Protocol Template for Prospective Investigator Initiated Studies involving patient contact

GENERAL INSTRUCTIONS

A complete description of the planned research (i.e., protocol) must be submitted with initial applications for IRB review (if submitting for expedited or full committee review). The research protocol should provide the information needed for reviewers to determine that the regulatory and Human Research Protection Program (HRPP) policy requirements have been met. There is no required format or template; different sections and formatting may be used, provided the necessary information is included. Please use this as a guide.

Note that **text in RED are instructions and points to consider;** do not use the RED text as an outline. Please **delete the RED text and complete the section with study appropriate information**.

1. This protocol template is to be used for studies that involve patient contact. Typically, these will be prospective studies. A prospective study is one that will generate some or all of the necessary data, documents or specimens after IRB approval, i.e. generating new data and samples.
2. Text that is **not** in **RED** is provided as **example** and may be kept or modified as necessary.
3. **If a section is not applicable, write "Not Applicable" under the header or delete the section.**
4. If you are adding sections, use heading font in "Styles" list found in the Home tab. This will ensure title appears in the table of contents.
5. To update the Table of Contents, move cursor to the Table (text will turn grey) and hit F9. Choose option to update entire table.

Version: MM/DD/YYYY (Very important to update the version date with each revision)

6. To insert references, use RefWorks application or the Insert/References/Endnotes function in Word. Contact Health Sciences Library for RefWorks training. http://geisinger.libguides.com/hslhome
7. Run spell check prior to submitting.
8. For assistance with sample size or statistical analysis plan, contact the Biostatistics Core (570-214-8688, biostatistics@geisinger.edu).*
9. For assistance with pulling data from Epic, or one of the Geisinger data bases, or creating a REDCap database, contact the Phenomic Analytics and Clinical Data Core (PACDC) by submitting a PACDC Service Request*: https://redcap.geisinger.org/surveys/?s=W99LCPWMFF
10. If your study will use MyCode data or samples, you must obtain approval from the MyCode governing board prior to IRB submission. Please reach out to Lance Adams to request the current MyCode forms: 1) MyCode Sample and Data Access Request and 2) DiscovEHR Project Concept Request Form. Submit the completed forms to him at ljadams1@geisinger.edu. Once approved, submit your MyCode approval documents to the IRB.*
11. If your study will use Geisinger Health Plan (GHP) data, you must obtain approval from GHP. For datasets that contain Protected Health Information (PHI), you must also execute a data sharing agreement between Geisinger Clinic and GHP. Submit the GHP Proposal Form and supporting documents to researchcontracts@geisinger.edu to start the process. Once approved, submit your GHP approval and Proposal Form to the IRB.*
12. Studies that include electronic transmission of patient data or institutional proprietary information will require Information Security Office and Privacy Office assessment and approval. These approvals will need to be included in the IRB application.
    a. Information Security Office: INFOSECURITY@geisinger.edu

b. Privacy Office: SYSTEMPRIVACYOFFICE@geisinger.edu and Deb Beaver @ dkbeaver@geisinger.edu.

13. Recruitment materials used for your study that include the Geisinger logo will need to be reviewed and approved by the Marketing team. Contact Megan Epler and Jeff Rowe (meepler@geisinger.edu and jfrowe@geisinger.edu) for **internal communications** and Matt Van Stone (mrvanstone1@geisinger.edu) for **external communications**.

14. Submit the protocol using the Geisinger iMedRIS electronic web-based IRB application https://irb.geisinger.edu/ and any other required information to the IRB.*

* If you are using project management support from the Investigator Initiated Research Operations group, they can manage your IRB submission, data approvals and coordination with other research support cores. Contact IIRO: IIRO@geisinger.edu

Please remove these 3 pages from your protocol.

GENERAL INFORMATION:

- Protocol Number is the IRB number assigned in iRIS
- Title of the Research Proposal
- Name of Principal Investigator
- Contact Information of Principal Investigator
- Co-Investigators can be listed on the IRB application in iRIS (recommendation is to not list Co-Investigators on the protocol to reduce the need for protocol revisions)
- Version Date (to be updated with changes)

Research Protocol - ####-#### (insert protocol number)

Insert Title

Version: DD MM YYYY

Principal Investigator: Name
Address
Telephone

TABLE OF CONTENTS (REMOVE IF LESS THAN 10 PAGES)

1 ABBREVIATIONS USED IN THE PROTOCOL

List all abbreviations used in alphabetical order or in the order referenced in the protocol; all abbreviations should be defined at first use and then used consistently thereafter.

Abbreviation	Term
AE	Adverse Event
CRF	Case Report Form
DMC	Data Monitoring Committee
EHR	Electronic Health Record
GIRB	Geisinger Institutional Review Board
HIPAA	Health Insurance Portability and Accountability Act
IRB	Institutional Review Board
MRN	Medical Record Number
PACDC	Phenomic Analytics and Clinical Data Core
PHI	Protected Health Information
PI	Principal Investigator
SAE	Serious Adverse Event

2 ABSTRACT

Every protocol should include an abstract.

Recommended Length: < 1 page

The abstract should be a summary of the most important aspects of the protocol. Detailed information should be put in the body of the protocol. For example, the synopsis should only contain the main inclusion criteria, while the body of the protocol should contain the complete list.

Be sure to define **study type**: Choose Interventional (i.e., experimental studies in humans to investigate the safety and/or efficacy of a drug, gene therapy, vaccine, behavior, device, or procedure) or Observational (i.e., studies in humans that record specific events occurring in a defined population without any significant clinical intervention by the researcher).

3 BACKGROUND AND SIGNIFICANCE

The **purpose** of the background and significance section is to state the problem to be investigated, the rationale for the proposed research, the current state of knowledge relevant to the proposal and the potential contribution of this research to the problem(s) addressed.

Summarize and synthesize the available research (including published data) to provide justification for the study. Evaluate prior research for relevance to the research question under study. When the proposed research is the first of its type to involve human participants, the results of relevant animal studies must be included. Discuss the anticipated results and potential pitfalls. Describe the significance of the research including potential benefit for individual participants or society at large. Discuss how public health and social welfare might be enhanced.

Recommended Length: Approximately 2-3 pages

The background and significance section should cover:

- The rationale for the proposed project
- The state of existing knowledge (including standard clinical practices at your institution), literature citations, and highlights of relevant data
- Gaps that the project is intended to fill
- Disease/diagnosis
- Population to be studied
- Endpoints

4 HYPOTHESIS AND SPECIFIC AIMS

The purpose of the study (research questions and/or study objectives) should be clearly stated. In experimental designs, objectives will be stated as hypotheses to be tested and specific aims.

The purpose of the hypothesis and specific aims is to describe concisely and realistically what the proposed research is intended to accomplish. Think of your hypothesis as the foundation of your application - the conceptual underpinning on which the entire structure rests. Choose an important, testable, focused hypothesis that increases understanding of biologic processes,

diseases, treatments, or preventions and is based on previous research. Your Specific Aims state what you plan to accomplish to test your hypothesis. As you prepare your protocol, you will design experiments that support your Specific Aims, linking them to the Study Design section.

If you are working with a Biostatistician, reach out to him/her for assistance with this section.

Recommended Length: The recommended length of the specific aims is ≤ 1 page.

4.1 Hypothesis

State hypothesis. Make sure it is understandable, testable and adequately supported by citations in the Background and by data in the Preliminary Results Sections. Example: [Procedure B] will result in significantly fewer [clinical outcomes] compared with [Procedure A].

4.2 Specific Aim 1

State aim 1. Example: To compare [clinical outcome] using [procedure A] and [procedure B].

4.3 Specific Aim 2

State aim 2 as appropriate.

Add new level 2 header for each specific aim

5 PRELIMINARY DATA (IF APPLICABLE)

Include pilot, unpublished or theoretical data not included in background.

6 STUDY DESIGN

6.1 Description

The research design should be identified and should be appropriate to answer the research question(s) under study. Describe the type of research proposed (e.g., experimental, correlational, survey, qualitative) and specific study design that will be used (e.g., pre-test /post-test control group design, cross-sectional design, prospective longitudinal cohort design, phase III double-blind randomized control group design).

e.g., This is a randomized, prospective….

If applicable, include randomization scheme, e.g., Qualifying subjects will be randomized 1:1 to receive either Treatment A or Treatment B.

e.g., This is a prospective collection of quality of life data using standard questionnaires…

6.2 Study Population

Target Population: Describe the general participant population such as age range, gender and ethnic background (specific inclusion/exclusion criteria will be provided below).

6.2.1 Approximate Number of Subjects

Define enrollment for the study and provide the number of participants planned to be enrolled.

Approximately X Geisinger subjects will participate in this study.

If study is a multi-center study, also state the number to be enrolled at all sites.
If Applicable - Describe the approximate number of subjects in each group.

6.2.2 Inclusion Criteria

Inclusion/Exclusion Criteria: List the inclusion/exclusion criteria (characteristics that people must have to be included or unable to participate in the research).

Inclusion criteria should be used to define your study population. Be aware of confusing negatives in the inclusion criteria. For example, "Patients who have not received heparin for ≥3 hours before surgery" might be better in the list of exclusion criteria as "Patients who have received heparin <3 hours before surgery". In general, an inclusion with "no" or "not" might be appropriately restated as an exclusion criterion.

Use a bulleted list to outline criteria, e.g.:

- Hospitalized male or female patients
- ≥18 years of age
- Able and willing to provide consent.

6.2.3 Exclusion Criteria

Exclusion criteria should be used to clarify what subset of patients will not be included in the study, and to define study population further from those who might meet inclusion criteria, but who are still not eligible for inclusion in the study. Be aware of confusing negatives in exclusion criteria. For example, "Patients who have had no more than 2 episodes of major hypoglycemia" in exclusion indicates you only want to include those who have had more than 2 episodes – if this is the case, better to put "Patients with more than 2 episodes of major hypoglycemia" in inclusion criteria to reduce confusion. If, on the other hand, the intention is to exclude those with more than 2 episodes, should be restated as "Patients with more than 2 episodes of major hypoglycemia" in exclusion criteria.

Do not restate negative inclusion criteria. For example, if you have "Patients who are able to provide consent" in inclusion, you do not need, "Patients who are not able to give consent" in exclusion. Use a bulleted list as you did for the inclusion criteria.

6.3 Recruitment

Describe the plan (when, where, how) to identify potential participants, including database/ medical record review if applicable. Explain who will be identifying and reviewing potential participants. Describe how the population will be identified and how initial contact will be made.

- Outline how you are getting your recruitment list. Provide information regarding access to the population (approvals to recruit when necessary).
- Specify if any advertising/recruitment materials will be used (e.g., print ad, physician letter, telephone script, etc.). Upload and attach recruitment materials with your iRIS submission. Materials that will be given to or seen by patients may require review and approval from Marketing and Communications prior to IRB submission (M&C: 570-271-6435).
- Examples of recruitment (avoid using the names of specific study team members when describing study processes in the protocol):
    - PI/study team will recruit his/her/their own employees/patients/students.
    - PI/study team will recruit individuals unknown to them (e.g., social network, posting flyers, direct approach).
    - PI/study team will send letters to colleagues asking for referrals.

- PI/study team will send letters to potential participants.
- Physicians not affiliated with the study can refer patients to your study (physician referral).

- Describe the screening process (confirming that potential participants meet inclusion/exclusion criteria). Explain what happens with screen failures and any data obtained from screen failures, if applicable.

6.4 Study Duration

Include a timeline for participant evaluations and the duration of participant participation.

6.4.1 Approximate Duration of Subject Participation

Subjects will participate in the study for approximately duration. This includes specific duration of each period, including any follow-up period (if applicable).

6.4.2 Approximate Duration of Study

This study will be completed in approximately duration. The end of the study is the last visit of the last subject or end of collection of data from the patient's electronic health record. OR Define the end of the study and provide the reason it is not the last visit of the last subject.

6.5 Procedures

Provide a thorough description of all study procedures, assessments and participant activities in a sequential format. You may want to describe procedures required at each study visit, if applicable. All interventions and interactions with patients must be described. Include methods for data collection. Describe how information will be captured (e.g., audio or video recorded, observations, note taking, etc.). Upload data collection documents/scripts/etc. in iRIS as supporting documents with your submission.

The following examples of information to include should be in paragraph format:

- **Description of processes based on type of study**
  - **Behavioral Intervention Studies**
    - Describe how the behavioral intervention with be developed or adapted for use.
    - Describe how the intervention will be administered.
    - Describe what the participant will be asked to do.
  - **Survey/Interview Studies**
    - Describe survey/interview methodology.
    - Describe development or selection of questionnaire, including whether it is validated (include as appendices).
  - **Focus Groups**
    - Describe the process/ design of the focus group(s).
    - Describe whether information drawn from the focus group will be shared with group participants.
  - **Studies that Use Medical Records, Data or Biospecimens**
    - Identify the sources of research material.
    - Describe what information (records, data, etc.) will be recorded and used.
    - Detail whether the data and/or specimens are identifiable and list the exact HIPAA identifiers to be accessed and used.
    - Describe how the data will be stored.
    - Describe any approvals or permissions that are required for obtaining existing data, records or specimens, as applicable.
    - Describe any specimens to be collected and the procedure for collecting and using them.
    - Describe any plans for retaining specimens including how long they will be kept, how they will be stored, who will have access, and the tracking labeling system to be used.
    - If data or specimens will be banked for future use, describe the process for providing researchers access.
  - **Studies Involving use of Medical Devices or Drugs**
    - Provide product details (name, manufacturer, etc.).

        - Describe route of administration, dosing, dosage regimen and duration.
        - State whether device or drug is FDA approved for the purpose being studied.
- **Participant Compensation**
    - Describe any compensation to participants including amounts, payment schedule and type.
- **Participant Withdrawal**
    - Describe procedures that will be followed when participants withdraw during data collection. Describe the process for participants to withdraw from the study after participation is complete, if applicable.
    - Describe conditions under which the investigators might withdraw a participant from the study.
    - Describe what will happen to data obtained from withdrawn participants.

6.5.1 Study Time and Events Table **(If Applicable)**

This table is a sample and may be useful for more complex studies but is not required. Modify for your study.

SAMPLE ONLY **Study Procedures**	**Days -21 to -1**	**Day 1**	**Day 7**	**Day 14**	**Day 21**	**Follow-up Visit**
Study Interval	Screening	Active Phase				Follow-up
Informed consent	X					
Demographics	X					
Medical history	X					
HIV, hepatitis B, C	X	X				
Urine drug screen	X					
Serum pregnancy	X					X
Weight	X					X
Physical examination	X	X				X
Vital signs	X	X	X	X	X	X
Laboratory evaluation	X	X	X	X	X	X
PK blood sample collection	X	X	X	X	X	X
Electrocardiogram	X	X	X	X	X	X
Questionnaires	X	X	X	X	X	X
Test article administration		X----------X				
Concomitant medications		X----------X				
Adverse events[a]	X----------X					

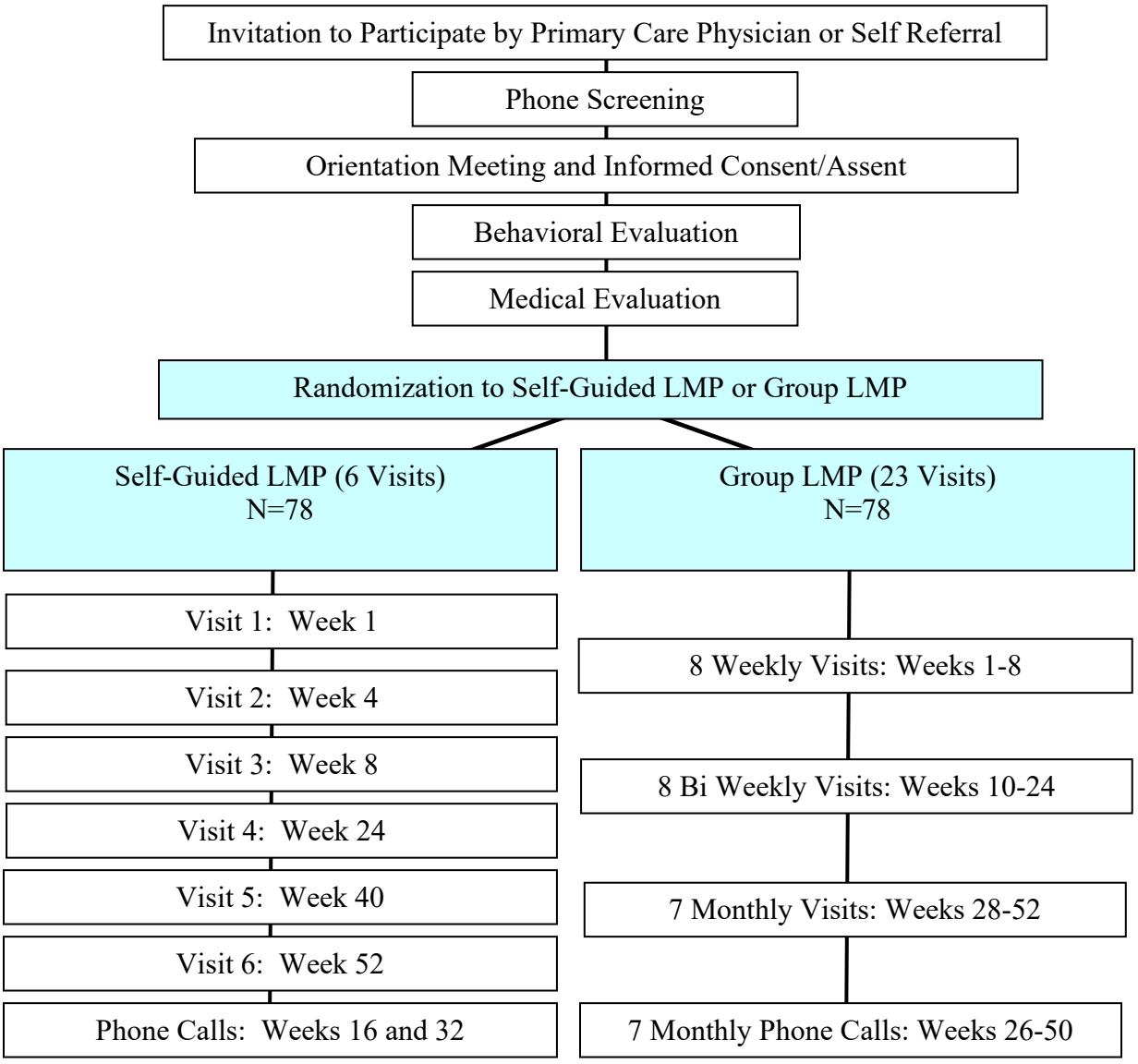
a. From the signing of the informed consent form to specify end of period.
HIV=human immunodeficiency virus; PK=pharmacokinetic.

The table should provide the time points for the procedures. To keep the footnotes clear and brief, the explanatory information about procedures should be in the body of the protocol and not in the footnotes whenever possible. Avoid abbreviations in the flowchart, or if they must be used, spell them out below the flowchart as shown above.

6.5.2 Study Flow Diagram (If Applicable)

This is a sample flow diagram and may be useful but is not required. Please note, it may be requested during your protocol review if it is felt to be needed. Modify for your study.

Figure 6.5.2-X: Study Flow Diagram **SAMPLE**



6.6 Primary Endpoints

The primary endpoint will be XX. Justify your choice of endpoint.

6.7 Secondary Endpoints

Secondary endpoints include XX.

6.8 Statistics

State who will perform the statistical analyses (e.g., Biostatistics Core). If you are working with a Biostatistician, reach out to him/her for assistance with this section.

6.8.1 Statistical Analysis Plan

Describe the statistical analysis plan:

- Outline analysis methods for each Specific Aim.
- If a study uses qualitative rather than quantitative methods, describe qualitative analysis.
- Describe how the data will be examined and statistically analyzed to answer study objectives.
- Describe randomization scheme in detail if applicable.

6.8.2 Statistical Power and Sample Size Considerations

Provide a brief sample size calculation or description of sample size calculation. Include methods and assumptions such as loss to follow-up, anticipated evaluability rate, power and clinical justification, as appropriate.

6.9 Data and Sample Management

6.9.1 Data Collection and Storage

- **Data Management Procedures and Confidentiality**
    - Describe what will happen with the data (electronic, paper, recordings, etc.) from the time it is collected until the data are permanently de-identified or destroyed.

- If applicable, describe who will have access to the data and how the data will be handled/maintained securely.
- Considerations for securely storing data include:
  - Paper records are locked in a secure location.
  - Electronic records are stored on a password protected or encrypted computer as appropriate based on sensitivity of data.
  - For data sets containing Protected Health Information (PHI), a coding system will be used to store data without identifiers, with the link stored separately.
- Provide specific information regarding where identifiable data and consent forms will be stored.
- If data will be transferred outside of Geisinger, describe procedures for data transfer. Specify where data will be sent. Indicate whether data will be identified or de-identified when transferring.
- Describe how the confidentiality of the study data will be maintained.

As appropriate provide details on how data will be collected and by whom; who creates the case report form (CRF) and/or database; how the data will be entered into the database and by whom; where data will be stored. If you collect PHI, how will the data be stored and will study ID numbers be assigned? If so, where will the "key" be stored? Describe who will have access to PHI (approved study staff and/or any organizations outside of Geisinger Clinic).

Example language:

Only IRB-approved study staff will have access to data collected for this research. Electronic data will be stored on Geisinger's secure network. Any hard copy data will be secured in a locked (area/suite/drawer/cabinet).

Example language if using Phenomic Analytics and Clinical Data Core (PACDC) for data pull:

The data will be pulled by a Phenomic Analytics and Clinical Data Core (PACDC) data broker from an institutional data warehouse. The PACDC broker will compile the final data set and send it in an Excel file to the study team. Once the data set is obtained, the research team will review it for analysis. The resulting analytic file will be stored in a password-protected database on

Geisinger's secure network. Only IRB-approved research team members will have access to the data file. The research team members will review the charts and gather all the needed information. The research team plans to perform manual chart reviews to access any required data elements that are not available through the initial data pull.

Provide an overview of the data collection variables to be collected for the research. **Optional:** Indicate which elements of PHI will be accessed/recorded (e.g., MRN, name, dates, etc.). Be sure to include any sensitive information that will be collected (e.g., mental health data, HIV status, etc.). If you list the PHI elements that will be accessed/recorded in the protocol, be sure that this information is consistent with the informed consent form and the IRB application. If this data is shared externally, these documents must also be consistent with the Data Use Agreement (DUA).

Example language:
The following data, including relevant dates, will be collected:

- Names
- Medical record number
- Date of birth/date of death
- Information relevant to all encounters, admissions/discharges, clinical procedures, medications administered, problem list entries, and lab values
- Baseline demographic variables of patients (age, sex, ethnicity, tobacco use, comorbidities)
- Clinical outcomes and procedural related complications

6.9.2 Sample Collection (If Applicable)

Provide details on the types of biological samples that will be collected and explain the purpose, timing, number of samples, etc. Also indicate who will collect each type of sample, how they will be processed and where will they be stored.

Samples are being collected for purposes related to this research such as purpose(s).

6.9.3 Total Volume of Blood Collected (If Applicable)

The total volume of blood collected from each subject will be approximately X.

6.9.4 Records Retention

Describe plans for destroying the data/samples or other handling once study is completed. Please note the following minimum research record retention requirements:

- Study records must be kept for at least 3 years after study completion.
- Federally-funded study records must be kept as determined by the funding agency.
- Signed consent/authorization, stand-alone authorization forms or documentation of verbal authorization must be kept for 6 years to comply with HIPAA requirements.
- FDA requires studies including investigational drugs or devices must be kept for 2 years after the last marketing approval or withdrawal of approval request.

Example language:

- Records of data/samples generated in the course of this study will/will not be de-identified and will be kept for at least XX years and then destroyed. Prior to destruction, data can be used for other IRB approved research.
- Records of data/samples generated in the course of this study will/will not be de-identified and kept indefinitely and can be used for other IRB approved research.
- Identifiable records of data/samples generated in the course of this study will be kept for at least XX years and then identifying information will be removed. A coded link will/will not be maintained for reidentification.

7 PROTECTION OF HUMAN SUBJECTS

7.1 Informed Consent and HIPAA Authorization

Optional: Consent and HIPAA authorization questions are addressed in the IRB application. If you include a consent and HIPAA authorization section in the protocol, be sure that this information is consistent with the IRB application.

The investigator will provide for the protection of the subjects by following all applicable regulations. The informed consent/authorization form will be submitted to the IRB for review and approval.

Please indicate if any of the following conditions apply to obtaining informed consent/authorization:

- Assent, alteration or waiver of authorization, waiver of consent, waiver of consent, or waiver of documentation of consent.
- Subjects who do not have adequate capacity to give consent.
- Minors who do not have sufficient psychosocial maturity.

Before any procedures specified in this protocol are performed, a subject must: (List may change based on study design – e.g., waiver of documentation of consent.)

- Be informed of all pertinent aspects of the study and all elements of informed consent.
- Be given time to ask questions and time to consider the decision to participate.
- Voluntarily agree to participate in the study.
- Sign and date an IRB-approved informed consent form.

Provide justification if a waiver of consent and/or HIPAA authorization is being requested from the IRB. Example waiver justification language for prospective data collection study with no patient contact:

We are requesting a full waiver of consent and HIPAA authorization for the patients identified in this study. The waiver of consent/authorization does not adversely affect the patients' rights and welfare. The investigator will provide for the protection of the subjects by following all applicable regulations. The proposed study involves data collection for all patients treated or admitted to any Geisinger Clinic hospital/location. The waiver is being requested for both retrospective and prospective data extraction, including PHI. Patient burden would be greatly heightened and, in some cases, impossible if we were required to consent the patient. Some patients that would be included in the retrospective data extraction may have moved away or have died and thus are not reachable for consent. Patients being seen may be lost to follow-up that is, they come in due for emergent care and are not followed in the Geisinger system post-visit or post-surgery. Therefore, their ability to sign a consent/authorization form may be compromised.

If the research study is not all inclusive, then it will have no research worth. For example, meaningful research cannot be conducted on a given health condition if all patients for whom consent could not be obtained were excluded. This would entail a cohort in which patients who died early in the hospital course, who were obtunded without immediate family available, who could not give consent because of delirium, etc., were not included. The resulting data would be fatally flawed and unacceptable by all known peer review standards. Inclusion of the patients in this study is an organizational task. The data collected is already or will be contained in the medical record and the research study represents a scientific ordering and accumulation of existing information.

The scientific and ethical equipoise for waiver of consent/authorization for this and similar type research is that these patients are receiving standard of care treatments and that identifiable data can only be used after IRB approval of this research proposal. The design, inception and consent/authorization waiver for this study has been validated throughout the country in numerous similar types of research studies. Thus, this application does not appear to be novel and does not establish or challenge current methodology or accepted ethical norms.

If requesting a waiver of documentation of consent, please make sure that appropriate measures have been taken to properly address obtaining HIPAA authorization, if it is applicable to your study. Generally, a valid authorization requires the signature and the date of the individual giving the authorization. When requesting a waiver of documentation of consent, if it is not practicable to obtain written HIPAA authorization (i.e. participants are never interacted with in person), then an alteration of HIPAA authorization and request for verbal authorization or a "waiver of documentation of HIPAA authorization" can be made and justified in the protocol.

7.2 Potential Risks/Benefits and Protection of Human Subjects Against Risks

Potential Risks

State any physical, psychological, social, economic, or legal risks and assess their likelihood and seriousness.

- The following examples of information to include should be in paragraph format:
    - Is there a potential for participants to become upset as a result of the research procedures and thus require psychological or medical attention?
    - Is there a potential for emotional stress or fatigue?

- Is there potential for loss of confidentiality and how serious would loss of confidentiality be? Describe the risks related to loss of confidentiality (e.g., loss of insurance or employment, etc.) and the precautions taken to minimize the risks (e.g., password protected files, encryption, locked cabinets). Consider breach of confidentiality or privacy as a risk for all study participants.
- Is there risk of physical harm from the intervention?
- Could the research create potential social stigmatization or legal action by authorities if research information became known outside of the research team?
- Are there potential risks to the participants related to the political, social, or economic context in which they live?
- Are there economic burdens the participants will encounter from participating in the research?

- State the plan for preventing or minimizing risks (e.g., screening to assure appropriate selection of participants, sound research design, de-identification of data, safety monitoring, and reporting).

Example language for precautions taken to minimize risks related to loss of confidentiality:
All electronic study data will be kept in password-protected computer files and hard copy data will be stored in a locked environment that is accessible only to the study team members. Data will be coded by linking a unique study identification number to patients' medical record numbers. Analysis will be performed using the coded data. Only aggregate data without personal identifiers will be included when presenting results or submitting manuscripts for publication.

Benefits

- Describe the potential benefits that individual participants may experience from taking part in the research.
- If there is no direct benefit, acknowledge that and describe the anticipated social benefit to the research.

Example language for studies with no direct benefit:
There will be no direct benefit to patients who are included in this study. We hope that what is learned from this study will help others in the future.

8 SAFETY MONITORING

Remove this section if study is minimal risk.

If your study is considered greater than minimal risk, describe the data and safety monitoring plan for the project and upload any supporting documents in iRIS.

8.1 Adverse Event Reporting (Example language follows; remove as applicable)

Clinical adverse events (AEs) will be monitored throughout the study. All AEs will be reported to the Institutional Review Board (IRB) regardless of whether they are considered study related. The date and time of onset and outcome, course, intensity, action taken, and causality to study treatment will be assessed by the study PI. In the event of a serious AE (SAE), this will be reported to the Geisinger IRB (GIRB) according to the GIRB guidelines. All other AEs will be summarized and submitted to GIRB during continuing review.

8.2 Definitions

An **adverse event** (AE) is any untoward, undesired, or unplanned event in the form of signs, symptoms, disease, or laboratory or physiologic observations occurring in a person given a test article or in a clinical study. The event does not need to be causally related to the test article or clinical study.

(Include as applicable to study)

An AE includes, but is not limited to, the following:

- Any clinically significant worsening of a preexisting condition.
- An AE occurring from overdose of a test article, whether accidental or intentional. Define overdose for each test article here or in the Overdose section. Overdose is a dose greater than that specified in the protocol. OR Overdose is a dose greater than that specified in the investigator's brochure/label. OR define overdose.
- An AE occurring from abuse (e.g., use for nonclinical reasons) of a test article.
- An AE that has been associated with the discontinuation of the use of a test article.
- For reports from post-marketing studies, any failure of expected pharmacologic action of a test article. For over-the-counter products, the recommended daily dose must be administered before failure of expected pharmacologic action can be attributed.

A **serious adverse event** (SAE) is an AE that:

- Results in death.
- Is life-threatening (see below).
- Requires inpatient hospitalization or prolongation of an existing hospitalization (see below).
- Results in a persistent or significant disability or incapacity (see below).
- Results in cancer.
- Results in a congenital anomaly or birth defect.
- Additionally, important medical events that may not result in death, be life-threatening, or require hospitalization may be considered SAEs when, based on appropriate medical judgment, they may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in hospitalization, or development of drug dependency or drug abuse.

Life-threatening refers to immediate risk of death as the event occurred per the reporter. A life-threatening experience does not include an experience, had it occurred in a more severe form, might have caused death, but as it actually occurred, did not create an immediate risk of death. For example, hepatitis that resolved without evidence of hepatic failure would not be considered life-threatening, even though hepatitis of a more severe nature can be fatal. Similarly, an allergic reaction resulting in angioedema of the face would not be life-threatening, even though angioedema of the larynx, allergic bronchospasm, or anaphylaxis can be fatal.

Hospitalization is official admission to a hospital. Hospitalization or prolongation of a hospitalization constitutes criteria for an AE to be serious; however, it is not in itself considered an SAE. In absence of an AE, a hospitalization or prolongation of a hospitalization should not be reported as an SAE by the participating investigator. This is the case in the following situations:

- The hospitalization or prolongation of hospitalization is needed for a procedure required by the protocol.
- The hospitalization or prolongation of hospitalization is part of a routine procedure followed by the center (e.g., stent removal after surgery). This should be recorded in the study file.

In addition, a hospitalization for a preexisting condition that has not worsened does not constitute an SAE.

Disability is defined as a substantial disruption in a person's ability to conduct normal life functions.

If there is any doubt about whether the information constitutes an SAE, the information is treated as an SAE.

A **protocol-related adverse event** is an AE occurring during a clinical study that is not related to the test article but is considered by the investigator or the medical monitor (or designee) to be related to the research conditions, i.e., related to the fact that a subject is participating in the study. For example, a protocol-related AE may be an untoward event occurring during a washout period or an event related to a medical procedure required by the protocol.

Other Reportable Information. Certain information, although not considered an SAE, must be recorded, reported, and followed up as indicated for an SAE. This includes:

- Pregnancy exposure to a test article, except for exposure to prenatal vitamins. If a pregnancy is confirmed, use of the test article must be discontinued immediately. Information about pregnancy exposure includes the entire course of pregnancy and delivery, and perinatal and neonatal outcomes, even if there are no abnormal findings. Both maternal and paternal exposure are considered other reportable information. For exposure involving the female partner of a male subject, the necessary information must be collected from the subject, while respecting the confidentiality of the partner.
- Lactation exposure to a test article with or without an AE.
- Overdose of a test article as specified in this protocol with or without an AE. Baby formula overdoses without any AEs are excluded.
- Inadvertent or accidental exposure to a test article with or without an AE.

8.3 Recording and Reporting

A subject's AEs and SAEs will be recorded and reported from the signing of the informed consent form to specify end of period in accordance with GIRB policy guidelines.

If a specific adverse event is expected, include follow-up procedures for that event. Describe any additional care for subjects after their participation in the study has ended if it differs from what is normally expected given the subject's medical condition.

8.4 Serious Adverse Event Reporting

The PI will notify GIRB of all study SAEs in accordance with policy guidelines. If an SAE has not resolved at the time of the initial report, a follow-up report including all relevant new or reassessed information (e.g., concomitant medication, medical history) will be submitted to GIRB. An SAE will be followed until either resolved or stabilized.

8.5 Data Monitoring Plan

This section can be removed from any protocols for studies that are minimal risk.

A Data Monitoring Committee (DMC) should be established for controlled trials with mortality or major morbidity as a primary or secondary endpoint. They may also be helpful in settings where trial participants may be at elevated risk of such outcomes even if the study intervention addresses lesser outcomes such as relief of symptoms. Refer to NIH guidelines: http://www.drugabuse.gov/Funding/DSMBSOP.html

Describe risks to participants and plans to mitigate those risks (e.g., close monitoring, adverse event reporting, PI review of safety data).

9 PUBLICATION PLAN (OPTIONAL)

You may choose to provide plans for meeting abstract submissions, grant applications, and/or journal publications.

Example language:

We plan to submit a scientific abstract to upcoming meetings and to publish the data as a manuscript in a peer-reviewed journal.

10 REFERENCES

Include a reference list of literature cited to support the protocol

Citation format from American Medical Association (AMA) Manual of Style, 9th edition shown below – may be modified based on requirements/preference. Use either RefWorks or Insert/Reference/Endnote function in Word to add references.

Contact Health Sciences Library for RefWorks training. http://geisinger.libguides.com/hslhome

[1] **Book - single author**

Shepard TH. Catalog of Teratogenic Agents. 7th ed. Baltimore, Md: Johns Hopkins Press; 1992.

[2] **Book - more than one author (list all authors if six or less, otherwise list first three followed by "et al.")**

Baselt RC, Cravey RH. Disposition of Toxic Drugs and Chemicals in Man. 4th ed. Foster City, Calif: Chemical Toxicology Institute; 1995.

[3] **Book - with editors**

Armitage JO, Antman KH, eds. High-dose Cancer Therapy: Pharmacology, Hematopoietins, Stem Cells. Baltimore, Md: Williams & Wilkins; 1995.

[4] **Chapter from a book**

Degner LF, McWilliams ME. Challenges in conducting cross-national nursing research. In: Fitzpatrick JJ, Stevenson JS, Polis NS, eds. Nursing Research and its Utilization: International State of the Science. New York, NY: Springer; 1994:211-215.

[5] **Article from journal - single author**

Moldofsky H. Sleep, neuroimmune and neuroendocrine functions in fibromyalgia and chronic fatigue syndrome. Adv Neuroimmunol. 1995;5:39-56.

[6] **Article from journal- - more than one author (list all authors if six or less, otherwise list first three followed by "et al.")**

Raux H, Coulon P, Lafay F, Flamand A. Monoclonal antibodies which recognize the acidic configuration of the rabies glycoprotein at the surface of the virion can be neutralizing. Virology. 1995;210:400-408.

[7] **Monographic series**

Davidoff RA. Migraine: Manifestations, Pathogenesis, and Management. Philadelphia, Pa: FA Davis; 1995. Contemporary Neurology Series, No. 42.

[8] **Online journals with volume and page information**

Simon JA, Hudes ES. Relationship of ascorbic acid to blood lead levels. JAMA [serial online]. 1999;281:2289-2293. Available from: American Medical Association, Chicago, Ill. Accessed August 24, 1999.

[9] **Online journals without volume and page information**

Gordon GF. Bypassing heart surgery. Alternative Medicine [serial online]. July 1999;issue 30.

[10] **Online web site**

Terre Haute Center for Medical Education. The THCME Medical Biochemistry page. Available at: http://web.indstate.edu/thcme/mwking/home.html. Accessed August 24, 1999.

11 ATTACHMENTS

11.1 Attachment 1: Title

This section is optional and can be removed if not applicable.

Copy and paste the sub-header above (i.e., 12.1 Attachment 1) to make attachments automatically number. Attachments should be numbered in the order they are mentioned in the protocol. Attachments should not be mentioned in the synopsis.

12 APPENDIX

12.1 Management of Multi-Site Research Where Geisinger/AtlantiCare is the Lead Site

Remove this section if not applicable.

Describe study activities that will be conducted at each site if they differ between sites.

Describe the plans for management of study activities, reporting requirements, and communication across sites. For example:

- Unanticipated problems involving risks to participants or others
- Modifications to study protocol, procedures, documents
- Interim study results