DX 10457

To: Elizabeth Holmes[eholmes@theranos.com]
From: Daniel Edlin
Sent: Mon 12/3/2012 11:50:17 PM
Importance: Normal
Subject: FW: Approved IRB Protocol for Theranos LOE
Received: Mon 12/3/2012 11:50:20 PM
Theranos LOE_Protocol Application for Existing Data and Specimens V 2 2 (2).doc
M-10278 Approval Memo.pdf
follstad_thern_AOstartLetter_6NOV12.pdf

Hi Elizabeth,

Attached is the CENTCOM LOE protocol for your records. Note that this is being adjusted to include Vancomycin, Pre-albumin, Random Cortisol, and Factor Xa.

I'll send this to Daniel as well.

Thanks,

Dan

From: Murphy, Christine L Maj MIL USAF USCENTCOM CCSG-AA [mailto:christine.l.murphy[redacted]
Sent: Friday, November 16, 2012 12:45 PM
To: Daniel Edlin; Christian Holmes
Subject: Approved IRB Protocol for Theranos LOE

Sirs,

For your reference please find attached the Approved Version of the protocol. Lab tech Officer as mentioned will be Capt Blanco, she is the only authorized hands on at this time. We will be submitting shortly an addendum to include the bridging Sergeant and Capt Blanco's replacement once that name is available. This is a common occurrence if any updates as to who is participating or minor updates in procedure occur to submit an addendum. I have also attached the IRB approval memo and the Approval To Start Letter from the theater Approval Authority for your reference. If there are any questions, please let me know. Thanks.

V/R

Maj Christine Murphy, USAF, BSC

Director, Joint Theater Blood Program

Human Protections Administrator/HPA

Clinical Laboratory Consultant

HQ USCENTCOM/CCSG

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MacDill AFB FL 33621

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christine.l.murphy@[redacted]

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U S Army Medical Research and Materiel Command
Office of Research Protections
Institutional Review Board Office

Initial Application for Research Involving Use of Existing Human Data and/or Specimens

Study Title:	Limited Objective Experiment (LOE) on the Theranos Point of Service Lab Device

Date of application: September 12, 2012

PART A.

1. Study Contacts

Principal Investigator:	Other Study Contact (if applicable)
Name and Degree: Eric Follstad, DAFC	Name and Degree: Maj Christine Murphy/MS/SBB
Title: Chief, Transformation & Concept Development	Title: Director, CENTCOM Theater Joint Blood Program Officer
Mailing Address: : HQ USCENTCOM/CCSG 7115 South Boundary Blvd MacDill AFB FL 33621	Mailing Address: HQ USCENTCOM/CCSG 7115 South Boundary Blvd MacDill AFB FL 33621
Phone Number: or [redacted]	Phone Number: [redacted] or [redacted]
Email Address: eric.a.follstad[redacted]il	Email Address: christine.l.murphy@c[redacted]
Fax Number: N/A	Fax Number: N/A

2. Key Study Personnel *(if more space is needed attach additional pages to the end of the application)*

List all key personnel **including the Principal Investigator (PI) and Other Study Contacts**, along with a brief statement of their study role(s) and responsibilities. If more space is needed, attach an additional page to the end of this application. NOTE: Key personnel are persons who have contact with identifiable data or specimens.

Key Personnel	Study Roles and Responsibilities
Name: Eric Follstad Affiliated Institute: CENTCOM HQ, CCJ8-ST	Study Role(s): Principal Investigator/Chief, Transformation & Concept Development Responsibilities: Lead S&T SME and coordinator for Theranos Limited Objective Experiment. Oversight of project coordination including LOE team alignment, development of protocol/test packet, device delivery, training, analysis, and final product .
Name: Maj Christine Murphy, USAF Affiliated Institute: CENTCOM HQ, CCSG	Study Role(s): CCSG Liaison/Other Study Contact Responsibilities: Lead CCSG Laboratory SME and direct liaison with Theranos for coordination of technical aspects of device and cartridges and delivery for Information Technology evaluation, theater delivery, and S&T LOE.
Name: Humberto Ibarra Affiliated Institute: USCENTCOM CCJ8-ST	Study Role(s): Lead Analyst Responsibilities: Develop LOE Test Plan and Final Report

Name: Capt Katrina Blanco, USAF Officer in Charge of Laboratory Affiliated Institute: Combined Joint Theater Hospital, Bagram Air Base	Study Role(s): On-site Investigator Responsibilities: Theater liaison to CCJ8 Analysis Team and Theranos. Coordination for initial setup of device, training of laboratory personnel in provision of de-identified specimens and results for the LOE, running of all samples on Theranos device, data collection, and entry of results.
Name: Affiliated Institute:	Study Role(s): Responsibilities:
Name: Affiliated Institute:	Study Role(s): Responsibilities:

3. Study Facilities

List all locations where study procedures will be performed	Briefly Describe Facility
Combined Joint Theater Hospital, Bagram Air Force Base, Afghanistan	Role III Military Treatment Facility. Testing will be performed in the clinical laboratory portion of the facility.

4. Additional Approvals – *(Copies of approval memoranda are required before final IRB approval will be granted)*

Check all that are required by your institution:

☐ Institutional BioSafety Committee	☐ Completed	☐ Review Pending
☐ Human Stem Cell Use Committee	☐ Completed	☐ Review Pending
☐ Radiation Safety Committee	☐ Completed	☐ Review Pending
☐ Data Use Agreement	☐ Completed	☐ Review Pending
☐ Material Transfer Agreement	☐ Completed	☐ Review Pending
☐ Other: _____	☐ Completed	☐ Review Pending
☐ NA		

5. Funding Information

☒ Internal Funding: _CENTCOM Research, Science, and Technology Development Funding through J8__

☐ External Funding *(List all sources that apply, including all Industry Sponsors; list award numbers. If more space is needed attach additional pages to the end of the application)*

Agency / Sponsor	Award Number
	Award #: _____
	Award #: _____

6. Target Population(s):

☐ Adults
☐ Children
☐ Pregnant Women
☐ Fetuses
☐ Active Duty Military
☐ Individuals Not Able to Provide Informed Consent
☐ Employees of the Performance Site
☐ Individuals/Legal Authorized Representative Not Able to Provide Advanced Informed Consent
☐ Prisoners
☒ Other: Pre-existing de-identified laboratory samples

7. **Waiver of the Informed Consent Process**. Ensure the protocol includes the supporting justification and/or information related to the waiver/alteration.

☐ **A. Not applicable** > skip to #8 below

☒ **B. Waiver of informed consent -** For the IRB to grant a waiver of informed consent, all of the following criteria must be addressed in the informed consent section of the protocol:

a) The research involves no more than minimal risk to the subject.
b) The waiver will not adversely affect the rights and welfare of the subjects.
c) The research could not be practicably carried out without the waiver of informed consent.
d) Subjects will be provided with additional pertinent information after participation, whenever appropriate.

8. **Documents Submitted**

☒ Protocol
☒ Request for waiver of HIPAA Authorization
☐ Data collection forms/CRFs
☐ Data Use Agreement
☐ Material Transfer Agreement

Part B. RESPONSIBILITIES OF THE PRINCIPAL INVESTIGATOR IN HUMAN SUBJECTS RESEARCH

The Principal Investigator is the individual who is primarily responsible for the execution of the research. He/she is responsible for the conduct of the study, obtaining subjects' consent, providing necessary reports, and maintaining study documents. The Principal Investigator and Associate Investigators will be familiar with all applicable regulations governing human subjects research, and will adhere to all requirements outlined in his/her institution's DoD Assurance of Compliance with the Human Subjects Protection Regulations as granted by the DoD, and/or by the institution's Federalwide Assurance granted by the Office for Human Research Protections, Department of Health and Human Services.

A. Initial Approval/Study Implementation

Research activities involving human subjects, to include recruitment, screening and/or enrollment, may not commence until the study has been reviewed and approved by the HQ, USAMRMC IRB's (hereafter referred to as the IRB). All study-related materials including, but not limited to, the protocol, informed consent form(s), recruitment materials, case report forms, etc., must be reviewed and approved by the IRB.

I acknowledge that I am responsible for assuring the quality of each subject's informed consent in accordance with current federal, DoD and Army regulations. This responsibility includes ensuring that any designee who obtains consent on my behalf is completely conversant with the protocol and is qualified to perform this responsibility.

I acknowledge that I am responsible for ensuring that the protocol has adequate ongoing data and safety monitoring.

B. Modifications/Amendments to the Protocol

I agree to submit all protocol amendments, changes, and/or modifications to the IRB for review and approval prior to implementation. Any changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to subjects or others. If such protocol changes or modifications are required, I will notify the IRB immediately.

C. Reporting Requirements for Unanticipated Events, SAEs, Deaths, Other

I agree that all unanticipated problems involving risk to subjects or others, all serious adverse events and all subject deaths related to participation will be promptly reported by phone (301-619-2165), by email (irboffice@amedd.army.mil), or by facsimile (301-619-4165) to the IRB. A complete written report will follow the initial notification. In addition to the methods above, the complete report can be sent to the U.S. Army Medical Research and Materiel Command, ATTN: MCMR-RP, 504 Scott Street, Fort Detrick, Maryland 21702-5012.

I will report immediately to the IRB the knowledge of a pending compliance inspection/visit by the FDA, OHRP, or other governmental agency concerning this DoD funded research; the issuance of Inspection Reports, FDA Form 483, warning letters or actions taken by any Regulatory Agencies (e.g. local, state, federal) including legal or medical actions; and any instance of serious or continuing noncompliance with the regulations or requirements.

Any significant findings that become known during the course of the research that might affect the willingness of subjects to enroll or to continue to take part, will be promptly reported to the IRB.

D. Deviations to the Protocol

Any deviations to the protocol that may have an effect on the safety or rights of the subject and/or the integrity of the study will be reported to the IRB as soon as the deviation is identified. I agree to report all deviations to the protocol in the continuing review report for the study and the final study report to the IRB.

E. Continuing Review Reports

A continuing review report for the research study will be submitted to the IRB. I will report progress of the approved research to the IRB as often as requested, but not less frequently than once per year. Should the protocol not receive approval of continuation by its expiration date, all study activity, including subject recruitment, screening, enrollment, data collection and/or data analysis must be discontinued except where necessary to protect the safety of participants.

F. Final Study Report

I will notify the IRB upon completion of the research study and submit a final study report.

G. Records Maintenance

I will maintain a Study File that must be kept for three years following completion of the study (if no IND/IDE used [32 CFR 219.115 (b)]). If IND products or IDE devices are used, the file must be kept for two years after Food and Drug Administration (FDA) approval of marketing application and can then be destroyed; or if no application is filed or approved, until 2 years after the study is discontinued and FDA notified [21 CFR 312.62 (c)]. This file may be inspected at any time by representatives of the IRB, the FDA (as applicable), and/or other regulatory agencies responsible for the oversight of research. Documents maintained in the Study File may include:

- The approved protocol, supporting materials (e.g., study instruments, case report forms, recruitment materials), all protocol amendments, and all continuing review reports.
- All approval memoranda from the IRB (e.g., granting approval to initiate the study, protocol amendments, approval to continue the study).
- Correspondence with the IRB, FDA and/or other pertinent agencies.
- Other applicable committee documentation (e.g., Radiation Safety Committee).
- Study tracking logs.
- Each informed consent/assent document signed by the subject.
- Reports of unanticipated problems, adverse events (initial, follow-up, medical monitor's report), deviations.
- Reports of any significant new findings found during the course of the study.
- All study documents generated from study data.
- Publications, abstracts, reprints resulting from study data.
- All information pertaining to an investigational drug or device (as per FDA regulations).
- Final study report and IRB closure acknowledgment.

I have read and agree to comply with the statements above which outline my responsibilities as a Principal Investigator.

As the Principal Investigator of this study, I assume full responsibility for the execution of this protocol. I also assume full responsibility for the oversight of all research team members and their activities related to this study.

Principal Investigator Signature:

Printed Name: Eric A. Follstad **DATE:** September 12, 2012

PART C. PROTOCOL

1. PROTOCOL TITLE: Limited Objective Experiment (LOE) on the Theranos Point of Service Lab Device

2. ABSTRACT This LOE will document the functionality of the Theranos Device in a field environment after deployment and transport from the United States. The LOE will also determine the Information Technology compatibility of the Theranos Device with pre-existing DoD network communications hardware and network security configurations. Also documented will be a direct comparison of user-friendly operability, turn-around-times, and lab results between the Theranos Devices and pre-existing laboratory instrumentation.

3. RESEARCH HYPOTHESES/OBJECTIVES. The objective of the LOE is to document the functionality of the Theranos in a deployed setting under field conditions and its operations on the DoD network. The comparison will provide information on if the Theranos device has potential to be an improvement over pre-existing lab technology through an improved user-friendly interface, faster turn-around-times, and an all inclusive lab testing device.

4. BACKGROUND AND SIGNIFICANCE. Current existing methodology utilized in theater provides many tests, but not all tests that are available in U.S. run laboratories. Several testing instruments are needed to complete the array of tests that doctors order for sick and injured Service members. Limitations on these instruments are based on the need for trained lab technicians who must troubleshoot, interpret results, quality control, and panic values, and manually enter results. The current methodology utilizes macro-sized technology and therefore requires a large amount of specimen to be collected from a patient. Depending on the test and if it needs to be sent to a referral laboratory, it may take hours to days before results are received so that doctors can treat their patients.

The Theranos Device is an instrument that utilizes micro-sampling and consists of nano-technology in a plug and play format depending on the customization of the user requirements and specifications. The device not only tests and contains lab information, but has the capability to enter other patient unique information as well such as symptoms, diet, pharmacy, physician notes, as well as other applications such as capture of biometric data (BP, pulse). The device can run one to six samples at a time depending on unit size and configuration and can run blood, urine, stool, tissue, swabs, washes, and potentially other samples as well. Excess sample can be saved. The device is validated to perform in a wide range of temperature, humidity, and atmospheric pressure conditions.

The cartridges contain all the required QC, calibrators, reagents, diluent that is required for the testing. The Cartridge can contain up to 60 assays with multiple areas of testing that can be performed in one cartridge with discrete testing and no cross reactivity. Test menus available includes drug testing, cytokine, hematology, chemistry, bacterial, viral testing, DNA technology as well as others. Tests that have not been developed yet can be developed in a short amount of time. Only actual tests run are charged for. Reflex testing is also available. Analysis run time can run from 10 to 40 minutes depending on the cartridge configuration, although faster run times may also be available. Cartridge storage includes room temperature and refrigeration storage.

Results of testing can be forwarded to Theranos affiliated pathology for review, locally, or both. The manufacturer noted that potentially a lab technician would not be needed to run the Device. Results and information are communicated from the device to a "cloud" multiple–Server type storage that can be accessed via a website. The information can also be sent to the local medical site information systems. As per user configuration requirements, the instrument may also display the results of lab testing or other application information.

Suggested areas of use could potentially be at Role III, II facilities (lab/patient care areas), MEDEVAC platforms, SOF units, and mortuary affairs for remains identification. The device has the potential to vastly improve the operations of the laboratory testing through user friendly operations, decreased need for trained lab techs, improving cost and turn-around-time, and enabling medical diagnoses with an all-inclusive device that can be used in multiple platforms on land, in the air, or at sea in a fixed or transportable mode including backpack configurations.

5. RESEARCH DESIGN AND METHODS.

- Limited Objective Experiment (Pilot Study)
- Two Theranos Devices will be sent from the U.S. to the CJTH Bagram Laboratory.
- Upon arrival, both Devices will be plugged into the existing DoD network as indicated by the pre-approved Interim Authority To Test (IATT). Once connected the Device will be able to communicate to the Theranos CLIA certified laboratory via a Theranos website.
- Capt Blanco will be provided training on the Devices by Theranos to the required level of expertise for independent operations and minor maintenance. Sample runs will be made to ensure proper operation, connectivity, end-to-end operation, and training objectives were met.
- For testing, Capt Blanco will start-up the Device. The Device will go through Start-up checks and provide screen readings that all start-up actions passed. During start-up the Theranos website will be accessed to determine that

Internet connections are on-line. Start-up and internet connection success will be recorded as per Device feedback.

- Theater configured cartridges will be used for the testing in the Device.
- Capt Blanco will receive specimens that have been de-identified per the standard operating procedures (SOP) in attachment 3 to prepare testing samples and record testing results.
- The LOE team and Capt Blanco will determine which tests will be run on each sample based on pre-existing clinical results (see SOP for procedures to keep sample de-indentified) and the matrix at Attachment 1.
- The matrix at Attachment 1 will be completed to the fullest extent possible based on sample availability, laboratory testing availability, and Theranos test funding.
- Device will perform analysis of the sample and electronically send preliminary results to Theranos. Theranos will review and finalize results sending back final results via Theranos website to Capt Blanco and on screen of Theranos Device.
- Results of turn-around time and laboratory results will be recorded from Theranos Device and pre-existing lab instrumentation. Turn-around-times will be measured in minutes and lab results will be measured according to the specific test. Recording vehicle will be on the LOE Analysis Team spreadsheet.
- Results provided by Capt Blanco will be analyzed by the LOE Analysis Team and findings will be recorded in the USCENTCOM Final Report.
- Capt Blanco will complete the Theranos LOE Questionnaire (see Attachment 2). These data will support findings documented in the USCENTCOM Final Report.

6. TARGET POPULATION. Samples will be selected from pre-existing laboratory specimens drawn for diagnostic related laboratory testing. No additional samples will be drawn from the patient for this LOE.

6.1 Sample Characteristics

Subjects. Samples will be selected from pre-existing, leftover laboratory specimens of active duty US service members (18 years of age or older) that will be de-identified prior to testing. These will be selected from leftover samples from physician ordered laboratory tests that are collected during the execution of the protocol. The testing will occur over a 28 day period and will consist of approximately 100 specimens, but may vary depending on the original sample and the type of testing performed on it. Depending on the test run the specimen may be required to be whole blood, serum, or plasma. The device test cartridges are capable of multiple tests per cartridge, so one specimen may have several tests run on it in one cartridge. The maximum expected number of tests/assays run will be 400 per device for a total of 800 tests. The maximum expected number of tests on the pre-existing instrumentation is half the number on the Theranos devices combined at 400 tests. Each sample will be run on each Theranos device and on the pre-existing instrumentation.

Attachment 1 lists the types of tests to be performed and the number of tests to be performed by each device for each type of test (8 to 12 tests per device for each type of test). On average, 4 to 6 samples will be tested per day during the 28 day period. Once on site, the actual number of tests per sample will be adjusted by the LOE Analysis Team and Capt Blanco based on sample availability; some samples will have less number of tests, some will have more. The specific types of tests to be tested for each sample will be selected to ensure that each type of test is performed at least once during the test period in the event that CJTH operational tempo (OPTEMPO) restricts lab analyses. (For example, tests 2 through 4 listed in Attachment 1 could be run on Sample 1, tests 5 through 8 listed in Attachment 1 could be run on Sample 2, and so on.)

The LOE Analysis Team and Capt Blanco will minimize the effect on lab resources by using pre-existing, de-identified clinical results. Priority will be given to selecting tests with known results first. Overall priority will be to ensure that each type of test is performed at least once during the test period.

The Protocol meets all requirements in 4.a through 4.g of the Guidance on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable dated 26 April 2006. Specifically, the protocol:

a) Meets the IDE exemption criteria at 21 CFR 812.2(c) (3) since the samples will be selected from leftover samples from physician ordered laboratory tests that are collected during the execution of the protocol and therefore:

(i) is noninvasive,

(ii) does not require an invasive sampling procedure that presents significant risk,
(iii) does not by design or intention introduce energy into a subject, and
(iv) is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.

b) The study uses leftover specimens, that is, remnants of specimens collected for routine clinical care or analysis that would have been discarded.

c) The specimens are not individually identifiable, i.e., the identity of the subject is not known to and may not readily be ascertained by the investigator or any other individuals associated with the investigation, including the sponsor. The CJTH SOP for de-identifying specimens (Attachment 3) will ensure that neither the investigator(s) nor any other individuals associated with the investigation or the sponsor can link the specimen to the subject from whom the specimen was collected, either directly or indirectly through coding systems. The LOE final report resulting from this investigation will not contain any patient identifiable information.

d) The specimens after de-identification will be accompanied by results of physician-ordered clinical tests. These clinical results will only be included in the study if like tests are performed on the Theranos devices. Clinical results not used in the study will be destroyed and not included in the study.

e) The individuals caring for the patients will be different from and do not share information about the patient with those conducting the investigation. The assessment team will use a dedicated laboratory technician, Capt Blanco, to participate in the LOE, who will not be involved in direct care of the patients from whom the specimens were taken.

f) The CJTH SOP for de-identifying samples will ensure specimens are provided to Capt Blanco without identifiers. The CJTH has established policies and procedures to ensure compliance with HIPAA requirement to prevent the release of personal information.

g) The study will be reviewed by an IRB in accordance with 21 CFR Part 56, except as described in section 7 of this guidance document.

6.2. Inclusion Criteria. Specimens will be utilized that will be consistent with the requirements of the particular test. This may include whole blood, serum, or plasma. Amount needed for test will be considered although this technology utilizes micro-samples so should be a minimal restriction. Specimen patient age should be 18 or older.

6.3. Exclusion Criteria. Specimens that do not meet testing criteria should not be used (example: if test requires whole blood, serum should not be used and vice versa.) Clotted, hemolyzed, lipemic, or other factors that could interfere with the test should not be used. Specimen patient age under 18 should not be used.

6.4. Informed Consent.

We are requesting the IRB allow the samples to be used in this study without gaining informed consent, and affirm that we will abide by all the requirements in the FDA Guidance Document for use of leftover specimens whereby the FDA states they will utilize enforcement discretion regarding informed consent provided specific requirements are met.

7.0. Data/Specimen Collection.

7.1 Collection Procedures.

- Candidate specimens will be hand selected by laboratory technicians not associated with the investigation and separated out into appropriate collection tubes. Selection of specimens will be based on quantity of specimen, age of patient (18 or older), and sample type required for the assay (whole blood, serum, plasma). Specimen will also be examined for anything that would interfere with the test (clots, hemolysis, fibrin, etc.). The de-identified samples tested on the Theranos devices and existing equipment for this research will be destroyed once testing is completed in accordance with the SOP.

- Data Elements To Be Collected:

Variable	Source	Operational Specification
IT Compatibility	Network Communications	N/A
User Friendly Operability	Direct Observation and User Surveys	N/A
Task Elapsed Times	Recorded Start/Stop Times	N/A
Lab Result Comparison	Device/Instrument Printout	N/A

Size, weight and floor space metrics	Direct measurement recorded on data logs	N/A

The LOE members are civilian personnel operating under approved orders, travel documents, and theater clearances (as required). The LOE Analysis Team will be deployed for 28 days to the CJTH Bagram Laboratory to observe the tests on the devices. Laboratory staff not associated with the investigation will provide de-indentified specimens from to be used on the Theranos device IAW the SOP. Capt Blanco will provide input on user operability of Device. The LOE members will record the test results and turn-around times for the existing laboratory equipment and the Theranos device.

- LOE Analysis Team will not have direct access to the de-identified specimens for testing. LOE Analysis Team will only be observing Capt Blanco operate the device with specimens that were previously de-identified by laboratory staff not associated with the investigation.
- Data will be assembled into a final report that will be provided to the CDR, US Central Command, and the Office of the Secretary of Defense for Acquisition, Technology, and Logistics (OSD/AT&L).

7.2 Data Management and Storage.

- The data will be collected both electronically and by hard copy in the laboratory.
- Analyzer equipment data will be collected off data logs, if available, from the analyzer equipment. For analyzers which do not provide electronic data logs, the analysis team will record test results manually via a hard copy test results log (Attachment 4). Both electronic logs and hard copy test results will be transferred to spreadsheets on the analysis team laptops which will use PGP whole disc encryption" software on their laptops for data protection.
- All partial electronic data logs and hard copies will be deleted or destroyed once the data has been entered into the analysis team laptops.
- Capt Blanco and the LOE Analysis Team will have access to the study data. Due to the operational nature of the study and the rotating lab personnel, additional names and positions of these government personnel will be documented prior to the start of the study. Current names and organizations follow:
    - Capt Katrina R. Blanco (CJTH)
- The following LOE Analysis Team will have access to the study data:
    - Mr. Humberto Ibarra (AMERICAN SYSTEMS Analyst)
    - Mr. Kenneth Sanchez (AMERICAN SYSTEMS Analyst)
    - Mr. Jason Pagan (AMERICAN SYSTEMS Analyst)
- At the completion of this study, data will be stored using approved hard disk encryption software by the Principal Investigator at HQ, USCENTCOM
- Data will be stored for 90 days following submittal of the final report.
- Data will be assembled into a final report that will be provided to the CDR, US Central Command, and the Office of the Secretary of Defense for Acquisition, Technology, and Logistics (OSD/AT&L).

7.3 Specimen Management and Storage.

- Previously run specimens that are selected for the study will be aliquoted into separate tubes from the original specimen and labeled in a de-indentified manner. (Example: Sample 1, Sample 2, etc.). Samples will be stored in test tube racks or equivalent at temperatures in accordance with the type of sample and test that is required. For example, some specimens require room temperature storage and others require refrigerated. On-site lab technicians will maintain proper storage before testing is performed and following completion of testing. Once results are recorded, specimens are no longer required.
- Storage of specimens will occur within the Bagram CJTH Laboratory.
- De-identified specimens will be stored until time of testing on all Devices and pre-existing lab equipment is complete and recorded properly.
- Specimens will be disposed of in accordance with standard disposal processes once testing is completed and recorded information is determined to be complete.

7.4 Confidentiality Protection.

- All specimens and collected results run on either the Device or the pre-existing instruments will be de-identified prior to release to Capt Blanco.. There will be no coded identifiers to link specimen to patient.
- There will be no unique identifiers linking the sample to the patient from whom the specimen originated. Generic labeling (Sample 1, Sample 2) will be utilized so results will be connected to de-identified specimen only.
- The only master list will be the sample numbers to link the results of the de-identified specimens run on the existing laboratory equipment to the specimens run on the Theranos device.

8.0 Statistical Analysis. There are four categories of data to be collected for the LOE:

1. Analyzer results (existing lab equipment and Theranos analyzer): There will be no statistical analysis performed on these data. The report will list the tests performed and the results of the tests for the existing laboratory equipment and the Theranos analyzer for each specimen sample.
2. Timed events (e.g., sample preparation times, analyzer run times): Depending on the results, the data will be presented as mean times with standard deviations noted, or, if warranted, plotted to show distribution, identified learning curve, etc. Outliers will be identified during the testing and investigated to determine their cause.
3. Hard metrics (size and weight of the analyzers, floor space, etc.): Metrics will be recorded and findings included in the final report. No statistical analysis will be performed on these data.
4. Subjective data (user ratings on specific characteristics of the devices): Data will be captured by the use of questionnaires (see Attachment 2) using a Likert scale, requesting the users to rate the different aspects of the analyzers. Results will be presented as bar charts showing the distribution of responses. Outliers will be identified and investigated during the execution of the LOE and results presented in narrative format in the final report.

8.1 Sample Size.
Each test will be performed on pre-existing equipment and on each Theranos device. Approximately a maximum total of 400 tests will be performed on each set of equipment. Each specific test will be run approximately 8 to 12 times as per Attachment 1 matrix. At this small sample size, there will be no statistical analysis accomplished. This sample size was determined based on the planned availability of the existing laboratory equipment due to an expected OPTEMPO, duration of test (28 days), the expected number of tests/test specimens available, and budgetary considerations. The analyzer results will be a simple side-by-side data comparison. The report will list the tests performed and the results of the tests for the existing laboratory equipment and the Theranos analyzer for each specimen sample.

9.0 Reporting Unexpected Problems to the IRB.

Unanticipated problems involving risk to volunteers or others will be promptly reported by phone (301-619-2165), by e-mail (irboffice@amedd.army.mil), or by facsimile (301-619-4165) to the U.S. Army Medical Research and Materiel Command's Office of Research Protections, Institutional Review Board Office. A complete written report will follow the initial notification. In addition to the methods above, the complete report will be sent to the U.S. Army Medical Research and Materiel Command, ATTN: MCMR-RP, 504 Scott Street, Fort Detrick, Maryland 21702-5012.

10.0 <u>Risks/Benefits Assessment.</u>

10.1 Risks.
Utilization of pre-existing specimens can potentially have risks in relation to breaching privacy or confidentiality, and may apply to individuals or groups to which they belong. In order to minimize the potential risk, specimens will be selected and de-identified by laboratory staff before being introduced for LOE analysis. Samples will be labeled generically as Sample 1, Sample 2, etc. and carry no identifying data. Clinical results accompanying the de-identified sample will not carry no identifying data or coding.

Potential risk to laboratory staff who de-identify the laboratory specimens and Capt Blanco will be exposure to body fluid substances in the form of whole blood, serum, or plasma and exposure to reagents in the testing device or pre-existing instrumentation. The laboratory staff and Capt Blanco will follow appropriate Body Fluid Exposure and Safety measures to protect against these potential risks. The laboratory will have and the laboratory staff who de-identify and Capt Blanco will utilize personal protective equipment to protect against exposure, which will include lab coat, gloves, eye protection when appropriate to prevent splash, hood if transfer is needed, and any other PPE appropriate to the procedure. The laboratory will have a Material Safety Data Sheet (MSDS) book available for safety reference on applicable reagents and supplies.

Potential risk to the LOE Analysis Team will be exposure to body fluid substances in the form of whole blood, serum, or plasma and exposure to reagents in the testing Device or pre-existing instrumentation. This exposure is assessed to be minimal since the LOE Analysis Team will not be physically handling any samples. However, the laboratory will provide personal protective equipment to protect against exposure, which will include lab coat, gloves, eye protection when appropriate to prevent splash, hood if transfer is needed, and any other PPE appropriate to the procedure. Body Fluid Exposure and Safety measures will be maintained as required by functional laboratories. The laboratory MSDS will also be available for the LOE Analysis Team.

10.2 Potential Benefits. The potential benefits is the determination that this new class of device technology works and provides benefits of nano-technology, micro-sampling, and one stop rapid turn-around-time testing in the treatment of ill and wounded military personnel both in the U.S. and deployment theater arenas. This technology could substantially improve the care and time to treatment of patients. The ultimate goal is to improve the chances of recovery and prevent unnecessary death.

11.0 REFERENCES.

1. Theranos Website – October 2011
2. Theranos Site Visit and Briefing – October 2011
3. Theranos Information Paper – Assembled by CENTCOM Surgeons Office – October 2011
4. Theranos Quad Chart – Assembled by CENTCOM Surgeons Office – January 2012
5. Guidance on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable - April 2006.

12.0 TIME REQUIRED TO COMPLETE THE RESEARCH (INCLUDING DATA ANALYSIS). Ninety Days.

Attachment 1
Proposed Types of Tests and the Number of Tests per Device

Theranos Suggested Test Numbers (Not Cartridges)				
Test Breakdown				
TEST TYPE	Specimen	Theranos Device 1 Test #	Theranos Device 2 Test #	Current Instrumentation
CBC	Whole Blood	12	12	12
Sodium	Plasma	12	12	12
Potassium	Plasma	12	12	12
Chloride	Plasma	12	12	12
Bicarb	Plasma	12	12	12
Blood Urea Nitrogen	Plasma	12	12	12
Creatinine	Plasma	12	12	12
Glucose	Plasma	12	12	12
Calcium	Plasma	12	12	12
Magnesium	Plasma	12	12	12
Phosphorus	Plasma	12	12	12
Anion Gap	Calculated	8	8	8
Total Protein	Plasma	12	12	12
Albumin	Plasma	12	12	12
Total Bilirubin	Plasma	12	12	12
Alkaline Phosphatase	Plasma	12	12	12
AST	Plasma	12	12	12
ALT	Plasma	12	12	12
Amylase	Plasma	12	12	12
Lipase	Plasma	12	12	12
PT	Whole Blood	8	8	8
PTT	Whole Blood	8	8	8
INR	Calculated	8	8	8
Creatinine Kinase	Plasma	12	12	12
Troponin I	Whole Blood	12	12	12
ABG	Whole Blood	6	6	6
Lactate	Plasma	6	6	6
Base Excess/Deficit	Whole Blood	8	8	8
ABO Blood Type	EDTA - RBC	12	12	12
Rh Blood Type	EDTA - RBC	12	12	12
Cholesterol	Plasma	12	12	12
Triglyceride	Plasma	12	12	12
HDL Chol	Plasma	12	12	12
LDL Chol	Plasma	12	12	12
VLDL Chol	Plasma	12	12	12
Chol/HDL Chol	Plasma	12	12	12
TOTAL for Current Instrumentation				400
TOTAL per Theranos Device		400	400	
TOTAL for Theranos Devices and Current Instrumentation		800		400

Attachment 2

Theranos LOE Questionnaire

*The information you provide will be on a **non-attribution** basis. Therefore, full freedom of expression is encouraged being that others will not later attribute your statements to you. Your name will only be used by data collectors for follow-up interviews when additional information is needed.*

Thank you for your participation.

Respondent Name (Title, First, Last): _____ Date: _____

Job Position: _____ Years in this Position: _____

Telephone Contact: _____ Email: _____

Please **circle** the most appropriate response and provide comments to amplify the response. Comments are highly encouraged as they provide the distinctions to qualify the answer. Comments are especially encouraged for "Highly Agree" or "Highly Disagree" responses.

1. The Theranos reporting file format was clear. Why?	Highly Agree	Agree	Disagree	Highly Disagree	N/A
Comments: _____					
2. The current laboratory systems reporting file format was clear. Why?	Highly Agree	Agree	Disagree	Highly Disagree	N/A
Comments: _____					
3. The Theranos reporting file format was clearer than the current laboratory systems reporting file format. Why?	Highly Agree	Agree	Disagree	Highly Disagree	N/A
Comments: _____					

4. The Theranos reporting delivery mode was clear. Why?	Highly Agree	Agree	Disagree	Highly Disagree	N/A
Comments:_____					
5. The current laboratory systems reporting delivery mode was clear. Why?	Highly Agree	Agree	Disagree	Highly Disagree	N/A
Comments:_____					
6. The Theranos reporting delivery mode was clearer than the current laboratory systems reporting delivery mode. Why?	Highly Agree	Agree	Disagree	Highly Disagree	N/A
Comments:_____					
7. The Theranos screen menus were easy to read and understand. Why?	Highly Agree	Agree	Disagree	Highly Disagree	N/A
Comments:_____					

8. It was easy to access the test results on the Theranos devices. Why?	Highly Agree	Agree	Disagree	Highly Disagree	N/A
Comments:_____					
9. It was easy to access the test results from the current laboratory devices. Why?	Highly Agree	Agree	Disagree	Highly Disagree	N/A
Comments:_____					
10. It was easier to access the test results on the Theranos devices than from the current laboratory devices. Why?	Highly Agree	Agree	Disagree	Highly Disagree	N/A
Comments:_____					
11. It was easy to download results on the Theranos devices. Why?	Highly Agree	Agree	Disagree	Highly Disagree	N/A
Comments:_____					

12. It was easy to access past test results on the Theranos devices. Why?	Highly Agree	Agree	Disagree	Highly Disagree	N/A

Comments:_____

_____

_____

_____

_____

13. It was easy to access past test results from the current laboratory devices. Why?	Highly Agree	Agree	Disagree	Highly Disagree	N/A

Comments:_____

_____

_____

_____

_____

14. It was easier to access past test results on the Theranos devices than from the current laboratory devices. Why?	Highly Agree	Agree	Disagree	Highly Disagree	N/A

Comments:_____

_____

_____

_____

_____

15. The Theranos device was easy to operate and program. Why?	Highly Agree	Agree	Disagree	Highly Disagree	N/A

Comments:_____

_____

_____

_____

_____

16. It was easy to select the appropriate cartridge for each specific set of tests. Why?	Highly Agree	Agree	Disagree	Highly Disagree	N/A
Comments:_____					
17. The Theranos device was easier to operate than the current laboratory equipment. Why?	Highly Agree	Agree	Disagree	Highly Disagree	N/A
Comments:_____					
18. The Theranos device was easier to set-up than the current laboratory equipment. Why?	Highly Agree	Agree	Disagree	Highly Disagree	N/A
Comments:_____					
19. The Theranos device and procedures overall training was adequate. Why?	Highly Agree	Agree	Disagree	Highly Disagree	N/A
Comments:_____					

20. The Theranos device hands-on training was adequate. Why?	Highly Agree	Agree	Disagree	Highly Disagree	N/A
Comments:_____					
21. The design of the Theranos device is adequate to allow a certified laboratory technician to operate it after initial training. Why?	Highly Agree	Agree	Disagree	Highly Disagree	N/A
Comments:_____					
22. The Theranos device manuals were adequate to support set-up of the system. Why?	Highly Agree	Agree	Disagree	Highly Disagree	N/A
Comments:_____					
23. The Theranos device manuals were adequate to support operation of the system. Why?	Highly Agree	Agree	Disagree	Highly Disagree	N/A
Comments:_____					

24. The Theranos device manuals were adequate to support trouble-shooting of the system. Why?	Highly Agree	Agree	Disagree	Highly Disagree	N/A

Comments:_____

_____

_____

_____

_____

25. The Theranos device manuals were adequate to support maintenance of the system. Why?	Highly Agree	Agree	Disagree	Highly Disagree	N/A

Comments:_____

_____

_____

_____

_____

26. The Theranos device operated on the Internet without incident. Please provide any examples.	Highly Agree	Agree	Disagree	Highly Disagree	N/A

Comments:_____

_____

_____

_____

_____

27. The Theranos device **did not** interfere with other clinic equipment. Please provide examples.	Highly Agree	Agree	Disagree	Highly Disagree	N/A

Comments:_____

_____

_____

_____

_____

28. The Theranos device **was not** interfered with by other clinic equipment. Please provide examples.	Highly Agree	Agree	Disagree	Highly Disagree	N/A
Comments:_____					
_____					
_____					
_____					
_____					

Attachment 3

BY ORDER OF THE CHIEF, LABORATORY SERVICES
TASKFORCE MED
24 Sept 2012
Bagram AB, Afghanistan

SGSAL 44-AD-140

Administration

LABORATORY DE-IDENTIFICATION SOP

1. PURPOSE: This operating instruction outlines sample de-identification for Theranos research testing.

2. SCOPE: This OI applies to all TF Med laboratory staff members providing de-edentified specimens to Capt Blanco for the Theranos Limited Objective Experiment.

3. PRINCIPLES: Research projects conducted in CJTH are sometimes run in the laboratory. Samples (and their associated results) for research must be de-identified for research projects.

4. MATERIALS NEEDED: Patient samples and associated results.

5. PROCEDURE:

5.1. Samples previously run for patient care will be selected for de-identification. The selection of samples will be based on the types of tests to be performed for any particular day. Capt Blanco and the LOE team will select the tests to be performed from the tests listed in Attachment 1. The selected tests will determine the type of specimen required to perform the tests (e.g., whole blood or plasma). Based on the specimen type required, the laboratory staff will randomly select the samples from available patient samples that match the sample type requirements for the day. Active duty (age 18 or older) samples will be pulled from the existing sample storage areas for Theranos study.

5.2. The results from testing already run on the patient sample will be pulled up in TC2.

5.3. Results will have all patient identification removed from them prior to printing and labeled as described in 5.4. The results will be printed for research use.

5.4. The sample will be aliquoted into a plastic pour off tube and labeled as Sample #1, etc. and provided to Capt Blanco along with the results from previous testing until enough samples are run for the study.

5.5. The aliquoted sample will be run on current lab instrumentation if any testing required has not already been run.

5.6. The aliquoted sample will be run on both Theranos analyzers and the results printed off.

Supersedes: N/A
OPR: TASKFORCE MED (Capt Blanco)

Certified by: Capt Blanco
Number of printed pages: 3

5.7. The results will be checked for completeness then the sample will be disposed of according to biohazard requirements.

5.8. De-identified results from current lab techniques and lab results from both research analyzers will be provided to the LOE Analysis Team.

Reviewed/Approved

This instruction has undergone supervisory review and is approved for implementations

SHEILA M. HANLEY, MSgt, USAF

Flight Chief, Clinical Laboratory Services

Annual Review

Name & Title	Signature	Date

Document Control

Number of Official Copies:

Location of Copies: Z:\EMDSS\EMDSS_SGSL_(Laboratory)\Admin\Current OIs\Admin OIs

Date of Implementation: _____

Revision Documentation: The following revisions were made to the OI following implementation. Training was accomplished prior to implementation of the revision.

				Initials/Date		
#	Date	Summary of Revision	Training Completed	Trainer	OIC	Med Dir
1						
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						

Attachment 4

Test Results Log

Sample #	Type of Test Performed	Results Theranos Device #1	Results Theranos Device #2	Existing Laboratory Equipment Results	
				Equipment Name	Results
Sample 1					
Sample 2					
Sample 3					
Sample 4					
Sample 5					
Samples 6-90 (Same as Sample 5)					

DEPARTMENT OF THE ARMY
US ARMY MEDICAL RESEARCH AND MATERIEL COMMAND
504 SCOTT STREET
FORT DETRICK, MD 21702-5012

MCMR-RPI 2 November 2012

MEMORANDUM FOR THE RECORD

SUBJECT: IRB Approval of the Protocol, "Limited Objective Experiment (LOE) on the Theranos Point of Service Lab Device," Principal Investigator: Eric A. Follstad, MS, Headquarters, US Central Command (USCENTCOM), MacDill AFB, FL; Performance Site: Craig Joint Theater Hospital, Bagram Air Field, Afghanistan, IRB Office Log Number M-10278

1. The Headquarters, US Army Medical Research and Materiel Command Institutional Review Board (HQ USAMRMC IRB) serves as the IRB for research conducted within the USCENTCOM Area of Operations. The above-referenced protocol has been reviewed for compliance with applicable human subject protection regulations. There are no outstanding human research protections issues to be resolved.

2. In accordance with 21 CFR 56.110(a,b), the protocol may be approved by expedited review because it involves no more than minimal risk and is included in the categories of research listed in the 9 November 1998 Notice in the Federal Register (63 FR 60364-60367) that may be reviewed by the IRB through an expedited review procedure, specifically, research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required (Category 1b); and research involving materials that have been collected, or will be collected solely for nonresearch purposes (Category 5).

3. The protocol (V 2.2, 26 September 2012, received 22 October 2012) is approved for a one-year period, 2 November 2012 – 1 November 2013, pending approval of the USFOR-A Joint Operations Area Approving Official.

4. This *in vitro* diagnostic device investigation is approved for the use of up to 100 leftover human specimens that are not individually identifiable.

5. This protocol meets the criteria set forth in the April 25, 2006 "Guidance for Sponsors, Institutional Review Boards, Clinical Investigators and FDA Staff: Guidance on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable" for use of specimens in FDA-regulated *in vitro* device studies without informed consent.

6. A waiver of the HIPAA Privacy Rule requirement to obtain authorization for the use of protected health information in research is approved as allowed under DOD 6025.18-R, C7.9.2.2.

7. The protocol must be reviewed for continuation. A continuing review report with a copy of the current protocol and supporting documents must be submitted in sufficient time for review and approval before the expiration date of 1 November 2013.

8. Any modifications (including, but not limited to, changes in the principal investigator, inclusion/exclusion criteria, number of specimens to be used, or procedures) must be submitted as a written amendment for the IRB's review and approval prior to implementation.

9. Any deviation to the protocol that may affect the safety or rights of the patients whose leftover specimens were used, or the integrity of the study must be reported to the IRB as soon as the deviation is identified.

10. Unanticipated problems involving risk to subjects or others must be promptly reported by telephone (DSN 312-343-6240), by e-mail (irboffice@amedd.army.mil), or by facsimile (DSN 312-343-4165) to the HQ USAMRMC IRB. A complete written report is to follow the initial notification.

11. A final report must be submitted to the HQ USAMRMC IRB.

12. The IRB Office point of contact for this protocol is Andrea Kline, MS, CIP at DSN 312-343-7801 or Andrea.Kline1@us.army.mil.

PITTMAN·PHILLIP·RICHARD·1114926 0 8 2

Digitally signed by PITTMAN·PHILLIP·RICHARD·1114926 0 8 2
DN: c=US, o=U·S· Government, ou=DoD, ou=PKI, ou=USA, cn=PITTMAN·PHILLIP·RICHARD·1114926 0 8 2
Date: 2012·11·02 1 0 :0 :40 -04'00'

PHILLIP R. PITTMAN, MD, MPH
Chair
Headquarters, US Army Medical Research and Materiel Command
Institutional Review Board

DEPARTMENT OF THE ARMY
TASK FORCE 44 MED
BAGRAM AFGHANISTAN
APO AE 09354

REPLY TO
ATTENTION OF:

TF44-MB-B

6 NOV 2012

MEMORANDUM FOR Eric Follstad (Research Site: Afghanistan)

SUBJECT: Protocol, "Limited Objective Experiment (LOE) on the Theranos Point of Service Lab Device" M-10278, PI: Eric Follstad

1. Congratulations. The U.S. Army Medical Research and Materiel Command's (MRMC) Office of Research Protections, Institutional Review Board has reviewed the above protocol and determined that it qualified for expedited review because it involves no more than minimal risk and is included in the categories of research listed in the 9 November 1998 Notice in the Federal Register (63 FR 60364-60367) that may be reviewed by the IRB through an expedited review procedure. The protocol is approved for a one-year period, 19 October 2012 – 18 October 2013.

2. As the USFOR-A Approving Official, I approve this research to be conducted within the Afghanistan Theater. You may begin work on the protocol.

3. Please retain a copy of this memorandum in your study file.

Encl

JON C. ALLISON
COL, MC, USA
Approving Official
US Forces-Afghanistan

CF:
US Army MRMC Office of Research Protections
JC2RT Study File