1. **Organization**

**Soteria Medical, LLC** is an FDA registered medical device developer and marketer incorporated in Florida during the first quarter of 2012 (www.FDA.gov – Soteria Medical, LLC – FDA Reg. # 3009723714). The devices which form the foundation of the firm are state-of-the-art noninvasive cardiovascular systems. The firm’s main focus is the primary and secondary prevention of coronary artery disease (CAD), the single leading cause of death in the United States and most countries of the developed world. Since incorporation, activities have focused on research, solidification of past and on-going product development, securing intellectual property, corporate infrastructure, manufacturing, and creation of business strategies for general operations, medical billing, product sales/placement, and market penetration. The Company was formed to expedite and capitalize technology created by Dr. Jeffrey K. Raines (Medical Device Inventor and Emeritus Professor of Surgery, Harvard University and University of Miami) for the early detection of CAD (**Appendix 1**). This new technology represents major scientific upgrades to systems Dr. Raines initially developed in the 1970’s for peripheral vascular disease and are currently found in virtually every vascular laboratory throughout the world. The new CAD technology is able to rapidly identify the presence of atherosclerosis literally decades in advance of symptoms, when intervention is effective. In 1994, Dr. Raines was the Inventor/Developer of technology related to the products and mission of **Soteria Medical, LLC**. At that time, **Vasocor, Inc.**, under Dr. Raines’ guidance, successfully developed an instrument platform which could perform 5 unique noninvasive tests that proved highly predictive of arterial disease (atherosclerosis). To-date, eight (8) United States Patents have been issued in his name for this work.
Clinical trials performed at Columbia University, Bowman Gray School of Medicine, Emory University, University of Miami, Leiden University (The Netherlands), and Groningen University (The Netherlands), involving nearly 1,000 patients, were successfully completed validating the claims of the technology and associated testing protocols. This is outlined in the firm’s extensive Bibliography (Appendix 2). In 2003, Credit Suisse First Boston (CSFB), withdrew further support and terminated the operating company. The reason given was poor business management by the team CSFB had installed and in no way was related to the technology. Dr. Raines was not a member of that executive team. These actions have enabled Dr. Raines to re-create medical devices based upon the earlier platform utilizing 2014 state-of-the-art technology and thereby improving the original measurements and protocols, while reducing the device footprint and operator dependence. The finished products are “disruptive technology” which is obvious to the markets the firm intends to serve. Soteria Medical, LLC will also capitalize on the following Vasocor data: (i) extensive clinical research/trial information, (ii) growing medical publications (20 to-date), (iii) successful FDA 510(k) filings in Dr. Raines’ name, and (iv) established reimbursement data. Device improvement began in March 2012; the Company Launch is scheduled for the Second Quarter of 2014.

2. Quality Policy

Soteria Medical, LLC is committed to employing the most advanced methods of research, development, manufacturing, and implementation for the purpose of introducing and establishing medical devices for the identification and monitoring of atherosclerosis which will result in reduced mortality and morbidity secondary to coronary artery, cerebrovascular, and peripheral vascular diseases.

Appendix 3 is FDA Part 820 Quality System Regulation. The information provided in this document is a response to this regulation in terms of activities directly associated with Soteria Medical, LLC. This is a central document for the company and will be updated on a regular basis with named Revisions (Rev).

The Soteria Cardiac Platform is the first product developed by Soteria Medical, LLC. Other Modules for this Platform and new products are currently in research and development phases. It is the stated intention of Soteria Medical, LLC to work closely with the FDA and comply with all components of Quality System Regulation 21 CFR 820. The first paragraph of this section is the Mission Statement for Soteria Medical, LLC. The goals of this mission require that the firm maintain the highest possible product quality and clear associated processes, procedures, and instructions.
3. **Personnel**

Dr. Jeffrey K. Raines is responsible for initiating and documenting the design plan, obtaining appropriate approvals, holding design review meetings, developing new products, and holding management review meetings. Other important members of the design team include: (i) Mr. Matt Kahn (Firmware Engineer), (ii) Mr. Artiom Bell (Software Engineer), (iii) Mrs. Gloria Raines (Office Manager/Tech), and staff working for Endeavor Manufacturing, Inc. (Contract Manufacturer) and Precision Metal Industries (Cart Manufacturer).

---

4. **Design Control**

4.1. **Design History File**

In terms of background, Dr. Raines (i.e. Soteria Medical, LLC) has obtained three Premarket notifications from the Federal Food and Drug Administration (FDA) which allow Soteria Medical, LLC to market their product line. This can be verified at [www.FDA.gov](http://www.FDA.gov). The 510(k) numbers are: K973659 (Pulse Volume Recorder (PVR) and Endogram), K990123 (Upgraded PVR and Endogram), and K011625 (Soterogram). The actual FDA Letter and the associated *Indications for Use Statement* for the last and most comprehensive submission (K011625) are given in Appendix 4. The 2014 FDA Registration is also provided in this Appendix.
4.1.1. 1st Design Concept (Atherosclerosis)

During this initial design period it became clear to many cardiovascular specialists, including Dr. Raines, that atherosclerosis was a process that involved: (i) smooth muscle cell migration from media of the arterial wall, (ii) associated thickening of the intima, (iii) complex disease of the arterial wall (i.e. lipid pools, thrombus, necrosis, fibrous caps, calcification, and plaque rupture), and (iv) disruption of the endothelial surface (interface between the wall and flowing blood). The following plates show a normal arterial cross-section on the right with a thin wall and intima and smooth endothelial surface. The diseased artery on the left shows the thickened wall, thickened intima, and irregular endothelial surface. This is a clear picture of early atherosclerosis.

4.1.2. 2nd Design Concept (Compliance - Δ volume / Δ pressure)

Jay N. Cohn, MD, a highly respected cardiologist from the University of Minnesota published a paper in the American Journal of Hypertension titled Arterial Compliance to Stratify Cardiovascular Risk: More Precision in Therapeutic Decision Making (Appendix 5). Dr. Cohn in the abstract of this publication opened with the following statement: “The focus of attention in preventing and treating cardiovascular (CV) disease is shifting toward the arterial wall. Evidence has been accumulating for several years that protecting the endothelium is key to reducing CV risk. Endothelial dysfunction results in reduced compliance, or increased arterial stiffness…” In this paper Dr. Cohn goes on to discuss arterial wall disease, hemodynamics (i.e. blood flow), and the relationship of arterial compliance (Δ volume / Δ pressure) in several disease states (i.e. diabetes).
4.1.3. 3rd Design Concept (Measurement Location)

Working from the tenet that early atherosclerosis increases the thickness of the arterial wall (occurring well in advance of blood flow alterations detected by other measures), Dr. Raines was given funding to seriously extend the design of his Pulse Volume Recorder to accurately and noninvasively measure arterial compliance in the lower extremity. It was well known, that the upper extremity arteries and even the carotid arteries did not reflect disease in the coronary arteries due to differences in distribution of elastin, collagen, and smooth muscle between these beds. The major technical challenge was to devise an accurate method to measure local arterial volume (i.e. $\Delta$ volume - the numerator in the definition of compliance). Dr. Raines realized this required an automated and internally calibrated system controlled by a small chip (i.e. microprocessor) within the system. A device was developed and built that could be used in the clinical setting to obtain accurate arterial compliance measurements in the lower extremity (thigh and calf levels). The thigh and calf levels were selected as the measurement sites for arterial compliance because the distribution of elastin, collagen, and smooth muscle mirror the distribution in the coronary arteries were are the target vessels. This device was initially called the Vasogram. Later it was known as the Atherogram and since 2012, the Soterogram. The names changes were secondary to the controlling firm’s name. Over the next few years Dr. Raines was awarded 8 United States Patents for this work; a complete patent listing is given in Appendix 1.

4.1.4. 4th Design Concept (How to Measure Compliance)

With Design Concepts 1 through 3 addressed, the critical design issue of how to accurately measure Arterial Compliance was still required. Compliance is calculated by knowing precisely the change ($\Delta$) in Arterial Volume produced by a change ($\Delta$) in Arterial Pressure. Accurate clinically oriented Blood Pressure Devices (NIBP Units) are available and when advanced arterial obstruction is not present in the upper extremity systemic circulation, Pulse Pressure (difference between Systolic Pressure and Diastolic Pressure) can be measured accurately and in a noninvasive manner. Further, pressure is a fundamental parameter for which there are direct transducers. Volume, while a fundamental parameter cannot be measured with a transducer in a direct fashion; an indirect method must be established.

Borrowing from Dr. Raines’ experience with Pneumatic Cuffs (flexible bladders covered by a semi-ridget cover) and general medical use of cuffs, it was decided that blood pressure cuffs could successfully be used in the measurement of segmental arterial volume change at the required locations (thigh and calf levels) as demonstrated in the following figure.
The remaining issue was to determine the most accurate and reproducible method of measuring segmental arterial volume change during the blood pressure transient from diastolic pressure to systolic pressure secondary to left ventricular contraction. Note that the cuff bladder with an internal pressure transducer constitutes a closed system in which the volume is reduced with arterial expansion resulting in a cyclic increase in bladder pressure corresponding to the cardiovascular pulse frequency. When the left ventricle expands the arterial volume decreases as does the bladder pressure.

For the Vasogram Dr. Raines built a pneumatic system that in closed-system format adds a piston which uses a step-function to expand the closed-system volume by a known value (Vcal). The Vcal expansion is accompanied by a step-change in bladder pressure (Pcal) which is measured. To improve measurement accuracy, the Vcal expansion is timed during the cardiac cycle to occur just as the left ventricle is beginning to expand after full contraction. To complete the bladder cycle measurements, the pressure change from the foot to the peak of the Bladder Pressure vs Time transient is determined (Pm). The expansion of the piston and its timing during the cardiac cycle are controlled by a computer. Computer Algorithms are used to measure Pcal and Pm. The arterial segmental volume expansion under the bladder/cuff is Vm and may be calculated directly using the following formula from the measured parameters.

\[ V_m = V_{cal} \times \left( \frac{P_m}{P_{cal}} \right) \]
The *Vasogram* Schematic is given below:

![Vasogram Schematic](image)

Linear Actuator
Drives
Calibration
Piston

The following diagram illustrates how the measurement are obtained:

![Vasogram Physiologic Tracing / Calibration](image)
This is the exact method and formulation used the the 510(k) submission which included the Multicenter Precision Study and the Multicenter Accuracy Study. These studies will be completely defined in the Verification and Validation Sections of this document.

4.1.5. Design Transition from the Vasogram to the Soterogram

Due to funding and business decision issues which had nothing to due with technology or medicine, the Vasogram was not launched commercially. In January 2010, Dr. Raines revisited the Vasogram. His review at that time included a listing of the positive points of the Vasogram Design and the negative points:

<table>
<thead>
<tr>
<th>Positive Design Points (Vasogram)</th>
<th>Negative Design Points (Vasogram)</th>
</tr>
</thead>
<tbody>
<tr>
<td>➢ Complete design with successful verification and validation.</td>
<td>➢ Hardware, firmware, and software were no longer state-of-the-art.</td>
</tr>
<tr>
<td>➢ The basic measurement of Compliance could now be significantly improved as regards reproducibility using new technology. The Compliance measurement required rapid air movement which was technically difficult and involved precise piston tracking/timing procedures which limited its use in broad populations.</td>
<td></td>
</tr>
<tr>
<td>➢ The Vasogram was never packaged for wide-scale clinical use.</td>
<td></td>
</tr>
</tbody>
</table>

Realizing the potential the Vasogram had in early identification of atherosclerosis and its ability to reduce cardiovascular morbidity and mortality, in January 2010, Dr. Raines began redesigning the Vasogram as a full-time activity. By that time he was Emeritus Professor at the University of Miami (2004) and was stepping down as Senior Partner at the Miami Vein Center (2004 – 2010). For a short period of time he changed the name of the procedure to Atherogram.
This is mentioned because some of the support documents carry that name. In the first quarter of 2012 Dr. Raines registered Soteria Medical, LLC with the State of Florida and changed the name of the procedure to *Soterogram*, its current name.

The first order of business was to completely re-design the technology used in the Compliance Measurement. Specifically, this involved two parameters: volume change and pressure change. The pressure change component was more easily and rapidly solved. In Dr. Raines’ *Vasogram* Design he had carefully selected the Colin Company Noninvasive Blood Pressure Module (NIBP). For the re-design he looked for an updated version of the Colin NIBP and found that Colin Company had been purchased by Omron Electronics, Inc. Omron continued the line of Colin NIBP Units under their name. Dr. Raines selected the M3600 Omron NIBP system for the re-design (*Soterogram*), after an evaluation process which will be described in another section of this document.

The remaining component of the Compliance Measurement was the method for the measurement of volume change. Dr. Raines began investigating the evolving field of Blind Signal Separation Mathematics (BSSM). BSSM is currently used for many applications including telephone and electrical line transmission monitoring and irrigation mechanics. The concept of BSSM can be described using the following example. The flow mechanics of River A includes the rise and fall of the river’s depth. The depth of River A may be accurately measured as a function of time. Actually, the flow mechanics of River A are determined by two other Rivers (River B and River C) which meet to an produce River A. For purposes of this example, consider the flow mechanics from Rivers B and C cannot be directly measured, however, limited information is known about River B, River C, or both. In a sense, the investigator is “blinded” regarding Rivers B and C. BSSM allows the investigator to reconstruct the depths of Rivers B and C as a function of time by knowing the details of River A and a few details from Rivers B and C (the majority of details being blinded from the investigator).

Fortunately, BSSM can be applied to the calculation of Vm, used to determine Compliance in the closed-system bladder described above. In this case a Cuff Pressure versus Time signal may be generated by a cuff bladder placed over an arterial segment of the lower extremity (thigh or calf level). This is referred to as a Physiologic Tracing and is like River B given in the example above. If a known Volume Change (Vcal) at a specific frequency was added by a piston to the closed-system bladder this would be like River C in the example given above. In medical terminology, tinctured means a solution composed of more than one part. Therefore, the pressure versus time signal derived from the physiologic signal (River B) and the superimposed signal generated by the piston (River C) produce a tinctured pressure versus time signal (River A). The following diagram illustrates this sequence.
A – **Tinctured Pressure Signal**  
(Combination of Physiologic Signal and Actual Sinusoid from Piston / GearMotor)

B – **Reconstructed Physiologic Pressure Signal**  
(Returns Max Amp – Pm)

C – **Reconstructed Sinusoid Pressure Signal** (Returns Max Amp – Pcal)

\[ V_m = V_{cal} \times \frac{P_m}{P_{cal}} \]

**Arterial Compliance** = \[\frac{\Delta \text{volume}}{\Delta \text{pressure}} = \frac{V_m}{(P_{sys} - P_{dia})}\]

Actual example signals for the Tinctured, Physiologic, and Piston Tracings are given in the next graph.
The hardware components required to generate these measurements are given in the next diagram.

This completes the most fundamental elements of the Design History for the Soterogram. The next section addresses the Design and Development Planning that moved the fundamental elements just described into a medical device that is known as the Soteria Cardiac Platform.

### 4.2. Design and Development Planning

Soteria Medical, LLC has the responsibility to establish and maintain plans that describe design and development activities and responsibility for implementation.

Soteria Medical, LLC is a small firm. Dr. Raines serves as the CEO and Chief Technical Officer. The projects associated with the firm’s product line and future development involve coordination, hardware, firmware, software, and manufacturing, placement of systems, client support, and service.
Dr. Raines will direct the administrative and technical activities of all projects. The initial projects include taking the design described in Section 4.1 and moving the Soteria Cardiac Platform to market. Additional projects will involve the development of additional modules for the platform.

Dr. Raines is currently supported by Gloria Raines (Office Manager), Matt Kahn (Firmware Engineer), Artiom Bell (Software Engineer), and Les Aguilera and Donald Lisiewski of Endeavor Manufacturing, Inc. (Contract Manufacturer). Endeavor Manufacturing, Inc. is abbreviated as EMI. Precision Metal Manufacturing (PMI) is the cart manufacturer for Soteria Medical, LLC. As additional staff is required to support operations, members will be added.

All projects will be managed by carefully prepared Statement of Work (SOW) documents. These documents are prepared by Dr. Raines and list: (i) description of project, (ii) start and stop dates for project, (iii) approved hours of work for project, and (iv) specific deliverables. An example SOW and Technical Memo Response is given in Appendix 6. All activities with EMI and PMI are managed by contract.

In the traditional fashion all activities will be supported by frequent written correspondence (document exchange, email, etc.), verbal correspondence, and face-to-face meetings. These activities will be ongoing and take place as needed.

This plan format shall be reviewed, updated, and approved as design and development evolves.

4.3. Design Inputs

4.3.1. Clinical Inputs

Design Input is defined as the physical and performance requirements of the Soteria Cardiac Platform used as the basis of the device design.

The Soteria Cardiac Platform consists of five modules: (1) Registration, (2) Framingham and Body Mass Index, (3) Ankle/Brachial Index, (4) PADogram, and the Soterogram. Each of these Modules has different clinical requirements which are discussed:

Registration: The Platform must have the ability of registering new patients and recalling information from previous patients.
Framingham and Body Mass Index: The calculations for Framingham Risk Profiles are widely described in the general medical literature. The Platform requires that the Framingham Calculations are accurately programmed in the Platform Code. The Platform also calculates Body Mass Index (BMI) which is defined by the following formula:

\[
\text{Body Mass Index} = \frac{\text{Weight in Kilograms}}{\text{Height in Meters}^2}
\]

The requirement is that given Subject Weight and Height, that the Body Mass Index be calculated and displaced accurately.
Ankle / Brachial Index (ABIgram) – This measurement requires that Systolic and Diastolic Blood Pressures be calculated at the brachial and ankle levels accurately and in conformance with American National Standard ANSI/AAMI SP10-1992. SP10 Specifications for NIBP Measurement and ABIgram testing results are given in Appendix 7.
PADogram – This measurement also requires that Systolic and Diastolic Blood Pressures be calculated at the brachial, thigh, calf, and ankle levels accurately and in conformance with SP10 Specifications for NIBP Measurement.

![Image](padogram.png)

**PADogram**

**Alpha 03 - Doe, John**

01/01/2014 1:07:07 PM

**PADogram Segmental Pressure Analysis**

<table>
<thead>
<tr>
<th>Level</th>
<th>Right</th>
<th>Left</th>
<th>Anatomic Location of Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brachial</td>
<td>130</td>
<td>147</td>
<td></td>
</tr>
<tr>
<td>Thigh</td>
<td>200</td>
<td>211</td>
<td></td>
</tr>
<tr>
<td>Calf</td>
<td>172</td>
<td>197</td>
<td>Distal SFA/Popliteal</td>
</tr>
<tr>
<td>Ankle</td>
<td>186</td>
<td>162</td>
<td>Tibial Vessels</td>
</tr>
</tbody>
</table>

**Soterogram** – As described in the Design History the basis requirements for determining the measurement (Compliance) provided by the Soterogram is segmental blood pressure and segmental arterial volume change (Compliance = Δ volume / Δ pressure). Requirements for the blood pressure component have been addressed (SP10 Specifications for NIBP Measurement). We have established a requirement that Δ volume be determined to an accuracy of +/- 5% when compared to our Soteria Calibration Device (described in Section 4.5). An example **Soterogram** report is given below.
4.3.2. Physical Inputs

The two major physical components of the Soteria Cardiac Platform are: (i) Pneumoelectric Package (PEP) and (ii) Soteria Diagnostic Cart. The PEP is a grouping of components that are controlled by a Software / Hardware Interface Module (SHIM) which is a Firmware Device (PCB) and software resident in a CPU and connected by a USB Cable. The following pictures illustrate the Soteria PEP.

Soteria Medical, LLC decided to design a proprietary Soteria Diagnostic Cart (SDC). The SDC simply houses the PEP and provides a workable solution for the device Operator. The SDC was designed by Soteria Medical, LLC in cooperation with Precision Metal Industries (PMI). PMI is responsible for manufacturing the SDC which is shown below. The SDC will be fully described, including specifications, in subsequent sections of this document.
The following picture is the front view of the *Soteria Cardiac Platform*.

![Soteria Cardiac Platform](image)

### 4.3.3. Functional Inputs

All functional requirements for the *Soteria Cardiac Platform* have been carefully defined and are captured in a detailed Functional Diagram ([Appendix 8](#)). This design feature and diagram has served as the central blueprint for the Platform Design extending from hardware to firmware to software.
4.3.4. Information from Previous Designs

As will be described under Verification and Validation Sections of this document, significant clinical studies were performed using earlier designs (i.e. Vasogram). In order to accurately use this previous data for the Soterogram, the Soterogram pneumatic gain should be adjusted to within +/- 5% of the pneumatic gain of the Vasogram. This was included as a requirement in the design of the Soterogram and is therefore a design input accomplished by the Soteria Calibration Device.

4.3.5. Risk Analysis / Safety

The Soteria Cardiac Platform is a noninvasive device (Class II). The only contact with the client is via standard blood pressure cuffs with pneumatic lines. There are no electrical connections. Further, the CPU and the SHIM operate at only 19 and 12 VDC, respectively, which is similar to working with a simple flashlight.

Careful analysis suggests that risk is limited to the pressure level exerted by the standard blood pressure cuffs during measurements. To mitigate pressure cuff risk, the design includes the following features:

- The cuff pressure level is constantly displayed (mmHg) to the Operator for all Modules.
- Each Platform Screen includes a RED Stop Button which the Operator can immediately depress, if necessary. This rapidly deflates the cuff.
- The PEP includes a Normally OPEN Exhaust Valve which immediately deflates the cuff, if necessary. If electrical power is lost for any reason, this valve rapidly opens on a mechanical basis.
- Finally, each Pneumatic Line has a Quick Release which the Operator can use to completely disconnect the subject.

4.3.6. Regulation

The Soteria Cardiac Platform is a Class II Medical Device. The Platform’s design manufacturing, and use is regulated by the FDA. It is the intention of Soteria Medical, LLC to carefully follow FDA guidelines.

4.3.7. Cost

Soteria Medical, LLC has determined the Target Cost to manufacture a Soteria Cardiac Platform using its current design is $5,000. This figure has been used in all Soteria Pro Forma. This may have to be adjusted secondary to contracting with Endeavor Manufacturing, Inc. (EMI).
4.4. Design Outputs

Soteria Medical, LLC acknowledges its responsibility to establish and maintain procedures for defining and documenting design output requirements in terms that allow an adequate evaluation of conformance to design input requirements. Soteria Medical, LLC has made a listing of design outputs and identifies where these design outputs may be found in this document (i.e. Quality System Regulation).

<table>
<thead>
<tr>
<th>Design Output</th>
<th>Location</th>
<th>Section</th>
</tr>
</thead>
<tbody>
<tr>
<td>Product Specifications including Engineering Prints, Drawings, and Diagrams</td>
<td>Device Master Record</td>
<td>5</td>
</tr>
<tr>
<td>Manufacturing Specifications</td>
<td>Device Master Record</td>
<td>5</td>
</tr>
<tr>
<td>Quality Plans including Inspections and Output Records</td>
<td>Quality Audit</td>
<td>4.8 and 9</td>
</tr>
</tbody>
</table>

The following Design Milestones may be informative.

<table>
<thead>
<tr>
<th>Date</th>
<th>Milestone</th>
</tr>
</thead>
<tbody>
<tr>
<td>January 2010</td>
<td><strong>Vasogram</strong> Design is revisited</td>
</tr>
<tr>
<td>June 2010</td>
<td>Breadboard of PEP built and tested</td>
</tr>
<tr>
<td>January 2011</td>
<td>Early PEP placed in Enclosure and connected to a CPU with Software</td>
</tr>
<tr>
<td>January 2012</td>
<td>Prototype PEP placed in Generic Cart and connected to a CPU</td>
</tr>
<tr>
<td>January 2014</td>
<td>Final PEP placed in Soteria Diagnostic Cart and connected to a CPU with Final Software</td>
</tr>
</tbody>
</table>

4.5. Design Verification

It is acknowledged that the developer and the manufacturer shall establish and maintain procedures for verifying the device design. This section is focused specifically on the developer and the confirmation that the design outputs meet the design input requirements. The inputs and outputs have been carefully discussed in Sections 4.3 and 4.4 and will not be repeated in this section.
**Alpha Testing** is a clinical test performed by the medical device developers within the developer’s environment. The purpose of the Alpha Test is to carefully compare the design results (outputs) with the device requirements and expectations (inputs). The Alpha Test allows the developer to make adjustments identified during testing without an audience. Soteria Medical, LLC elected to use the formality of the Alpha Test as a tool for Design Verification.

During the month of June 2013, Soteria Medical, LLC recruited 30 subjects for Alpha Test participation; 19 males and 11 females were enrolled after providing written Informed Consent. A formal Clinical Protocol was followed (Appendix 9). The average age of the Alpha subjects was 41 years of age with a range of 24 to 62 years of age.

Review of the Alpha Subjects on presentation suggested 16 (53%) were in excellent health and 14 (47%) with at least low-level cardiovascular disease (11 had hypertension, 8 had elevated blood lipids, and 3 demonstrated severe reduction in arterial compliance). All subjects underwent Registration, three-level Framingham Risk Assessment, ABIgram repeat measures, a single PADogram, and Soterogram repeat measures.

Summary highlights of Alpha Testing, suggested 14 (47%) required additional cardiovascular evaluation on the strength of measurements identified during the testing. The testing was extremely well-received by the participating subjects and their families.

The hardware, firmware, and software performed entirely as expected. Whenever possible hand calculations were compared to measured and displayed results in all five of the Modules included in the **Soteria Cardiac Platform**. No hardware or firmware changes were necessary on the strength of Alpha Testing. Minor software changes were suggested by the testing; these recommendations have been completed. Complete Records of this testing are being maintained at Soteria Medical, LLC. These records have undergone intense statistical review.

For this document Soteria Medical, LLC has assembled a grouping of verification and validation documents, for both Alpha and Beta Testing, which may be found in Appendix 10.

### 4.6. Design Validation

Validation is different than verification. In validation, the developer focus is on assuring that the device meets the standards set for its intended use.

Beta Testing differs from Alpha Testing in a number of important areas: (i) Beta Testing is performed within clinical centers which mimic target offices, clinics, and hospitals for the **Soteria Cardiac Platform**, (ii) while Soteria Medical, LLC personnel supported the Beta Testing, serious involvement by target personnel also took place, and (iii) the objective of the Beta Test is to use the Soteria Cardiac Platform in target environments and solicit/obtain review by local staff and participating subjects. The formal Beta Protocol is given in Appendix 11.
The firm’s goal was to include 3 to 5 clinical centers and 30-50 subjects in this Beta Test. Four clinical centers contributed 37 subjects. The four clinical centers were Naples Cardiology Group (Julian J. Javier, MD), Miami Rescue Clinic (Peter Gutierrez, MD), Palm Beach Surgical Group (Jack Zeltzer, MD), and Navarro Cardiovascular Center (Zoraida Navarro, MD – Palm Beach, FL). These Clinical Centers were selected from over 20 Clinical Centers wishing to participate. Selection was based on several factors which included a wide mix of clinic focus. In our case this ranged from busy to low-income primary prevention operation to cardiology to surgical services (secondary prevention).

The Beta Test was very successful. This can be documented by the fact that ALL Beta Sites want to participate in the Soteria Launch on a priority basis.

4.7. Design Transfer

Soteria Medical, LLC is based in Homestead, Florida. The Soteria Diagnostic Cart (SDC) manufacturer is Precision Metal Industries (PMI) located in Pompano Beach, Florida. PMI operates on an ISO-9001:2008, TUV registration # 12-1093, is ITAR certified, and is an established contractor for the United States Military. Endeavor Manufacturing, Inc (EMI) is located in Coral Springs, Florida and is an ISO 13485 registered facility. EMI is in the registering process with the FDA and anticipates registration very shortly. The distance between Homestead and Pompano Beach and Homestead and Coral Springs is 71 miles and 67 miles, respectively.

Soteria Medical, LLC has a contract with PMI to build all Soteria Medical, LLC carts (Appendix 12). The carts will be manufactured to Soteria Medical, LLC specifications and delivered directly to EMI. Soteria Medical, LLC also has selected EMI as its Contract Manufacturer; a contract is also in-process (Appendix 13). Further, Soteria Medical, LLC has completed the EMI Manufacturing Transfer Protocol (Appendix 14) and is presently involved with daily interaction with the intention of complete manufacturing transfer.

Soteria Medical, LLC acknowledges that various controls and procedures (i.e. Purchasing Controls, Complaint Files, Corrective and Preventive Actions, Quality Audit, and Management, Design, and Manufacturing Controls) will have overlap with EMI. When this is present, documents associated with the responsibilities of Soteria Medical, LLC and EMI will be clearly defined and included in this document.
4.8. Design Review / Changes and Quality System Regulation

Soteria Medical, LLC acknowledges its responsibility to establish and maintain procedures for the identification, documentation, document control, verification, validation, review, and approval of design changes where appropriate, before their implementation. This responsibility is also associated with Document Control.

Soteria Medical, LLC will assume as of May 1, 2014 the design is complete and that the complete design is given with adequate Design Transfer Information in the Master Device Record which is Section 5 of this document.

It is acknowledged in the course of operations that internal reviews, field work / experience, purchasing (Section 6), complaints (Section 7), corrective and preventive actions (Section 8), quality audits (Section 9), Management Review (Section 10), and advances in technology may dictate design changes. Some of these expected changes will be minor in scope as in the case of changing a simple hinge or lock. Some of these expected changes may be major as in the case of transient measurement error in the field or the identification of new technology that will enhance the performance of the Soteria Cardiac Platform. In any case a plan (procedures and forms) must be in-place to manage these situations. When Soteria Medical, LLC examined the requirements of a comprehensive Quality System Regulation plan three distinct areas emerged:

1. **Design Review:** After a design (i.e. Soteria Cardiac Platform) has been established and transferred to manufacturing and launch, information from various sources may trigger design changes as mentioned above. Procedures must be in-place to take advantage of this information which may have the effect of improving the goals of the current medical device or suggesting spin-off medical devices with different goals. In addition to design changes, this process must also include procedures associated with Document Control and Medical Device Report.

2. **Quality Audit:** Certainly, positive design change / review as discussed above, will lead to improved product quality; it is also possible that quality may be improved by constantly reviewing the active processes from design → development → manufacturing → client acceptance including servicing.

3. **Management Review:** Design Review, Quality Audit, and Manufacturing Audit performed by Endeavor Manufacturing, Inc. will address the majority of Quality System Regulation required by Soteria Medical, LLC for the Soteria Cardiac Platform and additional products. However, the firm would like to have a single entry point for its Quality System Regulation which will have the authority and responsibility to execute the necessary processes discussed above and for all other business processes.
The following diagram, discussion and table integrate all the components of the Soteria Medical, LLC Quality System Regulation, including meeting details and interactions.

**Soteria Medical, LLC – Quality System Regulation – Soteria Cardiac Platform**

For the 8 months of operations May 2014 through December 2014, separate monthly Design Reviews and Management Reviews will be chaired by Dr. Raines. All involved Staff, Consultants, and Contractors will participate. For each meeting, Minutes, approved by Dr. Raines, will be prepared and distributed for accuracy and correction. Document Control, Design Review / Changes, and Medical Device reporting will be made as needed and documented using:

(i) Document Control (Protocol and Form) – Appendix 15 Documents 1 and 2,

(ii) Medical Device Reporting Guidelines – Appendix 15 Documents 5 and 6,

(iii) Design Review Procedures (including training) – Appendix 15 Document 3,

These protocols, procedures and forms are found in **Appendix 15**. Beginning January 2015, less frequent (perhaps quarterly) Design Reviews and Device Reporting are anticipated.

<table>
<thead>
<tr>
<th>Focus</th>
<th>Meeting Frequency</th>
<th>Rev2 Section</th>
<th>Appendix</th>
</tr>
</thead>
<tbody>
<tr>
<td>Document Control</td>
<td>n/a</td>
<td>4.8</td>
<td>15</td>
</tr>
<tr>
<td>Medical Device Reporting</td>
<td>n/a</td>
<td>4.8</td>
<td>15</td>
</tr>
<tr>
<td>DESIGN REVIEW</td>
<td>1 / Month</td>
<td>4.8</td>
<td>15</td>
</tr>
<tr>
<td>Manufacturing Audit</td>
<td>Per EMI</td>
<td>4.8</td>
<td>n/a</td>
</tr>
<tr>
<td>Complaint File and Corrective and Preventive Measures</td>
<td>n/a</td>
<td>7</td>
<td>27, 28, and 29</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Purchasing</td>
<td>n/a</td>
<td>6</td>
<td>26</td>
</tr>
<tr>
<td>QUALITY AUDIT</td>
<td>Bimonthly</td>
<td>4.8 and 9</td>
<td>30</td>
</tr>
<tr>
<td>MANAGEMENT REVIEW</td>
<td>1 / Month</td>
<td>4.8 and 10</td>
<td>31</td>
</tr>
<tr>
<td><strong>ACTIONS</strong></td>
<td>As Needed</td>
<td>4.8 and 10</td>
<td>31</td>
</tr>
</tbody>
</table>

5. **Device Master Record**

Soteria Medical, LLC shall maintain Device Master Records (DMRs) prepared and approved in accordance with 820.40. The DMR for the **Soteria Cardiac Platform** is described in detail below.

5.1. **Device Specifications**

Device specifications include appropriate drawings, composition, formulation, component specifications, firmware specifications, and software specifications.
5.1.1. Basic Specifications

The *Soteria Cardiac Platform* employs hardware, firmware, and software in a combined effort to make measurements, perform analyses, and present clinical reports for five Modules. At the macro level the Platform: (i) performs digital calculations and stores data from digit input, (ii) performs reporting from pure digit input without measurement information (all Modules), (iii) performs reporting from measurement data which requires Blood Pressure measurements obtained by a NIBP System. The NIBP System functions specifically within the limits of FDA SP-10. Essentially, in most settings the error cannot exceed 3 mmHg (mean pressure), and (iv) performs reporting from measurement data which requires $\Delta$ volume measurements. Soteria Medical, LLC requires an error level for $\Delta$ volume not to exceed +/- 5% when compared to the “gold standard” which is the Soteria Calibration Device, designed specifically for this application and described under Design Verification and Production Process.

The Firmware Specifications and Testing are further addressed under Design Verification and Production Process. This is also the case for Software which is written in C Sharp using the .net Format.

5.1.2. Technical Memos

During the course of designing the *Soteria Cardiac Platform*, Technical Memos were prepared by Dr. Raines and distributed to the interested parties. A total of 29 of those Technical Memos have been raised to the level of significantly supporting specifications and are included in this section (Appendix 16). It should be noted that the information contained in these memos are covered in other areas of the DMR.

5.1.3. Bill of Materials (BOM)

Soteria Medical, LLC throughout the entire design phase has maintained an accurate BOM. This BOM lists every component used in the design (and now required for manufacturing) of the *Soteria Cardiac Platform*. Also included in this detailed tabulation are complete component specification, number of components used per unit, supplier/with contacts, component cost, and special notes, when indicated (Appendix 17).

5.1.4. Soteria Diagnostic Cart (SDC) Specifications and Drawings

The SDC is manufactured by Precision Metal Industries (PMI) to design specifications created by Soteria Medical, LLC. The design process was computer-assisted which produced illustrations, interference notes, design analysis, and engineering drawings. These files are very helpful in the manufacturing process. The SDC engineering drawings and specifications are found in Appendix 18.
5.1.5. Machined Parts Specifications and Drawings

The PMI Machine Shop also provides the following machined parts for each SDC: (i) PEP Plate, (ii) Pump Holder, (iii) Linear Actuator Holder, (iv) Linear Actuator to Piston Holder, and (v) SHIM Standoffs. The Machined Parts engineering drawings and specifications are found in Appendix 19.

5.1.6. Firmware Gerber Files

The PEP requires a Software / Hardware Interface Module (SHIM). This is a PCB which was designed by Soteria Medical, LLC Firmware Engineer Matt Kahn. The SHIM is a form of firmware and is used to control all hardware components on the PEP (Pump, NIBP, Linear Actuator, and Exhaust Valve). As suggested by its name, the SHIM interfaces with the CPU via a USB Cable and therefore receives real-time instructions from the Soteria Proprietary Software designed by Soteria Medical, LLC Software Engineer Artiom Bell. The Gerber Files are computer files that list all the SHIM Components and provide specifications and locations for PCB manufacturers. Gerber Files allow the PCB manufacturing to be transported. The Soteria SHIM Description is found in Appendix 20; the Gerber Files are safely stored at Soteria Medical, LLC and may be accessed on specific request.

5.1.7. Software Description and Code

The Soteria Cardiac Platform CPU is a Hewlett-Packard (HP) Pavilion 20 All-in-One System. This system includes a semi-robust processor which is powerful enough to meet the requirements of the Platform. HP has proven to be an excellent supplier for Soteria Medical, LLC. Upgrades occur approximately every 90 days. CPU replacement by HP is both local and excellent in response. A description of the Soteria Proprietary Software and a Software Hazard Analysis are given in Appendix 21. The complete Code is safely stored at Soteria Medical, LLC and may be accessed on specific request. The Code is written in C Sharp in the .net Format.

5.2. Production Process

Production process specifications include the appropriate equipment specifications, production methods, production procedures, and production environment specifications.

5.2.1. Assembly Instructions

Dr. Raines and the Soteria Medical, LLC Staff have taken their final design and fully constructed 10 PEPs, ordered and received 10 Soteria Diagnostic Carts, and married the PEPs and the Carts to create 10 operational Soteria Cardiac Platforms. The resulting Platforms were calibrated with the Soteria Calibration Device. This experience allowed Soteria Medical, LLC to generate a detailed 60-Step Assemble Instruction for the PEP and PEP insertion into the Cart.
5.2.2. Final Calibration

EMI will perform all manufacturing tasks with the exception of the Final Calibration; that task will be retained by Soteria Medical, LLC. For this task a comprehensive calibration will be undertaken for each completed Platform using the Soteria Calibration Device. The calibration adjustments (ADJ) are linear: ADJ = m * x + b where m is the adjustment slope and b is the y-axis offset (intercept). Final Calibration will involve minor software adjustments. The Final Calibration Protocol is found in Appendix 23.

5.2.3. Inventory Control

Before Soteria Medical, LLC decided to transfer manufacturing and manufacturing controls to Endeavor Manufacturing, Inc. (EMI), Soteria Medical, LLC created the following documents for control purposes: (i) BOM, (ii) Inventory Control Document (ICD), (iii) Unit History Document (UHD), and (iv) Bar Code Labeling. EMI also has an Inventory Control Process and Document. From the Soteria Medical, LLC we will follow Inventory Control Procedures and carefully monitor a tabulation that followed the BOM and list number of components in inventory available for manufacturing. This inventory will be updated on a monthly basis. Appendix 24 includes the Soteria Medical, LLC Inventory Control Procedures and Tabulation that will be used going forward.
5.2.4. Device History Record (DHR)

The DHR is intended to document the components, manufacturing, and distribution histories (provided to EMI by Soteria Medical, LLC) for each Soteria Cardiac Platform. Appendix 25 includes the Soteria Device History Record that will be used exclusively going forward.

5.3. Quality Assurance

Quality assurance procedures and specifications include acceptance criteria and the quality assurance equipment to be used.

5.3.1. Soteria Calibration Device

To support both manufacturing and quality assurance, Soteria Medical, LLC designed a very robust Soteria Calibration Device. This device is a computer-controlled system and is able to produce extremely accurate and reproducible system volume changes. These volume changes simulate exactly the volume changes experienced by the Soterogram module in the Soteria Cardiac Platform. To accurately simulate the clinical situation, the Soteria Calibration Device can produce a range of measured volume changes as a function of: (i) cuff size (calf or thigh) and (ii) system mean pressure, and subject heart rate. This device and the associated calibration protocols have been used to determine the accuracy of the Soterogram in measuring Δ volume and will be used in final calibration for each manufactured Platform.
5.4. Packaging and Labeling

5.4.1. Packaging

Soteria Medical, LLC has contacted several medical device manufacturers regarding the methods they use for packaging and shipping their devices. Firms that had cart-like instruments were targeted. The information obtained had a common theme. First, prior to a few years ago, these firms designed elaborate enclosures for their devices. These enclosures ranged from full enclosures with custom dimensions formed with polymer material that required return to the originating firm to custom wood pallets with custom wood or cardboard enclosures which were disposable. Second, the majority of firms that we contacted have recently changed their packaging protocols. These changes have been primarily driven by the more frequent use of vinyl wrapping and improved shipping protocols by carriers (USPS, UPS, FedEx, etc.). Simply stated the device enclosures have become less difficult to construct and less costly and have not resulted in increased shipping damage (picture).

With the above as background, Soteria Medical, LLC will package the Soteria Cardiac Platform using the following protocol:

- The complete Platform (Weight < 100 lbs) will be shipped together (i.e. single shipment, one unit).
- The CPU/Monitor will be in a separate padded box measuring 24” x 18” x 6”.
- The Keyboard will be shipped in its OEM packaging which measures 15” x 6” x 2”.
- The Soteria Cuff Set and Power Cord will be in a separate box measuring 16” x 8” x 3”.

[Image of a medical device]
> All other components of the Platform will be attached prior to shipping.

> The Keyboard and Soteria Cuff Set/Power Cord boxes will be shipped in the Client Storage Compartment of the Platform.

> The CPU/Monitor boxes will be strapped to the Platform Desktop for shipping.

> Four (4) corner cushions will be place on the coroners of the Platform Desktop.

> 12” Vinyl wrapping will applied from the Platform’s Lower Stalk, around the Central Compartments, to the Upper Stalk. This will firmly hold the CPU/Monitor Box which will be placed flat on the desktop surface.

> The wheels of the Platform will not be covered or locked on recommendation of our shippers.

> A detailed Packing Slip in an envelope will be securely taped to the Unit.

5.4.2. Labeling

Soteria Medical, LLC views Labeling as an integral part of quality control, business activity, and specifically tracking. For Labeling the firm has relied heavily and invested in Bar Code Technology (picture[s]).

Our Labeling Protocol starts with the generation of the Label itself. On each label the following information is inserted:

(i) Soteria Product (i.e. Soteria Cardiac Platform)

(ii) Product Component (i.e. PEP)

(iii) Bar Code representing the Serial Number of the Product

(iv) Serial Number

(v) Soteria Medical, LLC Website (www.soterogram.com)

(vi) Current Telephone Number for Soteria Medical, LLC

The Serial Number is defined by a series of four numbers:

> Year Manufactured (i.e. 2013 = 13)

> Month Manufactured (i.e. February = 02)

> Version (i.e. Version 1 = 001)

> Unit Manufactured within Version (7th Unit = 0007)
For the Soteria Cardiac Platform, labels will be attached to the following components:

(i) Soteria Diagnostic Cart (Back Surface of the Left Door of the Client Storage and the Back Surface of the Left Door of the Electronic Storage).

(ii) Pneumoelectric Package (Top Surface of Plate near the Manifold)

(iii) CPU / Monitor (Back Surface near Electrical Inputs)

(iv) CPU / Monitor Box (Top Surface – Upper Left-Hand Corner)

(v) Cuff Set / Power Cord Box (Top Surface – Upper Left Hand Corner)

When any Soteria Bar Code is scanned and entered into a Soteria Medical, LLC Computer the detailed Unit History Document (UHD) is displayed. The UHD is designed to contain all the information necessary to completely identify the unit, the history of the unit, and its location.
5.5. Installation, Maintenance, and Servicing

5.5.1. Installation

Soteria Medical, LLC will assume the responsibility of arranging for placement and Installation of all Soteria Cardiac Platforms. This process involves the following components: (i) before installation can take place a Contract between Soteria Medical, LLC and the Client (Hospital, Clinic, or Physician Office) must be executed between the parties. This document clearly describes the responsibilities of both parties, (ii) an Installation Date must be scheduled. Soteria Medical, LLC Staff will travel to each Client, (iii) the Soteria Cardiac Platform must be received in advance of the Installation Date, (iv) on the Installation Date, the Soteria Medical, LLC Staff will assemble and test the Soteria Cardiac Platform, this includes Software Installation and Soteria Server connection, (v) following successful assembly and testing of the Platform, a Soteria Medical, LLC Staff Member will present a PowerPoint Presentation which has been designed to provide clinical background associated with Platform measurements, patient presentations, and operating instructions for the Platform. This presentation will be open to all interested parties within the Client Office, and (vi) a minimum of 3 hours will be spent with the local Operator or Operators of the Platform. It is suggested that subjects for testing be selected by the Client Office and available for noninvasive testing.

The Operational Model for this testing requires that noninvasive clinical measurements be obtained locally. The measurement data is sent to the Soteria Central Server. The Soteria Professional Medical Association prepares a report. This report is sent back to the Client via the Soteria Server. Locally the report is again reviewed by a Physician and the results shared with the patient. This Operational Model allows for very careful monitoring of local activities and high quality assurance for each report.

If a Client or Operator within a Client Office is not performing well this will be obvious to Soteria Medical, LLC. Further, the Soteria Proprietary Software allows interactive monitoring between the local Operator and the Soteria Engineers and Physicians. This Installation and Monitoring Protocol has worked very well during the Platform Design Phase.

5.5.2. Maintenance

One-hundred percent of the local data, as well as, Platform performance are monitored centrally by Soteria Medical, LLC. Further, Soteria Software and Firmware Engineers can literally take control of a local Platform over the Internet. This means that maintenance can take place remotely in the vast majority of cases. When servicing is required, this will be accomplished by a full-time Soteria Medical, LLC Staff Member or a Local Contractor (described in the next section).

5.5.3. Servicing
Despite the fact that the *Soteria Cardiac Platform* has robust hardware, firmware, and software with remote monitoring and control, it is anticipated that circumstances will develop that require Client servicing.

The Platform electronics are located in a compartment that cannot be accessed by the Client. The Platform enjoys a modular design, along the lines of modern automobiles. The CPU and Monitor is one unit and may be removed with four proprietary screws. The locked Pneumoelectric Package (PEP) which houses all the electrical components and sensitive moving parts except the Battery, Charger, and Elevation System may be removed after access to the compartment with three screws. This means that the CPU / Monitor and the PEP which are believed to evoke the majority of servicing may be rapidly and easily exchanged. Soteria Medical, LLC believes this will lead to minimal Platform downtime and less complex Local Servicing. Soteria Medical, LLC is developing a network of local medical device service companies in the United States to assist in local servicing.

6. **Purchasing Controls**

The FDA 820 Regulation states that manufacturers shall establish and maintain procedures to ensure that all purchased or otherwise received product and services conform to specified requirements. Up to the point of Master Device File completion with manufacturing specification and manufacturing transfer, Soteria Medical, LLC has selected all consultants, suppliers and contractors. To this point these selections were made using the following criteria:

- Recommendations from respected sources for consultants, suppliers, and contractors.
- Direct previous experience with consultants, suppliers, and contractors.
- Direct current experience with consultants, suppliers, and contractors.
- Printed component specifications provided by suppliers.
- Component testing performed by Soteria Medical, LLC of units provided by suppliers.
- In the early stages of the design product application and performance were the major issues regarding selection. As the design matured, cost became slightly more involved in the selection process.

EMI from this point will be responsible for all manufacturing-related purchasing. EMI has in-place Purchasing Controls which they have derived from their medical device manufacturing experience. These controls include a Purchasing Control Procedure and Supplier Correction Request; this procedure and form will be active for this project and are given in Appendix 26.

7. **Complaint Files**
At this point in time the design and transfer to manufacturing is taking place. *Soteria Cardiac Platform* sales or placements have not occurred. Alpha and Beta Testing is considered part of design, therefore, there has been no potential for client (hospitals, clinics, and physician offices) complaints. With Platform distribution this will change immediately. Looking at the broad picture in terms of Soteria Medical, LLC operations, complaints may come from four sources (foci):

(i) general business operations,

(ii) manufacturing issues,

(iii) performance issues (including service), and

(iv) technology / medical issues.

Soteria Medical, LLC will manage the general business operations and technology/medical issues. The Soteria Complaint File, which includes both the Soteria Complaint Procedure and associated Form are described in *Appendix 27*.

EMI will have the responsibility of managing manufacturing, performance, and service issues. EMI has in-place procedures, protocols, and forms which they have derived from their medical device manufacturing experience. These controls which include post-production feedback and a customer satisfaction survey are EMI procedures and forms and will be active for this project. They are included in *Appendix 28* for completeness.

8. **Corrective and Preventive Measures**

At this point in time the design and transfer to manufacturing is taking place. *Soteria Cardiac Platform* sales or placements have not occurred. Alpha and Beta Testing is considered part of design, therefore, there has been no potential for client (hospitals, clinics, and physician offices) corrective and preventive actions. With Platform distribution this will change immediately. Looking at the broad picture in terms of Soteria Medical, LLC operations, corrective and preventive actions may come from four sources: (i) general business operations, (ii) manufacturing issues, (iii) performance issues (including service), and (iv) technology/medical issues. Soteria Medical, LLC will manage the general business operations and technology/medical issues. Soteria Medical Corrective and Preventive Measures (Procedures and Forms) are described in *Appendix 29*.

9. **Quality Audits**
Soteria Medical, LLC acknowledges its clear responsibility to conduct quality audits involving all aspects of its business. This ranges from design to design changes, to manufacturing to client services and complaints. At the moment we are a small firm, but expect to grow. For now we will conduct Quality Audits every other month (i.e. bimonthly). The Soteria Medical, LLC Quality Audit Procedures and Form are given in Appendix 30. Written Minutes from the Quality Audit Meetings (including Audit Form) will be forwarded to the Management Review Committee for final approval and ACTIONS (see Sections 4.8 and 10).

Soteria Medical, LLC has partnered with Endeavor Manufacturing, Inc. (EMI). In this arrangement EMI will serve as the contract manufacturer and therefore manage all manufacturing and monitoring of manufactured product. EMI has in-place procedures, protocols, and forms which they have derived from their medical device manufacturing experience.

10. Management Review

Soteria Medical, LLC acknowledges its responsibility to conduct and participate in careful review in the areas of Design, Quality (including Manufacturing) and Management. Committees, meetings, procedures and forms for these activities are in-place and are outlined in Sections 4.8, 9, and 10 of this document and associated appendices.

Soteria Medical, LLC acknowledges that management with executive responsibility shall review the suitability and effectiveness of the quality system at defined intervals and with sufficient frequency according to established procedures to ensure that the quality system is satisfied and effective. For 2014 Management Review Meetings will take place monthly. Written Reports and Recommendations from Design Review Meetings and Quality Audit Meetings will be referred to Management Review for FINAL approval, implementation, and follow-up.

Soteria Medical, LLC manages at least twenty suppliers, two engineering consultants (firmware and software), two legal consultants (general and medical), one accounting consultant, two major contractors (cart manufacturing and contract medical device manufacturing), medical billing company, national server host (Verizon) and a medical physician professional association. While the Soteria Medical, LLC Staff will increase after Launch, currently the full-time internal staff consists of Dr. Jeffrey K. Raines (President and CEO) and Gloria E. Raines (Office Manager and Technician).

The following chart provides via required transactions a prospective of the management activities and stakeholders in Soteria Medical, LLC once Launch activities begin. It should be understood that for the first 6 months of operation only 20 Clients will be selected to participate; over the following 6 months an additional 20 Clients will be added, for a total of 40 Clients. Soteria Medical, LLC believes this modest Launch will give the opportunity to learn all interactions and the ability to concentrate on quality and increasing efficiency.
For the next 8 months of operations (May 2014 through December 2014) Monthly Management Reviews will be chaired by Dr. Raines. All involved Staff, Consultants, and Contractors will participate. For each meeting, Minutes will be prepared and distributed for accuracy and correction. Management Changes will be made as needed and documented using the procedures and form found in Appendix 31. Dr. Raines will approve the Minutes and Management Review mandates going forward. Dr. Raines will be reviewed by the Office Manager, Senior Consultants, and EMI. Beginning January 2015, less frequent Management Reviews are anticipated.

Respectively submitted:

Jeffrey K. Raines

May 12, 2014
1. Curriculum Vitae – Dr. Jeffrey K. Raines
   - Printout
   - Electronic File

2. Bibliography and References – Soteria Medical, LLC
   - Printout
   - Main Text
   - Electronic File
   - File and Folder

   - Printout
   - Electronic File

4. FDA K011625 – Premarket Notification and Indication for Use Statement (Reg: 2014)
   - Printout
   - Electronic File

5. *Arterial Compliance to Stratify Cardiovascular Risk: More Precision in Therapeutic Decision Making* – American Journal of Hypertension
   - Printout
   - Electronic File

6. Statement of Work (SOW) – Example
   - Printout
   - Electronic File

7. ABIgram – SP-10 Publication
<table>
<thead>
<tr>
<th>Printout</th>
<th>Electronic File</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

8. Functional Flow Diagram (v1.9) – Soteria Cardiac Platform

<table>
<thead>
<tr>
<th>Printout</th>
<th>Electronic File</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

9. Design Verification – Alpha Protocol and Case Report Forms

<table>
<thead>
<tr>
<th>Printout</th>
<th>Electronic File - ONLY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

10. Design Verification and Validation – Assorted Calibration Studies

<table>
<thead>
<tr>
<th>Printout</th>
<th>Electronic Folder - ONLY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

11. Design Validation – Beta Protocol and Case Report Forms

<table>
<thead>
<tr>
<th>Printout</th>
<th>Electronic File - ONLY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

12. Precision Metal Industries (PMI) – Contract with Soteria Medical, LLC

<table>
<thead>
<tr>
<th>Printout</th>
<th>Electronic File</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

13. Endeavor Manufacturing, Inc. (EMI) – Contract with Soteria Medical, LLC
<table>
<thead>
<tr>
<th></th>
<th>Printout</th>
<th>Electronic File</th>
</tr>
</thead>
<tbody>
<tr>
<td>14.</td>
<td>Endeavor Manufacturing, Inc. (EMI) – Manufacturing Transfer Protocol</td>
<td></td>
</tr>
<tr>
<td>15.</td>
<td>Procedures and Form – Design Changes / Design Review) – Soteria Medical, LLC</td>
<td></td>
</tr>
<tr>
<td>16.</td>
<td>Technical Memos – DMR</td>
<td></td>
</tr>
<tr>
<td>17.</td>
<td>Bill of Materials (BOM)</td>
<td></td>
</tr>
<tr>
<td>18.</td>
<td>Soteria Diagnostic Cart (SDC) – Specifications and Drawings</td>
<td></td>
</tr>
<tr>
<td>19.</td>
<td>Machined Parts – Specifications and Drawings</td>
<td></td>
</tr>
</tbody>
</table>
20. Description of Software / Hardware Interface Module (SHIM)

21. Soteria Software Description

22. Assembly Instructions

23. Final Calibration Protocol and Form – Soteria Medical, LLC

24. Procedures and Form – Inventory Control – Soteria Medical, LLC

25. Form – Device History Record (DHR) - Soteria Medical, LLC

26. Procedures and Form – Purchasing Controls – Soteria Medical, LLC
27. Form – Complaint File – Soteria Medical, LLC

28. Procedures and Form – Complaint File – EMI

29. Procedures and Form – Corrective and Preventive Actions – Soteria Medical, LLC

30. Procedures and Form – Quality Audit – Soteria Medical, LLC

31. Form – Management Review – Soteria Medical, LLC