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TITLE: Development of a Hand Held Thromboelastograph

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14. ABSTRACT

The project objective is to develop a hand-held, ultra-portable thromboelastograph, ready for submission for FDA 510(k) clearance for clinical assessment of platelet function. Entegrion has designated the device as the *Portable Coagulation Monitor* (PCM).

This is a three year project, and this report summarizes progress to date at the end of year two (Y2). The overall summary of the Project Timeline is:

1- V 2.0 Prototype Design, Testing, Validation – months 1-12

2- Formal definition of Design Requirements & Specification – Months 13-15

3- Product Design & Development – Months 16-24

4- Certification Testing and subsystem design corrections if needed – months 25-30

5- Manufacturing Documentation – Months 30-36

6- FDA 510(k) Clearance – Months 30-36, concurrent with #5 above

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Introduction

Military Relevance

Trauma is known to induce hemostatic disorders such as trauma-induced coagulopathy (TIC), which evolves rapidly during the first few hours following injury. Commercially available devices for measuring blood-clotting status have many limitations that render them generally unsuitable for use in forward military treatment facilities and particularly during transport. These devices (Haemonetics' thrombelastography (TEG) and ROTEM thromboelastometry (TEM)) require clean, stable and vibration-free environments to properly validate their measurements. Coagulation assessment can take up to an hour on these machines. Entegrion has developed an alternative to these devices that will perform the necessary testing in a portable environment suitable for far forward and patient transport arenas. Use of this device will allow surgeons in level 1, 2, or 3 hospitals to make medical decisions based on the accepted state of a patient's coagulation profile.

The project objective is to develop a hand-held, portable thromboelastograph for 510(k) submission. Entegrion has designated the device as the *Portable Coagulation Monitor* (PCM). This is a three-year project, and this report summarizes progress to date at the end of year two (Y2).

The overall Project Timeline is:

1. Prototype Design, Testing, Validation – 12 months
2. Formal definition of Design Requirements & Specification – Months 13-15
3. Product Design & Development – Months 16-24
4. Certification Testing and Subsystem Design Corrections if needed-Months 25-30
5. Manufacturing Documentation – Months 30-36
6. FDA 510(k) Clearance – Months 30-36 (concurrent with #5 above)

Task	Year 1 (2011)				Year 2 (2012)				Year 3 (2013)				Status
	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	
1a													Complete
1b													Complete
1c													Complete
1d													Complete
1e													Continuing - delayed
1f													Complete
1g													Continuing – delayed
1h													Continuing – delayed
2a													Complete
2b													Complete
2c													Continuing - delayed
2d													Continuing - delayed
3a													In Progress
3b													In Progress
3c													Complete
3d													In Progress
3e													In Progress
3f													In Progress
4a													On Schedule
4b													On Schedule
4c													On Schedule
4d													On Schedule
5a													Complete
5b													Complete
5c													Complete
5d													In Progress
6a													Yet to Start
6b													Yet to Start
6c													Yet to Start
6d													Yet to Start

BODY

The objective is to develop a prototype system into a FDA 510(k) cleared, Complex Laboratory Institutional Accreditation (CLIA) classified "simple", hand-held portable device that replicates the user interface and basic functionality of commercially available thromboelastographic systems (TEG and ROTEM), but with greatly improved portability. The secondary objective is to decrease the sample analysis time and to improve the range of coagulation assessments possible over existing commercially available technologies.

Year 1 work was centered on designing production-based units and testing the Portable Coagulation Monitor (PCM) internal design. Year 2 work was centered on manufacturing the units designed in Year 1 and improving the manufacturing process of the cassettes to ensure a repeatable method.

FIGURE 1: Portable Coagulation Monitor (PCM)

Task 1: Portable Coagulation Monitor (PCM) V2.0 Prototype Development, Testing and Validation:

Subtask 1a: Establish electro-mechanical performance limits: dynamic range of motors
Subtask 1b: Ability to integrate a disposable sample cassette
Subtask 1c: Test protocols for coagulation at low, intermediate, and high shear rate
Subtask 1d: Robustness of device architecture: 1 meter drop test

Subtasks 1a – 1d are complete. The voice coil actuator (VCA) motors will generate a physical displacement of 0.5 mm in each direction at 1 Hz and 0.030 mm in each direction at 100 Hz. The cassette design enables the wicking of blood into the 75 µ gap between the two glass plates. A shear rate of 1000/s was chosen based on the data. A one-meter drop test was conducted in-house on a prototype model, and there was no indication of damage and was found to comply to IEC 61010-1. Currently, loss of calibration has not been evaluated, and it is recommended that the device calibration be re-evaluated for compliance after such a drop. Further testing will be carried out on a manufactured model.

FIGURE 2: Disposable Cassette

Subtask 1e: Basic data analysis to emulate commercially available TEG and ROTEM systems

Entegrion is currently developing algorithms to interpret the data generated by the PCM into emulations of commercially available TEG systems. The engineering teams at Entegrion and TriE Medical are actively involved in development of these algorithms. Task is delayed due to cassette and device manufacturing issues. Testing began in Year 2 – Q8 and will be evaluated in Year 3 – Q9. The delay is not expected to impact the overall timeline.

Subtask 1f: Basic user interface verification.

This task is complete. The display emulates the output of a ROTEM. The data is written to a micro-SD card that is embedded on the test cassette. This cassette can then be reinserted into the PCM device, and the data can be retrieved and saved to a computer via a USB interface. The graphic display has been programmed to resemble the ROTEM graphic output as see in Figure 3.

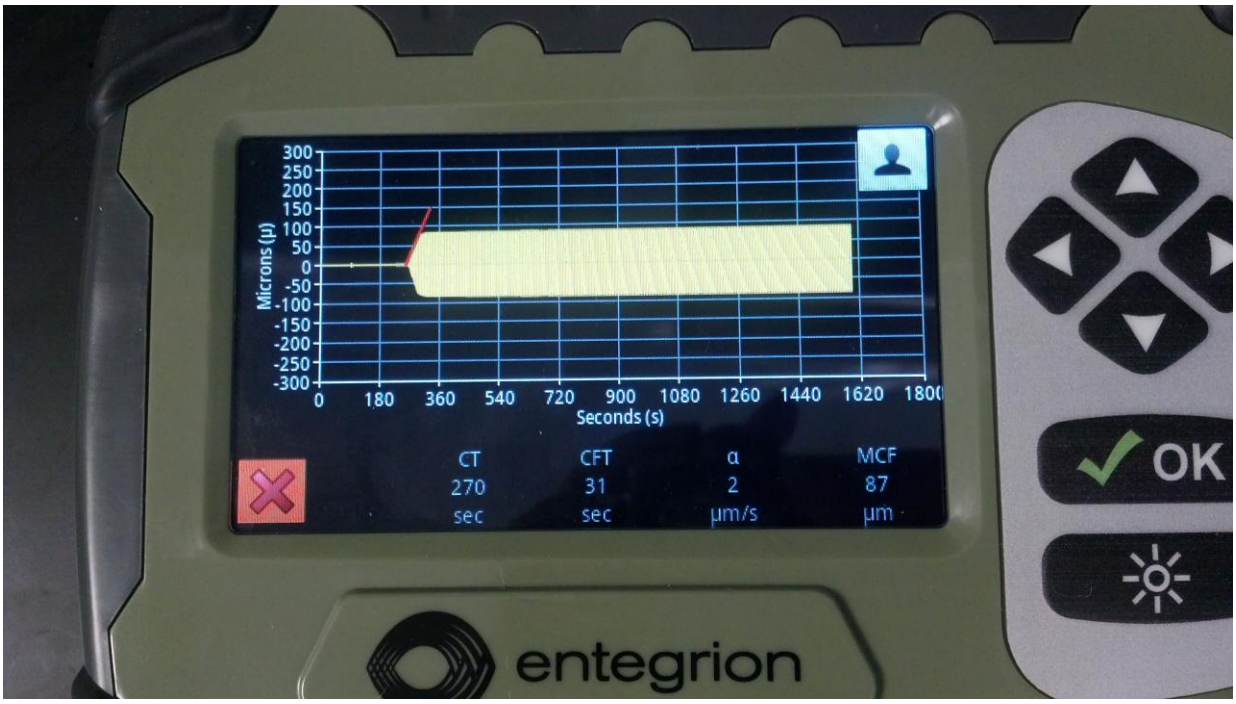

FIGURE 3: PCM Graphic Output

Subtask 1g: Blood sample temperature during test

The temperature control circuitry is in place but has not been fully tested. Testing on the sample temperature was delayed due to the component issues. Testing began in Year 2 – Q8 and will be evaluated in Year 3 – Q9.

Subtask 1h: Benchmark: quantitatively assess PCM vs. ROTEM on matched samples of whole blood

Task is delayed due to cassette and device manufacturing issues. Testing will begin Year 3 – Q1. The delay is not expected to impact overall timeline as testing sites will have access to high study subject throughput. This requirement will also be tested during clinical trials and reviewed by FDA in the 510(k) submission.

Task 2 - Formal definition of Design Requirements and Design Definition

Subtask 2a: Numbered Traceability as required by FDA.
Subtask 2b: Formal System Specification Documentation

Specifications documentation and numbered traceability on devices are complete.

Subtask 2c: Device Hazard Analysis, failure modes and countermeasures
Subtask 2d: Formal Design Review at the completion of all subtasks under Task 2

Device Hazard Analysis, failure modes, and countermeasures and Formal Design Review began in Year 2 – Q8 and will continue into Year 3 – Q9.

Task 3 - PCM Product Design and Development
Subtask 3a: Refine PCM design for manufacturability and compliance
Subtask 3b: Detailed evaluation of electronic design
Subtask 3c: Formal release of Design Documentation
Subtask 3d: Establishment of Integration Reports
Subtask 3e: In-house testing prior to certification testing
Subtask 3f: Military Standards testing

These tasks are underway and remain on schedule for completion, and Entegrion anticipates no problems.

Task 4 - PCM Certification Testing
Subtask 4a: IEC 60601-1
Subtask 4b: IEC 60601-1-2
Subtask 4c: ISO 10993
Subtask 4d: ISTA 2A

These tasks remain on schedule for both start time and completion as scheduled, and Entegrion anticipates no problems or delays.

Task 5 - Manufacturing Documentation
Subtask 5a: Device assembly drawings
Subtask 5b: Manufacturing assembly instructions
Subtask 5c: Wire and cable harness drawings
Subtask 5d: System Service Manual (English)

Device assembly drawings, manufacturing assembly instructions, and wire and cable harness drawings are completed for the initial build. Documentation will be updated during the next round of device manufacturing. The service manual is drafted and will be updated throughout the clinical trials.

Task 6 - FDA 510(k) clearance
Subtask 6a: Completed Design Portfolio, CFR 812 compliant
Subtask 6b: Finalized comparison with predicate devices
Subtask 6c: Written response from FDA
Subtask 6d: Clearance letter (510(k)) from FDA

Pre-IDE meeting held with FDA August 10, 2012. The FDA strongly recommended an additional reference range study be conducted prior to 510(k) filing in addition to increasing the subject size of the initially proposed clinical trial. These tasks remain on schedule for both start time and completion as scheduled, and Entegrion anticipates no problems.

KEY ACCOMPLISHMENTS

- Pre-IDE meeting with the FDA 10 August 2012 with clear path forward for 510(k) clinical trials and filing.
- Ten (10) PCM units built and functional for testing.
- Software for PCM/PC interaction developed.

REPORTABLE OUTCOMES

None

CONCLUSION

Year 2 involved bringing the PCM from a basic idea to a point in the design process that will allow it to be manufactured for medical personnel usage. Major effort was spent solving basic engineering issues bridging the initial theoretical design to actual practice. In addition, the clinical strategy for 510(k) filing has been discussed with the FDA. The overall project remains on track and within budget.

REFERENCES

None

APPENDICES

None