

BI IRB# 087-14 Acute and Short-Term Effects of CBD on Cue-Induced Craving in
Drug- Abstinent Heroin-Dependent Humans

NCT # 02539823

Version: March 12, 2017

Statistical Analysis Plan

A linear mixed-model repeated-measures analysis using the SAS procedure MIXED (SAS Institute, Cary, N.C.) was employed to assess the changes in cue- induced in-clinic VAS-C, VAS-A, and PANAS scores. Changes in the Heroin Craving Questionnaire out-of-clinic craving scale score were assessed using a repeated-measures analysis conducted with the MIXED procedure. At the first stage of all analyses, the distributional characteristics of all continuous explanatory and outcome variables were assessed using skewness and kurtosis indicators. If necessary, transformations were used to normalize a variable. To determine the effectiveness of the randomization procedure for assignment to the drug group, one-way analyses of variance were conducted on the session 1 baseline values of each of the outcome variables as a function of drug group. Nonsignificant drug group baseline differences were taken as indicators of effective randomization. Because a crossover design assumes that there are no carryover effects from one assessment period to the next, this possibility was tested using procedures in the Number Cruncher Statistical System User's Guide II. Once the analyses indicated that carryover effects were absent, the main analyses of the crossover design variables were undertaken.

Difference scores between the precue baseline scores and postcue scores within each session were calculated and used as outcomes in the analytic models. The models themselves were developed sequentially in which time was entered first (because there were multiple sessions and two events within each session for the crossover outcomes; that is, neutral and drug cues). This procedure was followed by entering the variable describing the sequence in which the drug and neutral cues were given, the drug group variable, and the cue indicator (neutral or drug cue). A single first-order interaction term (drug group by cue) was entered last because it was hypothesized that the cues would be responded to differentially depending on the drug group to which the research participant was assigned. Any significant mean differences for the main effect analyses or interaction terms were followed up by Tukey-adjusted post hoc mean comparisons.