STATISTICAL ANALYSIS PLAN FOR CAS-2; VERSION 2.0

290825

1. Study Design and Aims

This is a randomized, controlled trial evaluating coagulation activation in blood from four different central venous catheters (CVCs) using established laboratory methods. The primary aim is to investigate if four commonly used CVCs, with similar inner surface area, demonstrate different coagulation activation measured with clotting time (CT) in the ROTEM assay NATEM. Secondary aims include, but are not limited to, investigating if the four CVCs demonstrate different coagulation activation measured with additional ROTEM variables and coagulation markers, and if Sample 1 exhibits coagulation activation compared to Sample 2 within each CVC group. Blood samples will be drawn at two time points per catheter and analyzed for coagulation markers. Sample 1 will be collected within seconds after the catheter insertion and Sample 2 after flush and discard of blood.

2. Study Groups

Participants will be randomized to receive one of four commonly used CVCs with similar inner surface area.

Each group will consist of 20 individuals based on sample size calculations.

3. Primary Outcome

- Change in CT (ΔCT) between Sample 1 and Sample 2 across the four CVCs.

4. Secondary Outcomes

- Change in additional ROTEM variables (Δadditional ROTEM variables) between Sample 1 and Sample 2 across the four CVCs.
- Change in additional coagulation markers (Δadditional coagulation markers) between Sample 1 and Sample 2 across the four CVCs.
- Differences between Sample 1 and Sample 2 within each CVC group for all ROTEM variables and coagulation markers

5. Sample Size Calculation

- Based on prior data (ΔCT = 450s, SD = 152s), a one-way ANOVA with assumed group means of 450s, 275s, 350s, and 400s required n = 17 per group for 80% power at $\alpha = 0.05$.
- To account for likely non-normality and analysis failure, the sample size was increased to n = 22 per group (total 88 individuals).

6. Statistical Methods

- **Between-group comparisons** (differences in ΔCT and other markers between CVCs) → Kruskal-Wallis test with Dunn's multiple comparisons test if non-normality is detected. If normality is confirmed, one-way ANOVA with Tukey's post hoc test will be used.
- **Within-group comparisons** (Sample 1 vs. Sample 2) → Wilcoxon matched-pairs signed-rank test if non-normality is detected. If normality is confirmed, matched t-test will be used.
- **Between-group comparisons** (differences in ΔCT and other markers between CVCs) → Kruskal-Wallis test with Dunn's multiple comparisons test if non-normality is detected. If normality is confirmed, one-way ANOVA with Tukey's post hoc test will be used.
- **P-value <0.05** considered statistically significant.

7. Software

- GraphPad Prism 10.2.2 for statistical analysis and visualization.
- SAS Proc Power (version 9.4) for sample size determination.