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To Whom it May Concern:

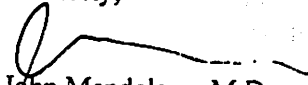
I have been asked to comment on the proposed MDMA study by Michael Mithoefer, MD and colleagues. I am a physician (board Certified in Internal Medicine) with considerable research publications relating to the cardiovascular effects of stimulants and other drugs of abuse. I was the senior author of the only study to investigate the acute cardiovascular effects of MDMA in healthy volunteers using 2-dimensional quantitative Doppler echocardiography (1).

The Mithoefer study proposes to administer two doses of 125 mg MDMA (each dose separated by several weeks) to twelve volunteers diagnosed with PTSD and who have failed to benefit from available pharmacotherapies. I am being asked to evaluate the cardiovascular risks of this protocol in light of recent research by Bryan Roth and colleagues. Roth's *in vitro* research indicates that MDMA (and its metabolite MDA) may, over time, induce heart valve changes similar to those reported in patients taking the anorectic fenfluramine.

Heart valve changes have not, to my knowledge, been reported in illicit users of MDMA. We saw no evidence of preexisting changes in the MDMA users included in our study, who had reportedly used MDMA 49 ± 65 times (range, 5-200 times). The acute cardiovascular effects of 1.5 mg/kg MDMA were well-tolerated by our volunteers. This study did not have adequate statistical power to detect a rare complication and recent studies with fenfluramine, though inconclusive, suggest that heart valve changes occurred in approximately 6% of patients taking fenfluramine on a daily basis for at least several months.

Given the lack of clinical reports of heart valve disease in illicit MDMA users and its low incidence in chronic fenfluramine patients, it currently appears that the risks of significant heart valve changes after two exposures to MDMA, as proposed in the Mithoefer study, are very low. It should be more than adequate to discuss this theoretical risk in the consent form (and related conversations). Echocardiograms, performed before and at least several weeks after completion of each volunteer's MDMA exposures, could be considered, although they appear unlikely to confirm or dispel this theoretical risk.

Sincerely,


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1. Lester SJ, Baggott M, Welm S, Schiller NB, Jones RT, Foster E and Mendelson J (2000) Cardiovascular effects of 3,4-methylenedioxymethamphetamine. A double-blind, placebo-controlled trial. *Ann Intern Med* 133:969-973).