TITLE: CLINICAL PHARMACOLOGY OF ELECTRONIC CIGARETTES

NCT02470754

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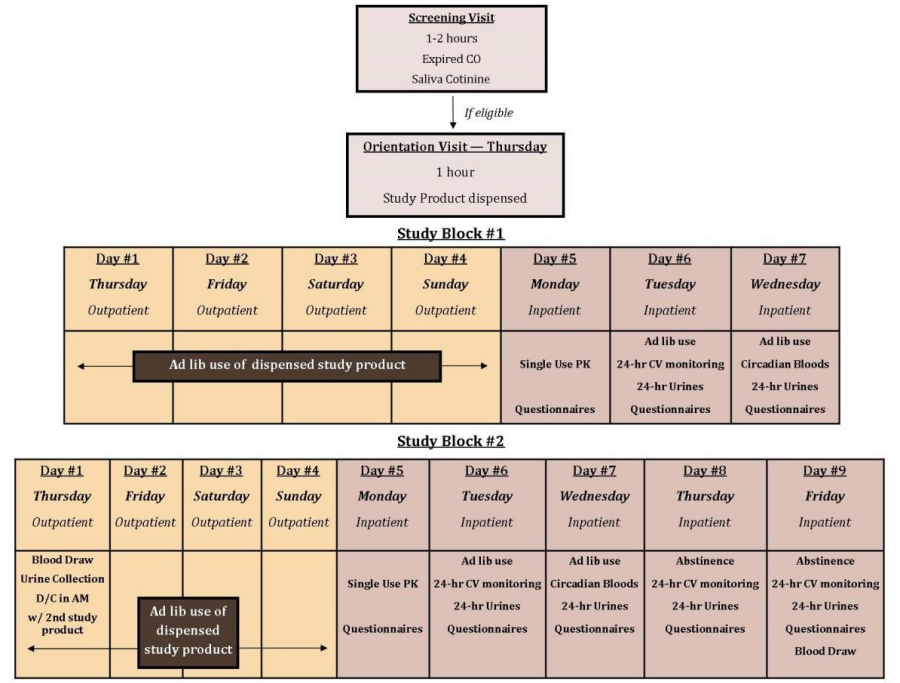
Abbreviations

EC	Electronic Cigarette
TC	Tobacco Cigarette (Commercially Manufactured or Available)
PK	Pharmacokinetic
CI	Confidence Interval
SD	Standard Deviation
BMI	Body Mass Index
HR	Heart Rate
SBP	Systolic Blood Pressure
DBP	Diastolic Blood Pressure
hr	Hour
AUCinf	Area under the plasma concentration time curve from zero to the last measured time
AUClast	Area under the plasma concentration time curve extrapolated from zero
CMAX	Peak Plasma Concentration
TMAX	Time of Peak Plasma Concentration
THalf	Half-Life
ANOVA	Analysis of Variance
SAS	Statistical Analysis System

Study Design

This is a within-subject two-arm crossover study design evaluating the safety and addictive potential of EC compared to TC



Study Endpoints

On the first hospital day in each treatment arm the subject will use their product at 9 AM in a standardized protocol. EC use will be one puff every puff every 30 seconds for a total of 15 puffs on 1st generation devices and 10 puffs on 2nd/3rd generation devices.

Endpoint (s): Systemic Nicotine Exposure - Baseline Adjusted AUC (Inf), TMAX, CMAX, Half-Life, and PK-Predicted Dose following the standardized puffing protocol. Additional PK Parameters may be calculated as deemed necessary.

Analysis: Linear mixed model

Descriptive Summary Statistics: N, n, arithmetic mean, SD, 95% CI will be used to describe continuous measures including nicotine intake [AUC Inf, AUC Last, PK-predicted dose] related to single use PK. Categorical Data will be described using frequency count and percentage of subjects in each category. Descriptive statistics will be calculated using standard methods.

Statistical Hypothesis

Distributional assumptions underlying the model will be examined by analysis of the residuals and plot of the residuals vs the fitted values.

Treatment effects will be compared by means of repeated measures ANOVA. All significance tests will be two-sided with an alpha level set at 0.05.

Primary Analysis

Crossover analysis was carried out following standard procedures. Following ln-transformation of plasma concentrations treatment effects were compared by means of repeated measures ANOVA. To account for the relatedness in the plasma nicotine measures within each subject during the two treatment periods, a linear mixed model was used to account for non-independence in sequential measurements.
In building the linear mixed-models, baseline-adjusted plasma nicotine concentrations were considered the dependent variable. These models included independent variables of treatment and a dichotomized variable defining order of product assignment. Participant IDs were used as group factor to estimate random effects.

Secondary Analysis

PK data will be presented in graphical and/or tabular form and will be summarized descriptively.
Mean Heart Rate, Mean Systolic Blood Pressure and Mean Diastolic Blood Pressure will also be described similarly. Additional toxicant exposure data may be described as necessary.