A Validation of the Assisted Fluid Management Feature

Statistical Analysis Plan

Medical Device: EV1000 Platform with Acumen™ Assisted Fluid Management Feature

Date: October 25, 2018

NCT03469570

Statistical Analysis Plan (SAP)

Data will be summarized using standard frequentist methods as appropriate per data type, i.e. frequencies (percentages) for categorical data, means, medians, measures of dispersion for continuous data and will be reported overall and by group. Any AE's will also be listed and summarized by site and group. All of the primary analysis will be on the intent to treat (ITT) population. Histograms and boxplots will be used to check distributions and for possible outliers for continuous variables. Mathematical transformations will be applied where appropriate in order to render the continuous variables to a normal distribution. Even if consistency with a normal distribution is found, all descriptive statistics will be reported with 97.5% confidence intervals, estimated from both bootstrapped and traditional estimation methods. Similarly, if not a normal distribution (i.e. proportion, etc.) then the point estimate and one-sided 97.5% confidence interval for the primary effectiveness endpoint recommended at the event level will also be computed using a bootstrap methodology and traditional estimation methods. Following the suggestions of Samuelson and Petrick (2006) a minimum threshold of 4000 bootstrap iterations is recommended for an alpha=0.025.

This approach is recommended for non-Gaussian distributions since it can accommodate correlated data. Any bootstrapping will follow procedure as discussed by Davison, AC and Hinkley, DV (1997). All statistical analysis will be conducted using SAS v9.4 or higher (Cary, NC) or NCSS v11 or higher (Kaysville, Utah, 2016) where specified.