Project Plan
for the

Patient-Initiated Emergency Response System (PIERS) Phase II

A Phase I Report of the NATIONAL HEART ATTACK ALERT PROGRAM

Reference # NLM 00-NHAAP/VMS

by
Johns Hopkins Medical Institutions
and the
Johns Hopkins University Applied Physics Laboratory

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1 BACKGROUND

This document describes the detailed project plan for Phase II development of the Patient Initiated Emergency Response System (PIERS), including the project development tasks/ activities, deliverables, schedule, cost, and any standards or guidelines to be used in the development.

Phase I of the project has produced preliminary medical requirements (Reference 1), system requirements (Reference 2), a preliminary system design (Appendix B to Reference 2), and a project plan for Phase II (this document). Phase II will include the following project activities:

1. Project and Inter-organization Coordination
2. Refinement of Medical and System Requirements
3. Define EMS Interactions
4. Refinement of System Top-Level Design
5. Detailed System Design
6. Development of Prototype Modules (System Components)
7. System Integration
8. System Demonstration
9. System Evaluation
10. System Documentation & Web Site
11. Preliminary Clinical Evaluation
12. Plan and Training for Clinical Trials
13. Plan for FDA Approval Process
14. Plan for System Production and Marketing

The last three are preparation for Phase III activities. Phase II activities include interaction with potential producer(s) of the system or components of the system. Selected modules, as appropriate, will be developed by adaptation of existing commercial products.

While system interactions with potential EMS agencies will initially focus on deployment in the Maryland State system, the design will be adaptable to systems and procedures of other states (and countries). (See section 2.2)

1.1 Project Overview

The major hardware/software components of the system, as depicted in Figure 2-1, are:

- Patient's Personal Module including an ECG element and a Data Management element
- System Server
- Client Modules for each interacting user of the system

These hardware and software components are used to achieve the following functionality:

- Rapid and transparent communication of data between participating elements of the system
- In-home ECG measurements and patient history retrieval
- Patient awareness, training and acceptance of system
- Tight coupling of personal physicians to system/process
- Support for interpretation of cardiac status
- Integration with Emergency Medical Services
- Common information between all participating medical personnel
- System/data operability and reliability diagnoses

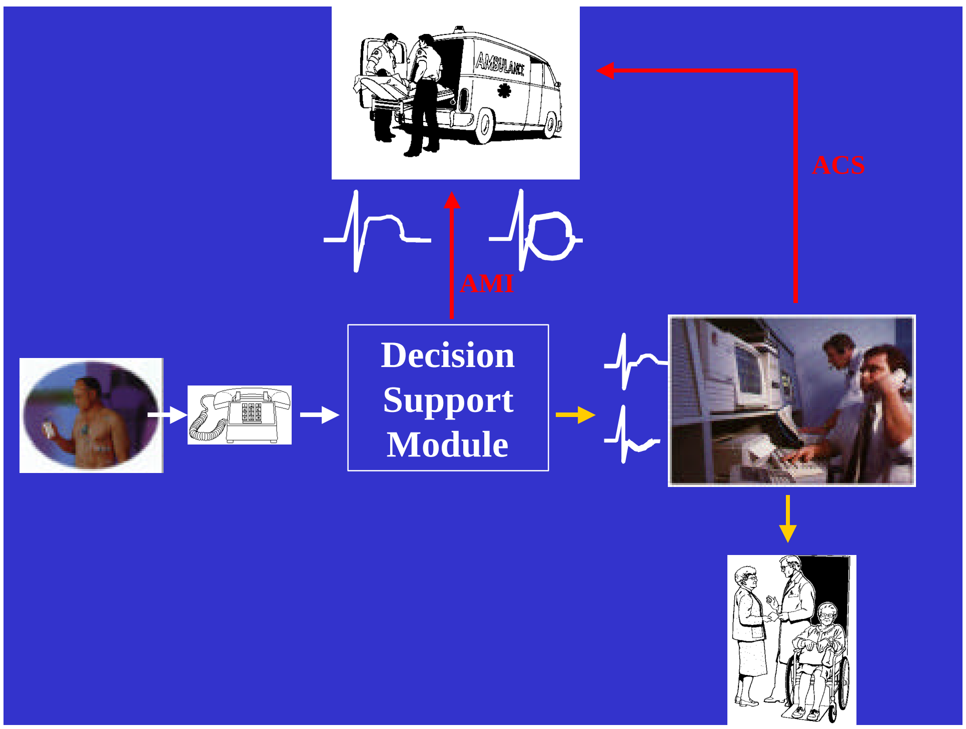


Figure 1-1
PIERS Concept

2. PROJECT TASKS/ACTIVITIES

This section describes each of the tasks planned for Phase II. A summary outline of all tasks including the approximate development time relationships is provided in a Gantt chart in Section 3 (Figure 3-1).

2.1 Refinement of Medical and System Requirements

The Phase I effort generated preliminary medical requirements and system requirements for each of the system modules. In Phase II the Medical and System Requirements Documents will be refined and updated through the life of the Phase II development effort. It will define the functional and performance requirements to be met by each of the system modules and the integrated system as developed through the requirements analysis process. As appropriate, these requirements have been and will be used as the basis for discussion with potential commercial manufacturers.

The requirements generated during Phase I are the result of a conceptual design and design feasibility study. These studies were performed, in part, by the application of a process modeling tool developed with the EXTEND simulation product (see Reference 2, Appendix D). The requirements establish the baseline performance of the *system* and enable the dramatic reduction in time between onset of chest pain and entering an ED. In Phase II these requirements will be refined based on detailed definition of protocols and procedures as well as the detailed design. The systems requirements analysis will translate and update any additional Phase II developed refinements of the medical requirements into requirements for the functionality and performance of the appropriate sub-system. Also, requirements on design variables such as data content and accuracy, data collection and processing speeds, connectivity to processes outside the system, data storage and archiving, user interaction, possible decision outcomes and others will be identified. Once refinements to the requirements have been defined and documented, a refinement of the system top-level design will be performed.

While system interactions with potential EMS agencies will initially focus on deployment in the Maryland State system, the design will be adaptable to systems and procedures of other states (and countries). We will survey the policies of several other states to determine the range of capabilities necessary to accommodate the needs and protocols of these states. The system requirements will then be adjusted to best provide for these needs. Where feasible, system options will be built into the system to implement the various state needs. For other system variants, adaptation will be accomplished by replaceable modules.

JHU/APL programs are assigned one of four quality assurance levels [ref x] depending upon the consequence of failures of the system. Where Level 1 invokes the most stringent QA process, the PIERS development will be conducted at Level 2. Level 2 provides for formal and strict configuration management while permitting the flexibility necessary for a prototype development.

2.2 Refinement of System Top-Level Design

The System Top-Level Design (Ref.erence 2, App. B) describes the system architecture (top level design) and design goals/constraints. Requirements are established for processing timelines, user features and input signal-conditioning requirements. Development risks and mitigation for future phases are identified. The system architecture addresses implementation of ECG acquisition and processing, historical data acquisition, decision support and user interaction, data transmission, and integration with legacy systems.

To reduce the risk in accomplishing the project aims and reduce the cost, the Johns Hopkins University plan for the development will leverage off of existing components, algorithms, tools, commercial communication capabilities, existing Emergency Medical Services (EMS) communications, and existing protocols for interacting with physicians in an Emergency Department (ED) or chest pain center to the maximum extent possible. Phase II will review the top-level design and identify commercial products that can be used. In particular, we plan to leverage commercial communication capabilities, existing EMS communications, and existing protocols for interacting with physicians in an ED or chest pain center. Hardware and software for ECG acquisition, processing and decision support will be adapted from one of the existing commercial products. The approach to software development is to use commercially available equipment and software wherever possible. For example, the System Server, the Client Modules (i.e., Cardiac Consultants Module, EMS Module, Emergency Department module, and Referring Physician's module) will each be implemented on commercial PC's and NT operating system. The design will be approached as generically as practical to permit the option of extending the eventual device to other medical applications.

The System Requirements Document includes any design requirements or constraints necessary to achieve system goals. The top-level design provides key parameters of each of the following system modules:

- Patient's Personal Module
- System Server
- Cardiac Teleconsultant's Module
- EMS Module
- Emergency Department Module
- Referring Physician's Module
- Service Provider Module

The detailed design for each module will be documented in a Detailed Design Document. For each of these modules, JHU will generate a functional description, inputs-outputs, communications requirements, preliminary human-computer interface designs, the design of the application module, and software language and processor requirements. This task will also include identification of commercial software suitable for this application and the provisions for incorporation of selected software.

2.3 Project and Inter-organization Coordination

The project Principal Investigator, a cardiologist at the Johns Hopkins Hospital, will provide overall project coordination, medical requirements oversight, coordination with state EMS agencies, and coordination of clinical evaluations. Engineering coordination, including system design, system prototype development, and system integration and testing, will be provided by a senior engineer at The Applied Physics Laboratory (APL). Individual components, such as the ECG element, may be coordinated within the companies providing the component.

Throughout Phase I and continuing in Phase II will be close interaction with representatives of the Maryland Emergency Medical Systems (MEMS) agency to assure that concepts and system design are compatible with typical current policies and procedures. While system interactions with potential EMS agencies will initially focus on deployment in the Maryland State system, the design will be adaptable to systems and procedures of other states (and countries). We will survey the policies and procedures of several other states to determine the range of capabilities necessary to accommodate the needs and protocols of these states. The system requirements will then be adjusted to best provide for these needs. All products of the Phase I activity have been reviewed by MEMS representatives.

Also integral to the Phase I, and continuing in Phase II, is the coordination with Dr. Raymond Bahr, Director of the Chest Pain Center at St. Agnes Hospital. Dr. Bahr brings invaluable insight to the project by virtue of his daily involvement with emergency diagnosis and treatment of chest pain.

For Phase II, we propose a major collaborative role for General Electric Medical Systems (GEMS). GEMS has a long history of successful collaboration with the Johns Hopkins Medical Institution (JHMI), particularly with the JHMI Division of Cardiology. GEMS, through the merger with Marquette, has world-renowned reputation for effective ECG interpretation algorithms. JHMI cardiologists are intimately familiar with the strengths (and limitations) of the Marquette algorithm. Therefore, the JHMI/GEMS team is ideally suited to application of the ECG interpretation technology for the [name] system. Furthermore, GEMS engineering and manufacturing resources bring the capability to produce and market the system worldwide.

JHMI has established agreements with GEMS regarding intellectual property and potential production of collaboratively developed systems. The Johns Hopkins University (JHU) and General Electric have initiated discussions with the goal of adapting an existing agreement related to GE's MRI product to this project.

While GEMS potentially provides a source for the ECG portion of the system, as a risk mitigation step, we have identified alternate commercial sources for elements of the Patient's Personal Module. Meridian and Montara Corporation both market portable 12-lead ECG devices and are possible alternate sources for the ECG device.

2.4 Detailed System Design

2.4.1 Patient's Personal Module

The Patient's Personal Module includes the ECG Element and a Data Management Element including memory to hold patient's relevant medical data and past ECGs, a patient entry and display interface, and the interface to the communications service. A telephone will also be integrated to provide an additional modality of system interaction.

<u>ECG Element</u>

Tasks for design of the ECG element include:

1. Select and coordinate with ECG Vendor
2. Adapt Existing ECG design and controls

3. ECG Waveform Storage
4. Adapt Electrode design (if necessary)

We expect that GEMS will provide the primary source for the ECG element of the system. The GEMS ECG device has been designed for digital interfacing and can be re-packaged into the PPM. GEMS has also developed an easy to use single piece electrode patch which is appropriate for PIERS use.

As a risk mitigation step, as described in Section 2.3, we will also seek an alternate commercial source for the ECG element of the Patient's Personal Module.

Data Management Element

Tasks within the Data Management Element include design of:

1. Communications protocol including:
    a. Protocol for transmitting ECG data to Communications Service (CS)
    b. Protocol for receiving questions/information from CS
    c. Data comms to/from CS
    d. Link to ECG element
2. Telecommunications interface
3. User controls

The collection and storage of historical data will be done in accordance with privacy standards. Patient's Personal Module and the patient's Referring Physician's Module are the only two places that patient data is stored. The content of the data collected will satisfy the medical requirements identified in the medical requirements document.

PPM Hardware Design

The PPM will be designed for portability and ease of use. The hardware design will integrate the ECG and Data Management elements into a pocket sized package. The approach to hardware design and development will emphasize the use of computer-aided design tools for circuit schematics, board layout and packaging design, to assure efficient transition to a commercial producer. Prior to final board design and fabrication a breadboard will be fabricated and tested.

The PPM design and fabrication will be performed in a manner that permits rapid, inexpensive fabrication of multiple PPMs. In Phase II, fabrication of 10 modules is planned. The PIERS would be developed in cooperation with General Electric Medical Systems. By maintaining close collaboration with GEMS, we expect that the PIERS design will be appropriate with minimal, if any, change for production of the system, including the Patient's Personal Module.

The PPM hardware design tasks are:

1. Electrical Interface requirements
2. Circuit schematics
3. Breadboard fabricate & test
4. Board layout
5. Packaging design
6. Packaging detail layout
7. Design review
8. Power circuit
9. Packaging – including ECG element

2.4.2 System Server

The requirements for the system server identified in the Requirements Document focus on controlling the flow of and validating the integrity of information.

Tasks related to the System Server include design of:

1. Interface to Communications Service
2. Interface to Client Modules
3. Workstation (Server & clients) configuration/design

2.4.3 Client Modules

In this context, "client modules" include the hardware and software to support all system users (except the patient):

- Cardiac Consultants Module
- EMS Module
- Emergency Department Module
- Referring Physician's Module
- Service Provider Module

Tasks for design of client modules are in some cases common to two or more client modules. Tasks include design of the following:

1. Receive & format data
2. ECG interpretation
3. ECG plot & data display
4. Cardiac Teleconsultant's controls & displays
5. EMS controls & displays
6. Emergency Department controls & displays
7. Prescribing Physician controls & displays
8. Service Provider controls & displays
9. EMS alertment
10. Communications operability check
11. Voice link & controls

The domain knowledge required to implement this decision support system already exists and has been demonstrated in other decision support systems. Sources of this knowledge include existing protocols used in emergency rooms and algorithms developed for automated ECG interpretation. The algorithm(s) employed for ECG processing will, to the extent possible, be an accepted industry standard and FDA approved. Software development will make maximum use of available software components and all custom components will be written in a high level language for the Microsoft Windows environment.

APL will perform a detailed design for each of these modules using standard software engineering principles, and knowledge engineering techniques to define human-computer interfaces.

2.5 Development and Integration of Prototype Modules

In Phase II, a prototype PIERS will be developed which includes all necessary data collection, data storage, signal conditioning, data processing, data interfaces, and user features. The patient portable portion of the working model, which will be small and battery powered, will provide a test-bed for testing and, if necessary, refining signal conditioning, data interfaces and user features, as well as testing potential patient and physician acceptability of the proposed device. The system server and client modules will each be hosted on NT-based personal computers. Communications among client modules will be web-based via an Internet Service Provider.

PPM Hardware Development

The PPM design and fabrication will be performed in a manner that permits rapid, inexpensive fabrication of multiple PPMs. In Phase II, fabrication of 10 modules is planned. The following tasks comprise the PPM hardware fabrication:

1. Procure parts
2. Electrodes
3. Board Fabrication
4. First board assembly
5. Package Fabrication
6. Test & Revise first PPM
7. Build 9 additional PPM's
8. Test PPM's

Software Development

APL will perform a detailed design for each of the software modules using standard software engineering principles, and knowledge engineering techniques to define human-computer interfaces. The domain knowledge will be extracted from existing EMS and ED protocols as well as the knowledge embedded in GEMS algorithm for ECG interpretation.

To facilitate implementation of patient data security, System Server and Client software will be primarily implemented with the Java language and related software libraries. PPM software will be implemented using an appropriate software development kit, such as Microsoft eMbedded Visual Tools for Windows CE. Encryption will be implemented using a commercial product (RSA BSAFE SSL-J & Crypto-J 2). A library has been selected for building client displays (KL Group Chart Bytecode). Legacy software and the corresponding language(s) will be used as appropriate to minimize development cost. For example the Home Link system is developed in Visual Basic.

Software modules will be developed using structured rapid prototyping with frequent module demonstrations using a pre-defined set of test data that includes all significant system behaviors. PIERS software integration will be accomplished by adding successive modules, starting with the Patient's Personal Module and System Server, until all client modules have been integrated.

PPM software development tasks include:

1. ECG Waveform Storage
2. ECG Interface Adaptation
3. Data comms to/from CS
4. Link to ECG Element
5. Phone interface
6. User Controls

Client Module software tasks include:

1. Receive & format data
2. ECG interpretation
3. ECG plots & data displays
4. Cardiac Teleconsultant's controls & displays
5. EMS controls & displays
6. Emergency Department controls & displays
7. Prescribing Physician controls & displays
8. Service Provider controls & displays
9. EMS Alertment
10. Comms operability check
11. Voice link & controls

2.6 System Demonstration

Selected scenarios will be defined and implemented to demonstrate the operability of the individual modules as well as the integrated system operating in Modes 1, 2, and 3. As a Mode 3 scenario example: 1) a patient calls with moderate chest pain, 2) an ECG measurement is reported, 3) the server processes the call and notifies the cardiac teleconsultant, 4) the ECG interpretation algorithm analyzes the ECG without a conclusive result, 5) the cardiac teleconsultant diagnoses the ECG as a likely MI and notifies the EMS, 6) relevant medical history data is transferred to the the EMS for relay to the dispatched EMS unit, 7) the patient is advised that the EMS has been dispatched, 8) the selected hospital emergency department is notified and preliminary data is transferred, 9) A record of findings is sent to the referring physician.

2.7 System Test and Evaluation

Specific tests will be designed for data collection, data storage, ECG data processing, ECG signal conditioning, data communication, and user interaction. Initial Phase II testing will verify inter-module communications and user controls and displays. The communications capabilities will be tested using communications simulators and the public telephone system via FCC approved interface devices. Additional engineering evaluation data (e.g., user interaction and communications infrastructure issues) will be collected and evaluated against criteria derived from the System Requirements Document.

System components which require evaluation separately and when integrated into the proposed system are the Patient's Personal Module, the System Server, and the Client Modules.

<u>Patient's Personal Module</u>: The function of the patient-carried component is to store, record and transmit historical and electrocardiographic information. Details of the testing of the individual elements which will make up this device depends upon the actual device selected and the detailed design of any components that may require custom fabrication. Once constructed, initial evaluation will consist of determining the ability of the patient module to store and telephonically transmit historical and electrocardiographic information, and record, store and transmit a patient-obtained ECG. As examples of specific tests:

1. Detailed comparison of ECG's recorded, stored and transmitted by the patient module with ECG's recorded by a technician on a standard electrocardiograph (overall interpretation, and quantification of intervals, T-waves and ST-segments) Comparisons will be made by both an expert physician panel and by a commercially available, automated 12-lead ECG interpretation program (eg. as available from Marquette).
2. Tests of the lead system – ease of use, reproducibility of placement and of recorded ECG's, and durability of training.

<u>Client Modules</u>: The Client Modules will provide data and ECG reports as appropriate to each of the system users and support interaction among users. Known data from the Patient's Personal Module will be presented at each client workstation and verified for accuracy and timeliness. All possible entries from client stations will be tested. Any decision support processing will be validated using actual test cases.

Once basic communications and operability is established, testing will next use pre-stored digitized ECG data associated with baseline pathologies and patient histories. Implemented algorithms will be tested to ensure that the baseline pathologies are accurately characterized by ECG processing. As the Phase II functional prototype matures, simulated ECG signals for the same pathologies will be used. A series of scenarios will be defined and implemented. Quantitative measures will be used to assess results.

The system will include on-line monitoring and data extraction features to support engineering evaluation in Phase II, clinical evaluation in Phase III and future operability tests.

2.8 Plan for Clinical Evaluation

In Phase II, a preliminary clinical evaluation will be conducted on the prototype. Study protocols will be developed which could be used for testing the efficacy of the proposed system in a clinical setting.

Initial real-world testing may involve patients in chest pain emergency rooms or, possibly, to patients being transported to emergency rooms by EMS from within the transport vehicle. Decisions made by the system when applied to these patients would be compared with actual decisions made by the emergency room physicians. An expert panel could resolve differences between system and physician decisions, and this information used to modify the decision support system, if appropriate. This essentially tests the correctness and timeliness of the system-supported triage decisions compared to a standard defined by current practice.

In a second Phase II efficacy study, high-risk patients (eg., those with known atherosclerotic disease) are randomly assigned to receive the device and system provided to them or to receive intensive education regarding seeking care early for symptoms potentially related to ACS. Over a period of a year, outcomes in the two groups could be compared (e.g., frequency of seeking treatment, delay in getting to treatment, death, incidence of myocardial infarction and other outcomes variables such as cost of care).

The appropriate Phase III trial would be an effectiveness clinical trial. For this type of trial, a REACT-type study design could be considered in which paired communities either do or do not use the proposed system (H, I). Alternatively, effectiveness outcomes (e.g. delay in treatment, death, incidence of myocardial infarction, cost of care, etc.) could be measured before and after implementation of the proposed system in one or more communities.

Additional plans for the preliminary clinical evaluation is provided in the Technical Proposal. Tasks associated with the preliminary clinical evaluation are:

1. Plan for Preliminary Clinical Evaluation (Phase II)
2. Nurse training
3. ECG electrode clinical evaluatio
4. ECG acquisition, transmission and training durability evaluationn
5. Interrogation algorithm identification, consultation, subset selection and modification
6. Interrogation algorithm initial clinical testing
7. Minimal PIERS configuration retrospective case simulation testing
8. Prototype PIERS preliminary patient testing

9. Training program development for patients, physicians, Cardiac Teleconsultants
10. Engineering support

2.9 Plan for FDA Approval Process

FDA new devices approval will probably be needed. The project Principal Investigator has discussed the proposed system with several individuals at FDA; opinion regarding what kind of FDA oversight will be required is not unanimous.

We have concluded that it is likely that pre-market approval will be required. Nevertheless, a 510k is not completely ruled out. The ECG technology, including its portability and telephonic transmission, are FDA approved. It could be argued, therefore, that the proposed system is similar to what already exists.

However, there are other elements of this system which suggest it will require pre-market approval. The proposed system will be used in real time, action will be taken upon receipt of the information, the patient population using the system is sick, and a new level of integration is being proposed. *Instead, the proposed system will need to go through pre-market approval.* ??? In terms of timing, FDA will be involved immediately. Donna Bea Tillman, Supervisor, Biomedical Engineering has offered to serve as a contact at FDA for this project and suggested arranging a meeting with representatives from the several FDA-areas that this project involves. Before a clinical trial is performed, FDA an IDE will be required – this requires 30 days for approval after application is made. It is not completely clear whether the proposed system will be eligible for consideration under 510k or whether pre-marked approval (PMA) will be required. It is most likely that PMA will be required. Following completion of the clinical trial and submission of the PMA application to FDA, a period of 6 months is generally required before approval.

2.10 Plan for System Production and Marketing

The PIERS would be developed in cooperation with a medical systems product developer. For Phase II, we propose a major collaborative role for General Electric Medical Systems. (See Section 2.3) By maintaining close collaboration with GEMS, we expect that the PIERS design will be appropriate with minimal, if any, change for production of the system, including the Patient's Personal Module. We propose a task in Phase II, to be conducted by GEMS, to plan for system production and marketing.

2.11 Maintaining Medical Data Privacy

Privacy and confidentiality of study subject will be maintained by blinding all data entered into the study database. All patients will be identified by study number only and data entered into the database by this identification number only.

Since clinical studies are not formalized at this point, it is unclear whether or to what extent patient or physician contact will be required for follow-up during longer-term studies. If such studies are done, however, which require long-term follow-up, a separate database will be kept that associates patient number with patient identifying demographics [name, address, phone number(s) and personal and physician contacts]. Access to this database will be on a "need-to-know" basis only. Such information is required so that study personnel can contact the patient by telephone or mail for follow-up, or to contact the patient's physician. Study personnel needing access to these data will be trained to understand the absolute requirement to protect patient privacy and confidentiality. Data so obtained will be entered into the main study database without any identifying information – i.e. by study number. Access to all databases will be password protected. Passwords will be available only to individuals requiring access to the databases (e.g. PI, study coordinators, data entry personnel). Data will be stored and analyzed on computers and backup storage media kept under lock-and-key at all times.

We recognize that transtelephonic transfer of patient information may be associated with specific problems related to patient privacy, given that data are stored and transmitted to electronic devices. Since the specific details of the proposed system are under development, the specific plans to minimize the potential for breech of patient privacy and confidentiality of medical information cannot be made. However, various encryption schemes would seem to be the simplest way of minimizing the potential problem with "hacked" computer-based information systems.

The computer providing data handling and call support will reside in an authorized medical facility with access only to authorized personnel. Access will be limited by both physical site protection and password protection.

The monitoring device will be provided with two features:

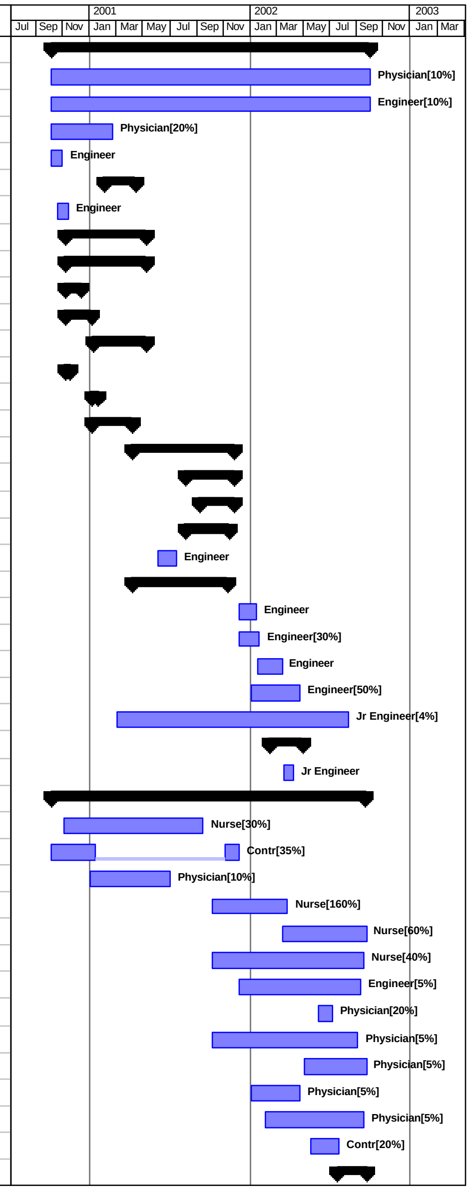
- An option to set up so as not to be associated with identifying information about the patient until added by a physician or medical technician at the data reception site, and
- Use of encryption for any patient identifying information.

We plan to apply to the Institutional Review Board (IRB) immediately after we are awarded this contract. Since initial studies will pose no risk to the patient (since the device will not be used to make medical decisions), we expect that IRB review and approval will take no longer than 30 days**.**

3.0 TASKS AND SCHEDULE

The following table provides a complete listing of planned Phase II tasks and the projected schedule for performing each task. Note, since the staffing level varies among tasks, the length of the schedule bar may not be proportional to staff time involved. For each task, an estimate of staff time has been made, forming the basis for the allocation of personnel proposed for the project.

ID	Task Name
1	**NHAAP Project**
2	**PI (Physician) Oversight and Reviews**
3	**Project/Engineering Coordination & Reviews**
4	**Refinement of Medical Requirements**
5	**Refinement of System Requirements**
6	**Define EMS Interactions**
9	**Refinement of System Top-Level Design**
10	**Detailed System Design**
11	**Patient's Personal Module (PPM)**
12	**ECG Element**
17	**Data Management Element**
21	**PPM Hardware Design**
30	**Communications Service (CS)**
32	**System Server**
36	**Client Modules**
49	**Development of Prototype Modules**
50	**Patient's Personal Module**
51	**Hardware Fabrication & Test**
60	**PPM Software**
67	**System Server Software**
68	**Client Modules Software**
80	**System Integration**
81	**Test Plan & Report**
82	**System Test, Evaluation, and Demonstration**
83	**System Refinement & Upgrades**
84	**Web sites development: (1) Informational and (2) Training**
85	**System Operators Manuals & Help Screens**
90	**System Design Document**
91	**Preliminary Clinical Evaluation (Phase II)**
92	Clinical ECG component & training evaluation
93	Interrogation algorithm identification, subset selection and modification
94	Interrogation algorithm initial clinical testing
95	Case simulation 1600
96	Prototype PIERS testing with ER patients (200)
97	Training program devel. for patients, physicians, Cardiac Teleconsultants
98	Engineering support for testing
99	**Plan for Clinical Trial (Phase III)**
100	**Phase III Clinical Trial Development**
101	**PIERS Cost-Effectiveness Analysis**
102	**Prepare & Submit IRB Documents**
103	**Plan for FDA Approval Process (Phase III)**
104	**Plan for System Production and Marketing**
105	**Project Plan & Proposal for Phase III**



APPENDIX A

REFERENCES

1. Aversano,Thomas, MD, Medical Requirements for the Patient Initiated Early Response System (PIERS), June 30, 2000

2. Aversano,Thomas, MD, System Requirements for the Patient Initiated Emergency Response System, June 30, 2000

3. JHU/APL, The Johns Hopkins University Quality Assurance Plan, April 16, 1990