

Official Study Title: Investigating the Cardiovascular Toxicity of Exposure to Electronic Hookah Smoking

Document Title: Statistical Analysis Plan

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Statistical Analysis Plan for Endothelial Function

Statistical analyses were performed using SAS (version 9.4). Data were analyzed by the Shapiro–Wilk test to determine distribution. Once normality was demonstrated, we tested within-participant pre- versus post-exposure changes using paired t tests. For non-normally distributed variables Wilcoxon signed-rank test was used. We applied paired t tests to compare the pre- versus post-changes induced by ascorbic acid versus e-hookah vaping for variables that were normally distributed, and Wilcoxon signed-rank test for non-normally distributed variables. Data are expressed as mean \pm SE. Data for plasma nicotine, exhaled carbon monoxide, and flow-mediated dilation normalized for shear were not normally distributed and were additionally expressed as median (interquartile range). Statistical significance was set at the 0.05 level.

Statistical Analysis Plan for Central Arterial Stiffness and Biomarkers of Oxidative Stress and Inflammation

Paired Student *t* tests were used to compare continuous variables between sessions before and after exposure. Because of the crossover study design, we used a general linear model approach for repeated measures to examine differences between e-hookah and traditional combustible hookah; the models included two within-subject factors (product type and time point relative to exposure session), and the sequence of type of product exposure was included as a between-group factor. The effect of primary interest was the interaction between the two within-subject factors, product type and time point relative to the exposure session. Effect sizes are for the interaction of product-by-time point relative to exposure in the general linear model repeated-measures analysis and translated from eta-square metric to d-metric. Statistical significance was set at 0.05 and analyses were conducted using SPSS Statistics version 24.0 software (IBM).