CMCVAMC SPECIFIC PROTOCOL SUMMARY
Corporal Michael J. Crescenz Department of Veterans Affairs Medical Center (CMCVAMC)
Institutional Review Board (IRB)

A. **Protocol Title**
   1. **Full Protocol Title:** Evaluating Individual and Patient-Selected Family/Friend/or Reciprocal Peer Notifications to Improve Statin Medication Adherence among Patients with Coronary Artery Disease

   2. **Date of Protocol Summary and Version #:** Date 02/04/2016; Version # 6

B. **Principal Investigator's Full Name and Degree:** Judith A. Long, MD

C. **Co-Investigator's Full Name and Degree**: Kevin Volpp, MD, PhD, Judd Kessler, PhD, David Asch MD, MBA, and Steven Marcus PhD

D. **Financial Sponsor** (Provide the name of the agency, organization, company or person providing funds for the research study.) **Center for Evaluation of Patient Care Aligned Teams**

E. **Grant** (Provide the name of individual who holds the grant and the grant number, if applicable.) **N/A**

F. **Protocol Number** (Provide the financial sponsor's protocol number, if applicable.) **Not Applicable**

G. **Institution(s) responsible for the project:**
   1. For single-site studies - CMCVAMC is the only institution involved. Yes ☒ No ☐
   2. For multi-center studies.
      2.1. CMCVAMC is the Coordinating Center in which the PI is the lead investigator. Yes ☐ No ☐ N/A ☐
      2.2. Provide the name of the Coordinating Center. Yes ☐ No ☐ N/A ☐
      2.3. List the name of the other sites involved.
      2.4. Provide the FWA numbers for each of the other sites involved.

THE FOLLOWING INFORMATION MUST BE CMCVAMC-SPECIFIC, THAT IS, SPECIFIC TO WHAT WILL BE DONE WITH CMCVAMC-RECRUITED VETERANS.

H. **Background and Significance** (Describe succinctly and clearly the past findings which justify the plan for this project. A summary of the relevant literature in the area of interest and reports of previous studies should be included.) **Improving patient medication adherence remains a major challenge in chronic disease management. In the United States, 33 to 69 percent of medication-related hospital admissions are due to poor medication adherence – at a cost in excess of $100 billion a year. In fact, one year after hospitalization for an acute coronary syndrome, nearly half of patients prescribed statins stop taking them. [1] Despite the importance of medication adherence, we have few effective tools to help patients improve taking their medications.**

One strategy to improve medication adherence is using newer technology to make engagement with patients significantly easier and more immediate. Devices such as Bluetooth enabled pill bottle caps can remind patients with daily alarms, monitor adherence, and create feedback reports on how well patients are doing in adherence to medications. Another strategy to engage patients is to recruit family, friends, and peers to create a social support networks that activate a patient to taking their medications. However, especially in veteran populations, there are few empirical studies evaluating how best to use these technologies and engage different support providers (family/friends/or peers) to improve medication adherence.

In March 2014, we amended the protocol inclusion criteria expanding eligible patients. The amendment is to expand eligible patients for our study to those with poor adherence as measured by a 16-month medication adherence rate (medication possession ratio - MPR) of less than or equal to 80%. In our original IRB application we identified a population of eligible patients based on an email communication. However, upon review VA chronic disease warehouse we found that our original sample of patients with CAD and 6-month MPR of less than 65% was limited to around 150 patients. In reviewing how the VA has calculated the medication possession ratio in the Primary Care Almanac we found that they use a 16-month period to calculate this adherence rate. In addition, previous literature identifies patients with less than or equal to 80% MPR as non-adherent. To increase our sample size of patients we are changing our protocol to recruit CAD patients with a 16-month MPR of less than or equal to 80% MPR.

I. **Purpose of the Project** (Clearly provide the purpose of this research project.) **In this study, we propose a randomized-control trial among veterans with coronary artery disease (CAD) and poor adherence to statins to test if simple feedback notifications around patient adherence to the individual or family/friends/or reciprocal partner can motivate patients to improved medication adherence**

This study will have three arms: 1. Usual care 2. Alarming pill bottle along with Individual feedback report and 3. Alarming pill bottle along with Individual plus patient-selected family/friend/or reciprocal partner feedback report. Adherence will be measured using a pill bottle medication-monitoring device (Vitality GlowCaps) that can flash and ring to remind people when they should take their medications, monitor adherence as well as help create notifications for different parties. The notification includes a weekly feedback adherence assessment report that will be received by the individual and either a patient-selected family member/friend or reciprocal partner with poor adherence to statin medications.

J. **Describe the Research Questions and Hypothesis**(that is, what questions are you trying to address by conducting the research.**)**

Primary Aim: To evaluate the impact of alarming pill bottles along with adherence feedback on medication adherence.
H1: Those who have alarming pill bottles and are receiving individual feedback alone will have better medication adherence at 3 months compared to usual care.
H2: Those who have alarming pill bottles and are receiving individual plus patient-selected family/friend/or reciprocal peer feedback will have better patient medication adherence at 3 months compared to usual care.

Secondary Aims
Aim 2: To evaluate the impact of alarming pill bottles and adherence feedback on patient activation/engagement.
H3: At 3 months, those receiving individual feedback and patient-selected family/friend/or reciprocal peer will have increased patient activation to a greater extent than usual care.
Aim 3: To evaluate the effect of patient-selected family/friend/or reciprocal peer feedback on improving patient perception of social support.
H4: At 3 months, those receiving family/friend/ or reciprocal peer feedback will improve patient perceived social support to a greater extent than usual care or individual notifications alone.
Exploratory Aims: Compare different feedback methods and persistent of effects.
H5: Those who receive individual with family/friend or individual plus reciprocal peer feedback will have better patient medication adherence compared to individual notifications alone.
H6: At 6 months, those randomized to the feedback intervention arms will have will have better patient medication adherence compared to usual care.

K. **Primary Outcome Variable(s)** (Define the primary outcome variable(s) used to support the study objectives (e.g. if the objective is to show that treatment A is superior to treatment B in the treatment

of subjects with essential hypertension, the primary outcome variable is blood pressure measurement.) **Adherence: Vitality GlowCaps will record when a pill bottle has been opened. While this is an indirect measure of adherence it has less bias than self-reported measures of adherence. Adherence will be measured using the following formula: [Number of times the pill bottle was opened/(Number of times a day each medication is prescribed to be taken multiplied by the total number of days in study)].**

L. **Secondary Outcome Variable(s)** (Define the secondary outcome variables. Such measured variables should also include the timing of measurement.) **Patient Activation Measure Survey: We will utilize the 13-item Patient Activation Measure (PAM) to measure an individual's activation level. This tool has been used in previous studies to predict self-efficacy for health behaviors, such as exercise and medications adherence. Response categories for each item are strongly agree, agree, disagree and strongly disagree. Responses are then scaled and transformed to a score ranging from 0 to 100. These scores are correlated with four stages of activation. This survey will be given at baseline, 3-months, and 6-months.**

Social Support (MPSS): The multidimensional scale of perceived social support will be given at baseline, 3-months, and 6-months. This is a 12-item questionnaire is a validated measure of social support. For each item, respondents must choose one answer that reflects their assessment of social support on a 7-point scale. The items divide into 3 main factors of support: Family, Friends, and Significant other.

LDL levels: We will obtain baseline LDL levels for each patient prior to the intervention. In addition to monitor impact of adherence to the statin medication we will obtain LDL levels baseline and 6-month time periods for all patients.

M. **Study Design and Methods:**

1. Is this a clinical trial? ☒YES ☐NO
   1.1. If yes, what type? Check all that apply.
   ☐ **Phase I** ☒ **Phase II** ☐ **Phase III** ☐ **Phase IV**
   1.2. If yes, this study must be registered on Clinicaltrials.gov.

2. **Design**
   2.1. What research methods will be used in the project? Check all that apply.

☒ Surveys/Questionnaires	☐ Interviews	☐ Audio Taping
☐ Behavioral Observations	☐ Chart Reviews	☐ Video Taping
☐ Focus Groups	☒ Randomization	☐ Double-Blind
☒ Control Group	☒ Placebo	☐ Withhold/Delay Treatment
☒ Specimen Collection	☐ Deception	☒ Telephone Survey
☐ Other (Describe)		

   2.2. Describe how randomization or other treatment assignment will be made. **After informed consent is obtained and the baseline interview is complete, participants will be randomized. A research study statistician using a permutated block randomization procedure will develop randomization lists of participants. The program specialist will assign the patient to a study arm using the randomized list of arm assignments. The primary investigators will be blinded to knowledge of participant's assigned intervention.**

   We calculated our sample size for a 3-arm randomized study with a primary outcome of adherence rate. We propose to randomize 224 patients (64 in Arm 1, 64 in Arm 2, and 96 in Arm 3). Assuming a 15% dropout this will yield 175 patients for analysis (50 in Arm 1, 50 in Arm 2, and 75 in Arm 3) (see power analysis section).

   2.3. For retrospective research studies, provide the "look-back" period. (e.g., December 1, 1999 through December 31, 2008.) **N/A**

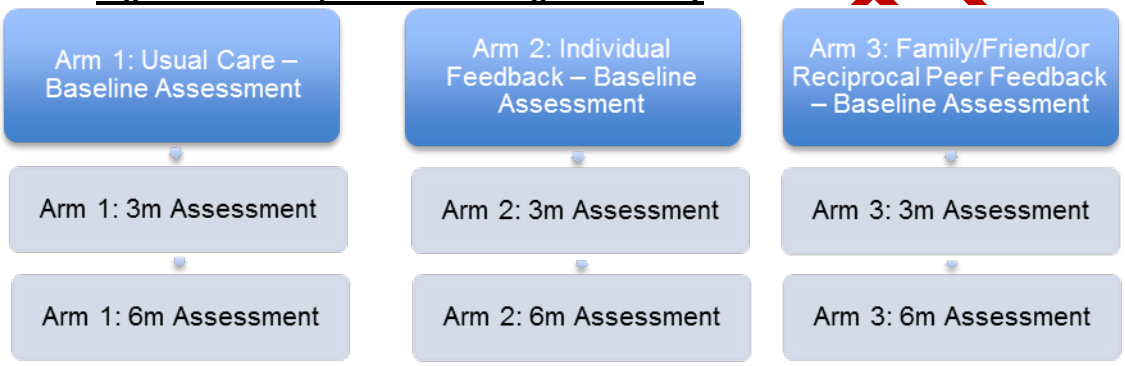
3. **Study Duration**

3.1. Provide the estimated length of time to enroll all subjects and complete the study.
We want to enroll a total of 224 veterans with CAD and poor adherence to statin medications. We project being able to enroll 8-10 people per week with a program specialist. We project that it will take 6-7 months to complete enrollment and another 6 months to complete follow-up for a total of 12-13 months. After that we anticipate it will take an additional 1-2 months to complete the analysis.

In August 2014, an amendment was submitted to allow for additional time to recruit patients. Our current ability to enroll patients has ranged from 2-7 per week.

3.2. Explain the expected duration of subject participation including any follow-up.
The active time for each participant will be 6 months. Figure 1 below depicts the flow of participants.

Figure 1: Participant flow through the study



3.3. Specify the projected date of completion of the proposed study. **If enrollment starts by October 1st, 2013, we anticipate completion of the study by November 1st, 2014. In August 2014, an amendment was submitted to extend IRB approval for an additional year. We did not start recruitment until April 2014. We anticipate completion of study by April 1st, 2015. In addition we anticipate an addition 3 months for analysis. We plan to complete of the study July 1st, 2015.**

4. **Drug Information** (If not applicable state, "Not Applicable.") **Not applicable**

4.1. Specify if the drug or biological agent is:
4.1.1. FDA approved
4.1.2. Used for off-label purposes
4.1.3. Not yet FDA approved.

4.2. Include the FDA Investigational New Drug (IND) number for all non-FDA approved and off-label drugs, biological agents or nutritional supplements. If not applicable state, "Not Applicable."

4.3. Provide all relevant information about the drug

4.4. Explain any wash-out periods, rescue medications permitted and any type of medications not permitted while enrolled in the study.

4.5. Describe blinding and un-blinding procedures.

4.6. Include the dosage, route of administration, previous use, and the safety and efficacy information on any drug used for research purposes.

4.7. Describe rationale for the dosage in this study.

4.8. Justify why the risks are reasonable in relation to anticipated benefits and/or knowledge.

4.9. Describe where drug preparation will be done.

4.10. All drugs for CMCVAMC subjects must be dispensed through the VA investigational pharmacy.

4.11. Describe where the study treatment will be administered.
4.12. Describe plan for tracking a non-compliant treatment study subject.
4.13. Summarize any pre-clinical data.
4.14. Describe the process for the storage, security, dispensing and return of an investigational drug.

5. **Investigational Device** (If not applicable state, "Not Applicable.") **Not applicable**
   5.1. The Investigational Device Exemption (IDE) number must be submitted for all significant risk devices and if an IDE exists for a non-significant device.
   5.2. Significant Risk or Non-significant Risk - If a device is not approved by the FDA, specify whether or not the sponsor has determined this device to be a "significant risk" or "non-significant risk" as defined by the FDA.
   5.3. Provide all relevant information about the device.
   5.4. Describe blinding and un-blinding procedures.
   5.5. Specify if device is:
      5.5.1. FDA approved
      5.5.2. Used for off-label purposes
      5.5.3. Not yet FDA approved.
   5.6. Explain if the investigational device will be delivered and/or stored by the Principal Investigator or Pharmacy Services.
   5.7. Describe the process for the storage, security, dispensing and return of an investigational device.
   5.8. For research involving an investigational device, describe the SOP or plan for device control.
   5.9. Address how the device will be stored in such a way that only research staff associated with the protocol will have access to the device.
   5.10. Describe measures that will be put into place to ensure that the device will only be used in participants of this research protocol.

N. **Does this project involve international research?** ☐YES ☒NO
   1. *For further instructions refer to VHA Directive 2005-050, Requirements for Conducting VA-Approved International Research Involving Human Subjects, Human Biological Specimens, or Human Data*
   2. *VHA Handbook 1200.05 definition of international research - VA international research is any VA-approved research conducted at international sites (not within the United States (U.S.), its territories, or Commonwealths); any VA-approved research using either human biological specimens (identified, de-identified, or coded) or human data (identified, de-identified, or coded) originating from international sites; or any VA-approved research sending such specimens or data out of the U.S. (see par. 56).* ***NOTE:*** *For the purposes of this Handbook, research conducted at U.S. military bases, ships, or embassies is not considered international research.*

O. **Study Procedure**
   1. **Study Procedures**
      1.1. Outline all study procedures - (*If necessary, include a table or flow chart, showing the schedule of the procedures and interactions. Distinguish between interventions that are experimental and carried out for research purposes vs. those that are considered standard of care. Routine procedures that are performed solely for research purposes should also be identified.)* **Overview: We will perform a randomized controlled trial with three arms. The ultimate aim of this type of study is to enhance efforts by Patient Care Aligned Teams (PACT) to improve medication adherence to statin medications among Veterans.**

Patients and Settings: We will enroll Veterans with CAD and poor adherence to statin medications who receive their care from the Corporal Michael J. Crescenz VA Medical Center (CMCVAMC). Veterans between the ages of 30 and 75 will be eligible for participation. There will be 3 arms: 1. Usual care 2. Individual feedback report alone and 3. Individual plus patient-selected family/friend/or reciprocal peer feedback reports. To ensure that we are studying a population who are most likely to benefit from improving medication adherence in the future, we are enrolling Veterans who are prescribed a statin by their provider and have a documented poor adherence as measured by a 6 month medication adherence rate (Medication Possession Ration) of < 65%. Dr George Tzanis (Director of Primary Care at CMCVAMC) has told us that he estimates that there are roughly 3,276 patients in Primary Care that meet this inclusion criteria. Due to an initial small sample from a review of pharmacy data, an amendment was submitted in March 2014, to expand eligible patients to those with poor adherence as measured by a 16-month medication adherence rate (Medication Possession Ratio) of less than or equal to 80%.

Potenial subjects will be identified by the Center for Evaluation of PACT (CEPACT) through VISN 4 Data Warehouse (VDW). With IRB approval, CEPACT will extract administrative, clinical and laboratory data through the VDW to identify eligible patients for this intervention. The VDW is updated regularly and thus an excellent source for up-to-date patient information. The identified patients will be sent a letter describing the study and then called. Current members of the PI's investigation team have used this method to identify Veterans with DM on many occasions – and has been successfully in enrolling between 60-70% of those contacted. Veterans who agree to participate will be invited into the Corporal Michael J. Crescenz VA to complete a consent procedure, baseline survey, and have their blood drawn to determine baseline LDL level at enrollment.

<u>Procedures:</u> As mentioned there will be 3 arms. Randomization into each arm is described above.

Control (Arm 1): They will complete all planned surveys, interviews, and blood draws (baseline, 3months, and 6 months). Patients will be given educational material on the importance of adherence to statin medications. The GlowCaps device will be explained and set to only record adherence.

Reminder/Individual Feedback (Arm 2): In addition to educational material on adherence to statin medications, the research coordinator will review set-up of personal reminders for the GlowCaps device which will be set to glow and buzz when the medication is missed. In addition, subjects will receive information on interpretation of the weekly adherence feedback report.

Subject-Selected Family/Friend/or Reciprocal Peer Notification (Arm 3): The subject will be given educational material on the importance of adhering to statin medications. The research coordinator will review set-up of alarm features of GlowCaps device. Similar to Arm 2, subjects will be given information on interpretation of weekly adherence feedback report. If the subject chooses a family/friend, the family/friend will be called and provided information on the interpretation of weekly adherence feedback report.

If the subject chooses a reciprocal peer, they will be assigned to another subject who has made a similar choice.
Subjects selecting this choice will complete the informed consent and surveys at the time of enrollment. The subject will be contacted after another subject has

been randomized into this arm. At this time the program specialist will coordinate a time to meet both subjects and review GlowCaps and interpretation of weekly adherence feedback reports. Thus, subjects who select a peer will have an extra research visit at the CMCVAMC.

An amendment was submitted in March 2014, to change the introduction of peers from a face-to-face meeting to a introduction via telephone call. Once amendment approval has been received, subjects in Arm 3, who choose a reciprocal peer, will proceed as follows: If the subject is the 1st participant in the pair they will complete the informed consent and baseline surveys at the time of enrollment. In addition, the research coordinator will review set-up of alarm features of the GlowCap Device. The 1st participant will be contacted by telephone when the 2nd participant who is randomized into this arm and chooses a reciprocal peer is assigned. This meeting of peers will be coordinated by telephone conference with the research coordinator. At this telephone conference, the research coordinator will facilitate an introduction of the peers and review the weekly adherence feedback report that will be exchanged to each partner. At the end of this meeting the GlowCaps device will be turned on at this time. If the 1st participant is unable to be reached the research coordinator will schedule a time with both participants to meet via a teleconference.

All participants from each group will be called at 3 months post-enrollment to complete social support and patient engagement surveys. At six months, they will be seen to return device, complete survey questionnaire, and complete blood test. This will complete the study period. If subjects do not come to the six month visit, they will be contacted to return for the visit by program specialist. At six months the GlowCaps device and information will be turned off.

<u>Data Collection:</u> All participants will complete a baseline survey, a 3 month and 6 months survey and a blood draw at baseline and 6 months. Arms 2 and 3 will be asked to respond to additional open-ended questions to better understand how the Veteran interacted with the intervention technology and feedback reports. The responses to these questions will be entered into the database by the research coordinator. These questions are attached in a separate document titled "Addition Qualitative Questions_GlowCaps". Table 1 identifies data to be collected at each time point and the source of the data.

For self-reported data we will use validated survey questions developed by the PI or other researchers in the field.

Table 1: Measurement Schedule

	Baseline	3 Mo	6 Mo
Main Dependent Variable Adherence (Continues GlowCaps)		x	x
Secondary Dependent Variables			
Direct LDL (blood)	x		x
Patient Activation Measure (self-report)	x	x	x
Social Support (self-report)	x	x	x
Moderators of Interest			
Demographics (self-report)	x		
General Health History (self-report)	x		

1.2. Explain if and how the follow-up of subjects will occur. **Follow-up will occur at three months post-enrollment with a brief phone call, and at 6 months post-enrollment with a visit at the Corporal Michael J. Crescenz VA Medical Center**

1.3. Describe where, how and who will be conducting study procedures. **Consent, study surveys baseline and 6 months will occur at the Corporal Michael J. Crescenz VA Medical Center and be performed by a program specialist. Evaluations of LDL level will be performed by the Corporal Michael J. Crescenz VA Medical Center lab.**

1.4. If a survey study, specify the estimated amount of time that subjects will need to complete the questionnaires/tools. **Based on experience, consent will take about 30 minutes and the baseline survey will take approximately 45 minutes. Follow-up visits will take about 60 minutes for survey completion. In total, we estimate the baseline visit will take approximately 1.5-2 hours in total. The telephone call will take approximately 30 minutes. The follow-up visit will take approximately 1 hour. The lab usually expedites tests for research and we expect patients will need to spend approximately 10 minutes getting their blood drawn. The total time commitment for consent and data collection is estimated to be around 3.5 hours.**

Table 2: Data Collection Step, Time to Complete and Mode of Collection

Procedure	Estimated Time to Complete	Number of Times to Perform
Consent	30 minutes	1 (in person)
Baseline Survey	45 minutes	1 (in person)
Lab Tests	10 minutes	2 (in person)
Follow-up Survey	30 minutes	1 (telephone)
Follow-up Survey	60 minutes	1 (in person)
Estimated Total Active Time		
Arm 1/2/3	210 minutes =~3.5 hours	

1.5. If a blood draw, specify the amount of blood to be drawn in milliliters and in teaspoonfuls or tablespoonfuls and specify how often and where the blood will be drawn. **Blood draws will occur at the Corporal Michael J. Crescenz VAMC lab. We anticipate a maximum of 5ccs or 1 teaspoon of blood will be required for each in-person visit at baseline and 6 months.**

2. **Data Collection** (Include all questionnaires and survey tools with the submission.)

2.1. Provide

2.1.1. the mode of data collection, e.g. telephone, in-person, questionn
Data will be collected mostly by in-person or telephone survey and lab tests. The participant will have data collected via GlowCaps to track daily adherence to medications. See Table 2 for details.

2.1.2. the precise plan for how data is to be collected or acquired, **Members of the research team created the "Way to Health" platform to provide close monitoring, feedback and reinforcement at a low cost to permit cost-effective flexible, scalable infrastructure. The platform was built at the University of Pennsylvania and the name derives from the 'The Way to Wealth', an essay written by Benjamin Franklin, which described how people can overcome difficulties in adopting good savings behaviors. *Way to Health* aims to improve health behaviors and consists of a portal with links to variety of peripheral devices (e.g., scales, pill bottles, glucometers) for assessing health behaviors and outcomes; the capacity to communicate back to patients using interactive voice recording; and the ability to automate the delivery of feedback reports. For this study, adherence reports will be sent to subjects (and if in "buddy group", reports will also be mailed to the buddy).**

Once patients have consented to be in the study and have their data managed by *Way to Health* (WTH), the WTH platform adherence tracking information will be stored according to a unique, random, patient identifier generated for the purposes of the study. To assure that subject, physician and other informant confidentiality is preserved, individual identifiers (such as name and medical record number) are stored in a single password protected system that is accessible only to study research, analysis and IT staff. This system is hosted onsite at the University of Pennsylvania (UPenn) and is protected by a secure identification number (ID). Any datasets and computer files that leave the firewall will be stripped of all identifiers and individuals will be referred to by their study ID. The study ID will also be used on all analytical files. An amendment was submitted on August 2014, to transfer these analytical files to the VA CHERP servers for further analysis. A detailed plan for transfer of these coded files is outlined in the section entitled: Information Security.

The University of Pennsylvania Biomedical Informatics Consortium (BMIC) is the hub for the hardware and database infrastructure. The data collected for *Way to Health* based studies is stored in MySQL databases on a BMIC-operated blade server environment devoted specifically to *Way to Health*. The data center is housed in the Information Systems and Computing at 3401 Walnut Street. All data are stored in a single relational database, allowing researchers to correct mistakes. Every SQL transaction, including accessing and changing data is logged for auditing purposes. Once a participant is consented and enrolled in the study, data are entered into the database through several different mechanisms. A program specialist will manually enter subjects' personal information and responses to survey questions through a PHP-based web interface. Researchers have a separate interface that allows them to manually enter

data if needed. This function will be used to enter data on LDL levels. All data collection and data entry done by the program specialists takes place at the Corporal Michael J. Crescenz VA Medical Center. Data from monitoring devices are uploaded automatically, imported from Vitality's web-based, password-protected platform. Vitality is the company that makes the GlowCap electronic pill bottles. No personally identifiable information is stored in Vitality's platform, only subject numbers and the cap data from the electronic pill bottles. The only data that is imported from Vitality's platform into *Way to Health* are the daily records of whether the cap was opened, which is how we will measure medication adherence. Datasets are blinded of all personally identifiable information when exported for analysis. The web application automatically removes all identifiers when a member of the research team requests an analytic dataset. The only people with access to identifiable participant information are pre-specified Program Specialists responsible for contacting participants. Personal information and research data will be stored in separate SQL tables and will be linked by a computer-generated ID number. All data for this project will be stored on the secure/firewalled servers for the BMIC Data Center, in data files that will be protected by multiple password layers. These data servers are maintained in a guarded facility behind several locked doors, with very limited physical access rights. They are also cyber-protected by extensive firewalls and multiple layers of communication encryption. Electronic access rights are carefully controlled by UPenn system managers. We believe this multi-layer system of data security, identical to the system protecting the University of Pennsylvania Health System medical records, greatly minimizes the risk of loss of privacy.

For example, data will be coded and Vitality is provided only with a study ID and a "cap ID(s)" for each participant. The *Way to Health* web developers have built an application that securely and automatically transmits data from the Vitality server to the *Way to Health* study server. All of the data is encrypted via https and transmitted from Vitality to the *Way to Health* web application and secure Penn servers. A HIPAA Business Associate Agreement is in place between this vender and Penn. Feedback reports are generated within the *Way to Health* platform and will be mailed to participants.

A program specialist will be read to participants survey questions and answers will either be directly input into a computer database or written onto paper forms and then transferred to a database at a later time. Paper records will be stored at CHERP behind an electronically locked entrance, a key-locked door and in a key-locked cabinet.

Lab results will be obtained from the lab or via CPRS and entered into the secure research database.

2.1.3. exact location where data will be collected, **Corporal Michael J. Crescenz VAMC and the Corporal Michael J. Crescenz VAMC Annex (for phone derived data.)**

2.1.4. exact location where data entry will take place. **All data entry will occur either at the Corporal Michael J. Crescenz VAMC or the Corporal Michael J. Crescenz VAMC Annex. Paper files for the study will be housed at the Corporal Michael J. Crescenz VAMC annex in locked filing cabinets. The data center and server for the *Way to Health* Platforms is at 3401 Walnut Street, Philadelphia, PA.**

2.1.5. the "title" of individual(s) collecting the data and analyzing the data, e.g. principal investigator, research coordinator. **A research coordinator will be collecting data and entering it into the database. The Principal investigator and Statistician/Programmer will be analyzing the data. Identifiable data will not be removed from Way to Health Platform. Access to identifiable data will be limited to those who require access including the program specialist, principal investigator, and the Statistician/Programmer.**

2.2. Provide a time line for each aspect of the study. **Baseline: Obtain consent, complete baseline survey, randomize, obtain blood. 3 months: Complete follow up survey, turn-off all feedback notifications. 6 months: Complete follow up survey, collect blood.**

2.3. Chart/Records/Data Review (retrospective and/or prospective)

2.3.1. Provide the planned or approximate number of charts/records/data to be accessed

2.3.1.1. CMCVAMC - **Given previous experience we anticipate having to screen between 1,600 and 1,700 charts to identify 224 people who will be eligible and willing to participate.**

2.3.1.2. Other site ☐

2.3.2. Does this protocol employ an Honest Broker? ☐YES ☒NO

2.3.2.1. If yes, provide name of individual. ☐

2.3.2.2. If no, explain who will access the charts/records. ☐

2.3.2.3. Describe from what database charts/records/data will be accessed. ☐

3. **Future Use of Data and Re-Contact**, if applicable. **Not Applicable**

3.1 If any of the participant's data are going to be retained after the study for future research, the following information must be provided to the participant:

3.3.1. Where will the data be stored? ☐

3.3.2. Who will have access to the data? ☐

3.2 If the subject is going to be re-contacted in the future about participating in future research, this must be specified. Describe the circumstances under which the participant would be re-contacted whether within the VA or outside the VA. ☐

3.2.1 If subjects will receive aggregate study results at the end of the study, the informed consent document must contain this information.

4. **Specimen Collection**

4.1. Give the source of all specimens and whether they were collected for research, treatment or diagnosis. **Blood will be drawn to assess direct LDL on two different occasions for research purposes. Treatment decisions will not be based on results by the research team.**

4.2. State where specimens will be stored, secured and when discarded. **Specimens will be drawn by the Corporal Michael J. Crescenz VA Medical Center lab and disposed of appropriately. We will not be storing blood for future use.**

4.3. Explain how destruction of samples will be substantiated. **The Corporal Michael J. Crescenz VA Medical Center lab will handle blood samples in the same way they handle samples for routine clinical care and subject to the oversight of routine clinical care.**

P. **Genetic Testing, if applicable**

1. Explain if the study is looking for an association between a genetic marker and a specific disease or condition, but at this point it is not clear if the genetic marker has predictive value. **Not Applicable**

1.1. The uncertainty regarding the predictive value of the genetic marker is such that studies in this category will not involve participant counseling.

1.2. Describe if the study is based on the premise that a link between a genetic marker and a specific disease or condition is such that the marker is clinically useful in predicting the development of that specific disease or condition. ☐

1.3. Will the subject be notified of the results and the provision for genetic counseling? ☐ Yes ☐ No ☒ N/A

1.3.1. If yes, explain further. ☐

1.4. If biological specimens are used in this protocol, please respond to the following questions by checking the appropriate box:

	YES	NO	N/A
a. Does the project involve genetic testing?	☐	☐	☒
b. Will specimens be kept for future, unspecified use?	☐	☐	☒
c. Will samples be made anonymous to maintain confidentiality? *(Instructions: Note: If there is a link, it is not anonymous. Coding is not anonymous.*	☐	☐	☒
d. Will specimens be destroyed after the project-specific use is completed?	☐	☐	☒
e. Will specimens be sold in the future?	☐	☐	☒
f. Will subjects be paid for their specimens now or in the future?	☐	☐	☒
g. Will subjects be informed of the results of the specimen testing?	☐	☐	☒
h. Are there any implications for family members based on specimen testing results? (If yes, they may be participants.)	☐	☐	☒
i. Will subjects be informed of results obtained from their DNA?	☐	☐	☒

1.5. Will specimens be de-identified? ☐YES ☐NO ☒ N/A

1.5.1. If yes, please describe the procedures to be used. ☐

1.5.2. Include at what point in the process the specimens will be de-identified. ☐

1.6. Describe what measures will be taken to minimize the following risks from breaches of confidentiality and privacy resulting from participating in **THIS aspect** of the research project:

1.6.1. physical ☐

1.6.2. psychological ☐

1.6.3. financial ☐

1.6.4. social ☐

1.6.5. legal harm ☐

Q. **Banking of Collected Specimens**

1. **Will collected specimens be banked**? ☐YES ☐NO ☒N/A

1.1. *IF BANKING SPECIMENS, IT MUST BE AT AN APPROVED VA REPOSITORY*. (*For additional information, refer to VHA Handbook 1200.12, Use of Data and Data Repositories in VHA Research - March 9, 2009.)*

1.2. If yes, specify the location where specimens will be banked.

1.2.1. If the location is a non-VA site, has the mandatory approval from the Chief Officer of Research and Development (CRADO) been obtained through submission of a tissue banking application (VA Form 10-0436 - Off-site Application for an Off-site Tissue Banking Waiver)? ☐YES ☐NO ☒N/A

1.2.2. If applicable, attach a copy of the VA Form 10-0436

1.3. Explain how destruction of banked samples will be substantiated. ☐

R. **Subject Recruitment** (characteristics of the study population): **The Veterans Health Affairs(VHA) health care system is the nation's largest integrated delivery health network. The VHA provides primary care for over five million veterans across 160 hospital-based and 783 community-based primary care clinics. Because veterans are typically older, sicker, and**

more socioeconomically vulnerable than patients outside VHA, this population is in need of better tools to monitor and improve patient adherence to medications.

1. **Provide the planned or targeted enrollment at**:
   - 1.1. CMCVAMC - **224 total participants**
   - 1.2. Other sites - ☐
   - 1.3. Not applicable; chart review or use of previously collected data - ☐

2. **Screening and/or Eligibility Requirements**
   - 2.1. Describe and provide justification for:
     Inclusion criteria - **All participants will have a diagnosis of CAD. To be eligible they must be between the ages of 30-75 years of age-to ensure we are targeting those most likely to benefit from improving control to these medications. Patients must have been prescribed a statin by their provider and a documented poor adherence as measured by a 6-month medication adherence rate (Medication Possession Ratio) of <65%. In a recent review of primary care patients in the Corporal Michael J. Crescenz VAMC roughly 3,276 patients met these inclusion criteria. An amendment was submitted in March 2014, to expand eligible patient to those with poor adherence as measured by a 16-month medication possession ratio of less than or equal to 80%.**
     - 2.1.1. Exclusion criteria - **Due to the use of the medication adherence reminder device, patients must speak English, have a home address, telephone number, and be willing and able to identify a friend or family member. We will exclude patients with active substance abuse, significant hearing loss, or reduced cognitive ability as determined from the patient's problem list.**
     - 2.1.2. List all screening and/or eligibility requirements. **We will electronically create a list of CMCVAMC patients with diagnosis codes for coronary artery disease (CAD) (ICD-9 code 414). Among these patient will review pharmacy database to identify patients with <65% of medication possession ratio in the previous 6 months. An amendment was submitted in March 2014, to expand eligible patient to those with poor adherence as measured by a 16-month medication possession ratio of less than or equal to 80%.**
   - 2.2. **We will exclude people if their current age is ≤ 30 and > 75 years of age. We will then review the list and determine who qualifies. Letters will be sent to potential participants letting them know that they may be eligible for a study with a brief description of the study and give them a number of they would like to learn more or to request no further contact. We will also notify potential participants that if we do not hear from them we will give them a call in the following weeks.**

     If the identified subject has not responded to either the mailed or 2 separate recruitment phone calls their information will be deleted from a list of potential participants.
   - 2.3. Explain any special test or evaluations potential subjects may have to undergo before they are actually determined to be eligible for the study. **When patients are contacted over the phone we will give them additional description of the study. If interested we will review the exclusion criteria with the participation – and exclude those who have the above exclusions.**
   - 2.4. Not Applicable; subjects not recruited; chart review. ☐

3. **If applicable, indicate what populations will be targeted for recruitment as participants. Check all that apply.**

Males	☒
Females	☒
Inpatients	☐

Outpatients	☒
VA Employees	☐
Non-English Speaking**	☐
Veteran Family members***	☐
Non-Veterans***	☐
Other (Specify)	☐
Not Applicable, chart review	☐

3.1. **For non-English speaking subjects - If an investigator proposes to use a participant population that does not speak or read English, a copy of the translated document, as well as the English version, needs to be forwarded to the IRB for approval. Translator certification is also required. ☐

3.2. ***If non-veterans will be recruited for this study, explain why sufficient veterans are not available to participate in the project [VHA Handbook 1200.5, paragraph 16a]. Veteran's spouses/partners, caregivers, etc. are considered non-veterans for the purposes of this study. ☐

3.3. ***Has approval to recruit non-veterans been received from the ACOS/R&D and Medical Center Director?

3.3.1. ☒ Not Applicable

3.3.2. ☐ Pending *(Non-veteran forms should be used. IRB office will obtain approval from ACOS/R&D and Medical Center Director.)*

4. **Does this project target a specific race or ethnic group as participants?** ☐YES ☒ NO
If yes, check all that apply.

Race	
American Indian or Alaskan Native	☐
Asian	☐
Black or African American	☐
Native Hawaiian or other Pacific Islander	☐
Black, not of Hispanic origin	☐
White, not of Hispanic origin	☐
Other	☐

Ethnicity	
Hispanic or Latino	☐
Not Hispanic or Latino	☐
Other	☐

4.1. Provide justification why this/these group(s) was/were chosen. ☐

5. **What is the age range of participants?** Check all that apply.

Children (Under 18) Requires Waiver from CRADO (VHA Directive 2001-028, Research Involving Children)	☐
Young Adults (18-21)	☐
Adults (22-65)	☒
Seniors (Over 65)	☒
Over 89	☐
Not Applicable, chart review	☐

6. **Are there specific reasons why certain populations (i.e., age, gender or ethnic groups) are excluded as participants?** ☒YES ☐NO ☐N/A

6.1. If yes, specify reasons. **Subjects who are greater than 76 may not benefit from improvements in statin medication adherence. In addition, subjects less than 30 may have other genetic contributing factors for elevated LDL levels.**

7. **Does the project require enrollment of the following classes of participants?**

	YES	NO
a. Employees	☐	☒
b. Individuals with impaired decision making capability	☐	☒
c. Pregnant women	☐	☒

d. Economically and/or educationally disadvantaged persons	☐	☒
e. Prisoners	☐	☒
f. Illiterate, limited, or no English language proficiency	☐	☒
g. Terminally ill patients	☐	☒

7.1. If applicable, what is the justification for including any of the above classes of participants in the project? ☐

7.2. If the project requires enrolling any of the above classes of participants describe any project-specific measures or special considerations, steps, or safeguards to ensure that these individuals are adequately protected. ☐

8. Describe the exact plan how subjects will be identified and recruited for the study.
Participants will be identified using the VISN 4 Data Warehouse (VDW). With IRB approval, CEPACT will extract administrative, clinical, and laboratory data from VDW on an ongoing basis. All eligible patients identified as meeting inclusion criteria will be sent a letter notifying them about the existence of the study, our intention to contact them, and our contact number in case they have questions. Mailings will be followed up with phone calls. This will be an ongoing process until recruitment is complete.

Veterans who agree to participate will be invited to the Corporal Michael J. Crescenz VA to complete a consent procedure, baseline demographic and social support survey, and initial blood test (direct LDL). In addition, all subjects will receive one-on-one training session on use of GlowCaps device.

8.1. Discuss methods, e.g., referrals from physician offices, clinics, programs, or through advertisements and brochures. ☐

8.2. If using a clinic, be specific about who will identify the potential subject and how that information will be transmitted to the research staff. ☐

8.3. If snowball method will be used, discuss the process and how the first individuals will be recruited. ☐

8.4. Describe how information will be disseminated to subjects, e.g. handouts, brochures, flyers and advertisements (*include all recruitment materials with this submission*). ☐

8.5. **Participants will be given a copy of the *Volunteering in Research* brochure and Notice of Privacy Practices, which explains what participants are expected to do in VA authorized studies**

9. **Informed Consent**

9.1. Informed Consent will not be sought. ☐

9.2. Written informed consent from participants (VA Form 10-1086 is attached). ☒

9.3. Written informed consent from participants' legally authorized representative (LAR) as required by VA policy and/or applicable state laws (VA Form 10-1086 is attached). ☐

9.4. Request Waiver of Documentation of Informed Consent ☐

9.5. List the **title** of the key personnel involved in the following activities:

9.5.1. Person Obtaining Consent

9.5.1.1. Provide the title(s) of individual(s) **Principal Investigator and/or Program Specialist**

9.5.1.2. Type of training received to perform this process **Program Specialist will have completed HIPPA and CITI research trainings on clinical research**

9.5.2. **Pre-Recruitment Screening** (the use of medical records and other data bases to determine populations and individuals eligible for the study), **Database Programmer and Program Specialist**

9.5.3. **Recruitment Process** (the process in which individuals are contacted and first introduced to the study and to the possibility of participating as subjects), **Program Specialist**

9.5.4. **Informed Consent Process** (the process by which recruited subjects are fully informed about participating in the study and then formally give their voluntary consent for participating), **Principal Investigator and/or Program Specialist**

9.5.5. **Screening of Recruited Subjects** (those activities in the protocol in which a final determination of eligibility of prospective subjects is made during the early phases of the study, using laboratory data, inclusion and exclusion criteria, and other person-specific information), **Program Specialist and Principal Investigator**

9.5.6. Include the breakdown of each individual's responsibilities:

9.5.6.1. Principal Investigator, **Judith A. Long, MD will be responsible for the oversight of this entire study**

9.5.6.2. Co-Principal Investigator, **David Asch MD, MBA and Kevin Volpp MD PhD are co-investigators who have created Way to Health Platform, Judd Kessler PhD will provide expertise on social incentives, and Steven Marcus PhD will be provider expertise on conducting VA related clinical trials**

9.5.6.3. Research Coordinator (**Program Specialist Pre-Recruitment Screening, Recruitment Process, Screening of Recruited Subjects , Obtaining informed consent**

9.5.6.4. Additional research staff by title, **Statistician**

9.6. Will informed consent be obtained from potential subjects prior to determining eligibility?
☐YES ☒NO ☐N/A

9.6.1. If no, provide justification and a HIPAA Waiver of Individual Authorization for Disclosure of Protected Health Information. **To make the recruitment process efficient we will need to screen for patients with CAD in the correct age range, with poor adherence to medications as described above. Please see the attached HIPAA Waiver of Individual Authorization for Disclosure of Protected Health Information for approval of this activity.**

9.7. Define when a subject is enrolled into the study, e.g. after the subject signs the informed consent or after randomized to treatment. **After the informed consent and HIPAA authorization are complete the patient will be enrolled in the study**

9.8. Describe:

9.8.1. The process when informed consent will be obtained and protecting patients' privacy. **Informed consent will be obtained at the Corporal Michael J. Crescenz VA Medical Center in a semi-private room with cubicles. This room usually has only one person working in it at a time and thus affords privacy. All study materials including informed consent forms will be read to the participant.**

9.8.2. Any waiting period between informing the prospective participant and obtaining consent. **No**

9.8.3. Steps taken to minimize the possibility of coercion or undue influence. **The consent process will explain how participation is voluntary and will not affect the care or services the patient is eligible from the Corporal Michael J. Crescenz VA Medical System. Participants will be told they can withdraw from the study at any time. Participants will only receive a reimbursement to defray the costs of the participant's time.**

9.9. Provide the language

9.9.1. used by those obtaining consent **English**

9.9.2 understood by the prospective participant or the legally authorized representative **English**

9.10. Provide location where informed consent will be obtained. **The Corporal Michael J. Crescenz VA Medical Center.**

10. **Waiver or Alteration of Informed Consent Requirements/Waiver of Requirement to Obtain Documentation of Informed Consent**

10.1. Are you requesting a waiver or alteration of informed consent? *(Check all that apply)*

10.1.1. No ☐

10.1.2. Yes; provide justification. ☒ **To make the recruitment process efficient we will need to screen for patients with CAD in the correct age range, with poor adherence to medications as described above. Please see the attached HIPAA Waiver of Individual Authorization for Disclosure of Protected Health Information for approval of this activity.**

10.1.3. Yes; for recruitment purposes only. ☐

10.2. **Are you requesting a waiver to obtain documentation of informed consent?**

10.2.1. No ☒

10.2.2. Yes; provide justification. ☐

S. **Compensation** *(The amount of compensation may not constitute an undue inducement to participate in the research.)*

1. Summarize any financial compensation that will be offered to subjects. **All subjects, regardless of the arm, will receive $50 for each in person visit (baseline, 6 months). Participants will also receive an additional $25 for completion of telephone survey at 3 months. An amendment was submitted in March 2014 to change payment form from cash to gift cards to CVS and/or Rite Aid depending on availability. For those patients who were enrolled prior to amendment approval, cash will still be provided. Once amendment approval is received, reimbursement will be in the form of gift cards.**
2. Provide the schedule for compensation.
   - **All enrollees are eligible for compensation up to $125 for completion of this study.**
   - **Subjects will receive $50 for completion of baseline survey and blood draw at visit one.**
   - **They will receive $75 at the second visit (at six months) if they complete the phone research questionnaire at 3months. If the phone questionnaire is not completed they will receive $50 at the second visit.**
   - **An amendment was submitted in March 2014 to change payment form from cash to gift cards. For those patients who were enrolled prior to amendment approval, cash will still be provided. Once amendment approval is received, reimbursement will be in the form of gift cards. The schedule for compensation will remain as explained above.**

   2.1. Per study visit or session. **$50 in person, $25 for 3 month telephone survey/ Post-Amendment: $50 gift card in person visit, $25 gift card for 3 month telephone survey**

   2.2. Total amount for entire participation. **$125**
3. Explain how compensation will be provided via cash, voucher, gift card, etc.
   - **Participants will be given vouchers which they can then redeem for cash from the Corporal Michael J. Crescenz VA cashier.**
   - **Post Amendment: Participants will be given gift cards equivalent to the amount specified above for the baseline and follow-up visits. This will be given to the Veteran by the research coordinator and recorded in a tracking database.**
4. If financial compensation will be prorated, explain the process. **N/A**
5. Not Applicable - ☐

T. **Withdrawal/Early Withdrawal**

1. Describe how and when a subject may withdrawal from the study. **Subjects may withdraw at anytime. Any request may either be expressed verbally or in writing.**
2. Provide procedures for the orderly termination of participation by the participant and if any consequences would result from early withdrawal from the study. **There will be no consequence of early withdraw. After submitting a request to withdraw or written or verbally the study participation will be terminated.**
3. Explain if survival data is required. If so, clarify how data will be obtained. **N/A**

4. Not Applicable; subjects not recruited; chart review. ☐

U. **Risk/Benefit Assessment**

1. **Potential Study Risk**s

1.1. Describe and assess all of the following risks that may be associated with the research:

1.1.1. Physical **Minimal - We are asking that all subjects get a blood test to measure LDL levels from the lab at each study visit. The blood test consists of inserting a needle into the arm and taking about a teaspoon of blood. Subjects may experience mild pain and swelling where the needle enters the skin and vein, bruising, infection and possibly fainting.**

1.1.2. Psychological **Minimal - Subjects may feel uncomfortable or embarrassed that someone else knows information about when they are taking their medication and that they may not be taking it as often as you should be**

1.1.3. Social **Minimal**

1.1.4. Economic **Minimal**

1.1.5. Monetary **Minimal**

1.1.6. Legal **Minimal**

1.1.7. Loss of confidentiality **Minimal - If subjects are in the Buddy group, there is a risk that the buddy may reveal the subject's name and phone number as well as information from their statin pill bottle reports to another person. We will instruct the buddy not to share any information with others. There is a risk that information could be accidentally released. We take great efforts to maintain confidential information**

1.1.8. Assess the likelihood and seriousness of such risks. **Minimal**

1.1.9. Other **N/A.**

1.2. Specify what steps will be taken to minimize these risks. **Subjects will need to complete a mini-quiz after completing the informed consent to assure the researchers they understand the study. Those who fail the mini-quiz will be given $50 for the in person visit but not enrolled in the study. All participants will be notified that participation is voluntary and they can terminate participation at any time. They will also be notified that their care will not be affected by their participation.**

The greatest risk to patients will be loss of confidentiality. Patient selected family, friend, or reciprocal peer will be informed that information around medication adherence is confidential and should not be shared. Participants will need to provide a current home address to receive adherence feedback reports.

Tracking data with identifiable information will be kept in a different data base than the analytic data base. All databases will be password protected and reside on the University of Pennsylvania WTH platform. Neither data base will be removed from the WTH server and will be behind VA firewalls. Paper files will be kept in locked filing cabinets and will not leave the Corporal Michael J. Crescenz VA or Annex. Papers will be kept in locked files when not being actively used. All participants will be given a study ID number and this will be the only link between the analytic files and the tracking database.

1.3. If methods of research create potential risks, describe other methods, if any, that were considered and why they will not be used. **N/A**

1.4. If chart review, breach of confidentiality is always a concern. Specify what steps will be taken to minimize these risks. **Charts will only be reviewed to determine if a potential subject may be eligible for the study. Only IRB approved study personnel will access charts from VA computers during working hours. Abstraction will be limited to determine eligibility only.**

2. **Potential Study Benefits**

2.1. Assess the potential benefits to be gained by the individual subject, as well as benefits that may accrue to society in general as a result of the planned work. **Using telemonitoring and feedback mechanisms for medication adherence can engage potential participants in those arms of the study to improve medication adherence. This study may lead to strategies that enhance adherence to medications. Adherence to medications can reduce the risk of an individual patient of having a heart attack – and on a population level has the ability to improve the quality and reduce the cost of healthcare. This study has the potential to add to our knowledge about how to use feedback reports and non-financial incentives to improve medication adherence.**

2.2. If the subject does not receive any direct benefit, then it must be stated here and in the consent form. **While we hope that subjects in some arms of the study might receive benefit it is likely that some participants will not benefit especially those who are randomized to usual care**

3. **Alternate Procedures**

3.1 Describe the alternatives available to the subject outside the research context. **N/A**

3.2 If none, state that the alternative is not to take part in this research study at all. **The only alternative is to not take part in the research study.**

V. **Data and Safety Monitoring Board (DSMB) or Data Monitoring Committee (DMC) (**All Phase III studies are required to have a DSMB. *However, the IRB has the right to require a DSMB with any study.)*

1. **Will an independent DSMB or DMC oversee the project?** ☐YES ☐NO ☒N/A

2.1. If yes, please provide contact information for the DSMB or DMC or Coordinating Center Representative and attach a copy of the charter.

Name: Phone Number:
Title: E-mail**:**

2. **If a DSMB or DMC will not monitor this study, who will monitor this study? Check all that apply.**

☒ Principal Investigator
☐ Sponsor
☐ VA Cooperative Studies Program
☐ Safety monitoring committee

W. **Data Monitoring** (*Monitoring plans describe how a monitor, independent of the study team, regularly inspects study records to ensure the study is adhering to the study protocol and applicable research regulations and CMCVAMC requirements. Monitoring plans do not necessarily require the use of an independent Data and Safety Monitoring Board (DSMB). Such independent boards are usually reserved for high-risk phase I studies, or large, multi-center phase III trials. Federally funded studies may require the use of an independent DSMB.)*

1. **Describe the data monitoring plan.** (All protocols must have a data monitoring plan appropriate for the potential risks and the complexity of the study.) **All serious adverse events will be reviewed by the PI and reported to the IRB. We do not expect events to differ by arm based on our prior research.**

Data not directly entered will be double entered to ensure fidelity. Paper consents will be reviewed routinely for completeness. All files will be regularly maintained and available for inspection upon request.

2. **Describe how protocol deviations, adverse events, serious adverse events, breaches of confidentiality, unanticipated adverse device effect (UADE), and unanticipated or unexpected problems will be reported to the CMCVAMC IRB and sponsor**. *(Refer to the CMCVAMC IRB Standard Operating Procedure (SOP) Manual for reporting guidelines.)* **Breaches of confidentiality will be reported within 24 hours of our awareness of said**

breach. Protocol deviations, adverse events, serious adverse events, breaches of confidentiality, unanticipated adverse device effect (UADE), and unanticipated or unexpected problems will be reported following the guidelines in the CMCVAMC IRB SOP.

2.1. Describe the management of information obtain that might be relevant to participant protections such as:

2.1.1. Unanticipated problems involving risks to subjects or others - **This is a low risk study. However, if unanticipated problems arise the study team will review them and report them immediately to the CMCVAMC IRB. If there are serious concerns about risks to subjects or others the study will be halted while an external group reviews the study to determine the risks.**

2.1.2. Interim results - **We are not planning an interim analysis**

2.1.3. Protocol modifications - **If we desire to modify the protocol we will submit a modification to the IRB and not act on the modification until it has been approved.**

3. **If applicable, define the plan for subjects if research shows results such as:**

3.1. Depression **n/a**

3.2. Suicide **n/a**

3.3. Abuse **n/a**

4. **Statistical Analysis**

4.1. Include statistical power calculations and the assumptions made in making these calculations. **Our sample size was determined using a power calculation where we seek to have 80% power to detect a Cohen's d=0.6 corresponding to a moderate-to-large effect of our intervention on the outcomes of interest. We assume alpha=.025 to account for multiple comparisons associated with the comparison of each of the two intervention arms with the control arm (i.e. alpha=.05/2=.025). Our power calculation suggests that a sample of 50 subjects in each of the three arms of the study will achieve this goal. However, Arm 3 of the study may include reciprocal pairs and, as such, the subjects cannot be considered to be independent. We assume a relatively large Intra Cluster Correlation of ICC=0.5 between the reciprocal pairs. This translates to a design effect of 1.5 which, in turn requires that the sample size for this arm be increased by 50% to n=75. We conservatively allow for 15% attrition and so will propose to randomize 64 subjects in Arms 1 and 2, and 96 in arm 3. Because this is a pilot study, the study was designed was to test if the intervention could detect an improved adherence of 5% between the groups.**

4.2. Define plans for data and statistical analysis, including key elements of the statistical plan, stopping rules and endpoints. **We will test the primary hypotheses using an unadjusted intent-to-treat analyses. Initial descriptive analysis of demographic and baseline clinical characteristics for all study patients will be conducted, including gender, age, race/ethnicity, income, education, type of statin medication, and initial measures of social support. For specific aim 1 (H1, H2), we will model using a one-way ANOVA model to test for differences the continuous outcome of percent of total medications taken at 3 months with study arm as the main independent predictor of interest. We will adjust for covariates not balanced at baseline. . For specific aim 2 and specific aim 3 (H3,H4), we will model using a one-way ANOVA model to test for differences the continuous outcome of change in patient activation and social support score with study arm as the main independent predictor of interest. We will adjust for covariates not balanced at baseline. If there is ceiling or floor effects with the patient activation and social support scores we will also adjust for baseline score. For H5 we will repeat the analysis for aim 1 including an interaction term to test difference between arms. For H6 we will repeat the analysis for aim 1 with the main independent variable being adherence at 6 months instead of 3 months. All**

analyses will compare each intervention arm to the control arm and use p=.025 as a critical value.

4.3. **Qualitative survey data collected will be read and coded for cultural themes by program specialist, and PI . Using these domains, we will conduct a descriptive analysis of Veterans attitudes toward GlowCaps, feedback reports, and feedback partners to improve medication adherence. This study will use a modified Grounded Theory approach and the constant comparative method for analyzing responses of veterans to the qualitative questions. Two members of the research team (PI, , and program specialist) will read a random sample of 10 veteran responses to identify and name concepts in the data, and to categorize data according to these concepts. Through consensus, a list of coding categories and their definitions will be developed; these codes will then be applied to all qualitative data by the program specialist, with regular meetings of the research team to discuss and resolve questions about codes and the application of codes to text. Once all responses have been coded to one or more coding categories, selective coding will be used to identify the core concept in the data and to relate the other concepts to this central concept. A theory will then be developed describing the relationship between concepts.**

X. **Privacy and Confidentiality** *(Privacy refers to persons and to their interest in controlling the access of others to themselves.) (Confidentiality refers to protecting information from unauthorized disclosure or intelligible interception.) (Investigator should contact the Privacy Officer for additional details.)*

1. **Indicate the type of data that will be received by the Principal Investigator. Check all that apply.**

1.1. ☐ De-identified – Without any identifiers that could link the data to a specific participant. (Contact Privacy Officer for assistance. *If data is coded, it is not considered de-identified.)*

1.2. ☒ Identified – Linked to a specific participant by identifiers sufficient to identify participants. (See HIPAA and Common Rule Criteria for list of identifiers.)

1.3. ☒ Coded – Linked to a specific subject by a code rather than a direct identifier. If coded is checked, specify: **An amendment was submitted in August 2014 on the transfer coded data for analysis at the VA. The data and process for coding was discussed with CMCVAMC Privacy Officer.**

1.3.1 Explain who will maintain the link or code. **PI, co-PI, program specialists**

1.3.2 Describe who will have access to the link or code. **PI, co-PI, program specialists**

1.3.3 Provide exact details for how the data is coded. **Veteran subjects will be assigned a code number that will be used in place of his or her name on study materials. Only the Principal Investigator, Co- Investigators, and program specialists will have access to the key linking codes to individual names.**

2. **Does the project require the use of existing Protected Health Information (PHI) from a database, medical records, or research records?** ☒YES ☐NO ☐N/A

2.1. If yes,

2.1.1. Specify the source of the existing PHI **VISN 4 VA Electronic Records**

2.1.2. Indicate the specific data elements/identifiers (e.g., name, address, phone numbers, etc.) on the below table. **For contact purposes and tracking: name, address, phone numbers, date of birth, and social security number.**

For determining eligibility: diagnosis codes of CAD, pharmacy record for medication possession ratio, and date of birth.

Please see the attached HIPPA waiver requesting permission to access this data.

2.2. If the study uses an existing database/data warehouse,
- 2.2.1. Provide a description of the database/data warehouse. **To identify potential eligible participants we will pull names from the VISN 4 data warehouse.**
- 2.2.2. Make clear who is responsible for maintaining it. **This warehouse is maintained by the VISN**
- 2.2.3. Cite any relevant Standard Operating Procedures (SOP) for the database/data warehouse. **N/A**
- 2.2.4. Provide a copy of the SOP.

3. Will PHI be collected prior to obtaining informed consent? ☒YES ☐NO ☐N/A
- 3.1. If yes, complete and provide a HIPAA Waiver of Individual Authorization for Disclosure of Protected Health Information with this submission.

4. HIPAA Identifiers - Indicate the PHI that will be collected from project participants directly or indirectly.
- 4.1. ☒ Name
- 4.2. ☒ All geographic subdivisions smaller than a State, including street address, city, county, precinct, zip code, and their equivalent geocodes, except for the initial three digits of a zip code if, according to the current publicly available data from the Bureau of the Census
- 4.3. ☒ All elements of dates (except year) for dates directly related to an individual, and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older.
  - 4.3.1. ☒ Birth Date ☒ Date of Death
  - 4.3.2. ☐ Discharge date ☐ Admission date
  - 4.3.3. ☐ Appointment Dates ☒ Other Dates (e.g. lab tests, x-rays, MRI, etc.) **Dates GlowCaps opened**
- 4.4. ☒ Telephone numbers
- 4.5. ☐ Fax numbers
- 4.6. ☐ Electronic mail addresses
- 4.7. ☒ Social Security/Medical Record Number
- 4.8. ☐ Health plan beneficiary numbers
- 4.9. ☐ Account Numbers
- 4.10. ☐ Certificate/license numbers
- 4.11. ☐ Vehicle identifiers and serial numbers, including license plate numbers
- 4.12. ☐ Device identifiers and serial numbers
- 4.13. ☐ Web universal resource locators (URLS)
- 4.14. ☐ Internet protocol (IP) address numbers
- 4.15. ☐ Biometric identifiers, including fingerprints, voiceprints, audio recordings
- 4.16. ☐ Full-face photographic images and any comparable images
- 4.17. ☐ Any other unique identifying number, characteristic, or code
- 4.18. ☐ Personal and Family History
- 4.19. ☐ History and Physical Examination ☒ Progress Notes
- 4.20. ☐ Discharge Summary(ies) ☐ Photographs, videotapes, other images
- 4.21. ☐ X-Ray ☐ HIV (testing or infectious disease) records
- 4.22. ☐ Diagnostic/Laboratory tests ☐ Sickle cell anemia
- 4.23. ☐ Drug Abuse Information ☐ Behavioral Health notes
- 4.24. ☐ Alcoholism or Alcohol Use ☐ Operative Reports
- 4.25. ☐ Billing records ☒ Medication List
- 4.26. ☐ Health Summary Reports ☐ Anatomic Pathology Report
- 4.27. ☐ Other Records:

5. Will participants be contacted from existing PHI? ☒YES ☐NO ☐N/A

5.1. If yes, clearly explain how participants will be contacted (NOTE: this would be the same information as listed under section R.8 identification and recruitment of subjects). **Potential participants once identified will first be sent a letter of introduction letting them know about the study and giving them a number if they would like more information or would like for us not to call them. A week after mailing out the letter, potential participants will be called and the study will again be introduced to them and they will be asked if they would be interested in participating in the study. See attached letter of contact and script for discussing the project with potential participants on the phone.**

6. Provide the titles of the exact individuals who will have access to the collected data. **The titles of the individuals with access are Principal Investigator, Program Specialist, and Statistician/Data Base Programmer**

6.1. Explain why these individual will have access to this data. **They will have access to identify, select, and enroll participants to be part of the study.**

Y. **Information Security** (*Contact the Information Security Officer for additional assistance regarding confidentiality (storage/security) of research data.)*

1. Provide the precise plan how data is to be collected or acquired (repeat the same information as listed under "Data Collection" section of this form. **Once patients have consented to be in the study and have their data managed by WTH, the WTH platform adherence tracking information will be stored according to a unique, random, patient identifier generated for the purposes of the study. To assure that patient, physician and other informant confidentiality is preserved, individual identifiers (such as name and medical record number) are stored in a single password protected system that is accessible only to study research, analysis and IT staff. This system is hosted onsite at the University of Pennsylvania (UPenn) and is protected by a secure identification number (ID). Any datasets and computer files that leave the firewall will be stripped of all identifiers and individuals will be referred to by their study ID. The study ID will also be used on all analytical files.**

The University of Pennsylvania Biomedical Informatics Consortium (BMIC) is the hub for the hardware and database infrastructure. The data collected for Way to Health based studies is stored in MySQL databases on a BMIC-operated blade server environment devoted specifically to Way to Health. The data center is housed in the Information Systems and Computing at 3401 Walnut Street. All data are stored in a single relational database, allowing researchers to correct mistakes. Every SQL transaction, including accessing and changing data is logged for auditing purposes. Once a participant is consented and enrolled in the study, data are entered into the database through several different mechanisms. A Program Specialist will manually enter subjects' information and enter responses to surveys through a PHP-based web interface. Researchers have a separate interface that allows them to manually enter data if needed. This function will be used to enter data on LDL levels. All data collection and data entry done by the program specialists takes place at the Corporal Michael J. Crescenz VA Medical Center. Data from monitoring devices are uploaded automatically, imported from Vitality's web-based, password-protected platform. Vitality is the company that makes the GlowCap electronic pill bottles. No personally identifiable information is stored in Vitality's platform, only subject numbers and the cap data from the electronic pill bottles. The only data that is imported from Vitality's platform into *Way to Health* are the daily records of whether the cap was opened, which is how we will measure medication adherence. Datasets are blinded of all personally identifiable information when exported for analysis. The web application automatically removes all identifiers when a researcher requests an analytic dataset. The only people with access to identifiable participant information are pre-specified Program Specialists responsible for contacting participants. Personal information and research data will be stored in separate SQL tables and will be linked by a computer-generated ID number. Additionally, any

information that leaves this system to communicate with third party data sources is stripped of any identifiers and transmitted in encrypted format. The same unique study ID is used to link these outside data to participants. All data for this project will be stored on the secure/firewalled servers for the BMIC Data Center, in data files that will be protected by multiple password layers. These data servers are maintained in a guarded facility behind several locked doors, with very limited physical access rights. They are also cyber-protected by extensive firewalls and multiple layers of communication encryption. Electronic access rights are carefully controlled by UPenn system managers. We believe this multi-layer system of data security, identical to the system protecting the University of Pennsylvania Health System medical records, greatly minimizes the risk of loss of privacy.

For example, data will be coded and Vitality is provided only with a study ID and a "cap ID(s)" for each participant. The Way to Health web developers have built an application that securely and automatically transmits data from the Vitality server to the Way to Health study server. All of the data is encrypted via https and transmitted from Vitality to the Way to Health web application and secure Penn servers. A HIPAA Business Associate Agreement is in place between this vender and Penn. Feedback reports are generated within the Way to Health platform and will be mailed to participants.

CEPACT will work with the CHERP Biostatistics and Informatics Core and WTH platform data team to develop a system to securely link limited data. The CHERP Biostatistics and Informatics Core will extract from the VDW IRB approved patient identifiers according to the criteria in for identifying potential participants. Identifiable data can only accessed by the Biostatistics and Informatics Core once IRB approval for the specific protocol has been obtained and only that data which is approved is abstracted for the PI. The VA data available to the WTH research coordinator will include listings of drug names and prescribing dates of related drugs and LDL laboratory information. This VA data will be linked to the Way to Health in a similar manner as above (similar to Vitality GlowCaps).

An amendment was submitted in August 2014 to transfer coded data from WTH server to the CHERP biostatistics and Informatics Core for analysis. As mentioned above, the datasets that leave the firewall will be stripped of all identifiers and individuals will be referred to by their study ID. The study ID will also be used on all analytical files. The data will not include and names, date of birth, date of pill bottle openings, or other PHI identifiers. The medication adherence data will include the time stamp for the pill bottle openings, but the time stamp will not be linked to a specific date of opening. These data will be transferred to the CMCVAMC using a password protected and encrypted CD/DVD as instructed by the VA ISO. On a monthly basis, this CD/DVD will be scanned by FITS to make sure there is no malware/virus to reduce the any risk to the VA (per VA ISO instructions). This data will be uploaded onto the secure password protected CHERP/CEPACT server. Once the data is uploaded the encrypted CD/DVD will be stored at Corporal Michael J. Crescenz VA Medical Center Annex, (file room 17) in a filing cabinet on the second floor. This room is located at CHERP, which is secured by a lock and key, and the filing cabinet containing the data will be secured by lock and key.

Subject questionnaires will be read to participants and answer will either be directly input into a computer database or written onto paper forms and then transferred to a database at a later time. Paper records will be stored at CHERP behind an electronically locked entrance, a key-locked door and in a key-locked cabinet.

Lab results will be obtained from the lab or via CPRS and entered into the secure research database

2. Provide a listing of the exact research data that will be stored, including but not limited to signed, original informed consent and HIPAA authorization forms, case report forms, etc. **Adherence to statin medication, self-reported demographics, survey data examining patient engagement in health behavior, social support, general health history, informed consent form, and HIPPA authorization form.**

3. Indicate how project's research data (original and all copies) will be stored and provide corresponding security systems. **Data must be used, stored, and secured according to the requirements of the VHA series 1200 Handbooks, other applicable VA and VHA requirements.**

The data collected for Way to Health based studies is stored in MySQL databases on a BMIC-operated blade server environment devoted specifically to Way to Health. The data center is housed in the Information Systems and Computing at 3401 Walnut Street. All data are stored in a single relational database, allowing researchers to correct mistakes. Every SQL transaction, including accessing and changing data is logged for auditing purposes. Once a participant is consented and enrolled in the study, data are entered into the database through several different mechanisms. A Program Specialist will manually enter subjects' information and enter responses to surveys through a PHP-based web interface. Researchers have a separate interface that allows them to manually enter data if needed. This function will be used to enter data on LDL levels. All data collection and data entry done by the program specialists takes place at the Corporal Michael J. Crescenz VA Medical Center. Data from monitoring devices are uploaded automatically, imported from Vitality's web-based, password-protected platform. Vitality is the company that makes the GlowCap electronic pill bottles. No personally identifiable information is stored in Vitality's platform, only subject numbers and the cap data from the electronic pill bottles. The only data that is imported from Vitality's platform into *Way to Health* are the daily records of whether the cap was opened, which is how we will measure medication adherence. Datasets are blinded of all personally identifiable information when exported for analysis. The web application automatically removes all identifiers when a researcher requests an analytic dataset. The only people with access to identifiable participant information are pre-specified Program Specialists responsible for contacting participants. Personal information and research data will be stored in separate SQL tables and will be linked by a computer-generated ID number. Additionally, any information that leaves this system to communicate with third party data sources is stripped of any identifiers and transmitted in encrypted format. The same unique study ID is used to link these outside data to participants. All data for this project will be stored on the secure/firewalled servers for the BMIC Data Center, in data files that will be protected by multiple password layers. These data servers are maintained in a guarded facility behind several locked doors, with very limited physical access rights. They are also cyber-protected by extensive firewalls and multiple layers of communication encryption. Electronic access rights are carefully controlled by UPenn system managers. We believe this multi-layer system of data security, identical to the system protecting the University of Pennsylvania Health System medical records, greatly minimizes the risk of loss of privacy.

Hard copy-based research data will be stored at the Corporal Michael J. Crescenz VA Medical Center Annex, (file room 17) in a filing cabinet on the second floor. This room is located at CHERP, which is secured by a lock and key, and the filing cabinet containing the data will be secured by lock and key. While files are actively in use, paper records will be held in the Corporal Michael J. Crescenz VA Medical Center Annex PROMISE (suite 200) in a key-locked filing cabinet behind an electronically locked entrance and a key-locked door. The data will be transported between the CMCVAMC hospital and CMCVAMC Annex in a locked case.

Project research data both original copies for hard-copies will be kept on VA property under lock and key in filing cabinets. Electronic data will be kept secure in password protected databases.

4. CMCVAMC, provide exact location where research data (original and all copies) will be stored and secured. **The information for eligible subjects will be stored via: The CHERP/CEPACT servers are located in the secure CMCVAMC server room, which is the OI&T Server Room that has double locks and a security alarm and cameras, which is located in Room 001 of Building 1 of the main CMCVAMC.**

   The filing room on the second floor of the Annex and is located at Room 17, and the cabinet is locked inside of Room 17. Active files will be stored in a locked filing cabinet (M133) in PROMISE, Suite 200, located on the second floor of the Annex.

5. Explain how data is to be transported or transmitted from one location to another. **No data will be transported from one location to another. Pre-enrollment screening will take place at the VA CHERP facilities. As stated above this information will identify patient who are eligible for our study.**

   Once a patient has completed the informed consent all information will entered through a web-based interface. This information includes all listed PHI, demographic and survey information listed above. The GlowCaps device will be linked to study ID and information on adherence will be collected and transmitted via wireless 3g network to secure servers kept at University of Pennsylvania.

   An amendment was submitted in August 2014, to transfer coded datasets from the WTH to the CMCVAMC medical center. To do this, as outlined in the information security section, the WTH Research Coordinator will download the coded data from the WTH server onto the encrypted CD/DVD. The Program Specialist and/or PI will transfer this CD/DVD to the CMCVAMC FITS to scan for viruses or malware. Once approved this data will be uploaded to secure password protected CHERP/CEPACT server.

   5.1. Informed Consent discloses PHI transported or transmitted off-site. YES☒ NO☐ ☐N/A

   5.2. HIPAA Authorization discloses entities to whom PHI will be transported or transmitted. ☒YES ☐NO ☐N/A

      5.2.1. List all entities or individuals outside CMCVAMC to whom data is to be disclosed, and the justification for such disclosure and the authority. University of Pennsylvania Biomedical Informatics -- Way to Health, Vitality GlowCaps

This project requires the use of electronic medication monitoring devices that records adherence information for the researcher and also sends reminders and adherence reports to the patient and a designated family member/friend or peer mentor. Electronic pill bottle caps are the preferred method among medical researchers to capture medication adherence data. In addition, the project requires IT infrastructure to collect patient surveys via a web based interface and integrate the survey data with medical adherence data. Due to the confidential nature of VA patient data, the service must provide a high level of data security acceptable for government funded medical studies.

   5.3. If yes, list the exact data that will be transmitted. **Name, Home address, telephone, DOB, Sex, Race, survey information, adherence and Medication list.**

   5.4. If yes, explain how data will be protected during transmission outside of CMCVAMC. **Transfer of information will happen via use of encrypted file and log-in through a secure server setup through the Way to Health platform**

   5.5. Off-site, provide exact location **The data center is housed in the Information Systems and Computing at 3401 Walnut Street Corporal Michael J. Crescenz, PA** (If off-site, attach at least one of the following.)

      5.5.1. Data Use/Transfer Agreement ☐YES ☐NO ☒N/A

5.5.2. Off-Site Storage/Transfer of Research Data ☒YES ☐NO ☐N/A
5.5.3. Memorandum of Understanding ☐YES ☐NO ☒N/A
5.5.4. *(Note: VA data disclosed to a non-VA investigator at an academic affiliate for research purposes needs to be approved by the Under Secretary of Health or designee.)*

6. List who is to have access to the data and how they are to access it (anyone who has access to the data is responsible for its security). **Judith A. Long, MD who is the Principal Investigator, the statistician and the program specialist.**

7. Describe who is to have access and be responsible for the security of the information (e.g., the Coordinating Center, the statistician, and PI who has ultimate responsibility). **Responsibility for the information security will be maintained by the PI. Hard copy-based research data will be stored at the Corporal Michael J. Crescenz VA Medical Center Annex, (file room) in a filing cabinet. This room is located at CHERP, which is secured by a lock and key, and the filing cabinet containing the data will be secured by lock and key. Paper records that are actively in use will be held in the Corporal Michael J. Crescenz VA Medical Center Annex PROMISE (suite 200) on the second floor, in a key-locked filing cabinet behind an electronically locked entrance and a key-locked door.**

The University of Pennsylvania Biomedical Informatics (BMIC) will be the hub for the hardware and database infrastructure for the Way to Health Platform. All data is stored on the secure/firewalled servers for the BMIC Data Center, in data files that will be protected by multiple password layers. These data servers are maintained in a guarded facility behind several locked doors, with very limited physical access rights. They are also cyber-protected by extensive firewalls and multiple layers of communication encryption.

Each investigator and staff member involved in the proposed study will sign and adhere to a Standard Operating Procedure for managing participant data through the WTH platform and has participated in required IRB/HIPAA compliance training. We will also continue to make use of password protection programs for all computerized records. In no instances will identifying information be publicly disclosed. Prior to conducting any analyses, all identifiers (e.g., names, medical record numbers, health plan enrollee numbers, birth dates, etc.) will be removed. Results from this part of the investigation will be reported in aggregate

8. Provide mechanisms used to account for the information. **The PI will have oversight over all information. Hard copy-based research data will be stored at the Corporal Michael J. Crescenz VA Medical Center Annex, (file room) in a filing cabinet. This room is located at CHERP, which is secured by a lock and key, and the filing cabinet containing the data will be secured by lock and key. Paper records that are actively in use will be held in the Corporal Michael J. Crescenz VA Medical Center Annex PROMISE (suite 200) on the second floor, in a key-locked filing cabinet behind an electronically locked entrance and a key-locked door.**

University of Pennsylvania informatics system managers will carefully control electronic access rights. They will keep log records and time-stamped information on people accessing the data through the WTH platform

9. Give security measures that must be in place to protect individually identifiable information if collected or used. **All identifiable information collected by hard copy paper-based data will be kept on VA property under lock and key in the cabinet located in the locked file room. All electronic data will have limited access, granted only to study staff, including the principle investigator and the program specialist under supervision of the database administrator.**

To assure that patient, physician and other informant confidentiality is preserved, individual identifiers (such as name and address) are stored in a single password protected system that is accessible only to study research, analysis and IT staff. This system is hosted on site at The University of Pennsylvania (UPenn) and is protected by a secure firewall. Once a participant is in this system, they will be given a unique study identification number (ID). Any datasets and computer files that leave the firewall will be stripped of all identifiers and individuals will be referred to by their study ID. The study ID will also be used on all analytical files.

Additionally, any information that leaves this system to communicate with third party data sources (biometrics devices, survey software, etc.) will be stripped of any identifiers and transmitted in encrypted format. The same unique study ID will be used to link these outside data to the participants.

The Way to Health (WTH) Research Data Center staff is responsible for preventing unauthorized access to the trial participant tracking system database. It is important to note that the Way to Health database server and individual study databases have never been compromised as a result of the extremely rigorous and secure network firewall technologies. The secure servers are located in a specially designed, highly secured facility at UPenn with dedicated uninterrupted power supply and strictly limited access. The study will utilize a client-server deployed Data Management System (DMS) rather than a 'Store and Forward' database configuration, obviating research site database security concerns. Confidential participant information will be entered into the database. If this information exists on paper CRFs, it will be filed under lock and key, with generation of a participant ID. Thereafter, confidential information will be made available to authorized users only as specifically needed. No one can gain access to an individual MySQL database table unless explicitly granted a user ID, password, and specific access. Even those with user names and passwords cannot gain access to the tables that contain the identifying participant information.

No results will be reported in a personally identifiable manner. All tracking system data will be password-protected with several levels of protection. The first will allow access to the operating system of the computer. The second will allow access to the basic menus of the integrated system; within certain menu options, such as database browsing, a third password will be required. Our prior research employing similar precautions has demonstrated that these techniques are very successful in assuring the protection of subjects.

The same procedure used for the analysis of automated data sources to ensure protection of patient information will be used for the survey data, in that patient identifiers will be used only for linkage purposes or to contact patients. The study identification number, and not other identifying information, will be used on all data collection instruments. All study staff will be reminded to appreciate the confidential nature of the data collected and contained in these databases.

Each investigator and staff member involved in the proposed study will sign and adhere to a Standard Operating Procedure for managing participant data through the WTH platform and has participated in required IRB/HIPAA compliance training. We will also continue to make use of password protection programs for all computerized records. In no instances will identifying information be publicly disclosed. Prior to conducting any analyses, all identifiers (e.g., names, medical record numbers, health plan enrollee numbers, birth dates, etc.) will be removed. Results from this part of the investigation will be reported in aggregate.

10. How and to whom a suspected or confirmed loss of VA information is to be reported. **CMCVAMC Information Security Officer and Privacy Officer will be notified within one hour of the improper use or disclosure, as well as the IRB, Associate Chief of Staff for Research (ACOS/R) and Research Compliance Officer.**

11. Identify any circumstances that may warrant special safeguards to protect the rights and welfare of subjects who are likely to be vulnerable including, but not limited to, those subjects who may be susceptible to coercion or undue influence, and describe appropriate actions to provide such safeguards. **Not applicable. We will not be recruiting patients who are considered vulnerable populations or those susceptible to coercion or undue influence.**

12. Electronic PHI will be stored on the following:
    - 12.1. CMCVAMC desktop computer with password protection and/or encryption. ☒YES ☐ NO ☐N/A
      - 12.1.1. If yes, identify where the desktop is located. **The CMCVAMC desktops are password protected, but not encrypted. The desktops will be located at Corporal Michael J. Crescenz VAMC or the Corporal Michael J. Crescenz VAMC Annex. Electronic PHI will be stored on VA servers behind the VA fire wall and will not be removed.**
    - 12.2. CMCVAMC secure server. ☒YES ☐NO ☐N/A
      - 12.2.1. If yes, identify the CMCVAMC server. **VISN 4, CMCVAMC/CHERP.CHERPNAS is a networked attached storage server inside the VA network. It provides space to store electronic data for all CHERP/CEPACT-related studies. It runs intel xeon 5600 series 3GHz (64 bit) CPUs with 48GB RAM and 146GB hard drive.**
      - 12.2.2. External drive that is password protected and/or encrypted. ☐YES ☒NO ☐N/A
        - 12.2.2.1. If yes, identify the external drive.
    - 12.3. Off-Site server ☒YES ☐NO ☐N/A (If off-site, attach at least one of the following.)
      - 12.3.1. Provide exact location and the name of the off-site server. **The data stored at University of Pennsylvania Biomedical Informatics Consortium (BMIC). The data center is housed in the Information Systems and Computing at 3401 Walnut Street.**
      - 12.3.2. Data Use/Transfer Agreement ☐YES ☐NO ☐N/A
      - 12.3.3. Off-Site Storage/Transfer of Research Data ☒YES ☐NO ☐N/A
      - 12.3.4. Memorandum of Understanding ☐YES ☐NO ☒N/A

13. Explain how data is to be transported or transmitted from one location to another. **The data collected for Way to Health based studies is stored in MySQL databases on a BMIC-operated blade server environment devoted specifically to Way to Health. The data center is housed in the Information Systems and Computing at 3401 Walnut Street. All data are stored in a single relational database, allowing researchers to correct mistakes. Every SQL transaction, including accessing and changing data is logged for auditing purposes. Data will be entered into the database through encrypted files and password-protected log-in into the Way to Health Platform.**

    An amendment was submitted in August 2014, to transfer coded datasets from the WTH to the CMCVAMC medical center. To do this, as outlined in the information security section, the WTH Research Coordinator will download the coded data from the WTH server onto the encrypted CD/DVD. The Program Specialist and/or PI will transfer this CD/DVD to the CMCVAMC FITS to scan for viruses or malware. Once approved this data will be uploaded to secure password protected CHERP/CEPACT server.

14. Informed Consent discloses PHI transported or transmitted off-site. ☒YES ☐NO ☐N/A

15. HIPAA Authorization discloses entities to whom PHI will be transported or transmitted. ☒YES ☐NO ☐N/A

16. List all entities or individuals outside CMCVAMC to whom data is to be disclosed, and the justification for such disclosure and the authority. **University of Pennsylvania _ Biomedical Informatics, Vitality GlowCaps This project requires the use of electronic medication monitoring devices that records adherence information for the researcher and also sends reminders and adherence reports to the patient and a designated family member/friend or peer mentor. Electronic pill bottle caps are the preferred method among medical researchers to capture medication adherence data. In addition, the project requires IT infrastructure to collect patient surveys via a web based interface and integrate the survey data with medical adherence data. Due to the confidential nature of VA patient data, the service must provide a high level of data security acceptable for government funded medical studies.**

17. Clarify what protection exists for a database. **Access is limited to study staff by the database administrator**
    17.1. Data is stored:
        17.1.1. With identifiers - ☒YES ☐NO
        17.1.2. Coded - ☒YES ☐NO
        17.1.3. De-Identified - ☐YES ☒NO
        17.1.4. Provide the exact list of identifiers that will be stored. **Name, social security number, phone number, address, date of birth, dates of GlowCap openings.**

18. Describe the plan for protecting research data from improper use or disclosure. **Only IRB approved study personnel will have access to study related materials. Study related materials will be kept in password protected files on a secure server. Paper files will be kept on the premises in locked filing cabinets.**
    18.1. The Investigator must notify the Information Security Officer, Privacy Officer, IRB, Associate Chief of Staff for Research and Research Compliance Officer within one hour of the improper use or disclosure.

19. Is there a plan to apply for a Certificate of Confidentiality? ☐YES ☐NO ☒N/A
    19.1. If yes, provide a copy of the certificate with this application or to the IRB Office as soon as received.

20. **Record Retention**:
    20.1. The required records, including the investigator's research records, must be retained until disposition instructions are approved by the National Archives and Records Administration and are published in VHA's Records Control Schedule (RCS 10-1). VHA Handbook 1200.05 §26.h
    20.2. Until a schedule for local research records is published, ALL records including identifiers must be retained." ORO/ORD Guidance on Informed Consent Form Modifications Addressing VA Record Retention Requirements (July 23, 2009)
    20.3. If there are additional procedures for record retention, explain further. **None**

Z. **Qualification of the Investigators**

Provide a description of the qualifications of each investigator/co-investigator and their specific role in the study. **The research conducted in this proposal will be led by Judith A. Long, MD (Principal Investigator). She is the Chief of General Internal Medicine and Assistant Professor of Medicine at University of Pennsylvania and Corporal Michael J. Crescenz VA Medical Center. In addition to being core faculty at Center for Health Equity Research and Promotion (VA CHERP) she is Associate Director of Center for Evaluation of Patient Aligned Care Team (CEPACT). She has experience conducting primary**

intervention trials at the Corporal Michael J. Crescenz VA and in the development of peer mentor models to improve adherence to medications.

Kevin Volpp MD PhD (Co-investigator) is a general internist and Professor of Medicine at University of Pennsylvania and Corporal Michael J. Crescenz VA Medical Center. He is the founding Director of the Center for Health Incentives and Behavioral Economics (CHIBE) and a core faculty member at VA CHERP.

Judd Kessler PhD (Co-investigator) is an Assistant Professor of Business Economics and Public Policy at the Wharton School at University of Pennsylvania.

Steven Marcus PhD (Co-Investigator) is an epidemiologist, statistician, computer scientist at the VA CHERP and Associate Professor in the School of Social Policy and Practice at the University of Pennsylvania.

David Asch MD MBA (Co-Investigator) is a general internist and Professor of Medicine at University of Pennsylvania, executive director of Penn Medicine Center for Health Care Innovation, and former director of VA CHERP.

1. If applicable, the Principal Investigator must identify a qualified clinician to be responsible for all study related healthcare decisions. **There will be no study related healthcare decisions. Dr. Long will review all serious adverse events and determine if they are potentially study related.**

2. PI should submit a current, dated CV with each new initial review. **Please see attached CV for Judith A. Long, MD.**