

ATTACHMENT 2

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Summary Table of Published Abuse Liability Studies of Oral
Immediate-Release Methylphenidate by Dose

Table 1. Published Abuse Liability Studies of Oral Immediate-Release Methylphenidate by Dose

Citation	Study Design	Population	Behavioral Endpoints	MPH Dose (mg)	MPH Form	Abuse Conclusions by MPH Dose
Heil SH <i>et al</i> 2002 ¹⁴	PC, DB, SD, CO	Light Drug Abusers (4M/12F)	Drug Effect VAS; ARCI; ARS	20, 40	IR tablets	Statistical differences from placebo detected for 40-mg but not for 20-mg on VAS, ARS, and some subscales of ARCI.
Jasinski DR 2000 ¹⁵	PC, DB, SD, CO	Polysubstance Abusers (24M)	Subject-Rated Questionnaires (VAS); ARCI; Observer Ratings	45, 90	IR tablets	Statistical differences from placebo detected for both 45- and 90-mg on Subject (Like and High scales) and Observer Ratings.
Roache JD <i>et al</i> 2000 ¹⁶	PC, DB, MD, parallel	Cocaine Abusers (21M/7F)	Profile of Mood States; ARCI; Cocaine Questionnaire (VAS)	(5 + 20) morning; 20 evening	5 mg IR tablet + 20 mg SR capsule	Statistical differences from placebo in mainly unpleasant or dysphoric ratings
Roache JD <i>et al</i> 2000 ¹⁶	PC, DB, SD, DR parallel	Cocaine Abusers (10M/2F)	Profile of Mood States; ARCI; Cocaine Questionnaire (VAS)	15, 30, 60	IR tablets	Statistical differences from placebo only for 60-mg dose in Shaking (VAS) Ratings and in the dysphoric LSD Scale of ARCI
Rush CR <i>et al</i> 2001 ¹⁷	PC, DB, SD, parallel	Healthy Nonabusers (4M/4F)	ARCI; Subject Ratings	20, 40	IR tablets	Statistical differences from placebo detected for 40-mg on "Any Effect" and "Like Drug" scales, but not for 20-mg. Neither dose separated from placebo on the "High" scale.
Rush CR and Baker RW 2001 ¹⁸	PC, DB, DR, CO	Polysubstance Abusers, Cocaine-Trained (6M)	ARCI; Drug-Effect Questionnaire; Observer-Rated Questionnaire	15, 30, 60, 90	IR tablets	Complete substitution for the cocaine discriminative stimulus only occurred with 60- and 90-mg, but relatively high levels of cocaine-appropriate responding were observed at 30-mg.

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Citation	Study Design	Population	Behavioral Endpoints	MPH Dose (mg)	MPH Form	Abuse Conclusions by MPH Dose
Rush CR <i>et al</i> 2002 ¹⁹	PC, DB, SD, CO	Polysubstance Abusers, Cocaine-Trained (4M/2F)	Cocaine-Sensitive Adjective Scale; Drug-Effect Questionnaire	60	IR tablets	Post-hoc analyses revealed statistical differences from placebo for 60-mg.
Rush CR <i>et al</i> 1998 ²⁰	PC, DB	Healthy, Non-abusers (2M/3F)	ARCI, POMS, Drug-Effect Questionnaire	5, 10, 20, 40	IR tablets	Across all dose groups, MPH produced discriminative-stimulus and participant-related effects virtually indistinguishable from d-amphetamine. The two highest MPH doses produced ≥ 75% drug appropriate responding.

Key ARCI - Addiction Research Center Inventory, ARS – Adjective Rating Scale; CO – crossover; DB – double blind, DR – dose response; F – female; IR – immediate release; MD - multiple dose; M – male, PC-placebo-controlled; POMS-Profile of Mood States, SD – single dose, SR – sustained release; VAS – visual analog scale.

¹⁴Heil SH, Holmes HW, Bickel WK, et al. Comparison of the subjective, physiological, and psychomotor effects of atomoxetine and methylphenidate in light drug users. *Drug Alcohol Dependence* 2002; 67: 149-56.

¹⁵Jasinski DR. An evaluation of the abuse potential of modafinil using methylphenidate as a reference. *J Psychopharm* 2000; 14: 53-60.

¹⁶Roache JD, Grabowski J, Schmitz JM, et al. Laboratory measures of methylphenidate effects in cocaine-dependent patients receiving treatment. *J Clin Psychopharm*. 2000; 20: 61-68

¹⁷Rush CR, Essman WD, Simpson CA, et al. Reinforcing and subject-rated effects of methylphenidate and d-amphetamine in non-drug abusing humans. *J Clin Psychopharm* 2001; 21(3):273-285.

¹⁸Rush CR, Baker RW. Behavioral pharmacological similarities between methylphenidate and cocaine in cocaine abusers. *Exp Clin Psychopharm* 2001; 9: 59-73

¹⁹Rush CR, Kelly TH, Hays LR, et al. Discriminative-stimulus effects of modafinil in cocaine-trained humans. *Drug Alcohol Dependence* 2002; 67: 311-322

²⁰Rush CR, Kollins SH, Pazzaglia PJ. Discrimination-stimulus and participant-rated effects of methylphenidate, bupropion, and triazolam in d-amphetamine trained humans. *Exp Clin Pharmacol* 1998;6(1):32-44.