Prospective Research Study Protocol Template

* **If you believe your activity may not meet the definition of “Human Research” subject to IRB oversight, complete and submit the Determination of Human Subject Research Form in IRBNet.**
* **Be sure that all study materials/documents are correct and consistent with the information in this protocol.**
* **Instructions and/or sample text is provided in *blue font* to generate ideas of what should be included in some of the sections. This should be deleted and substituted with information that pertains to the actual study.**
* **Two example protocols are given as sample text in *green font* and *orange font*, delete these examples. Additional example text is provided in *purple* text.**
* **The italicized bullet points below serve as general guidance to investigators on the kinds of information that may be applicable to include in each section. Please DELETE the italicized text in the protocol before submitting. Note that, depending on the nature of your research, some sections below will not be applicable. Indicate this as “N/A.” Do not delete the section.**
* **Slight adjustments may be made to the section headings text to better reflect specific study design.**
* **Appendices, if used, should be added after the Reference section.**
* **Delete this “Instructions” section from your final protocol.**

**Study Protocol Title:**

*Be consistent with the Title throughout your research application, protocol, and IRB documents.*

**Study Sponsor:**

AdventHealth Orlando

*AdventHealth Orlando is the default response. Please change if needed.*

*The sponsor is the person or organization who is responsible for the research study and may or may not be the funder. The sponsor develops/writes the study protocol or has it developed on its behalf, which may include collaboration with outside entities. The sponsor is responsible for satisfying all legal and regulatory requirements including but not limited to overseeing the conduct of the study, data integrity and analysis. The sponsor has the right to publish the results of the study.*

**Principal Investigator:**

Principal investigator:

# List of Abbreviations:

*Include commonly used abbreviations and acronyms.*

# Introduction

*The introduction should open with remarks stating this document is a research protocol and that the described study will be conducted in compliance with the following as applicable:*

 *institutional research requirements; Common rule; FDA; Good Clinical Practices (GCP)* *International Conference on Harmonization (ICH) Guidelines (E6) for GCPs standards. You must be familiar with the regulations governing this research.*

***Sample Text****: This document is a protocol for a human research study. This study is to be conducted in accordance with institutional research requirements and (insert applicable regulations specific to this research).*

# Background Information and Scientific Rationale

*Provide and summarize published (or available unpublished) data in the literature to build a rationale for the research question(s), study objectives, and research design.*

*If none is available, include a statement that there is no available research data to date on the intervention being investigated.*

*This section must provide a justification for the conduct of this study based on existing knowledge and should include your research question.*

*You may include a summary of epidemiological data, if relevant.*

# Study Objectives

*In a general fashion, summarize the purpose, aim, or objective of the study.*

## Primary Objective/Aim/Goal/Hypothesis

*Select the appropriate term (objective/aim/goal/hypothesis) for your research area and be consistent throughout the protocol*

*Include the details of the study’s primary objective (which is the main purpose for performing this study and should be focused on* ***one question****), outcome measures and method by which outcomes will be determined or state the hypothesis to be tested.*

***Sample Text:*** *The primary objective of this study is to evaluate the efficacy of three different antibiotics in the treatment of acute bronchitis by measuring time until symptoms (fever, shortness of breath and wheezing) have cleared. Antibiotic C is currently not approved for treating acute bronchitis.*

***Sample Text:*** *Does having access to a “health advocate” decrease the number of hospitalizations for patients with CHF?*

***Sample Text:*** *The primary objective of this study is to determine the presence of RNA in exosomes in human saliva and their correlation with tumor staging. Saliva samples will be collected from research subjects to determine the sensitivity of exosome detection as well as to relate it to evidence of disease.*

## Secondary Objective/Aim/Goal/Hypothesis

*Include secondary objectives (as many as relevant). These objectives may be dependent or independent of the primary objective.*

***Sample text:*** *The secondary objective of this study is to assess patients’ overall change in symptoms and return to daily activities after 2 weeks of antibiotic treatment. Information regarding patient health history will be obtained and tested as potential predictors of outcome.*

***Sample text:*** *The secondary objective will be to survey the patients and advocates regarding the pros and cons of the intervention.*

# Study Design

## Research Design

*Include the description of study type (randomized double-blinded, placebo-controlled, open/off label, parallel or crossover design), number of study arms and other study details. Type of study and design should be decided on the basis of primary and secondary objectives and availability of resources.*

***Sample Text:*** *This research will be carried out as a randomized double-blind, three-arm trial. Randomization will be conducted by a qualified study member who will be the only person with access to the randomized assignment information.*

***Sample text:*** *The research design is a randomized prospective clinical study. Details for the study visits are provided in the study visits section of the protocol.*

## Research Intervention Description

*This section describes the investigational component of the research. This includes drugs, devices, biologics, clinical intervention or other specific intervention, activities.*

If the research involves drugs or devices and is investigator-initiated, indicate whether there is any possibility that the results will be reported to FDA.

If the research involves drugs or devices, describe your plans to store, handle, and administer those drugs or devices so that they will be used only on subjects and be used only by authorized investigators.

If the drug is investigational (has an IND #) or the device has an IDE # or a claim of abbreviated IDE (non-significant risk device), include the following information as it’s applicable to the regulations outlined in the table:

* Identify the holder of the IND/IDE/Abbreviated IDE.

* If FH is the IND/IDE holder, explain the study team’s plan to comply with FDA’s sponsor requirements for the following when applicable:

**Example**: The principal investigator will ensure that [insert applicable regulations from below chart] are understood and met. This includes but is not limited to adhering to consenting requirements, protocol adherence, record keeping, coordinating reports to be submitted directly to the FDA such as serious, unexpected adverse reactions reports, annual reports, amendment submissions, study/project closures.

* If there is a claim of an abbreviated IDE (non-significant risk device) please defend the reasoning.

**Example:** The study device is an investigational device, i.e., has not been cleared for commercial use by the FDA. Therefore, this study will be conducted in accordance with requirements of 21 CFR part 812.2(b) Abbreviated requirements. We have determined that the device, <name>, is a non-significant risk device, as it will not be used as the final determinant of participant diagnosis. FDA has concurred with this determination as documented in their letter.

|  |
| --- |
| *Please reference this table in order to provide the relevant information above.* ***Remove from protocol after review.***  |
|  | ***Applicable to:*** |
| ***FDA Regulation*** | ***IND Studies*** | ***IDE studies*** | ***Abbreviated IDE studies*** |
| ***21 CFR 11*** | *X* | *X* |  |
| ***21 CFR 54*** | *X* | *X* |  |
| ***21 CFR 210*** | *X* |  |  |
| ***21 CFR 211*** | *X* |  |  |
| ***21 CFR 312*** | *X* |  |  |
| ***21 CFR 812*** |  | *X* | *X* |
| ***21 CFR 820*** |  | *X* |  |

## Study Site(s)/Location(s) and Number of Subjects

*Include the following information about number of sites and number of subjects. Keep in mind that you can have 1 site with multiple locations within that site. For example, AdventHealth Orlando is a single site but can have multiple locations such as campuses, outpatient clinics, outpatient surgery, imaging centers, or physician offices.*

*AdventHealth Orlando site locations (campus, physician offices, etc):*

*Estimated number of subjects at AdventHealth* *Orlando sites:*

*Name of external site(s) outside of AdventHealth Orlando:*

*Estimated number of subjects at external sites:*

*Total number of all sites:*

*Estimated number of subjects at all sites combined:*

## Multi-Site Research Logistics/Communication Plan

*Indicate n/a if there are no other sites other than AdventHealth Orlando.*

*AdventHealth Orlando is a single site but can have multiple locations such as campuses, outpatient clinics, outpatient surgery, imaging centers, or physician offices.*

*This section will be applicable to research that is conducted at AdventHealth Orlando (any location) and external institutions or facilities not affiliated with AdventHealth Orlando.*

If this is a multi-site study where you are the lead investigator and AdventHealth Orlando is the **coordinating center**, describe the processes to ensure communication among sites, such as:

* All sites have the most current version of the protocol, consent document, and HIPAA authorization.
* All required approvals have been obtained at each site (including approval by the site’s IRB of record).
* If an external site is not using their IRB of record or does not have an IRB of record to use, please describe what IRB will be used for that external site
* All modifications have been communicated to sites, and approved (including approval by the site’s IRB of record) before the modification is implemented.
* All engaged participating sites will safeguard data as required by local information security policies.
* All local site investigators conduct the study appropriately.
* All non-compliance with the study protocol or applicable requirements will be reported in accordance with local policy.

Describe the method for communicating to participating sites:

* Problems
* Interim results
* The closure of a study

If this is a multi-site study where AdventHealth Orlando is a **participating** **center**, describe the processes to ensure communication with the **coordinating center**.

## Research Conducted in a Foreign Country

*Indicate n/a if there are no sites in foreign countries.*

Any project that will be conducted in whole, or in part, at a location outside the United States must include answers to the following questions:

* List the study location and the primary language/dialect spoken by the proposed subject population.
* If this project has been, or will be, reviewed by a local IRB or Ethics Committee, provide the name, address, and contact information for the local IRB or ethics review committee at the foreign research site.
* If applicable, provide the name and contact information for any foreign investigator, collaborator, or institution assisting the PI in the conduct of the project.
* Briefly describe your knowledge of the intended population including knowledge of local customs, practices, and religions as they relate to this project.
* Describe your proficiency with the local language, or how information and communication will be translated throughout the project.
* Describe how the community will be notified, and information disseminated, regarding the results of the research project.
* Address any cultural, regional, or unique risks the IRB should be aware of when evaluating this research project.
* State how will you communicate with the IRB if you need to report an unanticipated problem (associated with risk to subjects or others associated with the study) or an amendment to the study.
* For student investigators, explain how the faculty sponsor will provide oversight for the study while you (or representatives) are conducting the research in the foreign country.

## Community-Based Participatory Research

*Indicate n/a if there is no community involvement in the design or conduct of the research.*

*Describe involvement of the community in the design and conduct of the research.*

Note: “Community-based Participatory Research” is a collaborative approach to research that equitably involves all partners in the research process and recognizes the unique strengths that each brings. Community-based Participatory Research begins with a research topic of importance to the community, has the aim of combining knowledge with action and achieving social change to improve health outcomes and eliminate health disparities.

# Subject Selection

## Vulnerable Populations (if applicable)

 *Indicate n/a if there are no vulnerable populations in the study.*

Provide justification if including any of the following populations in your study. For instance, consider whether the proposed research is directly important to the health and well-being of the vulnerable population; if it will answer a question affecting the health or welfare of the vulnerable population, or whether the study objectives can be met by using competent other subjects i.e. competent adults.

***Example:*** *Due to our target population, it is possible that some of these patients will be cognitively impaired adults. If cognitively impaired patients are not enrolled, this would compromise the validity of the study because* ***<fill in the blank>***

*Include a description of additional safeguards in place to protect the rights and welfare of any of the vulnerable populations. Any populations lacking justification may NOT be included.*

Cognitively Impaired Adults: (If the research involves cognitively impaired adults, review the **“HRP-414 WORKSHEET: ADULTS LACKING CAPACITY”** to ensure that you have provided sufficient information.)

Children: (If the research involves persons who have not attained the legal age for consent to treatments or procedures involved in the research (“children”), review the [**“HRP-310 CHECKLIST: Children”**](https://drupal02.floridahospital.org/irb/content/checklist-and-worksheets) to ensure that you have provided sufficient information.)

Pregnant Women: If the research involves pregnant women, review the [**“HRP-305 CHECKLIST: Pregnant Women”**](https://drupal02.floridahospital.org/irb/content/checklist-and-worksheets) to ensure that you have provided sufficient information.

Neonates of non-viable or uncertain viability: If the research involves neonates of uncertain viability or non-viable neonates, review the **HRP-306 CHECKLIST: Neonates of Uncertain Viability** or **HRP-307 CHECKLIST: Nonviable Neonates** to ensure that you have provided sufficient information..

Prisoners: If the research involves prisoners, review the [**“HRP-308 CHECKLIST: Prisoners”**](https://drupal02.floridahospital.org/irb/content/checklist-and-worksheets) and address each of the criteria for approval.

*Employees:*  ***(Refer to FH Policy 400.120 & FH SOP 400.120A)*** *When FH (or FH affiliate) employment status is part of the inclusion criteria, the FH Researcher must be able to provide a rationale other than convenience for selecting the FH employee as a subject. The recruitment method must not lead FH employees, especially when they are in a subordinate job position, to believe they will be compromised in any way by not participating. The compromised circumstances and fear of retribution, even subtle cues of compromise, can place FH employees in a position of involuntary participation in a research project. You must explain your plan to avoid coercion and make it clear that non-participation will not affect their employment status.*

*Recruitment through bulletin board advertisements (screened and approved by the IRB), or recruitment through a third party unassociated in a power/supervisory relationship with the employee are usually the best strategies.*

*NOTE: When a FH employee is recruited to be a study subject, but FH employment is not an inclusion criterion, it is suggested that during the consent procedure the relationship between the subject’s employment status and study participation be addressed so that it is made clear that non-participation will not affect employment status.*

Students: Provide a plan to avoid coercion when recruiting students and be clear that non-participation will not affect the potential subjects’ academic status.

## Inclusion Criteria

*Create a numbered list of criteria subjects must meet to be eligible for study enrollment (e.g. age, gender, target disease, concomitant disease if required, etc.) Consider clinical aspects that are appropriate for your protocol such as number of symptoms and length and/or severity of symptoms.*

1. *Age 18 – 89*
2. *Primary diagnosis of acute bronchitis (ICD-9:466.0)*

***Sample text:***

1. *Age 18 – 89*
2. *Diagnosis of Chronic Heart Failure (CHF)*
3. *NYHA classification I - III*
4. *Willing and able to provide a contact phone number*
5. *Resides in Central Florida*

**Sample text:**

1. Age 5-12 years of age
2. Undergoing MRI without sedation
3. Able to wear MRI distraction goggles
4. Mentally capable of comprehending study video

## Exclusion Criteria

*Create a numbered list of criteria that would exclude a subject from study enrollment. Consider clinical issues that are appropriate for your protocol such as contraindications to the study interventions, abnormal lab results, or history of cancer.*

*If exposure to certain medications or treatments at screening is prohibited, that must be noted in the exclusion criteria—if these are also prohibited concomitant medications during the study period that should be noted here as well. You may have exclusion criteria related to factors that may interfere with study completion, such as lives outside of the central Florida area, has active drug or alcohol dependence, participating in another research study that could impact subject safety and results of your study, etc.*

***Sample text:***

1. *Known allergies to the study medications.*
2. *Lives more than 50 miles from Dr. Xyz’s medical practice office*
3. *Diagnosed with any of the following co-morbidities (list here)*
4. *Active alcohol dependence as defined by patient report of > 14 alcohol beverages per week*

***Sample text:***

1. *Diagnosed with any of the following co-morbidities (list here)*
2. *Plans to relocate outside of Central Florida within a year*
3. *Diagnosed with renal disease within the past 5 years*

**Sample text:**

1. Reporting a pain score of 8-10 on the Visual Analog Scale prior to giving informed consent

# Resources Available

Describe your process to ensure that all persons assisting with the research are adequately informed about the protocol, the research procedures, and their duties and functions.

Include your plan for ongoing discussion of issues throughout the duration of the study such as reportable new information, implementing amendments, study progress, etc.

Describe the qualifications (e.g., training, experience, oversight) of you and your staff as required to perform their role. When applicable describe their knowledge of the local study sites, culture, and society. Provide enough information to convince the IRB that you have qualified staff for the proposed research.

Describe other resources available to conduct the research: For example, as appropriate:

* Justify the feasibility of recruiting the required number of suitable subjects within the agreed recruitment period. For example, how many potential subjects do you have access to? What percentage of those potential subjects do you need to recruit?
* Describe the time that you will devote to conducting and completing the research.
* Describe your facilities.
* Describe the availability of medical or psychological resources that subjects might need as a result of an anticipated consequences of the human research.

# Study Procedures

## Subject Recruitment and Screening

If this is a multicenter study and subjects will be recruited by methods not under the control of the local site (e.g., call centers, national advertisements), describe those methods.

Describe the methods that will be used to identify potential subjects.

Describe when, where, and how potential subjects will be recruited.

Describe materials that will be used to recruit subjects. (Include copies of these documents with the IRB submission. For advertisements, include the final copy of printed advertisements. When advertisements are taped for broadcast, include the final audio/video tape. (You may submit the wording of the advertisement prior to taping in order to avoid re-taping due to inappropriate wording but will still need the IRB to review the final audio/video tape.)

*Note: If you plan to access medical records for study development or feasibility, Reviews Prep to Research Form must be completed and submitted* ***PRIOR*** *to any access of medical records.*

*Note: If you plan to access medical records for screening and/or recruitment purposes prior to obtaining informed consent, Reviews Prep to Research Form must be completed and submitted* ***WITH*** *the initial application.*

***Sample Text:*** *Participants will be recruited from the clinical practice of Dr. Brown. A flyer advertising the study will be placed in the waiting room visible to patients.*

*Dr. Brown or one of the sub-Investigators will briefly describe the study to the patient and ask the patient if s/he would like more information. If the patient indicates s/he would like more information, a qualified researcher will approach the patient, in a private room, to provide an overview of the study.*

***Sample text:*** *Participants will be recruited from patients admitted to AdventHealth Orlando, Orlando campus with the primary diagnosis of CHF. An information sheet will be provided to patients immediately after admission as a way to introduce the advocate program.*

## Consent Process

*Indicate n/a if you are applying for a Waiver or Alteration of Informed Consent.*

If you are obtaining consent of subjects describe whether you will be following **“INVESTIGATOR GUIDANCE: Informed Consent (HRP-802) ”** If not, describe your consent process in similar detail.

 If you are documenting consent of subjects in writing describe whether you will be following **“INVESTIGATOR GUIDANCE: Documentation of Informed Consent (HRP-803)”** If not, describe your process to document informed consent in writing in similar detail.

## Subjects who are not yet adults (infants, children, teenagers)

* Describe the criteria that will be used to determine whether a prospective subject has not attained the legal age for consent to treatments or procedures involved in the research under the applicable law of the jurisdiction in which the research will be conducted. (E.g., individuals under the age of 18 years.)
* Describe whether parental permission will be obtained from:
	+ Both parents unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.
	+ One parent even if the other parent is alive, known, competent, reasonably available, and shares legal responsibility for the care and custody of the child.
* Describe whether permission will be obtained from individuals other than parents, and if so, who will be allowed to provide permission. Describe the process used to determine these individuals’ authority to consent to each child’s general medical care.
* Indicate whether assent will be obtained from all, some, or none of the children. If assent will be obtained from some children, indicate which children will be required to assent.
* When assent of children is obtained describe whether and how it will be documented. The IRB allows the person obtaining assent to document assent on the consent document and does not routinely require assent documents and does not routinely require children to sign assent documents.

## Cognitively Impaired Adults

* Describe the process to determine whether an individual is capable of consent.

## Adults Unable to Consent

* List the individuals from whom permission will be obtained in order of priority. (See: “POLICY: Legally Authorized Representatives Children and Guardians (HRP-021)”)
* Describe the process for assent of the subjects. Indicate whether:
	+ Assent will be required of all, some, or none of the subjects. If some, indicated, which subjects will be required to assent and which will not.
	+ If assent will not be obtained from some or all subjects, an explanation of why not.
	+ Describe whether assent of the subjects will be documented and the process to document assent. The IRB allows the person obtaining assent to document assent on the consent document and does not routinely require assent documents and does not routinely require subjects to sign assent documents.

## Documentation of Informed Consent Process

*Indicate n/a if you are applying for a Waiver or Alteration of Informed Consent.*

*NOTE: Documentation of the informed consent process is required to establish that the subject was accurately and adequately informed and that no study-related procedures were initiated prior to obtaining informed consent.*

*In this section, describe how you will document the Informed Consent process in source documentation such as using a checklist or documenting via a progress note. This requirement is separate from obtaining signatures on the consent document. For help to create a checklist, review* **TEMPLATE – Informed Consent Process Checklist**

***Sample Text:*** *A research team member will note in the source documentation the consent process, date consent was obtained and that consent was obtained prior to initiating any research procedures.*

## Waiver of Written Documentation of Consent or Waiver of Consent

**Waiver of Written documentation of Consent (consent will be obtained but signatures will not be required)**

*Indicate n/a if you are obtaining Informed Consent.*

* Indicate if you wish to request a Waiver of Written Documentation of Consent
* Review the [**“HRP-303 CHECKLIST: Waiver of documentation of Consent”**](https://drupal02.floridahospital.org/irb/content/checklist-and-worksheets) to ensure your study qualifies for the waiver.

**Waiver or Alteration of the Consent Process (consent will not be obtained, required information will not be disclosed, or the research involves deception)**

*Indicate n/a if you are obtaining Informed Consent.*

* Indicate if you wish to request a Waiver or Alteration of Consent of Consent
* Review the **“HRP-300 CHECKLIST:** [**Waiver Consent**](https://drupal02.floridahospital.org/irb/content/checklist-and-worksheets) **HHS”**
* If protected health information (PHI) is being used or disclosed, please complete and submit the **“FORM: Waiver of HIPAA Authorization Request (HRP-220)”**

## Non-English Speaking Subjects

* If you do not plan to enroll non-English speaking subjects, provide justification for the exclusion.
* If you plan to enroll non-English speaking subjects, consider the flow of the entire study and explain your plan to ensure that you are adequately prepared to conduct study procedures such as the consent process, study visits, directions, follow ups, etc., including how oral and written study material that is to be used will be presented.
* Indicate what language(s) other than English are understood by prospective subjects or representatives.
* For the consent process, indicate if you will have consent documents translated into a particular language or if you will follow HRP-804 INVESTIGATOR GUIDANCE Short Form Consent Process

## Randomization

*Indicate n/a if you are not randomizing subjects to study groups.*

*If relevant to this study, describe how subjects are going to be randomized. Note: flipping a coin is not considered a best practice for randomization.*

***Sample Text:*** *Randomization into three treatment groups will be done using statistical software by a trained team member. This information will only be released as the patients are enrolled. A master list of the patient names and intervention group will be stored in a limited access, confidential file.*

***Sample text:*** *Patients will be randomized to the treatment group (patient advocate) or to the control group. Patients in the treatment group will be assigned an advocate on a rotating basis so that each advocate has approximately the same number of patients. The group randomization will be based on web based software (randomizer.org) and the assignment of advocates will be a systematic selection process.*

## Study Visits

*In this section, describe the setting as well as all the procedures and treatments required at each visit delineated by visit. If appropriate, create a study procedures flowchart/table depicting the activities and procedures to be followed at each visit.*

*A study visit can consist of any subject contact for research purposes (e.g. face to face, phone, email) and in some cases may occur only once.*

***Sample Text:***

*Visit 1: Inclusion and exclusion criteria will be reviewed. If the patient meets criteria, s/he will be invited to participate in the research study. The patient will be given the informed consent and it will be reviewed with the patient and all questions will be answered. After the informed consent is signed, the patient will be randomized to the treatment groups (Antibiotic A, Antibiotic B, Antibiotic C). A questionnaire regarding symptoms will be completed with the assistance of a study team member. The patient will be given a diary for recording symptoms each day for the two week intervention period and instructed in its use. The patient will be instructed to record his or her temperature, any shortness of breath, or wheezing.*

*2-Day Phone Call Follow-up: Two days after Visit 1, the patient will be contacted by phone to review diary completion compliance and to answer any questions the patient may have. The patient will be contacted up to 3 times on this day, and if the patient cannot be reached, a reminder letter will be sent.*

*1-Week Phone Call Follow-up: One week after Visit 1, the patient will be contacted by phone to review diary completion compliance and to answer any questions the patient may have. The patient will be contacted up to 3 times on this day, and if the patient cannot be reached, a reminder letter will be sent.*

*Visit 2: After completing the two-week antibiotic regimen, the patient will return to the clinic for visit 2. At this visit, the patient will turn in his or her diary (given at visit 1) and complete a final symptom questionnaire.*

*The following table identifies the procedures in relation to the study timeline.*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| *STUDY VISIT SCHEDULE* | *Visit 1**Screening* | *Completed by patient on daily basis during treatment Period (2 weeks)* | *2 day phone call follow-up* | *1 week phone call follow-up* | *Visit 2**Two week follow-up (+2 days)* |
| *Inclusion and Exclusion Criteria* | *X* |  |  |  |  |
| *Informed Consent* | *X* |  |  |  |  |
| *Randomization* | *X* |  |  |  |  |
| *Temperature readings – diary* |  | *X* |  |  |  |
| *Shortness of Breath – diary* |  | *X* |  |  |  |
| *Wheezing – diary* |  | *X* |  |  |  |
| *Review diary compliance* |  |  | *X* | *X* | *X* |
| *Symptom and QOL Questionnaire* | *X* |  |  |  | *X* |

***Sample text:***

*Inpatient Phase:*

*After patients have been screened and have signed informed consent, they will be assigned to the advocate (intervention) group or the control group.*

*Control Group:*

*Patients in the control group will be provided standard medical treatment for CHF patients.*

*Advocate Group:*

*Patients in the intervention group will be assigned an advocate (rotating basis). There will be six advocates assigned to this study. On the first day of the patient’s hospital stay, the advocate will visit the patient and discuss what services are available. This will be recorded an electronic text entry. Services that may be provided during the patient’s hospital include:*

* *educational videos on CHF,*
* *visit from a registered dietitian,*
* *smoking cessation program information,*
* *general health counseling and*
* *assistance setting up additional physician appointments.*

*On each subsequent day the patient is in the hospital, the advocate will visit at least one time and document electronically the content of the discussion and services provided.*

*Follow-up Phone Call Phase:*

*Control Group: Control group patients will receive a phone call at the end of one year. Items addressed in the end of study phone call are provided in the document titled, “Control group – end of study phone call.”*

*Advocate Group: After returning home, the patient will receive a daily phone call with the last phone call occurring on day 30 from date of enrollment. After the initial period of daily phone calls ends, the patient will receive a phone call once a month for 11 months regardless of subsequent hospitalizations.*

***Sample Text:***

*Study Visit 1 – Inclusion and exclusion criteria will be reviewed. If the patient meets criteria, s/he will be invited to participate in the study. Informed Consent will be obtained. Saliva sample will be collected per Manual of Procedures. <if a Manual of Procedures is not available, then a description of the procedure could be placed in this section, such as the following: “The patient will be asked to refrain from eating or drinking for 1 hour. Demographic data will be collected during this time. After one hour of abstention from food and drink, the patient will be given bottled water and asked to rinse out their mouth 2 times. Ten minutes following this oral rinse, the subject will be given a sterile Falcon tube. They will be asked to tilt their head forward and to allow saliva to pool in their mouth prior to spitting saliva into the tube. The subject will be asked to repeat the pooling and spitting of saliva until a total of 10 ml of saliva is collected in the tube. The tube will be placed on ice between episodes of spitting. The patients will be instructed not to cough up mucus or phlegm during the collection period.”> The saliva sample will remain on ice until the laboratory analysis of the saliva occurs on the same day as sample collection.*

*Clinical data will be obtained from medical record review until clinical data collection is completed.*

*Laboratory Analysis: Exosomes will be purified from saliva. To isolate RNA, 25 ul of the protease inhibitor and 200 units of RNase inhibitor will be added per 5 ml of saliva. No inhibitors will be used for flow cytometry and electron microscopy. Saliva samples will be diluted 1:1 with phosphate buffered saline and centrifuged at 16 500 × g for 15 min to remove cells and debris. The supernatant will be filtered through a 0.2 μm vacuum filtration system, before ultracentrifugation at 120 000 × g for 60 minutes to pellet the exosomes. Additional information is contained in the Manual of Procedures.*

## Study Duration

*Include a projected start date.*

*Include the estimated duration to enroll all study subjects.*

*Provide the total length of time participants will remain in the study, including the active intervention and follow up period.*

*Provide an estimated date for investigators to complete the study (includes analysis).*

## Materials of Human Origin: Collection, Preparation, Handling and Shipping

*This section does not apply to obtaining blood samples or other specimens for safety monitoring, screening procedures, and/or diagnostic purposes as part of this research study. Indicate n/a if you will not be using Materials of Human Origin.*

*This section should be used if the focus of the study utilizes prospectively obtained materials of human origin (whether acquired from within AdventHealth* *Orlando or from another source) obtained as part of clinical intervention or prospective research study.*

*Describe the process for obtaining access to the materials of human origin, and the plan for the physical security of the materials after they are obtained, including:*

1. *How and from where it will be obtained.*
2. *Where the biological materials will be stored.*
3. *Who will have access to the stored biological materials and how will such access be secured and controlled?*
4. *What chain of custody for the Materials of Human Origin will be used throughout the trial, and how will the transfer of custody between departments, people, and/or institutions be documented?*
5. *Will the biological materials be sent anywhere outside of the AdventHealth Orlando system? If so, identify all locations.*
6. *What are your plans for disposition of data or human biological specimens that are identifiable in any way (directly or via indirect codes) once the study has ended?*

# Study Outcome Measures (Endpoints)

*In this section, provide a list of the endpoint/outcome measures/data elements to be studied along with a description of the endpoint/outcome measure.*

*NOTE: Data elements listed here should mirror your data collection sheet or case report form.*

*Depending on your study type, you may have endpoints or outcome measures, or both. For example, if you are conducting a cancer study, your endpoint might be progression of disease. If you are conducting an intervention study, your endpoint might be reduction of disease as measured by change in blood pressure.*

*Describe the primary and secondary study endpoints/outcome measures/data elements. These may be designated variables or may be safety related values (such as specific time points, evidence of liver toxicity, or inability to tolerate further treatment).*

*If the variable will be used as a safety measure, please define as such.*

***Sample Text:*** *Body Temperature: Temperature will be taken at 4 times each day using a digital oral thermometer. Data collection will indicate method and measurement scale used for temperature readings.*

***Sample Text:*** *Shortness of breath: Shortness of breath will be measured twice a day at (12:00 PM ± 1 hour and 6:00 PM ± 1 hour) using the Dyspnea Index (see Appendix). The scale is from 0 to 4, with 4 being the highest indication of shortness of breath.*

***Sample Text:*** *Wheezing: Wheezing will be measured using a peak flow meter twice a day at (12:00 PM ± 1 hour and 6:00 PM ± 1 hour). The numerical value is the peak expiratory flow rate (PEFR)*

***Sample Text:*** *Questionnaire: Patient information will be obtained using a paper questionnaire administered 2 weeks (plus 2 days) after starting antibiotic treatment. Questions regarding returning to normal activity as well as basic demographic information will be collected. Demographic information of age, gender, employment and smoking status will be self-reported items on the questionnaire.*

***Sample Text:*** *Number of hospitalizations: Count of the number of admissions during a 12-month period starting with patient enrollment in the study.*

 ***Sample Text:*** *Patient Interview: Information on the pros and cons of the intervention will be solicited from all patients and advocates involved with the study. This information will be gathered (audio recorded) by trained interviewers using five standard questions during a brief (approximately 15 minute) interview. Interview questions are provided in a separate document.*

***Sample Text:*** *Heart Rate (safety measure): Procedure will be stopped if the patient’s heart rate drops below 50 or goes above 150.*

***Sample Text:*** *The following data variables and materials will be collected for analysis in this study:*

* *Demographic variables: Patient age and gender*
* *Clinical variables: Date of tumor resection, pathology report with tumor description and grade, and past history of cancer*
* *Saliva sample: A saliva sample will be obtained. (Additional information is provided in the Materials of Human Origin section.)*

# Data Management and Quality Plan

*Throughout this section, address all mechanisms used to capture/store data including but not limited to paper copy, spreadsheets, databases, digital files (video or voice), device driven data collection, cloud storage.*

## Data De-identification

*Indicate n/a if you are not de-identifying data.*

If data will be de-identified, there will be a process of developing a code to be used for study subject numbers. This code usually consists of numerals, and may be a combination of numerals and letters. However, the code must not contain any unique identifiers. Please provide the following information related to this process.

* *How are unique identifiers being generated? Describe the format or taxonomy of the chosen code.*
* *How is data being linked to subjects’ identifying information?*
* *How and when will the link be used?*
* *Where will the linked data be stored?*
* *Who will have access to the linked data?*
* *How long will the linked data be stored?*
* *Will the link ever be destroyed so that the data or the samples will become de-identified?*
* *Describe any circumstances under which the link between the subject’s identity and assigned study subject number could be used to break the code.*

##

## Data Confidentiality, Storage, and Retention

*Describe how you plan to maintain confidentiality of study data.*

* Describe how data and records of any media type (e.g., paper, electronic, audio recordings, video recordings, blogs, and photographs) will be stored during the study and after the study has been completed.
* Describe data security measures for the storage of records (e.g., locked filing cabinet, password protected computer, etc.)
* Describe who will have access to the data and records.
* Describe how long data and records will be retained\*
* Describe how data and records will be disposed.

*\* FH policy requires study records be maintained a minimum of 7 years following study closure.* ***Refer to POLICY 400.070 HRP-070 Investigator Obligations record retention requirements at AdventHealth.***

## Data Quality

*Indicate n/a if you do not have a plan for insuring data quality.*

*Describe how the data quality is going to be checked.*

***Sample Text:*** *Data will be entered into a database form that will be programed to only allow certain values as entry. Randomly selected subjects will be reviewed and checked with source documentation. Data will be cleaned by using summary analysis and graphs, prior to data analysis.*

***Sample Text:*** *Data will be double entered by two different coders. All differences will be checked to source. After data set is finalized, the data set will be locked. A data management plan will be completed and stored with study records.*

*Sample text: Quality control procedures for this research study include source data verification by randomly selecting 10% of subject records with comparison between the paper case report form (CRF) and the electronic database record of those same data. If errors are common (higher than 20%), data will be completely checked prior to data analysis.*

## Data Sharing (outside of AdventHealth Orlando)

*Indicate n/a if you are not sharing data outside of AdventHealth Orlando.*

*If information is going to be shared with any other individual, organization or institution outside of AdventHealth* *Orlando, please complete this section. State the purpose of data sharing and provide a detailed description of all data elements that will be shared. (Note: Consult the Office of Sponsored Programs (OSP) regarding appropriate legal documents.)*

*Sample text: eCRFs will contain data pertaining to medical care and include the following PHI identifiers: Dates of diagnosis, surgery, discharge.*

# Sample Size Determination

*Describe how the sample size was determined for this study. The sample size should be based upon the primary outcome variable. If the authors have determined that sample size estimation was not computed, please provide the rationale.*

***Sample Text:*** *The primary outcome measure is time (hours). For this study there was a statistical power analysis used to determine the appropriate sample size of 24 patients in each group; the study has three treatment groups for a total of 72 patients. Calculation of sample size was done using alpha set to 0.05 and power of 80%. The estimated difference in time was based on expert opinion of Dr. Brown and was set to 5 hours.*

***Sample text:*** *The anticipated patient population for the Orlando campus is 450 patients per year. Of the patients with CHF, 40% of eligible patients are expected to enroll. Approximately 200 patients will be enrolled in the study, thus approximately 100 patients in the control group and 100 patients in the treatment group.*

# Statistical Analysis Plan

*Describe the statistical approach to the primary and secondary objectives of the study. This section should contain the key elements of the analysis plan. Describe how you will manage missing data.*

## Primary Objective Analysis

***Sample Text:*** *The primary variable of interest is Time in days measured as the initiation of antibiotic treatment until clearing of symptoms. Time will be compared between the three treatment groups using analysis of variance (ANOVA) for comparison of group means or an appropriate non-parametric comparison test.*

***Sample text:*** *The primary variable of interest is the number of hospitalizations over the one year period. The number of hospitalizations will be compared for the treatment and control groups using appropriate statistical methods depending on the distribution of values. Additional comparison of demographic information (age, gender and race/ethnicity) will be checked prior to analysis. Any variables determined to be a covariate will be included in the final analysis.*

## Secondary Objective Analysis

***Sample Text:*** *The secondary analysis will be focused on the changes in symptoms and return to normal activity (in days) as reported by the subject via a written questionnaire. Changes in symptoms for the different treatment groups will be compared using Chi-square test of independence. Return to normal activities will be analyzed using analysis of variance (ANOVA) for comparison of group means or an appropriate non-parametric comparison test.*

***Sample text:*** *Analysis of questionnaire information will be accomplished using Chi-square analysis for categorical information. Open ended questions (free text) will be summarized using qualitative methods, specifically thematic approach.*

# Potential Risks and Benefits

## Potential Benefits

*Describe potential benefits to the individual research subject (economic, physical, or other) as well as the benefits to science for this research study.*

Include the probability, magnitude, and duration of the potential benefits if these can be quantified or determined.

Indicate if there is no direct benefit.

## Potential Risks

List the reasonably foreseeable risks, discomforts, hazards, or inconveniences to the subjects related the subjects’ participation in the research.

Include as many as may be useful for the IRB’s consideration, describe the probability, magnitude, duration, and reversibility of the risks if these can be quantified/determined.

Consider physical, psychological, social, legal, and economic risks, and other risks as applicable to the study.

If applicable, indicate which procedures may have risks to the subjects that are currently unforeseeable.

If applicable, indicate which procedures may have risks to an embryo or fetus should the subject be or become pregnant.

If applicable, describe risks to others who are not subjects.

## Mitigation of Risks

*Describe what procedure(s) will be implemented to reduce subject risk(s) described above.*

Describe the availability of medical or psychological resources that subjects might need as a result of an anticipated consequences of the human research.

***Sample Text:*** *Side effects will be monitored during follow-up study visits.*

***Sample text:*** *Advocates will monitor patient reaction and provide access to counseling if the patient requests this type of support.*

## Provisions to Protect the Privacy Interest of Subjects

Describe the steps that will be taken to protect subjects’ privacy interests. “Privacy interest” refers to a person’s desire to place limits on whom they interact or whom they provide personal information.

Describe what steps you will take to make the subjects feel at ease with the research situation in terms of the questions being asked and the procedures being performed. “At ease” does not refer to physical discomfort, but the sense of intrusiveness a subject might experience in response to questions, examinations, and procedures.

Indicate how the research team is permitted to access any sources of information about the subjects.

***Sample Text:*** *Subjects will be assigned unique identifiers for study-related records. All precautions will be taken to make sure that only authorized individuals will access subject research records. The collection of sensitive information about subjects will be limited to minimum necessary to achieve the aims of the research, so that no unneeded sensitive information will be collected.*

***Sample text:*** *The initial phase of this study will be conducted while the subject is in the hospital. If the subject does not have a private room, the Advocate will meet with the subject in a private area such as a conference room. At the time of consent, the Advocate will inquire how the subject wishes to handle Advocate visits if the subject has visitors in his/her room at the time of the Advocate’s visit. Possible choices might include having the Advocate return at a later time or asking visitors to wait outside or conducting the visit with visitors present.*

*The second phase of this study involves telephone calls to the subject after hospital discharge. At the time of consent, the Advocate will inquire how the subject wishes to handle telephone calls and leaving messages for the subject.*

# Early Withdrawal of Subjects

## Investigator Withdrawal of Subjects

*NOTE: This section is* ***not*** *related to when a subject withdraws consent. This section is designed to describe the scenarios under which the* ***investigator*** *may withdraw a subject prior to the expected completion of that subject (e.g. safety reasons, failure of subject to adhere to protocol requirements, disease progression, loss to follow-up, etc.) Also, if abrupt termination of study treatment could affect subject safety (e.g. in an antihypertensive study, abrupt withdrawal without other intervention might cause hypertensive rebound), describe procedure to transition subject off the study drug or to alternate therapy. Describe the process to determine when a subject is lost to follow-up (e.g. number of phone calls to subject, phone calls to next-of-kin if possible, certified letters, etc.).*

***Sample Text:*** *Patients that did not complete the full course of antibiotics (e.g., adverse reaction, exacerbation requiring additional treatment or non-compliance) will be removed from the study. If patients are unable to complete the two weeks of antibiotic treatment, data collection will not continue but will be counted in the patient numbers and a reason will be recorded on the CRF. Patient compliance will be defined as completing 80% of the required medication during the two-week treatment period.*

***Sample Text:*** *Patients will be contacted via phone, for a follow-up appointment approximately, 1 day after the 2-week treatment. If patients cannot return for follow-up they will be sent a paper questionnaire to complete and return. A total of 5 phone calls and 2 paper questionnaires will be sent prior to concluding the patient is lost to follow-up.*

***Sample text:*** *Subjects may be withdrawn from the study if the advocate is unable to contact the subject by phone for more than 3 days in the initial month or for 2 or more months in the 11-month follow-up period. Patients will also be withdrawn if the patient does not allow the advocate to set appointments or will not provide information regarding primary physician contact information or other information such that the advocate can assist the patient.*

***Sample text:*** *If a patient is withdrawn from the study, a final phone call will be made to obtain the number of hospitalizations in the past year or patient disposition.*

## Subject Request for Withdrawal from Study

*Describe the process in which a subject may request withdrawal from the study. Also, if abrupt termination of study treatment could affect subject safety (e.g. in an antihypertensive study, abrupt withdrawal without other intervention might cause hypertensive rebound) describe procedure to transition subject off the study drug or to alternate therapy.*

## Data Collection and Follow-up for Withdrawn Subjects

*Even though subjects may be withdrawn prematurely from the study, it is important to describe how data will be handled for withdrawn subjects and be sure that this is consistent with information in the Informed Consent form.*

***Sample text:*** *Patients who request withdrawal or who are withdrawn by the PI from the study will have their data maintained in the research database up to the point of withdrawal. This data will be included in subsequent analysis because a subject may have withdrawn due to possible drug side effects and keeping these patients in the analysis is essential for study validity.*

***Sample text:*** *Patients who request to be withdrawn from the study will not be included in the final analysis of readmission rates. We will not be contacting patients via phone as this would not be appropriate for subjects requesting to not continue with the research study. The percentage of patients withdrawing will be calculated.*

# Adverse Event Reporting

*Include methods and timeline for assessing, recording, managing and reporting adverse events and safety parameters*

***Sample Text:*** *At each contact with the subject, the investigator will seek information on adverse events by specific questioning and, as appropriate, by examination. Information on all adverse events will be recorded immediately in the source document, and also in the appropriate adverse event module of the case report form (CRF). All clearly related signs, symptoms, and abnormal diagnostic procedures results will be recorded in the source document.*

***Sample Text:*** *All adverse events will be reported according to AdventHealth Orlando IRB guidelines.*

# Safety Monitoring Plan

*This section is REQUIRED for studies that are determined by the IRB to be more than minimal risk*

## Safety Monitoring*Indicate n/a if you do not have a Safety Monitoring Plan.*

*Monitoring is an ongoing review of the study throughout its duration. Plans for collecting data and protocol compliance should be included. The plan might include establishing a data monitoring committee (committee details should be provided in the next section).*

Describe:

* The plan to periodically evaluate the data collected regarding both harms and benefits to determine whether subjects remain safe.
* What data will be reviewed, including safety data, untoward events, and efficacy data.
* How the safety information will be collected (e.g., with case report forms, at study visits, by telephone calls with participants).
* The frequency of data collection, including when safety data collection starts.
* Who will review the data.
* How frequently there will be a review of cumulative data
* The statistical tests for analyzing the safety data to determine whether harm is occurring.
* Any conditions that trigger an immediate suspension of the research.

## Data and Safety Monitoring Board (DSMB) or Equivalent

*Indicate n/a if you do not have a DSMB or equivalent.*

*A Data and Safety Monitoring Board (DSMB) is a group of professionals, experienced in clinical care and/or clinical research, assembled to provide additional safety and oversight to a clinical study. This type of oversight committee includes medical and scientific experts and may include clergy, statisticians and other non-medical experts. These members may* ***not*** *be part of the study team. The DSMB will look only at de-identified data.*

*This section should describe these noted DSMB attributes.*

* *Number of members and roles (e.g. clinicians, biostatisticians, bioethicists, etc.). It is not necessary to list the names or contact information of DSMB members in the protocol. The names and contact information of DSMB members should be maintained in the regulatory files.*
* *How often the DSMB will meet (and if by phone, face-to-face, or web-assisted conferencing).*
* *Type of safety information that will be assessed for patient safety.*
* *How the safety data will be supplied to the DSMB.*
* *Summary of number and type of safety assessments the DSMB will conduct.*
* *How the DSMB will record the summary of its various meetings.*
* *How the DSMB will report its findings and/or recommendations, and to whom.*

# Ethical Considerations

*Indicate n/a if you do not have any Ethical Considerations.*

*Identify any ethical concerns and how you will address these. Including but not limited to the following:*

*Treatment: Address subject rights such as assigning subjects to placebo or non-standard of care or allowing subjects in the control group access to the treatment after study completion, if appropriate.*

***Example:*** *This is an extension study where a participant who failed treatment in the parent study may be re-randomized to the same dose of active drug/placebo. Based on current data for <drug>, it is not possible to make definitive conclusions about the impact of continued therapy in subjects not meeting response criteria, but the sponsor considers it possible that some subjects may see response with continued treatment and also considers the decision to enter the extension study is one based on individual risk:benefit assessment and a discussion between the subject and the investigator. The investigators at this site will carefully consider each potential participant’s entry into this study and address this issue during the consent process.*

***Deception:*** *If distress or deception must be experimentally induced, as in some psychological and physiological measurement research, the research design usually requires withholding certain information from the consent process in order to obtain unbiased results. After the subjects have completed participation, it is important to provide this information to subjects from whom it was withheld and to provide an opportunity for subjects to express their concerns and ask questions about the research. If the research design includes deception, please describe why it is needed. Describe the debriefing process of how subjects will be debriefed with a description of what really happened and why the research could not otherwise have been conducted.*

## *Sharing of Results with Subjects: Describe whether results (study results or individual subject results, such as results of investigational diagnostic tests, genetic tests, or incidental findings) will be shared with subjects or others (e.g., the subject’s primary care physicians) and if so, describe how it will be shared.*

# Funding Source

*Indicate n/a if you do not have a funding source.*

*This section should describe how the study will be financed, but should not contain specific dollar amounts.*

***Sample Text:*** *This study is supported by funding from National Institute of Neurological Disorders and Stroke and the National Center for Medical Rehabilitation Research (RO1 NS050506). AdventHealth Orlando has received a subaward from Duke University, who is the Prime Recipient of this grant. The IRBNet # for this grant is 412345.*

***Sample Text:*** *This study is funded in part by a gift given to the AdventHealth Orlando Foundation.*

# Subject Stipends or Payments

*Indicate n/a if you are not providing subject stipends or payments.*

*Describe any subject stipend, payment or gift here. Describe the amount, method, and timing of any payments to subjects*

# Publication Plan

*Indicate n/a if you do not have a publication plan.*

*Describe the plan for publication. Note: To the extent possible, roles and responsibilities of each research team member should be determined in advance. Additionally, if the research study will be published, there should be an additional plan that describes assignment of authorship and the contributions of each author. International Committee of Medical Journal Editors (ICMJE) has a policy to guide authorship.*

*Note: Review the Clinical Trials.gov guidelines on the Research Services website to determine if your study is required to be registered. For those studies of which it is not required by law, registration may still be required by your publishing journal.*

# References

*This is the bibliography section for any information cited in the protocol. It should be organized as any standard bibliography.*

1. Author, Title of work, periodical and associated information.
2. Author, Title of work, periodical and associated information.