Protocol Number: [redacted] CONFIDENTIAL
Version: 4.0
Date: 07 September 2022

TITLE PAGE

Protocol Title:
A prospective multi-center study to evaluate clinical equivalence (method comparison) between the BD Microtainer® Easy Collect Capillary Tube SST™ and BD Microtainer® Easy Collect Capillary Tube EDTA devices to respective comparators

Protocol Number: [redacted]

Version Number: 4.0

Study Device: [redacted] Tube SST™ [redacted] EDTA

Study Type:
Investigational Device Exemption (IDE)

Short Title: [redacted]

Sponsor Name: BD Integrated Diagnostic Solutions

Legal Registered Address: 1 Becton Drive; Franklin Lakes, NJ 07417
Sponsor Contact:
Nathan Loes
Sr. Clinical Project Manager
Nathan.Loes@BD.com

Regulatory Agency Identifier Number(s): Not applicable

National Principal Investigators	
[redacted]	[redacted] Becton Dickinson and Company 1 Becton Drive Franklin Lakes, NJ 07417 Vice President, Global Clinical Development [redacted]
[redacted]	

[redacted]

Protocol Number: [redacted] CONFIDENTIAL
Version: 4.0
Date: 07 September 2022

Version History:

Version Number	Date	Type
1.0	12/20/2021	Original
2.0	02/22/2022	Amendment
3.0	06/06/2022	Protocol updated to include interim analysis (Section 10.6). Sponsor Contact and team members/approvers were updated. Adverse Event (Section 9.1.1.) was updated to be consistent with changes being made to subsequent [redacted] protocols
4.0	09/07/2022	Protocol Updated to specify which Instrument Flags will be evaluated (Section 1.1 Protocol Synopsis pg 11; Section 3 Objectives & Endpoints pgs 23-24). Table 3 – Reference numbers for Vitamin D (10995719/10995720) & Total Protein (11097604) were updated to reflect the correct assay reference numbers used in the study. Previous Reference number for Vitamin D (11201772/11201773) was an invalid reference and Total Protein (11097524) is for urine analysis which were listed in error in the protocol.

[redacted]

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SPONSOR PROTOCOL APPROVAL

Signature below indicates approval of the protocol as written.

Individual or function	Name	Signature	Date
[redacted]	[redacted]	*This document is signed electronically in the eTMF system*	
[redacted]	[redacted]	*This document is signed electronically in the eTMF system*	
[redacted]	[redacted]	*This document is signed electronically in the eTMF system*	
[redacted]	[redacted]	*This document is signed electronically in the eTMF system*	
[redacted]	[redacted]	*This document is signed electronically in the eTMF system*	
[redacted]	[redacted]	*This document is signed electronically in the eTMF system*	

[redacted]

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PRINCIPAL INVESTIGATOR AGREEMENT PAGE

Investigator Responsibilities

1. Prior to participation in this study, the Investigator or Institution must sign the Clinical Study Agreement (CSA) and obtain written approval from the appropriate Institutional Review Board (IRB)/Ethics Committee (EC).
2. The Investigator must receive BD-sponsored training prior to site activation. The Investigator is responsible for ensuring that all Sub-Investigators and clinical staff are adequately trained prior to performing any data collection or study-related procedures.
3. The Principal Investigator shall ensure that the study is conducted in accordance with the study protocol, any modifications as requested by the IRB/EC, the signed CSA, the ethical principles of the Declaration of Helsinki, Good Clinical Practice (ICH E6) / ISO 14155), and applicable national/regional regulations and laws.
4. If applicable, ensure that written informed consent is obtained from each participant prior to the conduct of any study procedure, using the current IRB/EC approved Informed Consent Form.

I have read and understand the contents of this study protocol. I agree to follow and abide by the requirements set forth in this document. I agree to conduct the trial in accordance with the study protocol, the signed Clinical Study Agreement, and Good Clinical Practice (GCP) as well as applicable FDA and ISO regulations (e.g., 21 CFR Parts 812, 50, 54, 56; ISO 14155:2011E). I agree to participate in BD-Sponsored training prior to performing any data collection or study-related procedures.

Agreed to by (Investigator):

_____
Printed Name – Investigator

_____
Signature – Investigator

_____
Site Number

_____
Date

Abbreviations

ADE	Adverse Device Effect
AE	Adverse Event
AMR	Analytical Measurement Range
BD	Becton, Dickinson, and Company
CAL	Clinical Acceptance Limits
CAP	Capillary Collection
CBC	Complete Blood Count
CFR	Code of Federal Regulations
CI	Confidence Interval
COV	Close-out Visit
CRF	Case Report/Record Form
CSA	Clinical Study Agreement
CV	Coefficient of Variation
DMP	Data Management Plan
EDC	Electronic Data Capture
EDTA	Ethylenediaminetetraacetic acid
FDA	Food and Drug Administration
FDAAA	FDA Amendments Act of 2007
GCP	Good Clinical Practice
HbA1c	Hemoglobin A1c (glycosylated hemoglobin)
HIPAA	Health Insurance Portability and Accountability Act
ICF	Informed Consent Form
ICH	International Conference on Harmonization
IDE	Investigational Device Exemption
IDS-SM	Integrated Diagnostic Solutions – Specimen Management
IFU	Instructions for Use
IP	Interpretive Program
IRB/EC	Institutional or Independent Review Board/Ethics Committee
ISO	International Organization for Standardization
IUO	Investigational Use Only
MDL	Medical Decision Levels
NDA	Nondisclosure Agreement
OSI	Occurrence of Special Interest
PFH	Plasma Free Hemoglobin
PI	Principal Investigator
RMV	Routine Monitoring Visit
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SIV	Site Initiation Visit
SOP	Standard Operating Procedure
SST™	Serum Separator Tube
UADE	Unexpected Adverse Device Effect
US	United States
USADE	Unexpected Serious Adverse Device Effect
VP	Venipuncture
WHO	World Health Organization

1 PROTOCOL SUMMARY

1.1 Synopsis

Protocol Title	A prospective multi-center study to evaluate clinical equivalence (method comparison) between the B[redacted] [redacted] Tube SST™ and [redacted] [redacted] Capillary Tube EDTA devices to respective comparators
Short Title	[redacted] Capillary System Clinical Equivalence Study
Rationale	[redacted] The study is intended to assess clinical equivalence (method comparison) of the [redacted] Tube SST™ and [redacted] Tube EDTA to the respective comparators (listed below) [redacted]. Part A: [redacted] Tube SST™ versus Comparator product(s): • [redacted]® SST™ Blood Collection Tube [redacted] SST) • [redacted] SST™ Blood Collection Tube [redacted] SST) • [redacted] Tube with Clot Activator and Gel Separator [redacted] Part B: [redacted] Tube EDTA versus Comparator product(s): • [redacted] EDTA) • [redacted] EDTA) • [redacted] tube with K_2EDTA [redacted]
Objectives and Endpoints	Objectives and endpoints of this study are provided below.

Objectives	**Endpoints**
Clinical Equivalence	
SERUM	

Protocol Title	A prospective multi-center study to evaluate clinical equivalence (method comparison) between the [redacted] Tube SST™ and [redacted] Tube EDTA devices to respective comparators	
	To demonstrate clinical equivalence of the [redacted] Tube SST™ (Test Device SST) as compared to the relevant comparators for chemistry analytes listed in Table 3.	Average difference between Test Device SST and respective comparator device. • Test Device SST vs. [redacted] Serum (Venous Comparator) • Test Device SST vs. [redacted] SST (Capillary Comparator)
	EDTA	
	To demonstrate clinical equivalence of the [redacted] Tube EDTA (Test Device EDTA) as compared to the relevant comparators for whole blood parameters listed in Table 5.	Average difference between investigational device and respective comparator device. • Test Device EDTA vs. [redacted] EDTA (Capillary Comparator) • Test Device EDTA vs. [redacted] EDTA (Venous Comparator)
	Visual Observations and Supplemental Measurements: SERUM	
	Evaluation of the frequency of selected visual observations in the [redacted] Tube SST™ (Test Device SST) and all comparator tube types: • [redacted] SST • [redacted] SST • [redacted] Serum	Frequency of selected visual observations.
	To evaluate sample hemolysis as measured by Plasma Free Hemoglobin (PFH) for [redacted]	Mean and distribution of PFH values per tube type and frequency of PFH

[redacted]

Protocol Title	A prospective multi-center study to evaluate clinical equivalence (method comparison) between the [redacted] Tube SST™ and [redacted] Tube EDTA devices to respective comparators	
	[redacted] Tube [redacted] and comparators using the Siemens Atellica platform.	occurrence above 50mg/dL per tube type.
	To evaluate serum collection volume of the [redacted] (Test Device [redacted] tube).	Serum collection volume as measured by the weight of serum in the [redacted]
	To evaluate duration of sample collection for the [redacted] (Test Device [redacted] tube) and capillary comparator.	Mean time in seconds between puncture timestamp and additive/ blood mix start timestamp per tube type.
	Visual Observations and Supplemental Measurements: EDTA	
	Evaluation of the frequency of visual observations in the [redacted] (Test Device EDTA tube) and all comparator tube types: • [redacted] EDTA • [redacted] EDTA • [redacted] EDTA	Frequency of selected visual observations.
	Evaluation of the frequency of occurrence of instrument flags (both asterisks and IP messages of interest) in the [redacted] Tube EDTA (Test Device EDTA) and all comparator tube types. [redacted]	Frequency of occurrence of instrument flags. Confirmation of relevant flags by manual review of smears.

[redacted]

Protocol Title	A prospective multi-center study to evaluate clinical equivalence (method comparison) between the [redacted] Tube SST™ and [redacted] Tube EDTA devices to respective comparators	
	version 1.0 for instrument flags of interest.	
	To evaluate peripheral blood smears for samples with platelet clump instrument IP messages.	• Frequency of occurrence of platelet clump instrument flags, confirmed by peripheral smear review. • Frequency of instrument platelet clump flags with no platelet clumps identified on peripheral smear.
	To evaluate whole blood collection volume for the [redacted] Tube EDTA (Test Device EDTA).	Whole blood collection volume as measured by the weight of whole blood in the Test Device EDTA tube after collection.
	To evaluate duration of sample collection for the [redacted] Tube EDTA (Test Device EDTA) and capillary comparator.	Mean time in seconds between puncture timestamp and additive/blood mix start timestamp per tube type.
	Device Safety Assessment	
	To assess the safety of the Test Device SST and EDTA systems.	Device/procedure - related adverse events (AEs).
	For Informational Purposes Only:	
	SERUM	
	Evaluate clinical equivalence between comparator tubes for the chemistry analytes listed in Table 3.	Average difference for tube comparisons. • Test Device SST tube vs. [redacted] SST tube (Venous Comparator)

[redacted]

Protocol Title	A prospective multi-center study to evaluate clinical equivalence (method comparison) between the [redacted] Tube SST™ and [redacted] Tube EDTA devices to respective comparators	
		• [redacted] vs. [redacted] Serum • [redacted] SST vs. BD [redacted] SST tube • [redacted] SST tube vs. [redacted] Serum
	EDTA	
	Evaluate clinical equivalence between comparator tubes for all analytes listed in Table 5.	Average difference between the following devices • Test Device EDTA tube vs. [redacted] EDTA • [redacted] vs. [redacted] EDTA • [redacted] EDTA vs. [redacted] EDTA. • [redacted] EDTA vs. [redacted] EDTA
Design and Overview	This is a prospective, multi-center study designed to evaluate the safety and effectiveness of the [redacted] Tube SST™ and [redacted] Tube EDTA devices. This study will be conducted in two parts; Part A will evaluate the [redacted] Tube [redacted] device and Part B will evaluate the [redacted] Tube EDTA device. A minimum of 100 participants, and a maximum of 150 participants per part will be enrolled at a minimum of three various [redacted] site settings representative of the intended use environment [redacted] Samples will be collected by [redacted]. Comparator venous and conventional capillary tubes will be collected by Phlebotomists. Samples will be collected, clotted	

Protocol Title	A prospective multi-center study to evaluate clinical equivalence (method comparison) between the [redacted] Tube SST™ and [redacted] Tube EDTA devices to respective comparators
	(serum samples only) and centrifuged within 2 hours of collection (serum samples only) prior to testing, within 4 hours of collection (see Section 7). The study population will include apparently healthy participants and patient populations ≥18 years of age, covering a range of disease states (See Section 5). The goal is to maximize coverage of the assay measurable range for each analyte, including above and below medical decision levels and at the extremes of the range, with natural samples where possible. [redacted] Approximately 10 % contrived samples will be prepared for each analyte to cover the assay measurable range (AMR). Preparation of these samples will be described under a separate Spiking Plan. An overview of the spiking approach is provided in Appendix B.
Study Device	[redacted], Investigational Use Only (IUO) The BD Microtainer® Easy Collect Capillary Tube SST™ is a part of the prototype capillary collection device system that includes a capillary blood collection container with clot activator. Additional details are provided in Section 6.1 [redacted] Tube EDTA, Investigational Use Only (IUO) [redacted] Tube EDTA is [redacted] blood container with K_2EDTA anticoagulant. [redacted]
Participants	• Participants will fall under two groups: Natural Sample Group (uncontrived) and Contrived Sample Group. The Contrived Sample Group of participants will be enrolled [redacted]. The collection of blood, and preparation of the contrived samples from the blood collected from these subjects is outlined in the overview presented in Appendix B. Detailed instructions will be provided in a separate Spiking Plan.

[redacted]

Protocol Title	A prospective multi-center study to evaluate clinical equivalence (method comparison) between the [redacted] Tube SST™ and [redacted] Tube EDTA devices to respective comparators
	• Participants ≥18 years of age recruited [redacted] in-person, via phone, or via electronic communications using IRB-approved recruitment materials. In order to cover the assay measurable range (AMR) additional in- and out-patient hospital populations with disease states such as the below listed conditions may be enrolled. • Part A: Patients with hepatic, renal, endocrine, cardiovascular disorders and/or cancer. • Part B: Patients with hematological disorders, cancers, diabetes and/or allergies.
Intervention(s)/Procedure(s)	After completing the informed consent process and enrolling into the study, blood will be collected from participants using a predetermined randomization schedule which will include randomized collection type (venous or capillary) and tube draw order. Participants in study Part A will have [redacted] collections performed using the Test Device SST, and two (2) conventional [redacted] collections performed using the currently marketed [redacted] device. A standard venipuncture will also be performed to collect samples into [redacted] comparator tubes. An approximate blood volume of 10 mL will be collected from participants in Part A. Participants in study Part B will have [redacted] collection performed using the Test Device EDTA and [redacted] conventional [redacted] collection [redacted]. A standard venipuncture will also be performed to collect samples into the [redacted] EDTA and [redacted] EDTA comparator tubes. An approximate blood volume of 5 mL will be collected from participants in Part B. Samples will be mixed and processed per their respective IFUs. Samples will be transported to [redacted] laboratory for analysis within 4 hours of collection end time for serum tubes and within 4 hours of collection end time for EDTA tubes. The collection end time (additive/blood mix start timestamp) for each conventional and Test Device capillary tube collected from a participant will be noted on the CRF. For venous collections, the collection end time (additive/blood mix start timestamp) will be the time of the last tube collected [redacted]

[redacted]

Protocol Title	A prospective multi-center study to evaluate clinical equivalence (method comparison) between the [redacted] Tube SST™ and [redacted] Tube EDTA devices to respective comparators
	[redacted]. Analysis time is defined as the time at which the sample is aspirated by the instrument.
Investigational Sites	This study will be conducted at a minimum of 3 sites in the US. [redacted]
Data Monitoring Committee	Not applicable
Regulatory Status	IDE Exempt

1.2 Schema

Natural Sample Group
Part A

[redacted]

Part B

[redacted]

[redacted]

Contrived Sample Group
A Schema which provides an overview of the spiking approach is presented in Appendix B. Details of the collection of blood and preparation of the contrived samples will be provided in a separate Spiking Plan.

2 INTRODUCTION

BD Integrated Diagnostic Solutions – Specimen Management (IDS-SM) manufactures a range of tubes [redacted] for clinical testing.

Currently, the method for collection of a large volume of capillary blood (up to 600 µL) involves optional warming of the hand or finger prior to procedure, lancing of the fingertip, squeezing the fingertip by hand, and dripping the blood into an open non-sterile tube. The capillary blood collection process is considered cumbersome and lacks standardization in how much pressure is applied in squeezing of the finger which may lead to poor sample quality or insufficient blood volume. Common sample quality issues for capillary blood collection include hemolysis and dilution of sample with interstitial fluid, potentially causing bias in test results. Open collection also carries a risk of blood exposure for healthcare workers and potential risk of infection at the finger puncture site. [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

2.1 Rationale

[redacted]

2.2 Risk/Benefit Assessment

This study provides no direct health benefit to the participants but is associated with minimal risk. The risks to participants are in line with standard blood collection procedures.

More detailed information about the known and expected benefits and risks and reasonably expected adverse events of capillary blood collection may be found in the IFU.

[redacted]

2.2.1 Risk Assessment

Potential Risk of Clinical Significance	Summary of Data/Rationale for Risk	Mitigation Strategy
Study Intervention: [redacted]		
• Since the [redacted] blood collection tubes may contain	Package insert	• Venipuncture will be performed using commercially available sterile evacuated blood collection tubes

[redacted]

Potential Risk of Clinical Significance	Summary of Data/Rationale for Risk	Mitigation Strategy
chemical additives, backflow may cause adverse reactions. • There is a risk of blood exposure for study staff should a study tube leak or break.		following standard venipuncture procedure and best practices for venipuncture. During the venipuncture procedure the participant's arm will be placed in a downward position; tubes will be held with the stopper uppermost; The tourniquet should be released as soon as blood starts to flow; and care is taken to make sure the additives do not touch the stopper or end of the needle during venipuncture • Study staff will use Universal/Standard Precautions during all procedures where exposure to blood/blood components may be possible.
Study Procedures: Blood Specimen Collection		
Blood collection by venipuncture is known to be associated with: • Slight/moderate discomfort at the collection site • Bruising/hematoma • Scarring • Infection • Syncope • Nausea/vomiting	Common medical knowledge; package insert	• Venipuncture will be performed by phlebotomists. • Venipuncture will be performed at a location with sufficient medical facilities by phlebotomists to ensure participant safety and comfort.
Capillary blood collection using non-sterile collection tube and finger device (if applicable) may have a risk of non-sterile surfaces touching skin at the puncture site leading to a potential risk of infection	Instruction for use; package insert	• Disinfection of the finger puncture site and the interior surface of the finger device, that is in contact with the finger, with disposable alcohol wipe will be performed prior to capillary collections • [redacted] will be instructed to follow universal precautions/risk mitigation

Potential Risk of Clinical Significance	Summary of Data/Rationale for Risk	Mitigation Strategy
		procedures to minimize blood exposure. • New devices will be used for each individual [redacted] collection. • The [redacted] device will be disinfected prior to use • The skin at the puncture site will be disinfected prior to collection. • The [redacted] tool is [redacted] and will be discarded after each participant use.
Other		
Discomfort during capillary blood collection	Common medical knowledge	• Devices will be removed immediately upon participant request due to pain or discomfort. • Skin irritation or allergy from devices will be mitigated by immediate removal and discontinuation of the procedure.

2.2.2 Benefit Assessment

There are no direct benefits to the participant for participation in this study. The findings may reveal information that will allow for the development of a new capillary blood collection device that may improve sample quality and patient experience during capillary blood collection, and thus may improve medical care for persons that undergo blood collection procedures.

2.2.3 Overall Benefit: Risk Conclusion

While there are no direct benefits to participants in this study, it is possible that the information gathered could benefit patients in the future. There are no known or anticipated risks associated with the use of any study device other than those associated with general blood collection procedures. Potential risks for participants are well known, have been minimized as reasonably feasible. The risk is low with a little chance of prolonged sequelae.

3 OBJECTIVES AND ENDPOINTS

3.1 Acceptance Criteria

For each comparison, clinical equivalence will be demonstrated for an analyte if the mean biases with 95% limits are within the Clinical Acceptance Limits (CAL).

- If the mean bias is within the CAL but the 95% limit exceeds the CAL, it will be considered clinically non-equivalent, requiring further interpretation and assessment to determine whether the difference is clinically acceptable. This assessment will be made based on impact on patient diagnosis and treatment.
- If the mean bias exceeds the CAL at any medically relevant points, it will be considered clinically non-equivalent and will be considered clinically unacceptable, unless a rationale can be provided.

Objectives	**Endpoints**
Clinical Equivalence	
SERUM	
To demonstrate clinical equivalence of the [redacted] (Test Device SST) as compared to the relevant comparators for chemistry analytes listed in Table 3.	Average difference between investigational device and respective comparator device. • Test Device SST vs. [redacted] (Venous Comparator) • Test Device SST vs. [redacted] (Capillary Comparator)
EDTA	
To demonstrate clinical equivalence of the [redacted] (Test Device EDTA) as compared to the relevant comparators for whole blood parameters listed in Table 5.	Average difference between investigational device and respective comparator device. • Test Device EDTA vs. [redacted] EDTA (Capillary Comparator) • Test Device EDTA vs. [redacted] EDTA (Venous Comparator)
Visual Observations and Supplemental Measurements: SERUM	
Evaluation of the frequency of selected visual observations in the [redacted] (Test Device SST) and all comparator tube types: • [redacted] • [redacted]	Frequency of selected visual observations (Table 4).

• Greiner Vacuette Serum	
To evaluate sample hemolysis as measured by Plasma Free Hemoglobin (PFH) on Siemens Atellica platform for [redacted] and all comparator tube types: • [redacted]	Mean and distribution of PFH values per tube type and frequency of PFH occurrence above [redacted] per tube type.
To evaluate serum collection volume of the Test Device SST tube	Serum collection volume as measured by the weight of serum in the [redacted]
To evaluate duration of sample collection for [redacted] (Test Device SST tube) tube and capillary comparator [redacted]	Mean time in seconds between puncture timestamp and additive/ blood mix start timestamp per tube type.
Visual Observations and Supplemental Measurements: EDTA	
Evaluation of the frequency of visual observations in the [redacted] (Test Device EDTA tube) and all comparator tube types:	Frequency of selected visual observations (Table 4).
Evaluation of the frequency of occurrence of instrument flags (both asterisks and IP messages of interest) in the [redacted] (Test Device EDTA) and all comparator tube types: • [redacted]	Frequency of occurrence of instrument flags. Confirmation of relevant flags by manual review of smears.

[redacted]

To evaluate peripheral blood smears for samples with platelet clump instrument IP messages.	• Frequency of occurrence of platelet clump instrument flags, confirmed by peripheral smear review. • Frequency of instrument platelet clump flags with no platelet clumps identified on peripheral smear.
To evaluate whole blood collection volume for the [redacted] (Test Device EDTA)	Whole blood collection volume as measured by the weight of whole blood in the Test Device EDTA tube after collection.
To evaluate duration of sample collection for the [redacted] EDTA and capillary comparator-[redacted]	Mean time in seconds between puncture timestamp and additive/blood mix start timestamp per tube type.
Device Safety Assessment	
To assess the safety of the Test Device SST and EDTA systems.	Device/procedure - related adverse events (AEs).
For Informational Purposes Only:	
SERUM	
Evaluate clinical equivalence between comparator tubes for the chemistry analytes listed in Table 3.	Average difference for tube comparisons. • Test Device SST tube vs. [redacted] (Venous Comparator) • [redacted] SST vs. [redacted] Serum • [redacted] SST vs. [redacted] SST tube • [redacted] SST™ tube vs. [redacted] Serum
EDTA	
Evaluate clinical equivalence between comparator tubes for all analytes listed in Table 5.	Average difference between the following devices • Test Device EDTA tube vs. [redacted] • [redacted] EDTA vs. [redacted] EDTA • [redacted] EDTA vs. [redacted] EDTA

	• [redacted] EDTA vs. [redacted] EDTA

4 STUDY DESIGN

4.1 Overall Design

This is a prospective, multi-center randomized collection study designed to evaluate the safety and effectiveness of the [redacted] Blood Collection System using the [redacted] (SST™ and EDTA) and to provide the necessary data to demonstrate substantial equivalence of these Test Device tubes to their respective comparators.

This study will be conducted in two parts; Part A will evaluate the Test Device SST™ tubes and Part B will evaluate the Test Device EDTA tubes. A minimum of 100 participants, and a maximum of 150 participants per part will be enrolled at a minimum of three various [redacted] site settings representative of the intended use environment [redacted]. Additional participants may be enrolled in order to obtain 100 complete data sets for all analytes. All participants will be compensated at the completion of study procedures.

Natural Samples will be collected by representative future users of the [redacted] Blood Collection System who may not have prior blood collection experience. Persons who perform [redacted]. Prior to participation in the study, all users will receive training on use of study products. [redacted] tubes will be collected [redacted]. Persons who perform collection of the comparator [redacted] Samples will be collected, clotted (serum samples only), centrifuged (serum samples only), and transported prior to analyte testing at [redacted]. Note: Serum samples must be centrifuged within 2 hours of collection time (see Section 7).

The study population will include apparently healthy participants and patient populations covering a range of disease states (See Section 5). The goal is to maximize coverage of the assay measurable range for each analyte, including above and below medical decision levels and at the extremes of the range, with natural samples, where possible. An overview of the reference range, critical values, and assay measurable range for each parameter is provided in Appendix A.

To ensure measurements are obtained to cover the assay measurable range (AMR), approximately 10% contrived samples will be prepared for each analyte. Preparation of these samples will be described under a separate Spiking Plan. A separate group of approximately 20 participants will be enrolled [redacted]

[redacted]

4.2 Scientific Rationale for Study Design

This study is designed to determine the clinical performance of the Test Device tubes against currently marketed capillary and venous blood collection devices in testing of both serum analytes and whole blood analytes.

[redacted] collect [redacted] the comparator devices. [redacted] Test Device tubes, blood collection will be carried out by the targeted users of the Test Devices, [redacted]

The analytes selected to be tested in this study represent the intended use of the devices.

The patient population was selected in order to cover the assay measurable range (AMR) using natural (uncontrived) samples to reflect real-world use. Measurements of certain analytes at the extreme ends of the AMR may not be sustainable to life or it may just not be possible to recruit the participants to span the full range. Therefore, in order to cover this range, approximately 10% of the paired samples used in each analysis may be contrived.

4.2.1 Participant Input into Design

Not applicable.

4.3 End of Study Definition

A participant is considered to have completed the study after he/she has completed blood collection and is discharged from the collection location, even if not all the study tubes are collected.

The end of the study is defined as the date of the analysis of the samples collected from the last participant in the study.

5 STUDY POPULATION

Natural Sample Group

Participants will be recruited [redacted] in-person, via phone, or via electronic communications, such as social media, using IRB-approved recruitment materials. In order to cover the assay measurable range (AMR) additional in- and out- patient hospital populations with disease states such as the below listed conditions may be enrolled.

- Part A: Patients with hepatic, renal, endocrine, cardiovascular disorders and/or cancer.
- Part B: Patients with hematological disorders, cancers, diabetes and/or allergies.

Approximately equal number of female and male participants with a targeted enrollment of at least 30% of either gender [redacted]. The patient disease state and gender will be documented on a CRF.

Contrived Sample Group
Participants enrolled for the preparation of contrived samples [redacted]

5.1 Inclusion Criteria

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

1. Participants ≥18 years of age.
2. Not currently pregnant (self-reported)
3. Adequate access to four fingers [redacted] and inner elbows for blood collection procedures
4. Willing and able to comply with all study procedures and evaluations
5. Ability to read, write, and understand English language
6. Provision of signed and dated informed consent form

Contrived Sample Group
Participants enrolled for the preparation of contrived samples must meet the criteria laid out within the [redacted]. Participants who have been enrolled within [redacted] have already been screened according to the inclusion criteria for that program.

5.2 Exclusion Criteria

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

1. Evidence of skin issues such as infections, ulcerations, blisters, peripheral vascular disease, inflammation, extensive scarring or calluses, or healed burns at the [redacted] site.
2. Subject to post-study exclusion period for this or other related studies:
    a. A study participant may enroll once in study part A and once in study part B of this clinical study. They may not enroll more than once in a single study part.
    b. If a study participant has previously enrolled in one study part and would like to enroll in the second study part, they must wait [redacted] from the time of the first study part collection procedures to enroll in the second study part collection procedures.

3. Any condition which, in the opinion of the Investigator, would preclude participation in this study.

Contrived Sample Group
Participants enrolled for the preparation of contrived samples must meet the criteria [redacted]

5.3 Lifestyle Considerations

There are no required lifestyle considerations or restrictions.

5.4 Screen Failures

Screen failures are defined as participants who do not meet all eligibility criteria. Individuals who do not meet the criteria for participation in this study (screen failure) may not be rescreened.

6 STUDY INTERVENTIONS

6.1 Investigational/Test Device

[redacted]

- [redacted]

[redacted]

6.2 Comparator Devices/Standard of Care

Part A

- [T03-T04] [redacted] SST™ Tube [redacted] SST), 400-600 µl, [redacted], or equivalent.
- [T05] [redacted] SST™ Blood Collection Tube ([redacted] SST), [redacted], [redacted], or equivalent.
- [T06] [redacted] Blood Collection Tube with Clot Activator and Gel Separator [redacted] or equivalent.

Part B

- [T08] [redacted] EDTA), [redacted] or equivalent.
- [T09] [redacted] EDTA), [redacted] or equivalent.
- [T10] [redacted] EDTA), [redacted]

6.3 Ancillary Devices/Products

- [redacted]
- [redacted]
- [redacted]
- [redacted]

6.4 Device Labeling

Investigational devices (or the immediate packaging) shall be labeled in accordance with regulatory requirements, including the following statement: "For Investigational Use Only". The performance characteristics of this product have not been established."

The devices used during current venipuncture collection practices and capillary blood specimen collections are all commercially available and will be labeled as provided by the manufacturer.

For contrived samples blood will be collected from participants [redacted]

6.5 Measures to Minimize Bias

6.5.1 Randomization

All randomization schedules are to be provided by BD [redacted].

Natural Sample Group
Collection method (venous vs. capillary), tube collection order (within collection method), [redacted] location [redacted] will be randomized according to a draw schedule. [redacted]

Contrived Sample Group
For the contrived samples, indirect draw order will be randomized according to a draw schedule. Tube testing order on instrument will be randomized according to a test schedule.

6.5.2 Blinding/Masking

Not applicable, this is an open-label study.

7 STUDY PROCEDURES AND ASSESSMENTS

- Study procedures, assessments for natural samples and their timing are illustrated in the respective schemas provided in Section 1.2. Protocol waivers or exemptions are not allowed.
- Adherence to the study design requirements is essential and required for study conduct.
- Procedures conducted as part of the participant's routine clinical management (e.g., blood count) and obtained before signing of the ICF may be utilized for screening or baseline purposes provided the procedures met the protocol-specified criteria.
- The Instructions for Use (IFU) is a reference document for the investigational Test Device product; this study protocol will supersede the Test Device IFU.

7.1 Screening, Informed Consent, and Enrollment

Potential study participants will be screened against the inclusion and exclusion criteria outlined in Section 5. Participants will first be asked to provide written informed consent. Those who provide consent will be considered enrolled and will be assigned a unique participant number. Those meeting eligibility criteria will receive information regarding the study, including but not limited to test procedures, information to be collected, number and type of blood collection procedures, potential risks and benefits, and other pertinent information.

[redacted]

Part A
Natural Sample Group: [redacted]
Contrived Sample Group: [redacted]

Part B
Natural Sample Group: [redacted]
Contrived Sample Group: [redacted]

[redacted]

7.2 Blood Collection Procedure

Natural Sample Group
Study Part A:
For each participant, [redacted] one venipuncture using a [redacted] to collect blood into a [redacted] tube. The collection will be performed per the study site's standard operating procedure for venipuncture. In addition, [redacted] collections using [redacted]. A [redacted] the Test Device [redacted] system. The collection end time [redacted] for each conventional and Test Device capillary tube collected from a participant will be noted on the CRF. For venous collections, the collection end time will be the time of the last tube collected from a venipuncture draw. Duration of collection for all capillary collections (conventional and Test Device) will also be captured

on CRFs as described in section 7.7 of this protocol, Supplemental Measurements, Visual Observations, and Analyte Testing. Study Samples will be mixed and processed per their respective IFUs.

Study Part B: For each participant, [redacted] one venipuncture [redacted] to collect blood into a [redacted] tube. The collection will be performed per the study site's standard operating procedure for venipuncture. In addition, [redacted] one (1) conventional capillary collection [redacted] tube. [redacted] collection using the [redacted] Test Device EDTA system. The collection end time [redacted] for each conventional and Test Device [redacted] tube collected from a participant will be noted on the CRF. For venous collections, the collection end time will be the time of the last tube collected from a venipuncture draw. Duration of collection for all capillary collections (conventional and Test Device) will also be captured on CRFs as described in the supplemental measurements section, section 7.7 of this protocol, Supplemental Measurements, Visual Observations, and Analyte Testing.

Contrived Sample Group
An overview of the spiking approach for the preparation of contrived samples is outlined in Appendix B. If multiple sets of contrived specimens are prepared from a single participant, each unique set of contrived samples will be assigned a unique pool number.

7.3 Test Device Blood Collection Procedure

Natural Sample Group

[redacted]

[redacted]

- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]

[redacted]

- [redacted]
- [redacted]
- [redacted]

[redacted]

- [redacted]
- [redacted]

[redacted]

[redacted]

- [redacted]
- [redacted]

[redacted]

- [redacted]
- [redacted]

[redacted]

- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]

[redacted]

- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]

[redacted]

[redacted]

- [redacted]
- [redacted]
- [redacted]
- [redacted]

Step 9: Apply Gauze

- Apply the sterile gauze or pad to the puncture site. Direct the patient to hold and apply pressure if they are able to assist.

[redacted]

- [redacted]

[redacted]

- [redacted]

[redacted]

- [redacted]

The collection end time for each conventional and Test Device [redacted] tube collected from a participant will be noted on the CRF. For venous collections, the collection end time will be the time of the last tube collected from a venipuncture draw

Contrived Sample Group

The procedures for the collection of blood for the preparation of the contrived samples are outlined in the overview of the spiking approach in Appendix B.

Once the contrived samples are indirectly transferred into the study tubes, they will be processed in the same manner as the natural samples.

7.4 Repeat Collection

In cases of insufficient sample volume or loss of sample during collection, repeat collection may be needed. Repeat collection will vary based on blood collection method. Participants should be asked for their permission before attempting a repeat collection.

Natural Sample Group
Part A: SERUM

Capillary Collections – A total of four capillary collections will be performed [redacted] the event of an unsuccessful collection, the subject will be included in the study and the missing tubes will be noted.

Venipuncture – 1 additional venipuncture will be allowed, for a total of 2 venipunctures for Part A of this study.

Part B: EDTA

Capillary Collections – A total of two capillary collections will be performed [redacted]

Venipuncture: 1 additional venipuncture will be allowed, for a total of 2 venipunctures for Part B of this study.

Contrived Sample Group

Repeat collections on participants enrolled for the preparation of contrived samples [redacted]

[redacted]

7.5 Participant Compensation

Participants will be compensated for their time and participation after the study procedures are complete.

7.6 Natural and Contrived Sample Storage and Processing

[redacted]

[redacted]

[redacted]

Part A: SERUM

After tube inversions, all Serum tubes need to stand for their minimum clot times and then centrifuged as indicated in Table 1. [redacted]. All tubes from the same participant [redacted] will be centrifuged within the same timeframe. Remove samples from centrifuge as soon as centrifugation is completed. [redacted].

For Natural samples, all tubes from the same participant will be processed and tested at the same timeframe using the same lot of reagents. For contrived samples, all tubes from the same pool set will be processed and tested at the same timeframe using the same lot of reagents.

[redacted]

Part B: EDTA

Complete tube inversions as indicated in Table 1 for all EDTA tubes.

All tubes from the same participant will be processed and tested at the same timeframe using the same lot of reagents. Place Test Device container into adapter for automated processing on the instrument. [redacted]

[redacted]

[redacted]

[redacted]

Table 1: Tube Processing

Tube Number	Tube type	Inversions*	Minimum Clot Time	Centrifugation †	
				Time	G-force (g)
T01, T02	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
T03, T04	[redacted]	5	45 min	90 sec	6500
T05	[redacted]	5	30 min	10 min	1300
T06	[redacted]	5	30 min	10 min	1800
T07	[redacted]	[redacted]	N/A	N/A	N/A
T08	[redacted]	8	N/A	N/A	N/A
T09	[redacted]	8-10	N/A	N/A	N/A
T10	[redacted]	8-10	N/A	N/A	N/A

†All serum tubes will be centrifuged within 2 hours of their respective collection end time. All tubes from the same participant (Natural Sample Group) or from the same contrived sample pool will be centrifuged within the same timeframe
*Mix blood with additives in the tubes immediately after collection using the indicated number of tube inversions

[redacted]

7.7 Supplemental Measurements, Visual Observations, and Analyte Testing

- Duration of collection (applicable to only Natural Samples): Defined as time in seconds between puncture timestamp and additive/blood mix start timestamp per

[redacted]

tube type. This parameter will only be collected for tubes T01-T04, Capillary collections.

- Volume of Serum (applicable to only Natural Samples): [redacted]
- Plasma, Free Hemoglobin (applicable to Natural and Contrived Samples): As measured on Siemens Atellica.

The following visual observations will be assessed during part A for Natural Samples. For Contrived Samples all visual observations in Table 2 also apply with the exception of the visual observation for collection failure.

Table 2:Visual Observations for Part A

Visual Observation	Rating	Description	Ideal Rating	Note
Complete Fill	1, 2, (3)	[redacted]	2	Performed after collection, right before mix start timestamp
Collection Failure	0, 1, 2, 3, 4	[redacted]	0	

		[redacted]		
Fibrin mass (distinct from fibrin strands)	0, 1, 2, 3	[redacted]	0	Performed as soon as possible after centrifugation and prior to testing
Fibrin strands (distinct from fibrin masses)	Y/N	[redacted]	N	
Gel Barrier formation	0, I, C	[redacted]	C	
Red blood cells on barrier	0, 1, 2, 3	[redacted]	0	
Hemolysis	0, 1, 2, 3	[redacted]	0	

*Complete fill will be determined by visually comparing the venous tubes to an example tube set (reference tubes).

[redacted]

7.7.1 Part A: SERUM (Natural and Contrived Samples)

Serum samples from the Test Device [redacted] and comparator tubes will be tested ('analysis time') on the Siemens Atellica platform after centrifugation as noted in Table 3 and within 4 hours from the collection end time. For the contrived samples the full panel of analytes may not be run on each contrived sample set. The specific analytes to be tested for each contrived sample set will be detailed in the Spiking Plan. Analysis time is defined as the

[redacted]

time at which the sample is aspirated by the instrument. All serum samples from the same subject will be tested within the same timeframe using the same lot of reagents. Test Device SST tubes should be [redacted] to enable serum sampling from the primary tube. [redacted] tubes may be aliquoted into sample cups prior to analysis.

Table 3: Analytes to be Measured in Part A Natural and Contrived Samples

Analytes	Abbreviation	[redacted]	[redacted]
Immunoassays			
Thyroid-Stimulating Hormone	TSH	[redacted]	[redacted]
Vitamin D	Vit D	[redacted]	[redacted]
Enzyme			
Alkaline Phosphatase	ALP	[redacted]	[redacted]
Alanine Aminotransferase	ALT	[redacted]	[redacted]
Aspartate Aminotransferase	AST	[redacted]	[redacted]
Lipid			
High-Density Lipoprotein	HDL	[redacted]	[redacted]
Low-Density Lipoprotein	LDL	[redacted]	[redacted]
Total Cholesterol	CHOL	[redacted]	[redacted]
Triglycerides	TRIG	[redacted]	[redacted]
Metabolic			
Albumin	ALB	[redacted]	[redacted]
Total Bilirubin	TBIL	[redacted]	[redacted]
Blood Urea Nitrogen	BUN	[redacted]	[redacted]
Calcium	Ca	[redacted]	[redacted]
Carbon Dioxide	CO2	[redacted]	[redacted]
Chloride	Cl	[redacted]	[redacted]

[redacted]

Creatinine	CRE	[redacted]	[redacted]
Glucose	GLU	[redacted]	[redacted]
Potassium	K	[redacted]	[redacted]
Sodium	Na	[redacted]	[redacted]
Total Protein	TP	[redacted]	[redacted]

By default, TSH will be measured in capillary tubes T01 [redacted] and T03 [redacted] The remaining chemistry analytes will be tested from T02 (Test Device SST) and T04 [redacted]. If necessary, leftover serum from either tube of the same tube type, from the same participant can be used for repeat analysis, only for the analytes listed above.

7.7.2 Part B: EDTA

Supplemental Measurements:

- Duration of collection (applicable to only Natural Samples): [redacted]. This parameter will only be collected for [redacted], T07 and T08.
- Volume of Whole Blood (applicable to only Natural Samples): [redacted]
- Smear Reviews: (applicable to Natural and Contrived Samples) Peripheral smears will be reviewed in response to applicable instrument flags. Details on smear reviews provided below.

The following visual observations will be assessed during part B for Natural Samples. For Contrived Samples only the visual observation of complete fill will be assessed.

Table 4: Visual Observations for Part B

Visual Observation	Rating	Description	Ideal Rating	Note
Complete Fill	1, 2, (3)	[redacted]	2	Performed after collection, right before mix start timestamp

[redacted]

		[redacted]		
Collection Failure	0, 1, 2, 3, 4	[redacted]	0	

*Complete fill will be determined by visually comparing the venous tubes to an example tube set (reference tubes). [redacted] reference tubes will be provided to illustrate an acceptable fill volume [redacted]

Testing to be done in Part B includes the following whole blood parameters and instrument platforms (Table 5). EDTA samples from the Test Device EDTA and comparator tubes will be tested ('analysis time') within 4 hours from collection end time. For the contrived samples the full panel of analytes may not be run on each pooled set. The specific analytes to be tested for each pooled set will be detailed in the Spiking Plan. Analysis time is defined as the time at which the sample is aspirated by the instrument (instrument print out time). All tubes from the same participant will be processed at the same timeframe using the same lot of reagents. Test Device EDTA tubes will be [redacted] to enable primary tube sampling. Testing for EDTA Tubes will be performed at room temperature.

Table 5: Analytes to be measured in Part B Natural and Contrived Samples

Analytes	**Abbreviation**	[redacted]	**Instrument**
Basophils (%)	BA	[redacted]	Sysmex XN 1000
Eosinophils (%)	EO	[redacted]	

[redacted]

Erythrocyte Count	RBC	[redacted]	
Hematocrit	Hct	[redacted]	
Hemoglobin	Hgb	[redacted]	
Leukocyte Count	WBC	[redacted]	
Lymphocytes (%)	LY	[redacted]	
Mean Corpuscular Hemoglobin	MCH	[redacted]	
Mean Corpuscular Hemoglobin Concentration	MCHC	[redacted]	
Mean Corpuscular Volume	MCV	[redacted]	
Monocytes (%)	MO	[redacted]	
Neutrophils (%)	NE	[redacted]	
Platelet Count	PLT	[redacted]	
Red Cell Distribution Width (RDW-SD / RDW-CV)	RDW-SD / RDW-CV	[redacted]	
Instrument flags	N/A	[redacted]	
Hemoglobin A1c	HbA1c	[redacted]	Bio-Rad D-100

* [redacted]

Relevant instrument flags will be confirmed with manual blood smears. Blood smears will be prepared on all tubes with instrument flags (asterisks and IP messages), as appropriate. For platelet flags, 10 high power fields on the smear will be scanned for platelet clumps and rated according to the below criteria.

None Seen	[redacted]
Slight	[redacted]

Moderate	[redacted]
Marked	[redacted]

7.8 Natural and Contrived Sample Acceptance and Rejection Criteria for Analyte Testing

Part A: Samples with the following visual scores will be rejected:

- Complete Fill [redacted]
- Collection failure [redacted]
- Gel Barrier [redacted]
- Visual Hemolysis [redacted]

Part B: Samples with the following visual scores will be rejected:

- Complete Fill [redacted]
- Collection failure [redacted]

7.9 Repeat Testing Natural and Contrived Samples

For study part A and B, repeat analyte testing is to occur on a per analyte basis following analyzer test run errors or flags during testing of the analyte, as deemed appropriate by the laboratory staff per their procedures. Repeat analyte testing should occur within the prescribed test window for each study part (within 4 hours of collection for Part A, and within 4 hours of collection for Part B).

If upon the first run, a valid test result is not obtained due to any test run error or no numerical value is obtained, a repeat test should be run, volume permitting. Both the original and repeat test result will be provided and clearly marked.

For Part B, if a [redacted] instrument flag is noted on the test report, a smear will be prepared and reviewed. Check the sample for the following and repeat the test on the [redacted]

1. Adequate sample volume
2. Mix sample well, (observe for any "hang-up" in sample tube- smaller tubes need more time with the inversions to mix well)
3. Check sample integrity – no clots within sample or on tube top

The first valid result will be used for analysis. If both the first and repeat run is flagged by an asterisk, this data point should be documented with the asterisk in the study database and the first result with the asterisk will be used in the analysis.

7.10 Residual Sample Usage (Natural Sample Group Only)

After study objectives are met, [redacted] samples of sufficient quantity to collect data supporting the use of the Test Device for analysis of additional analytes. [redacted]

[redacted]

[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

[redacted]

[redacted]

[redacted]

[redacted] In the event of voluntary study participant withdrawal, bio-banked samples will be destroyed per the study participant request [redacted]

Contrived Sample Group
This section is not applicable to contrived samples. Contrived samples will be disposed of according to standard laboratory procedures after the completion of the clinical study testing.

7.11 Safety Evaluations

Natural Sample Group
Adverse events will be actively collected while the participant is at the site and collected via self-report through telephone calls over 7 days after blood collection.

Contrived Sample Group
Safety Evaluations are outlined in document [redacted]

8 PARTICIPANT DISCONTINUATION/WITHDRAWAL

8.1 Discontinuation/Withdrawal

Natural Sample Group

- A participant may withdraw from the study at any time at his/her own request or may be withdrawn at any time at the discretion of the investigator or sponsor for safety, behavioral, compliance, or administrative reasons. This is expected to be uncommon.
- At the time of discontinuing from the study, no further study assessments will be performed. Adverse events that occur and are self-reported by the participant to the PI and study staff will be documented for up to 7 days after discontinuation from the study.
- If the participant withdraws consent for disclosure of future information, the sponsor may retain and continue to use any data collected before such a withdrawal of consent.
- If a participant withdraws from the study, he/she may request destruction of any samples taken and not tested, and the investigator must document this in the site study records.

Contrived Sample Group

Safety Evaluations are outlined in document [redacted]

8.2 Lost to Follow-Up

Not applicable, study will be completed in one visit.

9 ADVERSE EVENTS AND DEVICE DEFICIENCIES

9.1 Definitions of Events

9.1.1 Adverse Events (AEs)

An adverse event is defined as any untoward medical occurrence, inappropriate patient management decision, unintended disease or injury, or untoward clinical signs in participants, users, or other persons, with any connection to study related activities, whether or not related to the IVD medical device under investigation (ISO 20916). In this study, participant AEs are limited to those occurring immediately before, during, and immediately after specimen collection. Also, based on the nature of the study, test results will not be used for patient management decisions.

For the purpose of this study, Adverse events will be collected by the study team from enrollment through completion of the study (once discharged). If an adverse event occurs during this time the PI is required to follow-up with the participant. The clinical course of the event will be followed according to accepted standards of medical practice until the event resolves, stabilizes, or in the opinion of the Investigator, is no longer considered clinically significant. The Investigator must document the adverse event outcome on the AE CRF through a follow-up call to the participant.

The participant may self-report any additional AEs that occur through 7 days post discontinuation by calling the site.

9.1.2 Serious Adverse Events (SAEs)

A serious adverse event is defined by ISO 20916 and/or 21 CFR 803.3 as an adverse event that:

a. led to death
b. led to serious deterioration in health that resulted in life-threatening illness or injury, resulted in permanent impairment
c. life threatening (refers to any event in which the subject was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe)
d. required intervention to prevent permanent impairment/damage
e. required inpatient hospitalization/prolonged hospitalization, or resulted in medical/surgical intervention to prevent life-threatening illness/injury or permanent impairment; or
f. led to fetal distress, fetal death, or a congenital abnormality or birth defect
g. important medical event that may require intervention to prevent one of the preceding conditions

9.1.3 Adverse Device Effect (ADE) / Serious Adverse Device Effect (SADE)

An adverse device effect is defined as any adverse event that is considered to be related to the use of an investigational medical device. This definition includes any event resulting from insufficiencies or inadequacies in the instructions for use, deployment, implantation, or operation or any malfunction of the investigational device (study device) and includes any event that is a result of a user error.

A serious adverse device effect (SADE) is defined as an ADE that has resulted in any of the consequences characteristic of an SAE.

9.1.4 Unanticipated (Serious) Adverse Device Effect (UADE/USADE)

An unanticipated (serious) adverse device effect (UADE/USADE) is any (serious) adverse device effect on health or safety or any life-threatening problem or death caused by, or associated with, a study device, which by its nature, incidence, severity, or outcome has not been identified in the current instructions for use and/or current version of the risk analysis report, or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of participants.

UADEs/USADEs will be reported to FDA as required by 21 CFR Part 812.

9.2 Severity of Adverse Events

Each AE shall be assessed for its severity, or the intensity of an event, experienced by the participant according to the criteria below.

Severity Rating	Description
Mild	Event, signs, or symptoms that do not interfere with the participant's daily activity, are usually considered self-limiting, can be treated with non-prescription type medications, and do not require medical intervention
Moderate	Event may interfere or cause low level inconvenience with the participant's daily activity. Requires medical intervention and/or treatment; however, unlikely to require hospitalization or be considered potentially life-threatening in nature
Severe	Event may cause significant discomfort to the participant and/or interferes with the participant's daily activity. Requires medical intervention and/or treatment to preclude a permanent impairment; may be life threatening and/or require hospitalization

9.3 Relationship of Adverse Event to Device(s)/Procedure

Each AE will be assessed for its relationship to the study device or procedure according to the following guidelines.

A. Assess each AE for its relationship to the device or procedure.

- Device Related: This category should be restricted to AEs directly attributable to any study device used during blood collection.
- Procedure: A procedure includes any study-related activity performed during the participant's study visit.

B. The following categories shall be used for assigning the certainty of the relatedness.

Relatedness	Description
Not Related	Event is independent of study intervention and/or evidence exists that the event is related to another etiology. There must be an alternative etiology documented by the clinician.
Unlikely Related	Event in which the temporal relationship to study intervention makes a causal relationship improbable (e.g., the event did not occur within a reasonable time of the study device use) and in which underlying disease provides plausible explanations (e.g.,

	the participant's clinical condition other concomitant treatments).
Likely Related	Event in which there is evidence to suggest a causal relationship and the influence of other factors is less likely. The event occurs within a reasonable time after use of the study device and is less likely to be attributed to concurrent disease.
Related	Event in which there is clear evidence to suggest a causal relationship and other possible contributing factors can be ruled out. The event occurs in a plausible time relationship to use of the study device and cannot be explained by concurrent disease.

9.4 Reporting of Events

For all adverse events, all sections of the appropriate Case Report Form (CRF) must be completed.

- All SAEs, SADEs, and/or UADEs/USADEs must be reported to the Sponsor within one (1) working day of the site/investigator becoming aware of the event.
- De-identified copies of all requested relevant documentation should be submitted to the Sponsor within 72 hours of knowledge, as appropriate.

It is the responsibility of the Investigator to report adverse events to individual Institutional Review Boards (IRBs)/Ethics Committees (ECs) and/or regulatory authorities according to the local regulations in each participating country.

9.5 Safety Committees

A safety committee will not be used.

9.6 Device Deficiencies

The Investigator will record a device deficiency if a device used in the study procedure failed to meet its performance specifications whether due to mechanical failure, malfunction, or defect. Device deficiencies also include use errors and inadequate labeling. This applies to: devices used to treat the participant, or devices in which the package was opened, but the device was not used for treatment, or devices with which treatment was attempted, but the device did not remain through the entire study procedure/period.

[redacted]

[redacted]

- [redacted]

If the device deficiency was associated with an AE, the reporting provisions for AEs, ADEs, SAEs, SADEs and UADEs/USADEs apply.

Reported deficiencies will be investigated and reported under 21 CFR part 803 Medical Device Reporting by the Sponsor if necessary. The site may be contacted to provide additional information to allow the Sponsor to conduct a thorough investigation.

It is the responsibility of the Investigator to notify the IRB/EC of such device deficiencies in accordance with the IRB/EC and/or the Competent Authority's local regulations.

10 STATISTICAL METHODS

The statistical analysis plan (SAP) will be finalized prior to database lock and will include a more technical and detailed description of the statistical analyses described in the following sections. This section includes a summary of the planned statistical analyses of the most important endpoints including primary and key secondary endpoints.

10.1 Overview of Study Design

This is a prospective, multi-center random sample collection study designed to evaluate the clinical equivalence of the blood collection device with Test Device [redacted] and EDTA tubes vs. respective comparators.

[redacted]

10.2 Sample Size Considerations

For clinical equivalence, 100 paired samples provide at least 90% power to ensure that mean biases and confidence intervals are within the clinically acceptable limits (CAL) at medical decision points, assuming no true bias between the tubes, residual SD, or CV ≤ CAL, and collected data extend past the medically relevant points.

10.3 Analysis Population

Safety analysis (summary of all device/procedure - related AEs) will be conducted on all enrolled participants.

[redacted]

All data collected will be reviewed for possible exclusion based on significant protocol deviations. Analysis will be performed on the resulting Per-Protocol (PP) dataset. Missing values will not be imputed and will not be included in any analyses.

Visual assessments: all collected tubes will be included in the summaries and analyses. For duration of sample collection, only tubes with complete fill will be included in the summaries and analyses.

Analytes: Pre-specified specimen exclusion criteria will be applied. Analysis will be performed on all first reported valid result unless a reason is provided for specific exclusions. Reasons for such exclusions will be included in the statistical report. If repeat tests are performed, a list of participants and tubes showing the initial and repeat results will be provided, showing which result is used in the analyses. For each investigational device vs. respective comparator device comparison, only participants with valid results in both tubes will be included in the bias analysis.

In addition, for study Part B, platelet analysis, a primary analysis of platelet results will be conducted excluding samples (from all tube types) with platelet flags confirmed with platelet clumps on smear review. Platelet flags and smear review data will be tabulated per tube type and sample type. An additional analysis will be done including all data, with and without platelet flags. [redacted]

10.4 General Considerations

An alpha level of 5% will be used for all analyses. For equivalence testing with analytes having a CAL, this corresponded to obtaining 90% confidence intervals (associated with 95% two 1-sided tests).

For all analytes and continuous response metrics summary statistics including sample size, mean, standard deviation (excluding analytes), range of data obtained (minimum and maximum value) will be provided for each device.

For visual observations and categorical observations, number of observations and percent in each category will be summarized for each device.

[redacted]

[redacted]

[redacted]

10.5 Analysis Methods

10.5.1 Clinical Equivalence Endpoints

For each analyte and each comparison, Deming regression (weighted Deming for analytes with percent CAL) or Passing-Bablok Regression will be used to estimate average differences between the investigational device and comparator device at medical decision levels (MDLs) for each analyte. Average differences with 95% confidence limits will be compared to the CALs to determine clinical equivalence between the devices.

10.5.2 Visual Observations and Supplemental Measurements Endpoints

The distribution of visual observation ratings for each tube type will be tabulated and summarized. No analysis will be performed on the visual observations data from this protocol alone; visual observations for Natural Samples from multiple protocols will be combined for analysis, as specified in a separate Meta-Analysis plan. For the Test Device [redacted] a meta-analysis plan will assess for the Natural Samples the plasma free hemoglobin, serum volume, duration of sample collection, fibrin mass, complete barrier formation, and complete fill. For the Test Device EDTA, a meta-analysis plan will assess for the Natural Samples the whole blood volume, complete fill, duration of sample collection, and instrument flag frequencies.

10.5.3 Safety Analysis Endpoints

A summary of all Device/procedure - related adverse events (AEs) will be provided.

10.6 Interim Analysis

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

11 DATA COLLECTION AND RECORD MAINTENANCE

11.1 Case Report Forms

The Investigator is responsible for ensuring the completeness and accuracy of all study documentation.

All required clinical data will be collected/documented in sponsor-provided paper source and electronic Case Report Forms (CRFs). FDA 21 CFR 11 is followed as well as other applicable legislation on the handling of electronic data. Modification of the CRFs will only be made if deemed necessary by the Sponsor and/or the appropriate regulatory body.

Site numbers and participant numbers will be used to track participant information throughout the study. Participant personal information will be pseudonymized/de-identified.

11.2 Source Documentation

Original or certified copies of all relevant clinical findings, observations, and other activities throughout the clinical investigation must be recorded and maintained in the study file of each enrolled participant. Where there is no prior written or electronic record of data, such as for subjective data (e.g., pain scales, questionnaires), these data may be recorded directly on the CRF(s) and the CRF is then considered to be the source.

11.3 Data Management

Data management is the responsibility of the Sponsor. Data from completed CRFs will be managed in a secured, controlled database. A Data Management Plan (DMP) will be developed that outlines the procedures used for data review, database cleaning and issuing/resolving data queries. Procedures for validations and data storage will also be contained within the DMP.

[redacted]

11.4 Record Retention

The Investigator shall retain all study records for a minimum of two (2) years after the later of the following two dates: the date on which the study is terminated/completed or the date that the records are no longer required for purposes of supporting a pre-market approval application or a notice of completion of a product development protocol (21 CFR Part 812.140). The data for some of these records may be available in computerized form but the final responsibility for maintaining study records remains with the Investigator.

The Investigator may withdraw from the responsibility to maintain records for the period required by transferring custody of the records to any other person who will accept responsibility for retaining them. Notice of a transfer shall be given to the Sponsor and FDA, if applicable, not later than ten (10) working days after the transfer occurs.

12 QUALITY CONTROL AND ASSURANCE

12.1 Control of Study Products

Investigational study products will be released only for use by Investigators who have obtained written IRB/EC approval (as required) for participation in this study, who have completed all required study documentation, and who have been qualified by the Sponsor. Investigators must maintain control over all study products, and ensure they are used in accordance with this protocol. Failure to do so may result in the Sponsor suspending or terminating the study at the Investigator's site.

The Investigator will ensure that study products are only dispensed to participants (or used for specimens) properly enrolled in the study. The Investigator must maintain records of receipt, disposition, return and/or destruction of all study products. All investigational study products released to the site must be accounted for at the unit level prior to study close out, regardless of disposition. The Sponsor-Monitor will regularly review all records regarding study product accountability.

The Sponsor will maintain records that document the shipment, receipt, disposition, return and/or destruction of study products.

12.2 Monitoring

The Sponsor will designate trained and qualified personnel to monitor the progress of this clinical study in accordance with established standard operating procedures and the study-specific Monitoring Plan.

Prior to study start, a study initiation visit (SIV) will be conducted to review with the Investigator(s) and staff the provisions and proper conduct of this study. This visit will include a detailed review of this protocol, verification that all necessary documents are on file at the investigational site and confirmation of IRB/EC approvals.

During the study, routine monitoring visits (RMVs) will be conducted to assure the site continues to adhere to the protocol, the investigator agreement, and regulations regarding conduct of clinical studies. The Sponsor-Monitor will confirm that the ICF to be used is the version approved by the IRB/EC, confirm the applicable national privacy laws have been followed, verify that all necessary documents are on file at the investigational site and confirm that there are provisions to continue and maintain all documents and records throughout the study as required by applicable regulations. These monitoring visits will assess continued protocol compliance, adequate participant enrollment, accurate data reporting, monitoring of participant safety through identification and/or review of any device-related AEs, UADEs, or SAEs, device accountability, continued maintenance, and calibration of study-specific equipment (if applicable), and continued IRB/EC acceptance of the study.

At the completion of the study, the Sponsor-Monitor will conduct a final close-out visit or COV. The purpose of this visit may include but is not limited to collecting all outstanding study data documents, confirming that the Investigator's files are accurate and complete, reviewing the record retention requirements with the Investigator, providing for the return of unused devices to the Sponsor, reviewing records which account for device shipments and ensuring that all applicable requirements for closure of the study are met.

12.3 Audits and Inspections

If the study is selected for audit by the Sponsor or if there is an inspection by the appropriate Health Authorities, the Investigator and his team will make themselves available during the visit. The Investigator must agree to the inspection of all study related records and give the auditor/inspector direct access to source documents for verification of data on CRFs. The participant's anonymity must be ensured, and data checked during the audit must remain confidential.

As soon as the Investigator is aware of an upcoming inspection/audit by the Health Authorities, he/she will promptly inform the Sponsor. As agreed with the Investigator, Sponsor personnel may be present at the site during the inspection.

12.4 Protocol Deviations

A protocol deviation is defined as an event where the Investigator or site personnel did not conduct the study according to the protocol.

Except when necessary to protect the life or physical well-being of a participant, protocol deviations are not permitted. The Sponsor and the investigational site's IRB/EC must be notified immediately if an emergency situation arises in which the safety of a participant may require immediate intervention different than that defined in the protocol. This must be followed by written confirmation that describes the emergency action and outcomes,

[redacted]

within five (5) working days from the date of the emergency action in accordance with the governing IRB/EC's requirement.

It is the Investigator's responsibility to ensure that there are no deviations from the Protocol. Except in an emergency, when a protocol deviation is planned or anticipated, the Sponsor should be contacted for approval. Any and all deviations must be recorded on the appropriate CRF regardless of whether medically justifiable or sponsor approved. Upon evaluation by the Sponsor, actions may be required to prevent additional deviations, such as retraining of the site, implementation of additional site procedures, and more frequent monitoring. If these steps fail, more serious measures, up to and including termination of enrollment at the site.

12.4.1 Occurrence of Special Interest

An occurrence of special interest (OSI) is defined as an event that is outside of the reasonable control of the study site or Principal Investigator. The event prevents completion of specimen processing and/or testing or could impact the integrity of the evaluation of data. Examples of OSI include but are not limited to specimen handling accidents, specimen shipping/transport mishaps, and instrument/ ancillary device malfunction (excluding study device).

An occurrence of special interest must be recorded on the appropriate CRF. Upon evaluation by the Sponsor, actions may be required to prevent additional occurrences, such as retraining of the site, implementation of additional site procedures, and/or more frequent monitoring.

13 ADMINISTRATIVE REQUIREMENTS

13.1 Investigator and Site Selection

The Investigator must be of good standing as an Investigator and knowledgeable in relevant areas of clinical research to ensure adherence to the requirements of this protocol, including the protection of human participants. Other site personnel must have appropriate research experience and infrastructure to ensure adherence to this protocol and enrollment of sufficient numbers of evaluable participants. The curriculum vitae of the Investigator(s), Sub-Investigator(s) and Study Coordinator(s) will be maintained in the Sponsor's files as documentation of qualification by training and experience.

The Principal Investigator will sign the Investigator Agreement pages of this protocol, agreeing to comply with all applicable regulations and the requirements of this study as per the clinical study agreement.

Any site that is deactivated prior to initial enrollment, either by the Sponsor or by the individual site itself, may be replaced.

[redacted]

13.2 Training

In addition to each Investigator and appropriate site personnel being trained on this protocol and study procedures during the Site Initiation Visit, product training will be provided by the Sponsor or designee and is required for each Investigator. Additional study staff (e.g., Sub-Investigator(s)) will also require device training provided from the Sponsor or proctoring by the PI. All training will be documented and filed at the investigational site and with the Sponsor.

13.3 Required Documents

An Investigator may not screen or enroll participants until authorized to do so by the Sponsor. At a minimum, the following documentation should be received by the Sponsor prior to the commencement of external study activities:

- Fully executed Non-disclosure Agreement (NDA) between PI/site and Sponsor;
- CVs., signed and dated within 2 years of study start for the PI and Sub-Investigator(s);
- CVs. for Study Coordinator(s);
- Signed CSA by PI/site (or designee);
- Signed Investigator Agreement Page by PI and Sub-Investigator(s);
- Signed Financial Disclosure Statement by PI and Sub-Investigator(s);
- Completed and Signed Training Log by PI and Sub-Investigator(s);
- Study Personnel Identification list;
- Written approval from the IRB/EC of both the protocol and ICF, and any other
- applicable protocol specific material; and
- IRB/EC Membership List, Assurance of Compliance Form, or equivalent.

13.4 Publication Policy

The sponsor believes that results of applicable clinical studies should be published in peer-reviewed literature in a timely, accurate, complete, and balanced manner, regardless of study outcomes, whenever possible. As such, at the conclusion of this study, an article may be prepared for publication in a reputable scientific journal. Formal presentation(s) or publication(s) of data collected from this study will be considered as a joint publication by the investigator(s) and the appropriate personnel of the Sponsor. Authorship will be based on generally accepted criteria of the ICMJE (International Committee of Medical Journal Editors) and determined by mutual agreement.

The publication of the principal results from any single-center experience within the study is not allowed until the preparation and publication of the multicenter results. Exceptions to this rule require the prior approval of the Sponsor. The analysis of other pre-specified and non-pre-specified endpoints will be performed by the Sponsor or its designee. Such analyses, as well as other proposed investigations or manuscripts will require the approval of the Sponsor.

[redacted]

13.5 Study Registration

In compliance with Title VIII of Public Law 110-85, known as FDA Amendments Act of 2007 (FDAAA), the Sponsor will register this study and disclose study results in a publicly accessible database (i.e., ClinicalTrials.gov). This study will be registered no later than 21 days after commencing enrollment. Study results will be posted to the website within 12 months after regulatory and health authority approval.

13.6 Termination of Study

The Sponsor reserves the right to suspend enrollment or terminate the study at any time for any reason. The Sponsor may suspend enrollment or terminate the study at a specific investigational site for reasons including, but not limited to, inadequate data collection, low participant enrollment rate, achievement of the total enrollment, conditions imposed by the reviewing IRB/EC and/or non-compliance with this protocol or other clinical research requirements. Written notice will be submitted to the Investigator in advance of such termination.

In the event of study suspension or termination, the Sponsor will send a report outlining the circumstances to the IRB/EC, and all Investigators and Regulatory Authorities as required by regulation.

14 ETHICAL AND REGULATORY CONSIDERATIONS

14.1 IRB/EC Approval

Investigators or designees must submit the study protocol, Informed Consent Form (if applicable), and all other locally required documentation to an appropriate IRB/EC and obtain study-specific written approval (favorable opinion) before being allowed to participate in the study. Before commencement of the study, the Investigator or designee must provide the Sponsor with written documentation of such approval. The IRB/EC must give written renewal of the original approval at least annually to continue the study. A copy of the written renewal must be provided to the Sponsor.

The IRB/EC will be notified of any amendments to the protocol, as well as possible associated information and consent form changes, where applicable, and written approval (favorable opinion) will be obtained prior to implementation, as applicable.

The Investigator or designee is responsible for fulfilling any conditions of approval imposed by the IRB/EC, such as regular safety reporting, study timing, etc. The Investigator or designee will provide the Sponsor with copies of such reports.

14.2 Informed Consent and Confidentiality (Natural Samples)

Prior to any study procedure, the Investigator (or designee) must explain to each participant in layman's terms, the nature of the study, its purpose, expected duration, and the risks and benefits of study participation. Also, participant will be informed of uses and disclosures of their medical information for research purposes, and their rights to access information about them. All applicable national privacy laws (e.g., HIPAA requirements in the US) will be followed in this study. The participants must be informed of their right to withdraw from the study at any time and for any reason without sanction, penalty, or loss of benefits to which they are otherwise entitled, and that withdrawal from the study will not jeopardize their future medical care. Participants will be informed of their right to new information and/or findings relating to the clinical study, and the process by which this information is made available. After this explanation, given sufficient time to decide whether to participate, before any study procedure is conducted, and before entering the study, the participant must voluntarily provide consent in accordance with 21 CFR Parts 50 and 56 and ISO 14155:2011(E). The participant will receive a copy of his/her signed ICF.

14.2.1 Confidentiality

Participant confidentiality must be strictly held in trust by the Investigator, study staff, and the Sponsor. Participant confidentiality and anonymity will be maintained by removal of identifiers from any data, documentation, or clinical samples submitted to the Sponsor.

Any data collected meeting the definition of protected/confidential health information or personal identifying information will be collected and maintained using the designated authorizations and following privacy procedures as specified in the applicable health authority regulations.

The Sponsor-Monitor, authorized representatives of the sponsor, and/or applicable Health Authorities may inspect all documents and records required to be maintained by the Investigator. The Investigator/Site will permit access to such records.

14.3 Regulatory Status

The Sponsor has determined and documented this to be an IDE Exempt study based on congruency with 21 CFR 812.3. This determination is based on the following assessment of the investigational device:

- Is not intended as an implant;
- Is not purported or represented to be for a use in supporting or sustaining human life;
- Is not intended for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health; and,
- Does not present a potential for serious risk to the health, safety, or welfare of a participant.

Classification of non-significant risk is documented in the Study Risk Assessment Form.

14.4 Statement of Compliance

This clinical investigation will be conducted in compliance with the protocol and following regulatory requirements:

- 21 CFR 50, 54, 56 and 812;
- 21 CFR 812.28(a)(1) (Good Clinical Practice);
- Ethical principles of the Declaration of Helsinki, in its current revision; and
- Applicable sections of the national laws and regulations.

The clinical investigation will not commence at a clinical site until approval (favorable opinion) from the respective IRB/EC has been received. All additional requirements imposed by the IRB/EC(s) will be followed. Involvement of the national competent authorities (e.g., by notification, seeking authorization) will be accomplished as required by national laws and regulations.

[redacted]

[redacted]

16 APPENDICES

Appendix A: Reference Ranges, Critical Values, and Assay Measurable Ranges per Parameter
Appendix B: Overview of Spiking Approach

[redacted]

[redacted]

[redacted]

[redacted]

Appendix B: Overview of Spiking Approach

Contrived Samples

Overview: Full details of the contriving approach and preparation steps to create abnormal low and abnormal high samples will be defined under a separate Spiking Plan. However, contrived samples will be created using the general approach below, using [redacted] and then prepared by addition of spiking/dilution material. Once contrived samples are prepared, they will be transferred into the Test Device and comparator tubes for processing. Multiple sets of contrived samples can be prepared from the blood collected from one participant. Collection metrics such as duration of collection, whole blood volume, and serum volumes will not be collected for contrived samples. All visual observations will be collected except for "collection failure" as these samples are indirectly collected. Following visual observations, all samples are expected to be processed and tested as per [redacted] handling, processing, and testing.

[redacted]

[redacted]

[redacted] -- [redacted]

[redacted]


[redacted]

[redacted]