Cover Page

Protocol Title:	A randomized controlled post-market study to assess the impact of peripheral intravenous catheter length and gauge on catheter indwell duration and haemolysis in human participants using a bilateral, cephalic vein cannulation model.
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Statistical Analysis Plan

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Protocol Title	A randomized controlled post-market study to assess the impact of peripheral intravenous catheter length and gauge on catheter indwell duration and haemolysis in human participants using a bilateral, cephalic vein cannulation model.
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Approval

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List of Abbreviations and Definitions

- **BD:** Becton Dickinson and Company
- **BMI:** Body Mass Index
- **cfHb:** Cell-free hemoglobin
- **CI:** Confidence Interval
- **CRF:** Case Report/Record Form
- **CTU:** Clinical Trials Unit
- **C/V:** Catheter to vein ratio
- **Device Configuration:** One of the following combinations of gauge and length
  - 22G & 1 inch
  - 22G & 1.75 inch
  - 20G & 1 inch
  - 20G & 1.75 inch
- **eCRF:** Electronic Case Report/Record Form
- **FDAAA:** FDA Amendments Act of 2007
- **GCP:** Good Clinical Practice
- **GCUH:** Gold Coast University Hospital
- **HIV:** Human Immunodeficiency Virus
- **IRB/HREC:** Institutional Review Board/Human Research Ethics Committee
- **LLAD:** Luer Lok Access Device
- **PIVC:** Peripheral intravenous catheter
- **PWD:** Pulse Wave Doppler
- **SD:** Standard Deviation
- **SOP:** Standard Operating Procedure
- **XLabS:** Experimental laboratory science group

1 Introduction

1.1 Background and Rationale

BD is investigating a specific PIVC device design factor (length and gauge) that may extend indwell time and consequently enable successful PIVC use (i.e. blood collection) throughout dwell time. Identifying device design factors that increase PIVC dwell time and reduce incidence of haemolysis would reduce associated workload costs (e.g., recollection of hemoglobin-free serum samples, PIVC reinsertion) for healthcare institutions.

1.2 Objectives

1.2.1 Primary Objectives

To assess patent indwell time for PIVCs of different length and gauge.

1.2.2 Secondary Objectives

- To assess haemolysis occurrence based on blood collection device, catheter device configuration.
- To evaluate blood draw fill time
- To determine the relationship, if any, between catheter blood draw patency indwell time and presence of intra/extravenous thrombi, catheter angle/tip location *in situ*, catheter length in vessel, vein depth from skin surface, C/V ratio, and vessel anatomy
- To evaluate changes in vessel dimensions, PIVC position (insertion angle and *in situ* tip position), and hemodynamics from baseline throughout indwell time

1.2.3 Exploratory Objectives

- To assess incidence of complications prompting device removal
- To evaluate manual flush variability (as applicable) using in-line pressure measurements

2 Study Description

2.1 Study Design

This is a single-center, open-label, multi-visit, self-controlled study design, in 40 healthy participants, randomized by gauge of peripheral intravenous catheter (PIVC) device into the lower arm cephalic vein of both arms. The purpose of this feasibility study is to assess impact of catheter length and gauge on PIVC indwell time over a multi-day (72 hour) period. This study will also evaluate the incidence of haemolysis from PIVC using a LLAD and vacutainer tube (2mL, 6mL) blood collection method compared to venipuncture from the antecubital fossa.

2.2 Study Population

Participants of clinical trials at the Clinical Trials Unit (CTU) based at the Griffith University Gold Coast campus are recruited through two primary mechanisms: 1) local advertising via digital and paper flyers; and 2) identification of suitable participants in the CTU volunteer registry (database). All advertising in the printed and audio-visual media has prior approval of the Griffith University Human Research Ethics Committee (HREC). The CTU volunteer registry has been maintained since 2015 and currently contains more than 700 volunteers.

Participants not meeting all criteria will be assessed by a medical monitor and included if patient safety is not adversely impacted.

2.2.1 Inclusion Criteria

In order to be eligible to participate in this study, an individual must meet all of the following criteria:

- Female or Male
- 18-65 years of age
- Not pregnant at time of recruitment within 48 hrs Day 1 procedures (self-reported)
- Normal coagulation results (prothrombin time 13-17 sec; activated partial thromboplastin time 27-37 sec)
- Normal platelet aggregation results for ADP, TRAP, and collagen induced maximal amplitude (>70% amplitude over 6 mins)
- Target cephalic veins readily cannulatable (i.e., $\geq \sim$2.55 mm to obtain C/V ratio less than 45% as indicated by standard 52 of the INS guidelines
- Able and willing to provide verbal and written consent
- Current Medicare card holder

2.2.2 Exclusion Criteria

Participants are excluded from the study if any of the following criteria apply:

- History of pro coagulative state/condition (e.g. previous deep vein thrombosis)
- Current hypertension (e.g., systolic >139 OR diastolic >89 mmHg)
- Currently on any anti-coagulant or platelet inhibitor medication. Use of NSAIDs and aspirin will be documented however not exclusionary.
- Hemophilia or any current or history of bleeding disorder or tendency
- Presence or report of current blood borne disease/infection (e.g. hepatitis, HIV, leukemia, lymphoma)
- Difficult vascular access (i.e., vein must be readily palpable and cannulatable - no less than $\sim$2.55 mm diameter to maintain $\leq$45% C/V ratio) as indicated by standard 52 of the INS guidelines27
- Allergy or sensitivity to chlorhexidine gluconate, isopropyl alcohol, latex, or skin adhesives
- BMI <18.5 kg/m^2 or $\geq$35 kg/m^2
- Positive results for the urine drug screen at screening or check-in (including opiates, methadone, cocaine, amphetamines)
- History or presence of alcoholism (self-reported) or drug abuse within the past 2 years
- A current or previous medical, physical, mental/cognitive disorders or anatomical conditions that, in the opinion of the investigator, would place the patient at risk, would make them unable to perform study procedures or has the potential to confound interpretation of the study results (e.g., musculo-skeletal injury, chronic back pain)
- Employed by Becton Dickinson, Teleflex Medical, Smiths Medical or B Braun (conflict of interest)

2.3 Randomization and Blinding

2.3.1 Randomization

Participants will be randomized using R statistical software (R 3.6.2 or higher). The generation of the randomization list will be conducted by a staff member not involved in data acquisition or analysis. Each randomization number will have a corresponding code (e.g., LA_20G_1.75 - indicating a Nexiva 20G 1.75 will be first inserted into the left arm). The participant will then have the other length PIVC of the same gauge inserted into the contralateral arm. Intervention kits will be created for each participant using large ziplock bags with all necessary (plus extra) consumables inside. Each kit will be separated via separate ziplock bags into consumables required for the right arm and left arm. Once the kits have been created, the appropriate randomization number will be recorded on the outside of each. Subsequently,

the corresponding code will be placed in an envelope and sealed with the randomization number written on the outside of the envelope. These envelopes will be produced in duplicate with the second envelope sealed in a locked cabinet in the CTU for the circumstance where unblinding is required. Thereafter, the randomization list excluding the corresponding code will be given to the postdoctoral research fellow for storage until a randomization number is requested for the study.

2.3.2 Blinding/Masking

Due to the concealment of intervention allocation, most staff members, other than the inserter and study manager (research assistant), will be blinded to which gauge and length catheter the participant is receiving. In order to avoid bias, sonographic data measurements (e.g., vessel diameter, C/V ratio, blood flow velocity) will be acquired on a separate day at the end of each working week. The acquisition of the sonographic measurements will be conducted by the sonographer). All concealed data will be transferred into an Excel spreadsheet that will be subsequently grouped into 2 groups in a separate Excel spreadsheet by a staff member not involved in data analysis and is unblinded. This will allow the researchers to analyze the data without having access to information about the allocation

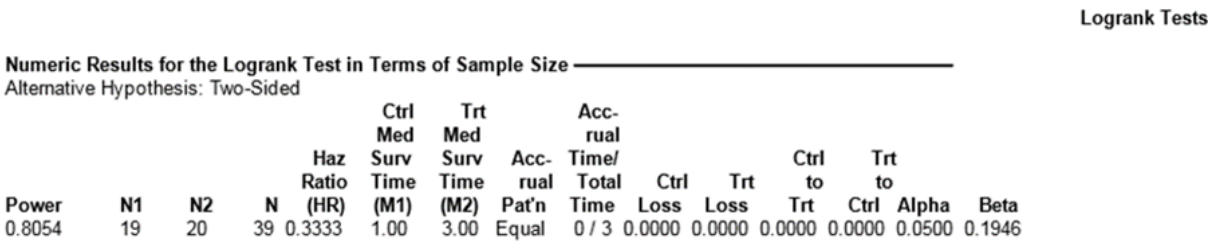
2.3.3 Procedures for Unblinding

In the unlikely scenario of a SAE, the study manager or post-doctoral research fellow will open the duplicate envelope located in the locked cabinet of the CTU that has the randomization number written on the outside and contains the corresponding code within. The information will be provided to any personnel that require the information (e.g., the study Medical Doctor) as deemed necessary by the Principal Investigator.

2.4 Sample Size

There is limited published data investigating the impact of PIVC catheter length on indwell time; a single article was found in the literature comparing catheter survival between a BD PIVC catheter (20 gauge; 4.78 cm/1.88-inch length) and midline catheter (POWERWAND™, 19.5 gauge; 6 cm/2.3-inch length). The indwell time results for this research were utilized to calculate a sample size estimate using the routine "Survival - Two Survival Curves - Logrank Tests" available in the software PASS 2019. Based on the available dataset, a sample size of ∼20 participants per PIVC length would be required, considering median failure times of catheter of different lengths of 1 and 3 days, as can be seen in Figure 2.4.1. The same calculation will be applied to investigating the impact of increased gauge, because the increased volume of catheters is similar in both condition (i.e., 1 versus 1.75 inch = 75% increased volume; 20 versus 22 gauge = 51% increased volume).

Figure 2.4.1: Details of sample size calculation



Logrank Tests

Numeric Results for the Logrank Test in Terms of Sample Size

Alternative Hypothesis: Two-Sided

Power	N1	N2	N	Haz Ratio (HR)	Ctrl Med Surv Time (M1)	Trt Med Surv Time (M2)	Acc-rual Pat'n	Acc-rual Time/ Total Time	Ctrl Loss	Trt Loss	Ctrl to Trt	Trt to Ctrl	Alpha	Beta
0.8054	19	20	39	0.3333	1.00	3.00	Equal	0 / 3	0.0000	0.0000	0.0000	0.0000	0.0500	0.1946

2.5 Interim Analysis

A formal interim analysis is not planned. However, after 5 participants have completed their follow-up visit (V6), the in-situ catheter positions will be compared to the expected position based on the catheter lengths. Only summary statistics related to the catheter length will be provided (mean, median, percentage) and no statistical test will be performed.

2.6 Preliminary Analysis

In order to answer critically urgent business questions, a preliminary analysis will be performed by an independent statistician prior to the final database lock. This analysis will be limited to the analysis of the following specific endpoints:

- Indwell time (as described in section 5.2.1.1) and ranking of factor influencing indwell time (as described in section 5.2.2.3 by item 7)
- Haemolysis as a continuous measurement by device configuration and over time, including baseline venipuncture rate as relative comparator, as described in section 5.2.2.1 by item 1 (including the preliminary Boruta analysis)
- Rate of occurrence of Haemolysis by device configuration and over time, including baseline venipuncture rate as relative comparator, as described in section 5.2.2.1 by item 2 (including the preliminary Boruta analysis)
- Thrombus observation by device configuration over time, as described in section 5.2.2.3 by items 1, 2, 3, 4 and 7
- Incidence of failure modes for device removal, as described in section 5.2.1.2

The results of the preliminary analysis will be communicated by the independent statistician to Christopher Rini (Associate Director - Biomedical Engineering) who will be responsible for sharing them with Jeff O'Bryan (Director - Product Development Engineering), select MDS designees, and Ron Pettis (Director/Principal Scientist - Parenteral Research). Preliminary analysis will not be shared beyond those required for making time-critical business decisions on behalf of the MDS business unit.

Every GCD employee involved in the study execution, especially the lead study statistician, as well as all site employees involved in the study execution, will remain blinded to the results of this preliminary analysis until database lock.

It is understood by all parties that the results of this primary analysis will be subject to confirmation after database lock and fulfillment of all the processes related to data quality described in the Data Management Plan.

2.7 Study Procedure

The time-windows for collection of the primary, secondary and exploratory endpoints are detailed in Table 2.7.1.

The primary endpoint data (catheter dwell time) and exploratory endpoint data (PIVC complications) will be collected over 7 time-windows (see text highlighted in orange on Table 2.7.1). The secondary endpoint data (cfHb, blood draw time) will be collected over 8 discrete timepoints (including baseline, see text highlighted in red on Table 2.7.1).

All other secondary endpoint data (e.g., blood flow velocity, vessel diameter), except incidence of extravenous thrombus (assessed once the catheter is removed), will be collected over 15 timepoints (see text

highlighted in blue and grey on Table 2.7.1). Please note that the cells that indicate 'Day' in Table 1 are indicating the interventional visit days and are not inclusive of the screening visit or follow-up visit.

The flush pressure profile exploratory endpoint data will be collected over 7 timepoints (see text highlighted in blue on Table 2.7.1).

Table 2.7.1: List of sampling time points for primary, secondary, and exploratory endpoints. cfHb: cell-free hemoglobin; TIP: catheter tip position; BFV: blood flow velocity; C/V: catheter to vein ratio; PRES: in vivo pressure; PIVC: peripheral intravenous catheter; FILL: blood draw fill time. Time T+00:00 is the time of insertion

Day	Visit	Timepoint code	Approximate Time (hh:mm)	Measurements taken
Day 1	Baseline	D1.1	T-00:60	**TIP, BFV, C/V via ultrasound (no indwelling catheter)**
		D1.2	T-00:40	**cfHb via venipuncture**
	Morning	D1.3	T+00:15	**TIP, BFV, C/V via ultrasound, PRES via PIVC during flush**
		D1.4	T+00:25	**cfHb, FILL via PIVC**
		D1.5	T+00:35	TIP, BFV, C/V via ultrasound
	Afternoon	D1.6	T+06:00	**TIP, BFV, C/V via ultrasound, PRES via PIVC during flush**
		D1.7	T+06:15	**cfHb, FILL via PIVC**
		D1.8	T+06:25	**TIP, BFV, C/V via ultrasound**
Day 2	**Morning**	D2.1	T+24:00	**TIP, BFV, C/V via ultrasound, PRES via PIVC during flush**
		D2.2	T+24:15	**cfHb, FILL via PIVC**
		D2.3	T+24:25	**TIP, BFV, C/V via ultrasound**
	Afternoon	D2.4	T+30:00	**TIP, BFV, C/V via ultrasound, PRES via PIVC during flush**
		D2.5	T+30:15	**cfHb, FILL via PIVC**
		D2.6	T+30:25	**TIP, BFV, C/V via ultrasound**
Day 3	**Morning**	D3.1	T+48:00	**TIP, BFV, C/V via ultrasound, PRES via PIVC during flush**
		D3.2	T+48:15	**cfHb, FILL via PIVC**
		D3.3	T+48:25	**TIP, BFV, C/V via ultrasound**
	Afternoon	D3.4	T+54:00	**TIP, BFV, C/V via ultrasound, PRES via PIVC during flush**
		D3.5	T+54:15	**cfHb, FILL via PIVC**
		D3.6	T+54:25	**TIP, BFV, C/V via ultrasound**
Day 4	**Morning**	D4.1	T+72:00	**TIP, BFV, C/V via ultrasound, PRES via PIVC during flush**
		D4.2	T+72:15	**cfHb, FILL via PIVC**
		D4.3	T+72:25	**TIP, BFV, C/V via ultrasound**

2.8 Endpoints

2.8.1 Primary Endpoint

The primary endpoint is the catheter indwell time, defined as the time from catheter insertion to time of catheter failure. It is measured in hours.

2.8.2 Secondary Endpoints

- Haemolysis measured in three different ways with cfHb, AU480 and visual assessment: Quantification of cell free hemoglobin and frequency of samples exceeding a concentration of 50 mg/dL.
- Blood draw fill time. Defined as the duration from attachment of vacutainer to time when blood fills to pre-defined fill level. It is measured in seconds.
- Relationship, if any, between catheter blood draw patency indwell time and presence of intra/extravenous thrombi, catheter angle/tip location *in situ*, catheter length in vessel, vein depth from skin surface, C/V ratio, and vessel anatomy assessed via the incidence of:
  - Intravenous thrombus (mural, at tip)
  - Vein collapse
  - Presence and location of a valve relative to catheter tip
  - Side branches relative to catheter tip detected through ultrasound
- Evaluation of changes in vessel dimensions (Catheter to vein ratio), PIVC position (insertion angle and *in situ* tip position), and hemodynamics from baseline throughout indwell time evaluated using:
  - Vessel diameter or Catheter to vein ratio (C/V ratio)
  - Blood flow velocity
  - *In situ* tip position
  - Extravenous thrombus visually observed upon device removal within:
    - Catheter hub
    - Needleless connector
    - Extension tubing via visual observation

2.8.3 Exploratory Endpoints

- Incidence of complications prompting device removal assessed by the frequency of occurrence of the following events:
  - Vein collapse
  - Phlebitis
  - Venous thrombosis
  - Dislodgement
  - Infiltration (called Extravasation in the protocol)
  - Accidental removal
- Manual flush variability will be evaluated using duration of flush and characteristics of Flush pressure profile (peak force) obtained on in-line pressure measurements

2.9 Acceptance Criteria

No acceptance criteria have been established for this study.

3 Intended Statistical Software and Data Information

The analysis will be conducted with R version 4.0.3 (2020-10-10) [1] or a more recent version. The extraction of the pressure profile and duration of flush characteristics will be performed by BDTI R&D

using LabView 2020 with the script PIVC linedraw, version 1.1.2. Results will be provided to the study statistician in a csv file.

4 Analysis Population Set(s)

4.1 Population Definitions

In the unforeseen circumstance of a protocol deviation (e.g., 20G PIVC instead of 22G PIVC; blood was collected into 6mL vacutainer before 2mL for a specific participant), the data will be analyzed "as treated" - that is, data will be analyzed as the participant's actual received intervention. However, in the unforeseen circumstance of a protocol deviation whereby a participant receives the wrong intervention (e.g., two different gauge catheters; two 20G catheters of the same length), they will be treated as per protocol (PP) and thus their data will be excluded from the study because paired comparison of catheter length will not be possible.

5 Statistical Analysis/Calculations

5.1 Derived Variables

Below is a list of variables that require calculation or transformation of data that will be used for derived outcomes. Any variables that are not listed below do not have derived outcomes.

5.1.1 Haemolysis: Quantification and frequency of occurrence

To quantify cfHb, whole blood collected and anticoagulated with Ethylenediaminetetraacetic acid (EDTA), will be centrifuged at 1200 x g for 10 min. The top half of the supernatant will be added to 0.01% Na_2CO_3 (1:6) and the absorbance of each sample will be measured at 380, 415 and 450 nm using a spectrophotometer (MultiSkan GO, Thermo Fisher Scientific; MA, USA). The cfHb will subsequently be calculated from these absorbances using the Harboe method 45, as described in Equation 1.

$$\text{cfHb}\left(\frac{\text{mg}}{\text{dL}}\right) = \left(\frac{167.2\text{Abs}_{415} - 83.6\text{Abs}_{450} - 83.6\text{Abs}_{380}}{10}\right) \times \frac{1}{\text{dilution in } Na_2CO_3} \quad (1)$$

Additionally, an automated biochemistry analyzer (AU480, Beckman Coulter, USA) will be employed for a clinical measurement of haemolysis and assessing the frequency of cfHb above a threshold of 50 mg/dL. The accuracy of the device is not sensitive to measurements below 50 mg/dL. Lastly, visual assessment of haemolysis will be checked, and photographs taken of each sample.

5.1.2 Dominant arm

The identification of the dominant will be performed for each subject crossing information from the VENIPUNCTURE CRF questions "Arm Venipuncture Performed from?" and "Was this the Non-Dominant Arm?", available in the variables DELOC and DENDARM, respectively, from the table VPVP.

5.1.3 Blood draw fill time

The blood draw fill time (seconds) will be calculated manually using a stopwatch - from connection to blood reaching predetermined fill line.

5.1.4 Intravenous thrombus

The presence of an intravenous thrombus (mural, at tip) will be ascertained using ultrasound.

5.1.5 Vessel diameter, Catheter to vein ratio

The vessel diameter, and C/V ratio (Catheter to vein ratio) will be derived from the mean average of three cross-sectional, B-mode scans to be taken with the indwelling PIVC in view. The vessel diameter

will be calculated from the horizontal axis using the internal calculations of the ultrasound. The data will be reported as the average of the values taken from three images. The catheter diameter will be derived from the device specifications, where catheter outer diameter is reported to be 0.90 mm and 1.10 mm, respectively for 22G and 20G catheters.

5.1.6 Blood flow velocity

The blood flow velocity calculations (i.e. maximum and mean velocity of 5 seconds of data) will be derived from the area underneath the velocity spectrum boundary using the internal measurement tool of the ultrasound.

5.1.7 Flush pressure profile and duration of flush

The flush pressure profile (i.e. duration and peak pressure) will be derived from the pressure trace from a 3 to 10 mL saline flush performed upon first accessing the device at each time point indicated in Table 2.7.1. Pressure (P) will be recorded prior to commencement of the flush and this will be defined as "baseline" pressure. Commencement of the flush will induce a spike in positive pressure, and this will be defined as "time point zero" (t_0). The time point at which the spike in positive pressure returns to baseline will indicate completion of the flush and will be defined as the "completion time point" (t_c). Subsequently, the duration of the flush will be derived by subtracting time point zero from the completion time point, as described in Equation 2.

$$\text{flush duration} = t_c - t_0 \tag{2}$$

Alternatively, the duration of the flush could be reduced to the time between the max pressure and the completion time point, as described in Equation 3.

$$\text{alternative flush duration} = t_{max} - t_0 \tag{3}$$

The pressure reading with the maximal value between the two time points will be recorded as the peak pressure, defined as in Equation 4.

$$\text{flush peak pressure} = \max_{t_0<t<t_c} P(t) \tag{4}$$

5.2 Analysis Methods

The following section defines hypothesis that will be tested. However, given the feasibility nature of the study no acceptance criteria were defined and estimating absolute effects and statistical significance of difference between device configuration is of similar importance.

5.2.1 Statistical Analysis of Primary Endpoint

5.2.1.1 Indwell Time

It is hypothesized that:

- PIVC indwell time will be greater for longer catheters
- PIVC indwell time will be greater for catheters of smaller gauge (larger bore)

In order to test these hypotheses, catheter indwell time will be assessed using survival analysis, including:

- Kaplan-Meier survival curves including Log-Rank test p-value
- Cox Proportional Hazards Model with Hazard Ratios for each device vs. default device condition (BD Nexiva 20G x 1 inch) and associated 95% Confidence Intervals. Effect of the following covariates will be investigated: gender, age, BMI and dominant arm.

Main analysis will be performed stratified by device, depending on the results pooled analyses by gauge or by catheter length might be performed. An example of the Kaplan-Meier curve and associated metrics is provided in Appendix B by Figure B.1.1. An example of the Hazard Ratios extracted from the Cox Proportional Hazards models is provided in Appendix A by Table A.4.2.

For the purpose of this survival analysis, device failure (inability to flush or draw blood, see section 6.6) will be identified as follows:

- Blood Draw: Variables DEBLDCS equal to "N" and DEBLDRS equal to "N" from table INBCINBC
- Flush: Variables DEFLSSU equal to "N" and DEFLSRS equal to "N" from table INFL

Failure can occur during any of the 7 repeats of the blood draw (for either tube volumes) or flush processes, as highlighted in orange on Table 2.7.1, for right or left arm, per randomization schedule. Date-time of failure is then given by the aggregation of variables DEDTN & DEFTM, from tables INBCINBC or INFL, respectively for blood draw or flush.

Additional Indwell Time summary statistics and graphical representation will be provided as represented in Appendix A by Table A.4.1 and in Appendix B by Figure B.2.1, respectively.

5.2.1.2 Additional Description of Failure Modes

Failure mode counts will be summarized overall, per device, per day and per device per day, as represented in Appendix A by Tables A.5.1, A.5.2, A.6.1 and A.6.2, respectively. A list of the failure modes available in the free form text field describing the "Other" category will be provided. Companion bar plots will be generated for each of these tables.

Note: It is possible that despite a failure having been observed during a 2mL, a draw was attempted at 6mL, such situation would result in failures being counted twice. To avoid this, any failure information with a time stamp ulterior to the time stamp associated with the first failure record will be discarded from the data used to generate the principal tables summarizing the count of failure modes. A separate table will included providing counts of consecutive failures (defined as a failure occurring in a 6mL draw when a failure has already been observed for the immediately preceding 2mL).

5.2.1.3 Additional Description of Failure Remediation

Failure remediation counts, which steps are described in the PIVC rescue decision trees for flush and aspiration procedures represented in Appendix D by Figures D.1.1 and D.1.2, will be summarized for each step overall and per device per day, as represented in Appendix A by Tables A.7.1 and A.7.2, respectively.

5.2.2 Statistical Analysis of Secondary Endpoints

5.2.2.1 Haemolysis

It is hypothesized that:

- The cfHb concentrations observed in blood samples (all vacutainers, at all timepoints) collected from shorter catheters will be greater than that observed in longer catheters.

- The cfHb observed in blood samples (all vacutainers, at all timepoints) collected from catheters with a larger gauge (smaller bore) will be greater than blood collected from smaller gauge (greater bore).
- The cfHb observed in blood samples (all catheters) collected into greater volume vacutainers will be greater than blood collected into smaller volume vacutainers.

Haemolysis will be assessed through:

1. Quantification of average cfHb concentrations measured at each time point listed in red in Table 2.7.1. A linear mixed effect model will be used with cfHb as response and subject as random effect. Time, gauge, length, vacutainer volume and baseline (at D1.2) cfHb (2ml, 6ml measures will be used as separate continuous variables and will be retained in the model if significant) will be fixed effects. An example of the summary statistics table and associated graphical representation are provided in Appendix A by Table A.10.2 and in Appendix B by Figure B.3.1, respectively.
2. Rate of occurrence measured using the results of the cfHb concentrations at each time point listed in red in Table 2.7.1. Samples will be considered positive for haemolysis for cfHb concentration $\geq$ 50mg/dL[1]. A logistic mixed effect model will be used with haemolysis occurrence as response and subject as random effect. Time, gauge, length, vacutainer volume and baseline (at D1.2) cfHb will be fixed effects. Tables summarizing occurrence rates per device per time point and associated graphical representation will be similar to the one provided for rate of occurrence measured using the results of the AU480 analysis (see next item) in Appendix A by Table A.10.2 and in Appendix B by Figures B.4.1 and B.4.2, respectively. Contrast based multiple comparisons will be used to compare haemolysis rate between conditions (between gauge, between length) at each timepoint.
3. Rate of occurrence measured using the results of the AU480 Analysis at each time point listed in red in Table 2.7.1. Samples will be considered positive for haemolysis for AU480 output of + (50-99mg/dL), ++ (100-199mg/dL), +++ (200-299mg/dL), ++++ (300-500mg/dL) and +++++ (>500mg/dL), i.e. anything different from N (<50mg/dL)[2]. A logistic mixed effect model will be used with haemolysis occurrence as response and subject as random effect. Time, gauge, length, vacutainer volume and baseline (at D1.2) cfHb will be fixed effects. Examples of the table summarizing occurrence rates per device per time point and associated graphical representation are provided in Appendix A by Table A.10.2 and in Appendix B by Figures B.4.1 and B.4.2, respectively. Contrast based multiple comparisons will be used to compare haemolysis rate between conditions (between gauge, between length) at each timepoint.
4. Rate of occurrence measured using the results of the visual assessment at each time point listed in red in Table 2.7.1. Samples will be considered positive for haemolysis for visual values $\geq$ 50mg/dL, as shown on the reference chart. A logistic mixed effect model will be used with visually observed haemolysis occurrence as response and subject as random effect. Time, gauge, length, Vacutainer tube volume and baseline (at D1.2) cfHb will be fixed effects. An example of the table summarizing occurrence rates per device per time point is provided in Appendix A by Table A.10.2. Graphical representation will be similar to the ones given as example for the AU480 analysis. Contrast based multiple comparisons will be used to compare haemolysis rate between conditions (between gauge, between length) at each timepoint.

In each case, i.e. for cfHb, AU480 and visual assessment, modeling will be preceded by an assessment of the importance of potential covariates using the Boruta algorithm. The covariates of interest will include,

[1] A separate assessment of the relationship between the cfHb and AU480 measurements will be performed in order to check the validity of this threshold, which could be modified upon review of these results.

[2] A separate assessment of the relationship between the cfHb and AU480 measurements will be performed in order to check the validity of this threshold, which could be modified upon review of these results.

but will not be limited to:

- Presence of thrombus
- Size of thrombus
- Proximity of thrombus to tip of catheter
- Draw rate
- Screening Blood Testing (as provided by Blood Testing CRF)
  - Coagulation Panel: PT & aPTT
  - Platelet Aggregometry: ADP, TRAP & Collagen Induced Maximal Amplitude
  - Blood Screening: Blood Glucose & Triglycerides
  - Liver Panel: ALT Average Measurement & AST Average Measurement

The significance of the most important features will be assessed by inclusion in the corresponding models and only significant covariates will be retained in the final model.

5.2.2.2 Blood draw fill time

It is hypothesized that:

- The blood draw duration observed for blood samples (all vacutainers, at all timepoints) collected from shorter catheters will be decreased when compared to longer catheters of the same gauge.
- The blood draw duration observed for blood samples (all vacutainers, at all timepoints) collected from smaller gauge (larger bore) catheters will be decreased when compared to larger gauge (smaller bore) catheters of the same length, over time.
- The blood draw duration observed for blood samples (all catheters, at all timepoints) collected into greater volume vacutainers will be increased when compared to smaller volume vacutainers.

A linear mixed effect model will be used with blood draw fill time as response and subject as random effect. Time, device configuration (gauge, length and their interaction), Vacutainer tube volume and baseline (at D1.2) blood draw fill time will be fixed effects. Contrast based multiple comparisons will be used to compare blood draw fill time between conditions (between gauge, between length) at each timepoint. Example tables for summary statistics (overall and per time point for each Vacutainer tube volume are given in the Appendix section by Table A.9.1 and Table A.9.2, respectively. Graphical representations of distribution of blood draw time per device is provided in Figure B.5.1 and of average blood draw time is shown in the Appendix section by Figure B.5.3. Example tables for ANOVA tables (Table A.9.3) and multiple comparisons (Table A.9.4) can be found in the Appendix A

5.2.2.3 Relationship between catheter blood draw patency indwell time and presence of intra/extravenous thrombi, thrombus length, thrombus type catheter angle/tip location *in situ*, catheter length in vessel, vein depth from skin surface, C/V ratio, and vessel anatomy

Relationship, if any, will be assessed through the computation of:

1. Summary statistics stratified by indwell time considered as a discrete variable (0, 6, 24, 30, 48, 54, 72 hours)
2. Scatter plot showing time between initial Thrombus observation to time of removal per Device Configuration
3. Bar plot showing percentage of thrombus for each time point per device configuration
4. Scatter plot showing thrombus length as a function of time grouped by device configuration
5. Relationship between flush technique and presence of Thrombus
6. Summary statistics and boxplot showing time between time of initial thrombus observation and device removal per device configuration

7. Importance of covariates will be computed with Boruta algorithm with a survival random forest model (an example output from the algorithm is provided in the Appendix by Figure B.7.1).
8. Test of predictive performance for the most important features (confirmed by the Boruta algorithm) using a leave-one-out strategy

In addition to the variables used in the primary endpoint survival model (device gauge and length), investigated baseline characteristics will be:

- Venous thrombosis
- Thrombus Length
- Thrombus Type
- Angles of insertion (Acute Inferior and Superior)
- Catheter to vein (C/V) ratio
- Catheter length in vessel
- Presence of side branches and/or intravenous valves
- Age
- Gender
- Height
- Weight
- BMI
- Dominant arm
- Medical history questionnaire responses
- Exploratory endpoints:
  - Vein collapse
  - Phlebitis
  - Dislodgement
  - Extravasation

  item Screening Blood Testing (as provided by Blood Testing CRF)
  - Coagulation Panel: PT & aPTT
  - Platelet Aggregometry: ADP, TRAP & Collagen Induced Maximal Amplitude
  - Blood Screening: Blood Glucose & Triglycerides
  - Liver Panel: ALT Average Measurement & AST Average Measurement

The Boruta algorithm does not require specific formatting and generally works well with continuous and categorical variables. In some cases, it might be interesting to move from continuous format to a categorical one (e.g. age) depending on the final analysis. Categorization rules will be detailed whenever performed.

5.2.2.4 Evaluation of changes in vessel dimensions, PIVC position (insertion angle and *in situ* tip position), and haemodynamics from baseline throughout indwell time

These will be evaluated using:

- C/V ratio
- Catheter Length in Vessel (mm)
- Catheter Insertion Angle - acute inferior border angle (deg)
- Catheter Insertion Angle - acute superior border angle (deg)
- Blood Draw Time (sec)
- Blood Flow Velocity (cm/sec)
- *In situ* tip position (Mid-Stream & Wall Contact)

For each of these characteristics, summary statistics by indwell time considered as a discrete variable (0, 6, 24, 30, 48, 54, 72 hours) and line and bar plots will be generated on average for continuous and by proportion for categorical responses, respectively.

Line plots will be similar to the example provided for cfHb in Figure B.3.2 and bar plots will be similar to the example provided for Haemolysis occurrence in Figure B.4.1, both represented in Appendix B.

Mixed effect models will be used with corresponding response and subject as random effect. Time, gauge, length, Vacutainer tube volume and baseline measurement of response will be fixed effects. Depending on the type of the response variable, the models will be:

- Linear: C/V ratio, catheter length, catheter insertion angles and blood flow velocity
- Logistic: Tip positions

Depending on model results, contrast based multiple comparisons will be used to compare means between conditions (between gauge, between length) at each timepoint. Results will be provided in Tables similar to the example given for Blood Draw Fill time in Tables A.9.3 and A.9.4, as can be found in the Appendix A.

The relationship between C/V ratio and Blood Draw Time as well as between C/V ratio and Blood Flow Velocity will be investigate using relevant graphical representation (scatter plots) and measure of association.

5.2.3 Statistical Analysis of Exploratory Endpoints

5.2.3.1 Incidence of complications prompting device removal

Assessment of the incidence of reasons for removal, device handling descriptors and complication prompting device removal will include assessment of the frequency of occurrence of the following events:

- Reasons for removal:
  - End of study
  - Accidental Dislodgement
  - Flush Failure
  - Blood Draw Failure
  - Adverse Event
- Device handling descriptors:
  - Failure modes for Flush/Draw (2/6mL) by Device configuration
  - Success of specific remediation steps
  - Remediation occurrence rate by day and percentage of success
- Vein collapse
- Phlebitis
- Presence of Venous thrombosis
- Catheter Dislodgement from Vein
- Extravasation
- Accidental removal
- Catheter Dislodgement from Vein

For each of these characteristics, summary statistics by indwell time considered as a discrete variable (0, 6, 24, 30, 48, 54, 72 hours) and longitudinal line and bar plots will be generated on average for continuous and by proportion for categorical responses, respectively.

Lineplots will be similar to the example provided for cfHb in Figure B.3.2 and bar plots will be similar to the example provided for Haemolysis occurrence in Figure B.4.1, both represented in Appendix B.

Relationship between the occurrence of these events will be investigated using complementary approaches:

- Predictive Power over time (similar to Kramer's V but no need to transform variables)
- Boruta algorithm with a survival random forest model (an example output from the algorithm is provided in the Appendix by Figure B.7.1) where the variables coding for these events will be predictors.
- Boruta algorithm applied at each time point with failure up to current time point as response. A graphical representation of feature importance vs time will be generated similar to the one provided in the Appendix by Figure B.7.2
- Kramer's V evaluated at each time point and represented as a function of time (which will require categorization of continuous variables, to be performed *ad hoc*). A graphical representation of pairwise feature association Kramer's V vs time, similar to the one provided for the Boruta algorithm output represented in he Appendix by Figure B.7.2 will be provided.

Based on the outcome of these exploratory steps, models might be used to investigate further the relationship between these variables and indwell time.

5.2.3.2 Flush pressure profile

Manual flush variability will be evaluated using duration of flush and characteristics of Flush pressure profile obtained on in-line pressure measurements. They will be comprised of:

- Peak pressure
- Flush duration (sec.)

For each of these characteristics, summary statistics by indwell time considered as a discrete variable (0, 6, 24, 30, 48, 54, 72 hours) and longitudinal line and bar plots will be generated on average for continuous and by proportion for categorical responses, respectively.

Lineplots will be similar to the example provided for cfHb in Figure B.3.2 and bar plots will be similar to the example provided for Haemolysis occurrence in Figure B.4.1, both represented in Appendix B.

Relationship between the occurrence of these events will be investigated using the Boruta algorithm with a survival random forest model (an example output from the algorithm is provided in the Appendix by Figure B.7.1) where the variables coding for these events will be predictors.

Based on the outcome of the Boruta algorithm, models might be used to investigate further the relationship between these variables and indwell time.

5.2.4 General Considerations

- For categorical data, count and percentage with 95% confidence interval will be calculated.
- For continuous data, average, standard error, 95% confidence interval, median, inter-quartiles, minimum and maximum will be provided.
- p-values less than 0.05 will be considered statistically significant. Multiple comparisons adjustments (Tukey's or Sydak's) will be made when appropriate
- Importance of factors/variables might be evaluated using machine learning tools such as the Boruta algorithm (random forest all-relevant approach)

- Whenever possible, effects of the following covariates will be investigated: gender, age and BMI
- Initially, all factors/variables will be included into the model as well as any two-way/three-way interactions.
- Variables or interactions which are not significant (p-value < 0.05) will be removed from the final model. Models adjusted with significant effects (and significant interactions if any) will be used for analysis whenever possible.
- Use of models will be preferred to non-parametric tests whenever possible.
- Residual plots for each model will be drawn and reviewed to ensure there are no systematic patterns.
- Transformation of response and/or explanatory variables will be investigated whenever modeling assumptions are not satisfied.

5.2.5 Approaches and Analyses for Missing Data and Other Data Issues

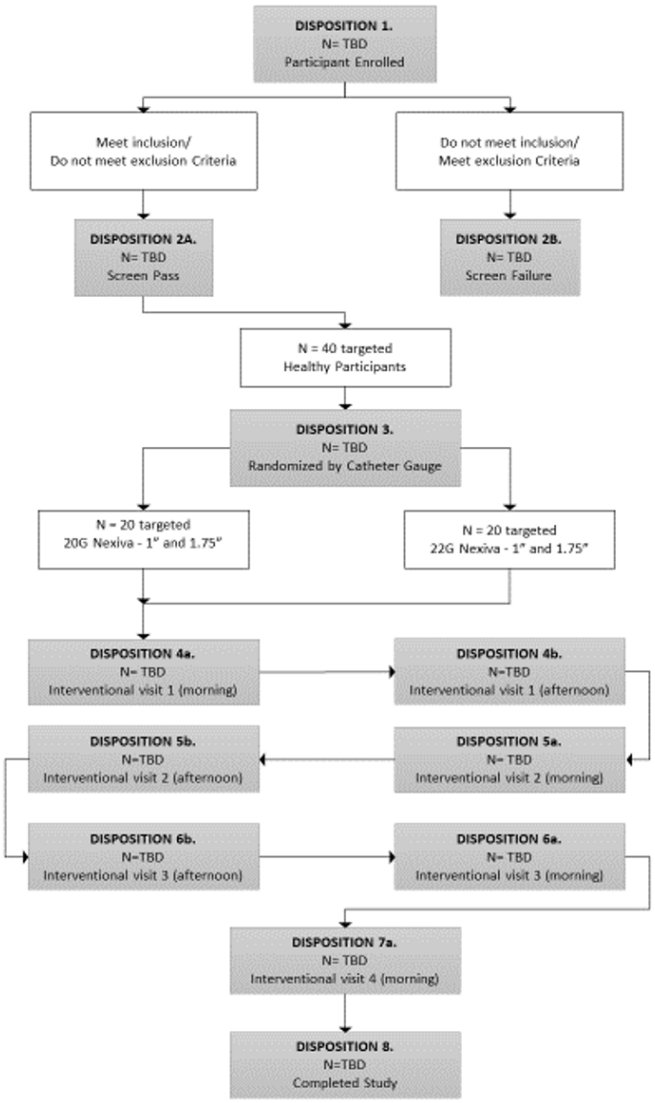
Missing data will not be imputed and will be considered missing for data analysis, resulting in a possible reduced sample size.

6 Summary of General Study Data

6.1 Subject Disposition

Participants will be provided the PISCF and once informed, written consent is provided they will be enrolled into the study. Participants will then be screened to ensure they meet the inclusion criteria and do not meet any of the exclusion criteria. Subsequently, participants who are identified as suitable for the study will be provided a unique participant code. The number of participants enrolled and those that failed screening will be recorded. For those that participate in the study, the stage that they reach will also be recorded (e.g., interventional visit 2, as depicted in Figure 6.1.1). For those that participate in the study and drop out, individual responses will be asked to be provided and recorded. Population membership (ITT, PP, etc.) is provided in section 4.1.

Figure 6.1.1: Skeleton flow diagram depicting participant disposition



6.2 Protocol Deviations

Specific protocol deviations are listed below and categorized as either a major deviation (i.e., data to be excluded) or minor (i.e., data to be included).

6.2.1 Major deviations

- **Failure to attend:** If a participant fails to attend two subsequent visits (e.g. interventional visits 2 & 3), the individual data collected from the participant will be excluded.
- **Suspicion of tampering:** If it is suspected that the participant has tampered with their PIVCs, as evidenced by breakage of the anti-tampering device, leakage from the extension, perforated dressing the data collected from the participant will be excluded.
- **Insertion of alternate gauge PIVCs:** Data will be excluded from participants where, in the unanticipated circumstance, a 20G PIVC has been inserted into one arm (e.g., left) of the participant and a 22G PIVC has been inserted into the other arm (e.g., right). Participants will be asked to re-enroll and re-consent after a period of 2 weeks.
- **Insertion of identical length PIVCs:** Data will be excluded from participants where, in the unanticipated circumstance, two PIVCs of the same length are inserted into the participant regardless of the gauge. Participants will be asked to re-enroll and re-consent after a period of 2 weeks.
- **Contraction of a common cold/respiratory infection:** If a participant contracts a common cold/respiratory infection during their interventional visit, the individual data collected from that participant will be excluded and they will be removed from the study.

6.2.2 Minor deviations

- **Incorrect order for collection of blood:** The order in which blood is collected into two alternate size vacutainers (2mL and 6 mL) will be randomized. In the unanticipated circumstance whereby the order of blood collection is incorrect, the data will be included and analyzed "as treated".
- **Incorrect order for PIVC insertion:** The order in which the PIVCs are inserted into the arm will be randomized. In the unanticipated circumstance whereby the order of PIVC insertion is incorrect, the data will be included and analyzed "as treated".
- **Incorrect allocation of PIVC length:** The alternate PIVC lengths will be randomized to the participants arms. In the unanticipated circumstance whereby allocation of PIVC length is incorrect (e.g., the 20G 1.0 inch PIVC is inserted into the participant's right arm when it was intended for the participant's left arm), the data will be included and analyzed "as treated".

6.3 Demographics and Baseline Variables

Demographic variables will include all medical history questionnaire responses, and each of the following variables at time of intervention:

- Age
- Height
- Weight
- Resting blood pressure
- Gender
- BMI
- Menstrual cycle phase (women only)

Table A.1.1 provides an example of demographic variables summary table, per study group and overall.

Baseline variables will include all sonographic data prior to PIVC insertion and cfHb collected via

venipuncture. Tables A.3.1 and A.3.2 provide examples of baseline variables summary table, per study group and overall, including blood analysis.

6.4 Concurrent Illnesses and Medical Conditions

This study does not aim to recruit individuals with current illnesses. However, in the opinion of the primary investigator and or associated medical opinion, a participant with specific conditions that may not affect blood coagulation and bleeding risk may be considered for inclusion. A list of some illnesses and medical conditions that would result in exclusion and/or may be considered acceptable are indicated below. Please note, specific coding for medical conditions is based upon the International Classification of Diseases (ICD version 11, https://icd.who.int/browse11/l-m/en). Searching the parent classification will provide examples of specific conditions. For brevity, we have provided only codes and descriptions for ICD-11_03 (Disease of the blood or blood-forming organs).

Table 6.4.1: List of medical conditions that will exclude participants from participating in this trial

Parent Classification	Code/s	Description
ICD-11_01	—	Any and all infections will exclude volunteers from participating
ICD-11_02	—	Any and all neoplasms will exclude volunteers from participating
ICD-11_03 Disease of the blood or blood-forming organs	3B10	Hereditary factor VIII deficiency
	3B11	Hereditary factor IX deficiency
	3B12	Von Willebrand disease
	3B13	Haemophilia C
	3B14	Other inherited coagulation factor deficiency with bleeding tendency
	3B15	Inherited coagulation factor deficiency without bleeding tendency
	3B20	Disseminated intravascular coagulation
	3B21	Haemorrhagic disorder due to circulating anticoagulants and coagulation factors
	3B22	Acquired haemophilia
	3B50	Inherited fibrinolytic defects
	3B51	Acquired fibrinolytic defects
	3B60	Non-thrombocytopenic purpura
	3B61	Thrombophilia
	3B62	Qualitative platelet defects
	3B63	Thrombocytosis
	3B64	Thrombocytopenia
	3B65	Thrombotic microangiopathy, not elsewhere classified
	3B80	Congenital disorders of spleen
	3B81	Acquired disorders of spleen
ICD-11_04	—	Any and all diseases of the immune system will exclude volunteers from participating
ICD-11_05	—	Any and all endocrine, nutritional or metabolic diseases will exclude volunteers from participating
ICD-11_06	—	Specifically, the following codes will be excluded: 6A20-6A25, 6A40, 6A40, 6A60-6A62, 6A71-6A73, 6B01-6B03, 6B06, 6B23, 6B25, 6B40-6B43, 6B61-6B66, 6B80-6B85, 6C00, 6C01, 6C20, 6C21, 6C40-6C4H, 6C50, 6C51, 6C70-6C73, 6C90, 6C91, 6D30-6D36, 6D50, 6D51, 6D70-6D72, 6D80-6D86, 6E40, 6E60-6E-69. The inclusion of participants with mental, behavioural or neurodevelopmental disorders not specifically listed here (including sub-classifications) will be decided by the PI on a 'case-by-case' basis.
ICD-11_07	—	Any and all sleep-wake disorders will exclude volunteers from participating
ICD-11_08	—	Specifically, the following codes will be excluded: 8A00-8A07, 8A20-8A23, 8A40-8A46, 8A60-8A68, 8B00-8B03, 8B10, 8B11, 8B20-8B26, 8B40-8B44, 8B60-8B62, 8B85, 8B86, 8B88, 8B90-8B94, 8C00-8C03, 8C10-8C12, 8C20, 8C21, 8C60-8C62, 8C70-8C78, 8C80-8C84, 8D20-8D23, 8D40-8D44, 8D60-8D68, 8D80-8D8C, 8E00-8E03, 8E20-8E22, 8E40-8E4A, 8E60-8E66. The inclusion of participants with diseases of the nervous system not specifically listed here (including sub-classifications) will be decided by the PI on a 'case-by-case' basis.
ICD-11_09	—	Specifically, the following codes will be excluded: 9A01, 9A02, 9A10, 9A11, 9A21-9A23, 9A60, 9A61, 9A71, 9A73, 9A76, 9A80-9A83, 9A91, 9A96, 9B50, 9B51, 9B63, 9B65, 9B66, 9B71-9B78, 9B82, 9B83, 9C20-9C22, 9C60, 9C61, 9D20-9D25. The inclusion of participants with diseases of the visual system not specifically listed here (including sub-classifications) will be decided by the PI on a 'case-by-case' basis.
ICD-11_10	—	Specifically, the following codes will be excluded: AA00-AA04, AA90, AA91, AB00, AB01, AB10-AB1B, AB30-AB36, AB53, AB70, AB71, AB90-AB93. The inclusion of participants with diseases of the ear or mastoid process not specifically listed here (including sub-classifications) will be decided by the PI on a 'case-by-case' basis.

ICD-11_11	—	Any and all diseases of the circulatory system will exclude volunteers from participating
ICD-11_12	—	Any and all diseases of the respiratory system will exclude volunteers from participating
ICD-11_13	—	Any and all diseases of the digestive system will exclude volunteers from participating
ICD-11_14	—	Specifically, the following codes will be excluded: EA00, EA10-EA12, EA20, EA50, EA51, EA60, EA89, EB00, EB04, EB05, EB10-EB31, EB40-EB44, EB50, EB51, EB61, EB90, EC20, EC30-EC33, EC40, EC90-EC92, ED00-ED02, ED30, ED50-ED56, ED60, ED62, EE00, EE02, EE20, EE21, EE40, EE41, EE50, EE70, EE80, EE81, EE90, EE91, EF20, EF30, EF31, EF40, EF50, EF60, EG00-EG02, EH77, EH90-EH93, EJ10, EJ30, EJ70, EJ71, EK00-EK02, EK10-EK12, EK70, EL10, EL50-EL54, EL60-EL62, EL70-EL73, EL80. The inclusion of participants with diseases of the skin not specifically listed here (including sub-classifications) will be decided by the PI on a 'case-by-case' basis.
ICD-11_15	—	Specifically, the following codes will be excluded: FA10-FA13, FA-FA27, FA36, FA70-FA72, FA80-FA85, FA90-FA92, FB00, FB10, FB30-FB33, FB40-FB43, FB50-FB56, FB80-FB86, FC01. The inclusion of participants with diseases of the musculoskeletal system or connective tissue not specifically listed here (including sub-classifications) will be decided by the PI on a 'case-by-case' basis.
ICD-11_16	—	Specifically, the following codes will be excluded: GA00-GA07, GA20-GA23, GA30, GA91, GB07, GB08, GB21, GB23, GB40-GB42, GB50-GB59, GB60, GB61, GB70, GB71, GB80-GB83, GB90, GC00-GC08. The inclusion of participants with diseases of the genitourinary system not specifically listed here (including sub-classifications) will be decided by the PI on a 'case-by-case' basis.
ICD-11_17	—	None to consider
ICD-11_18	—	Any and all conditions associated with pregnancy, childbirth or puerpium will exclude volunteers from participating
ICD-11_19	—	Not applicable
ICD-11_20	—	Specifically, the following codes will be excluded: LA00-LA07, LA70-LA77, LA80-LA8G, LA90, LB00, LB20-LB22, LB30, LB31, LB72-LB74, LB90-LB92, LB96, LB96, LB99, LC00-LC02, LC20, LC50-LC52, LC60, LC80, LD20, LD23, LD24, LD26-LD29, LD2C-LD2H, LD40-LD47, LD90. The inclusion of participants with developmental anomalies not specifically listed here (including sub-classifications) will be decided by the PI on a 'case-by-case' basis.
ICD-11_21	—	Any and all symptoms, signs, or clinical findings not elsewhere classified will exclude volunteers from participating
ICD-11_22	—	Any injury, poisoning or certain other consequences of external causes except for NC50 and ND10, will exclude volunteers from participating
ICD-11_23	—	Not applicable

6.5 Prior and Concurrent Medications

This study does not aim to recruit individuals who are regularly taking medications. However, in the opinion of the primary investigator and or associated medical opinion, a participant taking medications that may not affect blood coagulation and bleeding risk may be considered for inclusion. A list of some drug classes and example drugs that would result in exclusion and/or may be considered acceptable are indicated below.

Please note, specific coding for drugs, based upon the ATC/DDD Index 2020 (https://www.whocc.no/atc_ddd_index/) are listed to provide some specific examples. Searching the drug classes can provide specific examples. Specific examples of drugs within the B01A Antithrombotic Agents class are given for example.

Table 6.5.1: List of current drug use resulting in exclusion (1/2)

Class	Parent Classification	Drug Class	Drug Class Description	Drug	Description
B01 Antithrombotic Agents	B01A Antithrombotic Agents	B01AA	Vitamin K Antagonists	B01AA03	Warfarin
		B01AB	Heparin Group	B01AB01	Heparin
		B01AC	Platelet Aggregation Inhibitors Excl. Heparin	B01AC04	Clopidogrel
				B01AC06	Acetylsalicylic Acid
				B01AC16	Eptifibatide
				B01AC24	Ticagrelor
		B01AD	Enzymes	B01AD01	Streptokinase

		B01AD04	Urokinase
		B01AD11	Tenecteplase
B01AE	Direct Thrombin Inhibitors	B01AE06	Bivalirudin
B01AF	Direct Factor Xa Inhibitors	B01AF01	Rivaroxaban
B01AX	Other Antithrombotic Agents	B01AX01	Defibrotide

Table 6.5.2: List of current drug use resulting in exclusion (2/2)

Class	Parent Classification	Drug Class	Drug Class Description
J01	J01A	-	
Antibacterials for Systemic Use	Tetracyclines		
	J01B	-	
	Amphenicols		
	J01C	-	
	Beta-lactam Antibacterials, Penicillins		
	J01D	-	
	Other Beta-lactam Antibacterials		
	J01E	-	
	Sulphonamides and Trimethoprim		
	J01F	-	
	Macrolides, Lincosamides and Streptogramins		
	J01G	-	
	Aminoglycoside Antibacterials		
	J01M	-	
	Quinoline Antibacterials		
	J01R	-	
	Combinations of Antibacterials		
	J01X	-	
	Other Antibacterials		
J02	J02A	J02AA	Antibiotics
Antimycotics for systemic Use	Antimycotics for Systemic Use	J02AB	Imidazole Derivatives
		J02AC	Triazole Derivatives
		J02AX	Other Antimycotics for Systemic Use
J04	J04A	-	
Antimycobacterials	Drugs for Treatment of Tuberculosis		
	J04B	-	
	Drugs for Treatment of Lepra		
J05	J05A	-	
Antivirals for Systemic Use	Direct Acting Antivirals		
J06	J06A	-	
Immune Sera and Immunoglobulins	Immune Sera		
	J06B	-	
	Immunoglobulins		
J07	J07A	-	
Vaccines	Bacterial Vaccines		
	J07B	-	
	Viral Vaccines		
	J07C	-	
	Plant Alkaloids		
	J07X	-	
	Other Vaccines		
L01	L01A	-	
Antineoplastic and Immunomodulating Agents	Alkylating Agents		
	L01B	-	
	Antimetabolites		
	L01C	-	
	Plant Alkaloids and Other Natural Products		
	L01D	-	
	Cytotoxic Antibiotics and Related Substances		
	L01X	-	
	Other Antineoplastic Agents		
L04	L04A	L04AA	Selective Immunosupressants
Immunosupressants	Immunosupressants	L04AX	Other Immunosupressants

An example of other drug classes which may not result in exclusion, but will trigger deeper investigation

for their effect on platelet function/thrombosis is provided in Table 6.5.3.

Table 6.5.3: List of current drug use trigerring deeper investigation for their effect on platelet function/thrombosis

Class	Parent Classification	Drug Class	Drug Class Description
G03	G03A	G03AA	Progestogens and Estrogens, fixed combinations
Sex Hormones and Modulators of the Genital System	Hormonal Contraceptives for Systemic Use		
		G03AB	Progestogens and Estrogens, sequential preparations
		G03AC	Progestogens
N02	N02A	N02AA	Natural Opium Alkaloids
Analgesics	Opioids	N02AB	Phenylpiperidine Derivatives
		N02AC	Diphenylpropylamine Derivatives
		N02AD	Benzomorphan Derivatives
		N02AE	Oripavine Derivatives
		N02AF	Morphinan Derivatives
		N02AG	Opioids in Combination with Antispasmodics
		N02AJ	Opioids in Combination with Non-opioid Analgesics
		N02AX	Other Opioids
	N02B	N02BA	Salicylic Acid and Derivatives
	Other Analgesics and Antipyretics	N02BB	Pyrazolones
		N02BE	Anilides
	N02C	N02CA	Ergot Alkaloids
	Antimigraine Preparations	N02CB	Corticosteroid Derivatives
		N02CC	Selective Serotonin (5HT1) Agonists
		N02CD	Calcitonin Gene-related Peptide (CGRP) Antagonists
		N02CX	Other Antimigraine Preparations

6.6 Device Failure, Malfunctions and Defects

PIVC failure in the current study is defined as:

1. An inability to flush or collect blood through the PIVC
2. The removal of the PIVC based on medical doctor's assessment of an AE

A device rescue decision tree (see Appendix 16.5 of the study protocol) will be utilized to identify if the PIVC has failed.

7 Safety Analysis

Sufficient detail on summarizing safety data, e.g., information on severity, expectedness, and causality; details of how adverse events are coded or categorized; how adverse event data will be analyzed is provided in a separate document (i.e., a safety management plan).

8 Interim Analysis Plan

No interim analysis has been planned.

9 References

[1] R Core Team. *R: A Language and Environment for Statistical Computing*. R Foundation for Statistical Computing, Vienna, Austria, 2016. URL https://www.R-project.org/.

[2] Miron B. Kursa and Witold R. Rudnicki. Feature selection with the Boruta package. *Journal of Statistical Software*, 36(11):1–13, 2010. URL http://www.jstatsoft.org/v36/i11/.

10 SAP Revision History

Version Number	Rationale for Change	Section or Page Affected	Description of Change
1.0	Original SAP		

11 Appendix

A Tables

A.1 Demographics

Table A.1.1: Numerical Summary of Subjects Demographics, per Group (i.e. Gauge) and Overall

Characteristic	20G	22G	Overall
Age (years)			
Mean	42.35	39.87	41.11
95% Mean CI	37.42, 47.07	34.77, 44.98	37.51, 44.70
Median	45.15	39.45	42.15
SD	11.22	12.14	11.61
Min, Max	24.2, 56.3	23.9, 57.4	23.9, 57.4
Total Count	20	20	40
Gender			
F	11 (55.0%)	9 (45.0%)	20 (50.0%)
M	9 (45.0%)	11 (55.0%)	20 (50.0%)
Total	20	20	40
Ethnicity			
Non Hispanic / Latino	18 (90.0%)	19 (95.0%)	37 (92.5%)
Hispanic / Latino	2 (10.0%)	1 (5.0%)	3 (7.5%)
Total	20	20	40
Race			
Asian	6 (30.0%)	8 (40.0%)	14 (35.0%)
Other	7 (35.0%)	6 (30.0%)	13 (32.5%)
White / Caucasian	7 (35.0%)	6 (30.0%)	13 (32.5%)
Total	20	20	40
Height (cm)			
Mean	166.06	168.64	167.35
95% Mean CI	161.10, 171.26	163.55, 173.65	163.63, 171.10
Median	161.05	168.20	166.65
SD	12.09	11.78	11.85
Min, Max	151.2, 185.6	150.4, 188.6	150.4, 188.6
Total Count	20	20	40
Weight (kg)			
Mean	67.92	76.78	72.34
95% Mean CI	63.44, 72.27	73.23, 80.32	69.18, 75.43
Median	72.50	76.10	74.75
SD	10.41	8.34	10.34
Min, Max	52.8, 81.6	63.5, 88.7	52.8, 88.7
Total Count	20	20	40
BMI (kg/m^2)			
Mean	22.40	22.90	22.65
95% Mean CI	21.25, 23.55	21.85, 24.00	21.88, 23.45
Median	23.00	23.50	23.00
SD	2.68	2.55	2.60
Min, Max	18, 27	19, 27	18, 27
Total Count	20	20	40

A.2 Family Medical History

Table A.2.1: Numerical Summary of Familiy Medical History, per Group (i.e. Gauge) and Overall

Characteristic	20G	22G	Overall
Blood Disorder or Bleeding or Clotting Problem			
No	20 (100.0%)	18 (90.0%)	38 (95.0%)
Yes	0 (0.0%)	2 (10.0%)	2 (5.0%)
Total	20	20	40

Table A.2.1: Numerical Summary of Familiy Medical History, per Group (i.e. Gauge) and Overall continued

Characteristic	20G	22G	Overall
Cancer			
No	19 (95.0%)	19 (95.0%)	38 (95.0%)
Yes	1 (5.0%)	1 (5.0%)	2 (5.0%)
Total	20	20	40
Heart Disease			
No	20 (100.0%)	20 (100.0%)	40 (100.0%)
Yes	0 (0.0%)	0 (0.0%)	0 (0.0%)
Total	20	20	40
High Blood Pressure (Hypertension)			
No	13 (65.0%)	19 (95.0%)	32 (80.0%)
Yes	7 (35.0%)	1 (5.0%)	8 (20.0%)
Total	20	20	40
Diabetes Type 2			
No	19 (95.0%)	14 (70.0%)	33 (82.5%)
Yes	1 (5.0%)	6 (30.0%)	7 (17.5%)
Total	20	20	40

A.3 Baseline Characteristics

Table A.3.1: Numerical Summary of Baseline PIVC Characteristics, per Group (i.e. Gauge) and Overall

Characteristic	20G	22G	Overall
Tip Position Mid-Stream			
Yes	16 (80.0%)	15 (75.0%)	31 (77.5%)
No	4 (20.0%)	5 (25.0%)	9 (22.5%)
Total	20	20	40
Tip Position Well Contact			
No	16 (80.0%)	17 (85.0%)	33 (82.5%)
Yes	4 (20.0%)	3 (15.0%)	7 (17.5%)
Total	20	20	40
Blood Flow Velocity (cm/sec)			
Mean	161.94	161.86	161.90
95% Mean CI	159.06, 164.96	159.05, 164.73	159.86, 163.97
Median	160.97	162.27	161.69
SD	6.90	6.61	6.67
Min, Max	150.46, 173.71	150.97, 173.28	150.46, 173.71
Total Count	20	20	40
Catheter-to-Vein ratio			
Mean	38.70	35.92	37.31
95% Mean CI	36.95, 40.42	34.27, 37.56	36.02, 38.61
Median	38.88	35.06	36.93
SD	4.13	3.91	4.21
Min, Max	32.11, 44.91	30.23, 42.67	30.23, 44.91
Total Count	20	20	40

Table A.3.2: Numerical Summary of Baseline Venipuncture Blood Analysis, per Group (i.e. Gauge) and Overall

Tube Volume	Characteristic	20G	22G	Overall
2mL	cfHb (mg/dL)			
	Mean	199.31	200.93	200.12
	95% Mean CI	175.48, 222.22	174.31, 228.18	182.19, 218.30
	Median	201.03	199.82	199.82
	SD	53.78	64.40	58.57
	Min, Max	56.99, 324.24	111.27, 317.8	56.99, 324.24
	Total Count	20	20	40

Table A.3.2: Numerical Summary of Baseline Venipuncture Blood Analysis, per Group (i.e. Gauge) and Overall continued

Tube Volume	Characteristic	20G	22G	Overall
	Haemolysis - AU480 (Yes/No)			
	No	10 (50.0%)	10 (50.0%)	20 (50.0%)
	Yes	10 (50.0%)	10 (50.0%)	20 (50.0%)
	Total	20	20	40
	Haemolysis - Visual (Yes/No)			
	Yes	14 (70.0%)	12 (60.0%)	26 (65.0%)
	No	6 (30.0%)	8 (40.0%)	14 (35.0%)
	Total	20	20	40
	Blood Draw Fill Time (sec)			
	Mean	39.48	39.15	39.31
	95% Mean CI	37.86, 41.08	37.41, 40.86	38.10, 40.51
	Median	39.40	39.92	39.74
	SD	3.83	4.06	3.90
	Min, Max	32.77, 46.32	32.06, 46.4	32.06, 46.4
	Total Count	20	20	40
6mL	cfHb (mg/dL)			
	Mean	194.94	200.96	197.95
	95% Mean CI	174.19, 215.28	178.16, 223.07	182.86, 213.25
	Median	212.88	193.48	207.24
	SD	47.91	52.64	49.77
	Min, Max	86.01, 275.98	103.33, 311.35	86.01, 311.35
	Total Count	20	20	40
	Haemolysis - AU480 (Yes/No)			
	Yes	12 (60.0%)	9 (45.0%)	21 (52.5%)
	No	8 (40.0%)	11 (55.0%)	19 (47.5%)
	Total	20	20	40
	Haemolysis - Visual (Yes/No)			
	Yes	13 (65.0%)	13 (65.0%)	26 (65.0%)
	No	7 (35.0%)	7 (35.0%)	14 (35.0%)
	Total	20	20	40
	Blood Draw Fill Time (sec)			
	Mean	99.94	101.73	100.83
	95% Mean CI	97.33, 102.41	98.61, 105.01	98.85, 102.95
	Median	101.04	100.15	100.15
	SD	5.98	7.49	6.75
	Min, Max	86.61, 108.96	91.1, 116.4	86.61, 116.4
	Total Count	20	20	40

A.4 Indwell Time

Table A.4.1: Numerical Summary of Subjects Indwell Time in hours, per Device Configuration (Gauge and Length) and Overall

Characteristic	BD Nexiva (22G x 1 inch)	BD Nexiva (22G x 1.75 inch)	BD Nexiva (20G x 1 inch)	BD Nexiva (20G x 1.75 inch)	Overall
Indwell Time (Hours)					
Mean	44.76	55.84	59.72	69.82	57.54
95% Mean CI	36.08, 53.42	45.68, 64.78	52.74, 65.55	68.08, 71.24	53.19, 61.60
Median	42.84	66.22	64.09	72.00	66.97
SD	20.38	22.59	14.76	3.83	18.97
Min, Max	9.4, 72	0.07, 72	15.76, 72	58.6, 72	0.07, 72
Total Count	20	20	20	20	80

Table A.4.2: Proportional Hazard Ratios computed from Cox Proportional Hazards model for Indwell time

	HR(95%CI)	P(Wald's test)	P(LR-test)
device: ref.=BD Nexiva (22G x 1 inch)			0.002
BD Nexiva (22G x 1.75 inch)	0.6 (0.28,1.26)	0.175	
BD Nexiva (20G x 1 inch)	0.57 (0.27,1.2)	0.141	
BD Nexiva (20G x 1.75 inch)	0.2 (0.08,0.49)	< 0.001	

A.5 Indwell Failure Mode

Table A.5.1: Failure Modes Count Overall

Failure Mode	Flush	Draw (2mL)	Draw (6mL)
Unsecure Luer Connection	2	0	1
Locked Clamps	2	0	0
Catheter Dislodgement	5	0	0
Catheter Kinking	2	2	0
Vasospasm	0	0	0
Thrombus	24	10	7
Infiltration	2	0	0
Other	9	0	1

A list of the failure modes available in the free form text field describing the "Other" category will be provided.

Table A.5.2: Failure Modes Count Per Device Configuration

Device	Failure Mode	Flush	Draw (2mL)	Draw (6mL)
BD Nexiva (22G x 1 inch)	Luer Connection	0	0	0
	Clamp	1	0	0
	Tube Kinking	0	0	0
	Dislodgement	0	0	0
	Catheter Kinking	1	0	0
	Vasospasm	0	0	0
	Thrombus	9	2	2
	Infiltration	0	0	0
	Other	5	0	0
BD Nexiva (22G x 1.75 inch)	Luer Connection	0	0	1
	Clamp	0	0	0
	Tube Kinking	0	0	0
	Dislodgement	2	0	0
	Catheter Kinking	0	0	0
	Vasospasm	0	0	0
	Thrombus	6	1	2
	Infiltration	1	0	0
	Other	2	0	0
BD Nexiva (20G x 1 inch)	Luer Connection	1	0	0
	Clamp	1	0	0
	Tube Kinking	0	0	0
	Dislodgement	2	0	0
	Catheter Kinking	1	1	0
	Vasospasm	0	0	0
	Thrombus	7	3	3
	Infiltration	1	0	0
	Other	1	0	1
BD Nexiva (20G x 1.75 inch)	Luer Connection	1	0	0
	Clamp	0	0	0
	Tube Kinking	0	0	0
	Dislodgement	1	0	0
	Catheter Kinking	0	1	0
	Vasospasm	0	0	0
	Thrombus	2	4	0
	Infiltration	0	0	0
	Other	1	0	0

A.6 Indwell Failure Mode Per Day

Table A.6.1: Failure Modes Count Overall Per Day

Failure Mode	Day 1: Flush	Day 1: Blood Draw (2mL)	Day 1: Blood Draw (6mL)	Day 2: Flush	Day 2: Blood Draw (2mL)	Day 2: Blood Draw (6mL)	Day 3: Flush	Day 3: Blood Draw (2mL)	Day 3: Blood Draw (6mL)	Day 4: Flush	Day 4: Blood Draw (2mL)	Day 4: Blood Draw (6mL)
Luer Connection	0	0	0	0	0	0	1	0	0	1	0	1
Clamp	0	0	0	0	0	0	2	0	0	0	0	0
Tube Kinking	0	0	0	0	0	0	0	0	0	0	0	0
Dislodgement	0	0	0	0	0	0	2	0	0	3	0	0
Catheter Kinking	1	0	0	0	0	0	1	0	0	0	2	0
Vasospasm	0	0	0	0	0	0	0	0	0	0	0	0
Thrombus	2	1	1	6	2	0	9	2	2	7	5	4
Infiltration	0	0	0	0	0	0	1	0	0	1	0	0
Other	2	0	0	2	0	0	3	0	0	2	0	1

Table A.6.2: Failure Modes Count Per Device Configuration

Device	Failure Mode	Day 1: Flush	Day 1: Blood Draw (2mL)	Day 1: Blood Draw (6mL)	Day 2: Flush	Day 2: Blood Draw (2mL)	Day 2: Blood Draw (6mL)	Day 3: Flush	Day 3: Blood Draw (2mL)	Day 3: Blood Draw (6mL)	Day 4: Flush	Day 4: Blood Draw (2mL)	Day 4: Blood Draw (6mL)
BD Nexiva (22G x 1 inch)	Catheter Kinking	1	0	0	0	0	0	0	0	0	0	0	0
	Clamp	0	0	0	0	0	0	1	0	0	0	0	0
	Dislodgement	0	0	0	0	0	0	0	0	0	0	0	0
	Infiltration	0	0	0	0	0	0	0	0	0	0	0	0
	Luer Connection	0	0	0	0	0	0	0	0	0	0	0	0
	Other	2	0	0	2	0	0	1	0	0	0	0	0
	Thrombus	2	0	0	5	1	0	2	0	1	0	1	1
	Tube Kinking	0	0	0	0	0	0	0	0	0	0	0	0
	Vasospasm	0	0	0	0	0	0	0	0	0	0	0	0
BD Nexiva (22G x 1.75 inch)	Catheter Kinking	0	0	0	0	0	0	0	0	0	0	0	0
	Clamp	0	0	0	0	0	0	0	0	0	0	0	0
	Dislodgement	0	0	0	0	0	0	0	0	0	2	0	0
	Infiltration	0	0	0	0	0	0	0	0	0	1	0	0
	Luer Connection	0	0	0	0	0	0	0	0	0	0	0	1
	Other	0	0	0	0	0	0	0	0	0	2	0	0
	Thrombus	0	1	1	1	0	0	1	0	0	4	0	1
	Tube Kinking	0	0	0	0	0	0	0	0	0	0	0	0
	Vasospasm	0	0	0	0	0	0	0	0	0	0	0	0
BD Nexiva (20G x 1 inch)	Catheter Kinking	0	0	0	0	0	0	1	0	0	0	1	0
	Clamp	0	0	0	0	0	0	1	0	0	0	0	0
	Dislodgement	0	0	0	0	0	0	2	0	0	0	0	0
	Infiltration	0	0	0	0	0	0	1	0	0	0	0	0
	Luer Connection	0	0	0	0	0	0	1	0	0	0	0	0
	Other	0	0	0	0	0	0	1	0	0	0	0	1
	Thrombus	0	0	0	0	1	0	5	1	1	2	1	2
	Tube Kinking	0	0	0	0	0	0	0	0	0	0	0	0
	Vasospasm	0	0	0	0	0	0	0	0	0	0	0	0
BD Nexiva (20G x 1.75 inch)	Catheter Kinking	0	0	0	0	0	0	0	0	0	0	1	0
	Clamp	0	0	0	0	0	0	0	0	0	0	0	0
	Dislodgement	0	0	0	0	0	0	0	0	0	1	0	0
	Infiltration	0	0	0	0	0	0	0	0	0	0	0	0
	Luer Connection	0	0	0	0	0	0	0	0	0	1	0	0
	Other	0	0	0	0	0	0	1	0	0	0	0	0
	Thrombus	0	0	0	0	0	0	1	1	0	1	3	0
	Tube Kinking	0	0	0	0	0	0	0	0	0	0	0	0
	Vasospasm	0	0	0	0	0	0	0	0	0	0	0	0

A.7 Failure Remediation

Table A.7.1: Remediation Steps Count Overall

Step	Flush	Draw (2mL)	Draw (6mL)
No remediation	0	0	0
Secure Luer	0	0	0
Clamp Release	0	0	0
Tube Unkink	0	0	0
Digital Pressure	0	0	0
Dressing Replacement	0	0	0
Dressing w/Digital Pressure	0	0	0
First tourniquet	0	0	0
Tourniquet w/Digital Pressure	0	0	0
Heat Pack	0	0	0
Heat Pack w/Digital Pressure	0	0	0
Second tourniquet	0	0	0
Tourniquet w/Digital Pressure	0	0	0
Unable to Rescue	0	0	0

A similar table will be provided detailing counts per Device Configuration.

Table A.7.2: Remediation Characteristics Count per Device Configuration per Day

Device	Characteristic	Day 1	Day 2	Day 3	Day 4
BD Nexiva (22G x 1 inch)	Total Number of Attempts	0	0	0	0
	No Remediation	0	0	0	0
	Success with Remediation	0	0	0	0
	Unsuccessful with Remediation	0	0	0	0
BD Nexiva (22G x 1.75 inch)	Total Number of Attempts	0	0	0	0
	No Remediation	0	0	0	0
	Success with Remediation	0	0	0	0
	Unsuccessful with Remediation	0	0	0	0
BD Nexiva (20G x 1 inch)	Total Number of Attempts	0	0	0	0
	No Remediation	0	0	0	0
	Success with Remediation	0	0	0	0
	Unsuccessful with Remediation	0	0	0	0
BD Nexiva (20G x 1.75 inch)	Total Number of Attempts	0	0	0	0
	No Remediation	0	0	0	0
	Success with Remediation	0	0	0	0
	Unsuccessful with Remediation	0	0	0	0

A.8 Blood Analysis

Table A.8.1: Numerical Summary of Subjects Blood Analysis, for each time point, per Device Configuration (Gauge and Length) and Vacutainer tube and Overall

Time Point (hours)	Characteristic	BD Nexiva (22G x 1 inch) - 2mL	BD Nexiva (22G x 1 inch) - 6mL	BD Nexiva (22G x 1.75 inch) - 2mL	BD Nexiva (22G x 1.75 inch) - 6mL	BD Nexiva (20G x 1 inch) - 2mL	BD Nexiva (20G x 1 inch) - 6mL	BD Nexiva (20G x 1.75 inch) - 2mL	BD Nexiva (20G x 1.75 inch) - 6mL	Overall
0	cfHb (mg/dL)									
	Mean	196.10	178.14	164.49	172.33	172.62	159.97	149.22	147.86	167.59
	95% Mean CI	171.35, 219.19	158.51, 197.03	150.93, 178.84	160.06, 184.58	159.35, 186.12	143.55, 177.42	139.16, 160.00	139.67, 155.47	161.88, 173.62
	Median	195.08	180.15	155.63	167.18	162.05	157.74	152.27	151.02	160.67
	SD	55.75	45.54	32.54	28.87	31.76	39.52	24.26	18.39	38.54
	Min, Max	76.06, 303.33	97.93, 260.95	108.78, 234.07	128.96, 230.49	128.66, 228.95	103.03, 242.28	100.59, 215.9	98.15, 179.49	76.06, 303.33
	Total Count	20	20	20	20	20	20	20	20	160
	Haemolysis - AU480 (Yes/No)									
	No	12 (60.0%)	14 (70.0%)	16 (80.0%)	16 (80.0%)	14 (70.0%)	17 (85.0%)	19 (95.0%)	20 (100.0%)	128 (80.0%)
	Yes	8 (40.0%)	6 (30.0%)	4 (20.0%)	4 (20.0%)	6 (30.0%)	3 (15.0%)	1 (5.0%)	0 (0.0%)	32 (20.0%)
	Total	20	20	20	20	20	20	20	20	160
	Haemolysis - Visual (Yes/No)									
	No	6 (30.0%)	10 (50.0%)	15 (75.0%)	11 (55.0%)	12 (60.0%)	13 (65.0%)	19 (95.0%)	20 (100.0%)	106 (66.2%)
	Yes	14 (70.0%)	10 (50.0%)	5 (25.0%)	9 (45.0%)	8 (40.0%)	7 (35.0%)	1 (5.0%)	0 (0.0%)	54 (33.8%)
	Total	20	20	20	20	20	20	20	20	160
6	cfHb (mg/dL)									
	Mean	191.24	188.75	166.15	172.37	173.04	170.39	145.77	152.51	169.50
	95% Mean CI	171.53, 208.22	165.51, 209.21	150.82, 181.25	158.32, 186.25	159.51, 189.07	155.95, 184.03	137.91, 153.45	141.88, 162.78	163.72, 175.30
	Median	188.49	199.50	168.11	164.19	163.48	176.50	145.60	153.00	165.28
	SD	41.29	48.75	35.17	31.34	35.02	32.98	17.97	24.42	36.51
	Min, Max	75.26, 250.08	64.44, 276.65	96.55, 218.81	108.5, 221.35	119.11, 280.54	98.34, 215.76	115.71, 179.55	101.31, 205.98	64.44, 280.54
	Total Count	18	18	19	18	20	20	20	20	153
	Haemolysis - AU480 (Yes/No)									
	No	11 (61.1%)	9 (50.0%)	16 (84.2%)	13 (72.2%)	17 (85.0%)	16 (80.0%)	20 (100.0%)	19 (95.0%)	121 (79.1%)
	Yes	7 (38.9%)	9 (50.0%)	3 (15.8%)	5 (27.8%)	3 (15.0%)	4 (20.0%)	0 (0.0%)	1 (5.0%)	32 (20.9%)
	Total	18	18	19	18	20	20	20	20	153
	Haemolysis - Visual (Yes/No)									
	No	6 (33.3%)	5 (27.8%)	12 (63.2%)	11 (61.1%)	13 (65.0%)	10 (50.0%)	20 (100.0%)	18 (90.0%)	95 (62.1%)
	Yes	12 (66.7%)	13 (72.2%)	7 (36.8%)	7 (38.9%)	7 (35.0%)	10 (50.0%)	0 (0.0%)	2 (10.0%)	58 (37.9%)
	Total	18	18	19	18	20	20	20	20	153
24	cfHb (mg/dL)									
	Mean	167.54	189.19	171.23	171.64	152.95	163.34	143.22	155.87	163.37
	95% Mean CI	143.70, 191.58	165.61, 213.07	161.63, 180.64	156.24, 187.69	131.63, 175.36	147.13, 180.21	134.65, 151.83	145.77, 165.09	157.14, 169.70
	Median	160.38	182.91	170.18	163.25	136.96	158.61	143.07	161.72	161.40
	SD	50.25	50.21	21.05	34.06	51.48	38.17	20.33	22.85	39.02
	Min, Max	68.3, 248.91	116.04, 283.39	128.92, 208.47	116.1, 232.11	59.98, 271.69	84.58, 243.42	106.41, 179.48	106.81, 182.01	59.98, 283.39
	Total Count	16	16	18	17	20	19	20	20	146
	Haemolysis - AU480 (Yes/No)									
	No	12 (75.0%)	10 (62.5%)	16 (88.9%)	13 (76.5%)	15 (75.0%)	16 (84.2%)	20 (100.0%)	20 (100.0%)	122 (83.6%)
	Yes	4 (25.0%)	6 (37.5%)	2 (11.1%)	4 (23.5%)	5 (25.0%)	3 (15.8%)	0 (0.0%)	0 (0.0%)	24 (16.4%)
	Total	16	16	18	17	20	19	20	20	146

Table A.8.1: Numerical Summary of Subjects Blood Analysis, for each time point, per Device Configuration (Gauge and Length) and Vacutainer tube and Overall continued

Time Point (hours)	Characteristic	BD Nexiva (22G x 1 inch) - 2mL	BD Nexiva (22G x 1 inch) - 6mL	BD Nexiva (22G x 1.75 inch) - 2mL	BD Nexiva (22G x 1.75 inch) - 6mL	BD Nexiva (20G x 1 inch) - 2mL	BD Nexiva (20G x 1 inch) - 6mL	BD Nexiva (20G x 1.75 inch) - 2mL	BD Nexiva (20G x 1.75 inch) - 6mL	Overall
	Haemolysis - Visual (Yes/No)									
	No	10 (62.5%)	8 (50.0%)	12 (66.7%)	11 (64.7%)	15 (75.0%)	14 (73.7%)	20 (100.0%)	18 (90.0%)	108 (74.0%)
	Yes	6 (37.5%)	8 (50.0%)	6 (33.3%)	6 (35.3%)	5 (25.0%)	5 (26.3%)	0 (0.0%)	2 (10.0%)	38 (26.0%)
	Total	16	16	18	17	20	19	20	20	146
30	cfHb (mg/dL)									
	Mean	185.52	210.60	167.79	169.92	158.51	162.12	153.68	150.67	166.82
	95% Mean CI	156.51, 212.85	184.63, 239.48	151.42, 183.66	158.34, 182.34	140.63, 177.80	145.08, 178.00	146.47, 161.67	141.87, 159.93	160.26, 173.39
	Median	196.62	197.89	173.95	169.28	150.21	164.66	148.96	148.17	162.70
	SD	54.86	50.87	34.25	25.29	42.43	37.41	17.77	21.35	38.84
	Min, Max	92.32, 255.62	132.23, 298.24	110.07, 213.18	133.8, 228.66	81.58, 247.7	69.02, 250.81	124.97, 200.12	123.78, 188.76	69.02, 298.24
	Total	13	12	16	16	19	19	20	20	135
	Count									
	Haemolysis - AU480 (Yes/No)									
	No	7 (53.8%)	7 (58.3%)	12 (75.0%)	14 (87.5%)	16 (84.2%)	17 (89.5%)	19 (95.0%)	20 (100.0%)	112 (83.0%)
	Yes	6 (46.2%)	5 (41.7%)	4 (25.0%)	2 (12.5%)	3 (15.8%)	2 (10.5%)	1 (5.0%)	0 (0.0%)	23 (17.0%)
	Total	13	12	16	16	19	19	20	20	135
	Haemolysis - Visual (Yes/No)									
	No	6 (46.2%)	3 (25.0%)	10 (62.5%)	11 (68.8%)	13 (68.4%)	14 (73.7%)	18 (90.0%)	16 (80.0%)	91 (67.4%)
	Yes	7 (53.8%)	9 (75.0%)	6 (37.5%)	5 (31.2%)	6 (31.6%)	5 (26.3%)	2 (10.0%)	4 (20.0%)	44 (32.6%)
	Total	13	12	16	16	19	19	20	20	135
48	cfHb (mg/dL)									
	Mean	212.51	219.02	178.49	174.76	158.17	168.39	148.86	149.54	169.38
	95% Mean CI	190.93, 234.07	195.34, 245.23	166.08, 190.73	158.24, 190.35	143.31, 173.95	152.88, 184.93	143.20, 154.62	142.42, 156.99	163.17, 175.78
	Median	215.34	209.73	180.08	175.33	151.59	167.16	149.97	146.95	161.69
	SD	34.84	38.74	25.15	32.48	32.70	33.84	13.33	17.01	34.74
	Min, Max	157.99, 269.46	175.61, 284.53	135.55, 212.02	110.22, 233.24	94.86, 223.68	116.07, 242.81	129.66, 170.4	119.31, 188.16	94.86, 284.53
	Total	9	8	15	15	16	16	20	20	119
	Count									
	Haemolysis - AU480 (Yes/No)									
	No	2 (22.2%)	3 (37.5%)	10 (66.7%)	12 (80.0%)	14 (87.5%)	13 (81.2%)	20 (100.0%)	20 (100.0%)	94 (79.0%)
	Yes	7 (77.8%)	5 (62.5%)	5 (33.3%)	3 (20.0%)	2 (12.5%)	3 (18.8%)	0 (0.0%)	0 (0.0%)	25 (21.0%)
	Total	9	8	15	15	16	16	20	20	119
	Haemolysis - Visual (Yes/No)									
	No	2 (22.2%)	2 (25.0%)	7 (46.7%)	8 (53.3%)	13 (81.2%)	11 (68.8%)	20 (100.0%)	19 (95.0%)	82 (68.9%)
	Yes	7 (77.8%)	6 (75.0%)	8 (53.3%)	7 (46.7%)	3 (18.8%)	5 (31.2%)	0 (0.0%)	1 (5.0%)	37 (31.1%)
	Total	9	8	15	15	16	16	20	20	119
54	cfHb (mg/dL)									
	Mean	180.69	220.07	166.77	164.29	170.58	151.13	144.48	154.89	162.77
	95% Mean CI	157.23, 208.83	186.70, 252.39	148.36, 184.87	149.35, 177.62	147.01, 194.87	132.11, 168.79	136.31, 152.67	146.58, 163.53	156.17, 169.79
	Median	167.93	222.47	165.77	172.10	169.55	149.39	146.47	151.33	159.28
	SD	36.32	48.41	36.08	27.18	45.87	33.97	18.73	18.62	35.50
	Min, Max	141.72, 243.15	169.64, 268.91	104.92, 222.54	116.32, 196.82	108.07, 250.53	94.07, 197.64	116.47, 178.69	123.45, 194.23	94.07, 268.91
	Total	6	6	14	13	13	12	19	18	101
	Count									
	Haemolysis - AU480 (Yes/No)									
	No	4 (66.7%)	3 (50.0%)	11 (78.6%)	13 (100.0%)	10 (76.9%)	12 (100.0%)	19 (100.0%)	18 (100.0%)	90 (89.1%)
	Yes	2 (33.3%)	3 (50.0%)	3 (21.4%)	0 (0.0%)	3 (23.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	11 (10.9%)
	Total	6	6	14	13	13	12	19	18	101

Table A.8.1: Numerical Summary of Subjects Blood Analysis, for each time point, per Device Configuration (Gauge and Length) and Vacutainer tube and Overall continued

Time Point (hours)	Characteristic	BD Nexiva (22G x 1 inch) - 2mL	BD Nexiva (22G x 1 inch) - 6mL	BD Nexiva (22G x 1.75 inch) - 2mL	BD Nexiva (22G x 1.75 inch) - 6mL	BD Nexiva (20G x 1 inch) - 2mL	BD Nexiva (20G x 1 inch) - 6mL	BD Nexiva (20G x 1.75 inch) - 2mL	BD Nexiva (20G x 1.75 inch) - 6mL	Overall
	Haemolysis - Visual (Yes/No)									
	No	4 (66.7%)	2 (33.3%)	8 (57.1%)	8 (61.5%)	7 (53.8%)	9 (75.0%)	19 (100.0%)	16 (88.9%)	73 (72.3%)
	Yes	2 (33.3%)	4 (66.7%)	6 (42.9%)	5 (38.5%)	6 (46.2%)	3 (25.0%)	0 (0.0%)	2 (11.1%)	28 (27.7%)
	Total	6	6	14	13	13	12	19	18	101
72	cfHb (mg/dL)									
	Mean	184.83	211.15	190.26	181.81	143.39	185.70	148.12	138.60	165.03
	95% Mean CI	156.46, 214.29	171.81, 250.48	175.38, 204.42	154.09, 209.57	129.77, 162.99	155.46, 213.94	136.82, 159.65	129.95, 147.59	156.23, 174.25
	Median	180.15	204.68	198.61	177.06	135.06	202.90	138.18	142.76	153.87
	SD	40.42	49.86	21.32	41.43	27.98	45.62	24.00	16.89	38.68
	Min, Max	134.72, 235.61	156.91, 270.1	158.71, 217.83	128.38, 236.34	120.09, 213	110.75, 239.34	122.85, 182.83	118.5, 168.81	110.75, 270.1
	Total	6	5	7	7	9	8	16	13	71
	Count									
	Haemolysis - AU480 (Yes/No)									
	No	4 (66.7%)	2 (40.0%)	4 (57.1%)	4 (57.1%)	8 (88.9%)	4 (50.0%)	16 (100.0%)	13 (100.0%)	55 (77.5%)
	Yes	2 (33.3%)	3 (60.0%)	3 (42.9%)	3 (42.9%)	1 (11.1%)	4 (50.0%)	0 (0.0%)	0 (0.0%)	16 (22.5%)
	Total	6	5	7	7	9	8	16	13	71
	Haemolysis - Visual (Yes/No)									
	No	3 (50.0%)	2 (40.0%)	2 (28.6%)	4 (57.1%)	8 (88.9%)	3 (37.5%)	14 (87.5%)	13 (100.0%)	49 (69.0%)
	Yes	3 (50.0%)	3 (60.0%)	5 (71.4%)	3 (42.9%)	1 (11.1%)	5 (62.5%)	2 (12.5%)	0 (0.0%)	22 (31.0%)
	Total	6	5	7	7	9	8	16	13	71

A.9 Blood Draw Fill Time

Table A.9.1: Numerical Summary of Blood Draw Fill Time in seconds for each Vacutainer tube, per Device Configuration (Gauge and Length) and Overall

tube	Characteristic	BD Nexiva (22G x 1 inch)	BD Nexiva (22G x 1.75 inch)	BD Nexiva (20G x 1 inch)	BD Nexiva (20G x 1.75 inch)	Overall
2mL	Blood Draw Fill Time (sec)					
	Mean	59.30	60.29	59.53	60.95	60.10
	95% Mean CI	58.23, 60.33	59.36, 61.20	58.67, 60.39	60.06, 61.82	59.64, 60.57
	Median	59.27	60.16	59.37	61.52	60.00
	SD	5.08	4.91	4.82	5.25	5.05
	Min, Max	45.83, 72.19	46.29, 73.76	46.69, 70.86	48.88, 77.06	45.83, 77.06
	Total Count	88	109	117	135	449
6mL	Blood Draw Fill Time (sec)					
	Mean	100.29	100.60	99.14	98.97	99.67
	95% Mean CI	98.90, 101.73	99.15, 101.98	97.77, 100.49	97.83, 100.16	98.99, 100.33
	Median	99.29	101.14	99.48	97.99	99.33
	SD	6.74	7.44	7.37	6.90	7.14
	Min, Max	84.03, 118.89	82.55, 118.55	84.03, 115.48	84.56, 119.35	82.55, 119.35
	Total Count	85	106	114	131	436

Table A.9.2: Numerical Summary of Blood Draw Fill Time in seconds for each Vacutainer tube, for each time point, per Device Configuration (Gauge and Length) and Vacutainer tube and Overall

Tube	Time Point (hours)	Characteristic	BD Nexiva (22G x 1 inch)	BD Nexiva (22G x 1.75 inch)	BD Nexiva (20G x 1 inch)	BD Nexiva (20G x 1.75 inch)	Overall
2mL	0	Blood Draw Fill Time (sec)					
		Mean	58.77	61.25	60.41	59.01	59.86
		95% Mean CI	57.34, 60.13	59.28, 63.32	58.37, 62.49	56.57, 61.52	58.83, 60.89
		Median	58.92	61.46	60.54	58.64	59.34
		SD	3.29	4.70	4.87	5.69	4.74
		Min, Max	51.27, 63.83	53.66, 70.59	51.38, 69.45	49.33, 69.93	49.33, 70.59
		Total Count	20	20	20	20	80
2mL	6	Blood Draw Fill Time (sec)					
		Mean	60.94	58.40	58.76	62.05	60.04
		95% Mean CI	59.21, 62.74	56.21, 60.58	57.19, 60.43	59.89, 64.32	59.03, 61.09
		Median	59.90	59.05	58.06	62.15	59.43
		SD	3.98	4.94	3.79	5.22	4.70
		Min, Max	53.83, 68.83	46.29, 69.44	52.58, 65.84	52.49, 75.85	46.29, 75.85
		Total Count	18	19	20	20	77
2mL	24	Blood Draw Fill Time (sec)					
		Mean	56.85	60.95	58.56	60.95	59.41
		95% Mean CI	54.47, 59.10	58.49, 63.48	57.07, 60.08	58.34, 63.31	58.23, 60.56
		Median	58.67	61.31	58.66	62.31	59.64
		SD	4.92	5.57	3.54	5.82	5.21
		Min, Max	48.08, 64.9	52.09, 72.58	50.83, 66.75	48.88, 68.39	48.08, 72.58
		Total Count	16	18	20	20	74
2mL	30	Blood Draw Fill Time (sec)					
		Mean	61.60	59.05	59.24	60.83	60.12
		95% Mean CI	58.68, 64.23	57.27, 60.80	57.19, 61.40	58.69, 63.00	58.99, 61.22
		Median	61.98	59.51	58.57	60.79	60.00
		SD	5.35	3.74	4.81	5.12	4.79
		Min, Max	48.68, 69.78	53.62, 65.95	49.69, 70.86	51.25, 70.69	48.68, 70.86
		Total Count	13	16	19	20	68

Table A.9.2: Numerical Summary of Blood Draw Fill Time in seconds for each Vacutainer tube, for each time point, per Device Configuration (Gauge and Length) and Vacutainer tube and Overall continued

Tube	Time Point (hours)	Characteristic	BD Nexiva (22G x 1 inch)	BD Nexiva (22G x 1.75 inch)	BD Nexiva (20G x 1 inch)	BD Nexiva (20G x 1.75 inch)	Overall
2mL	48	Blood Draw Fill Time (sec)					
		Mean	59.11	60.82	59.95	62.41	60.86
		95% Mean CI	54.40, 63.75	59.28, 62.22	56.89, 62.73	60.51, 64.39	59.48, 62.16
		Median	59.57	61.03	60.23	61.85	60.73
		SD	7.70	3.04	6.27	4.47	5.31
		Min, Max	45.83, 72.19	54.24, 65.8	46.69, 67.65	55.83, 73.5	45.83, 73.5
		Total Count	9	15	16	20	60
2mL	54	Blood Draw Fill Time (sec)					
		Mean	57.51	60.69	59.66	60.80	60.11
		95% Mean CI	53.32, 61.67	57.75, 63.88	56.50, 62.79	58.77, 62.72	58.66, 61.60
		Median	57.25	58.89	61.26	62.02	61.07
		SD	5.84	6.02	5.97	4.59	5.43
		Min, Max	49.39, 65.32	49.53, 73.76	49.17, 68.98	51.95, 68.15	49.17, 73.76
		Total Count	6	14	13	19	52
2mL	72	Blood Draw Fill Time (sec)					
		Mean	59.78	61.94	61.16	60.52	60.82
		95% Mean CI	55.13, 63.86	57.39, 66.20	57.83, 64.25	58.00, 63.49	59.04, 62.61
		Median	60.20	61.65	62.14	61.05	61.56
		SD	5.99	6.54	5.25	5.87	5.67
		Min, Max	49.86, 66.61	51.2, 70	52.68, 67.56	53.7, 77.06	49.86, 77.06
		Total Count	6	7	9	16	38
6mL	0	Blood Draw Fill Time (sec)					
		Mean	98.51	98.75	96.41	98.84	98.13
		95% Mean CI	95.59, 101.39	95.38, 102.18	93.48, 99.30	95.70, 101.94	96.55, 99.67
		Median	98.97	96.66	97.19	97.70	98.08
		SD	6.80	8.05	6.76	7.36	7.19
		Min, Max	84.03, 112.86	82.55, 112.09	84.24, 110.49	84.56, 115.29	82.55, 115.29
		Total Count	20	20	20	20	80
6mL	6	Blood Draw Fill Time (sec)					
		Mean	101.60	97.88	101.11	99.86	100.13
		95% Mean CI	98.10, 105.23	94.19, 101.56	97.86, 104.39	96.86, 102.68	98.43, 101.82
		Median	99.10	99.15	102.04	99.57	99.61
		SD	8.02	8.07	7.64	6.77	7.60
		Min, Max	84.14, 115.25	85.32, 111.59	88.65, 114.36	85.37, 113.48	84.14, 115.25
		Total Count	18	18	20	20	76
6mL	24	Blood Draw Fill Time (sec)					
		Mean	100.36	99.57	98.44	99.57	99.45
		95% Mean CI	98.03, 102.98	96.38, 103.02	95.35, 101.50	98.15, 101.16	98.16, 100.79
		Median	99.59	99.91	100.11	98.67	99.58
		SD	5.19	7.03	6.89	3.54	5.72
		Min, Max	93.63, 112.08	89.85, 116.46	86.57, 111.26	95.3, 108.19	86.57, 116.46
		Total Count	16	17	19	20	72
6mL	30	Blood Draw Fill Time (sec)					
		Mean	102.86	103.11	100.07	97.88	100.64
		95% Mean CI	99.28, 106.87	101.19, 104.96	95.85, 104.16	94.85, 101.24	98.86, 102.44
		Median	103.15	103.39	99.95	94.68	101.98
		SD	7.06	3.96	9.59	7.48	7.60
		Min, Max	92.33, 118.89	96.36, 109.89	84.03, 115.48	89.66, 116.71	84.03, 118.89
		Total Count	12	16	19	20	67
6mL	48	Blood Draw Fill Time (sec)					
		Mean	99.82	102.54	100.42	100.89	101.04
		95% Mean CI	96.37, 103.42	98.47, 106.69	96.88, 103.91	97.84, 103.92	99.21, 102.87
		Median	99.01	103.16	99.16	99.86	99.71
		SD	5.52	8.37	7.45	7.13	7.25
		Min, Max	92.46, 108.6	85.27, 118.55	87.77, 113.06	87.61, 111.31	85.27, 118.55
		Total Count	8	15	16	20	59
6mL	54	Blood Draw Fill Time (sec)					
		Mean	101.97	102.69	99.12	98.57	100.21
		95% Mean CI	96.33, 107.41	99.67, 105.60	97.09, 101.31	94.83, 102.79	98.28, 102.16
		Median	104.34	102.21	98.58	97.15	100.00
		SD	7.89	5.72	3.87	8.77	6.98
		Min, Max	92.02, 112.6	91.76, 112.19	93.56, 107.26	85.32, 119.35	85.32, 119.35
		Total Count	6	13	12	18	49

Table A.9.2: Numerical Summary of Blood Draw Fill Time in seconds for each Vacutainer tube, for each time point, per Device Configuration (Gauge and Length) and Vacutainer tube and Overall continued

Tube	Time Point (hours)	Characteristic	BD Nexiva (22G x 1 inch)	BD Nexiva (22G x 1.75 inch)	BD Nexiva (20G x 1 inch)	BD Nexiva (20G x 1.75 inch)	Overall
6mL	72	Blood Draw Fill Time (sec)					
		Mean	95.07	101.64	97.92	96.13	97.57
		95% Mean CI	92.50, 97.64	94.92, 108.95	93.41, 102.73	92.96, 99.59	95.19, 100.10
		Median	94.85	104.38	97.71	95.10	95.91
		SD	3.29	10.30	7.11	6.43	7.30
		Min, Max	91.29, 99.09	90.24, 118.23	88.42, 109.56	87.75, 109.13	87.75, 118.23
		Total Count	5	7	8	13	33

Table A.9.3: ANOVA table for Blood Draw Duration linear mixed effect model

	Chisq	Df	Pr(>Chisq)	Result
(Intercept)	1829.42	1.00	<0.001	Significant
timepoint	6.47	6.00	0.372	NS
device	2.21	3.00	0.53	NS
tube	420.57	1.00	<0.001	Significant
timepoint:device	14.15	18.00	0.719	NS
timepoint:tube	5.09	6.00	0.532	NS
device:tube	2.76	3.00	0.43	NS
timepoint:device:tube	13.80	18.00	0.742	NS

Table A.9.4: Multiple Comparisons Based on linear mixed effect model for Blood Draw Duration. Sidak's adjustement for multiple comparisons was used.

Tube	Time (hours)	Contrast	Estimate	Lwr	Upr	p-value	Result
2mL	0	BD Nexiva (22G x 1 inch) - BD Nexiva (22G x 1.75 inch)	-2.48	-7.47	2.51	0.576	NS
		BD Nexiva (22G x 1 inch) - BD Nexiva (20G x 1 inch)	-1.64	-6.64	3.36	0.834	NS
		BD Nexiva (22G x 1 inch) - BD Nexiva (20G x 1.75 inch)	-0.24	-5.24	4.76	0.999	NS
		BD Nexiva (22G x 1.75 inch) - BD Nexiva (20G x 1 inch)	0.84	-4.16	5.84	0.973	NS
		BD Nexiva (22G x 1.75 inch) - BD Nexiva (20G x 1.75 inch)	2.24	-2.76	7.24	0.655	NS
		BD Nexiva (20G x 1 inch) - BD Nexiva (20G x 1.75 inch)	1.40	-3.59	6.39	0.888	NS
	6	BD Nexiva (22G x 1 inch) - BD Nexiva (22G x 1.75 inch)	2.55	-2.64	7.75	0.585	NS
		BD Nexiva (22G x 1 inch) - BD Nexiva (20G x 1 inch)	2.19	-2.95	7.33	0.691	NS
		BD Nexiva (22G x 1 inch) - BD Nexiva (20G x 1.75 inch)	-1.10	-6.24	4.04	0.946	NS
		BD Nexiva (22G x 1.75 inch) - BD Nexiva (20G x 1 inch)	-0.36	-5.43	4.71	0.998	NS
		BD Nexiva (22G x 1.75 inch) - BD Nexiva (20G x 1.75 inch)	-3.65	-8.72	1.42	0.248	NS
		BD Nexiva (20G x 1 inch) - BD Nexiva (20G x 1.75 inch)	-3.29	-8.28	1.70	0.325	NS
	24	BD Nexiva (22G x 1 inch) - BD Nexiva (22G x 1.75 inch)	-4.12	-9.54	1.30	0.206	NS
		BD Nexiva (22G x 1 inch) - BD Nexiva (20G x 1 inch)	-1.73	-7.03	3.58	0.836	NS
		BD Nexiva (22G x 1 inch) - BD Nexiva (20G x 1.75 inch)	-4.12	-9.43	1.19	0.189	NS
		BD Nexiva (22G x 1.75 inch) - BD Nexiva (20G x 1 inch)	2.39	-2.75	7.53	0.628	NS
		BD Nexiva (22G x 1.75 inch) - BD Nexiva (20G x 1.75 inch)	-0.00	-5.14	5.14	1	NS
		BD Nexiva (20G x 1 inch) - BD Nexiva (20G x 1.75 inch)	-2.39	-7.38	2.60	0.605	NS
	30	BD Nexiva (22G x 1 inch) - BD Nexiva (22G x 1.75 inch)	2.54	-3.35	8.43	0.683	NS
		BD Nexiva (22G x 1 inch) - BD Nexiva (20G x 1 inch)	2.35	-3.34	8.04	0.711	NS
		BD Nexiva (22G x 1 inch) - BD Nexiva (20G x 1.75 inch)	0.76	-4.87	6.39	0.985	NS
		BD Nexiva (22G x 1.75 inch) - BD Nexiva (20G x 1 inch)	-0.19	-5.55	5.18	1	NS
		BD Nexiva (22G x 1.75 inch) - BD Nexiva (20G x 1.75 inch)	-1.78	-7.08	3.52	0.824	NS
		BD Nexiva (20G x 1 inch) - BD Nexiva (20G x 1.75 inch)	-1.59	-6.64	3.46	0.849	NS
	48	BD Nexiva (22G x 1 inch) - BD Nexiva (22G x 1.75 inch)	-1.75	-8.39	4.89	0.905	NS
		BD Nexiva (22G x 1 inch) - BD Nexiva (20G x 1 inch)	-0.86	-7.44	5.71	0.987	NS
		BD Nexiva (22G x 1 inch) - BD Nexiva (20G x 1.75 inch)	-3.33	-9.67	3.00	0.528	NS
		BD Nexiva (22G x 1.75 inch) - BD Nexiva (20G x 1 inch)	0.89	-4.79	6.56	0.978	NS
		BD Nexiva (22G x 1.75 inch) - BD Nexiva (20G x 1.75 inch)	-1.58	-6.98	3.81	0.873	NS
		BD Nexiva (20G x 1 inch) - BD Nexiva (20G x 1.75 inch)	-2.47	-7.75	2.81	0.624	NS
	54	BD Nexiva (22G x 1 inch) - BD Nexiva (22G x 1.75 inch)	-3.25	-10.93	4.43	0.695	NS
		BD Nexiva (22G x 1 inch) - BD Nexiva (20G x 1 inch)	-2.17	-9.95	5.61	0.889	NS
		BD Nexiva (22G x 1 inch) - BD Nexiva (20G x 1.75 inch)	-3.35	-10.73	4.03	0.645	NS
		BD Nexiva (22G x 1.75 inch) - BD Nexiva (20G x 1 inch)	1.08	-4.99	7.15	0.968	NS
		BD Nexiva (22G x 1.75 inch) - BD Nexiva (20G x 1.75 inch)	-0.10	-5.66	5.45	1	NS
		BD Nexiva (20G x 1 inch) - BD Nexiva (20G x 1.75 inch)	-1.18	-6.85	4.48	0.949	NS
	72	BD Nexiva (22G x 1 inch) - BD Nexiva (22G x 1.75 inch)	-2.24	-11.01	6.53	0.913	NS
		BD Nexiva (22G x 1 inch) - BD Nexiva (20G x 1 inch)	-1.37	-9.69	6.95	0.974	NS
		BD Nexiva (22G x 1 inch) - BD Nexiva (20G x 1.75 inch)	-0.80	-8.35	6.76	0.993	NS
		BD Nexiva (22G x 1.75 inch) - BD Nexiva (20G x 1 inch)	0.87	-7.08	8.82	0.992	NS
		BD Nexiva (22G x 1.75 inch) - BD Nexiva (20G x 1.75 inch)	1.44	-5.71	8.59	0.954	NS
		BD Nexiva (20G x 1 inch) - BD Nexiva (20G x 1.75 inch)	0.57	-5.99	7.14	0.996	NS
6mL	0	BD Nexiva (22G x 1 inch) - BD Nexiva (22G x 1.75 inch)	-0.24	-5.23	4.75	0.999	NS
		BD Nexiva (22G x 1 inch) - BD Nexiva (20G x 1 inch)	2.11	-2.90	7.11	0.7	NS
		BD Nexiva (22G x 1 inch) - BD Nexiva (20G x 1.75 inch)	-0.33	-5.33	4.67	0.998	NS
		BD Nexiva (22G x 1.75 inch) - BD Nexiva (20G x 1 inch)	2.34	-2.66	7.34	0.623	NS
		BD Nexiva (22G x 1.75 inch) - BD Nexiva (20G x 1.75 inch)	-0.09	-5.10	4.91	1	NS

	BD Nexiva (20G x 1 inch) - BD Nexiva (20G x 1.75 inch)	-2.44	-7.42	2.55	0.591	NS
6	BD Nexiva (22G x 1 inch) - BD Nexiva (22G x 1.75 inch)	3.72	-1.54	8.98	0.264	NS
	BD Nexiva (22G x 1 inch) - BD Nexiva (20G x 1 inch)	0.49	-4.65	5.63	0.995	NS
	BD Nexiva (22G x 1 inch) - BD Nexiva (20G x 1.75 inch)	1.75	-3.39	6.89	0.818	NS
	BD Nexiva (22G x 1.75 inch) - BD Nexiva (20G x 1 inch)	-3.23	-8.37	1.91	0.368	NS
	BD Nexiva (22G x 1.75 inch) - BD Nexiva (20G x 1.75 inch)	-1.98	-7.12	3.16	0.755	NS
	BD Nexiva (20G x 1 inch) - BD Nexiva (20G x 1.75 inch)	1.25	-3.73	6.24	0.916	NS
24	BD Nexiva (22G x 1 inch) - BD Nexiva (22G x 1.75 inch)	0.77	-4.73	6.27	0.984	NS
	BD Nexiva (22G x 1 inch) - BD Nexiva (20G x 1 inch)	1.90	-3.47	7.27	0.799	NS
	BD Nexiva (22G x 1 inch) - BD Nexiva (20G x 1.75 inch)	0.77	-4.54	6.08	0.982	NS
	BD Nexiva (22G x 1.75 inch) - BD Nexiva (20G x 1 inch)	1.13	-4.16	6.41	0.947	NS
	BD Nexiva (22G x 1.75 inch) - BD Nexiva (20G x 1.75 inch)	-0.00	-5.22	5.22	1	NS
	BD Nexiva (20G x 1 inch) - BD Nexiva (20G x 1.75 inch)	-1.13	-6.18	3.93	0.94	NS
30	BD Nexiva (22G x 1 inch) - BD Nexiva (22G x 1.75 inch)	-0.25	-6.28	5.77	1	NS
	BD Nexiva (22G x 1 inch) - BD Nexiva (20G x 1 inch)	2.79	-3.04	8.62	0.607	NS
	BD Nexiva (22G x 1 inch) - BD Nexiva (20G x 1.75 inch)	4.98	-0.79	10.75	0.118	NS
	BD Nexiva (22G x 1.75 inch) - BD Nexiva (20G x 1 inch)	3.04	-2.32	8.41	0.462	NS
	BD Nexiva (22G x 1.75 inch) - BD Nexiva (20G x 1.75 inch)	5.23	-0.07	10.54	0.054	NS
	BD Nexiva (20G x 1 inch) - BD Nexiva (20G x 1.75 inch)	2.19	-2.86	7.24	0.679	NS
48	BD Nexiva (22G x 1 inch) - BD Nexiva (22G x 1.75 inch)	-2.76	-9.66	4.13	0.73	NS
	BD Nexiva (22G x 1 inch) - BD Nexiva (20G x 1 inch)	-0.63	-7.46	6.20	0.995	NS
	BD Nexiva (22G x 1 inch) - BD Nexiva (20G x 1.75 inch)	-1.11	-7.71	5.50	0.973	NS
	BD Nexiva (22G x 1.75 inch) - BD Nexiva (20G x 1 inch)	2.13	-3.54	7.81	0.766	NS
	BD Nexiva (22G x 1.75 inch) - BD Nexiva (20G x 1.75 inch)	1.66	-3.73	7.05	0.857	NS
	BD Nexiva (20G x 1 inch) - BD Nexiva (20G x 1.75 inch)	-0.48	-5.76	4.80	0.996	NS
54	BD Nexiva (22G x 1 inch) - BD Nexiva (22G x 1.75 inch)	-0.78	-8.55	6.98	0.994	NS
	BD Nexiva (22G x 1 inch) - BD Nexiva (20G x 1 inch)	2.87	-5.01	10.75	0.784	NS
	BD Nexiva (22G x 1 inch) - BD Nexiva (20G x 1.75 inch)	3.35	-4.08	10.78	0.651	NS
	BD Nexiva (22G x 1.75 inch) - BD Nexiva (20G x 1 inch)	3.65	-2.66	9.96	0.443	NS
	BD Nexiva (22G x 1.75 inch) - BD Nexiva (20G x 1.75 inch)	4.13	-1.60	9.87	0.248	NS
	BD Nexiva (20G x 1 inch) - BD Nexiva (20G x 1.75 inch)	0.48	-5.38	6.35	0.997	NS
72	BD Nexiva (22G x 1 inch) - BD Nexiva (22G x 1.75 inch)	-6.57	-15.81	2.67	0.258	NS
	BD Nexiva (22G x 1 inch) - BD Nexiva (20G x 1 inch)	-2.76	-11.75	6.24	0.859	NS
	BD Nexiva (22G x 1 inch) - BD Nexiva (20G x 1.75 inch)	-1.09	-9.40	7.22	0.987	NS
	BD Nexiva (22G x 1.75 inch) - BD Nexiva (20G x 1 inch)	3.82	-4.35	11.99	0.624	NS
	BD Nexiva (22G x 1.75 inch) - BD Nexiva (20G x 1.75 inch)	5.48	-1.92	12.88	0.225	NS
	BD Nexiva (20G x 1 inch) - BD Nexiva (20G x 1.75 inch)	1.67	-5.42	8.75	0.93	NS

A.10 Thrombus Occurrence

Table A.10.1: Numerical Summary of Thrombus Occurrence, per Device Configuration (Gauge and Length) and Overall

Characteristic	BD Nexiva (22G x 1 inch)	BD Nexiva (22G x 1.75 inch)	BD Nexiva (20G x 1 inch)	BD Nexiva (20G x 1.75 inch)	Overall
Thrombus (Yes/No					
Yes	62 (63.3%)	72 (62.1%)	99 (79.8%)	68 (49.3%)	301 (63.2%)
No	36 (36.7%)	44 (37.9%)	25 (20.2%)	70 (50.7%)	175 (36.8%)
Total	98	116	124	138	476

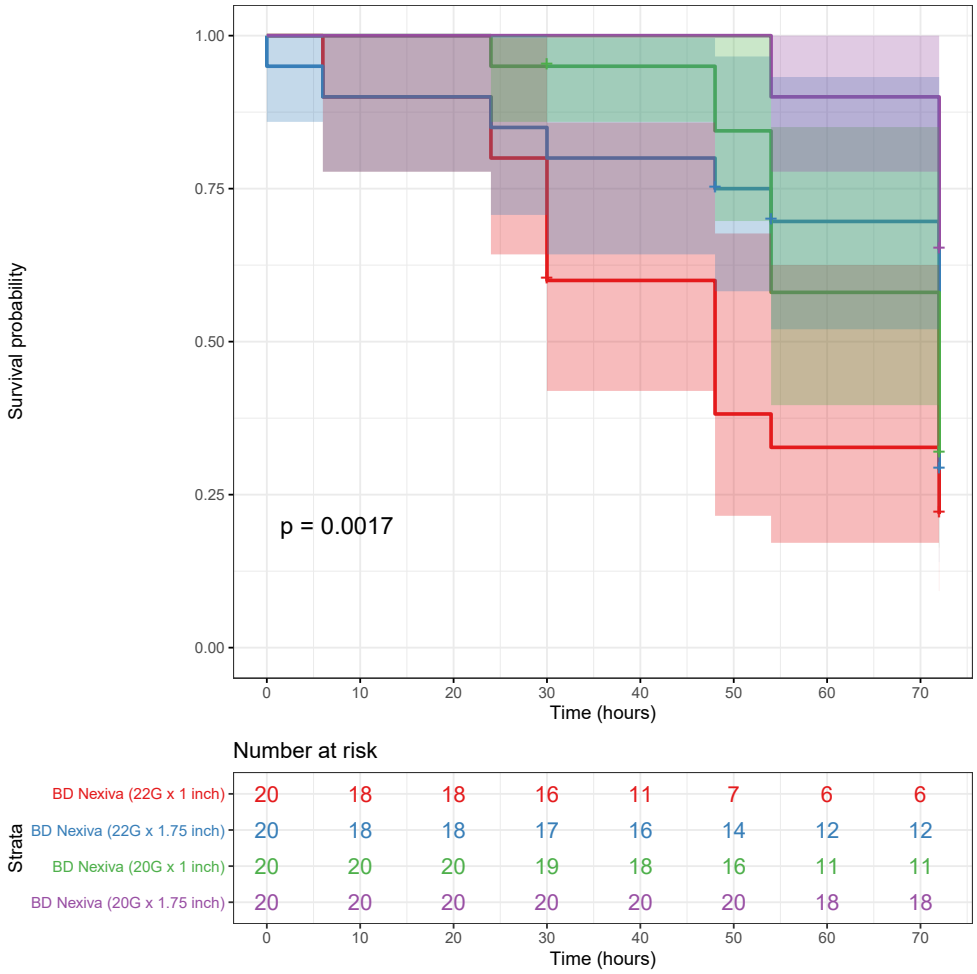
Table A.10.2: Numerical Summary of Thrombus Analysis, for each time point, per Device Configuration (Gauge and Length) and Overall

Time Point (hours)	Characteristic	BD Nexiva (22G x 1 inch)	BD Nexiva (22G x 1.75 inch)	BD Nexiva (20G x 1 inch)	BD Nexiva (20G x 1.75 inch)	Overall
0	Thrombus (Yes/No					
	Yes	14 (70.0%)	13 (65.0%)	16 (80.0%)	10 (50.0%)	53 (66.2%)
	No	6 (30.0%)	7 (35.0%)	4 (20.0%)	10 (50.0%)	27 (33.8%)
	Total	20	20	20	20	80
6	Thrombus (Yes/No					
	Yes	14 (70.0%)	12 (63.2%)	16 (80.0%)	10 (50.0%)	52 (65.8%)
	No	6 (30.0%)	7 (36.8%)	4 (20.0%)	10 (50.0%)	27 (34.2%)
	Total	20	19	20	20	79
24	Thrombus (Yes/No					
	Yes	12 (66.7%)	11 (61.1%)	16 (80.0%)	10 (50.0%)	49 (64.5%)
	No	6 (33.3%)	7 (38.9%)	4 (20.0%)	10 (50.0%)	27 (35.5%)
	Total	18	18	20	20	76
30	Thrombus (Yes/No					
	Yes	10 (62.5%)	11 (64.7%)	15 (78.9%)	10 (50.0%)	46 (63.9%)
	No	6 (37.5%)	6 (35.3%)	4 (21.1%)	10 (50.0%)	26 (36.1%)
	Total	16	17	19	20	72
48	Thrombus (Yes/No					
	Yes	6 (54.5%)	10 (62.5%)	15 (83.3%)	10 (50.0%)	41 (63.1%)
	No	5 (45.5%)	6 (37.5%)	3 (16.7%)	10 (50.0%)	24 (36.9%)
	Total	11	16	18	20	65
54	Thrombus (Yes/No					
	Yes	3 (42.9%)	8 (57.1%)	13 (81.2%)	10 (50.0%)	34 (59.6%)
	No	4 (57.1%)	6 (42.9%)	3 (18.8%)	10 (50.0%)	23 (40.4%)
	Total	7	14	16	20	57
72	Thrombus (Yes/No					
	Yes	3 (50.0%)	7 (58.3%)	8 (72.7%)	8 (44.4%)	26 (55.3%)
	No	3 (50.0%)	5 (41.7%)	3 (27.3%)	10 (55.6%)	21 (44.7%)
	Total	6	12	11	18	47

B Figures

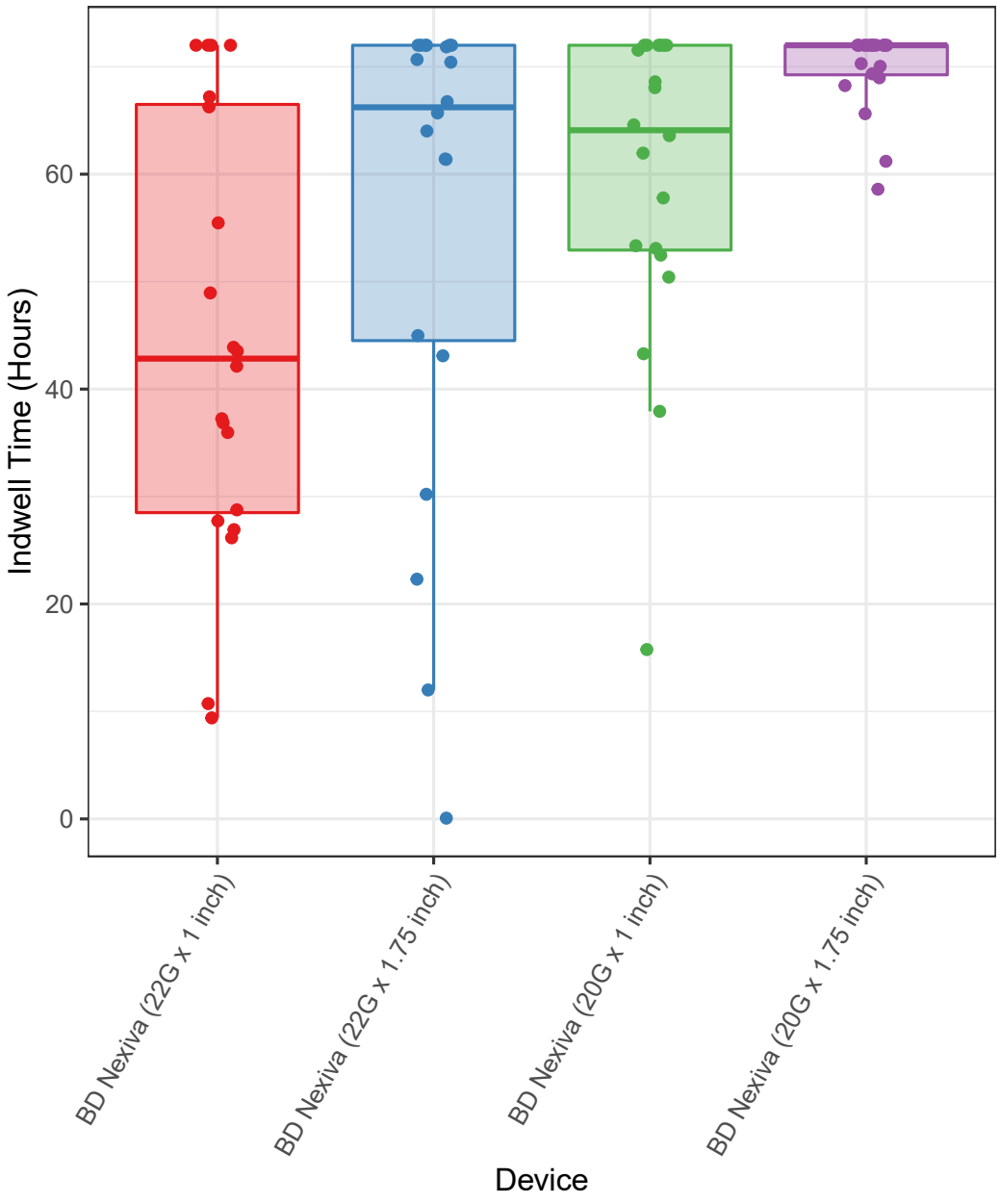
B.1 Survival

Figure B.1.1: Survival Curve for Indwell Time per Device Configuration. Color bands represent 95% Confidence Intervals



B.2 Indwell Time

Figure B.2.1: Boxplot for Indwell Time per Device Configuration



B.3 Blood Analysis

B.3.1 cfHb

Figure B.3.1: Boxplot for cfHb per Device Configuration for each Timepoint

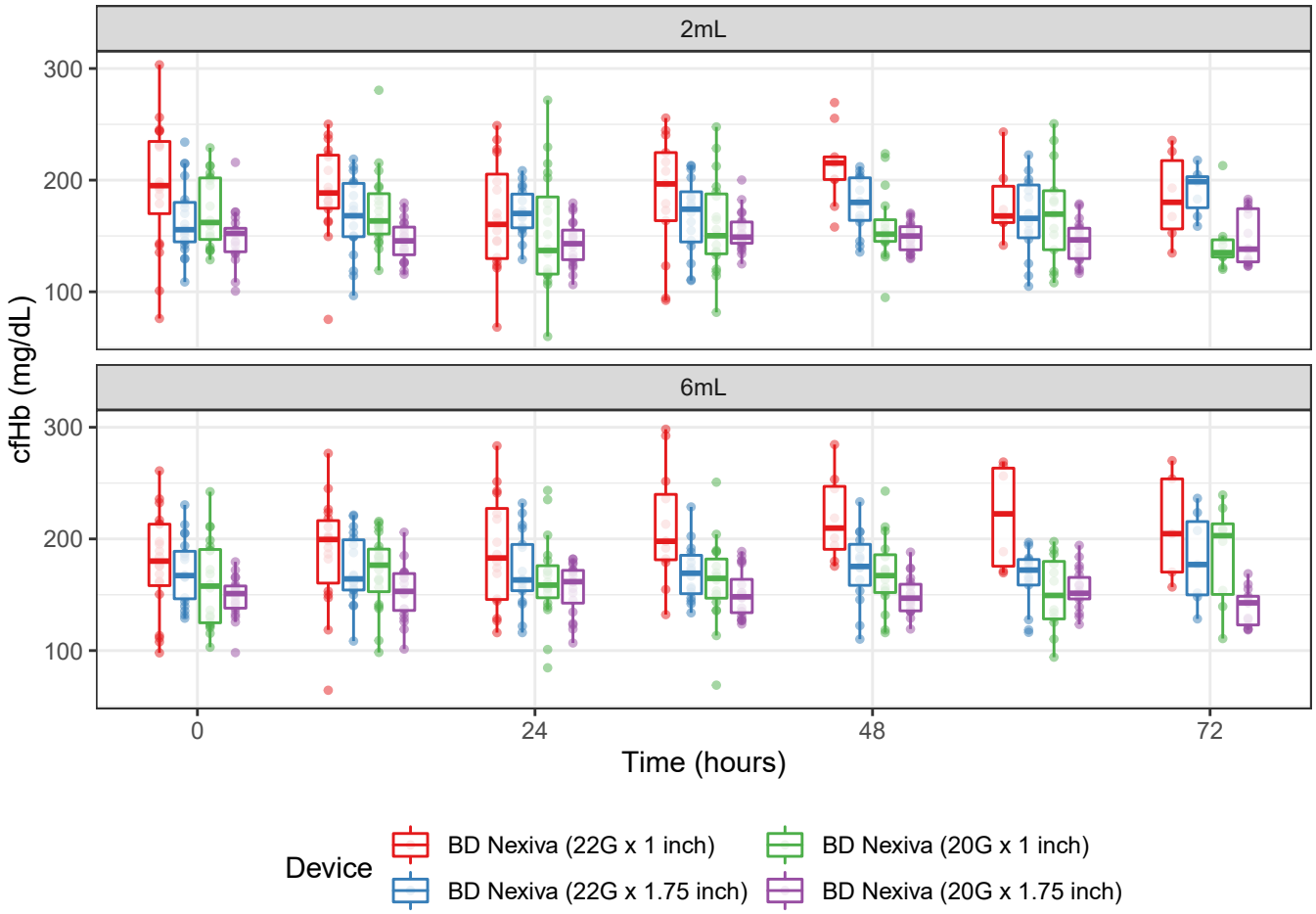
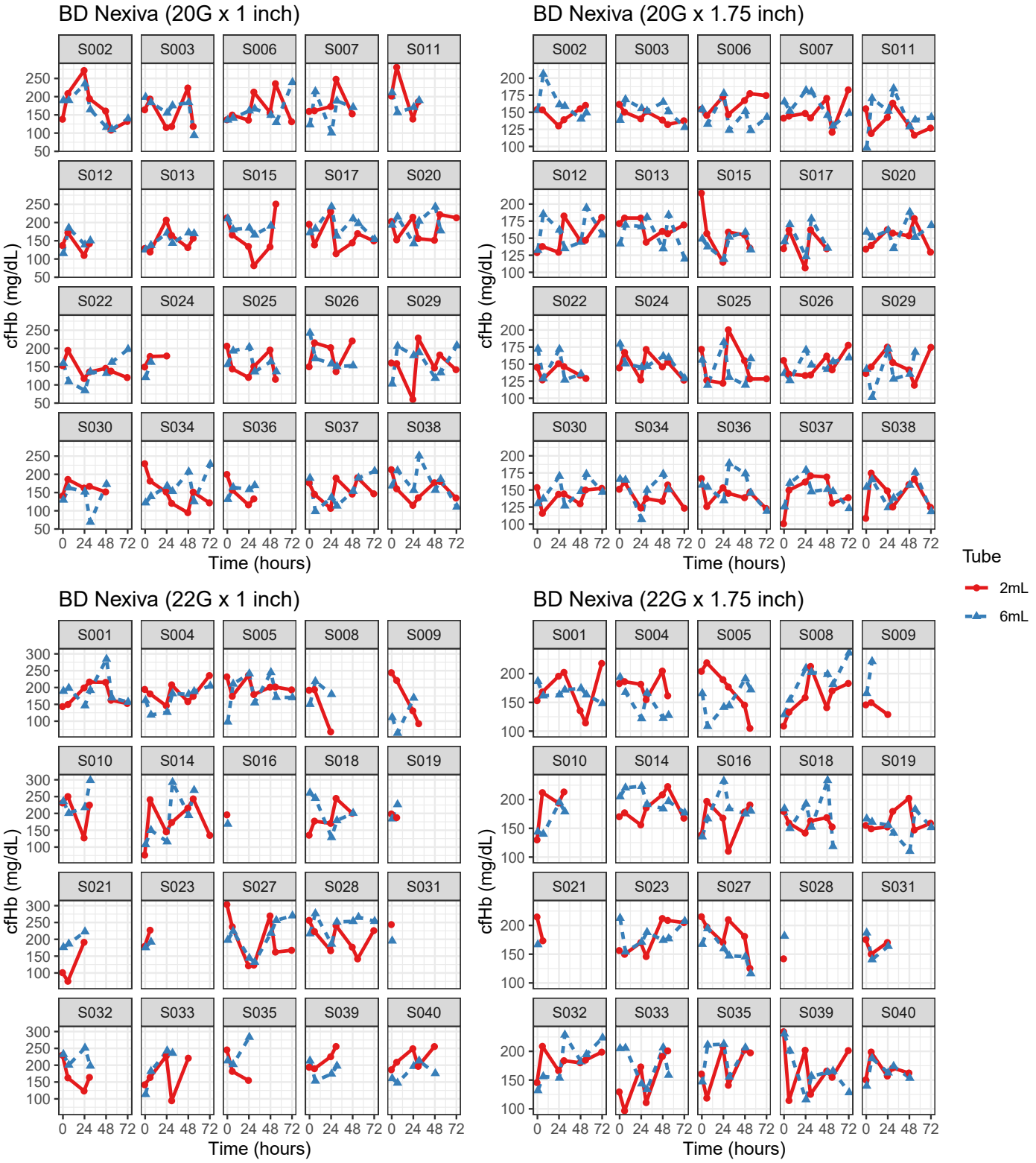


Figure B.3.2: Lineplot for cfHb per subject and Device Configuration over time



B.4 Haemolysis Occurrence

Figure B.4.1: Barplot for Haemolysis Occurence (assessed with AU480) per Device Configuration

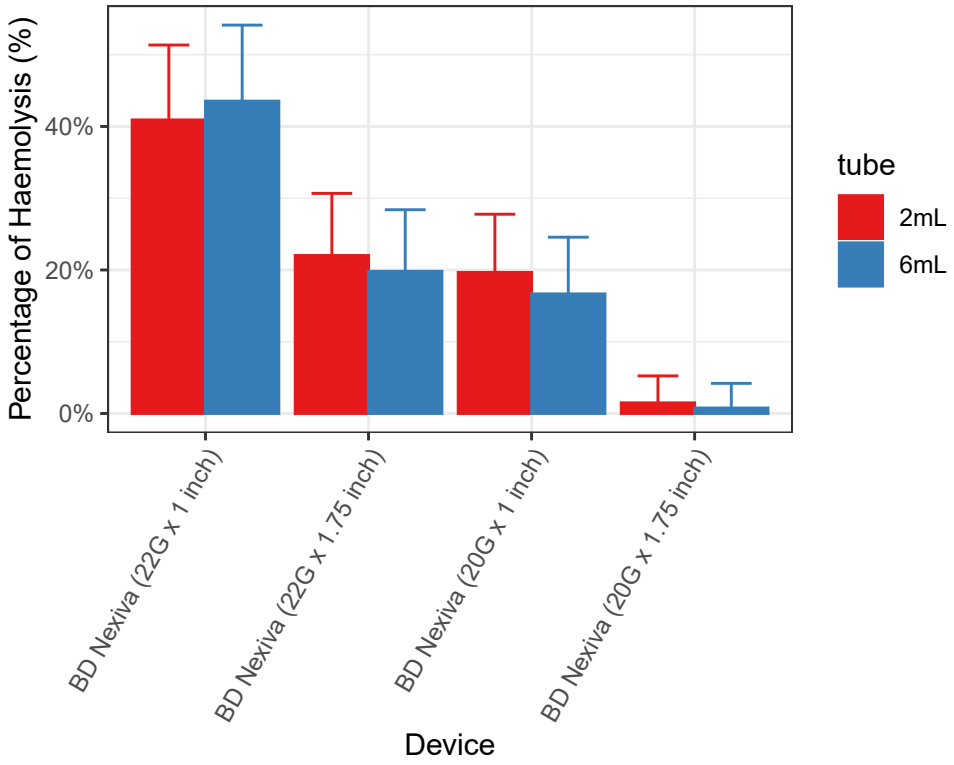
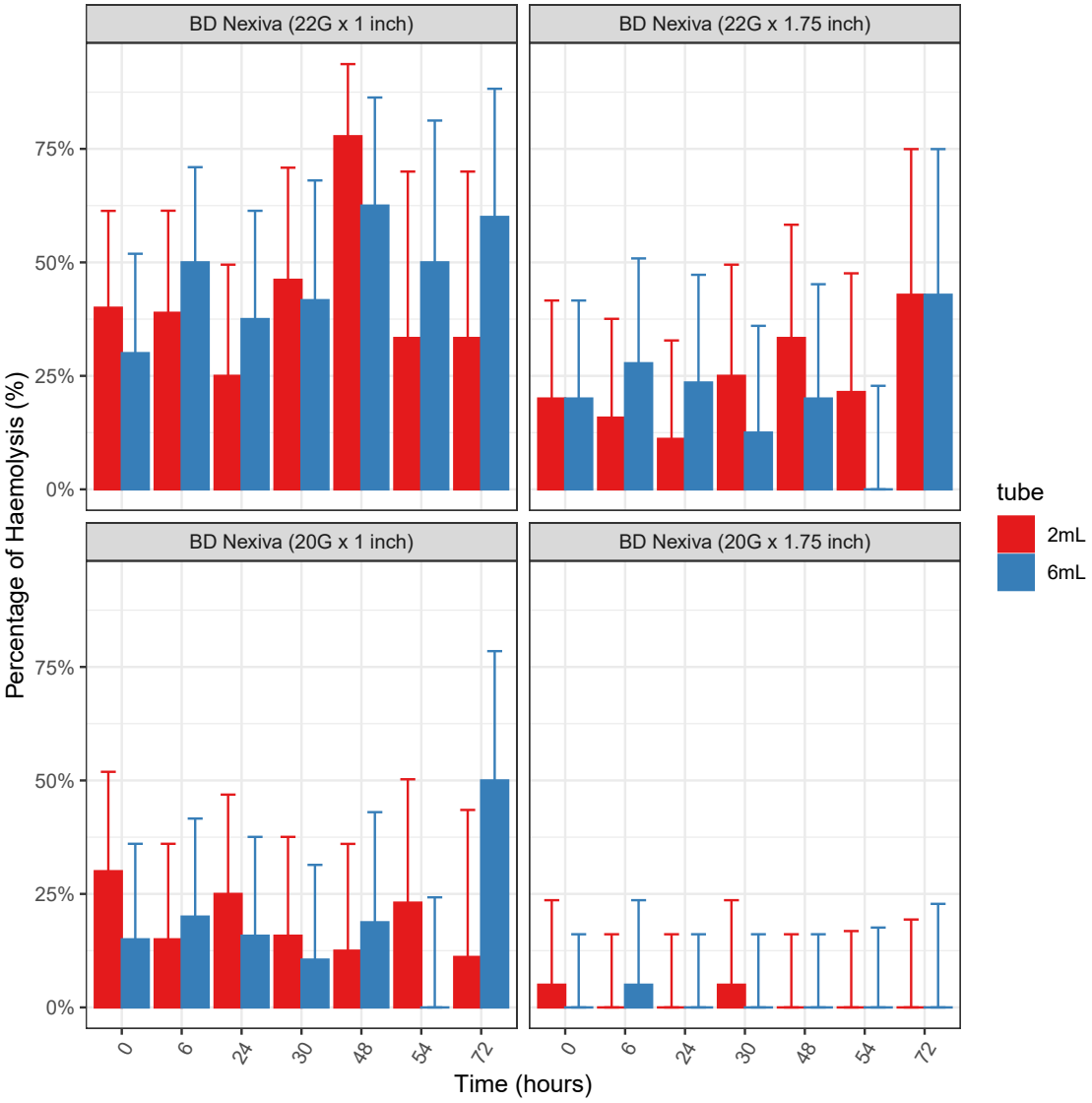


Figure B.4.2: Barplot for Haemolysis Occurence (AU480 measurements) per Device Configuration for each Timepoint



B.5 Blood Draw Fill Time

Figure B.5.1: Boxplot for Blood Draw Fill Time per Device Configuration

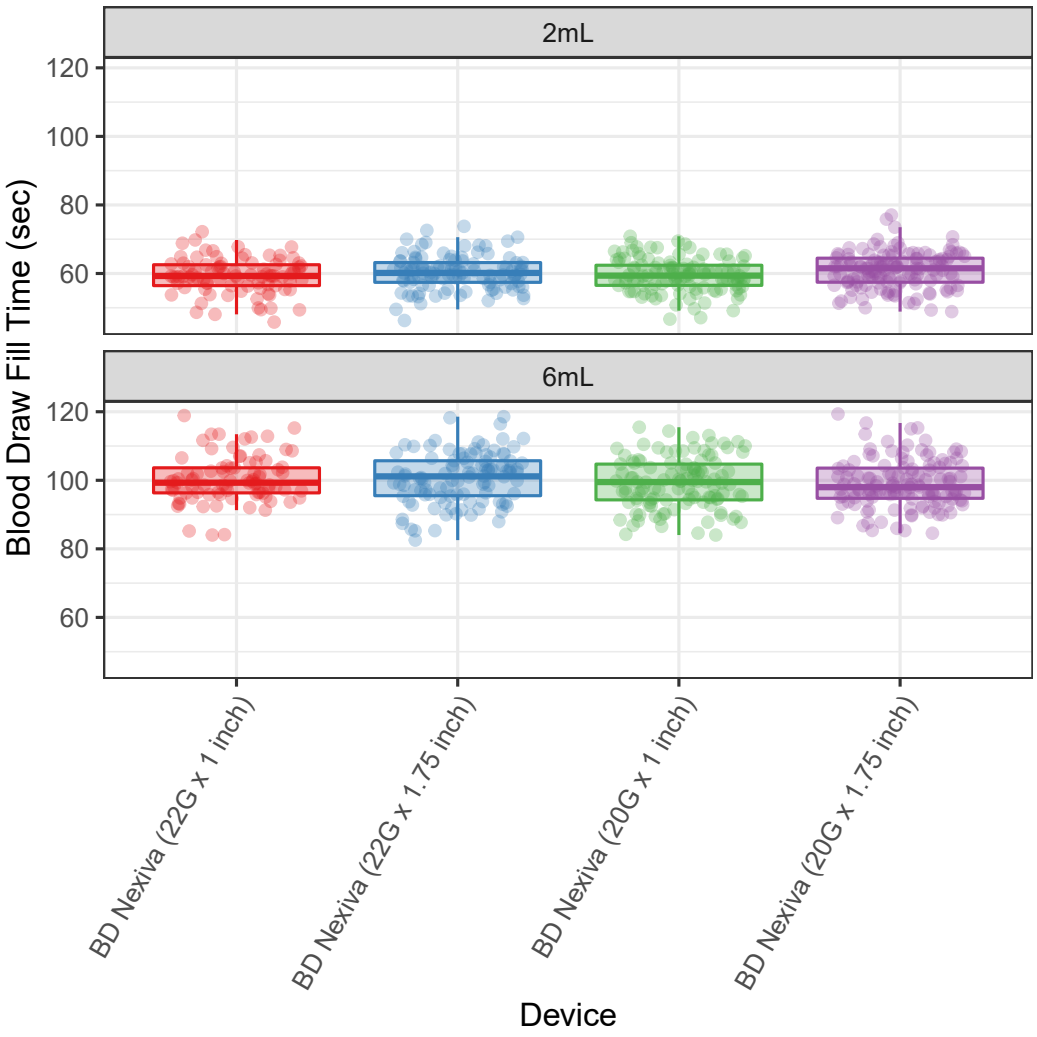


Figure B.5.2: Estimated Blood Draw Fill Time Difference (with 95% CI) between Device Configurations for 2 and 6mL Vacutainer tubes

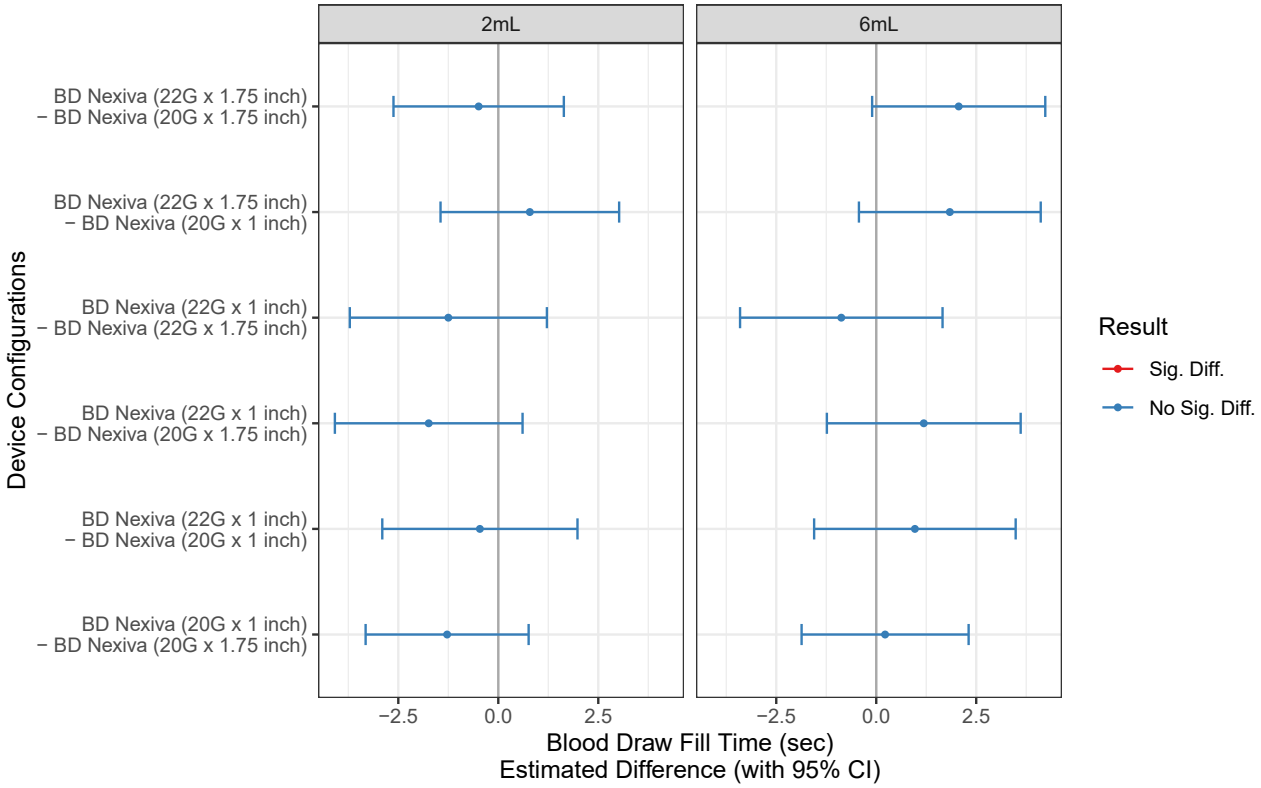


Figure B.5.3: Lineplot for Blood Draw Fill Time per Device Configuration at each captured timepoint

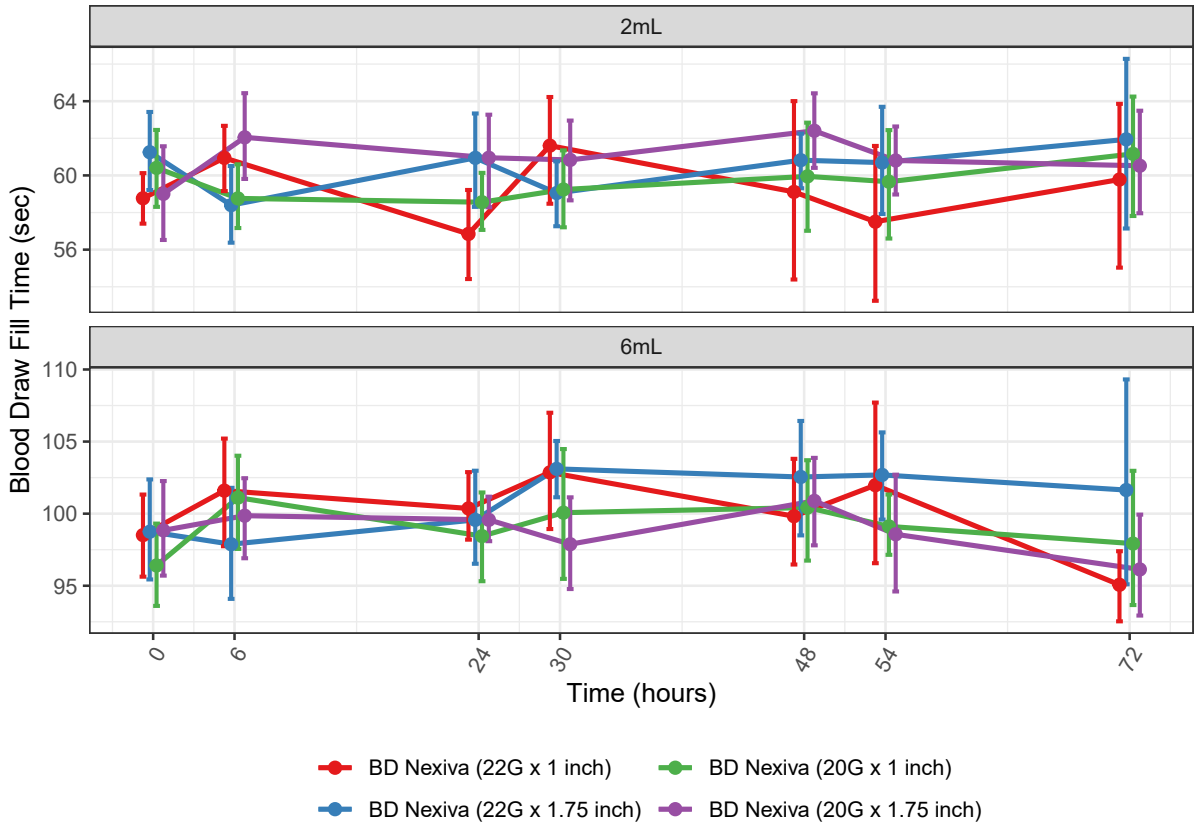
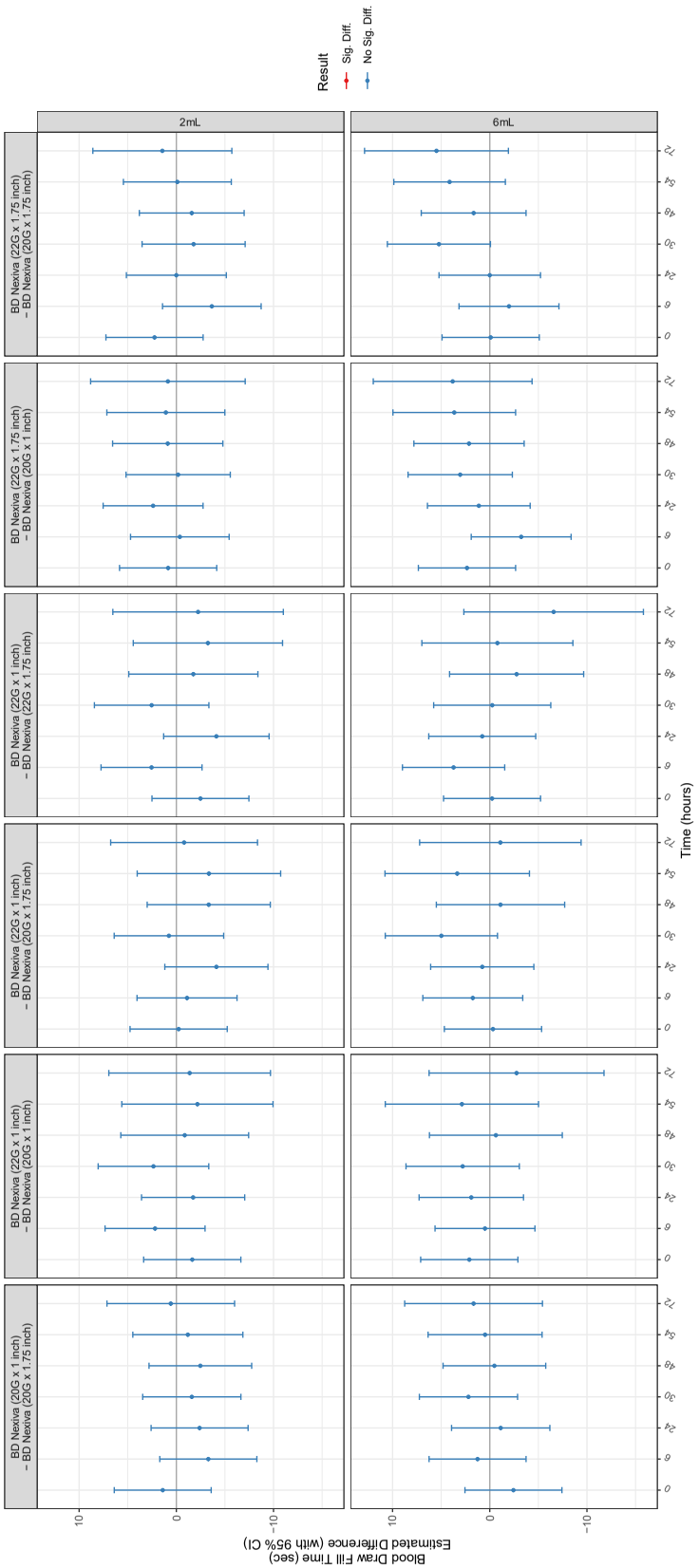


Figure B.5.4: Estimated Blood Draw Fill Time Difference (with 95% CI) between Device Configurations for 2 and 6mL Vacutainer tubes per Time Point



B.6 Thrombus Occurrence

Figure B.6.1: Barplot for Thrombus Occurence per Device Configuration

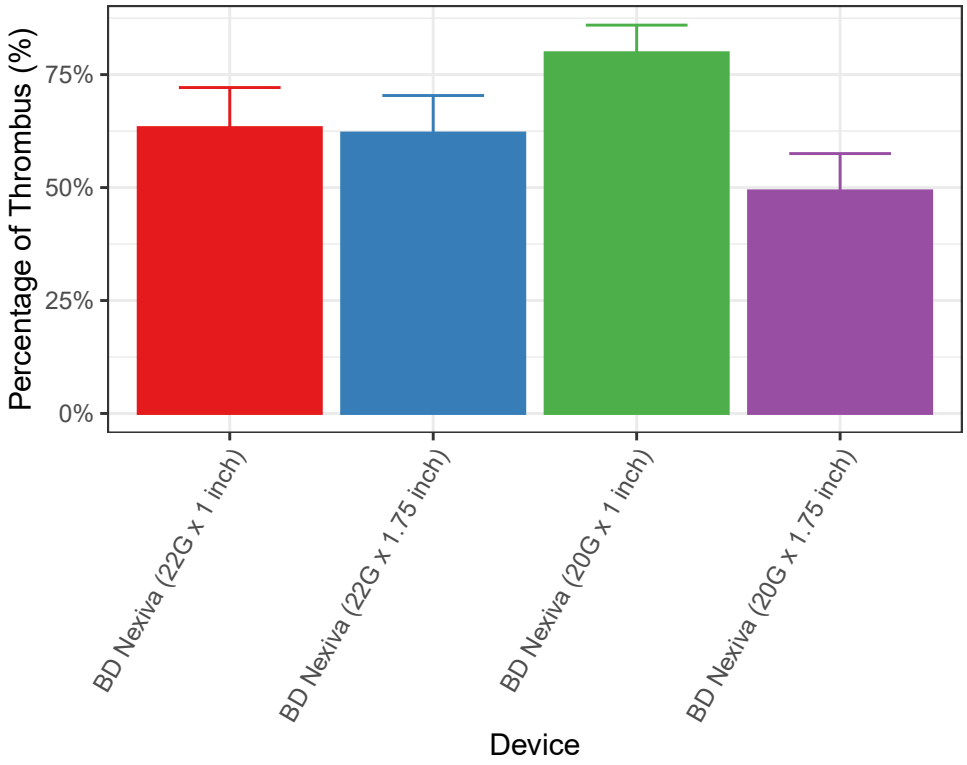
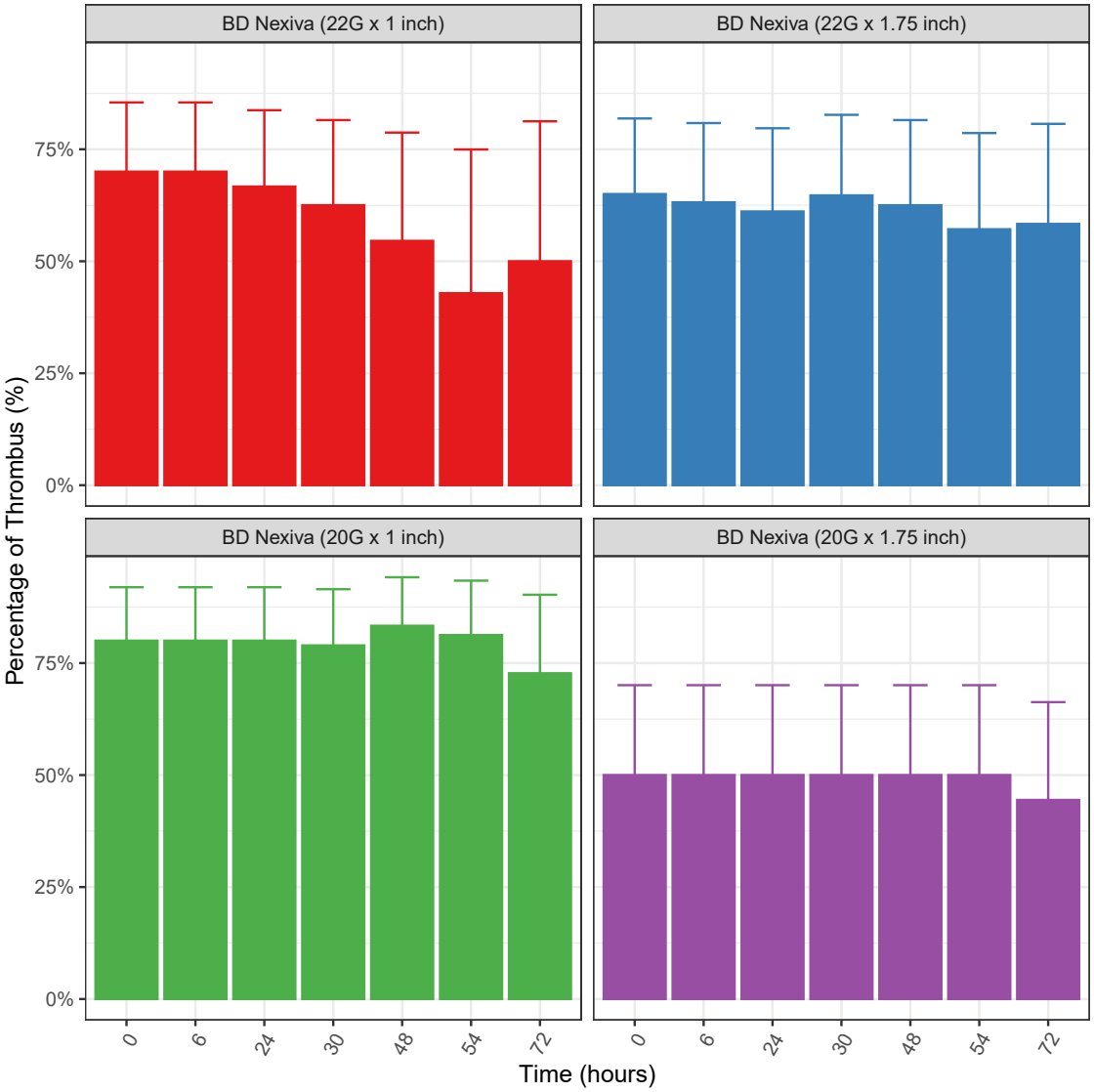
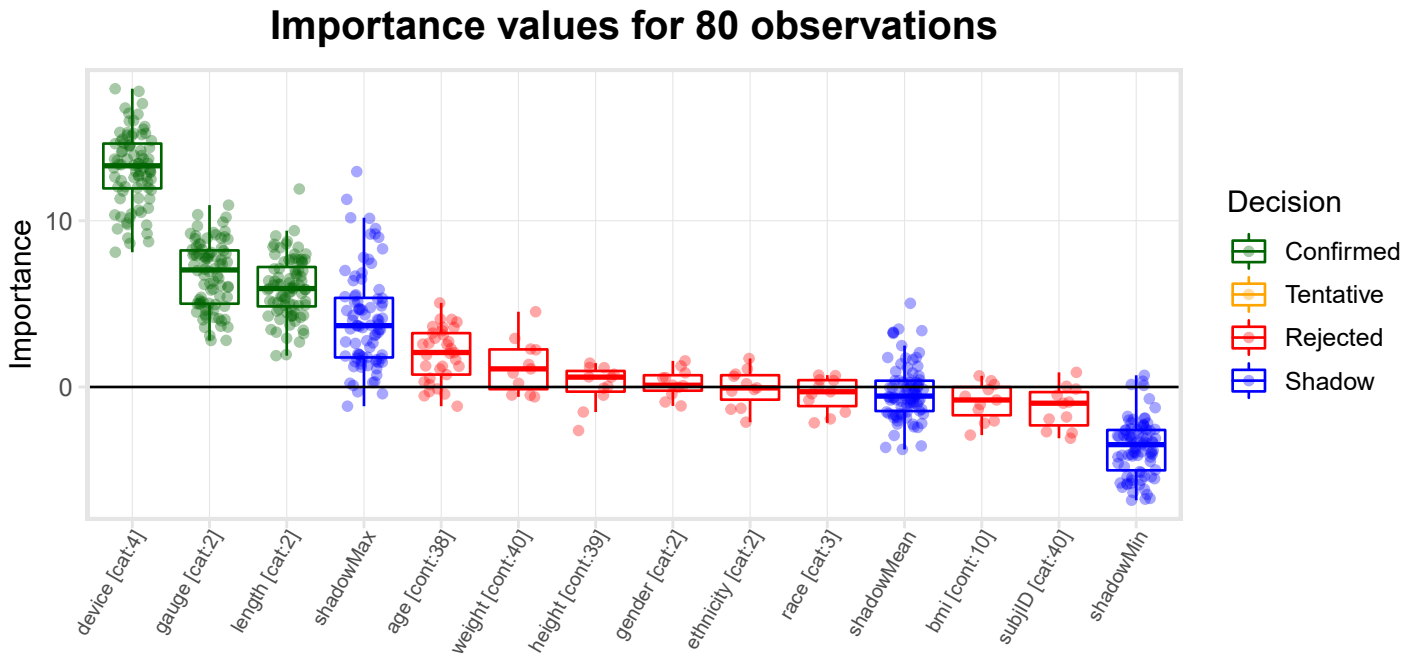


Figure B.6.2: Barplot for Thrombus Occurence per Device Configuration for each Timepoint



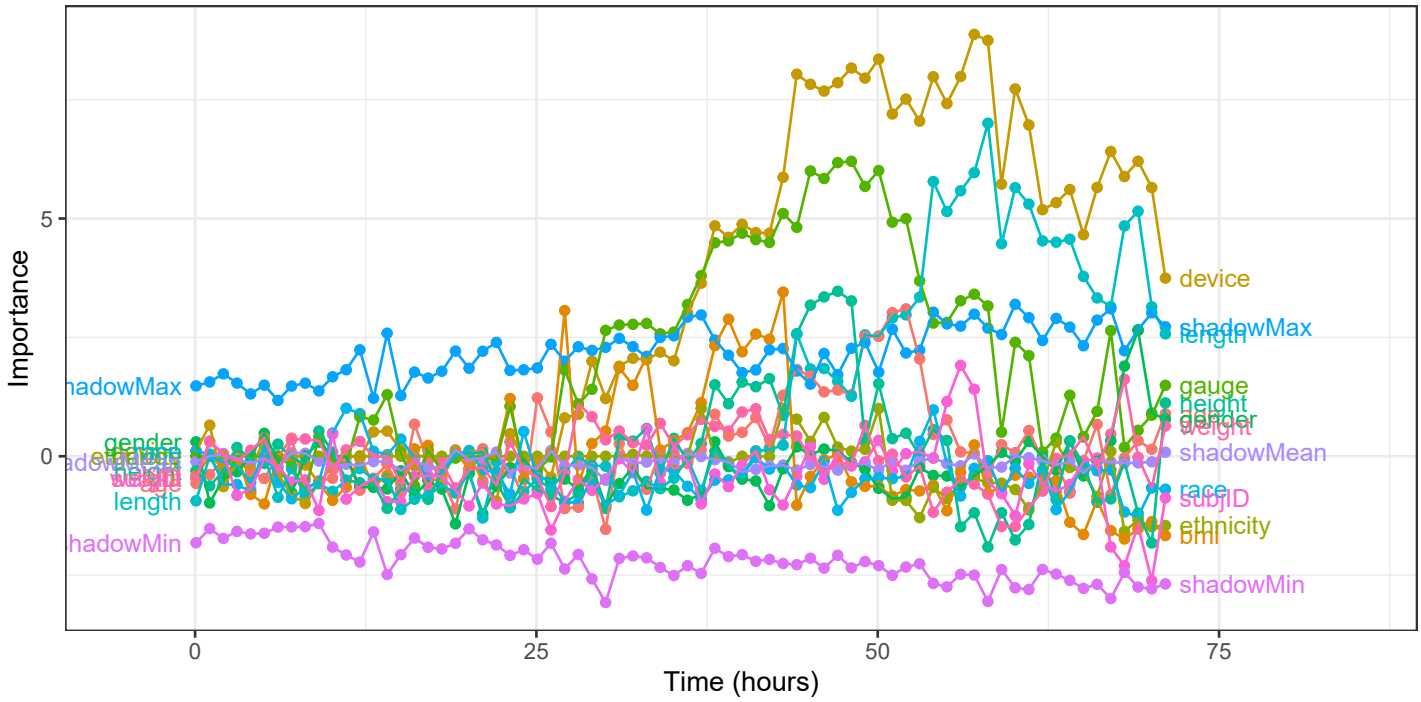
B.7 Feature Importance with Boruta Algorithm

Figure B.7.1: Boruta plot showing survival predictive importance of features



Note: The output of the Boruta algorithm represents the predictive importance of each feature. The algorithm statistically compares the importance of each feature to the importance of random features called "shadow variables" (obtained from the random permutation of the features available in the dataset). Features are assessed as being "Confirmed" when showing a significantly higher importance than the best shadow variables (shadowMax). For more details, please refer to [2].

Figure B.7.2: Boruta plot showing evolution of predictive importance of features over time



Note: The output presented in Figure B.7.2 represents the evolution of the output of the Boruta algorithm when considering median importance of predictors for device failure observed up to any considered time point, therefore potentially showing how different predictors can predominantly be associated with failures over time.

C Listings

Table C.0.1: Dummy randomization list (rows 1 to 40).

subjID	randoID	gauge	order	arm_length	arm	length	device
S001	101001.00	22G	1	RA_1.75 inch	Right	1.75 inch	BD Nexiva (22G x 1.75 inch)
S001	101001.00	22G	2	LA_1 inch	Left	1 inch	BD Nexiva (22G x 1 inch)
S002	101002.00	20G	1	LA_1.75 inch	Left	1.75 inch	BD Nexiva (20G x 1.75 inch)
S002	101002.00	20G	2	RA_1 inch	Right	1 inch	BD Nexiva (20G x 1 inch)
S003	101003.00	20G	1	LA_1 inch	Left	1 inch	BD Nexiva (20G x 1 inch)
S003	101003.00	20G	2	RA_1.75 inch	Right	1.75 inch	BD Nexiva (20G x 1.75 inch)
S004	101004.00	22G	1	LA_1 inch	Left	1 inch	BD Nexiva (22G x 1 inch)
S004	101004.00	22G	2	RA_1.75 inch	Right	1.75 inch	BD Nexiva (22G x 1.75 inch)
S005	101005.00	22G	1	RA_1 inch	Right	1 inch	BD Nexiva (22G x 1 inch)
S005	101005.00	22G	2	LA_1.75 inch	Left	1.75 inch	BD Nexiva (22G x 1.75 inch)
S006	101006.00	20G	1	RA_1.75 inch	Right	1.75 inch	BD Nexiva (20G x 1.75 inch)
S006	101006.00	20G	2	LA_1 inch	Left	1 inch	BD Nexiva (20G x 1 inch)
S007	101007.00	20G	1	RA_1 inch	Right	1 inch	BD Nexiva (20G x 1 inch)
S007	101007.00	20G	2	LA_1.75 inch	Left	1.75 inch	BD Nexiva (20G x 1.75 inch)
S008	101008.00	22G	1	LA_1.75 inch	Left	1.75 inch	BD Nexiva (22G x 1.75 inch)
S008	101008.00	22G	2	RA_1 inch	Right	1 inch	BD Nexiva (22G x 1 inch)
S009	101009.00	22G	1	RA_1.75 inch	Right	1.75 inch	BD Nexiva (22G x 1.75 inch)
S009	101009.00	22G	2	LA_1 inch	Left	1 inch	BD Nexiva (22G x 1 inch)
S010	101010.00	22G	1	LA_1 inch	Left	1 inch	BD Nexiva (22G x 1 inch)
S010	101010.00	22G	2	RA_1.75 inch	Right	1.75 inch	BD Nexiva (22G x 1.75 inch)
S011	101011.00	20G	1	RA_1 inch	Right	1 inch	BD Nexiva (20G x 1 inch)
S011	101011.00	20G	2	LA_1.75 inch	Left	1.75 inch	BD Nexiva (20G x 1.75 inch)
S012	101012.00	20G	1	LA_1 inch	Left	1 inch	BD Nexiva (20G x 1 inch)
S012	101012.00	20G	2	RA_1.75 inch	Right	1.75 inch	BD Nexiva (20G x 1.75 inch)
S013	101013.00	20G	1	RA_1.75 inch	Right	1.75 inch	BD Nexiva (20G x 1.75 inch)
S013	101013.00	20G	2	LA_1 inch	Left	1 inch	BD Nexiva (20G x 1 inch)
S014	101014.00	22G	1	LA_1.75 inch	Left	1.75 inch	BD Nexiva (22G x 1.75 inch)
S014	101014.00	22G	2	RA_1 inch	Right	1 inch	BD Nexiva (22G x 1 inch)
S015	101015.00	20G	1	LA_1.75 inch	Left	1.75 inch	BD Nexiva (20G x 1.75 inch)
S015	101015.00	20G	2	RA_1 inch	Right	1 inch	BD Nexiva (20G x 1 inch)
S016	101016.00	22G	1	RA_1 inch	Right	1 inch	BD Nexiva (22G x 1 inch)
S016	101016.00	22G	2	LA_1.75 inch	Left	1.75 inch	BD Nexiva (22G x 1.75 inch)
S017	101017.00	20G	1	RA_1 inch	Right	1 inch	BD Nexiva (20G x 1 inch)
S017	101017.00	20G	2	LA_1.75 inch	Left	1.75 inch	BD Nexiva (20G x 1.75 inch)
S018	101018.00	22G	1	LA_1 inch	Left	1 inch	BD Nexiva (22G x 1 inch)
S018	101018.00	22G	2	RA_1.75 inch	Right	1.75 inch	BD Nexiva (22G x 1.75 inch)
S019	101019.00	22G	1	RA_1.75 inch	Right	1.75 inch	BD Nexiva (22G x 1.75 inch)
S019	101019.00	22G	2	LA_1 inch	Left	1 inch	BD Nexiva (22G x 1 inch)
S020	101020.00	20G	1	LA_1.75 inch	Left	1.75 inch	BD Nexiva (20G x 1.75 inch)
S020	101020.00	20G	2	RA_1 inch	Right	1 inch	BD Nexiva (20G x 1 inch)

Table C.0.2: Dummy Demographics listing (rows 1 to 40).

subjID	gauge	age	gender	ethnicity	race	height	weight	bmi
S001	22G	48.60	M	Hispanic / Latino	Asian	181.70	84.80	22.00
S002	20G	47.90	F	Hispanic / Latino	White / Caucasian	151.20	57.90	20.00
S003	20G	47.20	M	Non Hispanic / Latino	Other	159.00	59.00	19.00
S004	22G	49.60	F	Non Hispanic / Latino	Asian	165.20	68.10	20.00
S005	22G	57.10	F	Non Hispanic / Latino	White / Caucasian	160.30	76.30	20.00
S006	20G	56.30	F	Non Hispanic / Latino	Other	159.30	58.80	18.00
S007	20G	31.70	F	Non Hispanic / Latino	Asian	158.20	80.50	24.00
S008	22G	57.40	F	Non Hispanic / Latino	White / Caucasian	172.50	63.50	22.00
S009	22G	32.90	F	Non Hispanic / Latino	Other	174.90	86.20	24.00
S010	22G	39.80	M	Non Hispanic / Latino	Asian	174.80	65.50	25.00
S011	20G	25.20	M	Non Hispanic / Latino	White / Caucasian	160.40	52.80	19.00
S012	20G	54.40	F	Non Hispanic / Latino	Other	170.40	56.20	23.00
S013	20G	43.40	F	Non Hispanic / Latino	Asian	177.10	74.20	23.00
S014	22G	28.50	M	Non Hispanic / Latino	White / Caucasian	155.50	73.70	26.00
S015	20G	39.20	M	Non Hispanic / Latino	Other	185.60	77.30	27.00
S016	22G	32.50	F	Non Hispanic / Latino	Asian	150.40	69.10	24.00
S017	20G	25.40	F	Non Hispanic / Latino	White / Caucasian	181.20	71.50	25.00
S018	22G	24.30	M	Non Hispanic / Latino	Other	180.70	75.50	19.00
S019	22G	55.50	M	Non Hispanic / Latino	Asian	188.60	84.40	24.00
S020	20G	49.00	M	Non Hispanic / Latino	White / Caucasian	153.50	54.20	23.00
S021	22G	28.30	M	Non Hispanic / Latino	Other	169.70	71.80	23.00
S022	20G	46.00	F	Non Hispanic / Latino	Asian	184.50	76.80	20.00
S023	22G	54.60	M	Non Hispanic / Latino	White / Caucasian	185.30	82.40	26.00
S024	20G	24.20	M	Non Hispanic / Latino	Other	156.30	79.90	23.00
S025	20G	28.10	M	Non Hispanic / Latino	Asian	185.20	59.50	19.00
S026	20G	55.10	M	Non Hispanic / Latino	White / Caucasian	161.70	75.30	26.00
S027	22G	29.30	F	Non Hispanic / Latino	Other	157.00	75.90	19.00
S028	22G	39.10	F	Non Hispanic / Latino	Asian	155.20	84.20	24.00
S029	20G	44.30	M	Non Hispanic / Latino	White / Caucasian	170.70	81.60	21.00
S030	20G	52.30	F	Non Hispanic / Latino	Other	152.50	77.70	25.00
S031	22G	26.50	M	Non Hispanic / Latino	Asian	178.80	69.60	25.00
S032	22G	45.00	M	Non Hispanic / Latino	White / Caucasian	166.70	88.70	20.00
S033	22G	28.10	M	Non Hispanic / Latino	Other	166.60	63.90	27.00
S034	20G	52.20	F	Non Hispanic / Latino	Asian	169.40	54.70	22.00
S035	22G	55.50	F	Non Hispanic / Latino	White / Caucasian	179.50	82.50	21.00
S036	20G	29.90	F	Hispanic / Latino	Other	153.50	61.10	21.00
S037	20G	55.70	F	Non Hispanic / Latino	Asian	177.20	73.50	26.00
S038	20G	39.60	M	Non Hispanic / Latino	White / Caucasian	154.30	75.80	24.00
S039	22G	23.90	F	Non Hispanic / Latino	Other	158.40	88.60	21.00
S040	22G	40.90	M	Non Hispanic / Latino	Asian	150.90	80.80	26.00

Table C.0.3: Dummy Family Medical History listing (rows 1 to 40).

subjID	gauge	bloodDisorderClotting	cancer	heartDisease	highBloodPressure	diabetesType2
S001	22G	No	No	No	No	Yes
S002	20G	No	No	No	No	No
S003	20G	No	No	No	No	No
S004	22G	No	No	No	Yes	No
S005	22G	Yes	No	No	No	Yes
S006	20G	No	No	No	Yes	No
S007	20G	No	No	No	No	No
S008	22G	Yes	No	No	No	Yes
S009	22G	No	No	No	No	Yes
S010	22G	No	No	No	No	No
S011	20G	No	No	No	No	Yes
S012	20G	No	No	No	No	No
S013	20G	No	No	No	Yes	No
S014	22G	No	No	No	No	No
S015	20G	No	No	No	Yes	No
S016	22G	No	No	No	No	No
S017	20G	No	No	No	Yes	No
S018	22G	No	No	No	No	No
S019	22G	No	No	No	No	No
S020	20G	No	No	No	Yes	No
S021	22G	No	No	No	No	No
S022	20G	No	Yes	No	Yes	No
S023	22G	No	No	No	No	No
S024	20G	No	No	No	No	No
S025	20G	No	No	No	Yes	No
S026	20G	No	No	No	No	No
S027	22G	No	No	No	No	Yes
S028	22G	No	Yes	No	No	No
S029	20G	No	No	No	No	No
S030	20G	No	No	No	No	No
S031	22G	No	No	No	No	No
S032	22G	No	No	No	No	No
S033	22G	No	No	No	No	No
S034	20G	No	No	No	No	No
S035	22G	No	No	No	No	Yes
S036	20G	No	No	No	No	No
S037	20G	No	No	No	No	No
S038	20G	No	No	No	No	No
S039	22G	No	No	No	No	No
S040	22G	No	No	No	No	No

Table C.0.4: Dummy Baseline listing (rows 1 to 40).

subjID	gauge	tipMidStream	tipWallContact	bfv	cv_ratio
S001	22G	Yes	No	162.86	35.70
S002	20G	Yes	No	169.78	33.96
S003	20G	Yes	Yes	157.73	39.69
S004	22G	Yes	Yes	151.31	42.67
S005	22G	No	No	165.24	36.42
S006	20G	No	No	164.16	44.91
S007	20G	Yes	No	168.51	35.11
S008	22G	No	No	163.64	30.23
S009	22G	Yes	No	173.14	33.27
S010	22G	Yes	No	164.40	40.57
S011	20G	Yes	No	159.85	41.06
S012	20G	No	No	173.71	37.45
S013	20G	Yes	Yes	160.25	42.14
S014	22G	Yes	No	166.91	31.00
S015	20G	Yes	No	155.56	44.65
S016	22G	Yes	No	159.83	35.38
S017	20G	Yes	No	163.14	42.58
S018	22G	Yes	No	161.69	38.99
S019	22G	No	No	159.15	34.75
S020	20G	Yes	No	151.37	43.20
S021	22G	Yes	No	163.94	34.72
S022	20G	Yes	Yes	169.70	42.95
S023	22G	No	No	164.49	40.26
S024	20G	Yes	No	161.92	32.11
S025	20G	Yes	No	173.03	42.02
S026	20G	No	No	154.34	33.76
S027	22G	Yes	Yes	155.45	41.91
S028	22G	Yes	Yes	155.20	30.45
S029	20G	Yes	No	169.53	33.37
S030	20G	Yes	No	157.41	35.70
S031	22G	Yes	No	150.97	33.86
S032	22G	Yes	No	157.20	33.50
S033	22G	Yes	No	158.89	33.09
S034	20G	Yes	Yes	161.70	38.45
S035	22G	No	No	173.17	39.35
S036	20G	Yes	No	158.18	39.31
S037	20G	No	No	150.46	33.90
S038	20G	Yes	No	158.48	37.64
S039	22G	Yes	No	173.28	40.17
S040	22G	Yes	No	156.54	32.07

Table C.0.5: Dummy Indwell Time listing (rows 1 to 40).

subjID	device	lifeTime	indwellTime_cont	status	eventType	indwellTime_disc
S001	BD Nexiva (22G x 1 inch)	67.20	67.20	1.00	blood_draw_6mL	72.00
S001	BD Nexiva (22G x 1.75 inch)	72.53	72.00	1.00	blood_draw_6mL	72.00
S002	BD Nexiva (20G x 1 inch)	80.58	72.00	0.00		72.00
S002	BD Nexiva (20G x 1.75 inch)	68.25	68.25	1.00	flush	72.00
S003	BD Nexiva (20G x 1 inch)	57.79	57.79	1.00	blood_draw_6mL	54.00
S003	BD Nexiva (20G x 1.75 inch)	91.75	72.00	0.00		72.00
S004	BD Nexiva (22G x 1 inch)	66.26	66.26	0.00		72.00
S004	BD Nexiva (22G x 1.75 inch)	86.02	72.00	1.00	flush	72.00
S005	BD Nexiva (22G x 1 inch)	90.85	72.00	0.00		72.00
S005	BD Nexiva (22G x 1.75 inch)	66.75	66.75	1.00	flush	72.00
S006	BD Nexiva (20G x 1 inch)	64.59	64.59	0.00		72.00
S006	BD Nexiva (20G x 1.75 inch)	69.34	69.34	0.00		72.00
S007	BD Nexiva (20G x 1 inch)	61.96	61.96	1.00	flush	54.00
S007	BD Nexiva (20G x 1.75 inch)	72.67	72.00	0.00		72.00
S008	BD Nexiva (22G x 1 inch)	35.96	35.96	1.00	flush	30.00
S008	BD Nexiva (22G x 1.75 inch)	95.55	72.00	0.00		72.00
S009	BD Nexiva (22G x 1 inch)	37.24	37.24	1.00	blood_draw_2mL	30.00
S009	BD Nexiva (22G x 1.75 inch)	22.31	22.31	1.00	blood_draw_2mL	24.00
S010	BD Nexiva (22G x 1 inch)	28.76	28.76	0.00		30.00
S010	BD Nexiva (22G x 1.75 inch)	44.98	44.98	1.00	flush	48.00
S011	BD Nexiva (20G x 1 inch)	43.29	43.29	1.00	flush	48.00
S011	BD Nexiva (20G x 1.75 inch)	93.55	72.00	0.00		72.00
S012	BD Nexiva (20G x 1 inch)	37.93	37.93	0.00		30.00
S012	BD Nexiva (20G x 1.75 inch)	83.98	72.00	0.00		72.00
S013	BD Nexiva (20G x 1 inch)	74.79	72.00	1.00	flush	72.00
S013	BD Nexiva (20G x 1.75 inch)	70.04	70.04	0.00		72.00
S014	BD Nexiva (22G x 1 inch)	73.05	72.00	1.00	blood_draw_2mL	72.00
S014	BD Nexiva (22G x 1.75 inch)	70.67	70.67	0.00		72.00
S015	BD Nexiva (20G x 1 inch)	53.34	53.34	1.00	blood_draw_2mL	54.00
S015	BD Nexiva (20G x 1.75 inch)	92.07	72.00	1.00	flush	72.00
S016	BD Nexiva (22G x 1 inch)	10.73	10.73	1.00	flush	6.00
S016	BD Nexiva (22G x 1.75 inch)	61.41	61.41	0.00		54.00
S017	BD Nexiva (20G x 1 inch)	68.60	68.60	0.00		72.00
S017	BD Nexiva (20G x 1.75 inch)	58.60	58.60	1.00	flush	54.00
S018	BD Nexiva (22G x 1 inch)	43.54	43.54	1.00	blood_draw_6mL	48.00
S018	BD Nexiva (22G x 1.75 inch)	64.02	64.02	1.00	flush	72.00
S019	BD Nexiva (22G x 1 inch)	26.92	26.92	1.00	flush	24.00
S019	BD Nexiva (22G x 1.75 inch)	82.65	72.00	0.00		72.00
S020	BD Nexiva (20G x 1 inch)	73.47	72.00	1.00	blood_draw_2mL	72.00
S020	BD Nexiva (20G x 1.75 inch)	87.35	72.00	0.00		72.00

Table C.0.6: Dummy Blood Analysis listing (rows 1 to 40).

subjID	device	lifeTime	Indwell Time (cont.)	Indwell Time (cat.)	baselineCfHb	timepoint	tube	cfHb	haemolysis - AU480	haemolysis - Visual	Blood Draw Duration (sec.)
S001	BD Nexiva (22G x 1 inch)	67.20	67.20	72.00	191.86	0.00	2mL	143.26	No	No	62.52
S001	BD Nexiva (22G x 1 inch)	67.20	67.20	72.00	191.86	0.00	6mL	189.17	No	Yes	102.54
S001	BD Nexiva (22G x 1 inch)	67.20	67.20	72.00	191.86	6.00	2mL	149.51	No	No	59.28
S001	BD Nexiva (22G x 1 inch)	67.20	67.20	72.00	191.86	6.00	6mL	198.38	No	Yes	84.14
S001	BD Nexiva (22G x 1 inch)	67.20	67.20	72.00	191.86	24.00	2mL	198.79	No	Yes	62.80
S001	BD Nexiva (22G x 1 inch)	67.20	67.20	72.00	191.86	24.00	6mL	146.22	No	No	102.12
S001	BD Nexiva (22G x 1 inch)	67.20	67.20	72.00	191.86	30.00	2mL	216.39	Yes	Yes	59.31
S001	BD Nexiva (22G x 1 inch)	67.20	67.20	72.00	191.86	30.00	6mL	191.83	No	Yes	105.70
S001	BD Nexiva (22G x 1 inch)	67.20	67.20	72.00	191.86	48.00	2mL	215.34	Yes	Yes	59.57
S001	BD Nexiva (22G x 1 inch)	67.20	67.20	72.00	191.86	48.00	6mL	284.53	Yes	Yes	94.84
S001	BD Nexiva (22G x 1 inch)	67.20	67.20	72.00	191.86	54.00	2mL	162.19	No	No	65.32
S001	BD Nexiva (22G x 1 inch)	67.20	67.20	72.00	191.86	54.00	6mL	169.64	No	No	103.54
S001	BD Nexiva (22G x 1 inch)	67.20	67.20	72.00	191.86	72.00	2mL	152.62	No	No	64.50
S001	BD Nexiva (22G x 1 inch)	67.20	67.20	72.00	191.86	72.00	6mL	156.91	No	No	94.85
S001	BD Nexiva (22G x 1.75 inch)	72.53	72.00	72.00	191.86	0.00	2mL	153.01	No	No	57.46
S001	BD Nexiva (22G x 1.75 inch)	72.53	72.00	72.00	191.86	0.00	6mL	186.75	No	Yes	109.77
S001	BD Nexiva (22G x 1.75 inch)	72.53	72.00	72.00	191.86	6.00	2mL	168.11	No	No	56.58
S001	BD Nexiva (22G x 1.75 inch)	72.53	72.00	72.00	191.86	6.00	6mL	161.64	No	No	109.21
S001	BD Nexiva (22G x 1.75 inch)	72.53	72.00	72.00	191.86	24.00	2mL	195.47	No	Yes	53.42
S001	BD Nexiva (22G x 1.75 inch)	72.53	72.00	72.00	191.86	24.00	6mL	163.25	No	No	107.81
S001	BD Nexiva (22G x 1.75 inch)	72.53	72.00	72.00	191.86	30.00	2mL	202.26	Yes	Yes	59.02
S001	BD Nexiva (22G x 1.75 inch)	72.53	72.00	72.00	191.86	30.00	6mL	171.86	No	No	101.98
S001	BD Nexiva (22G x 1.75 inch)	72.53	72.00	72.00	191.86	48.00	2mL	135.55	No	No	61.49
S001	BD Nexiva (22G x 1.75 inch)	72.53	72.00	72.00	191.86	48.00	6mL	174.44	No	No	97.01
S001	BD Nexiva (22G x 1.75 inch)	72.53	72.00	72.00	191.86	54.00	2mL	114.32	No	No	49.53
S001	BD Nexiva (22G x 1.75 inch)	72.53	72.00	72.00	191.86	54.00	6mL	163.32	No	No	106.43
S001	BD Nexiva (22G x 1.75 inch)	72.53	72.00	72.00	191.86	72.00	2mL	217.83	Yes	Yes	64.70
S001	BD Nexiva (22G x 1.75 inch)	72.53	72.00	72.00	191.86	72.00	6mL	148.19	No	No	105.51
S002	BD Nexiva (20G x 1.75 inch)	68.25	68.25	72.00	176.53	0.00	2mL	153.96	No	No	54.68
S002	BD Nexiva (20G x 1.75 inch)	68.25	68.25	72.00	176.53	0.00	6mL	153.11	No	No	95.97
S002	BD Nexiva (20G x 1.75 inch)	68.25	68.25	72.00	176.53	6.00	2mL	153.49	No	No	64.35
S002	BD Nexiva (20G x 1.75 inch)	68.25	68.25	72.00	176.53	6.00	6mL	205.98	Yes	Yes	96.23
S002	BD Nexiva (20G x 1.75 inch)	68.25	68.25	72.00	176.53	24.00	2mL	130.04	No	No	62.57
S002	BD Nexiva (20G x 1.75 inch)	68.25	68.25	72.00	176.53	24.00	6mL	161.20	No	No	104.41
S002	BD Nexiva (20G x 1.75 inch)	68.25	68.25	72.00	176.53	30.00	2mL	139.05	No	No	68.95
S002	BD Nexiva (20G x 1.75 inch)	68.25	68.25	72.00	176.53	30.00	6mL	158.97	No	No	95.09
S002	BD Nexiva (20G x 1.75 inch)	68.25	68.25	72.00	176.53	48.00	2mL	155.15	No	No	59.26
S002	BD Nexiva (20G x 1.75 inch)	68.25	68.25	72.00	176.53	48.00	6mL	140.26	No	No	95.75
S002	BD Nexiva (20G x 1.75 inch)	68.25	68.25	72.00	176.53	54.00	2mL	160.11	No	No	61.84
S002	BD Nexiva (20G x 1.75 inch)	68.25	68.25	72.00	176.53	54.00	6mL	149.46	No	No	94.52

Table C.0.7: Dummy Blood Analysis Baseline listing (rows 1 to 40).

subjID	gauge	tube	cfHb	haemolysis_AU480	haemolysis_Visual	bloodDrawDuration
S001	22G	2mL	148.74	No	No	43.72
S001	22G	6mL	234.99	Yes	Yes	111.18
S002	20G	2mL	224.05	Yes	Yes	32.77
S002	20G	6mL	129.02	No	No	104.25
S003	20G	2mL	212.55	Yes	Yes	33.82
S003	20G	6mL	263.10	Yes	Yes	86.61
S004	22G	2mL	135.19	No	No	40.63
S004	22G	6mL	259.57	Yes	Yes	98.93
S005	22G	2mL	202.30	Yes	Yes	37.65
S005	22G	6mL	244.32	Yes	Yes	100.27
S006	20G	2mL	223.75	Yes	Yes	42.84
S006	20G	6mL	216.52	Yes	Yes	95.40
S007	20G	2mL	56.99	No	No	43.10
S007	20G	6mL	225.63	Yes	Yes	102.07
S008	22G	2mL	148.56	No	No	35.68
S008	22G	6mL	185.07	No	Yes	100.02
S009	22G	2mL	197.34	No	Yes	42.94
S009	22G	6mL	311.35	Yes	Yes	92.57
S010	22G	2mL	210.10	Yes	Yes	42.49
S010	22G	6mL	262.42	Yes	Yes	97.18
S011	20G	2mL	197.32	No	Yes	42.06
S011	20G	6mL	143.21	No	No	93.79
S012	20G	2mL	264.69	Yes	Yes	36.38
S012	20G	6mL	210.89	Yes	Yes	88.81
S013	20G	2mL	196.52	No	Yes	36.05
S013	20G	6mL	219.72	Yes	Yes	104.09
S014	22G	2mL	124.86	No	No	43.14
S014	22G	6mL	197.42	No	Yes	106.31
S015	20G	2mL	132.21	No	No	42.66
S015	20G	6mL	214.86	Yes	Yes	108.96
S016	22G	2mL	237.06	Yes	Yes	38.79
S016	22G	6mL	167.25	No	No	101.38
S017	20G	2mL	191.75	No	Yes	42.19
S017	20G	6mL	275.98	Yes	Yes	103.73
S018	22G	2mL	171.68	No	No	32.80
S018	22G	6mL	227.78	Yes	Yes	91.10
S019	22G	2mL	155.16	No	No	44.12
S019	22G	6mL	165.42	No	No	116.40
S020	20G	2mL	204.74	Yes	Yes	41.08
S020	20G	6mL	216.52	Yes	Yes	94.47

D Additional Figures

D.1 PIVC Rescue Decision Tree

Figure D.1.1: PIVC Rescue Decision Tree for Flush Procedures

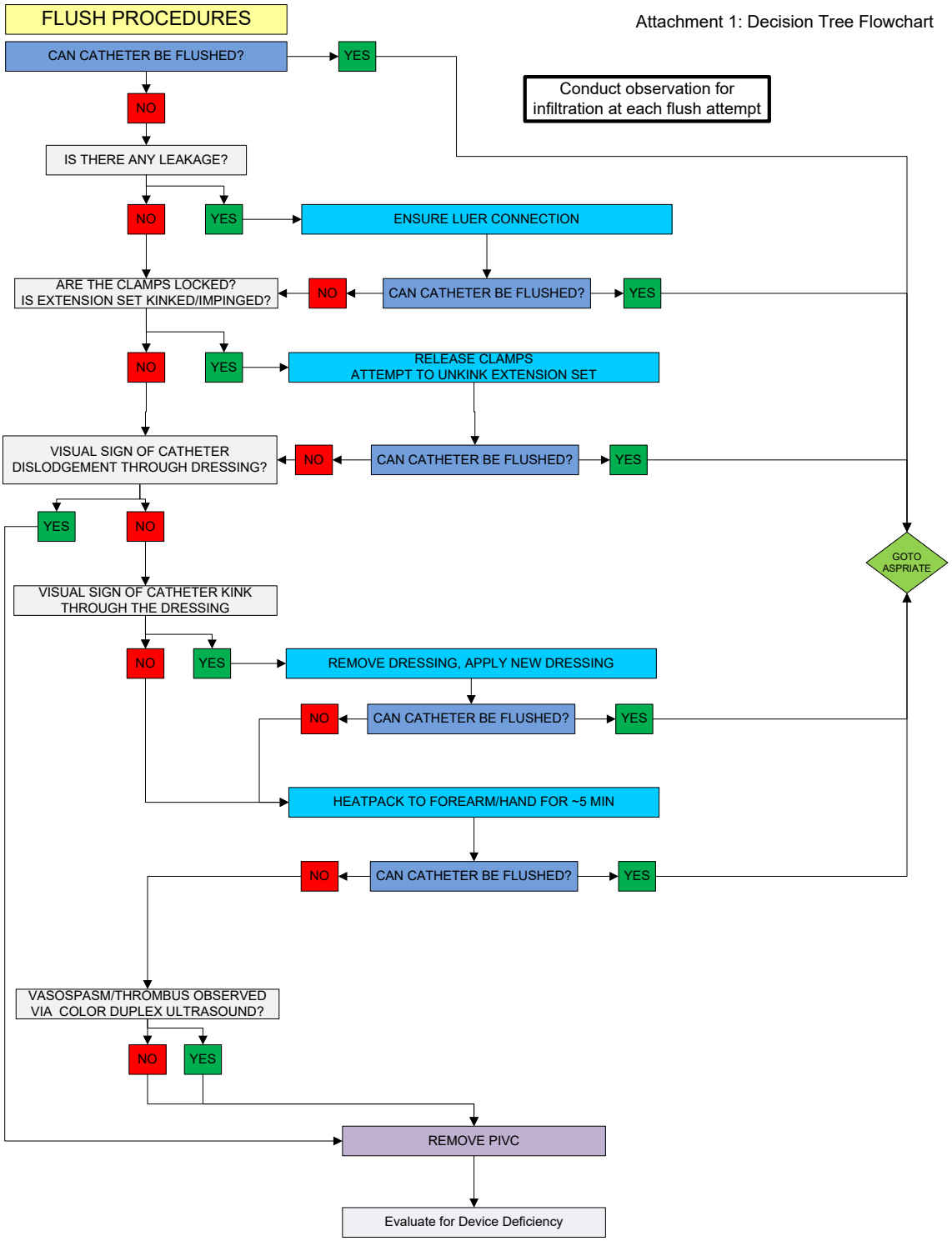


Figure D.1.2: PIVC Rescue Decision Tree for Aspiration Procedures