic minipump." (p. 191); all mice were housed singly for the duration of the experiment (3 weeks). Dose: desmethylimipramine in saline (10–11.5 mg/kg/d) in a 35–40 g mouse, fluoxetine dissolved at the same concentration in 50% DMSO; haloperidol dissolved in 25%DMSO at 0.3–0.34 mg/kg/day (2 mg/ml) and diazepam in 100% DMSO at 1–1.1 mg/kg/day (6.66 mg/ml).

**P8816:** A. M. Depino, *et al.* GABA homeostasis contributes to the developmental programming of anxiety-related behavior. *Brain Research* 2008;1210(189-199)

**ALZET Comments:** Diazepam; DMSO; propylene glycol; SC; Mice; mice (neonate); 1002; 2002; 14 days; Controls received mp w/ vehicle; dose-response (Fig. 1); no stress (see pg. 193); post op. care (flumazenil); animal info (C57BL/6 x 129/SvJ, male, 14 days old, 60 days old); 50% DMSO used; behavioral testing (maze); wound clips used; 50% propylene glycol used.

**P5972:** T. K. Hensch, *et al.* Columnar architecture sculpted by GABA circuits in developing cat visual cortex. *Science* 2004;303(5664):1678-1681

**ALZET Comments:** Diazepam; Propylene Glycol; CSF/CNS (visual cortex); Cat (kitten); 2004; 2ML4; 4 weeks; Diazepam is a benzodiazepine agonist.

**P5275:** M. Fagiolini, *et al.* Inhibitory threshold for critical-period activation in primary visual cortex. *Nature* 2000;404(6774):183-186

**ALZET Comments:** Diazepam; Propylene glycol; CSF/CNS (visual cortex); Mice; 1007D; 4 days; Controls received mp w/ vehicle; comparison of icv injections vs. mp; 50% propylene glycol used.

**P7957:** T. K. Hensch, *et al.* Local GABA Circuit Control of Experience-Dependent Plasticity in Developing Visual Cortex. *Dynamics* 1997;210(53)

**ALZET Comments:** Tetrodotoxin; diazepam; Propylene glycol; CSF/CNS (visual cortex); Mice; 1007D; 1 week; Controls received mp w/ vehicle; half-life (p. 1508), rapid breakdown (diazepam); monocular deprivation, localization of cannula delivery confirmed with dye.

**P3556:** M. I. Arnot, *et al.* Dimethyl sulfoxide/propylene glycol is a suitable solvent for the delivery of diazepam from osmotic minipumps. *J. Pharm. & Tox. Meth* 1996;36(29-31)

**ALZET Comments:** Diazepam; Clonazepam; flumazenil; DMSO; Propylene glycol; Tetraglycol; <sup>3</sup>H tracer; Radio-isotopes; in vitro (egg); 2ML4; no duration posted; no comment posted.

**P3118:** C. D. Torchin, *et al.* A system for testing the development and reversal of anticonvulsant tolerance to benzodiazepines in mice. *Epilepsy Res* 1993;16(27-35)

**ALZET Comments:** Diazepam; flumazenil; flunitrazepam; ZK-93426; Tetraglycol; SC; mice; 2001; no duration posted; controls received mp with vehicle; tolerance; tetraglycol chosen as solvent because PEG, propylene glycol, tween, DMSO, saline, molecusol, and methyl cellulose did not maintain benzodiazepines in solution or proconvulsant activity was seen (see pg. 30); flumazenil is RO-15-1788; infusion delayed in some animals by using saline-filled catheter tubing; some animals received benzodiazepine + antagonist concomitantly.

**P2618:** K. Rasmussen, *et al.* The CCK-B antagonist LY288513 blocks effects of diazepam withdrawal on auditory startle. *NeuroReport* 1993;5(2):154-156

**ALZET Comments:** Diazepam; Water; Tween 80; SC; Rat; 2ML2; 12 days; no comment posted.

**P3033:** J.-L. Moreau, *et al.* Physical dependence induced in DBA/2J mice by benzodiazepine receptor full agonists, but not by the partial agonist Ro 16-6028. *Eur. J. Pharmacol* 1990;190(269-273)

**ALZET Comments:** Triazolam; Alprazolam; Diazepam; Propylene glycol; SC; mice; 2001; 7 days; controls received mp with vehicle; functionality of mp verified by receptor binding study; comparison of oral alprazolam vs. mp; ". . .the use of implantable minipumps. . .permitted. . .development of behavioral tolerance associated with downregulation of benzodiazepine receptor binding and GABA receptor function. . ."; dependence.



**P1392:** M. Hawkins, *et al.* Desensitization of adenosine A2 receptors in the striatum of the rat following chronic treatment with diazepam. *Neuropharmacology* 1988;27(11):1131-1140

**ALZET Comments:** Diazepam; Propylene glycol; Water;; SC; Rat; 2ML1; 7 days; functionality of mp verified by sectioning; neuroscience.

**P0886:** W. Loscher. Development of tolerance to the anticonvulsant effect of GABA<sub>mimetic</sub> drugs in genetically epilepsy-prone gerbils. *Pharmacol. Biochem. Behav* 1986;24(1007-1013

**ALZET Comments:** Aminobutyric acid, Y-acetylenic Y-; Aminooxyacetic acid; Diazepam; THIP; Valproic acid; Saline; SC; Rat; 2ML2; 2 weeks; controls received mp w/saline; diazepam too unstable to be used in mp; epilepsy; functionality of mp verified after 14 day exper. period - all 50 mps worked accurately; stability of VPA, THIP, GAG and AOAA.

**P0433:** A. Turmel, *et al.* Sensitization of rat forebrain neurons to serotonin by adinazolam, an antidepressant triazolobenzodiazepine. *Eur. J. Pharmacol* 1984;99(241-244

**ALZET Comments:** Adinazolam; Diazepam; Benzyl alcohol; Ethanol; Propylene glycol; Sodium benzoate; Water; IP; Rat; 2002; 5 and 14 days; comparison of adinazolam. iv injec vs. mp infusion; comparison of agents effects; adinazolam. used with water vehicle, Diaz. with combination vehicle.

## 6. Lorazepam

**P8188:** J. M. Fahey, *et al.* The effect of chronic lorazepam administration in aging mice. *Brain Research* 2006;1118(13-24

**ALZET Comments:** Lorazepam; PEG 400; SC; Mice; 1, 14 days; Controls received mp w/ vehicle; functionality of mp verified by lorazepam plasma concentrations; tolerance; animal info (male, CD-1, 2-3 months old, 10-12 months old, 22-24 months old).

**P4914:** J. M. Fahey, *et al.* Pharmacodynamic and receptor binding changes during chronic lorazepam administration. *Pharmacology Biochemistry and Behavior* 2001;69(1-8

**ALZET Comments:** Lorazepam; PEG 400; SC; mice; 1 or 14 days; controls received mp w/ vehicle; plasma lorazepam levels; brains examined postmortem for membrane binding; lorazepam is a benzodiazepine with anxiolytic and anti-insomnia properties;

**P4593:** M. H. J. Tehrani, *et al.* Sequestration of g-Aminobutyric acid<sub>A</sub> receptors on clathrin-coated vesicles during chronic benzodiazepine administration in vivo;. *The Journal of Pharmacology and Experimental Therapeutics* 1997;283(1):384-390

**ALZET Comments:** Lorazepam;; PEG 400;; SC;; mice;; 2001;; 7 days;; controls received mp w/vehicle; tolerance;;

**P3328:** M. Mortensen, *et al.* The effect of lorazepam tolerance and withdrawal on metabotropic glutamate receptor function. *J. Pharmacol. Exp. Ther* 1995;274(1):155-163

**ALZET Comments:** Lorazepam; PEG 400; SC; mice; 2001; 7 days; tolerance.

**P3673:** J. J. Byrnes, *et al.* Chronic benzodiazepine administration. *Psychopharmacology* 1993;111(91-95

**ALZET Comments:** Alprazolam; Lorazepam; PEG 400; SC; mice; 2001; 2002; 7, 8, or 14 days; controls received vehicle; tolerance.

**P2501:** L. G. Miller, *et al.* Chronic benzodiazepine administration. x. concurrent administration of the peripheral-type benzodiazepine ligand PK11195 attenuates chronic effects of lorazepam. *J. Pharmacol. Exp. Ther* 1992;261(1):285-289

**ALZET Comments:** Lorazepam; PK 11195; SC; mice; no duration posted; controls received mp w/ vehicle; tolerance; Lorazepam and PK11195 infused separately and together; PK11195 is a peripheral-type site ligand; pumps chosen because they produce "constant plasma and brain concentrations".

**P2332:** G. B. Kaplan, *et al.* Effects of benzodiazepine administration on A1 adenosine receptor binding in-vivo and ex-vivo. *J. Pharm. Pharmacol* 1992;44(700-703

**ALZET Comments:** Alprazolam; Lorazepam; PEG 400; IP; mice; 2001; 6 days; controls received mp w/ vehicle.





**P2610:** A. M. Allan, *et al.* Effects of lorazepam tolerance and withdrawal on GABA receptor operated chloride channels in mice selected for differences in ethanol withdrawal severity. *Life Sci* 1992;51(12):931-943

**ALZET Comments:** Lorazepam; PEG 400; SC; mice; 7 days; controls received mp w/ vehicle; tolerance.

**P2080:** A. M. Allan, *et al.* Effects of lorazepam tolerance and withdrawal on GABA-A receptor-operated chloride channels. *J. Pharmacol. Exp. Ther* 1992;261(2):395-402

**ALZET Comments:** Lorazepam; PEG 400; SC; mice; 7 days; tolerance.

**P2362:** L. Miller, *et al.* Prenatal benzodiazepine administration, II. lorazepam exposure is associated with decreases in [35S]TBPS binding but not benzodiazepine binding. *Pharmacol. Biochem. Behav* 1991;40(4):29-432

**ALZET Comments:** Lorazepam; PEG 400; SC; mice (pregnant); 2001; 7 days; teratology.

**P1591:** A. Schatzki, *et al.* Lorazepam discontinuation promotes 'inverse agonist' effects of benzodiazepines. *Br. J. Pharmacol* 1989;98(4):51-454

**ALZET Comments:** Lorazepam; PEG 400; SC; mice; 2001; 2002; 7 days; no comment posted.

**P1290:** L. G. Miller, *et al.* Chronic benzodiazepine administration II: discontinuation syndrome is associated with upregulation of gamma-aminobutyric acid receptor complex binding and function. *J. Pharmacol. Exp. Ther* 1988;246(1):177-182

**ALZET Comments:** Lorazepam; PEG 400; SC; mice; 2001; 7 days; tolerance; functionality of mp verified by plasma, brain levels.

**P1319:** L. G. Miller, *et al.* Chronic benzodiazepine administration. 1. tolerance is associated with benzodiazepine receptor downregulation and decreased gamma-aminobutyric acid receptor function. *J. Pharmacol. Exp. Ther* 1988;246(1):170-176

**ALZET Comments:** Lorazepam; PEG 400; SC; mice; 2001; 2002; 14 days; dose-response (graph, text); tolerance; functionality of mp verified by plasma levels.

**P1396:** J. Bell, *et al.* Increased central noradrenergic activity during benzodiazepine withdrawal: an electrophysiological study. *Neuropharmacology* 1988;27(11):1187-1190

**ALZET Comments:** Alprazolam; Lorazepam; Ethanol; Propylene glycol; Saline; SC; Rat; 2ML2; 12 days; no comment posted.

## 7. Triazolam

**P2656:** C. Cohen, *et al.* Tolerance, cross-tolerance and dependence measured by operant responding in rats treated with triazolam via osmotic pumps. *Psychopharmacology* 1994;115(86-94)

**ALZET Comments:** Triazolam; Propylene glycol; SC; Rat; 2ML2; 14 days; controls received mp w/ vehicle; tolerance; dependence.

**P2115:** L.-W. Zhou, *et al.* Triazolam blocks the initial rotational effects of quinpirole but permits the later developing reduction of dopamine D2-mediated rotational behavior and dopamine D2 receptors. *Eur. J. Pharmacol* 1992;218(2):19-227

**ALZET Comments:** Quinpirole HCl; Sulpiride; Triazolam; Ascorbic acid; DMSO; SC; mice; 2001; 6 days; Quinpirole is a dopamine agonist; antidepressant; stability verified in vitro for 7 days.

**P3033:** J.-L. Moreau, *et al.* Physical dependence induced in DBA/2J mice by benzodiazepine receptor full agonists, but not by the partial agonist Ro 16-6028. *Eur. J. Pharmacol* 1990;190(2):69-273

**ALZET Comments:** Triazolam; Alprazolam; Diazepam; Propylene glycol; SC; mice; 2001; 7 days; controls received mp with vehicle; functionality of mp verified by receptor binding study; comparison of oral alprazolam vs. mp; ". . .the use of implantable minipumps. . .permitted. . .development of behavioral tolerance associated with downregulation of benzodiazepine receptor binding and GABA receptor function. . ."; dependence.

