# Clinical Trials: Processes and Procedures

*By Jennifer Hosford*

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Pre-Clinical Trial Activities

I. Before a clinical trial is considered, often a PI and his team will want to review the clinical research protocol so they can decide whether or not they want to participate.

II. Depending on the nature of the trial, this will probably involve the implementation of a Non-Disclosure Agreement (NDA) and/or a Confidential Disclosure Agreement (CDA):
   http://research.ufl.edu/research/doc/nda.doc

III. All of these types of documents must be reviewed and approved by Division of Sponsored Programs (DSP), via the following process:
   I. Send the NDA/CDA the company gives you to the Research Administration and Compliance (RAC) Office at com-rac-l@lists.ufl.edu for initial review.
   II. Include the name, address, telephone number and email address of your contact at the company and make sure you include any initial questions or concerns you may have about the agreement before the first review has commenced.
   III. RAC will review the agreement, negotiate the terms (if needed), collect DSP signature and return it to the other party/sponsor.
   IV. If the Investigator’s signature is needed to acknowledge the terms of the agreement, RAC will collect said signature prior to signing and returning the NDA/CDA to the company.
   V. Once DSP receives a fully executed NDA/CDA, a copy will be sent to the Investigator and the exchange of confidential information can begin.

First Steps in Preparing Your Trial

IV. If it is decided that the investigator would like to participate in the trial, the Principle Investigator (PI) or PI staff should provide COM (College of Medicine)-RAC with a copy of:

1. The proposed Clinical Trial Agreement (CTA; word Standard Clinical Trial Agreement)
2. Study letter if Master CTA is being used
3. A copy of the protocol
4. Clinical Trial Checklist
   (http://www.research.ufl.edu/research/pdf/clinical_trial_checklist.pdf)
5. A company/sponsor contact person as early in the process as possible.
V. The CTA Checklist must accompany the CTA or other contracts with funding that functions on a “paid-per-patient” basis when a project is submitted to the RAC and DSP offices.

VI. The CTA Checklist includes questions about Payment Consideration, Intellectual Property Ownership, Publications, and Clinicaltrials.gov, and provides necessary information to help DSP negotiate an accurate and effective contract for University of Florida (UF).

Contractual Elements of a CTA

VII. Each CTA is reviewed on a case-by-case basis; however there are a number of contractual items that are common to most CTA agreements.

VIII. The following is just a sample of common elements found in a CTA that may need to be negotiated by DSP or RAC with the Sponsor:

VI. Parties to the Agreement

I. The parties to the Agreement should be by and between the University of Florida and the Sponsor. The Investigator as an employee of the university should not be named as a legal party to the Agreement. We do allow the Investigators to sign CTA’s as Read and Acknowledged if the Sponsor insists.

VII. Publications

I. Agreements must allow the Investigator the ability to publish results of the study. We do afford the sponsor a right of prior review for purposes of identification of proprietary or confidential information or intellectual property protection.

II. Where UF is one site of a multi-site trial we do allow sponsors to coordinate timing of publications among the sites.

VIII. Publicity

I. The University of Florida does not allow the sponsor to freely use our name or the name of the University’s project staff in any publicity, advertising, or press release without the express prior written approval of an authorized representative of University.

IX. Intellectual Property

I. The drug or device being tested in the clinical trial is normally proprietary and owned by the sponsoring party and may already be covered by patent protection. Although each CTA must be reviewed on its own merit, it is the University of Florida’s general policy that title to inventions arising from projects conducted by faculty and staff will be owned by the University.

X. Indemnification
I. The sponsoring party, and the actual owner of the study drug or device if an intermediary is involved, normally shall provide to indemnify and hold harmless the University of Florida from any and all liabilities, claims, actions or suits for personal injury or death arising from the conduct of the CTA.

II. **The University of Florida cannot provide indemnification.**

**XI. Governing Law**

I. Agreements should be governed by the laws of the State of Florida or this provision must be absent from the agreement.

**XII. Subject Injury Compensation Language**

I. It is DSP procedure to negotiate appropriate compensation language for subject injury in all CTA’s. The language should be similar to one of the variations vetted and approved by UF General Counsel.

**XIII. VA Approved Contract Language**

I. If the UF Clinical Trial Checklist identifies that the study is supported by the VA or conducted at a VA facility or targets VA subjects then the CTA must include VA approved contract language. This is one of UF’s roles to help the VA maintain its AAHRPP accreditation.

**VA Approved Contract Language**

**XIV. Background: FYI**

I. The checklist gathers information about whether or not the VA is involved in the conduct of the trial, and when the VA is involved DSP should include in the agreement specific VA approved contract language found below or at a minimum secure language that satisfies the principles set forth by the VA approved language.

II. If a sponsor rejects the language in whole or in part, discuss with PI and Study Coordinator to see if the study can be conducted without VA involvement.

III. If it is determined that study cannot be conducted without VA involvement, bring to the attention of Stephanie Gray or Brian Prindle within the Division of Sponsored Programs for further discussion and direction.

**XV. Human Subject Protection**

I. The research to be conducted under this Agreement (or equivalent) involves Human Subjects or human tissues within the meaning of 38 C.F.R. Part 16 and all research to be performed under this Agreement (or equivalent) will conform to applicable Federal laws and regulations and local IRB policies and procedures.
II. Additional information is available from the HHS Office for Human Research Protections (http://www.hhs.gov/ohrp/).

III. Sponsor (or equivalent) and UF on behalf of the VA shall immediately notify each other upon identifying any aspect of the protocol, including information discovered during site monitoring visits, or the study results that may adversely affect the safety, well-being, or medical care of participants, or that may affect the willingness of participants to continue participation in the research, influence the conduct of the study, or that may alter the IRB’s approval to continue the study, UF on behalf of the VA shall promptly notify the IRB of any such events.

IV. When participant safety or medical care could be directly affected by study results, UF on behalf of the VA will send study participants a written communication about the results.

XVI. Research Related Injury

I. Sponsor (or equivalent) shall be responsible for reasonable and customary costs incurred for treatment of physical injury to the subject if Sponsor (or equivalent) reasonably determines, after consulting with UF on behalf of the VA, that the Adverse Event was reasonably related to administration of the Test Article or Protocol; provided, however, that:

   I. The Adverse Event is not attributable to VA Employees’ negligence or willful misconduct;

   II. The Adverse Event is not solely attributable to any underlying illness, whether previously diagnosed or not; and

   III. The Protocol drug or Protocol procedure was administered in accordance with the Protocol.

XVII. Presentations and Publications

I. UF, VA and Sponsor (or equivalent) have the right to make publicly available the results of their research and development activities and are encouraged to do so.

II. Unless otherwise required by the authorship guidelines or requirements of the meeting or other forum at which the presentation will be made or the journal in which the publication will appear, authorship should reflect a substantial contribution to:

   I. The conception, design and/or conduct of the clinical trial,

   II. The acquisition, evaluation and/or interpretation of the results of the clinical trial and/or

   III. The drafting and revising of the manuscript and its final approval.
XVIII. Depending upon his or her level of participation in the performance of the clinical trial, the contribution of each participant should be recognized appropriately in all resulting presentations and publications, either as a named author or contributor or in an acknowledgement. The final determination shall be made by mutual agreement of UF, VA and Sponsor (or equivalent).

XIX. A manuscript of each proposed presentation or publication of the results of the clinical trial shall be submitted to UF, VA and Sponsor (or equivalent) for review prior to submission to anyone who is not employed by UF, VA or Sponsor (or equivalent) and under an obligation of non-disclosure and non-use at least substantially identical to that imposed on UF and Sponsor (or equivalent) by this Agreement in order to permit UF, VA and Sponsor (or equivalent) to:

I. Evaluate the manuscript for accuracy,

II. Ascertain whether Information (other than the results of the clinical trial) is being improperly disclosed,

III. Provide information which may not have yet been made available by UF, VA or Sponsor (or equivalent),

IV. Provide input for consideration regarding the content and/or conclusion(s) of the manuscript and

V. Determine whether the manuscript discloses any potentially patentable invention(s).

XX. UF, VA and Sponsor (or equivalent) shall be afforded a review period of fifteen (15) working days for manuscripts not exceeding two (2) double-spaced pages in length (or the equivalent thereof) and thirty (30) working days for all other manuscripts.

   I. A working day is any day other than a Saturday, Sunday or Federal holiday.

   II. Upon receipt of UF, VA and Sponsor (or equivalent)’s written consent to release the manuscript or, if later, upon the conclusion of the review period with no request, input or notification having been received from UF, Sponsor (or equivalent) and VA, the manuscript may be submitted to anyone.

XXI. By mutual agreement of UF, VA and Sponsor (or equivalent), any Confidential Information (other than the results of the clinical trial) contained therein shall be excised from the manuscript and reasonable consideration shall be given to all other input received from Sponsor (or equivalent).

XXII. If Sponsor (or equivalent) determines that any manuscript submitted to it for review in accordance with this paragraph contains or describes one or more potentially patentable inventions that should be made the subject of one or more patent applications, Sponsor (or equivalent) shall provide notice to UF on behalf of VA of this determination prior to the expiration of the review period.
I. Sponsor (or equivalent) shall have two (2) months from its receipt of such additional information to file such patent application(s).

II. UF, VA and Sponsor (or equivalent) shall not submit the manuscript to anyone who is not a UF, VA or a Sponsor (or equivalent) employee and who is not under an obligation of non-disclosure and non-use at least substantially identical to that imposed on both UF and Sponsor (or equivalent) by this agreement except by mutual agreement.

XXIII. If the clinical trial is part of a multicenter clinical trial, the data resulting from the performance of the clinical trial shall be pooled with the data from other centers (final pooled dataset) and analyzed as stipulated in the Protocol.

I. Without the consent of the steering committee of the multicenter clinical trial, no presentation or publication of the results obtained from datasets other than the final pooled dataset (either of data from one center alone or of data from more than one but less than all of the centers) shall be made prior to the presentation or publication of the pooled dataset.

II. Thereafter, should results obtained from datasets other than the final pooled dataset be published for sound scientific reasons, adequate reference shall be made to the primary publication.

III. In no event shall UF or VA be restricted from presenting or publishing independently after the expiration of twelve (12) months from the completion of the Clinical Trial provided that all other provisions of this paragraph have been satisfied and provided that the publication adequately describes the results as obtained from a dataset other than the final pooled dataset, if that is the case.

The Research Protocol

XXIV. Clinical Trial Protocol Development

I. Every clinical investigation begins with the development of a clinical protocol.

II. The protocol is a document that describes how a clinical trial will be conducted (the objective(s), design, methodology, statistical considerations and organization of a clinical trial,) and ensures the safety of the trial subjects and integrity of the data collected.

III. A research protocol is a document that describes the background, rationale, objectives, design, methodology, statistical considerations, and organization of a clinical research project (above is the link is to UCFS’s Clinical Trials Protocol Template, one of the best templates I have found).

IV. According to the ICH Good Clinical Practice guidelines, a protocol should include the following topics:
I. Title Page (General Information)

II. Background Information

III. Objectives/Purpose

IV. Study Design

V. Selection and Exclusion of Subjects

VI. Treatment of Subjects

VII. Assessment of Efficacy

VIII. Assessment of Safety

IX. Adverse Events

X. Discontinuation of the Study

XI. Statistics

XII. Quality Control and Assurance

XIII. Ethics

XIV. Data handling and Recordkeeping

XV. Publication Policy

XVI. Project Timetable/Flowchart

XVII. References

XVIII. Supplements/Appendices

V. The NIH provides many resources for protocol development to assist investigators in writing and developing clinical research protocols that are in compliance with regulatory/GCP requirements.

VI. Some NIH institutes have a mandatory requirement for using their protocol template.

XXV. Sample Protocol Templates and Resources:

I. Protocol Template

II. DMID-Minimal Risk Template

III. DMID-Greater Than Minimal Risk Template

IV. DMID-Interventional Template
Research Administration and Compliance

IX. When submitting a study to the Research Administration & Compliance (RAC) Office for a Billing Compliance Review, the Principal Investigator must compile a Study Registration & Initiation Packet that contains information about the study.

X. The forms needed in the packets depend on the type of study and the specific requirements of the protocol, contract, award and budget:

**Study Registration and Initiation Checklist (SRIC)**

a) The Study Registration & Initiation Checklist (SRIC) will lead researchers through a series of questions to determine what other documents and forms are needed for the Study Registration & Initiation Packet:

   i. **Part A: Study Information**

      1. **Study Title**

         a. In the free-text field, enter the title of the research study.

      2. **Study Short Name**

         a. In the free-text field, enter the study’s acronym or short title, if applicable (30 character limit).

            i. *Note: For studies uploaded into Epic, this Short Name will be one of two ways that the study can be searched. Please select a short name that the study team will remember easily.*

      3. **Sponsor Protocol #**

         a. In the free-text field, enter the study’s protocol # as listed in the sponsor’s protocol (if available).

      4. **Will any part of this study be conducted at North Florida/South Georgia Veteran Health System?**

         a. Click the appropriate box.

         b. If YES, STOP and review the shorter VA-Only SRIC to see if it may be used in place of the standard checklist.
5. **College**  
   a. From the drop-down field, select your college.

6. **Department**  
   a. In the free-text field, enter your department, center, or institute.

7. **Division**  
   a. In the free-text field, enter your division. Enter “N/A” if you are not part of a division.

8. **Select IRB Used**  
   a. From the drop-down field, select the IRB you will be using.

9. **IRB Number**  
   a. In the free-text field, enter the IRB number if already assigned.
   
   b. Click the “pending” box if the study is not yet approved.

10. **ClinicalTrials.gov**  
    a. Select the box that describes what the ClinicalTrials.gov status of this study is.
    
    b. Most industry sponsor-initiated studies are registered by the sponsor.
    
    c. For more information on which studies require registration, see [http://rac.med.ufl.edu/manage_study/guide-clinicaltrials-gov/app-clinicaltrials/](http://rac.med.ufl.edu/manage_study/guide-clinicaltrials-gov/app-clinicaltrials/).
    
    d. **Note:** If your study is **NOT** registered with ClinicalTrials.gov, you may not be able to publish study results. You also may not bill Medicare for any study services, including protocol-required “Standard of Care”.

11. **Study Funding and Support Source(s), Sponsor Name, Explanation/ Comments**  
    a. From the drop-down field(s), select all applicable Funding and Support Source(s).
    
    b. This should include original sponsors of flow-through studies (e.g. Department of Defense, National Institute of Health, etc.).
    
    c. Also indicate any entity that is providing drugs, devices, equipment, or any items or services at no cost to the study.
    
    d. In the adjacent free-text field(s), enter the sponsor name and any explanation/comments.
    
    e. If your funding source is not a listed option, select “Other” and provide an explanation in the adjacent free-text field(s).
12. Department Contacts
   a. In the free-text fields, list all of the contact information for the requested study roles.
   b. Use the “Other” row to describe an additional study contact, if applicable.

13. Signatures Required for ALL Submissions
   a. The following are required before submitting the form to the RAC Office:
   b. Signature of Department Chairman(s) – *Note: For “departmental” funding/support, each Chair of any department providing study funding/support must acknowledge the support and ensure that the appropriate effort will be captured in the UF Effort Reporting system.*
   c. Signature of Principal Investigator
   d. Signature of Person Completing the Form
   e. RAC will obtain the following signatures:
      i. RAC Reviewer
   ii. Part B: Funding/Budget Questions
      1. Does this study require the use of any drugs/substances, devices or any technical/professional medical services OR any activity that could result in subject injury?
         a. If YES, continue to question #1.
         b. If NO, you may skip the remainder of Part B and Part C and continue on to IRB questions as indicated.
      2. Does study protocol REQUIRE the application implantation or use of any specifically-named medical devices?
         a. If yes, complete the Device Table.
            i. *Note: Only non-generic devices specifically named in the protocol, contract, award, budget, or informed consent need to be listed.*
         b. A “device” is an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part or accessory which is:
            i. Used in the diagnosis of disease or other conditions and/or
ii. Used in the cure, mitigation, treatment, or prevention of disease and/or

iii. Intended to affect the structure or any function of the body but **NOT**
    through chemical action or metabolism

3. **Does study involve any FDA IDE Category A devices, FDA IDE Category B devices, or PMA/510(K) device related to carotid artery stenting (CAS), or FDA Humanitarian Use Device?**

   a. If YES, attach a copy of the FDA Approval Letter, and be sure to read and understand the Shands pre-notification/CMS pre-approval requirements and then check the box showing you did so.

4. **Does study protocol REQUIRE the administration, ingestion or use of any drug, biologic, nutritional supplement, or any other substance (investigational, FDA approved, or other)?**

   a. If YES, complete the Drug Table.

5. **Sponsor/Study pays for all protocol required activities?**

   a. If NO, and the Principal Investigator plans to bill the participant/third party for some of the services, submit a Detailed Budget.

   b. **Note:** A detailed budget must show how EACH protocol-required service or activity will be paid – i.e. which ones will be “billed out” and which ones will be covered by the study (either through study payment or salary support)

   c. If YES, submit a copy of the budget negotiated with Sponsor or attached to award, or create a Limited Budget.

   d. **Timesaver Tip:** If you already have a budget from the sponsor, or have one that you created for the award or proposal, then you do NOT need to create an additional budget using the Limited Budget template. Submit the budget you already have as the “Limited Budget”.

6. **Does study objective or aim involve**

   a. Investigational treatment, **OR**

   b. Investigational drug/substance, **OR**

   c. New indication for FDA approved drug/substance(s)

   d. **Note:** “Investigational” here means “only available to participants inside the research study”. If the item or service being studied is available for this specific use/indication outside of a research study (either here at UF or elsewhere in the
U.S.A.), then it would be considered “Standard of Care”, and the answer would be “NO”.

e. If NO, continue to part C.

f. If YES, submit a completed Medicare Coverage Analysis Worksheet unless the sponsor is paying for all services OR this study involves an IDE, HUD or CAS PMA/510(k) device following Shands & Medicare device rules.

**Medicare Qualifying Studies**

**XI.** Effective for items and services furnished on or after September 19, 2000, through issuance of a National Coverage Determination (NCD), the Center for Medicare and Medicaid Services (CMS) expanded Medicare coverage to include “routine costs” of “qualifying” clinical research studies.

a. Both “routine costs” and “qualifying” are terms that CMS has defined as detailed below.

**XII.** Visit the CMS Medicare Clinical Trial Policies website for the original Medicare National Coverage Determination (NCD) for Routine Costs document.

a. Note: Medicare has confirmed that even though the NCD was originally drafted for clinical trials, the rules also apply to any research studies.

**Medicare Coverage Analysis Worksheet**

**XIII.** If the study billing plan includes billing “routine costs” to participants or their insurance, the Principal Investigator must perform a Medicare Coverage Analysis to ensure that the study “qualifies” for coverage of routine costs.

**XIV.** This worksheet incorporates the Medicare “qualifying” requirements from the Medicare National Coverage Determination (NCD) for research studies.

1. “Routine costs” of a clinical research study include all items and services that are otherwise generally available to Medicare beneficiaries (i.e., there exists a benefit category, it is not statutorily excluded, and there is not a national non-coverage determination) that are provided in either the experimental or the control arms of a study.

**XV.** Note: If the study involves an IDE category A, IDE category B, or PMA/510(k) carotid artery stenting (CAS) device, do NOT use this worksheet to determine if the study “qualifies” for coverage. These studies must be pre-approved prior to study start-up by the local Medicare contractor First Coast Service Options.

a. **Study Title**

   a. In the free text field, type in the study title (limit 256 characters).
I. **Step 1:** Principal Investigator must confirm that **ALL THREE** of the following are true:

1. The subject or purpose of the study must be the evaluation of an item or service that falls within a *Medicare benefit category* (e.g., physicians’ service, durable medical equipment, diagnostic test) and is not statutorily excluded from coverage (e.g., cosmetic surgery, hearing aids).

2. The study must not be designed exclusively to test toxicity or disease pathophysiology. It must have **therapeutic intent**.

3. Studies of therapeutic interventions must enroll *patients with diagnosed disease* rather than healthy volunteers. Studies of diagnostic interventions may enroll healthy patients in order to have a proper control group.

II. If the answer is “NO” to any of these three statements, then the study does not “qualify” for coverage.

4. No protocol -required services may be billed to Medicare or any third party payers that follow Medicare rules. Principal Investigator must sign and date the “**Study Does NOT Qualify**” box.

III. If the answer is “YES” to all three, then proceed to STEP TWO.

IV. **Step two:** Principal Investigator must then confirm that **AT LEAST ONE** of the following is true:

5. The study is funded by NIH, CDC, AHRQ, CMS, DOD, and VA.

6. The study is supported by centers or cooperative groups that are funded by the NIH, CDC, AHRQ, CMS, DOD and VA.

7. The study is conducted under an investigational new drug application (IND) reviewed by the FDA.

8. The study is a drug study that is exempt from having an IND under 21 CFR 312.2(b)(1).

V. On the worksheet, circle which ones apply. If none of these apply, then the study does not “qualify” for coverage.

9. No protocol -required services may be billed to Medicare or any third party payers that follow Medicare rules. Principal Investigator must sign and date the “**Study Does NOT Qualify**” box.

VI. If at least one of these applies, the study “qualifies” for coverage of “routine costs”. Principal Investigator must sign and date the “**Study is Medicare Qualifying**”. 

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Note: This worksheet is not intended to stand alone. It is to be used in conjunction with the Medicare National Coverage Determination (NCD). There are a few types of studies that, when run through the analysis worksheet, seem to be “non-qualifying”, but when analyzed using the NCD, may be “qualifying”. If the Principal Investigator thinks the study may be one of these exceptions, please contact the RAC office for assistance.

RAC Required Tables

Device Table

The Device Table (Device Table) documents all specifically-named, non-generic devices required by the protocol and/or mentioned in the protocol/informed consent/contract. In addition, it lists ANY device provided by the study sponsor.

There are three compliance reasons why these specifically-named devices must be documented with the RAC office:

I. Some types of investigational devices pose an incredibly high risk for billing compliance issues/errors.

II. If the devices referenced in the protocol or ICF fall into the high-risk types, then the RAC office must ensure that the study team is aware of applicable device considerations and the device is put on a special tracking log that is monitored by Shands and RAC.

III. If a particular device is being provided by a sponsor, it must be documented in order to ensure that the contract/agreement with the sponsor includes language that shows that the sponsor is promising to provide the device.

1. If a particular device is being stored in Shands or UFP Clinic space, Shands/UFP needs to be informed and location/storage procedures must be followed.

b. Note: For the purposes of this form, the definition of a “device” loosely follows the FDA definition of a device, but on a simpler level. It boils down to this: **If the specially-named medical “thing” that we are discussing is not a DRUG, then it is a DEVICE.**

IV. The RAC Device Table is only used to evaluate billing risks. It is not shared with IRB or FDA.

c. Instructions
d. **Study Short Name**  
a. In the free-text field, enter either the study’s short name.

e. **Name/Description of Device**  
a. In the free-text field, enter either the name or description of the device required by the protocol and/or provided by the sponsor.

b. This name/description should match the way the device is referenced in the protocol, informed consent, and/or contract.

f. **FDA Device Type**  
a. From the drop-down field, select the FDA classification of this device.

b. Sponsors of device studies should have an FDA letter that confirms the type. See FDA Device Classifications for more information.

g. **FDA #**  
a. For IDEs or PMA/S10(k) Carotid Artery Stenting (CAS) devices only, enter the FDA number in the free-text field.

b. These are 6 digit numbers proceeded with a “G” for IDEs, “P” for PMAs, and “K” for 510(k)s.

h. **Funding Source**  
a. From the drop-down field, select the funding source for the device.

i. **Location of Device Use**  
a. In the free-text field, describe where the device will be used or implanted.

b. *Note: Shands Operating Rooms require that study teams contact them prior to starting a device study that will involve their operating rooms.*

j. **Does Shands Need to Purchase/Receive?**  
a. If Shands will need to purchase or receive the device in order to have it in stock, click “YES”; otherwise, click “NO”.

b. *Note: When a study involves a device that has to be purchased or received by Shands Healthcare, the Shands Healthcare contracting office should be contacted as early in the start-up process as possible.*

k. **Storage Location**  
a. In the free-text field, describe where the device will be stored until it is used.
b. If the device will be stored at Shands, Shands needs to be notified prior to the study starting.

Drug Table

XVIII. The Drug Table (Drug Table) is used to document all specifically-named drugs, biologics, nutritional supplements, or any other ingested/applied substances required by the study protocol: This includes Investigational & Non-Investigational items.

l. This information is used by Shands Investigational Drug Service (IDS) and Shands non-investigational pharmacy to help ensure that study drugs are available when needed.

m. The table is also reviewed by the Research Administration & Compliance (RAC) office and the Division of Sponsored Programs (DSP) to determine drug provision language in contracts with outside sponsors.

n. Instructions

o. Study Short Name

a. In the free-text field, enter the study’s short name (30 character limit).

p. Name of Item

a. List any specifically-named drug, biologic, nutritional supplement, or any other ingested/applied substance required by the study protocol OR provided/paid for by the sponsor.

b. Note: There is no need to include items merely suggested or recommended unless they are to be paid for by the sponsor. Sponsor-funded pre-meds or concomitant meds obtained from a non-investigational pharmacy can be listed generically as long as you have a Confirmation of Services from the applicable pharmacy that acknowledges that these drugs will be invoiced to the study.

q. Use of Item

a. Click on the field and then click the arrow on the right.

r. From the drop-down list, select one of the following to describe who will receive each item:

a. Conditional: Items required by protocol for SOME subjects in SOME circumstances (e.g. adverse event, lab results, etc.)

b. All Subjects: Items required by protocol for ALL subjects (including items that are randomized)
Drug with placebo can either be listed on one or two lines, as shown in the following examples:

a. `<line 1> “Drug xyz/placebo” “All subjects” (or “conditional”, as applicable)

OR

b. `<line 1> “Drugxyz” “Conditional”
c. `<line 2> “Placebo” “Conditional”

t. **FDA Drug Type**

a. Click on the field and then click the arrow on the right.

b. From the drop-down list, select the FDA status of the item.

c. If the item does not fit any of the options, select “Other” and explain in the comments section at the bottom of the form.

u. **FDA IND#**

a. If the item has an FDA IND (Investigational New Drug) number, enter it into the free-text field.

v. **Funding Source**

a. Click on the field and then click the arrow on the right.

b. From the drop-down list, select the option that describes how the item will be paid for. If the options are not applicable, select “Other” and explain how the item will be provided or paid for in the comments section at the bottom of the form.

w. **Administration Location**

a. Click on the field and then click the arrow on the right.

b. From the drop-down list, select the option that describes where the item will be administered to the participant.

x. **Storage Location**

a. Click on the field and then click the arrow on the right.

b. From the drop-down list, select the option that describes where the item will be stored prior to administration to participant.
c. If the options are not applicable, select “Other” and explain where the item will be stored in the comments section at the bottom of the form.

y. Confirmation of Services

a. An IDS Confirmation of Services is required for any item that will be billed to/provided by the sponsor AND stored/administered in a location marked with an asterisk (*).

Part C: Billing Questions

b. **ALL studies must submit a billing plan using the Billing Grid.**
   
   i. Provide estimated study start and end dates in the free-text fields provided.
   
   ii. Provide estimated number of study subjects that you expect to consent.
   
   iii. Using RAC Billing Grid, grid **ALL** protocol-required services and activities (Exception: Administrative activities such as “Informed Consent” “Adverse Event Reporting” “QOL” etc. may be omitted).
   
   iv. Include modifier codes as directed by “Medicare Qualifying” status question at top of the grid (see information on “Use of V70.7 & Q0Q1 Modifiers”).
   
   v. Submit either Pricing Tool Output OR service department COS Forms for all study-funded services or UF CRC-funded services. (“S” or “C” on the Billing Grid)
   
   vi. If UF CRC will be involved, an additional UF CRC COS Form is required.

c. **Does this study involve any requests for a “Reading Exception”?**
   
   i. This refers to a request for no professional reading and/or interpretation from the department in which the service is performed.
   
   ii. This can include exceptions such as: Principal or Co-Investigator is performing the read, or the technical portion is being sent to a centralized core-lab to perform the read.
      
      d. The results may or may not be provided to the PI.
   
   i. If Yes, Make sure to explain “Reading Exception” scenario on the billing grid.
   
   ii. Please read policy on “Reading Exception”.
   
   iii. The Informed Consent must include IRB template language about the reading exception(s).
      
      e. Please contact UF IRB office for more info.
i. Follow individual service department procedures/processes to ensure proper billing procedures are implemented.

f. **Part D: Study Plan/Agreement Questions**

i. Does this study require the use of an Informed Consent Form (ICF) that includes costs and subject injury financial language?

   g. If NO, skip to question 9. No FLA is required.

   h. If YES, provide a copy (in Word) of the Informed Consent Forms (ICF) that you intend to submit to the IRB or WIRB.

i. **Please indicate when you would like to receive the FLA.**

   i. The RAC office will issue a Financial Language Assessment (FLA) for the ICF at the time point you indicate.

   ii. If this study is tissue/data bank or study with a consent waiver, RAC will issue a “No ICF” FLA.

   iii. If the study requires a contract to be negotiated, the timing of the FLA can help reduce the risk of conflict between the fiscal language in the ICF and the final executed contract.

   iv. If a FLA for IRB-01 is requested immediately after RAC review, the ICF sent **MUST** be the **FINAL** version (in Word). RAC staff will be inserting FLA language into the ICF for you and sending directly to IRB-01.

   v. In all cases, it is the PI and Study Team’s responsibility to reconcile the ICF and contract language **BEFORE** the first patient is consented.

   j. **Note:** WIRB, IRB-01 & IRB-03 require the FLA form for all new ICF submissions.

k. Is this study solely funded internally by UF PI or PI’s department(s)?

   i. If the study is receiving any funding or support from outside of UF, click “NO”.

l. Does this study include a contract, human subject research agreement, Clinical Trial Agreement, or any similar “Paid per Patient” agreement?

   i. If YES, submit a Clinical Trial Agreement Checklist.

m. Submit a copy of sponsor’s agreement/contract, approval letter, or award notice, etc. (draft, executed or proposed, as appropriate) with budget attached.

n. **Protocol**

   i. Always provide the protocol/human subject plan/scope for the study.
**Is the Principal Investigator in the College of Medicine?**

i. Principal Investigators in the College of Medicine (COM) must submit their submission via the PeopleSoft system.

ii. Principal Investigators in other HSC, non-COM colleges may submit their submissions via the PeopleSoft system, via hard copy (with DSR-1), or via email to (with DSR-1).

**RAC Billing Grid**

p. The RAC Billing Grid depicts the study billing plan in a table format.

q. The grid should be an accurate representation of all study-related services and activities required by the protocol.

r. It identifies which services will generate either technical fees that will be billed by Shands Patient Financial Services (PFS) and/or professional fees that will be billed by University of Florida Physicians (UFP).

s. The grid also shows payment sources for each service/activity (e.g., participant/third party payer, sponsor-funding, UF CRC, etc.):

   i. **STEP 1: Determine if the study “Qualifies” for Medicare coverage of “Routine Costs”**.
      1. Before building the grid, the Principal Investigator must determine if the research study qualifies for coverage according to Medicare rules.

   ii. **STEP 2: Identify the Protocol-Required Services**.
      1. Carefully review the protocol and Schedule of Events (SOE) table to identify all required clinical services that must be completed over the course of the entire study.
      2. Be sure to review the entire protocol, as it is common for additional requirements to be excluded from the SOE table.

   iii. **STEP 3: Build the Grid**.

      t. **Row 1 – Hyperlink to Form Instructions**

      u. **Row 2 – Study Short Name**
         1. This should match the “Study Short Name” that is entered on the RAC Study Registration and Initiation Checklist.

      v. **Row 3 – Medicare Qualifying Question**
         i. This question must be answered for ALL studies.

      w. **Row 4 – Medicare Status**
i. This row holds a drop-down box that contains possible answers to the Medicare Qualifying questions.

ii. Click on the red text and a small arrow will appear on the right side.

iii. Click the arrow and then click on the answers to see the full text that will display for that choice.

iv. *Note: The Medicare Qualifying Status must be provided, verified and confirmed by the Principal Investigator. See Medicare Coverage Analysis Worksheet.*

v. The text for this field has been formatted based on columns A-P remaining stable “as is”.

vi. Increasing/decreasing the width of these columns or deleting/adding columns between A-Q may affect the formatting in this field.

x. **Row 5 thru 12 – Key**

i. This area defines the various abbreviations used in the grid body to describe who will be paying for that particular item, services, activity or visit.

y. **Row 13 – Header Rows**

i. This row labels the columns on the grid.

z. **Column B – Location**

i. Indicate where the service will take place. This should be specific enough that any reviewer will know exactly where the service will take place (e.g. “sponsor’s central lab” or “Inpatient” or “MBI” or “Dr. X’s research Lab” or “Cardiology West Clinic”).

ii. If the activity could happen in various locations, list all applicable locations.

iii. This field will automatically wrap text and increase in height as text is entered. If the width of this column is manually changed, it may affect the formatting in the Row 3 Medicare Status field.

aa. **Column C - Procedure Code**

i. This column is required for the following:

1. items/services/activities that create a bill that must be paid with study funds (“S”),
2. items/services/activities that create a bill that must be paid by UF CRC (“C”),

3. UFP clinic visits paid via salary support (“SAL”).

4. UFP clinic eye exams paid via salary support (“SAL”).

5. For “S” or “C” services, use the procedure code that was referenced by the service provider on the Confirmation of Services form (or the Pricing Tool output if it was used in lieu of a Confirmation of Services form).

6. For salary-supported clinic visits, type in the code range 99201-99215.

7. For salary-supported clinic eye exams, type in the code range 92002-92014.

bb. **Column D - Name or Short Description of Item, Service, Activity**

   i. Enter the name or short description of each protocol-required item, service or activity.

   ii. This list will look very much like the items listed on the protocol “Table of Events”.

   iii. Most item/service/activities should be listed one per row, but in some cases, items/services/activities may be grouped together if they will be provided at the same time and location.

       1. For example, an Office Visit may be listed as “Office Visit (to include vitals, height, weight, physical exam)” if all these services were listed in the protocol and were going to be provided in the clinic during the visit.

   iv. Exception: Administrative activities such as consenting, QOL questionnaires, AE reports may be omitted.

   v. This field will automatically wrap text and increase in height as text is entered. If the width of this column is manually changed, it may affect the formatting in the Row 3 Medicare Status field.

cc. **Column E - Pro-Tech Indicator – Use for Shands/UFP services only**

   i. In this column, click any empty field in this column to display the drop-down choices.
ii. Use the drop-down to indicate if this item/service/activity will generate a professional (pro) fee or a technical (tech) fee, or both.

iii. In some cases, the study may have a service where the pro and tech fees will be paid differently – for example a chest X-ray where the tech fee will be billed to the study (“S”) and the pro fee will be waived because the PI doing the reading (“NB”).

iv. In these cases, either indicate the difference in billing scenario by creating two rows (one for pro and one for tech) OR create one row for the service and indicate “tech” (or “pro” if appropriate) and add a comment to the comments column that explains how the other piece will be done (e.g. “Reading will be done by PI. No pro fee”).

v. *Note: Some activities do not have the potential to create any type of fee (e.g., consenting, questionnaires, etc.)*

1. In these cases, the pro/tech indicator may be left blank.

dd. **Columns F thru P – Time-point Labels**

i. These fields can be edited to reflect time-points in the study (should match the time-point labels in the protocol “Schedule of Events”).

ii. If the width of these columns is manually changed, or if these columns are deleted, it may affect the formatting in the Row 3 Medicare Status field.

e. **Column Q – Comments**

i. This field is used to make comments about the specific service in this row. It can be used to indicate “reading exceptions”, expand on location, or explain other variables that may affect billing plan.

ii. For any “NB” services, the Study Team must explain in the comments what steps are taking place to ensure a bill is not generated (e.g., “Provider is billing PI directly” or “Study services will be conducted in a research-only clinic room” or “study coordinator will perform service”).

ff. **Rows 14 thru ∞ – Study Details**

i. Use each field to enter the details of the each service, item or activity.

ii. Once you get to Columns E-P, click the empty field to display the drop-down choices for the billing plan for this service at this time-point.
iii. Identify the funding source for each service listed by carefully reviewing the financial compensation/budget section of the agreement, contract or award.

iv. S = Study/Sponsor pays participant bill generated by Shands or UFP – The bill(s) generated must be directed to the study team for payment.

v. SAL = Clinic visit (CPT code 99201-99215) or clinic eye exam (CPT code 92002-92014) cost covered via study salary support. This indicates that the service provider is part of the study team, and that the study will pay the provider service directly via salary-support from that provider’s home department. The patient charge will be “zeroed” out and no bill will be generated by University of Florida Physicians.

vi. C = UF CRC pays – UF CRC has indicated on its Confirmation of Service that it will pay for this service. The bill(s) generated must be directed to UF CRC for payment.

vii. NB = No participant bill generated by Shands or UFP – This would apply to activities/services being provided in non-Shands non-UFP locations (e.g. research space, McKnight Brain Institute, core labs, outside labs such as Quest, etc.).

1. This would also apply to services where a “reading exception” has been requested.

2. Note: for locations other than research space, you will need to explain in the comments column what will happen to any bill that might be generated by the service provider.

viii. M = Item is to be billed to Medicare/Insurance/Patient without V70.7 or modifiers – For services /items that are being billed to participants or their insurance, but do NOT require modifiers.

1. See Use of V70.7 Diagnosis Code and Q0 Q1 Modifier.

ix. MQ0 = Item/Service under investigation in a “Qualifying” study to be billed to Medicare/Insurance/Participant with V70.7 & Q0.

x. MQ1 = “Routine Cost” in a “Qualifying” study to be billed to Medicare/Insurance/Participant with V70.7 & Q1.

xi. Note: Services that have an “S” or “C” in any column will need to have a Confirmation of Service (COS) form completed by the Service Provider.

xii. Reminders
1. List ALL protocol-required services and activities conducted by research personnel, a core/central facility, or service provider (exception: administrative activities may be omitted).

2. Be sure to attach Confirmation of Service (COS) Forms or Pricing Tool Output for any items designated “S”.

   xiii. Attach a UF CRC COS for any items designated as “C” or performed in UF CRC space.

   xiv. Tips

   1. To add ROWS, copy and insert at bottom.

   2. To add 1-2 TIME-POINTS, insert between column P and Q and adjust “comments” column.

   3. To add more than 2 TIMEPOINTS, do not insert columns. Use Supplemental RAC Billing Grid to indicate continuation of visit time=points or different arm.

RAC Review Process – Monitoring and Audits

XIX. All research involving human subjects conducted at the University of Florida will be in compliance with applicable State and Federal regulations and may be subject for review by the RAC.

   a. All Principal Investigators and their designees are required to support the execution of the study to promote proper billing procedures are followed for all concurrent payers such as the sponsor (contracting or granting agency), study participants, and/or their third party payers, including Medicare and other government payers.

XX. The RAC Auditors may conduct various types of fiscal compliance reviews and audits at different stages of a research study and for varying reasons.

XXI. The Auditors may review a study by examining a minimal amount of documents and/or systems in order to determine the type of audit needed:

   1. Limited Audits are a targeted review of a limited set of documents, systems, and/or participant activity involved with a specific research study.

   2. Full Audits consist of a complete investigation of all applicable documents, systems and participant activity related to a specific research study.

XXII. A study may be reviewed for the following reasons:

   1. Interim Audit: This is a full audit, usually randomly selected from the RAC database of submissions, for a study in which participants have been enrolled.
2. **For Cause**: This review is initiated when an actual or potential fiscal compliance concern is identified. These reviews may become limited or full audits.

3. **Closeout**: This review will take place after all study services are completed and are required before funding projects are closed out by Contracts and Grants. These reviews may become limited or full audits.

4. **Tracking Monitoring**: This is a review of the tracking log, study registration documents, R99 agreement, and billing grids, for an ongoing study. These reviews may take place any time during the life of a study and could potentially be expanded to limited or full audits.

XXIII. For more information, questions, concerns, or submission of a tracking log for closeout review, please contact CTC-Auditors@ufl.edu.


XXV. Examples of potential violations and probable consequences that exist under current University rules are also available: [Billing Compliance Assurance Information](https://www.fnas.ufl.edu/college-of-medicine-office-of-billing-compliance/billing-compliance-assurance-information).

### Clinical Trial Budget

XXVI. Clinical studies are usually funded on a per-patient basis with provisions for pro-rated payment for patients who do not complete the study.

XXVII. All costs necessary to conduct the study, including salaries, procedures, services, supplies and indirect costs, should be considered when determining the fixed per-patient amount.

XXVIII. Sponsors usually apply one of two options when presenting a budget:

   a. They may offer a certain amount per patient and ask that you work within that amount

   b. They may ask you to formulate a budget for them

XXIX. Either way, it is important to ensure that the amount agreed upon will adequately cover all costs associated with conducting the study.

XXX. The budget period for a clinical trial will equal the trial’s contractual date or the IRB end date whichever occurs first.

XXXI. Upon IRB renewal and notice to DSP’s Award Administration at ufawards@ufl.edu, your project end date will be adjusted accordingly in the accounting system.

**Research Budgeting & Pricing Tool**
XXXII. The UF Research Budgeting and Pricing Tool was designed to assist faculty and staff during the early stages of budget analysis by providing a convenient and efficient way to obtain a Medicare cost estimate for simple, straight-forward research services when the CPT code and location is known.

i. You will no longer need to send an inquiry and wait for a Confirmation of Service from ancillary departments in this situation.

ii. You will be able to find the answer yourself within minutes, on your own computer, and at a time that is convenient to you.

XXXIII. Access the Tool

i. For general outpatient research-funded services, proceed to the UF Research Budgeting and Pricing Tool to obtain a price estimate.

ii. You will need to know and enter the CPT code and planned service location to obtain an accurate pricing estimate. If you are not sure which CPT code to use for a service, please contact the ancillary/service providers for clarification or confirmation before using the tool.

iii. Click on this link to access the Tool: http://cms-pricing.ctsi.ufl.edu. You might want to bookmark the URL for future reference. Be sure to read the User Guide before you use the tool.

iv. Please note that access to the tool is restricted to UF and Shands networks. If you are off-campus, please use the UF VPN service or the Shands VPN service to access to access the Tool.

XXXIV. When NOT to Use the Tool?

i. Although the Tool was designed for convenience and efficiency, it does have specific limitations: It is important that it be used only when the correct CPT code and location are known with certainty.

   1. This will avoid unanticipated errors that may cause unexpected increased costs.

   2. Remember, the Tool only provides an estimated study cost at the time you use the Tool; the study will be charged for the actual service that is ordered, and the cost will be the Medicare rate applicable on the day the service is rendered.

   3. In addition, there are some other situations where the Tool should not be used, and the standard Confirmation of Services process should be followed instead.

   ii. If your study involves research-funded services meeting the following criteria, DO NOT USE THE TOOL.

   iii. Instead, please contact the service providers directly to obtain research price estimates, following their instructions for the Confirmation of Service (COS) processes.
iv. Ancillary/service provider contact information may be found on the Shands & UFP Contacts page of the RAC website.

XXXV. **The tool may NOT be used for:**

1) **Inpatient stays:** For research-funded inpatient stays, contact Theresa O’Connell at oconta@shands.ufl.edu or 352-265-7965 ext. 86465 for Technical Fee price estimates and the individual UFP department(s) for Professional Fee price estimates.

2) **Implantation and explanation of investigational devices or PMA/510k carotid artery stenting:** Contact Theresa O’Connell and the individual UFP department(s) for price estimates.

3) **Complicated services:** For complicated services or procedures (e.g., surgical procedures; services involving more than one code such as ECGs), obtain a COS from the ancillary/service provider. Forward the COS to Theresa O’Connell and the individual UFP department(s) for price estimates.

4) **Pathology services:** For pathology services/procedures (e.g., biopsy tissue or slides), follow the UFL Laboratory/Pathology instructions to obtain a COS.

5) **Cytogenetics services:** For Cytogenetics services, request a COS from Brian Gray via e-mail (grayb@pathology.ufl.edu). Complete the COS form and return it to Brian with a copy of the protocol.

6) Investigational Drug Services and Non-investigational pharmacy services: For investigational drug and non-investigational pharmacy services, click here and follow the Investigational Drug Services (IDS) instructions to obtain a COS form.

7) **UF-CRC services:** For services performed at the University of Florida Clinical Research Center (UF-CRC), contact Jill Sandersen at sanderjn@ufl.edu or 352-265-8909.

8) **Services not found in the Tool** or any **service with multiple options for codes where you are uncertain which code to use:** Obtain a COS from the ancillary/service provider. Forward the COS to Theresa O’Connell and the individual UFP department(s) for price estimates.

9) **Innovative procedures or services not previously performed at UF or Shands:** Contact Theresa O’Connell and the individual UFP department(s) for price estimates.

10) **Services not performed at UF or Shands:** Contact the outside service providers directly for pricing.

11) **Shands “send-out” labs:** Follow the UFL Laboratory/Pathology instructions to obtain a COS.

12) **Training for the Tool**

See RAC809 RAC Hot Topic – Research Budgeting and Pricing Tool.

XXXVI. **Negotiating Budget With Sponsor**

**Covering Costs**
1. Investigators should be entering into budget negotiations with the intention of at least covering their costs.

2. An investigator and University of Florida, cannot bear losses on clinical trials, which are generally not activities supported by other revenue sources (such as state dollars).

3. Sponsors should not expect you to cost-share on clinical trials and you should not have that expectation either.

4. Shortages should be clearly identified during the Pre-Award stage to ensure that all parties are agreeable to this type of arrangement—not identified after a contract is executed.

5. If conducting the clinical trial is in the best interest of the institution and patients, and sponsor funding is not sufficient the amount of the shortage, and who will cover this cost must be identified and agreed upon during the Pre-Award stage.

   ii. Before beginning any negotiations with the Sponsor, it is critical to build an accurate detailed budget based on actual costs.

   iii. By providing the Sponsor with accurate cost data, a positive outcome is more likely:

       1. Sponsors routinely allocate an initial budget amount to each participating site.

       2. This budget may contain details of each cost, offer a per-patient total or provide a detailed schedule of payments depending on the work performed.

       3. The initial amount offered may or may not cover what it will actually cost to conduct the study.

       4. By preparing a detailed budget, you have the opportunity to contact the sponsor and negotiate adequate funding based on your costs.

       5. Usually, the sponsor is willing to work with you to the satisfaction of both parties.

       6. However, there may be situations that may require serious consideration as to whether or not it makes sense to conduct the clinical trial.

           7. **This decision must be made prior to the signing of the contract or agreement.**

   XXXVII. **Grand Total Cost**

       1. The total cost of conducting the study needs to equal the total funding for the study.

       2. Contingencies need explanation or justification.
b. The more clear the explanation is of what costs are paid using the Sponsor’s funding (what the sponsor is paying for and what they are not paying for) the less risk and increased protection which will produce a solid budget that is defensible of our budget and billing plan.

1. Verify that your final budget negotiated with the sponsor matches the budget and payment terms in the clinical study agreement.

2. The budget and payment terms in the signed clinical study agreement are the official budget documents.

XXXVIII. Lack of Funds

1. Careful preparation of the budget by adhering to the Standards should minimize the occurrence of lack of funds.

2. If it is determined that the cost of performing the study is greater than the Sponsor’s funding offer, renegotiating the budget with the sponsor is expected.

3. If the sponsor will not fully cover the cost of performing the study or the study is internally funded, it is the responsibility of the principal investigator, in conjunction with the division chief and/or department chair to determine the source of the alternative funding and secure the signed approval of the appropriate individual for the study to proceed.

XXXIX. Large Overage of Funds

1. Payments for clinical trials should reflect the fair market value of the work being done.

2. It is important to emphasize that this does not mean that the payment may only cover the total costs of the study.

3. However, if our detailed budget indicates that the payment will actually result in compensation that is significantly more than the total costs of the study, it is advisable to consult either the RAC or UF General Counsel’s Office to explore the matter more fully and ensure that there are no regulatory concerns.

XL. Budget Negotiating Tips

i. As is true for any type of negotiation, the two parties rarely offer their best or final offer at the beginning of negotiations.

ii. Sometimes a Sponsor may tell you that they can’t afford higher costs.
b. Remember that the Sponsor has a great deal to gain by your participation, and you don’t know if you don’t ask.

i. Typically, not enough money is budgeted for startup and documentation preparation tasks. Be sure to ask for these costs as early as possible, and that these are paid upon contract execution.

ii. If the Sponsor decides to not continue the study before the contract is signed, asked for those costs to be paid.

c. The more accurate and detailed your internal budget is, the more likely it becomes funded. Be firm, especially when negotiating administrative time. This is often an area that is perceived to be fully covered by indirect costs when in fact, they are not.

i. Many Sponsors prefer to work with investigators from Academic Health Centers.

iii. If this is a Sponsor that you already have worked with, it is important to remind them of the high quality and reliable work that you produced on their previous trials.

iv. If all costs in the budget are agreeable except for the hospital and/or professional services, negotiate with the Sponsor to be sure they have provided you with the highest reimbursement rate for those services.

v. Always start your negotiations with the List or Negotiation Price for each service.

1. Remember the basic rate is only an estimate, the study will be charged the actual rate on the date of service, which may be higher than the basic rate you obtained from the from the Pricing Tool/confirmation of service.

2. Plan for this in determining the minimum you can accept from the sponsor for each service.

3. If you cannot cover your costs after negotiating with the Sponsor and/or service providers, consider using another service provider who can provide the same service for a lower cost.

vi. If you are conducting a study that involves an inpatient admission, many of these inpatient costs may not be anticipated at the point of negotiating the budget and may not be covered by the sponsor.

1. Consider including a clause in your contract stating that these unanticipated inpatient costs will be covered by the sponsor.

2. A good example of language to insert in the contract is as follows: “Because [study] involves an inpatient admit for research reasons, sponsor will reimburse site for actual cost plus overhead for personal medications administered during inpatient hospitalization period and for any other supplies, labs, etc. required during the inpatient hospitalization period.”
vii. Be sure that the person who is negotiating with the Sponsor is knowledgeable and confident in their approach, knowing what is needed to obtain the necessary results.

viii. If you are the PI of the clinical research study, consider obtaining negotiating assistance from peers, the department, Research Administration and Compliance (RAC) or Division of Sponsored Programs (DSP).

1. If you are negotiating on behalf of the PI, be sure to obtain the PI’s input regarding the negotiations, and arrange for them to participate in the negotiations when appropriate.

2. Don’t hesitate to obtain help from others who have negotiated budgets before.

ix. Carefully review the budget and payment terms in the contract or agreement and verify that these budget and payment terms match your negotiated budget.

1. The final clinical study agreement (CTA) negotiations and signature authority are the responsibility of DSP.

2. If you have entered into any negotiated changes, be sure to explain this important step to the Sponsor.

x. For additional help in developing and negotiating study budgets take the class: Building a Detailed Budget (Course# RAC803).

**Budget Templates**

b) The budget clearly identifies all services/activities that are required by the study protocol, along with other costs necessary to conduct the study, and indicates what services/activities/costs the Sponsor is (or is not) paying for.

**When is a Detailed Budget required?**

**c) Download Detailed Budget Template**

a. A Detailed Budget is completed when any claims for study-required clinical services will be billed to the participant/third party payer.

b. It is recommended a Detailed Budget be created when a sponsor/grant is funding any study services or activities.

c. This budget is used to ensure the sponsor/grant is providing sufficient funding to cover all study costs.

d. It also demonstrates the study team’s plan for how the sponsor’s/grant’s money will be used to pay study expenses.
d) What is a **Detailed Budget**?
   
a. The detailed budget is a document which lists all expenses of conducting a study including: services, activities, personnel, supplies and equipment, document storage, etc., and the cost for each item listed in the budget.
   
b. The detailed budget is used to determine the actual cost of the study and for negotiating the budget with a sponsor or submission of a grant application.

e) How do I create a **Detailed Budget**?
   
a. A Detailed Budget may be created using any of the following, provided it includes all the costs of conducting the study as explained below:
   
i. RAC Detailed Budget template.
   
ii. Template provided by the sponsor.
   
iii. PI/department’s budget template.
   
iv. Any other document that includes the required information.

f) How do I complete the **Detailed Budget** Template?
   
a. Carefully review the protocol table of events, procedures, appendixes, and other study documents to identify all the services/activities required by the protocol. Then complete each section of the template as explained below.

**g) Study Start-Up Costs**
   
a. Non-refundable, one-time costs that are generally due upon execution of the contract.

**h) Considerations**
   
a. Feasibility costs (e.g. protocol review & budget evaluation).
   
b. Investigator meetings.
   
c. Site Evaluation/Initiation Visits.
   
d. Document submission (e.g. IRB/Regulatory documents).
   
e. Pharmacy set-up.
   
f. Sponsor-required training.
   
g. Advertising.
   
h. Long-term record retention.
   
i. Materials/supplies.
j. Equipment

i. The sponsor should provide all equipment.

ii. If the equipment is being loaned, review the contract to see if it is to be returned at the end of the study. It could be considered an incentive if the sponsor does not require the equipment to be returned.

iii. If materials or supplies are required before beginning enrollment, try to recover the cost at start-up so reimbursement is not enrollment based.

i) Instructions

a. Enter the direct cost for each line item.

b. Add additional rows if necessary and make sure to double check the formulas.

c. Non-applicable cells can be left blank, deleted, or a “0” can be entered.

j) Visit Schedule

i. Carefully review the protocol and Schedule of Events (SOE) table to identify the time points for all activities that must be completed over the course of the entire study. Be sure to review the entire protocol and study documents as it is common for additional requirements to be provided in the procedures, appendixes, or other study documents such as manuals.

ii. Enter the schedule (Baseline, Visit 1, Cycle 1, Month 3, etc) for all tests, procedures, or activities required by the protocol.

k) Personnel including Fringe Benefits

a. Amount of time (effort) each individual will spend working on the study.

l) Considerations

i. Principal Investigator (PI) oversight.

ii. Screening of medical records/interviewing subjects to determine eligibility.

iii. Consenting a subject including reviewing the consent with the subject, making copies, and documenting the consent process.

iv. Scheduling tests, procedures and follow-up visits.

v. Collecting, processing and shipping laboratory/pharmacokinetic samples.

vi. Conducting study questionnaires.
vii. Completing case report forms.


m) Instructions

a. Use one row for each individual and enter their name and study role.

b. Add additional rows if necessary and make sure to double check the formulas.

c. Obtain each individual’s annual salary and fringe benefit cost from PeopleSoft.

d. Use the following formula to calculate each individual’s hourly salary & fringe cost:

   i. \[
   \text{[Annual salary & fringe cost]} / 2088
   \]

e. Use the following formula to calculate each individual’s per visit cost and enter it in each appropriate cell:

   i. \[
   \text{[Time per visit]} \times \text{[Hourly salary & fringe cost]}
   \]

f. Use the following formula to calculate each individual’s total percentage of effort and enter it in each appropriate cell:

   i. \[
   \text{[Per Participant cost]} \times \text{[Number of Participants]} / \text{[Annual salary & fringe cost]}
   \]

g. The worksheet will automatically calculate the “per participant” cost for each individual and the category subtotal.

n) Expenses/Materials/Supplies

a. Additional materials, supplies, or other expenses required to conduct the study. These are usually not listed in the schedule of events.

o) Considerations

a. If materials or supplies are required before beginning enrollment, try to recover the cost at start-up so reimbursement is not enrollment based.

b. Investigational Drug Service dispensing fees.

c. Maintenance fees for equipment.

d. Laboratory supplies (e.g. gloves, shipping containers, dry ice/ice packs, slides, tubes, etc.)

e. Phone, fax or data port.

f. Copies.
g. Stamps or express mail service.

p) Instructions
   a. Use one row for each expense, material or supply.
   b. Add additional rows if necessary and make sure to double check the formulas.
   c. Enter each per visit cost.
   d. The worksheet will automatically calculate each per participant expense, material, or supply cost and the category subtotal.

q) Subject Travel and Stipends

r) Considerations
   a. Consider a flat-rate participant stipend instead of calculating travel costs.
   b. Ensure you follow all UF Travel rules.

s) Instructions
   a. Use one row to list each traveler.
   b. Add additional rows if necessary and make sure to double check the formulas.
   c. Enter each per visit cost.
   d. The worksheet will automatically calculate each per participant travel cost and the category subtotal.

t) Participant Care Costs

u) Considerations
   a. You must include per visit costs for all study required tests, procedures, visits, or activities that will be funded by a sponsor.
   b. This includes tests/procedures/office visits that are billed directly to the research account (R99), or tests/procedures/visits that are billed directly to the PI by the provider, including any outside vendor services.
   c. Ensure you budget all the test or procedure costs (technical and professional or global).

v) Instructions
   a. Carefully review the protocol, Schedule of Events, appendixes, and other study documents to identify all required activities over the course of the entire study.
b. Be sure to review the entire protocol, not just the Schedule of Events Table, as it is common for additional requirements to be found in other sections of the protocol.

c. Although not required, it is recommended to include study required services that will be billed to insurance/participant with a $0 charge in the budget.

i. This will provide a complete list of all services/activities and how each will be paid (billed to study or billed to third party payer/participant).

ii. *NOTE: Only routine care in a Medicare Qualifying Study may be billed to third party payer/participant. See Medicare Qualifying Studies.*

d. Use one row to list each test, procedure, visit or activity.

e. Add additional rows if necessary and make sure to double check the formulas.

f. Enter each per-visit cost to be paid from the study account.

i. Sponsors should be charged the list price from the Confirmation of Service Form (COS) or Negotiation Rate from the Pricing Tool for each service.

g. Enter the number of times each service is to be performed at each time point

w) **Subtotals & Totals**

a. The budget template will automatically calculate:

i. All category subtotals.

ii. Total “per participant” direct cost.

iii. Grand total “per participant” cost.

iv. Grand total with 5% allowance for potential price increase at time of service.

b. Enter the total number of patients you plan to enroll per year and the worksheet will calculate:

i. Grand total participant cost over 5 years.

ii. Add or deletes years if necessary and make sure to double check the formulas.

x) **Invoicable Costs**

a. Costs for services/activities that may or may not occur but need to be included in the contract.

y) **Considerations**

a. Screen failures.

b. IRB submissions
c. Amendments.

d. IND/safety reports.

e. Annual renewals.

f. If you are using WIRB, try to negotiate contract language to bill all WIRB costs directly to the Sponsor so that institutional overhead and personnel effort can be avoided. Suggested language might read, “The University of Florida will utilize Western Institutional Review Board and all fees associated with its use will be billed directly to the Sponsor.”

g. FDA or Sponsor audits.

h. Professional travel to conferences for presentations or other associated with the study. Ask the sponsor to arrange & pay for all professional travel for investigator meetings or conferences.

i. Supplies, equipment or materials not included in the per participant costs.

j. Tests or procedures that do not apply to every subject, such as:
   i. Pregnancy tests.
   ii. Tests or procedures that only need to be obtained in select scenarios (i.e. test required at screening if not performed prior to consenting).
   iii. Note: All tests/procedures/items provided to a participant at no cost must be provided at no cost to all participants in the study.

k. Unanticipated costs
   i. If you are conducting a study that involves an inpatient admission, many of these inpatient costs may not be anticipated at the point of negotiating the budget and may not be covered by the sponsor.
   ii. Consider including a clause in your contract stating that these unanticipated inpatient costs will be covered by the sponsor.
   iii. A good example of language to insert in the contract is as follows:

   1. “Because [study] involves an inpatient admission for research reasons, sponsor will reimburse site for actual cost plus overhead for personal medications administered during inpatient participant hospitalization period and for any other supplies, labs, etc. required during the inpatient hospitalization period.”

2) Instructions (except for Unanticipated Costs)

   a. Enter the direct cost for each line item.
b. Add additional rows if necessary and make sure to double check the formulas.

c. Non-applicable cells can be left blank, deleted or a “0” can be entered.

d. Use the “Other” row to include an invoicable cost that is not outlined.

e. The worksheet will automatically calculate each line item indirect and total cost.

**aa) Review & Evaluate Fiscal Feasibility**

a. Compare the actual costs in the Detailed Budget against the Sponsor’s budget.

**bb) Lack of Funds?**

a. If it is determined that the cost required to conduct the study is greater than the sponsor’s funding offer:

   i. Renegotiate the budget.

   ii. Identify additional funding.

1. If the sponsor will not fully cover the cost or the study is internally funded, it is the responsibility of the principal investigator, in conjunction with the division chief and/or department chair, to determine the source of the alternative funding and secure the signed approval of the appropriate individual for the study to proceed.

   iii. Do not conduct the study.

**cc) Large Overage of Funds?**

a. Research payments should reflect the fair market value for the work being done. It is important to emphasize that this does not mean that the payment may only cover the total costs of the study.

b. However, if your detailed budget indicates that the payment will actually result in compensation that is significantly more than the total costs of the study, it is advisable to consult either the RAC Office or General Counsel’s Office to explore the matter more fully and ensure that there are no regulatory concerns.

**When is only a Limited Budget required?**

**c.** The study does not require any clinical services.

**OR**

**d.** The sponsor is funding all study-required clinical services; therefore, NO claims will be submitted to the patient/third party payer.

e. **NOTE:** Although not required for RAC submission when the sponsor is paying for all study-required clinical services, it is recommended that an internal Detailed Budget be developed for all studies to
accurately determine all the costs of conducting the study to ensure adequate funding is obtained from the sponsor or grant.

f. What is a **Limited Budget**?

   i. The format of a Limited Budget can vary; however, it must include, at minimum, the following elements:
      1. Study Title.
      2. Principal Investigator’s Name.
      3. List of all personnel (salary and fringe) costs.
      4. If applicable, list of all patient care costs (any tests, procedures, or other services) funded by a sponsor.

g. My study meets the criteria for a Limited Budget, but I don’t have any type of budget. What should I do?

   i. Use the Limited Budget template to create a budget with the required elements.

   ii. Create a budget using any template that has the required elements listed above.

   iii. *Please note: If your study does not have any salary support or patient care costs, a statement to that effect signed by the Principal Investigator can take place of a limited budget.*

h. I already have a budget for my study. Can I use it as a Limited Budget?

   i. As long as the elements listed above are included, any pre-prepared budget can be used. Some examples of what can be submitted as a “limited” budget include:

      1. The budget provided by the sponsor.
      2. The budget submitted by Principal Investigator when he/she applied for the grant or award.
      3. The PeopleSoft budget submitted via the PeopleSoft Proposal module.
      4. The budget presented to Department Chair’s when using departmental funds.
      5. A Detailed Budget

**Indirect Costs**

dd) The established Indirect costs (IDC) rate for non-federal clinical trials at the University of Florida is 28% of total direct costs (TDC).

ee) When payment is received, 21.875% of total cash received is assessed for indirect costs while the remaining direct component is released into the 214 project for spending.

ff) For example, if a $15,000 payment is received from a clinical trial sponsor; then the payment will be split into directs and indirects as follows: $15,000 payment x 21.875% = $3,281.25 for indirects, leaving $11,718.75 for the direct costs.
IRB and WIRB Fees

All investigators are required to use WIRB (IRB-04) for industry sponsored Clinical Trials, unless an exemption is granted by the College of Medicine’s Dean’s Office.

gg) The WIRB fees (http://irb.ufl.edu/WIRB/wirbcosts.html) may be charged directly to the industry sponsored CTA, or the sponsor may elect to pay WIRB directly. If the latter is the case, the WIRB invoice must be sent to the sponsor for payment.

hh) Be sure to budget in advance for these expenses as appropriate. Be aware that WIRB will charge for every revision to the protocol. Take this into consideration in your budgeting as this is frequently a place where trials lose money.

Billing Plans

ii) The first step in developing a reasonable budget is to generate a billing plan that shows who will be paying the costs of all items, services and activities required by the protocol.

jj) Since all medical procedures must be billed consistently to all payors, if the contract states that the sponsor will pay for Procedure A, then the sponsor must be billed for every occurrence of Procedure A across all accrued subjects, i.e. you cannot bill Medicare for Procedure A performed on Subject XYZ and bill the sponsor for Procedure A performed on Subject LMN.

   a. Expenses related to your clinical trial must be treated consistently across:

      i. All study documents from the Informed Consent form in the protocol to the signed contract (which includes the clinical trial budget) to billing submissions

      ii. All sources of payment such as Medicare, the patient, the patient’s insurance carrier, and the sponsor

      iii. All expenses related to the conception, execution, and close-out of a clinical trial need to be captured and accounted for in the budget and billing processes. Expenses include but are not limited to:

         1. All procedures listed in the protocol study table – be sure to include any procedures resulting in a cost that might be necessary though not specifically stated.

            a. Example: the study table might include a CBC with platelet count but not list the blood draw necessary to run the test. The blood draw has an associated cost that should be included in the budget.
2. All activities in the protocol outside of the study table that represent a cost. Example: the protocol may require that samples be shipped.

   a. Those shipping costs need to be accounted for in the budget.

3. Pre-study and Start-up costs:

   a. For example: pre-award services, pharmacy set-up costs, radiology start-up fee, IRB review fees, etc. Sponsors may ask for a breakdown of expenses included in specific start-up fees. Each unit (Pharmacy, Radiology, CHR, etc.) that charges a start-up fee can provide the breakdown of costs.

4. Costs for financial management of the trial. This includes billing the sponsor and costs related to maintaining billing compliance, such as using the OnCore clinical trial management system.

5. Follow-up phone calls after treatment completion.

6. Close-out costs which may include storage of study documents and auditing.

kk) If an expense is not included in the budget in the signed contract, then it may not be billed to the sponsor. If you wish to bill the sponsor for an expense not included in the current agreement, the sponsor must agree to the additional charges and an amendment to the contract would need to be negotiated and signed, if possible. If the sponsor refuses to pay for expenses that have not been included in the budget, the PI and their respective department will be responsible for those costs.

ll) Depending on PI discretion and protocol design, the study may have items/services that are:

Sponsor-Funded

mm) Research-funded items/services generate a bill that needs to be re-directed to the study’s billing account number or “R99.” These items/services pose the biggest billing compliance risk.

nn) If sponsor-funded items and services are not correctly identified, they could end up being billed out to the participants or their insurance companies.

   a. In many cases, these trigger the False Claims Act, which places the Principal Investigator and his/her UF department at risk of fines.

oo) The UF HSC has many processes in place to circumvent this billing risk:

   a. They include the Confirmation of Services and R99 process, use of research order forms, and Tracking Logs for sponsor-funded services.
b. The study team must make certain that all of these processes are followed in order to ensure that the billing plan is followed correctly.

**Billable directly to the participants and/or their insurance companies (third party payers)**

pp) These are items/services that are “qualified” to be billed out to participants and/or their insurance companies (third party payers).

a. The University of Florida uses the [Medicare National Coverage Determination (NCD) for Routine Costs](https://www.cms.gov) and [Medicare Investigational Device Rules](https://www.cms.gov) as a basis for determining what study items and services may be “billed out” to research participants and/or their third party payers, i.e. study service that are standard of care (SOC).

b. “Routine costs” of a clinical research study include all items and services that are otherwise generally available to Medicare beneficiaries (i.e., there exists a benefit category, it is not statutorily excluded, and there is not a national non-coverage determination) that are provided in either the experimental or the control arms of a study.

1. **Routine Costs include:**

   a. Items or services that are typically provided absent a study (e.g., conventional care);

   b. Items or services required solely for the provision of the investigational item or service (e.g., administration of a non-covered chemotherapeutic agent);

   c. The clinically appropriate monitoring of the effects of the item or service, or the prevention of complications; and

   d. Items or services needed for reasonable and necessary care arising from the provision of an investigational item or service in particular, for the diagnosis or treatment of complications.

2. **Routine Costs DO NOT include:**

   a. The investigational item or service itself (unless otherwise covered outside of the study);

   b. Items and services provided solely to satisfy data collection and analysis needs and that are not used in the direct clinical management of the patient (e.g., monthly CT scans for a condition usually requiring only a single scan); and

   c. Items and services customarily provided by the research sponsors free of charge for any enrollee in the trial.

qq) In order for a study to be considered “Qualifying” is must meet all of the following three requirements:

   a. The subject or purpose of the trial must be the evaluation of an item or service that falls within a Medicare benefit category (e.g., physicians’ service, durable medical equipment, diagnostic test) and is not statutorily excluded from coverage (e.g., cosmetic surgery, hearing aids).
b. The trial must not be designed exclusively to test toxicity or disease pathophysiology. It must have therapeutic intent.

c. Trials of therapeutic interventions must enroll patients with diagnosed disease rather than healthy volunteers. Trials of diagnostic interventions may enroll healthy patients in order to have a proper control group.

rr) These things are, however, necessary but not sufficient to consider a trial to be “Qualifying.” Studies also should have the following seven desirable characteristics:

   a. The principal purpose of the trial is to test whether the intervention potentially improves the participants’ health outcomes.

   b. The trial is well-supported by available scientific and medical information or it is intended to clarify or establish the health outcomes of interventions already in common clinical use.

   c. The trial does not unjustifiably duplicate existing studies.

   d. The trial design is appropriate to answer the research question being asked in the trial.

   e. The trial is sponsored by a credible organization or individual capable of executing the proposed trial successfully.

   f. The trial is in compliance with Federal regulations relating to the protection of human subjects.

   g. All aspects of the trial are conducted according to the appropriate standards of scientific integrity.

ss) There are four types of studies that CMS has deemed to automatically meet the following seven desirable characteristics requirement above:

   a. Studies funded by NIH, CDC, AHRQ, CMS, DOD, and VA.

   b. Studies supported by centers or cooperative groups that are funded by the NIH, CDC, AHRQ, CMS, DOD, and VA.

   c. Studies conducted under an investigational new drug application (IND) reviewed by the FDA.

   d. Drug studies that are exempt from having an IND under 21 CFR 312.2(b)(1).

tt) The Medicare Coverage Analysis Worksheet incorporates the qualifying criteria discussed above and is to be used by the Principal Investigator if the study is a “qualifying” study.

uu) The Medicare Analysis Worksheet is NOT to be used for Investigational Device studies or studies involving Carotid Artery Stenting (CAS).

vv) If the study is not a Medicare qualifying study, then we cannot bill any services associated with the study and the cost of all study required services must be paid by study funds.
a. Study Does Not Qualify for Medicare Reimbursement:

i. If the study is not a Medicare-qualifying or pre-approved study, then UF cannot bill out any “routine costs” associated with the study.

ii. All of the study budget projections must reflect that lack of income.

iii. The study team must ensure that the patients considering entering the study know that it will likely be their personal responsibility to pay.

iv. Alternatively, we can ask the sponsor to pay for ALL protocol-required services, including “routine costs” and/or standard of care services associated with the study.

v. Also, it is possible that the Sponsor may be able to make changes to the study so that it will meet Medicare Qualifying rules.

vi. Keep in mind that many third party payers are agreeing to follow the Medicare policy, and there are many patients under the age of 65 who have Medicare as their payer, so age is not always a factor.

vii. Each potential study participant’s payment source will have to be evaluated individually so bills are not sent out to payers incorrectly and so participants have all the fiscal information they need to make an informed decision.

viii. Misrepresentation of Studies as “Qualified” to Gain Medicare Coverage:

1. All claims submitted to Medicare for coverage as “routine costs in a qualifying study” are subject to review and audit by the Center for Medicare and Medicaid Services Chief Clinical Officer. If a study is found to not qualify, then:
   a. Medicare coverage of routine costs is denied.
   b. Medicare enrollees are not liable for the costs.
   c. Principal Investigator’s department and billing providers are liable for the costs where appropriate.
   d. Billing providers and Principal Investigators are subject to fraud investigation.

ww) Once the Principal Investigator has determined that the study is a “qualifying study”, each billable item/service in the study must be pre-identified as “MQ0” or “MQ1” on the billing grids so that the study team will know the correct coding for claims.

xx) In addition, the Investigators (or their designees) are responsible for providing the billing offices with necessary information so that these offices can code the correct information on claims submitted to Medicare for services rendered in a qualifying clinical study as follows:

1. Each claim for an outpatient hospital/technical service must include the diagnosis code V70.7 as the secondary diagnosis (primary for healthy controls) with either Q0 or Q1 modifier attached.

2. Each claim for inpatient hospital/technical service or must include the diagnosis code V70.7 as the second or higher diagnosis (modifiers are not needed).

3. Each claim for a professional service (both inpatient and outpatient) must include the diagnosis code V70.7 as the secondary diagnosis (primary for healthy controls) with either Q0 or Q1 modifier attached.
yy) The use of the QO and Q1 modifiers and V70.7 diagnosis codes is the Principal Investigator’s attestation that the services are provided in a study that meets all criteria of a Medicare qualifying study.

zz) Clear documentation must be provided in the patient’s chart. The following information must be placed in the beneficiary’s medical record:

1. Study name
2. Sponsor’s name
3. Sponsor-assigned protocol number

aaa) If Medicare initiates a medical review, a copy of the signed informed consent must be readily supplied upon request. Additionally, the billing provider must submit a detailed itemization of items and services billed as routine costs in the study.

i. IND & IND-Exempt Study Sponsor Identification:

1. Sponsors of IND and IND-exempt studies must identify themselves to Medicare via email at clinicaltrials@cms.hhs.gov and include the following information in the notification:
   a. Study sponsor’s name and contact information
   b. Information on drug under study (name, route of administration, etc.)
   c. Disease being investigated
   d. Expected enrollment and length of study
2. Study teams should obtain verification from the Sponsor that the above notification has been sent to Medicare.

ii. Coverage with Evidence Development:

1. On July 12, 2006 CMS released a guidance document titled National Coverage Determinations with Data Collection as a Condition of Coverage:

   iii. Coverage with Evidence Development (CED). This document concerns the circumstances under which CMS would issue a national coverage determination (NCD) requiring, as a condition of coverage, collection of additional patient data to supplement standard claims data. See Centers for Medicare and Medicaid Services Website for more details.

Studies with Investigational Components

bbb) These are studies where the aim or objective of the study involves an “investigational component.” “Investigational component” is defined as a service, item, treatment or procedure that is NOT standard of care (SOC) and not available outside of the study. Some examples are:
a. Study of a drug with an FDA Investigational New Drug (IND) number.

b. Study of an FDA-approved drug being used in a new indication.

c. Study of a device with an Investigational Device Exemption (IDE).

d. Study of a new treatment regimen, such as radiation being used on a body site where it is not SOC to use radiation or radiation being offered at different levels/intervals than is SOC.

As long as the sponsor is NOT paying for or providing the item or service, UF policy allows the following types of study items/services to be “billed out” (accompanied by correct codes and modifiers):

a. Devices and “routine costs” provided in a device study pre-approved by Medicare.

b. “Routine costs” in a study that “qualifies” using rules established under the Medicare National Coverage Determination (NCD) for Routine Costs. See Medicare Qualifying Studies.

c. Complications (if not covered by study sponsor). See Complications and Subject Injury.

d. Note: Study services performed for research purposes only (e.g., data collection or eligibility services that are not standard of care) may NOT be billed out. They must be paid for or provided by the sponsor.

Studies with NO Investigational Components

ddd) These are studies where the aim or objective of the study does NOT involve an “investigational component.” Some examples are:

a. Study comparing two standard-of-care treatment regimens.

b. Observational studies (no change to standard of care).

c. Chart review studies (no change to standard of care).

d. Data collection studies (no change to standard of care).

What May Be Billed Out In Studies with NO Investigational Components:

a. Regular standard of care items and services (if not covered by study sponsor).

b. Complications (if not covered by study sponsor).

c. Note: Study services performed for research purposes only (e.g., data collection or eligibility services that are not standard of care) may NOT be billed out. They must be paid for or provided by the sponsor.
Items/services activities that are provided in such a way that no bill is generated

fff) These items/services/activities are provided in a manner or location where no participant bills can be generated. Some examples are:

a. Services provided in a research-only room in a clinic.

b. An MRI conducted at the McKnight Brain Institute.

c. An extra tube of research blood drawn off a standard of care phlebotomy.

d. Activities conducted at a health science fair.

e. Under most circumstances, these items/services/activities pose low billing compliance risk, **but if the location of the activity changes, the risk could change dramatically.**

f. Another example of increased risk is when these “No Bill Generated” items/services/activities are being provided in a clinic setting where they could be confused with a participant’s standard of care services unrelated to the study.

   i. Great care must be taken to ensure that the Study Team understands the billing plan and the clinic procedures so that the items intended as “No Bill Generated” do NOT, in fact, generate a charge.

**Use of V70.7 Diagnosis Code and Q0 Q1 Modifiers**
Principal Investigators are responsible for determining and providing the appropriate V70.7 diagnosis code and the appropriate Q0/Q1 modifier needed on any claims to research participants or their insurance for clinical services or items rendered in the following type of clinical research studies:

a. Any study that the Principal Investigator has determined to be a “qualifying clinical trial/research study” under the rules of Medicare Clinical Trials National Coverage Determination (NCD) using a Medicare Coverage Analysis;

b. Any Investigational Device Exemption (IDE) trial that has been pre-approved by our local Medicare office;

c. Any study supported by Medicare under a pre-approved Medicare Coverage with Evidence Development (CED).

For these types of studies ONLY, Principal Investigators must provide the V70.7 diagnosis code and the appropriate Q0/Q1 modifier on clinical encounter forms, ancillary order forms, or the electronic medical record for services that are to be billed out.

a. If fields for these codes are not available on the forms or in the electronic medical record, the V70.7 diagnosis code and the appropriate Q0/Q1 modifier must be identified in the medical notes or comments.

Some examples of research studies that DO NOT require the V70.7 diagnosis code and the Q0/Q1 modifiers are:

a. Studies that do not involve any investigational items, services or treatment (studying Standard of Care);

b. Observational Studies (no change to Standard of Care);

c. Chart Review Studies (no change to Standard of Care);

d. Data Collection Studies (data collection-only services must be paid by sponsor);

e. Studies where sponsor is paying for all services (no billing to study participants or their insurance).

Please note: The V70.7 diagnosis code and modifier should not be used without verification by the Principal Investigator.

The use of the Q0 and Q1 modifiers and V70.7 diagnosis code attest that Principal Investigator has determined that the services are provided according with Federal regulations and that:

a. The item or service is provided in one of the three types of studies described above;
b. The item or service is not already being paid for or provided by the sponsor; and

c. The item or service is billable under the applicable NCD, IDE pre-approval or CED rules.

III) For more details about what items or services need coding and modifiers, please see Medicare Billing & Coding Logic Diagram.

mmm) Additional Study Medical Record Requirements

a. The following information must be recorded in the beneficiary’s medical record (this information does not need to be submitted with the claim but must be provided if requested for medical review):

   i. Study name

   ii. Sponsor’s name

   iii. Sponsor assigned protocol number

   iv. If Medicare initiates a medical review, a copy of the signed informed consent must be readily supplied upon request.

   v. Additionally, the billing provider must submit a detailed itemization of items and services billed as routine costs in the study.

nnn) Misrepresentation of Studies as “Qualifying” to Gain Medicare Coverage

a. All claims submitted to Medicare for coverage as “routine costs” in an NCD “qualifying” study, pre-approved device study, or Medicare CED study are subject to review and audit by the Center for Medicare and Medicaid Services Chief Clinical Officer.

b. If a study is found to not qualify, then:

   i. Medicare coverage of routine costs are denied;

   ii. Medicare study enrollees are not liable for the costs;

   iii. Billing providers are liable for the costs where appropriate;

   iv. Billing providers and Principal Investigators are subject to fraud investigation.

ooo) V70.7 – Diagnosis Code
a. This diagnosis code identifies a patient as a subject in either a:

i. Medicare NCD qualifying clinical research study;

ii. Pre-approved Investigational Device Exemption (IDE) study or;

iii. Pre-approved Medicare CED study.

b. Billing claims should include the V70.7 diagnosis code as a secondary diagnosis (primary for those research participants who are normal healthy volunteers in therapeutic control groups).

ppp) Q0 – Investigational Item or Service

a. This modifier identifies investigational items or services.

i. These are defined as those items and services that are being investigated as an objective within the qualifying study (e.g. Investigational Cochlear Implant with an IDE Number).

b. Please note: Most investigational Items or services cannot be billed to research participants or their insurance, and are typically paid for or provided by the research sponsor. Some exceptions may include:

i. The investigational item or service itself if it would be covered outside of the clinical research study;

ii. A Pre-Approved FDA Category B Investigational Device with an IDE number.

qqq) Q1 – Routine Cost

a. This modifier identifies a “routine cost”.

i. These are defined as those items and services covered for Medicare beneficiaries outside of the research study; used for direct patient management within the study; and are not investigational items or services as described in the “Q0” section above.

b. “Routine Costs” include:

i. Items or services that are typically provided absent a clinical research study (e.g., conventional care);

ii. Items or services required solely for the provision of the investigational item or service;
iii. Items or services that are required for clinically appropriate monitoring of the effects of the investigational item or service;

iv. Items or services that are required for the prevention of complications;

v. Items or services needed for reasonable and necessary care arising from the provision of an investigational item or service—in particular, for the diagnosis or treatment of complications.

c. “Routine Costs” do NOT include:

i. The investigational item or service itself (unless otherwise covered outside of the study);

ii. Items and services provided solely to satisfy data collection and analysis needs;

iii. Items and services that are not used in the direct clinical management of the patient;

iv. Items and services used only to determine eligibility;

v. Items and services customarily provided by the research sponsors free of charge for any enrollee in the study.

rrr) Coding Requirements for Shands Hospital Technical Services Claims

a. Insurance claims for Shands hospital or technical services ordered as part of:

i. Medicare NCD qualifying clinical trial/research study,

ii. Pre-approved Investigational Device Exemption (IDE) study or

iii. Pre-approved Medicare CED study

b. These must include:

i. V70.7 as the secondary diagnosis (primary for healthy volunteers);

ii. Q0 or Q1 modifiers for each item/service (except for inpatient items/services);

iii. IDE Number (for Investigational Device Studies);

iv. Condition Code 30 (Qualifying Clinical Trial/Research Study).
a. When completing a paper order for hospital ancillaries for each study item/service to be billed out, the Principal Investigator will need to apply the V70.7 code, Q0/Q1 modifier, plus the IDE number (if applicable) on the order.

b. The hospital will ensure the V70.7 and the modifiers are applied to the charges through the charging system to Patient Financial Services (PFS). If the modifiers cannot be sent through the charging system, a process will be put in place to respond to the SSI bill hold request for modifiers as given from the order.

c. The order will be sent to Health Information Management (HIM) to be scanned into IHIRM.

(ttt) Accounts Coded by HIM (E, G, & Y patient type)

a. When a patient is in Emergency Room, Observation, or ambulatory setting, and ancillary orders are online (not sent by paper), the Principal Investigator will need to write the following into the patient’s chart:

   i. The name of the study;

   ii. The V70.7, diagnosis code;

   iii. A modifier Q0 or Q1, for each item/service;

   iv. IDE number (if applicable).

b. This information can also be documented in the online order systems when a note field is supplied.

c. Note: This is for information-only purposes and does not achieve passing the code or modifier to Patient Financial services (PFS).

(uuu) Missing Modifier Procedure for Shands Ancillaries

a. If the V70.7 is written in the paper order, but the modifier is missing, the hospital ancillary will make an effort to call the ordering person.

b. For the online accounts that hit the SSI bill-hold-edit-report and are patient type Y, E, or G, Patient Financial Services (PFS) will send these requests to HIM for the correct modifier.

c. HIM will contact the auditors in the Research Administration and Compliance Office (RAC) to help identify the Principal Investigator as necessary to ensure proper modifier coding.

(vvv) Coding Requirements for University of Florida Physicians (UFP) Claims
a. Insurance claims for UFP professional services ordered as part of:
   i. Medicare NCD qualifying clinical research study,
   ii. Pre-approved Investigational Device Exemption (IDE) study or
   iii. Pre-approved Medicare CED study

b. These must include:
   i. V70.7 as the secondary diagnosis (primary for healthy volunteers);
   ii. Q0 or Q1 modifiers for each item/service;
   iii. IDE Number (for Investigational Device Studies);
   iv. Condition Code 30 (Qualifying Clinical Trial/Research Study).

UFP Clinical Services Orders

a. Principal Investigators must provide the V70.7 diagnosis code and the appropriate Q0/Q1 modifier on clinical encounter forms.

b. If the encounter involves “mixed” services (i.e. some items/services are not study-related, or there are both Q0 and Q1 items/services), the Principal Investigator can write the V70.7 code and appropriate modifier next to each item or service for which the code and modifier apply.

Device Studies


a. Other clinical research involving investigational drugs or investigational treatments were typically not covered by Medicare until 2000 when the National Coverage Determination (NCD) for Routine Costs was written.

If a study involves both devices and investigational drugs or other treatments be sure to follow both sets of rules.

FDA Device Classification
The Food and Drug Administration (FDA) has established multiple classifications and categories for medical devices.

a. The classifications are based on the risk the device presents to the patient and the level of regulatory control the FDA determines is needed to legally market the device.

b. Several device categories and processes have been set up by FDA to enable providers to use a device in a clinical study in order to collect safety and effectiveness data before the device can be marketed.

c. The FDA also has a classification for the humanitarian use of a device that would not otherwise be available. These are called Humanitarian Use Devices (HUDs):

aaaa) A HUD is a device intended to benefit patients by treating or diagnosing a disease or condition that affects or is manifested in fewer than 4000 individuals in the United States per year.

bbbb) The costs of research and development for such devices could exceed the returns when treating such small populations.

cccc) The HUD provision of the regulations is intended to provide incentive for the development of devices which might provide benefit to these small populations of individuals.

dddd) More information about HUDs can be found on the FDA website.

Humanitarian Device Exemptions (HDE):

eeee) To obtain approval for an HUD, a humanitarian device exemption (HDE) application is submitted to FDA.

ffff) An HDE application is not required to contain the results of scientifically valid clinical investigations demonstrating that the device is effective for its intended purpose.

gggg) The application, however, must contain sufficient information for FDA to determine that the device does not pose an unreasonable or significant risk of illness or injury.

hhhh) In addition, HUDs may only be used after an IRB has approved the use of the device to treat or diagnose the specific disease. More information on HDEs can be found on the FDA website.

iii) Medicare Coverage Criteria for HUD Devices:

a. Medicare has no specific rules, regulations or instructions with regard to HUDs.

b. Medicare does not require nor is there any process for obtaining prior approval for HUDs.

c. Medicare does not perform “prior authorizations” for insertion of these devices.

jjjj) Coverage under general Medicare rules indicates most HUDs are not covered by Medicare. For more information on Medicare coverage of HUDs, see our local Medicare contractor’s website, First Coast Service Options.
Shands Pre-notification for HUDs

a. Before using any HUD, provider must:
   i. Obtain RAC & IRB approval
   ii. Submit HUD device document packet to Shands Patient Financial services (PFS)
       through :Kimberly Ellis hillkd@shands.ufl.edu
   iii. Email Device-Trials-L@LISTS.UFL.EDU before each use of the HUD.

Medicare Claims for HUDs

a. Medicare claims for HUDs may be reviewed pre or post payment.

b. Documentation must support that the services were reasonable and necessary.

c. No prior approval will be provided for these devices even if the patient is a participant in a research study.

d. Documentation, if requested, supporting the medical necessity of the procedure/device for the beneficiary must be made available to First Coast Service Options (FCSO) (through Shands) upon request and includes:
   i. Details about the specific device, including the device number and documentation that the device is classified by the FDA as a humanitarian use device (HUD) and has been approved by the FDA under a humanitarian device exemption (HDE).
   ii. A description of the clinical indications for the patient and why the device is needed. Medical records should document why the benefits of use of the device outweigh the risks, considering both other available devices and other available therapies.
   iii. A copy of the institution’s IRB approval letter for each individual patient.

Advanced Beneficiary Notice (ABN) for HUDs

Given the complexities of determining whether a device is reasonable and necessary when it has not been proven effective for its intended use, providers may wish to discuss this issue with their patients and consider the use of an advanced beneficiary notice (ABN). Additional information on the beneficiary notice initiative may be found at http://www.cms.gov/bni/.

a. Device manufacturers should have an official FDA letter that indicates what classification a particular device falls under. The study team should obtain a copy of this letter so it can be forwarded to the IRB, RAC office, Shands, Medicare, etc. as required.

b. Medicare may provide coverage and reimbursement for certain investigational devices and services related to the use of those devices (i.e., services necessary to the use of the device, as part of the preparation for the use of the device, or for the follow-up care after device use).
c. “Routine costs” (i.e., routine and medically necessary items or services that are typically provided absent a study) associated with the device study may also be covered.

d. For some device studies, coverage is contingent upon pre-approval from our local Medicare contractor, First Coast Services Options Inc. (FCSO), which has pre-approval information posted on their website. Currently, the device studies that require pre-approval from FCSO are:

   i. Investigational Device Exemption (IDE) Category A and Category B

      1. Post-Approval and 510(K) extension studies for carotid artery stenting (CAS)

         i. Medicare does not perform “prior authorizations” for insertion of Humanitarian Use Devices (HUDs). Claims for these devices may be reviewed pre or post payment. For HUD requirements, see:

   ii. Humanitarian Use Device (HUD)

      a. All other device studies do not require pre-approval. These studies fall under the Medicare National Coverage Determination (NCD) rules. See Medicare Qualifying Studies.

      b. Devices Purchased or Received by Shands:

   iii. When a study involves a device that has to be purchased or received by Shands Healthcare, the Shands Healthcare contracting office should be contacted as early in the start-up process as possible.

      1. Study teams should give their sponsors Shands contact information to make the appropriate arrangements for device procurement.

   iv. Sponsors should contact the following: Dawn Watkins, at 352-733-0370 or email: watkid@shands.ufl.edu

      a. Prior to study start-up, the study team should also contact the ancillary where the device is going to be implanted and/or used (i.e. OR).

      b. Most of the operating rooms require additional paperwork regarding the device.

      c. Please email Michele Scanlan or the Device Trial ListServ at Device-Trials-L@LISTS.UFL.EDU to ask for more detail.

**Investigational Device Exemptions (IDEs)**

The U.S. FDA places all IDEs into one of two categories:
a. **Category A** – experimental: These devices consist of novel, first-of-a-kind technologies. These are innovative devices for which initial questions of safety and effectiveness have not been resolved and the absolute risk of the device type has not been established. The FDA has insufficient evidence to determine whether these device types can be safe and effective. The Category A device itself is not subject to Medicare reimbursement; however, the routine care costs may be covered.

b. **Category B** – investigational, non-experimental: These devices are newer generation devices of already-proven technologies where the initial questions of safety and effectiveness of these devices have been resolved. The Category B device as well as the routine care costs may be covered.

oooo) **Medicare Coverage Criteria for IDE Devices:**

a. The device must be used in the context of an FDA and IRB approved study.

b. Coverage is limited to a predetermined number of patients and a predetermined number of sites as specified in the FDA-approval letter and/or study protocol.

c. **NOTE:** You must obtain a copy of the FDA Letter designating the device’s CMS Reimbursement Category (A or B) from your sponsor. The FDA Letter must state that the device has received final approval, not contingent approval.

pppp) The device must be used according to the study’s approved patient protocols.

qqqq) The device must have an assigned investigational device exemption (IDE) number.

a. This identification number allows the Medicare contractor to establish the specific claims processing procedures associated with the study.

rrrr) The device must meet all Medicare coverage requirements:

a. It must fall within a benefit category.

b. In the event that the device itself and/or the associated services fall within the scope of a national or local coverage determination (NCD/LCD) it must meet the criteria set forth in the NCD/LCD.

c. In the absence of an NCD/LCD, it must be considered reasonable and necessary in accordance with section 1862(a)(1)(A) of the Social Security Act.

d. Use of the device and the provision of associated services must be furnished in a setting appropriate to the patient’s medical needs and condition.

e. The Medicare pre-approval letter must be obtained from First Coast Service Options Inc. (FCSO) before enrolling any participants.

ssss) Obtaining the IDE Medicare Coverage Determination & Pre-Approval Letter:
a. If the IDE study will involve **any** billing to participants/insurers, a Medicare coverage determination **MUST** be performed **BEFORE** enrollment of any subjects.

b. You must collaborate with Shands Patient Financial Services (PFS) to provide any and all information about the device, the associated services and the protocol that our local Medicare contractor, First Coast Service Options, Inc. requires to make a coverage determination.

c. Forward the following list of all documents and materials required for Medicare submission to **Kimberly Ellis** at Shands PFS:

   i. Investigational device exemption (IDE) number: GXXXXX

   ii. Identification of the sponsor of the clinical trial and of the funding agency and/or organization if different from the sponsor.

   iii. Identification of the principle investigator (PI) and sub-investigators of the clinical trial.

      1. Please include a list of all other contact persons (anyone we are allowed to exchange information with regarding the clinical trial and phone numbers or e-mail addresses).

   iv. Identification of the facility (place of service of the clinical trial) including the provider number(s) and the address of the facility/hospital/institution.

   v. A copy of the complete FDA approval letter(s) provided to the PI and/or the sponsor or manufacturer of the device.

      1. Redacted letters and/or letters with blacked-out areas are not acceptable.

      2. Conditional letters are accepted if all patient safety issues have been addressed.

      3. Sending only page one of the FDA letter is not acceptable. Each site requesting an IDE approval letter must provide the entire FDA letter.

   vi. The number of traditional Medicare patients the facility is requesting to enroll for the first year of the clinical study.

      1. In the event that the number of patients requested exceeds the number based on the ratio approved in the FDA letter, an e-mail or letter from the sponsor requesting a larger total number of patients is required.

   vii. A copy of the approval letter from the Institutional Review Board (IRB) with the meeting date and the expiration date and the identifiers of the PI and sponsor listed.

   viii. A description of the action(s) taken to conform to any applicable FDA and/or IRB special controls and/or other requirements.

   ix. A copy of the complete study protocol, including patient inclusion criteria. Abbreviations or summaries of the protocol are not acceptable.
1. **NOTE: Ensure your sponsor has approved the protocol for release to the Medicare contractor.**

x. A copy of the IRB-approved informed patient consent form with PI and sponsor identifiers listed.

xi. A copy or description of the protocol for obtaining informed patient consent.

xii. Copies of all agreements between the sponsor and the PI, including but not limited to, complete financial agreements, any and all payments for each aspect of the study with PI and sponsor identifiers listed.

1. **NOTE: Confirm with UF Division of Sponsored Research that your sponsor has approved all contractual agreements for release to the Medicare contractor.**

xiii. Notification of any and all costs by code to be billed in association with the study.

1. Identification of all services as either routine care costs or data acquisition/clinical trial related costs, by code, including the anticipated frequency of billing.

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Once Shands PFS receives your complete packet of information, they will submit the request for coverage determination directly to our Medicare contractor, First Coast Service Options, Inc. (FCSO), who will make a coverage determination within 45 days.

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**Annual IDE Continuing Coverage Extension Requests:**

a. Pre-approved Medicare IDE coverage is limited to a pre-determined number of participants and length of time, which is usually tied to the IRB approval date. This means you will need to re-apply for pre-approval each time your IRB approval is updated.

b. NO additional participants can be enrolled until a continuing coverage determination is received from the First Coast Service Options, Inc. Forward the following list of all documents and materials required to Kimberly Ellis at Shands PFS:

   i. The IDE name & number GXXXXX

   ii. A copy of the last approval letter you received from FCSO.

   iii. An updated copy of the Investigational Review Board (IRB) letter including the meeting date and expiration date.

   iv. A list of the traditional Medicare beneficiaries enrolled in the clinical study for the past year including their names, Medicare numbers, and the dates of the initial device service/procedure.

1. In the event that no traditional Medicare patients were enrolled, please include a statement in the cover letter to convey this information.
v. List any changes to the study since the most recent FCSO approval letter was sent to you.

1. If any changes have occurred to any part of the clinical study since your original request and approval, please include the revised documents such as new protocol, new consent, new coding and cost form, new Food and Drug Administration (FDA) letter.

vi. Anticipated completion date of study and anticipated data publication date.

vvvv) Once Shands PFS receives your complete packet of information, they will submit the request for coverage determination directly to our Medicare contractor, First Coast Service Options, Inc. (FSCO), who will make a continuing coverage determination within 45 days.

wwww) Private Insurance Coverage of Investigational Devices:

   a. If any subjects have private insurance, you MUST obtain written pre-authorization for the IDE from the carrier BEFORE enrollment.

      i. Some private insurers will follow the Medicare benefit policy; however, they also have discretion to deny coverage regardless of Medicare’s coverage determination.

xxxx) IDE Device Claims Coding

   a. Once First Coast Service Options, Inc. has sent the pre-approval letter for an IDE to Shands, ensure that each billable item/service in the study is pre-identified as “MQ0” or MQ1” on the billing grids so that the study team will know the correct coding for claims. For more details, please see Medicare Billing & Coding Logic Diagram and Use of V70.7 &Q0Q1 Modifiers.

yyyy) IDE Device ListServ

   a. For any studies involving an IDE, send an email to the Device Trial ListServ Device-Trials-L@LISTS.UFL.EDU to notify Shands Hospital and University of Florida Physicians (UFP) billing staff of all participants enrolled in the device trial as soon as they are enrolled and prior to provision of any study services (including follow-up services) so that claims can be coded and properly processed.

Post-Approval and 510(k) Extensions Studies for Carotid Artery Stenting (CAS)

zzzz) NOTE: Except for post-approval and 510(k) extension studies for carotid artery stenting (CAS), our Medicare contractor, First Coast Service Options, Inc., has determined that PMA and 510K devices do not require Medicare pre-approval prior to participant enrollment. Routine Costs for these studies follow Medicare National Coverage Determination (NCD) rules.

aaaaa) Obtaining the CAS Medicare Coverage Determination & Pre-Approval Letter

   a. If the CAS post-approval and 510(k) extension study will involve any billing to participants/insurers, a Medicare coverage determination MUST be performed BEFORE enrollment of any subjects.
b. You must collaborate with Shands Patient Financial Services (PFS) to provide any and all information about the device, the associated services and the protocol that our local Medicare contractor, First Coast Service Options, Inc. requires to make a coverage determination. Forward the following list of all documents and materials required for Medicare submission to **Kimberly Ellis** at Shands PFS:

i. Post-approval for CAS study number: PXXXXX

ii. Post-approval for 510K extension studies: IXXXXX

iii. The name of the study and the stent (both trade, common or usual and classification name) and a narrative description of the stent.

   1. Include a statement as to the stent similarities and differences from other stents if not explicitly and clearly indicated in submitted documents.

iv. Identification of the sponsor of the study and of the funding agency and/or organization if different from the sponsor.

v. Identification of the principal investigator (PI) and sub-investigators.

   1. Please include a list of all other contact persons (anyone we are allowed to exchange information with regarding the study and phone numbers or e-mail addresses).

vi. The facility name, address, and Medicare facility provider number as it appears on the CMS carotid artery stenting facilities approved facilities list, found online at the following website: [https://www.cms.gov/Medicare/Medicare-General-Information/MedicareApprovedFacilities/index.html](https://www.cms.gov/Medicare/Medicare-General-Information/MedicareApprovedFacilities/index.html)

vii. A copy of the complete FDA approval letter(s) provided to the PI and/or the sponsor or manufacturer of the carotid stent. Redacted letters and/or letters with blacked out areas are not acceptable.

   1. Conditional letters are acceptable if all of the patient safety issues have been addressed.

   2. Sending only page one of the FDA letter is not acceptable.

   3. Each site requesting a Post-Approval for CAS approval letter must provide the entire FDA letter(s).

viii. The number of traditional Medicare patients the facility is requesting to enroll for the first year of the study. In the event that the number of requested exceeds the number based on the ratio approved in the FDA letter, an email or letter from the sponsor requesting a larger total number of patients is required.
ix. A copy of the approval letter from the institutional review board (IRB) with the meeting date and the expiration date listed and including the PI and sponsor identifiers.

x. A description of the action(s) taken to conform to any applicable FDA and/or IRB special controls and/or other requirements.

xi. A copy of the complete study protocol, including patient inclusion criteria. Abbreviations or summaries of the protocol are not acceptable.

   1. **NOTE: Ensure your sponsor has approved the protocol for release to the Medicare contractor.**

xii. A copy of the IRB-approved informed patient consent with PI and sponsor identifiers listed.

xiii. A copy of the CMS letter providing coverage for the post–approval extension study.

xiv. A copy or description of the protocol for obtaining informed patient consent.

xv. Copies of all agreements between the sponsor and the PI, including but not limited to, complete financial agreements, any and all payments for each aspect of the study with PI and sponsor identifiers listed.

   1. **NOTE: Confirm with UF Division of Sponsored Programs that your sponsor has approved all contractual agreements for release to the Medicare contractor.**

xvi. Notification of any and all costs by code to be billed in association with the study.

   1. Identification of all services as either routine care costs or data acquisition/clinical trial related costs, by code, including the anticipated frequency of billing.

   2. **Note: Data acquisition/clinical trial related costs are not billable to Medicare.**

b. Once Shands PFS receives your complete packet of information, they will submit the request for coverage determination directly to our Medicare contractor, First Coast Service Options, Inc. (FCSO), who will make a coverage determination within 45 days. For more information on the FCSO PMA approval requirements, see FCSO website.

ccc. **Annual CAS Continuing Coverage Extension Requests:**

   a. Pre-approved Medicare CAS coverage is limited to a pre-determined number of participants and length of time, which is usually tied to the IRB approval date.

      i. This means you will need to re-apply for pre-approval each time your IRB approval is updated.
ii. NO additional participants can be enrolled until a continuing coverage determination is received from the First Coast Service Options, Inc. Forward the following list of all documents and materials required to Kimberly Ellis at Shands PFS:

1. Post-approval for carotid artery stenting (CAS) study name & number PXXXXX
2. A copy of the last approval letter you received from FCSO.
3. An updated copy of the investigational review board (IRB) letter including the meeting date and expiration date.
4. A list of the traditional Medicare beneficiaries enrolled in the study for the past year including their names, Medicare numbers, and the dates of initial stent placement procedure.
5. In the event that there were no traditional Medicare patients enrolled in the study for the past year, please include a statement in the cover letter to convey this information.

b. List any changes to the CAS study since the most recent MAC J9 FCSO approval letter was sent to you.

c. If any changes have occurred to any part of the study since your original request and approval, please include the revised documents such as new protocol, new consent, new coding and cost form, and/or new Food and Drug Administration (FDA) letter.

d. Once Shands PFS receives your complete packet of information, they will submit the request for coverage determination directly to our Medicare contractor, First Coast Service Options, Inc. (FCSO), who will make a continuing coverage determination within 45 days. For more information on the FCSO PMA approval requirements, see FCSO website.

ddddd) Device Claims Coding

a. Once First Coast Service Options, Inc. has sent the pre-approval letter for a CAS to Shands, ensure that each billable item/service in the study is pre-identified as “MQ0” or “MQ1” on the billing grids so that the study team will know the correct coding for claims.

i. For more details, please see Medicare Billing & Coding Logic Diagram and Use of V70.7 &Q0Q1 Modifiers.

eeeee) For any studies involving a CAS PMA /501(k), send an email to the Device Trial ListServ Device-Trials-L@LISTS.UFL.EDU to notify Shands Hospital and University of Florida Physicians (UFP) billing staff of all participants enrolled in the device trial as soon as they are enrolled and prior to provision of any study services (including follow-up services) so that claims can be coded and properly processed.

Investigational Device Exemptions (IDEs)

fffff) An Investigational Device Exemption (IDE) is a request for authorization by the Food and Drug Administration to evaluate an investigational device in humans in order to collect safety and
effectiveness data to support a Premarket Approval (PMA) application or a Premarket Notification (510[k]) submission to the FDA.

   a. This authorization, unless deemed unnecessary, must be obtained prior to interstate shipment of the device and its evaluation in humans.

    ggggg) FDA regulations governing the IDE process, investigator and sponsor obligations, compliant performance of clinical research, annual reporting, safety reporting, etc. are contained in Title 21, Code of Federal Regulations, Part 812

hhhhh) Clinical evaluation of devices that have not been approved requires:

   iiiii) An IDE approved by an institutional review board

   a. If the study involves a significant risk device, the IDE must be approved by the FDA. See Guidance: http://www.fda.gov/downloads/regulatoryinformation/guidances/ucm126418.pdf

   b. Informed consent from all subjects prior to use of the device.

   c. Labeling for investigational use only.

   d. Monitoring of the study.

   e. Required records and reports.

    jjjjj) An overview of Device Regulation and Guidance is available at http://www.fda.gov/medicaldevices/deviceregulationandguidance/default.htm

    kkkkk) Guidance Documents for Clinical Trials and IDEs are available at http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfIDE/daIDEgd_print.cfm

lllll) Overview of the IDE Process

   a. Investigations with devices covered by 21 CFR 812 are subject to regulatory controls specific to the determined level of risk.

   b. The IDE regulation distinguishes between significant and non-significant risk device studies.

   c. The procedures for obtaining approval of the study are specific to the determined level of risk.

      i. Guidance on distinguishing between significant and non-significant risk are outlined in the FDA document "Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors: Significant Risk and Nonsignificant Risk Medical Device Studies."

      ii. Some types of studies are exempt from the IDE regulations.

   d. Significant risk device

      i. A significant risk device presents a potential for serious risk to the health, safety, or welfare of a subject and include:
1. Implants

2. Devices that support or sustain life

3. Devices that are significantly important in diagnosing, curing, mitigating, or treating disease or in preventing impairment to human health.

ii. Examples:

1. Sutures
2. Cardiac pacemakers
3. Hydrocephalus shunts
4. Orthopedic implants

iii. Studies of devices that pose a significant risk require both FDA and an Institutional Review Board approval prior to initiation of the clinical study.

iv. In order to conduct a study involving a significant risk device, a sponsor must:

1. Submit a complete IDE application to FDA for review and obtain approval;
2. Submit the investigational plan and report of prior investigations to the IRB at each institution where the investigation is be conducted for review and approval; and
3. Select qualified investigators, provide them with all necessary information on the investigational plan and report of prior investigations, and obtain signed Investigator Agreements from them.

e. After the FDA receives an IDE application, it notifies sponsors in writing of the date the FDA received the original application and the IDE number assigned (receipt of supplements and amendments are not acknowledged).

f. Once the FDA has acknowledged receipt of the IDE application, the sponsor must wait 30 calendar days before initiating any clinical trial.

g. During this period, the FDA may inform the sponsor that the IDE is approved, approved with conditions, or disapproved.

i. In cases of disapproval, the sponsor may respond to the cited deficiencies and/or request a regulatory hearing.

h. Non-significant risk Device

i. Non-significant risk devices are devices that do not pose a significant risk to human subjects. Examples include:

1. Contact lenses and lens solutions
2. Ultrasonic dental scalers

3. Foley catheters

ii. A non-significant risk device study requires only IRB approval prior to initiation of the clinical study.

iii. Sponsors of studies involving non-significant risk devices are not required to submit an IDE application to the FDA for approval.

iv. Sponsors must, however, present an explanation to the IRB as to why the device does not pose a significant risk.

v. If the IRB disagrees and determines that the device poses a significant risk, the sponsor must report this finding to the FDA within five working days.

**IDE Application Process**

A sponsor of a significant risk device study must submit a complete IDE application to the FDA, along with obtaining CPHS approval, before beginning clinical research.

Unlike an IND application, there are no pre-printed forms for an IDE application. Instead, there are required information elements that must be submitted in the order specified below:

1. Name and address of the sponsor.

2. Report of prior investigations, which must include reports of all prior clinical, preclinical, and laboratory testing of the device necessary to justify the proposed research.

   a. This report must include:

      i. References for all publications, both supportive and adverse, that are relevant for the evaluation of safety and effectiveness of device

      ii. Copies of all published and unpublished adverse effect information

      iii. Copies of other significant information if requested by an IRB or the FDA

      iv. Summary of all published and unpublished information (both supportive and adverse) that is relevant to the evaluation of safety and effectiveness of the device

      v. If nonclinical laboratory data are provided, a statement that such studies were performed in compliance with Good Laboratory Practice (21 CFR 58).

         1. If such studies were not conducted in compliance with the GLP regulation, include a brief statement of the reason for noncompliance.

3. Investigational plan:

   a. Purpose (name and intended use of the device; objectives and duration of the clinical investigation)
b. Protocol (include analysis of scientific soundness)

c. Risk analysis (description and analysis of all increased risks to the research subjects and how these risks will be minimized; justification for the investigation

d. Description of patient population including number, sex, age, condition)

e. Description of device (each important component, ingredient, property, and principle of operation and any anticipated modifications to the device during the clinical investigation)

f. Monitoring procedures

g. Additional records and supports, other than those already required by IDE application

4. Description of the methods, facilities, and controls used for manufacture, processing, packaging, storage, and installation of the device.

5. Example of the agreement to be signed by the investigators and a list of names and addresses of all investigators (see 21 CFR 812.43)

6. Certification that all investigators have signed the agreement, that the list from #5 above includes all investigators participating in the study, and new investigators will sign the agreement before being added to the study.

7. List of names, addresses, and chairpersons of all IRBs that have or will be asked to review the investigation and approval letters (if available).

8. Name and address of any other institution where a part of the investigation may be conducted.

9. The amount, if any, charged for the device and an explanation of why this cost does not constitute commercialization.

10. Copies of all labeling for the device.

11. Copies of all informed consent forms and all related information materials to be provided to the subjects.

12. Any other information requested by the FDA. Previously submitted information may be referenced.

13. An Environmental Assessment is no longer required.

Suggested Content for the IND Application Cover Letter

1. It is recommended that the cover letter include the following information in the order listed:
   a. Statement that the information provided is an original IDE application
   b. Device information:
i. Name of device
ii. Intended use

c. Sponsor contact information
   i. Name
   ii. Address
   iii. Contact person
   iv. Telephone number
   v. Facsimile number

d. Manufacturer information
   i. Name
   ii. Address
   iii. Contact person
   iv. Telephone number
   v. Facsimile number

e. Applicant information:
   i. If the organization submitting the application is not the sponsor, provide full contact information.

f. Provide the following information, if available, for Pre-IDE submission(s) and Pre-IDE meeting(s)
   a. If Pre-IDE was submitted, state the Pre-IDE number and name of FDA reviewer.
   b. If Pre-IDE meeting occurred, provide name of FDA contact person and a copy of meeting minutes.
   c. Waiver requests, if applicable.
   d. References files.

Suggested format for IDE Submissions:
   a. Use 8 ½” by 11” inch paper.
   b. Use at least a 1 ½” wide left margin to allow for binding into jackets.
c. Use 3-hole punched paper to allow for binding into jackets.

d. If submission exceeds 2" in thickness, separate into volumes and identify volume numbers.

e. Clearly identify type of submission (i.e. initial application, annual report, etc).

f. For submissions subsequent to initial application, identify the FDA assigned document number, the reason for the submission, and the type of submission.

g. All three copies of a submission must be identical.

h. Do not combine submissions for different devices.

i. Unless the IDE sponsor has delegated authority in writing for another person to submit information on the sponsor’s behalf, only the IDE sponsor may amend, supplement, or submit reports for the IDE.

j. Sequentially number the pages, provide a detailed table of contents, and use tabs to identify each section.

rrrrr) Mail Address for IDE Applications and Subsequent Correspondence with the FDA

a. Three signed copies of the “Application for Investigational Device Exemption” with cover letter must be submitted.

b. The cover page must identify the submission as an application for an IDE and must be signed by the sponsor.

c. The initial application and all subsequent communications with the FDA must be mailed to:

Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center (HFZ-401)
9200 Corporate Boulevard
Rockville, Maryland 20850-3223

d. The subsequent IDE correspondence must be submitted in triplicate and reference the IDE number.

e. The outside cover of each submission should identify the content (“IDE Application”, “Waiver” etc).

IDE Modifications

A sponsor may need to obtain approval from CPHS and the FDA prior to implementing a change to an investigational plan.

Changes in investigational plan that require prior approval (21 CFR 812.35).

The following types of protocol changes require an approved IDE supplement because the FDA believes that they are likely to have a significant effect on the scientific soundness of the trial design and/or the validity of the data resulting from the trial:
1. Change in indication

2. Change in type or nature of study control

3. Change in primary endpoint

4. Change in method of statistical evaluation

5. Early termination of the study (except for reasons related to patient safety)

The FDA also believes that expanding the study by increasing either the number of investigational sites or number of study subjects affects the rights, safety, and welfare of subjects.

Therefore, these actions also require approval before implementation.

The IDE supplement must be identified by IDE number on the cover sheet and submitted in triplicate.

The outside covering of the submission should identify it as "Supplement IDE."

Changes in the investigational plan that do not require prior FDA approval:

1. Notice of the following modifications to the device and/or investigational plan must be provided to the FDA within 5 working days of making the change:
   a. Emergency Use
   b. Certain Developmental Changes
   c. An FDA-approved supplement is not required for developmental changes in the device, including manufacturing changes, that do not constitute a significant change in design or basic principles of operation and that are made in response to information gathered during the course of the clinical investigation.
      i. Credible information to support developmental changes in the device includes data generated under design control procedures (see 21 CFR 812.30), preclinical/animal testing, peer reviewed published literature, or other reliable information such as clinical information gathered during the trial or marketing.
      ii. Generic types of device and manufacturing changes include changes to the control mechanism, principle of operation, energy type, environmental specifications, performance specification, ergonomics of patient-user interface, dimensional specifications, software or firmware, packaging or expiration dating, sterilization, and manufacturing process (including the manufacturing site).
   d. All developmental changes need to be reported to the CPHS in the sponsor's annual report.
i. Changes may also be subject to CPHS review when they are made.

2. Certain changes to the clinical protocol
   a. An FDA-approved supplement is not required for changes to clinical protocols that do not affect:
      i. Validity of the data or information in the approved protocol, or the subject risk-to-benefit relationship relied upon to approve the protocol.
      ii. Scientific soundness of the investigational plan
      iii. Rights, safety, or welfare of human subjects involved in the investigation.
   b. The determination is made by the sponsor and must be based on credible information. Examples of such changes include:
      i. Modification of inclusion/exclusion criteria to better define the target subject population
      ii. Increasing the frequency at which data or information is gathered
      iii. Inclusion of additional patient observations or measurements
      iv. Modifying the secondary endpoints (which usually support a secondary labeling claim and are not used to determine the safety or effectiveness of the device).
   c. For a protocol change, the notice to the FDA within 5 working days of the change must include:
      i. Description of the change ("track changes" version of the document)
      ii. Assessment supporting the conclusion that the change does not have a significant impact on the study design or planned statistical analysis
      iii. Summary of the information that served as credible information supporting the sponsor’s determination that the change did not affect the rights, safety, and welfare of the subjects.

 yyym) Changes to be submitted in the annual progress report

 1. Minor changes in the following areas (which do not meet the criteria listed above in the section for changes that must be submitted for FDA approval prior to augmentation) may be reported in the annual progress report:
   a. Purpose of the study
   b. Risk analysis
c. Monitoring procedures

d. Labeling

e. Informed consent materials

f. CPHS information

IDE Safety Reports

zzzzz) The sponsor of an IDE is required to promptly review and report to the FDA and investigators all information relevant to the safety of the investigational device from any source, foreign or domestic (Table 1).

aaaaaa) The investigator also is required to review and report to the FDA and the manufacturer all information relevant to the safety of the investigational device (Table 2).

bbbbbb) The investigator will also need to report to CPHS.

cccccc) Each written notification of an unanticipated adverse device effect (UADE) must be submitted on FDA Form 3500A. FDA Form 3500A and instructions can be accessed and submitted electronically on the FDA webpage Instructions for Completing Form FDA 3500A.

a. If the FDA determines that additional data are needed, it will contact the sponsor.

ddddd) Table 1: Summary of Reporting Requirements for Manufacturers

<table>
<thead>
<tr>
<th>Reporter</th>
<th>What to Report</th>
<th>Report Form #</th>
<th>To Whom</th>
<th>When</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manufacturer</td>
<td>30-day reports of deaths, serious injuries and malfunctions</td>
<td>Form FDA 3500A</td>
<td>FDA</td>
<td>Within 30 calendar days from becoming aware of an event</td>
</tr>
<tr>
<td>Manufacturer</td>
<td>5-day reports on events that require remedial action to prevent an unreasonable risk of substantial harm to the public health and other types of events designated by FDA</td>
<td>Form FDA 3500A</td>
<td>FDA</td>
<td>Within 5 work days from becoming aware of an event</td>
</tr>
<tr>
<td>Manufacturer</td>
<td>Baseline reports to identify and provide basic data on each device that is subject of an MDR report. At this time, FDA has stayed the requirement for denominator data requested in Part II,</td>
<td>Form FDA 3417</td>
<td>FDA</td>
<td>With 30 calendar, and 5 work day reports when device or device family is reported for the first time. Interim and annual updates</td>
</tr>
</tbody>
</table>
Items 15 and 16 on Form 3417 are also required if any baseline information changes after initial Manufacturer Annual Certification Form FDA 3381 FDA Coincide with firm’s annual registration dates.

Investigational New Drug (IND) Applications

Per the FDA, an IND application is submitted by a physician who both initiates and conducts an investigation, and under whose immediate direction the investigational drug is administered or dispensed.

a. A physician would submit an IND to propose a study of an unapproved drug, or a study of an approved product for a new indication or in a new patient population.

Does My Study Need an IND?

a. When the principal intent of the investigational use of a test article is to develop information about the product’s safety or efficacy, submission of an IND may be required.

b. Use this checklist to determine whether your protocol is exempt from IND review and submission. All criteria below must be met to constitute exemption:

i. The study drug is lawfully marketed in the United States;

ii. The study is not intended to be reported to the FDA as a well-controlled study in support of a new indication or use; or support any significant change in the drug’s labeling;

iii. The study is not intended to support a significant change in the advertising for a prescribed drug;

iv. The study does not involve a change in route of administration, dosage level, patient population, or other factors that significantly increases the risks associated with use of the drug product;

v. The study complies with IRB evaluation and informed consent requirements; and

vi. The study sponsor and/or investigator do not represent in a promotional context that the drug is safe and effective for the purposes in which it is under investigation.

c. If all of the above criterion are met, your protocol is exempt from IND review and submission.
d. Note that situations do arise when studies can be exempt from IND submission even though they do not meet all the criteria above.

e. Usually, such exemptions are granted because significant information about these treatments already exists in the literature - e.g., when a drug has been used clinically off-label regularly for the treatment of the studied condition and there is significant information in the literature about this use.

f. In a situation of this kind, only the FDA can determine that the protocol is exempt. If you have doubts about whether your study requires an IND, contact the appropriate department at the FDA.

g. For guidance in deciding whether a study of marketed drugs or biological products for treating cancer falls within the exemption under 21 CFR 312.2(b)(1) from the general requirement to submit an investigational new drug application, please review the FDA guidance entitled, IND Exemptions for Studies of Study Lawfully Marketed Drug or Biologic Products for the Treatment of Cancer (pdf).

h. FDA Determination of Exemption

a. Although 21 CFR 312.2(b)(1) does not require a submission for a determination of exempt status, whenever an IND application is submitted, FDA staff perform an initial limited review of the application to determine whether the study is exempt.

b. The protocol-related criterion used to assess exemption is (#4 above):

i. The investigation must not involve a route of administration or dosage level or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of risks) associated with the use of the drug product.

ii. If the FDA's initial limited review determines that a study protocol is exempt from the requirement for an IND, no further review of the study is performed.

iii. A letter is sent to the sponsor giving notice of the exemption.

h. The IND Application Process: How to File an IND

a. The following are the key components of an initial IND application:

i. IND Cover Letter (pdf)

ii. IND Application (pdf)

iii. Investigational New Drug Application -Form 1571 (pdf)

iv. Statement of the Investigator - Form 1572 (pdf)

FDA guidance on how to fill out Forms 1571 and 1572 (pdf)

v. Certification Form 3674 (pdf), if applicable.
1. Typically, you must submit Form 3674 with a new IND.

2. Protocol amendments will require resubmission of this form
   a. FDA Guidelines associated with certification requirement.
   b. Number of copies: Submit the original IND or IDE application and two copies to the FDA; file a copy for yourself in your Regulatory Binder
   c. Where do I send my IND Application?
      i. Initial Application
         Food and Drug Administration
         Center for Drug Evaluation and Research
         Central Document Room
         5901-B Ammendale Road
         Beltsville, MD. 20705-1266
      ii. Subsequent Submissions
         Send all subsequent submissions to your Project Manager using the address given on the IND/IDE 'Letter of Acknowledgement,'

iii. When can I begin my study once I have submitted my IND to the FDA?
   a. You will receive a letter with an IND number and Name of the Project Manager after the FDA receives your initial submission.
   b. The IND/IDE goes into effect 30 days after the FDA has received the application, unless the FDA notifies the sponsor-investigator that the investigation is subject to a clinical hold.
      i. You WILL NOT receive an approval letter.
   c. Note: In addition to having your IND go into effect, you must receive formal University of Florida approval from both the IRB and the RAC Office before your study may begin.

jjjjjj) Maintaining an IND
   a. Once your IND has gone into effect, you are responsible for its maintenance which includes:
      i. Protocol Amendments
         1. New protocol
         2. Significant changes in a protocol, including:
            a. Increase in drug dosage or duration of exposure, increase in # of subjects
            b. Significant change in design (e.g., addition or dropping of a control group)
c. Addition of new test or procedure; dropping of test intended to monitor safety

d. New Investigator (adding an additional site for the conduct of the study previously approved under the IND)

ii. Information Amendments

1. Information Amendments can include new toxicology, new chemistry, or other technical information

iii. IND Safety Reports

1. Required written reports

   a. For adverse experience associated with the use of the drug that is both serious and unexpected, or any finding from preclinical tests that suggests significant risk for humans:

      i. Report on the MedWatch 3500A Form (pdf)
         Your IND number should be placed on the Medwatch 3500A Form and the form should be submitted to your FDA project team.

      ii. Instructions for completing the MedWatch 3500A Form

      iii. The written report must be submitted within 15 calendar days after notification

      iv. Your IND number should be placed on the MedWatch 3500A Form, and the form should be submitted to your FDA project team

      v. Include an IND Safety Report Cover Letter (pdf)

2. Telephone and facsimile transmission reports for unexpected fatal or life-threatening experiences

   a. The telephone call or facsimile must be made within 7 calendar days of notification and should be followed with a written report within 8 calendar days

   b. Follow-up information should be submitted as soon as the relevant information is available

iv. Annual Report

1. The Annual Report should be submitted within 60 days of the anniversary date that the IND went into effect.
2. See **IND Annual Report Template** (pdf)

3. **Note:** All IND Maintenance documents sent to the FDA should be accompanied by a cover letter and a Form 1571 specifying what updated information is being sent to FDA.

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**Regulatory Responsibilities of the Sponsor-Investigator**

a. As defined in FDA regulations (21 CFR 312.3 and 812.3{o}), a sponsor-investigator is an individual who both initiates and conducts a clinical investigation, and under whose immediate direction an investigational drug or device is administered, dispensed, or used.

b. The requirements of a sponsor-investigator include both those applicable to an investigator and those applicable to a sponsor.

c. The following three documents can be helpful in understanding these obligations.

   i. **Understanding FDA Regulatory Requirements for Investigational New Drug Applications for Sponsor-Investigators** (pdf) M. E. Blair Holbein, PhD

   ii. The **FDA Sponsor and Investigator Responsibility Checklist** (pdf) can help you ensure that you maintain all required regulatory paperwork for Sponsor-Investigators.

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**Additional IND Resources**

a. **FDA Information for Sponsor-Investigators Submitting Investigational Drug Applications (INDs)**

b. **Clinical Protocol Template** (DOC)

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**Confirmation of Services (COS) Process**

A COS is used to communicate with Shands and UFP service providers about upcoming research studies that will involve study-funded services.

a. It is also used to obtain estimated prices for study-funded services so that study teams can negotiate budgets with sponsors.

**Research Pricing and Medicare Estimates:** clinical research services performed at Shands service locations have both a technical fee and a professional fee (with the exception of labs, where the professional fee is waived for research).

a. Services performed at University of Florida Physicians (UFP) locations have only professional fees.

For UF research studies that begin after September 26, 2010, Shands Healthcare and UFP services receive a discount based on the Medicare rate on the date of service.
In the pricing process, study teams will receive two different prices for the technical and/or professional component of each service:

a. **List Price** = Full Price that Shands or UFP would charge for an item/service if not related to research (base price for all discounts).

b. **Medicare Estimate** = Estimate of the actual price that Shands and UFP will charge study for an item/service

c. The Confirmation of Services process is used for the following types of study-funded services:
   
i. Any service where the study team is not absolutely sure of the CPT code.
   ii. Inpatient services.
   iii. Implantation/explantation of investigational devices or PMA/510k carotid artery stenting.
   iv. Complicated services/procedures.
   v. Pathology services.
   vi. Cytogenetics services.
   vii. UF-CRC services.
   viii. Innovative procedures or services not previously performed at UF or Shands.
   ix. Shands “send-out” laboratory services.

For study-funded services with which the study team is familiar (i.e., the study team has had experience with both the specific services, the service provider, and is absolutely certain of the CPT code and location of the service) the UF Research Budgeting and Pricing Tool output may be used in place of the standard COS form.

i. The study team will no longer need to send an inquiry and wait for a Confirmation of Service from ancillary departments or UFP in this situation.

**Confirmation of Services vs. UF Research Budgeting and Pricing Tool:**

i. The UF Research Budgeting and Pricing Tool may be used to obtain pricing estimates for general outpatient research-funded services when one is certain of the CPT codes and planned service locations. If unsure of which CPT code to use for a service, contact the ancillary/service providers for clarification or confirmation before using the tool, or use the Confirmation of Services process described below to obtain pricing for the service.

**How to Prepare for the Confirmation of Services Process:**
Before the Confirmation of Services process begins, the study team (including the Principal Investigator) needs to review the protocol and identify all possible services and activities that will be required by the study.

1. The study team should then review the budget, ICF draft, and contract draft provided by the sponsor to determine who is expected to pay for which services/activities.
2. Next, they need to determine who will perform each service and activity and where the service/activity will take place.
3. The study services/activities must be documented in a billing plan by entering all services/activities on a billing grid.

Steps in the Confirmation of Services Process:

a. For protocol-required study-funded services that will either be performed at a Shands ancillary service department or provided by a University of Florida Physicians (UFP) professional, the study team will need to contact the appropriate Shands ancillary department(s) and UFP department(s) to discuss the feasibility of the study tests/procedures and confirm the correct CPT and service codes. This can be done via e-mail before a formal COS is requested. See Shands & UFP Contacts.

b. The study team will obtain written confirmation of feasibility and estimated pricing for study-funded services from Shands Ancillaries and UFP by using the Confirmation of Services (COS) Form template.

c. Shands ancillary departments/UFP department(s) will either respond to the initial COS request from the Research Team within 2-5 business days by sending a completed COS form as an e-mail attachment to the study contact, or in the case of more complex studies, ancillaries/UFP department(s) will send an e-mail reply requesting any additional information they may need from the study team (e.g., protocol, PI clarification).

d. UFP department(s) will provide both the “List Price” and Medicare estimate for professional services.

e. Most Shands ancillaries will provide only the “List Price” for technical services.

i. If Medicare estimates are needed for technical services, the COS should be forwarded to Shands Financial Planning and Analysis to obtain these estimates.

f. The pricing information on the COS Forms from Shands ancillaries and UFP areas can be used for negotiations with the Sponsor and in developing the study budget.
i. All COS Forms must accompany the Study Registration and Initiation Packet when submitting the proposal to Research Administration & Compliance (RAC), along with other applicable paperwork.

ii. RAC reviews all documents and uploads the following to SharePoint for final review by Shands and UFP:

iii. Study Registration & Initiation Checklist

iv. Billing Grids

v. Confirmation of Services Forms

vi. Shands and UFP confirm final pricing (list price and Medicare estimate).

vii. Shands sets up a unique R99 number for the study.

g. After the final pricing and R99 number are provided by Shands and UFP, a staff member from RAC will e-mail the research team this information along with the final Study Registration and Initiation Checklist and billing grids. This stage of the process should take less than 10 business days to complete after the study team receives approval of their proposal packet from RAC. E-mail COM-RAC-L@LISTS.UFL.EDU with any inquiries regarding the final pricing/ R99 number e-mail.

i. What if the Study-Funded Services Change:

1. Any amendments to prior submissions for additions/deletions to study-funded services will need to follow the COS steps and report the changes to RAC using the Amended Study Registration Form.

R99 Numbers

uuuuuu) Any study with study-funded services being billed by Shands Patient Financial Services (PFS) or the University of Florida Physicians (UFP) must have an R99 number.

vvvvv) An R99 number identifies each individual study and facilitates the process of billing services to the study funded account.

a. You must have an assigned R99 number prior to scheduling patients for study-related clinical services.

b. This number is issued by Shands Patient Financial Services following approval of your Study Registration packet by the RAC Office.

Medicare Rates for Research

wwwww) Shands and University of Florida have approved Medicare rates for study-funded services conducted in any Shands and/or University of Florida Physicians (UFP) facility, effective September 27, 2010.
Medicare rates will be applied to all new clinical research studies (regardless of the study sponsor) submitted to the College of Medicine Research Administration and Compliance (RAC) office and that request a new R99 number on or after the specified effective date.

Obtain Medicare Rate Estimates for New Studies

i. If Medicare rates are needed for budget negotiation purposes, researchers should follow one of the processes specified below to obtain an estimated Medicare rate for study-funded services.

ii. Researchers may obtain a Confirmation of Services (COS) form from appropriate ancillary/service provider.

iii. Shands ancillary or UFP department contact will work with researchers to ensure the correct test/procedure is selected with appropriate service/CPT code, and to provide the List Price (full price) for the service.

iv. Researchers then forward the COS to Theresa O’Connell at oconta@shands.ufl.edu or 352-265-7965 ext 86465 for technical fee Medicare estimates, and/or the individual UFP department(s) for professional fee Medicare estimates.

v. Researchers can use the UF Research Budgeting and Pricing Tool to obtain a Medicare rate estimate for a simple, straight-forward research service when the CPT code and service location is known.

   1. The Tool will also provide an estimated List Price for each service.

vi. Note that the actual charge for the service will be the actual Medicare rate on the date of service, and may be different from the estimated Medicare rate obtained through the COS or the Tool.

Budget Building Tips

i. The Medicare rate quotes obtained through the COS or the Tool are estimates of the final charges and are based on the current Medicare rates.

ii. Researchers are encouraged to use the actual or estimated List Price or discounted List Price when building the budget to ensure sufficient funding for the study.

   a. Note: Industry Sponsors should be paying as close to List Price as can be negotiated (NOT Medicare estimate).

iii. The actual Medicare rates at the time of service may be affected by the following:

   1. Medicare rates are updated quarterly.
2. The service was performed with other services that may affect the Medicare reimbursement amount.
3. Modifiers selected at the time of the service may significantly increase or decrease the actual Medicare reimbursement amount. Be sure to consult with the Principal Investigator (PI) regarding potential modifiers that may be added to the service/CPT codes, and take these into consideration when obtaining pricing for building your budget.
4. The location of the service has changed.
5. Additional CPT coded services were ordered on the date of service that were not originally included in the estimate.
6. The service ordered was different than the service budgeted.

iv. When using Medicare rates to build your budget, be sure to apply an allowance (e.g., 5%-10% at a minimum) to the estimated Medicare rates taking into consideration the factors as described above to cover potential price increases at the time of service which could exceed 5-10%.

v. For budgetary purposes on multi-year studies, plan for a 5% price increase each year.

vi. The Detailed Budget Template has been revised to calculate the markup and 5% per year price increase.

vii. Researchers are encouraged to create a master budget template with CPT codes used for their studies so that the study team can look up pricing using the UF Research Budgeting and Pricing Tool.

Reconciliation Tips

a. Estimated Medicare rates obtained through COS or the Tool are provided for budgetary purposes only.

i. They might be different from the final prices (actual Medicare rates on the date of service) charged to the study. When researchers reconcile the study claims against their R99 plan or budget, the prices will not always match.

ii. There may be scenarios where the R99 plan and final charges have bundled or unbundled items differently. Researchers are advised to reconcile the claims and their billing plan carefully, and promptly contact Shands PFS or UFP billing personnel for issues or questions.

Existing Studies

a. The Medicare rates will NOT be applied retroactively to existing studies approved with discounted research rates.

b. Amended services for existing studies (with existing R99 numbers) will be priced at the discounted research prices following the old pricing scheme.
Research Series Account

Shands Admissions creates Research Series Accounts in the hospital billing system for participants who are receiving study-funded services. The purposes of the Research Series Account are:

i. To set up a research-only participant account in the hospital billing system for study-funded services.

ii. To help UFP identify professional fees associated with study-funded hospital services (technical fees) for a participant.

iii. To prevent inappropriate claims from going to 3rd party payers or participants.

To request a Research Series Account, the study team must follow guidelines specified in the following sections:

Hospital Inpatient Visit

Inpatient Mixed Visit on a Clinical Unit

i. When a patient admitted for a clinical inpatient stay is scheduled to receive study-paid services, Shands hospital will set up a Research Series Account for the patient’s study-paid services.

ii. To accomplish this and before the study-paid research services are conducted, the principal investigator (PI) or study coordinator (SC) will notify Shands Admissions, Patient Financial Services (PFS), and University of Florida Physicians (UFP) billing personnel by sending an e-mail to the Inpatient Listserv RESEARCH-INPT-L@LISTS.UFL.EDU.

iii. The e-mail will include:
   1. Patient Name
   2. Patient Medical Record Number
   3. Study R99 Number
   4. Ordering Physician Name
   5. Date(s) of Service
   6. Description of any research-required inpatient items/services that are to be billed to the study
   7. Note: RAC Billing Grids may be attached instead of descriptions

iv. To order research services, the PI must order the service in Epic.

v. In addition, and to ensure correct billing, the PI/SC must complete and the PI sign the hard-copy ancillary-specific research form and fax or deliver to the appropriate ancillary area per the instructions on the form.
vi. The PI/SC retains the original or copy of the research form in the research record.

vii. Following receipt of the research form, the ancillary department will ensure the research charges are posted to the Research Series Account.

1. If the charge has an associated professional fee, posting the charge to the Research Series Account will also serve to alert UFP to the patient’s research status.
2. This will prompt UFP staff to review the patient’s charges, so they are billed to the appropriate payer.

viii. **NOTE: Special Procedure for Blood Drawn by Study Nurse**

1. PI/SC completes lab research form, PI signs, Study Nurse draws sample, and delivers sample and research form to Lab.
2. Lab staff uses the research form to enter the order in Epic.
3. Lab staff sends original research form to Lab Administration at Rocky Point Labs (RPL).

ix. With the receipt of the research form, Lab staff will ensure the research service charges post to the Research Series Account.

x. Ancillary department will facilitate the scanning of the research form into iHIRM.

xi. Upon completion of all inpatient research services, the PI/SC will send an e-mail to the Inpatient Listserv `RESEARCH-INPT-L@LISTS.UFL.EDU` to notify all parties of the date after which inpatient services should no longer be billed to the study.

Inpatient Research Only Visit on a Clinical Unit

i. When a patient is scheduled for a research-only inpatient admission on a clinical unit where all services are to be paid by the study, Shands Healthcare will need to set up an inpatient research account with appropriate plan code for the patient.

ii. Before the patient is admitted, the Principal Investigator (PI)/Study Coordinator (SC) submits an Admission Request Form (ARF) to Shands Healthcare with an indication the admission is for research only.

iii. Once the patient is admitted and before the study-paid research services are conducted, the PI/SC will notify Shands Admissions, Shands Patient Financial Services (PFS), and University of Florida Physicians (UFP) billing personnel by sending an e-mail to the Inpatient Listserv `RESEARCH-INPT-L@LISTS.UFL.EDU`.

iv. The e-mail will include:

1. Patient Name
2. Patient Medical Record Number
3. Study R99 Number
4. Admitting Physician Name
5. Admission Date

v. To order research services, the PI must order the service in Epic.

1. In addition, and to ensure correct billing, the PI/SC must complete and the PI must sign the hard-copy ancillary-specific research form and fax or deliver to the appropriate ancillary area per the instructions on the form.

vi. The PI/SC retains the original or copy of the research form in the research record.

vii. With the receipt of the research form, the ancillary department will facilitate the scanning of the form into iHIRM.

viii. Upon discharge, the inpatient stay will be coded and all charges posted to the patient’s inpatient research account.

ix. NOTE: If Standard of Care services are provided during the Research Only hospital stay, you will need to e-mail the Inpatient Listserv RESEARCH-INPT-L@LISTS.UFL.EDU with a detailed description of the services which should be billed to the patient/insurance instead of the research study.

Study Participants Not in Epic Yet

i. For studies that have been uploaded into Epic, study teams are responsible for identifying any study participants who will be:
   1. Receiving protocol-required billable, or potentially billable (e.g., salary support, no read) study services at a Shands or UFP facility AND/OR
   2. Receiving an investigational drug or device.

ii. Study teams must attach these participants to the appropriate study in Epic BEFORE the participant receives protocol-required billable services or an investigational drug or device, or BEFORE any protocol-required billable services are ordered.
   1. See Participant Registration in Epic for more information.

iii. If a study participant has received study services before you have had a chance to attach the participant to the study in Epic OR the participant’s Epic Active Start Date was not set in time to include a study service, email details of the study-funded charges to Shands and UFP billing personnel so they can direct the study charges to correct account:
   1. Shands PFS: PFSResearchGroup@shands.ufl.edu
   2. UFP: UFPBARClinicalTrialsBillingTeam@shands.ufl.edu
Hospital Outpatient Visit

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Hospital Outpatient Mixed Visit:

i. When the patient is receiving research services that are to be billed to the study and clinical services that are to be billed to the patient/insurance, Shands admissions will set up a Research Series Account for the individual patient’s study-paid services and a clinical account for the services that are to be billed to the patient/insurance.

ii. This requires **separate orders for study-paid and clinical services** to ensure proper billing. Clinical orders will be entered into Epic by the PI.

   1. Clinical orders for study-related CMS qualifying “Routine Costs” must include the V70.7 diagnosis code. Q0/Q1 modifiers should be entered in Order Comments, as appropriate.

iii. For study-paid services, the PI/SC must complete and the PI sign the hard-copy ancillary-specific research form and fax, deliver, or send it with the patient to the appropriate ancillary area.

iv. Upon receipt of the research form, an ancillary staff member verifies that the patient has an active Research Series Account.

   1. If no Research Series Account, a financial representative in the ancillary area establishes a Research Series Account.

v. The ancillary staff member enters the research order in Epic.

vi. The ancillary staff member uses the research form to ensure charges are posted to the Research Series Account.

iiiiii) Hospital Outpatient Research Only Visit

i. When the participant is receiving study-funded services, Shands admissions will set up a Research Series Account for the participant.

ii. The PI/SC must complete and the PI sign the hard-copy ancillary-specific research form and fax, deliver, or send it with the patient to the appropriate ancillary area.

iii. Upon receipt of the research form, an ancillary staff member verifies the patient has an active Research Series Account.

   1. If no Research Series Account, a financial representative in the ancillary area establishes a Research Series Account.
iv. The ancillary staff member enters the order in Epic.

v. The ancillary staff member uses the research form to ensure charges are posted to the Research Series Account.

jjjjjjj) Study Participants Not in Epic Yet

i. For studies that have been uploaded into Epic, study teams are responsible for identifying any study participants who will be:

   1. Receiving protocol-required billable, or potentially billable (e.g., salary support, no read) study services at a Shands or UFP facility.

   AND/OR

   2. Receiving an investigational drug or device.

ii. Study teams must attach these participants to the appropriate study in Epic BEFORE the participant receives protocol-required billable services or an investigational drug or device, or BEFORE any protocol-required billable services are ordered. See Participant Registration in Epic for more information.

iii. If a study participant has received study services before you have had a chance to attach the participant to the study in Epic OR the participant’s Epic Active Start Date was not set in time to include a study service, email details of the study-funded charges to Shands and UFP billing personnel so they can direct the study charges to correct account:

   1. Shands PFS: PFSResearchGroup@shands.ufl.edu
   2. UFP: UFPBARClinicalTrialsBillingTeam@shands.ufl.edu

Doctor’s Office Visit

kkkkkk) Doctor’s Office Mixed Visit

i. Schedule Mixed Visit Type in Epic (see Scheduling Research Visits in Epic).

ii. Patient presents at check-in for combination study/clinical visit.

iii. Study encounter form and clinical encounter forms are printed and kept with the chart.

   b. If no study encounter form has been created, a clinical encounter form is printed and the physician will identify which services are study-related.

   i. Physician enters documentation in EPIC.
ii. Check-out staff uses the encounter forms to enter charges with the correct Guarantor (e.g. “Research/clinical trials study” for study funded services and patient/insurance for study “Routine Costs” and non-study “Standard of Care” services).

iii. If an ancillary clinical service is needed it would be ordered through EPIC.

iv. Ancillary services to be paid by the study will be ordered separately following the Hospital Outpatient Mixed Visit guidelines 3-6.

llllll) Doctor’s Office Research Only Visit

i. Schedule “Research/Clinical Trial” Visit Type in Epic (see Scheduling Research Visits in Epic).

ii. Patient presents at check-in for study visit.

iii. Study encounter form is printed and kept with the chart. If no study encounter form has been created, a clinical encounter form is printed, and the physician will identify somewhere on the form the patient is part of a study.

iv. Physician enters documentation in EPIC.

v. Check-out staff uses the encounter form to enter charges (including charges that should be “zeroed out”) with the correct Guarantor (research/clinical trials study).

vi. If an ancillary service is needed, the guidelines 1-5 for Hospital Outpatient Research Only Visit will be followed.

mmmmmmm) Study Participants Not in Epic Yet

i. For studies that have been uploaded into Epic, study teams are responsible for identifying any study participants who will be:

1. Receiving protocol-required billable, or potentially billable (e.g., salary support, no read) study services at a Shands or UFP facility.

    AND/OR

2. Receiving an investigational drug or device.

ii. Study teams must attach these participants to the appropriate study in Epic BEFORE the participant receives protocol-required billable services or an investigational drug or device, or BEFORE any protocol-required billable services are ordered. See Participant Registration in Epic for more information.
iii. If a study participant has received study services before you have had a chance to attach the participant to the study in Epic OR the participant’s Epic Active Start Date was not set in time to include a study service, email details of the study-funded charges to Shands and UFP billing personnel so they can direct the study charges to correct account:

1. Shands PFS: PFSResearchGroup@shands.ufl.edu
2. UFP: UFPBARClinicalTrialsBillingTeam@shands.ufl.edu

UF Clinical Research Center (CRC) Visit

nnnnnn) UF CRC Inpatient Visit:

a. When a patient is scheduled for a research-only admission to the Clinical Research Unit (CRC), CRC staff will notify the Admissions Department to open a Z account (with A31 plan code) for the patient. Use of the Inpatient Listserv is not required.

b. For admissions where both clinical and research services are expected, CRC staff may request either a Z or C as the primary account, based on whether the majority of services will be for research or clinical care (i.e. billed to the patient/insurance), respectively.

i. The admission may also require the establishment of a Research Series Account for services not funded by the CRC but required to be billed to the study.

c. For research services funded by the CRC, specific CRC research order worksheets will be created by CRC staff and given to the PI to sign.

i. Services provided by Shands ancillary departments will be entered into EPIC by the CRC staff.

ii. CRC staff will post charges to the appropriate account.

1. Copies of the research order worksheets will be sent to iHIRM.

d. To order study-funded services, the PI/SC must order the service in EPIC.

i. In addition, and to ensure correct billing, the PI/SC must complete and the PI sign the hard-copy ancillary-specific research form and fax or deliver it to the appropriate ancillary area per the instructions on the form.

e. With the receipt of the research form, the ancillary department will post the charges to the Research Series Account.

i. The ancillary department will facilitate the scanning of the research form into iHIRM.
f. To order clinical services, the PI must enter the order in EPIC. If necessary, charges will be moved to the clinical account by PFS staff with direction from the CRC.

**UF CRC Outpatient Visit**

a. When a patient is scheduled for a research-only visit to the CRC, CRC staff will notify the Admissions Department to open a patient Research Series Account, referencing the CRC R99#.

b. When the patient is receiving research-funded services and clinical services that are to be billed to the patient/insurance, the CRC will request both a Research Series Account and a clinical account.

c. This requires separate orders for research-paid and clinical services to ensure proper billing.

i. Clinical orders will be entered into EPIC by the PI.

ii. Clinical orders for study-related CMS qualifying “Routine Costs” must include the V70.7 diagnosis code. Q0/Q1 modifiers should be entered in Order

iii. Comments, as appropriate.

d. For research services funded by the CRC, specific CRC research order worksheets will be created by CRC staff and given to the PI to sign.

i. Services provided by Shands ancillary departments will be entered into EPIC by the CRC staff.

e. CRC staff will ensure all charges are posted to the CRC Research Series Account. Copies of the research order worksheets will be sent to iHIRM.

f. To order study-funded services, the PI/SC must complete and the PI sign the hard-copy ancillary-specific research form and fax, deliver, or send it to the appropriate ancillary area.

g. The ancillary staff member enters the order in EPIC.

h. The ancillary staff member uses the research form to ensure charges are posted to the Research Series Account.

i. The ancillary staff member facilitates the scanning of the research form into iHIRM,

j. Shands PFS works with CRC to separate “K” account charges by funding source and bill the responsible party.

**IDS Medication Orders**
With the implementation of Epic II on July 19, 2013, all medication orders (including chemotherapy and investigational drugs) will be submitted electronically through Epic.

i. This is a practice consistent with all other medication orders throughout University of Florida Health.

b. Recognizing that some research teams do not have a nurse coordinator to assist with pending Epic medication orders for physician investigator signature, the Investigational Drug Service (IDS) will continue to accept paper orders via fax transmission if investigator entry presents a significant hardship.

i. The goal is not to create a barrier to investigational medication management, but rather align with the standard practice of medication processing through UF Health.

c. Regardless of the method of medication order submission, all research participants must have an active Epic Research Series Account (encounter) in order for IDS to label and dispense investigational medications.

Research Series Account for IDS Orders

i. All Investigational Drug Service (IDS) medication orders will be processed in Epic. In order for this to occur, each patient requiring IDS medications must have an active Research Series Account.

ii. Prior to submitting a medication order to IDS, the study coordinator must verify in Epic that the patient has an active Research Series Account for the current month.

iii. If not, the study coordinator must request a Research Series Account from Shands Admissions via either the Inpatient Listserv `RESEARCH-INPT-L@LISTS.UFL.EDU` (for inpatients only) or by contacting Shands Admissions directly (for outpatients).

iv. In the e-mail, include the following information:

1. Patient Name
2. Patient Medical Record Number
3. Study R99#. If the study does not have an R99#, write “IDS Only”.
4. Ordering Physician Name
5. Date of Service

v. Admissions will verify the establishment of the Research Series Account by return e-mail and provide the account number.

1. For studies without R99 numbers, the Research Series Account will use the letters “IDS” as a substitute for the R99 number.
vi. Special Instructions – Renewal of Research Series Account:

1. If a Research Series Account is used exclusively for IDS activity, the Research Series Account will close on the last day of the month in which it was established.
2. If IDS services are anticipated in any subsequent month, a new Research Series Account will need to be requested.
3. IDS services alone will not keep a Research Series Account active.

rrrrrr) Detailed Guide to Ordering IDS Medications

i. For more information about ordering IDS medications, see Investigational Drug Ordering in Epic.

ssssss) Getting Help

i. If you need assistance with placing an investigational medication order, please do not hesitate to contact one of the IDS Pharmacists at one of the following numbers:

1. IDS Main Pharmacy: 265-0680 extension 4-4237 or 4-4716
2. CTSI IDS Pharmacy: 294-5894
3. IDS On-Call Pager: 413-2086

Unexpected Sponsor-Funded Services

ttttttt) UNEXPECTED (or emergent) services are defined as any service that was not in the original Study Registration & Initiation R99 information plan and is a service that is to be paid for by the study.

i. This could include added-on or new services that are urgent and/or related to subject injury, or services that were missing in error on the original Study Registration & Initiation packet.

uuuuuuuu) PATIENT SPECIFIC Unexpected Services

i. Use these procedures if the unexpected service applies to an individual study participant and will not affect other participants.

1. Research Study with an Existing R99

   a. When ordering services emergently for a patient during a clinical research study, steps include:

      i. Ordering the emergent service(s) by adding the service name to the corresponding research form for that study.
ii. After service is rendered, add the service name, service date, and service location to the Participant Service Tracking Log for that particular patient.

iii. Reconcile your Participant Service Tracking Log with Shands PFS and UFP monthly, as needed, if any study participants have had study funded services during the current month and there are any problems or outstanding invoices.

2. Research Study without an Existing R99

a. Research teams that do not have an existing R99 for that study and will be ordering services emergently must utilize the following procedure:

i. Obtain and utilize a “blank” research form for that particular ancillary department by contacting the ancillary department directly.

ii. See Who Can Help? for ancillary contact information.

iii. Check the box at the top of the research form titled, “NO R99#, BUT STUDY-FUNDED SERVICES (including participant specific) ARE UNEXPECTED or URGENT,”

iv. Enter the name of the Principal Investigator; Study Coordinator Name and Phone Number; Study Name; Department to Be Invoiced and PO Box #; Study Billing Contact and Phone#.

1. This information must be given to the scheduler for scheduled services also, to ensure that Shands Admissions creates the account correctly.

v. After service is rendered, add the service name, service date, and service location to the Participant Service Tracking Log for that particular patient.

b. Reconcile your Participant Service Tracking Log with Shands PFS and UFP monthly, as needed, if any study participants have had study funded services during the current month and there are any problems or outstanding invoices.

3. STUDY SPECIFIC Unexpected Services

a. Use these procedures if the unexpected service applies to all participants on the study.
4. **Research Study with an Existing R99**

a. When ordering services emergently for a patient during a clinical research study, it is permissible to add the name of the emergent service(s) to the corresponding research form for that study.

b. Subsequently, it is required that you amend your RAC Study Registration & Initiation documents and alert Shands Patient Financial Services (PFS) and/or University of Florida Physicians (UFP) billing personnel as soon as possible. Steps include:

   i. Order the emergent service(s) by adding the service name to the corresponding research form for that trial.
   ii. Obtain a Confirmation of Services from the appropriate ancillary department for the new service.
   iii. Complete the Amended Study Registration Form.
   iv. Revise the original billing grid to reflect the additional service and its corresponding payor.
   v. Submit these documents to the RAC office, who will email you with the updated Pricing Worksheet from Shands PFS and/or UFP within 10 business days of RAC approval.
   vi. Add the service name, service date, and service location to the Participant Service Tracking Log for all patients.
   vii. Reconcile your Participant Service Tracking Log with Shands PFS and UFP monthly, as needed, if any study participants have had study funded services during the current month and there are any problems or outstanding invoices.

5. **Research Study without an Existing R99**

a. Research teams that do not have an existing R99 for that study and will be ordering services emergently must utilize the following procedure:

   i. Obtain and utilize a “blank” research form for that particular ancillary department by contacting the ancillary department directly. See Who Can Help? for ancillary contact information.

   ii. Check the box at the top of the research form titled, “NO R99#, BUT STUDY-FUNDED SERVICES (including participant specific) ARE UNEXPECTED or URGENT”.

   iii. Enter the name of the Principal Investigator; Study Coordinator Name and Phone Number; Study Name;
Department to Be Invoiced and PO Box #; Study Billing Contact and Phone#.

1. This information must be given to the scheduler for scheduled services also, to ensure that Shands Admissions creates the account correctly.

iv. Obtain a COS from the appropriate ancillary department(s), update your RAC Study Registration & Initiation documents, and submit to the RAC office as soon as possible following the rendering of the service(s).

v. Complete the Amended Study Registration Form.

vi. Revise/create appropriate billing grid to reflect the new service and its corresponding payor.

vii. Submit to the RAC office as soon as possible following the rendering of the service(s).

1. RAC office will send you the Pricing Worksheet from Shands PFS and/or UFP and the R99 number for the study within 10 business days of RAC approval.

viii. Add the service name, service date, and service location to the Participant Service Tracking Log for all patients.

ix. Reconcile your tracking log with Shands PFS and UFP monthly, as needed, if any study participants have had study funded services during the current month and there are any problems or outstanding invoices.

6. Study Participants Not in Epic Yet

a. For studies that have been uploaded into Epic, study teams are responsible for identifying any study participants who will be:

i. Receiving protocol-required billable, or potentially billable (e.g., salary support, no read) study services at a Shands or UFP facility.

AND/OR

ii. Receiving an investigational drug or device.
b. Study teams must attach these participants to the appropriate study in Epic BEFORE the participant receives protocol-required billable services or an investigational drug or device, or BEFORE any protocol-required billable services are ordered. See Participant Registration in Epic for more information.

7. If a study participant has received study services before you have had a chance to attach the participant to the study in Epic OR the participant’s Epic Active Start Date was not set in time to include a study service, email details of the study-funded charges to Shands and UFP billing personnel so they can direct the study charges to correct account:
   a. Shands PFS: PFSResearchGroup@shands.ufl.edu
   b. UFP: UFPBARClinicalTrialsBillingTeam@shands.ufl.edu

8. What Procedures Should be Followed if a Study Participant Experiences Subject Injury/Adverse Event?
   a. See Reporting and Billing of Subject Injury/Adverse Events.

Services with “Reading Exceptions”

“Reading Exception” refers to a request for no professional reading/interpretation from the department in which the service is performed. This can include exceptions such as:

i. PI/Investigator is performing the read, or
ii. The technical portion is being sent to a centralized core-lab to perform the read. The results may or may not be provided to the PI.

b. Reading Exception Policy

i. Reading Exceptions are only allowed for Research study-paid services and must be included in the study billing plan as outlined in the Study Registration & Initiation documents and confirmed with the ancillary/service department through the Confirmation of Services/R99 process prior to study start-up.

ii. Each individual Shands/UFP ancillary department is required to develop, provide and monitor a billing process to ensure proper reading and billing procedures are followed.


   c. The Informed Consent for the study must provide the details of the “Reading Exception” to the study subject and identify each service as applicable using the following statement:
i. “Tests done only for research purposes will not be evaluated or used to diagnose or treat any of your medical problems. This/these test(s) may need to be repeated if required for your medical care in the future”

d. Note: If the services are required as part of the patient’s Standard of Care, the reading MUST be performed by the service department and must meet billable service requirements. The results are part of the patient’s medical record.

e. Study Team Responsibilities

i. For allowable “Read Exceptions” the Principal Investigator/Study Team will:
   1. Indicate a “Reading Exception” in the RAC Study Registration & Initiation documents;
   2. Notify the IRB and patient of the “Reading Exception” through appropriate ICF language (as outlined above);
   3. Follow individual service department procedures/processes to ensure proper billing procedures are followed. A liability waiver is no longer required with the Ancillary Department.

If the study participant receives at least one monthly study-funded service on the Research Series Account, the Research Series Account will remain in effect until Shands Patient Financial Services (PFS) is notified that the services for that study participant have ended. If the study participant did not have any study-funded services in the previous month, a new Research Series Account must be requested by the study team.

a. **Participants in More Than One Study:** since two Research Series Accounts cannot be created for one patient during the same time period, attention to the registration process is critical.
   1. When registering the study participant for multiple studies, the study team must inform all registration personnel that the participant will have multiple R99 numbers on the Research Series Account and that the initial R99 number must be entered in a manner that permits multiple numbers and orders.
   2. If possible, detailed information about what services correspond to each R99 number should be entered into the comment section to assist with ordering.
   3. An e-mail should also be sent to Shands Patient Financial Services (PFS) and University of Florida Physicians (UFP) notifying them that the patient is enrolled in more than one study and that there are multiple R99 numbers:
      a. **Shands PFS:** PFSResearchGroup@shands.ufl.edu;
      b. **UFP:** UFPBARClinicalTrialsBillingTeam@shands.ufl.edu

   4. The e-mail should include the date(s) of service, service(s) provided, medical record number, patient name, Principal Investigator name(s) and the corresponding R99 numbers.
Tracking Study Funded Services

This is the process by which all study-funded services performed are identified and monitored to ensure fiscal compliance.

a. Tracking logs are required for all studies with activity after June 2007.

Each study should have a designated tracking team which must include the study coordinator and the person paying the bills. Excellent communication between study coordinators and fiscal personnel is essential for this process to be effective, and monthly reconciliation of tracking logs is required (see reconciliation section below).

a. Why Do Study Teams Need to Track:

a. A study tracking log must be maintained in order to:

1. Monitor all study-funded services associated with the study.
2. Confirm that all services performed have been charged to the appropriate payer (e.g. grant, sponsor, third-party payer).
3. Confirm that all costs associated with the study have only been paid once.
4. Financially protect study participants, investigators and the institution.
5. Ensure compliance with all State and Federal Regulations.
6. Ensure that the study team is following the billing plan.
7. Ensure compliance with UF Health Science Center Policy and Standards.

b. If a tracking log is not maintained, revenue and/or billing compliance issues may occur. Some examples include:

i. Charges for study-funded services may be billed to patients and/or third-party payers.
ii. Invoices may be paid multiple times.
iii. Multiple payments may be made for the same service.
iv. Payments may be made for services not performed for the study.
v. Payments may be made for services for a person who is not a study participant.
vi. Professional fees paid by research salary support may be billed to patients or third-party payers in error.
vii. Professional fees for non-research services may be incorrectly written off as study services.

c. The tracking team MUST track:

i. All study-funded services that will generate a participant bill. This includes services billed by Shands Patient Financial Services (PFS-technical services),
University of Florida Physicians (UFP-professional services), or outside vendors (e.g. Quest labs).

ii. “Reading exception” (e.g., study-only chest X-ray that will be sent to the sponsor for interpretation). In this case, what needs to be verified is that a professional fee was NOT generated.

iii. A study physical exam/office visit that an investigator will perform via salary support in a clinic. Again, what needs to be verified is that a professional fee was NOT generated.

d. If your study has these types of services, it is essential that they are tracked and that the tracking log is sent to PFS and UFP on a monthly basis to ensure that fees are not billed to patients or third-party payers in error (see reconciliation below).

e. Study teams should also be aware of situations where it is possible that an **unintended bill** will be generated by a study service. Some examples are:

   i. A test/assessment provided by the study coordinator or other study team member in a clinic where that type of test/assessment is billable. (e.g., an ECG, walk test).

   ii. A billable service that the study team performs and does not plan to enter into the billing system.

   iii. Study-funded laboratory testing that is mistakenly placed on a participant’s billable account, then later moved to a study-funded account. (For example, when a lab charge is originally placed on a billable account, both a technical fee AND a professional fee may be generated. If the correction is only made to the technical fee, the professional fee may still stay on the patient’s billable account, which is then billed out in error.)

f. These **potentially** billable items can pose a high risk for billing errors. Study teams, charge entry and billing personnel must understand the billing plan and carefully follow correct clinic/ancillary procedures to ensure that these situations do not create unintended bills.

g. The tracking log should include the following information:

   i. Study identification (i.e. study title, PI, R99 number, study project number).

   ii. Expected service time points (i.e. “screening”, “visit 1”, “end of study”).

   iii. Names of items/services.*

   iv. Service/CPT codes.

   v. Anticipated pricing.

   vi. Responsible payer(s).

   vii. Participant names and medical record numbers.

   viii. Date that each study-funded service was actually provided (i.e. scheduled visits, admissions.)

   ix. Service providers/locations.
x. Invoice numbers and dates.
xi. Payment information (i.e., voucher numbers, payment amounts, payment dates).
-xii. Explanations for special circumstances.
-xiii. * If the study includes bundled services/items (e.g., technical services billed based on an inpatient DRG) which generate professional fee bills, these items/services should be listed separately on the tracking log (e.g., “CT scan of abdomen/pelvis”, “lab testing”).

h. Study identification data should be pre-filled into the study-specific tracking log.

ii. Note: This should be done prior to study start-up during a face-to-face meeting with all tracking team members. The study billing grid and tracking log should be reviewed and discussed so that all tracking team members understand the study billing and tracking plan.

VIII. Participant identification data should be entered by the study coordinator as each participant is enrolled.

IX. Service data should be entered by the study coordinator immediately after a participant’s study visit.

X. Invoice data should be entered as soon as each invoice is received.

XI. Payment data should be entered as each payment is made.

XII. What Format Should I Use for a Tracking Log:

1. As long as your tracking system creates a log that has the data elements mentioned above, you may use it for tracking. Most study teams choose to track using an Excel file on a shared drive. The Research Administration & Compliance (RAC) office has a customizable tracking log template which includes the required data elements.

2. RAC also offers a monthly class RAC805 Tracking Research Services, and RAC Auditor/Monitors are available for one-on-one consultations regarding the tracking process.

XIII. What is Reconciliation:

I. At least once a month, the study tracking team should perform an internal reconciliation of the tracking log. The team should compare the study-funded services performed to the study invoices received to ensure that:

   I. All study-funded services have been recorded in the tracking log.
II. All invoices have been received for those services.
III. The invoices received are for services that actually belong to the study.
IV. If there are any missing or incorrect items, send the most updated tracking log to UFP and PFS as soon as these problems are identified:

I. Shands PFS: PFSResearchGroup@shands.ufl.edu
II. UFP: UFPBARClinicalTrialsBillingTeam@shands.ufl.edu

XIV. Reminder: If the study includes potentially billable services (see What Services Need To Be Tracked above), the study team should send the tracking log to PFS & UFP any month that a potentially billable service was rendered, so that these offices can confirm that no unintended bill was generated.

I. For questions or assistance with participant service tracking, contact the RAC Auditors at CTC-Auditors@ufl.edu.

Participant Services Tracking Log

zzzzzzz) The tracking log is used to identify and monitor the occurrence and payment data for all study-funded services to ensure fiscal compliance.

XV. Instructions

XVI. Row 1 - Study Title

1. Enter the title of the research study.

XVII. Row 2 - Study Identifier (Short Name)

1. Enter the study’s acronym or short title as listed on the Study Registration & Initiation Checklist (SRIC).

XVIII. Row 3 – R99 Number

1. Enter the R99 number assigned to the study or N/A if there is not an R99 number.

XIX. Row 4 – P.I.

1. Enter the full name of the Principal Investigator.

XX. Row 5 – Special Circumstances (optional)

1. Use this space to include any notes/reminders to the study coordinator or fiscal personnel regarding any issues unique to the study that provide relevant information to the tracking
and/or payment of study services such as reading exceptions, items to be invoiced to the sponsor, etc.

XXI. Row 6 – Reminders

1. This line is used by the Research Administration and Compliance Office to provide a link to important policy information.

XXII. Row 7 – Column Headers

1. **Last Name:** This is the last name of the study participant.
2. **First Name:** This is the first name of the study participant.
3. **Study ID:** (optional) This is the number used to track participants within a study (also called a “participant ID”).
4. **DOB:** This is the study participant’s date of birth.
5. **Hospital Acct #:** This is the number used in the Shands HIS system and on invoices from Shands to identify a specific patient account (also called an “encounter” or “patient number”).
6. **Medical Record #:** This is the patient’s medical record number used by UF/Shands Healthcare system to identify a patient.
7. **Service Name:** This is the name or a description of the study service being tracked.
8. **Service Time-point:** This is the description of the study service time-point as referenced by the protocol and informed consent (e.g. “screening”, Visit 3”, “day 24”).
9. **Service Location:** This is the name of the location where the study service was conducted (e.g. “Shands BMT Clinic”, “Quest Lab”, “UF CRC”)
10. **Service Date:** This is the study visit date or the date the study service was performed.
11. **CPT/Service Code Tech Fees:** This is the expected CPT Code or Service code used by the vendor for the technical portion of a study service (for example, as listed on the Shands HealthCare Technical Pricing sheet.
12. **Medicare Rate Est. Tech Fees (on post 9/26/10 log):** This is the estimated Medicare Rate for the technical charges for a study service as provided by Shands on the Shands HealthCare Technical Pricing sheet. For other vendors (e.g. Quest Lab), use the negotiated research price provided to you by that vendor.
13. **Quoted Price Tech Fees (on pre 9/27/10 log):** This is the discounted research price for the technical charges for a study service as provided by Shands on the Shands HealthCare Technical Pricing sheet. For other vendors (e.g. Quest Lab), use the negotiated research price provided to you by that vendor.
14. **Invoice Date Tech Fees:** This is the date on an invoice for payment received from Shands or an outside vendor for technical charges.
15. **Invoice Number Tech Fees:** This is the invoice number on an invoice for payment received from Shands or an outside vendor for technical charges. (If the invoice is from Shands, it should match the Hospital Account #.)
16. **Invoice Amount Tech Fees:** This is the amount billed for the technical charge for a study service.
17. **Amount Paid by Study Tech Fees:** This is the amount paid for the technical charge for a study service.
18. **Date Paid Tech Fees:** This is the date that the payment voucher is created in PeopleSoft or a P-card payment is made for an invoice for technical charges.
19. **Voucher # Tech Fees:** This is the payment voucher number as assigned in PeopleSoft for payment of a technical fee invoice. If a P-card is used for payment, the voucher number used to pay the P-card charges should be entered.
20. **CPT Code Pro Fees**: This is the expected CPT Code used by the vendor for the professional portion of a study service (for example, as listed on the UFP Professional Pricing sheet.

21. **Medicare Rate Est. Pro Fees (on post 9/26/10 log)**: This is the estimated Medicare Rate for a study service as provided by UFP on the UFP Professional Pricing sheet. If applicable for other vendors (e.g. non-UF physician services), use the negotiated research price provided to you by that vendor, if applicable.

22. **Quoted Price Pro Fees (on pre 9/27/10 log)**: This is the discounted research price for a study service as provided by UFP on the UFP Professional Pricing sheet. If applicable for other vendors (e.g. non-UF physician services), use the negotiated research price provided to you by that vendor.

23. **Invoice Date Pro Fees**: This is the date on an invoice for payment received from UFP or an outside vendor for professional charges.

24. **Invoice Amount Pro Fees**: This is the amount billed for the professional charge for a study service.

25. **Amount Paid Pro Fees**: This is the amount paid for the professional charge for a study service.

26. **Date Paid Pro Fees**: This is the date that the payment voucher is created in PeopleSoft or a P-card payment is made for an invoice for professional charges.

27. **Voucher # Pro Fees**: This is the payment voucher number as assigned in PeopleSoft for payment of a professional fee invoice. If a P-card is used for payment, the voucher number used to pay the P-card charges should be entered.

XXIII. **Comments/Notes**: (optional) This column may be used to provide any additional information for explanation or documentation purposes.

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**Study Admin Record in Epic**

Per [UF HSC policy](#), beginning December 1, 2011, all UF clinical research studies that meet at least ONE of the following criteria must be uploaded into the Epic electronic medical record system:

- The study has protocol-required potentially billable service(s) that will be conducted in a Shands or University of Florida Physicians (UFP) facility (regardless of payer).

AND/OR

- The study involves an investigational drug or device.

AND/OR

- The study requires a ClinicalTrials.gov NCT number on billing claims.

*Note: A study that does not meet the above criteria may need to be uploaded into Epic after study start-up in the event of a study-related adverse event or injury.*

**Epic Training and Access**

Study team members who work with studies in Epic must have the appropriate access to the study’s administrative record **BEFORE** the study starts. See [Help with Epic Training and Access](#) for more information.

**Study Upload**
During its review process, the Research Administration & Compliance (RAC) office will identify studies that require Epic upload (see criteria above). The study team will be informed that the study qualifies for Epic upload via the RAC Study Initiation Letter.

The study administrative record will be created in Epic after IRB approval. After IRB approval, if you cannot find your study in Epic, send an Epic study upload request to EpicUploadRequest-L@lists.ufl.edu. Be sure to attach a Study Upload Template with all fields completed. Note: The study team will NOT be responsible for creating the study administrative record.

Searching for the Study Administrative Record

Once a study is approved by IRB-01 or WIRB, the study team is responsible for verifying, maintaining, and updating the study administrative record. To find the study administrative record in Epic:

1. Sign onto to Epic.

2. Navigate to Epic > Patient Care > Research Study Maintenance.

The Study Select screen will appear.

1. Search by the study short name or by the IRB# in the search box.
   - To search by study short name: type the first few letters of the study short name (e.g., CCTRN).
   - To search by IRB#: type “irb.” followed by the first few characters of the IRB#, including dashes (e.g., irb.27-2008).

Can’t Find the Study in Epic?
First, make sure your search syntax is correct (see section above). If your study is still not found in Epic, contact the RAC Office by sending an email to EpicUploadRequest-L@lists.ufl.edu. Be sure to attach a Study Upload Template with all fields completed.

Managing the Study Administrative Record

Once a study is uploaded, the study team is responsible for verifying, maintaining, and updating the study administrative record. In the administrative record, study teams can:

- Update the “Study Name” (study nickname/short name used to search for the study in Epic).
- Update “Guarantor Demographics” fields:
  - “Contact” (use for study’s departmental billing contact name).
  - “Address” (use for UF departmental address where study invoices should be sent).
  - “City (or ZIP)” (use for UF EMAIL address of study billing contact).
  - “State” (enter FL).
  - “ZIP” (enter UF departmental Zip Code).
  - “Phone” (enter UF phone number for study billing contact).
  - “Fax” (enter UF Fax number for study billing contact).
- Add or update names of Study Coordinators associated with the study.

No other fields should be changed in the study administrative record without emailing and consulting RAC personnel. See the RAC Guide to Fields in Epic Research Screens and Epic research training modules for more information on how to manage the study administrative record.

FAQs

For handout on Epic Research Module “Frequently Asked Questions”, see Epic FAQS

Participant Registration in Epic

Per UF HSC policy, beginning December 1, 2011, all UF clinical research studies that meet at least ONE of the following criteria must be uploaded into the Epic electronic medical record system:

a. The study has protocol-required potentially billable service(s) that will be conducted in a Shands or University of Florida Physicians (UFP) facility (regardless of payer).

   AND/OR

b. The study involves an investigational drug or device.

   AND/OR
c. The study requires a ClinicalTrials.gov NCT number on billing claims.

d. *Note:* A study that does not meet the above criteria may need to be uploaded into Epic after study start-up in the event of a study-related adverse event or injury.

**XXIV. Epic Training and Access**

1. Study team members who work with studies in Epic must have the appropriate access to the study’s administrative record **BEFORE** the study starts. See Help with Epic Training and Access for more information.

**XXV. Attaching Study Participants to a Study in Epic**

1. For studies that have been uploaded into Epic, study teams are responsible for identifying any study participants who will be:
   
   I. Receiving protocol-required billable, or potentially billable (e.g., salary support, no read) study services at a Shands or UFP facility.

   AND/OR

   II. Receiving an investigational drug or device.

2. Study teams must attach these participants to the appropriate study in Epic **BEFORE** the participant receives protocol-required billable services or an investigational drug or device, or **BEFORE** any protocol-required billable services are ordered.

3. After logging into Epic, navigate to Epic > Patient Care > Pt Research Studies.

4. The Patient Lookup screen will appear; search by the Name/MRN or SSN.

5. The Research Studies screen will appear.

6. Using the search box, click the “Add” button.

   ![Add a new study to list](image)

   Search for your study by either “irb.IRB#” or the first few letters of the Short Name. Once found, double-click on the study. Make sure you input the appropriate status and **Active Start/End dates**.

**XXVI. Participant Enrollment Status**

1. Study teams must maintain the participant enrollment status field in each participant’s Epic research record.

   II. This status will appear in a “research flag” or “research banner” whenever a service provider or billing person is viewing the participant’s electronic medical record.
III. See the RAC Guide to Fields in Epic Research Screens and the Epic research training modules for more information on how to set and update the participant status field.

I. Participant Start-End Dates – Triggering Pre-Bill Reviews

1. After a participant has been attached to an active research study in Epic, the study team must maintain the “Active start date” and “Active end date” fields in each participant’s research record.

   I. “Active start date” should be the first day that the participant will receive a protocol-required, BILLABLE service that either needs to be paid by study funds OR needs V70.7 and Q0Q1 modifiers added. If the “Active start date” field is blank, NO charges for the participant will be reviewed, and the possibility of billing error greatly increases.

   II. “Active end date” should be the last day that the participant will receive a protocol-required, BILLABLE service that either needs to be paid by study funds OR needs V70.7 and Q0Q1 modifiers added. The “Active end date” field can be left blank until the final service date is confirmed for that participant.

2. ANY and ALL professional services provided to the participant between these dates will be routed to a research billing work queue for pre-bill review.

3. This includes all professional charges that are NOT related to the study, so study teams should use great care in selecting start and end dates – see RAC Guide to Fields in Epic Research Screens for more information.

4. The research billing work queue will be reviewed by UFP billing personnel, who will then route charges to the appropriate account based on the study billing grids.

5. The study coordinator and the billing contact identified for each study will be required to respond in a timely fashion to any billing inquiries.

6. Note: If a study participant has received study services before you have had a chance to attach the participant to the study in Epic OR the participant’s Epic Active Start Date was not set in time to include a study service, email details of the study-funded charges to Shands and UFP billing personnel so they can direct the study charges to correct account:

   I. Shands PFS: PFSResearchGroup@shands.ufl.edu
   II. UFP: UFPBARClinicalTrialsBillingTeam@shands.ufl.edu

II. FAQs

1. For handout on Epic Research Module “Frequently Asked Questions: see Epic FAQs

Scheduling Research Visits in Epic

Per UF HSC policy, all research visits conducted in a UFP/Shands Clinic on and after December 1, 2011 must be scheduled into Cadence (the Epic scheduling system). However, the Epic system currently has some limitations that need to be addressed before all research visits can be processed in the Epic billing system. The following instructions will help researchers determine which visits must be scheduled in Epic Cadence during this transitional phase.

Note: Also see Participant Registration in EPIC and Help on EPIC Training and Access for more information on other research functions in Epic.
Clinic Visits that include “Qualifying” Research Services to be Billed Out

Any visit that includes a protocol-required service to be billed to the study participant/third party payer as a “routine cost” in a “qualifying” clinical research study must be scheduled in Epic Cadence. Study teams must be sure to provide the Diagnosis Code V70.7 and Q0&Q1 modifiers as appropriate per the study billing plan. See Use of V70.7 Diagnosis Code and Q0 Q1 Modifiers.

Clinic Visits with Research Services to be Paid by Study

Any visit that includes a research protocol-required professional service that should be paid by the study must be scheduled in Epic Cadence. Study teams must indicate the service as PAID BY STUDY in the notes, research form or encounter form (as applicable) and include the study R99 number (or study billing contact information as needed).

Clinic Visits with Research Services Covered via “Salary Support”

Any visit that includes a research protocol-required professional service that will be covered by “salary support” must be scheduled in Epic Cadence. Study teams must indicate the service as covered by STUDY SALARY SUPPORT in the notes, research form/encounter form (as applicable) and include the study R99 number (or study billing contact information as needed).

“Mixed” Clinic Visits

“Mixed” clinic visits include some items/services that will be billed to the patient and other items/services that are funded by the study. Examples:

Items or Services to be Billed to Patient/Insurance

- “Standard of Care” or “Conventional Care” items or services (unrelated to the study)
- Protocol-required qualifying “Routine Costs” (claim must have V70.7 code and Q0 or Q1 modifiers)

Items or Services Funded by the Study

- Protocol-required items or services that should be paid for by the study through R99 process
- Protocol-required items or services that are provided via “salary support” (the charge generated must be “zeroed out”)
- Protocol-required items or services that are provided by the study team in such a way that no charge is generated.

It is the responsibility of the PI (through the study coordinator) to understand the billing plan for each study visit so that all items or services for the visit are scheduled, documented and ordered correctly.

For “mixed” visits, depending what is included in the visit, study teams may have to schedule two appointments in Epic Cadence: one for items/services to be billed to patients/insurance and one for the items/services to be billed to the study or “zeroed out”.

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- Bill Out Appointment: The study team must ensure that study-related qualifying “Routine Costs” are marked with the V70.7 and Q0/Q1 modifier and that the non-study-related “Standard of Care” items/services are marked as “non-study SOC”. The medical record for this part of the mixed visit MUST FULLY SUPPORT either the “Routine Costs” or any “Standard of Care” items/services that will be billed out.

- Study Appointment: For the study-funded part of the visit, the study teams must indicate each item/service as either “PAID BY STUDY R99” or “NO CHARGE – PROVIDED THROUGH STUDY SALARY SUPPORT” in the notes, research form/encounter form (as applicable). Be sure to include the study R99 number (or study billing contact information) as needed.

Study Visit in “Research Space”

Until further notice, if a study visit is conducted EXCLUSIVELY in “research space” (either inside a clinic or elsewhere), and there is no way that a bill can be generated for this visit, the visit does NOT need to be scheduled in Epic Cadence.

Study Visit Conducted by non-Service Provider

Until further notice, if a study visit is conducted EXCLUSIVELY by a study team member who is not an Epic Service Provider, and there is no way that a bill can be generated for this visit, the visit does NOT need to be scheduled in Epic Cadence.

Logic Table for Scheduling in Epic (Cadence)

<table>
<thead>
<tr>
<th>Visit Includes</th>
<th>Must be scheduled in Epic (Cadence)?</th>
<th>Encounter Must be Closed by</th>
<th>Notes / Research Form / Encounter Form must include:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any protocol-required professional service that will be billed out to study participant or 3rd party as a “routine cost” in a “Medicare qualifying” study (&quot;MQ0&quot; or &quot;MQ1&quot; on the study billing grid)</td>
<td>YES</td>
<td>Service Provider</td>
<td>□V70.7 and correct modifier(s)</td>
</tr>
<tr>
<td>Any service that will generate a billable professional fee that needs to be paid by the study (&quot;S&quot; on the study billing grid)</td>
<td>YES</td>
<td>Service Provider</td>
<td>□Indication that the service should be billed to a research study</td>
</tr>
<tr>
<td></td>
<td>Visit Type = Research/Clinical Trial</td>
<td></td>
<td>□R99 number (or study contact info if no R99)</td>
</tr>
<tr>
<td></td>
<td>Guarantor = Study</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any service that would normally create a billable professional fee for a Service Provider but is being “zeroed out/waived” because it will be covered by study via “Salary Support” (might be listed as “S” or “NB” on the study billing grid or “Non-Grid”).</td>
<td>YES</td>
<td>Service Provider</td>
<td>□Indication that the service should be waived/zeroed out as “study salary support”</td>
</tr>
<tr>
<td></td>
<td>Visit Type = Research/Clinical Trial</td>
<td></td>
<td>□R99 number (if study has one)</td>
</tr>
<tr>
<td></td>
<td>Guarantor = Study</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NO billable services. ALL services are being provided in a way that ensures that NO possible participant bill would be generated.</td>
<td>NO</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>
Investigational Drug Pharmacy

Investigational Drug Ordering in Epic

With the implementation of Epic II on July 19, 2013, all medication orders (including chemotherapy and investigational drugs) will be submitted electronically through Epic.

a. This is a practice consistent with all other medication orders throughout University of Florida Health. Recognizing that some research teams do not have a nurse coordinator to assist with pending Epic medication orders for physician investigator signature, the Investigational Drug Service (IDS) will continue to accept paper orders via fax transmission if investigator entry presents a significant hardship.

b. The goal is not to create a barrier to investigational medication management, but rather align with the standard practice of medication processing through UF Health.

c. Regardless of the method of medication order submission, all research participants must have an active Epic Research Series Account (encounter) in order for IDS to label and dispense investigational medications.

How to Find and Verify an Active Research Series Account in Epic

a. Prior to submitting a medication order to IDS, the Study Coordinator must verify in Epic that the patient has an active Research Series account for the current month:

   i. Using the Citrix icon, start Epic, and log in with your user name and password.

   ii. Use the Patient Station feature to select the patient (name or MRN). Note: If you use the Patient Lookup, you may not find a valid encounter.
b. Through Patient Station, you can view the encounter screen and the Research Series account (encounter) number.

How to Request an Active Research Series Account for IDS Orders

a. If the patient does not have an active Research Series account for the current month, the study coordinator must request a Research Series account from Shands Admissions:
i. **For inpatients**, use Listserv RESEARCH-INPT-L@LISTS.UFL.EDU.

ii. **For outpatients**, contact Shands Admissions directly. In the e-mail, include the following information:

1. Patient Name
2. Patient Medical Record Number
3. Study R99#. If the study does not have an R99#, state “IDS Only”.
4. Ordering Physician Name
5. Date of Service

b. Admissions will verify the establishment of the Research Series account by return e-mail and provide the account number.

c. For studies without R99 numbers, the Research Series Account will use the letters “IDS” in place of the R99 number in the member/subscriber ID coverage fields.
Renewal of Research Series Account for IDS Orders

a. If a Research Series account is used exclusively for IDS activity, the account will close on the last day of the month in which it was established.

b. If IDS services are anticipated in any subsequent month, a new Research Series account will need to be requested.

c. IDS services alone will not keep a Research Series account active.

Orders for “Take Home” Ambulatory Medications

a. For investigational medications that will be administered in the home setting ("Take Home"), orders should be placed in an "Orders Only" encounter.

How to Create an “Orders Only” Encounter

a. If an “Orders Only” encounter does not currently exist for your PI Provider, Research Coordinators with a nurse or nurse practitioner Epic access security template may create and use Orders Only Encounter to pend orders for the patient.

   i. Select the patient through Patient Station

   ii. From Red Epic Button, select Patient Care -> Encounters -> Encounters

   iii. Select New

b. OR if you have a “New Encounter” Button Create an Orders Only Encounter using the link on the screen.
c. Fill in Type = Orders Only, Provider, and Department.

d. Select Accept or OK.

hhhhhhhh) How to “Pend” an Order Using Smart Groups

a. Once you have verified that an Orders Only Encounter has been created, follow the instructions below to “Pend” an Ambulatory Investigational Medication order (“Take Home”):

i. Go to Order Entry.
ii. Select Study Smart Groups for Order Entry – During the protocol implementation process, the Investigational Drug Service Pharmacy will work with the research team to set-up all new “Smart Groups” that will be used to order medications associated with a specific research protocol.

iii. Smart Groups are sorted by the IRB or WIRB number.

iv. When you enter the IRB number or any synonym associated with the protocol, you will be presented with a list of corresponding “Smart Groups”.

v. There may be an Inpatient/Clinic Administered option and/or and Ambulatory Ordering option. Select the one that applies to the situation and protocol.
b. Depending on the protocol, you may be presented with one option or multiple options. All options will be specific to your protocol as each Smart Group is customized by protocol requirements.
c. Fill in all required fields as indicated below:

i. Make sure to review the “Patient Sig” in the highlighted box.

ii. This is the information IDS Pharmacy will use for instructions on the label.

iii. Note that this field populates from both the dose buttons and the text box.

iv. You can use the “Notes to Pharmacy” to communicate additional instructions.

1. For example, you can use this field to communicate “Kit #” or “Bottle “.
2. If you are preparing this in advance of obtaining a Kit/Bottle number, you may include the following statement “Will fax IVRS confirmation with Kit/Bottle number corresponding to this Visit XX”.
3. Please also use the “Notes to Pharmacy” to indicate your requested pick-up date/time.
4. The “Dispense” quantity should correspond with your protocol package size. Please familiarize yourself with the package sizes (e.g., 60 count bottles, 35 count blister cards, etc.).
5. If you are unsure, please call the IDS Pharmacy.
6. Guessing will only slow the process because the IDS Pharmacist will have to clarify the order with the physician.
v. Whenever you see *** (three asterisks together), you must fill in the information requested.

vi. If you do not fill in the corresponding information, you will not be able to advance beyond the red stop signs. These informational stop signs are placed intentionally by IDS to request data.

d. After all information is entered, the screen may look like this:
e. When you are satisfied with the order, click the Accept button.

f. **Pending or Signing Orders:** You now have the option to “Pend” the orders for final review by the physician investigator.

   i. Alternatively, the physician may sign and release the orders now.
g. Once the order is signed by the physician, it will be released to the Investigational Drug Service Pharmacy. If the Ambulatory Smart Group is used as described above, the order will only go to IDS Pharmacy and no other outside retail pharmacy.

h. The “INV” prefix is an important designation for investigational medications.

i. This helps route orders to the Investigational Pharmacy and ensures that investigational medications are not inappropriately billed to the patient and his/her insurance.

iii. Orders for Injectable Medications to be Administered in Clinic

a. For injectable medications that will be administered onsite, the investigational medication should be ordered using a Smart Group within the Research Series Encounter.

b. Once inside the Research Series Encounter, select “Order Entry” and then “New Order”.

c. At the “New Order” prompt, enter the Smart Group name (IRB number or common synonym).

d. From the “Facility List” select the corresponding Smart Group, and compete the order.
e. When the order opens, complete all of the open boxes and address any “Stop Signs.”

f. Once all of the information is complete, this order may be pended for later signature by the physician investigator.

Summary

a. Investigational Order Entry:

   i. To summarize, you will order medications based on medication type in one of the following encounters.

   ii. Select “Smart Groups” corresponding to your IRB number from the appropriate medication/smart group lists within Epic.

<table>
<thead>
<tr>
<th>Medication Type</th>
<th>Encounter to Use</th>
<th>Search this List to Find Smart Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inpatient medication</td>
<td>Admission Encounter</td>
<td>Facility List</td>
</tr>
<tr>
<td>Clinic Administered Medication</td>
<td>Research Series Encounter</td>
<td>Facility List</td>
</tr>
</tbody>
</table>
Assistance Needed?

a. If you need assistance with placing an investigational medication order, please do not hesitate to contact one of the IDS Pharmacists at one of the following numbers:

i. IDS Main Pharmacy: 265-0680 extension 4-4237 or 4-4716
ii. CTSI IDS Pharmacy: 294-5894
iii. IDS On-Call Pager: 413-2086

Project Set-Up

IRB Requirements for PIs

At University of Florida, we provide training for all principle investigators and other study staff regarding Institutional Review Board requirements.

a. Effective January 7, 2013, the IRB education requirements must be met in order for a protocol to be reviewed by IRB-01 (Health Center IRB).

   i. This includes all investigators, sub-investigators, research coordinators and any other study staff involved in the conduct of a human subject research study (i.e.: those previously listed in Addendum A).

b. The following chart outlines the required training to conduct human subject research; the items in RED are the new requirements.

   i. The NIH Extramural Education is already required if you obtain NIH funding. The “Local IRB Video” requirement is currently available and may be accessed via http://my.ufl.edu.

   ii. Directions on how to access all of the training modules are located at http://irb.ufl.edu/education/trainreq.htm.

   iii. All requirements are available to complete now, but again, it will be mandatory for you to have completed them by January 7, 2013.

c. Please note, if you are a UF or Shands investigator, and you wish to conduct research at the NF\SG VAMC, you must comply with the VA’s Educational Requirements. Please contact the VA at 352-376-1611 x4917.

<table>
<thead>
<tr>
<th>Ambulatory Med (“Take Home”)</th>
<th>Orders Only Encounter to order (BY COORDINATOR)</th>
<th>Database Lookup</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IDS PHARMACY will dispense through Research Series Encounter</td>
<td></td>
</tr>
</tbody>
</table>
Researchers must comply with all UF policies and procedures*(see below) as well as all applicable federal*, state, and local laws regarding the protection of human subjects in research, including, but not limited to the following:

i. Obtaining IRB approval prior to involving any human subjects (including their data or tissue) in research studies.

ii. Only the IRB may determine if research is exempt from Federal regulations (investigators may not make the final determination of exemption).

iii. Ensuring that only qualified personnel conduct the study according to the approved Protocol, and in compliance with each individual's scope of practice.

iv. Insuring the rights and welfare of each research subject, and that the subject's rights and welfare must take precedence over the goals and requirements of the research.

v. Implementing no changes in the approved Protocol or Informed Consent Form without prior Institutional Review Board (IRB) approval, except in an emergency, if necessary to safeguard the well-being of human subjects.

vi. Ensuring that anyone obtaining informed consent has read the protocol and has sufficient knowledge of all information provided in the informed consent document.

vii. Obtaining legally effective informed consent from human subjects or their legally responsible representative before any research-related screening or intervention commences and using only the currently approved, stamped Informed Consent Form, when applicable.
viii. Providing each subject enrolled in the study a copy of the IRB-approved informed consent document at the time of the consent, unless the IRB has specifically waived this requirement.

ix. Unless specified otherwise, all signed informed consents and other research related documents (including but not limited to paperwork submitted to and approved by the IRB) should be retained throughout the study and for an additional three years after the study is completed/closed with the IRB.

x. Promptly reporting any injuries or unanticipated problems to the IRB in writing within 5 working days of occurrence or discovery of occurrence.

xi. Reporting progress of approved research to the appropriate IRB, as often as and in the manner prescribed by the IRB on the basis of risks to subjects, but not less than once per year. This includes submitting a closure report to the IRB once the research is completed.

xii. Completing investigator training as required by the Institutional Review Board.

xiii. Research investigators will advise the IRB and the appropriate officials of this Institution and other institutions of the intent to admit human subjects who are involved in research protocols. When such admission is planned or a frequent occurrence, those institutions must possess an applicable OHRP-approved Assurance prior to involvement of such persons as human subjects in those research protocols.

xiv. If conducting research involving products regulated by the Food and Drug Administration (FDA), the investigator will comply with all applicable FDA regulations and fulfill all investigator responsibilities (or investigator-sponsor responsibilities, where appropriate), including those described at:

1. 21 CFR 312: Investigational New Drugs
2. 21 CFR 812: Investigational Device Exemptions

xv. If unavailable to conduct or direct this research personally, as when on sabbatical, leave, or vacation, to:

1. Arrange for a co-investigator to assume research related responsibilities in the researcher's absence

2. Notify the IRB in writing of this change prior to the absence.

xvi. In the event that employment with the university is discontinued, to do one of the following with each approved/active study prior to leaving the university:

1. Transfer the study to a new principal investigator or
2. Close the project.

3. These changes must be sent in writing to the IRB by submitting either a formal revision or a Continuing Review/Study closure report.

4. This notification must be submitted in advance (prior to the termination of employment).

xvii. No research investigator will seek to obtain research credit for, or use data from, patient interventions that constitute the provision of emergency medical care without prior IRB approval.

1. A physician may provide emergency medical care to a patient without prior IRB review and approval, to the extent permitted by law (see Section 116[f]).

2. Such activities will not be counted as research nor the data used in support of research.

xviii. All investigators should review and be familiar with:


IRB-01 Manual for Principle Investigators and Other Study Staff

The University of Florida has published a manual of Policies & Procedures (THIS IS THE WHOLE MANUAL: SEE BELOW FOR CHAPTERS) for PIs and other personnel on UF run research studies. This contains a lot of very useful information about the process of research at the University and the rules and regulations surrounding why we do things the way that we do.

The following subjects are outlined in this manual:

a. Institutional Authority
   i. Limitation on Institutional Authority

b. Applicability

c. Authority of the IRB

d. Mission and Purpose

e. Ethical Mandate to Protect Human Subjects

f. Scope of Authority
   i. Definition of Human Subjects Research
   ii. Determination of Human Subjects Research
   iii. Human Subjects Research Exempt from IRB Review
      1. Exceptions to Exempt Criteria
      2. Determinations of Exemption
g. IRB-01 Relationships
   i. UF Administration
      1. Division of Sponsored Research (DSP)
      2. Office of General Counsel
   ii. Other Committees
      1. Human Use of Radioisotopes and Radiation Committee (HURRC)
      2. Institutional Biosafety Committee (IBC)
      3. General Clinical Research Center (GCRC) Advisory Committee
      4. University of Florida Shands Cancer Center (UFSCC) Multidisciplinary Organ
         Site Groups (MOSG) and Protocol Review and Resource Utilization Committee
         (PRRUC)
   iii. Research Investigators
      1. Responsibilities
      2. Training
   iv. Other Institutions
      1. Shands Teaching Hospitals and Clinics, Inc
      2. North Florida/South Georgia Veterans Health System (NF/SG VHS)
   v. Regulatory Agencies
h. IRB Membership
   i. Number of Members
   ii. Qualifications of Membership
   iii. Diversity of Membership
   iv. Appointment of Members
   v. Alternates
   vi. Responsibilities
   vii. Attendance
   viii. Performance Appraisal
i. IRB Management
   i. IRB Chair
   ii. Vice-Chairs
   iii. Executive Committee
   iv. Training of IRB Chair and Membership
   v. Compensation of IRB Members
   vi. Member Liability
   vii. Consultants
   viii. Conflict of Interest
   ix. IRB Administrative Staff
   x. Office Hours and Location
   xi. Resources
j. IRB Functions
   i. Review of Research
      1. General Information
      2. Scientific Review of Proposed Research
      3. Criteria for approval of Research
      4. Determination of the CR date
      5. Management of Protocols with Lapsed Approvals
         a. Grant Review
b. **Types of Review**

   i. **Full Board**

      1. Initial Review
      2. Continuing Review
         a. Longitudinal Review
      3. Revisions
      4. Tabled Response
      5. Unanticipated Problems Involving Risk to Subjects or Others and Adverse Events
      6. Other (Miscellaneous, Deviations, etc)

   ii. **Expedited Review Process**

      1. Initial Review
      2. Continuing Review
      3. Revisions
      4. Unanticipated Problems Involving Risk to Subjects or Others and Adverse Events
      5. Other (Miscellaneous, Deviations, etc)
      6. Study Closures

   iii. **Exempt/Non-human** Research

      1. Exempt
      2. Non-Human Subjects Research

   iv. **Reportable Events**

      1. Noncompliance Pertaining to Human Subjects Research
      2. Unanticipated Problems Involving Risk to Subjects or Others and Adverse Events
      3. Project Suspension/Termination
      4. Reporting Requirements (“Reporting Policy”)

   v. **IRB Actions and Decisions**

      1. Item Approved as Submitted
      2. Item Approvable Subject to Explicit Changes
      3. Item Tabled
      4. No Action/Further Action Needed
      5. Item Disapproved
      6. Project Suspension/Termination

   vi. Reporting IRB Findings and Decisions

   vii. Reviews Requiring Special Consideration

      1. **Vulnerable Subjects**
         a. Pregnant Women, Fetuses, Neonates
         b. Prisoners
         c. Children
         d. Adults Unable to Provide Consent
         e. Employees and Students

   viii. **FDA-Regulated Test Articles**

      1. Devices
      2. Investigational Drugs
      3. Emergency Use of a Test Article without IRB Review
4. **Emergency Use of a Test Article without Informed Consent Humanitarian Use** Device (HUD) with Humanitarian Device Exemption (HDE)

   ix. **Research Conducted Off-site or at Multiple Sites**

   k. **IRB Operations**
      i. **Meetings**
         1. Meeting Time, Place and Location
         2. IRB Meeting Convened via Telephone Conference Call
         3. Deadlines for Meeting Agendas
         4. Attendance
      ii. **Reviewer Assignment**
      iii. **Joint Gainesville/Jacksonville Review of Projects**
      iv. Pre-meeting distribution to members
      v. **Principal Investigator’s Participation during IRB-01 Meetings**
         1. Investigator Conflict of Interest
      vi. **Voting Requirements**
         1. Meeting Quorum
      vii. **Communication from the IRB**
      viii. **Appeal of IRB Decisions**
   ix. **Temporary Transfer of PI Responsibilities**
   x. **Disposition of Research when Principal Investigator Leaves UF**
      1. Administrative Changes to IRB Documents (Approved 9/21/2005)

l. **IRB Documentation and Records**
   i. **Documentation**
      1. **Correspondence to the IRB**
         a. Receipt of Documents from the PI
         b. Receipt of Comment Sheets from the Reviewer
      2. Required IRB Documentation
         a. Membership Roster
         b. Convened Meeting Agenda
         c. Minutes
            i. Informational Minutes
            ii. Minutes of Convened Meetings
         d. Policies and Procedures
   ii. **Records**
      1. Record Maintenance
         a. Record Access
         b. Record Content (name)
      2. Record Retention
      3. Record Inspection
      4. Confidentiality of Records

m. **Quality Assurance**

n. **HIPAA**

The Regulatory Binder
Essential Documents

a. The ICH GCP Guidelines define Essential Documents as those documents which individually and collectively permit evaluation of the conduct of a trial and the quality of data produced.

b. These documents serve to demonstrate compliance with standards of Good Clinical Practice and with all applicable regulatory requirements.

c. Filing essential documents in a timely manner can greatly assist in the successful management of a clinical trial.

d. The Regulatory Binder is often the first document reviewed during audits and inspections.
   i. Not all the essential documents are available at the start of the study.
   ii. Documents can be grouped into those that are generated before study initiation, those that are generated during trial conduct and those that are generated after study completion.

e. Not all documents have to be filed in one single binder.

f. The Regulatory Binder may sometimes consist of several binders that are stored in the same or different locations.

g. It is important to know where all these documents are located to be able to pull them out when needed in a timely manner.

h. The Regulatory Binder is referred to synonymously as the Study Files, Investigator Files or Investigator Binder:
   i. REGULATORY RECORDS/REGULATORY BINDER CHECKLIST
   ii. Regulatory Binder Template - IRB
   iii. IRB-01 Researcher Tools

Financial Set-up

To have a clinical trial project established in the University’s financial system the following documentation is required:

a. Completed Sponsored Projects Approval Form (DSP-1) or PeopleSoft Grants Workflow equivalent

b. Fully executed CTA

c. Institutional Review Board (IRB) approval letter
d. Provide DeptID for projects in Fund 214

The budget period for a clinical trial will equal the trials contractual date or the IRB end date plus three (3) years whichever occurs first. Upon IRB renewal and notice to DSP’s Award Administration at ufawards@ufl.edu, your project end date will be adjusted accordingly in the accounting system.

**Using Fund 214**

This new fund was established to support the University’s Industry Sponsored Clinical Trial Business. Fund 214 offers less central administration and more local control. Fund 214 is cash based which matches how we operate clinical trials.

**IV. Fund 214 Rules**

I. Patient Service Costs must be charged to the appropriate trial project directly at the time of the service or, if an unrestricted account was used in advance, such as the administrative operational project, miscellaneous donors project or overhead project, those cost must be transferred to the Clinical Trial project as quickly as possible once sufficient revenue has been received.

II. The earned payments during the life of the clinical trial should be used to support the clinical trial being conducted in accordance with the clinical trial agreement.

III. Transferring reasonable amounts of earned payments to a clinical trial administrative operating project to cover incidentals and administrative labor to run the clinical trial program of a unit or individual Principal Investigator’s trial program will be allowed.

**Invoicing and Payments**

We recognize the Principal Investigator and the UF Trial administrative staff are in the best position to know when a payment is owed. In this regard, the University allows the PI and their staff to be responsible for requesting payments, by invoicing their trial sponsors.

In this process please indicate to your sponsor how important it is to include the **UF project number on the check or check information** so when the payment is received it can be easily and rapidly identify and credit to your project.

Departments will be responsible for confirming payment has been received.

All checks are to be named payable to the University of Florida and remitted to:

a. **For Fund 214**: University of Florida
   Office of Research Business Office – Clinical Trials
1. Spending authority for fund 214:

   I. DSP will issue a onetime NOA upon full execution of the agreement and IRB approval.
   II. A 214 project is initially established at $0.
   III. As payments are received and identified to a project, the Office of Research Clinical Trial Business Unit will release 78.125% of the cash into the project for spending with the other 21.875% released to the DSP indirect cost project for end of year distribution.
   IV. When the Office of Research Business Office-Clinical Trials receives payment, and the project has been identified, a deposit transmittal is prepared and sent to University Cashier, Room S-113 Criser Hall for posting.
   V. As a communication tool, DSP will continue to issue NOA’s for each payment received, deposited and credited to a project in fund 214. The NOA will be after the fact of deposit and credit to the project.
   VI. The NOA be distributed only to the PI and department NOA contact person.
   VII. Additional NOA’s will be issued by DSP for administrative changes to the project such as: change in Principal Investigator, DeptID, date changes, or contractual changes.

b. For Fund 209: University of Florida
   Contracts and Grants
   123 Grinter Hall
   Gainesville, FL 32611

2. Spending authority for fund 209:

   I. As payment is received, C&G Accounting will request DSP to authorize the release of budget equal to the payment received. DSP authorizes the release by issuing a NOA

Payment Log and Cash Balance

Payment Log

II. All payments received will be logged into the Fund 214 Payment Log.

III. Trial payments are very difficult to identify to a UF project number, regardless of fund, so we ask PI’s and project staff to help to identify payments to projects, by frequently visiting the Payment Log, especially when you know a payment is due.

IV. When you identify a payment that needs to be applied to your project or you see a correction that needs to be made please contact Rachel Hurley of the Office of Research’s Business Office. Rachel manages the log and check deposit process for Fund 214.
V. The myUFL Grant Project Summary Page has been upgraded to include our cash based Funds 211, 212, 213, and, most importantly, fund 214, which was created specifically for industry sponsored clinical trials.

VI. If you have a project is fund 214 and you would like to know the available balance of the cash on hand, you can log into myUFL and, in two clicks (Grants>Grants Summary Pages), access the Project Summary Page and quickly see the available cash balance.

**Extensions and Amendments**

YYYYYYYY) **Clinical Trial Extensions**

a. Upon request or notification to DSP’s Award Administration Office at ufawards@ufl.edu internal extensions for clinical trials can be granted to accommodate an administrative close of a trial, generally a 3-month period, where no further human subject activity will take place.

b. All other extensions would require sponsor approval by a clinical trial amendment.

ZZZZZZZ) **Clinical Trial Amendments**

a. An amendment changes the terms of a previously executed agreement.

b. Amendments may be monetary, non-monetary or both. Amendments to CTA’s must be reviewed, approved and executed by the legal authorities at the Division of Sponsored Programs (DSP).

c. In most cases a Sponsored Projects Approval Form (DSP-1) is not required. Simply fax, email, or send a hard copy of the amendment to RAC or DSP for processing, as appropriate.

**Close-Outs**

AAAAAAA) **Close-Outs**

Upon close of a trial any cash balance remaining, DSP with the completed fixed price close memo can approve the direct component of the cash be transfer to the PI’s miscellaneous donor project and/or a clinical trial operations project where the funds may be spent at their discretion in support of research.

a. If your trial has ended prior to the accounting system known end date please contact C&G Accounting or DSP at ufawards@ufl.edu and request the close out process begin.

b. For Fund 214 projects, trials that remain at $0 after 24 months will be closed by C&G Accounting in coordination with DSP.

c. When all research study participants have completed all study activities, there are several UF offices that should be informed. These include, but are not limited to:

i. IRB – UF Institutional Review Boards
ii. DSP – Division of Sponsored Research Programs Handbook
iii. C&G – Contracts & Grants
iv. RAC- COM-RAC-L@lists.ufl.edu

bbbbb) Trial Never Started?

a. When a trial is closed before you are able to enroll a subject, you should immediately request a reasonable amount to cover your startup costs.

b. In the past with DSP approval we have allowed small sums to be deposited in a miscellaneous donor’s project without assessment of IDC.

c. Contact DSP’s Brian Prindle with particulars so we may assist and decide what project the payment shall be deposited to.

Final Invoice and Tracking Log Reconciliation

cccccc) All research study charges should be settled prior to study closure.

dddddd) All payments should be reviewed to ensure that they were made from the appropriate payment source, and that all services billed to research study participants and their third party payers were not paid with study funds.

eeeee) The study team should ensure that all applicable laws and regulations were followed.

ffffffff) The PI is ultimately responsible for ensuring that payments to Shands, UFP and/or other vendors have been made according to the study billing plan.

ggggg) Clear evidence of what charges were paid by which payment sources should be well documented on the study tracking log and in applicable study files.

hhhhh) At closeout, the RAC office requires that study team send the completed study tracking log for review to CTC-Auditors@ufl.edu. Tracking logs are required for all studies with activity after June 2007.

iii) All billing errors should be corrected before closing a research study with Contracts and Grants and the study team should send their tracking log to Shands and/or UFP for review.

jjjjjjjj) If the study team finds any error(s), they should work directly with Shands and UFP to correct the error(s) prior to sending the tracking log to the RAC auditors for closeout review.

kkkkk) The contacts for Shands and UFP are listed below.

a. Shands PFS: PFSResearchGroup@shands.ufl.edu
b. UFP: UFPBARClinicalTrialsBillingTeam@shands.ufl.edu

llllll) The RAC office may also request additional supporting documentation such as financial agreements and Medicare-approved routine costs.
These should be included in the study closure information.

Examples of additional documentation which may be needed to review your project for closeout are listed below:

a. Study budgets, including any revisions
b. R99 Agreement(s) – current and revised (post 2/14/07 Study Registration Form)
c. Protocol – original and amendments
d. Contracts and amendments
e. IRB/WIRB Approved Consent (Current)
f. IRB/WIRB Closure Letter – required if study is in Epic

Once the RAC office completes the review and determines that the project does not have outstanding or unresolved billing issues, the RAC office will notify the study team (and C&G contact if the name has been provided) that C&G may proceed with the closeout.

RAC Review Before C&G Closeout

Any Health Science Center study (federal and non-federal) involving human subjects and participant care costs (“services”) needs to be reviewed by Research Administration & Compliance (RAC) before the study is “closed-out” and/or any residual funds are transferred.

These studies can be identified by the PeopleSoft certification code CLSVC (clinical services).

a. NOTE: This field has only been in place for a few years, so many older studies that have participant care costs (i.e. that should be reviewed by RAC) may not have this field checked.

The process is as follows:

a. RAC receives an e-mail from C&G or the study team when the project is ready to close. RAC reviews the requests in the order they are received.
b. Once a closeout comes into the CTC-Auditors@ufl.edu inbox, RAC contacts the study team to request their study tracking log and any applicable study-related documents needed to review for closeout (if RAC has not already received this information).
c. RAC Auditors review the study tracking log for any billing and Epic compliances issues.
d. If RAC finds issues, RAC then works with the PI, study team, Shands, UFP, Contracts and Grants, and outside vendors (e.g. Quest Diagnostics) to resolve both billing and Epic compliance issues and outstanding balances.
e. Once the RAC Auditor completes the review and determines that the project does not have outstanding or unresolved billing issues, RAC will notify the PI/study team via an official e-mail indicating that they may proceed with study closure.
f. The C&G contact is copied if the contact name has been provided.
g. C&G may ask for a copy of this email before they proceed with the closeout.
Note: The study team is responsible for resolving any billing error(s) with Shands and UFP before closing a study. The number of subjects enrolled, billing compliance issues, outstanding balances, cooperation from the departments, etc, may impact how long it takes for a closeout to actually be finalized and the official e-mail sent from the RAC office.

Document Retention & Storage

The Institutional Review Board (IRB), The University of Florida (UF), and outside grant sponsors all have their own requirements for on-site and off-site records retention, and those should be followed. Please see the links below for the IRB and UF records retention information.

A review of your outside agency contract and or guidelines is necessary to locate each individual sponsor’s records retention policy.

a. IRB: http://irb.ufl.edu/irb01/data.html

b. Other University of Florida Links:


   ii. CTSI-Principal Investigators and Deans Email and Record Retention:  

   iii. Division of Sponsored Programs:  
        http://www.research.ufl.edu/research/handbook/researcher_handbook/section11.html

   iv. UF Records Management Information:  
       http://cms.uflib.ufl.edu/records/Records

   v. UF Health Shands Hospital Medical Records  
      https://ufhealth.org/uf-health-shands-hospital-medical-records

   vi. UF Records Preservation Memorandum from VP and General Counsel concerning certain research, financial and employment records relating to National Science Foundation and other federal awards.

ClinicalTrials.gov

Regulations for Registration of Studies in ClinicalTrials.gov

1) FDAMA requires registration of any study as of 02/29/2000 involving one or more of the following:

   • Drugs and biologics to treat serious or life-threatening diseases and conditions where the likelihood of death is high unless the course of the disease is interrupted
- Group C cancer drug (as defined by the National Cancer Institute)

2) **FDAAA** requires registration of any study ongoing or initiated after 9/27/2007 involving drugs, biologics and devices in one or more of the following categories:

- Phase II, III and IV clinical trials
- Controlled trials with health outcomes
- Pediatric post-market surveillance studies
- Studies conducted under an IND/IDE
- Registration must occur within 21 days of enrolling the first study subject into the study. The registration process can take up to 45 days, so Investigators must register their ACTs as soon as possible.

*Warning: Penalties for failure to register a FDAAA study will include a $10,000 warning letter to become compliant in 30 days. If not compliant in 30 days, a $10,000 a day fine will be assessed until the study is posted on ClinicalTrials.gov registry. If the study is funded by the NIH, the NIH can request the return of NIH funds for the entire project, part of the project, or any funded projects.*

3) **CMS** requires, effective January 1, 2014, that the 8-Digit Clinical Trial Number (NCT) from the ClinicalTrials.gov registry be included on claims for items and services provided in clinical trials that are qualified for coverage in the Medicare NCD Manual. This includes claims with the following codes:

- Condition code 30;
- ICD-9 code of V70.7/ICD-10 code Z00.6 (in either the primary or secondary positions) and
- Modifier Q0 and/or Q1, as appropriate (outpatient claims only)

4) Thus, any study must be registered that requires billing out for services provided to beneficiaries during their participation in a clinical trial, a clinical study, or a registry. Any bills not containing an 8-digit clinical trial number will be returned as un-processable to the provider for inclusion of the trial number.

5) NIH encourages (but does not require) registration of all NIH-supported clinical trials, regardless of whether or not they are subject to FDAAA. Note: UF also encourages registration of human subject research projects that involve a medical intervention for a health outcome.

6) **ICMJE** requires registration of studies in one or more of the following categories:

- Pilot studies through Phase I-IV trials
- Studies that prospectively assign human subjects to intervention and comparison groups to study the cause-and-effect relationship between a medical intervention and health outcome
- Any medical intervention used to modify a health outcome
- Drugs, surgical procedures, devices, behavioral treatments, process-of-care changes, Pharmacokinetic studies, etc.
- At least one prospectively assigned concurrent control or comparison group
- Projects investigating the biology of disease
- Projects involving health care providers, rather than patients, of intervention and comparison/control groups. If the purpose of the trial is to examine the effect of the provider intervention on the health outcomes of the providers’ patients, then investigators should register the trial.
- Ongoing studies that began study subject enrollment before 7/1/2005

Note: ICMJE requires registration prior to enrolling the first subject into the study. Member journals will refuse to publish a study that has not been properly registered. Because ICMJE journal membership increases yearly, UF Investigators should verify the current ICMJE membership of the journal to which they intend to submit an article. Also, other journals may require registration in ClinicalTrials.gov.

7) Acronyms
- CMS – Centers for Medicare & Medicaid Services
- FDAAA – Food and Drug Administration Amendments Act of 2007
- FDAMA – Food and Drug Administration Modernization Act of 1997
- ICMJE – International Committee of Medical Journal Editors
- IDE – Investigational Device Exemption
- IND – Investigational New Drug
- NIH – National Institutes of Health

CMS NCT Numbers

i) Mandatory Reporting of an 8-Digit Clinical Trial Number on Claims

(1) Effective January 1, 2014, it will be mandatory to report a clinical trial number on claims for items and services provided in clinical trials that are qualified for coverage as specified in the “Medicare National Coverage Determination (NCD) Manual,” Section 310.1.


ii) The clinical trial number to be reported is the same number that has been reported voluntarily since the implementation of CR 5790, dated January 18, 2008.

iii) That is the number assigned by the National Library of Medicine (NLM) [http://clinicaltrials.gov/](http://clinicaltrials.gov/) website when a new study appears in the NLM Clinical Trials data base.

iv) This number is listed prominently on each specific study’s page and is always preceded by the letters ‘NCT’.

v) The Centers for Medicare & Medicaid Services (CMS) uses this number to identify all items and services provided to beneficiaries during their participation in a clinical trial, clinical study, or registry.
vi) Furthermore, this identifier permits CMS to better track Medicare payments, ensure that the information gained from the research is used to inform coverage decisions, and make certain that the research focuses on issues of importance to the Medicare population.

**NIH Clinical Trial Requirements (Pub Med)**

vii) Public Law 110-85 (also known as FDAAA), enacted on September 27, 2007, amends the Public Health Service Act to mandate registration of “applicable clinical trials” (ACTs) in ClinicalTrials.gov.

1. As a result NIH requires grantees and their investigators to register their ACTs in [ClinicalTrials.gov](http://ClinicalTrials.gov).

2. Additionally, NIH encourages registration and results reporting for all NIH-supported clinical trials, regardless of whether or not they are subject to FDAAA.

viii) Investigators can find information to determine if a trial needs to be registered at the following sites:

1. [NOT-OD-08-14](http://NOT-OD-08-14)
2. [NOT-OD-08-023](http://NOT-OD-08-023)
3. [NOT-OD-09-030](http://NOT-OD-09-030)

ix) The [NIH smart chart](http://NIH smart chart) also helps Investigators determine if a study needs to be registered. **When in doubt, Investigators are advised to register the study.**

x) **UPDATE**

1. Effective July 1, 2013 NIH moved to the enforcement stage of its Public Access Policy, requiring full compliance with the Policy before continuing year (type 5) funds will be released.

2. Final, peer-reviewed manuscripts must be posted to the NIHMS upon acceptance for publication, and be made publicly available on Pub Med Central (PMC) **no later than 12 months after the official date of publication.**


xii) We wanted to share what we have learned regarding the implementation so far:

1. Awards are being held if there are publications not in compliance with the policy.

2. Alternatively, awards have been released but restricted so **NO SPENDING IS ALLOWED** until the publication is in compliance.

3. This may mean that charges are not allowed between the end of the prior year and the publication being in compliance.
(4) Any salaries, supplies purchased, or travel during the period after the last non-competing year before you receive a release of any restrictions may have to be placed on discretionary or unrestricted funds (you IDC return).

xiii) NIH is identifying non-compliant articles during the progress report submissions. In preparing the report, the PI is instructed to identify new publications associated with the award.

(1) There has been an instance where these articles are not in the PubMed Central database and through the progress report are identified and considered non-compliant.

(2) As a result NIH has withheld the award funds.

Publication Requirements (ICMJE Requirements)

xiv) In September 2004, ICMJE announced as a prerequisite to publish study results in ICMJE member journals the clinical trial must be registered with a public registry that meets the ICMJE’s minimal registration data set of 20 items. ClinicalTrials.gov meets those criteria and is the registry recommended for UF studies. Please see the ICMJE website.

xv) ICMJE requires registration of studies in one or more of the following categories:

(1) Pilot studies through Phase I- IV trials
(2) Studies that prospectively assign human subjects to intervention and comparison groups to study the cause-and-effect relationship between a medical intervention and health outcome
(3) Any medical intervention used to modify a health outcome
(4) Drugs, surgical procedures, devices, behavioral treatments, process-of-care changes, Pharmacokinetic studies, etc.
(5) At least one prospectively assigned concurrent control or comparison group
(6) Projects investigating the biology of disease
(7) Ongoing studies that began study subject enrollment before 7/1/2005

xvi) Note: For ICMJE, registration must occur prior to enrolling the first subject into the study. The registration process can take up to 45 days, so Investigators must register their study as soon as possible.

b) Member journals will refuse to publish a study that has not been properly registered. Because ICMJE journal membership increases yearly, UF Investigators should verify the current ICMJE membership of the journal to which they intend to submit an article. Also, other journals may require registration in ClinicalTrials.gov.

PRS Protocol Record Registration and Compliance

i) Registration

(1) ACTs are registered in PRS according to the following guidelines:
(a) At UF, Investigators are responsible to determine if their studies are ACTs and whether to register for NIH, FDAAA or ICMJE purposes and then to ensure all registration and compliance requirements are met.

(b) Under FDAAA, ACTs must be registered in full no later than 21 days after the first patient is enrolled.

   (i) **Note**: The registration process can take up to 45 days, so Investigators must register their ACTs as soon as possible.

(c) Investigators can register clinical trials for other reasons, such as ICMJE or other journal editor requirements that are broader than those of FDAAA.

   (i) **Note**: ICMJE requires study registration *prior to the first study subject being enrolled*.

(d) UF’s Organizational PRS account is under the name: UFlorida.

   (i) **Note**: In the ClinicalTrials.gov PRS system, UF is the designated sponsor and responsible party. The Investigator is responsible for the accuracy and compliance of the Protocol Record.

(e) To register the ACT in ClinicalTrials.gov, the Investigator must become a registered PRS user under UF’s organizational account. To do so, the Investigator requests by email a meeting with one of the DSP Administrators listed below to initiate the Investigator’s user account and to receive initial training on the PRS system.

(f) As a PRS user, the Investigator can log into the PRS system and register the ACT by completing all required data elements to create the Protocol Record.

(g) Once the Protocol Record is created, the Investigator will click the “Next Action: Complete” button at the top on the Protocol Record outline in a redbox.

(h) The PRS system notifies DSR Administrators to review, approve and release the Protocol Record into the ClinicalTrials.gov website for Quality Assurance (Q&A) review and comments.

(i) The ClinicalTrials.gov PRS Q&A review comments must be addressed prior to releasing the Protocol Record for public view. The release process may take up to 45 days to complete.

(j) Within three to five days after the Protocol Record is released, the PRS system will assign a ClinicalTrials.gov identifier, called the NCT number, to be used in all correspondence with PRS.

   (i) **Note**: The Protocol Record is not considered registered until the NCT number is assigned.

   **ii) Compliance**
(1) The Investigator is responsible for complying with all current FDAMA, FDAAA and ClinicalTrials.gov PRS laws, rules and regulations, including but not limited to the following responsibilities:

(a) Correct all Protocol Record errors and warnings and address all PRS Q&A review comments as soon as possible.

(b) Update the Protocol Record every 6-months.

(c) Update the Protocol Record regarding any protocol changes.

(d) Enter the Protocol Record’s primary results within 12 months from the Primary Completion Date (“The date that the final subject was examined or received an intervention for the purposes of the final collection of data for the primary outcome, whether the clinical trial concluded according to the pre-specified protocol or was terminated.”).

   (i) **Note:** Posting results can be a difficult and time-consuming process, so Investigators and their departments should develop resources to assure accurate and timely reporting. UF CTSI provides biostatistical support as needed.

(e) Post all secondary outcomes once they have been accomplished.

(f) Update the Protocol Record if the Investigator or study staff changes.

   (i) **Note:** Please notify the DSP Administrators immediately and follow the directions below:

(g) Contact Investigator’s department chair and DSP Administrators if the Investigator leaves UF:

   (i) If the study is ongoing, gain departmental approval to transfer the record to the new institution; if the study is closed or the Protocol Record must remain at UF, transfer the record to a designated record owner with the knowledge and approval of the department chair.

iii) **Training**

(1) UF offers training modules and direct assistance to UF Investigators and study staff regarding all aspects of ClinicalTrials.gov PRS protocol record management—from registration to maintaining compliant records, and ultimately to posting final results. [Access all training modules and registration instructions here.](#)

(2) **To Submit Requests for Assistance**

   (a) Please contact the Protocol Registry at PROTOCOLREGISTRY-L@LISTS.UFL.EDU.

(3) **DSP Contact Information**
DSP PRS Administrators are available to assist throughout the life of the ClinicalTrials.gov PRS Protocol Record:

(b) Gainesville:
   (i) Jane-Ann Norton: janeann@ufl.edu (352) 294-5189
   (ii) Becky Wichman, rwichman@ufl.edu, (352) 273-7656
   (iii) Anthe Hoffman: antheh@ufl.edu; or Brian Prindle: prindle@ufl.edu

(c) Jacksonville
   (i) Tina Bottini: tina.bottini@jax.ufl.edu (904) 244-9478

How to Register a Study in ClinicalTrials.Gov

ClinicalTrials.Gov at the University of Florida

iv) The University of Florida already has a Protocol Registration System account

(1) In order to enter a study on ClinicalTrials.gov, you need to contact Jane-Ann Norton:
   janeann@ufl.edu (352) 294-5189

(2) She will give you a PRS user account and you will receive an e-mail which look like this:

(a) Message generated by ClinicalTrials.gov Protocol Registration System

A PRS user account has been created for you.

The PRS URL is https://register.clinicaltrials.gov. To login, you will need the following information:

Organization: UFlorida
User Name: YourGatorLinkID
Password: Some combination of letters and numbers

Please login and change your password as soon as possible.
Also verify that the following information is correct.

Full Name: Your Name
E-Mail: Your Institutional e-mail

If you have questions about the system or have trouble logging in, please contact your organization's PRS administrator (tina.bottini@jax.ufl.edu, millerbc@ufl.edu, janeann@ufl.edu, prindle@ufl.edu, antheh@ufl.edu).

(3) You will also receive an e-mail from Jane-Ann Norton which looks like this and has some very important information:
Hi Your Name,

I have just registered you on Clinicaltrials.gov. Here is some information you’ll need to know.

Please login in at this website https://register.clinicaltrials.gov/prs/app/template/Login.vm

Organization: UFlorida

Username: YourGatorLinkID

The ClinicalTrials.gov system will send you an email shortly with further instructions and password information that allows you to login and change your password.

Please note that the requirement to update a record is every 6-months. When a trial is complete, you are also required to upload the study results within 12-months from the final data collection of the primary outcome. In March 2012, new punitive damages (up to $10K a day fines) will be assessed for records delinquent in posting results one year from study closure.

v) Once you receive your login information, you go to the PRS Login page: https://register.clinicaltrials.gov/prs/app/template/Login.vm

(1) You enter your login information and you will come to a menu—this is the Standard Function menu for ClinicalTrials.gov.

(a) Before you start, you are going to need to change your password

(b) Review the available documentation:

   (i) Quick Start Guide and User’s Guide

ClinicalTrials.Gov: Facts and Information

vi) PRS User Roles and Responsibilities:

(1) PRS User

   (a) Enters study data
   (b) Ensures that the data are correct
   (c) Updates records in a timely manner, as needed

(2) PRS Administrator

   (a) Reviews data for errors

   (b) Releases records for posting on ClinicalTrials.gov

   (c) Oversees the PRS account on behalf of their organization (e.g., creates user accounts)
(d) Serves as a point of contact for ClinicalTrials.gov

ClinicalTrials.Gov: The Process

**PRS: Login**

![Login screenshot from ClinicalTrials.gov](http://register.clinicaltrials.gov)

**PRS: Main Menu**

![Main menu screenshot from ClinicalTrials.gov](http://register.clinicaltrials.gov)
vii) Items to Consider Before Registering a Protocol

(1) Studies subject to FDAAA must be registered by the Responsible Party (study sponsor or designated principal investigator [PI])

(2) Each protocol can only be registered once

   (a) Avoid duplicate registrations (i.e., multiple records for same study)

       (i) Agree on the sponsor and the responsible party ahead of time

       (ii) Multisite studies are NOT registered by each individual site

       (iii) Multi-collaborator/funder studies need to designate a single entity to register the study

(3) See the “Protocol Registration Definitions and Instructions with Examples” section of this manual for hints on preparing a registration record
Create a Record

To enter your protocol into the system, click on “Create”

This will take you into a Web-based data entry system where you can enter information on your trial.

Sample PRS Data Entry Screen

Title: A Randomized Double-blinded Active-controlled Clinical... ID: M3-12A

Unique Protocol ID: M3-12A

Brief Title: Example: Safety Study of Recombinant Vaccinia Virus Vaccine to Treat Prostate Cancer

Official Title: Example: Phase 1 Study of Recombinant Vaccinia Virus That Expresses Prostate Specific Antigens in Metastatic Adenocarcinoma of the Prostate

Study Type: Interventional, Observational

FDA Regulated Intervention?: Yes

FIND/IDE Protocol?: Required by ClinicalTrials.gov; Required to comply with US Public Law 110-85, Section 801
## Entering Arms and Interventions

### 1. Specify Each Study Arm (3x)

<table>
<thead>
<tr>
<th>Arm Label</th>
<th>Arm Type</th>
<th>Arm Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug X</td>
<td>Experimental</td>
<td>5 mg daily + Penicillin 1 to 2 million units IV every 4 days.</td>
</tr>
</tbody>
</table>

- **Active Comparator**: Low Dose
- **Placebo Comparator**: Control

### 2. Specify Each Intervention (4x)

<table>
<thead>
<tr>
<th>Intervention Name</th>
<th>Intervention Description</th>
<th>Intervention Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug X</td>
<td>1 mg tablet</td>
<td>Drug</td>
</tr>
</tbody>
</table>

- **Active Comparator**: Low Dose
- **Experimental**: High Dose
- **Placebo Comparator**: Control
**Entering Arms and Interventions**

1. Specify Each Study Arm (3x)

<table>
<thead>
<tr>
<th>Arm Label</th>
<th>Active Comparator: Low Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug X, 1 mg daily + Penicillin 1 to 2 million units IV every 4 hours for 14 days.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Arm Type</th>
<th>Experimental</th>
</tr>
</thead>
</table>

| Arm Description | Drug X, 5 mg daily + Penicillin 1 to 2 million units IV every 4 hours for 14 days. |

<table>
<thead>
<tr>
<th>Arm Label</th>
<th>Experimental: High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug X, 5 mg daily + Penicillin 1 to 2 million units IV every 4 hours for 14 days.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Arm Type</th>
<th>Placebo Comparator: Control</th>
</tr>
</thead>
</table>

2. Specify Each Intervention (4x)

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Type: Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name: Drug X</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Intervention Description</th>
<th>1 mg tablets</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Arms</th>
<th>Active Comparator: Low Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experimental: High Dose</td>
<td></td>
</tr>
<tr>
<td>Placebo Comparator: Control</td>
<td></td>
</tr>
</tbody>
</table>

3. Assign Each Intervention to One or More Study Arms
After Data Entry Is Finished

- Review the information on the Edit Protocol screen for accuracy and completeness
  - **ERROR** - Study cannot be released, must be addressed
  - **WARNING** - FDAAA* item; should be addressed
  - **NOTE** - Helpful hints
- Review entry for consistency with Protocol Detailed Review Items ([prsinfo.clinicaltrials.gov/fdaaa.html](prsinfo.clinicaltrials.gov/fdaaa.html))
- When your review is complete, click on "Next Action: Complete"

---

viii) After Data Entry Is Finished
(1) PRS administrator will “approve” and “release” the record to be displayed publicly at ClinicalTrials.gov

(2) After the record is “released,” ClinicalTrials.gov staff will review the record for consistency with minimum quality review criteria.

(3) See our “ClinicalTrials.gov Review of Protocol Submissions” section of this manual for what they will be looking for during their review.

ix) Receive a ClinicalTrials.gov Identifier (NCTxxxxxxx)

(1) Records should be available at ClinicalTrials.gov within 2 to 5 business days of release by the administrator

(2) Where to find the ClinicalTrials.gov Identifier

   (a) Email: Sent to the “record owner” once QA reviewer has posted it

   (b) PRS Account: Appears in the “ClinicalTrials.gov ID” field

   (c) ClinicalTrials.gov: Search using your Unique Protocol ID; the NCT number is listed at the top

(3) A study is not registered until it receives a ClinicalTrials.gov Identifier (NCT number)
(4) Check the public site to ensure that your study is properly registered

- Modifying an existing CT.gov record
(1) Click “Modify” on the Main Menu and select the record to be modified

(2) Make changes to the relevant section of the record and save changes by clicking “OK”

(3) Review record for ERRORS, WARNINGS, NOTES and check against review criteria

(4) Update Record Verification Date

(5) Click on “Next Action: Complete”
ClinicalTrials.gov Review of Protocol Submissions

xi) Background

(1) Protocol information must be clear and informative and information must be consistent with the ClinicalTrials.gov Protocol Data Element Definitions (DRAFT): http://prsinfo.clinicaltrials.gov/definitions.html.

(2) ClinicalTrials.gov reviews protocol information for apparent validity, meaningful entries, logic and internal consistency, and formatting.

(a) It is the responsibility of the data provider to ensure that records are consistent with these criteria.

(b) The public posting of a registration record by ClinicalTrials.gov does not necessarily mean that all of these criteria have been met.

(c) At times, ClinicalTrials.gov may note problems and request revisions after a record has been posted publicly.
xii) General Registration Review Criteria

(1) Record is in English (with possible exception for the Official Title).

(2) Acronyms and abbreviations are spelled out fully (with acronym or abbreviation in parentheses) at least the first time they are used in the Protocol Section.

(3) Acronyms used to identify the study are entered in the Acronym data element.

(4) No spelling errors exist. Hint: The Spelling Tool on the “View Protocol Record” page may be used to identify possible spelling errors.

(5) No formatting problems exist, including any unreadable characters or symbols. Hint: Unicode, UTF-8 format, is the standard for ClinicalTrials.gov.

(6) In general, the Brief Title is in lay language and includes the condition and intervention evaluated in the study.

(7) Board approval (by an ethics committee) is required for all Interventional studies.

   (a) For trials with an Overall Recruitment Status of “Not Yet Recruiting,” a Board Approval Status of “Submitted, Pending” or “Request not yet submitted” is acceptable.

   (b) Once participant recruitment begins, a Board Approval Status of “Approved” and the Review Board Name and contact information (either phone or email) is required.

xiii) Internal Consistency

(1) Information must be consistent throughout the record.

   (a) Overall Recruiting Status is consistent with Study Start Date and Primary and Study Completion Dates.

   (b) Study Type is consistent with other information in the record (see Study Type below).

   (c) Intervention Names are the same throughout the record (see Intervention Information below).

   (d) Study Design data elements are consistent with Official Title and other information in the record.

xiv) Brief Summary and Detailed Description

(1) Information is provided in complete sentences and is not written in the first person.

(2) References are not provided in this section.
(a) All references must be entered in the Citation field.

(3) Compensation/reward information is not present.

(4) Results-type data (“results” or “conclusions” of the study) are not present. Results may be entered in the results section of the record (see additional information about entering results at https://prsinfo.clinicaltrials.gov/fdaaa.html).

xv) Study Type

(1) Designation of study as ‘Observational’ or ‘Interventional’ is consistent with other information in the record and with the ClinicalTrials.gov Protocol Data Element Definitions:

(a) Interventional

(i) **Definition:** Studies in human beings in which individuals are assigned by an investigator based on a protocol to receive specific interventions. Subjects may receive diagnostic, therapeutic or other types of interventions. The assignment of the intervention may or may not be random. The individuals are then followed and biomedical and/or health outcomes are assessed.

1. **Hint:** Randomized studies are interventional. Studies with investigational drugs or devices are likely to be interventional.

(b) Observational

(i) **Definition:** Studies in human beings in which biomedical and/or health outcomes are assessed in pre-defined groups of individuals. Subjects in the study may receive diagnostic, therapeutic, or other interventions, but the investigator does not assign specific interventions to the subjects of the study.

xvi) Outcome Measures

(1) The Primary and Secondary Outcome Measure Titles and Descriptions (if provided) are as specific as possible.

(2) The Outcome Measure information includes the name of the specific measure (e.g., Systolic Blood Pressure) and a description of the metric that will be used to characterize the measure (e.g., Change in Systolic Blood Pressure).

(a) **Hint:** “Bioequivalence,” “pharmacokinetics,” and “pharmacodynamics” are not specific descriptions of an Outcome Measure because they do not specify by which measures bioequivalence, pharmacokinetics or pharmacodynamics will be assessed.
Examples of Outcome Measure Titles to assess these parameters include:

(i) “Area under the plasma concentration versus time curve (AUC) of ‘drug x’”

(ii) “Peak Plasma Concentration (Cmax) of ‘drug x’”

(c) Hint: “Safety,” “tolerability,” and “feasibility” are not specific measures. Similarly, “Adverse events” by itself is not sufficient. “Number of participants with adverse events” is specific.

(3) The Outcome Measure information describes WHAT will be measured, not why it is measured.

(a) Hint: Generally, verbs should not be included in the Outcome Measure Title.

(4) Outcome Measure Time Frame

(a) Each Outcome Measure includes a time point at which the outcome is assessed for the specific metric used.

(b) Most outcome measures will have one time point.

(c) If multiple outcomes are based on the same underlying measure (e.g., Outcome Measure Title “Change from Baseline in Hamilton Depression Rating Scale”) assessed at different time points (e.g., “8 weeks and 12 weeks”), then each unique combination of measurement and Time Frame is entered as a separate Outcome Measure (e.g., “Change from Baseline in Hamilton Depression Rating Scale at 8 weeks” and “Change from Baseline in Hamilton Depression Rating Scale at 12 weeks”).

(d) “Change” Outcome Measures – Generally two time points (e.g., “baseline and 8 weeks”) are entered to indicate the time period over which the change occurred.

(e) Time-to-Event Outcome Measures – This measure describes plans to assess the time to occurrence of an “event” (e.g., “death”) for studies involving survival analysis

(i) The Time Frame should, at a minimum, include the estimated period of time over which the event will be assessed (e.g., “up to 100 weeks”).

(ii) The Time Frame may also include information on how the event will be determined and over what estimated period of time (e.g., “From date of randomization until the date of first documented progression or date of death from any cause, whichever came first, assessed up to 100 months”).

(f) Pharmacokinetic Outcome Measures (e.g., Cmax, AUC) – These assessments rely on multiple measurements over time and the Time Frame may include multiple time points describing the
interval at which data are collected (e.g., “0, 1, 2, 3, 4, 6, 8, 12, 24, 48, 72, 96 hours post-dose”).

(i) **Hint:** “At follow-up” or “end of study” is usually not an adequate Time Frame. At a minimum, the

(g) Time Frame should include the maximum length of follow-up that is currently planned (e.g., “up to 3 years”).

(h) Exceptions are possible, for example, in measures that are assessed at the particular time the intervention is administered (e.g., “at time of surgery”).

xvii) Conditions or Focus of the Study

(1) Only the primary disease or condition being studied is listed. If the focus of the study is not a disease, a brief description is provided (e.g., “Medical Errors”).

xviii) Intervention Information

(1) Each intervention is entered separately using the Intervention Type, Name, and Description data elements.

xix) Intervention Names

(1) **Drug Names:** The generic name of the drug must be used, if available.

(2) If more than one drug name is being used for the same drug (e.g., a generic name and a brand name), clearly indicate that one drug is the same as the other.

(3) The preferred format is to include one drug name in parentheses next to the other drug name, for example: “Advil (ibuprofen).”

(4) **The Other Intervention Names data element is not currently viewable on the public site; therefore the content of the record must be clear and consistent in the use of Intervention Names.**

   (a) More than one drug name can be confusing to the public, particularly a patient audience.

(5) **Device and Other (non-Drug) Names:** A specific device name or other descriptive name is provided with sufficient detail so it can be distinguished from other similar interventions.
xx) Intervention Type

(1) List each Intervention Name and Intervention Type that is used in the study; each Arm may include more than one Intervention Type.

(2) Procedures frequently involve a drug or device. Whenever possible, the other relevant Intervention Types used in the procedure (e.g., Drug, Device) are selected and specific Intervention Names are listed.

(3) Each unique intervention is entered separately using the Intervention Type and Intervention Name data elements.

xxi) Arm Information - Each intervention is assigned to the corresponding Arm.

(1) Arm Type

(a) “Active Comparator” or “Placebo Comparator” cannot be the only Arm Type for a “Single Group Assignment” study design.

(b) The presence of a “Comparator” suggests that there is more than one Arm (to what the "Active Comparator" is being compared).

(c) If an intervention is assigned to an Arm, “No Intervention” is not an appropriate Arm Type.

xxii) Eligibility

(1) A list of key Inclusion Criteria and Exclusion Criteria is included.

(2) Criteria are bulleted (preferred format) or numbered.

xxiii) Locations

(1) If Central Contact is provided, only City, State and Country of locations are required.

(2) If there is no Central Contact, additional information is required (contact number or email).
Protocol Registration Definitions and Instructions with Examples

* Required by ClinicalTrials.gov

FDAAA  Required to comply with US Public Law 110-85, Section 801

(FDAAA) May be required to comply with US Public Law 110-85, Section 801

1. Titles and Background Information

Organization's Unique Protocol ID  * FDAAA
Definition: Unique identification assigned to the protocol by the sponsoring organization, usually an accession number or a variation of a grant number. Multiple studies conducted under the same grant must each have a unique number.
(Limit: 30 characters)
Examples:
ABT-1233-RV
Merck-023
ACTG 021

Secondary IDs  FDAAA
Definition: Other identification numbers assigned to the protocol, including unique identifiers from other registries and NIH grant numbers, if applicable. (Limit: 30 characters)

ID Type  Select one. Provide additional information, depending upon selected ID Type, as noted below.
(Limit: 119 characters)

- US NIH Grant/Contract Award Number - in the Secondary ID field, include activity code, institute code and 6-digit serial number. Other components of the full award number (type code, support year and suffix, if applicable) are optional.
  Examples: R01DA013131, UO1HL066582, 5R01HL123451-01A2

- Other Grant/Funding Number - also provide name of grantor.

- Registry Identifier - also provide name of clinical trials registry.

- EudraCT Number - from European Union Drug Regulatory Authorities Clinical Trial System.

- Other Identifier - also provide brief description (i.e., what organization issued the ID).
**Brief Title**

Definition: Protocol title intended for the lay public. (Limit: 300 characters)
Example: Safety Study of Recombinant Vaccinia Virus Vaccine to Treat Prostate Cancer

**Acronym**

Definition: Acronym or initials used to identify this study, if applicable. Enter only the acronym. If supplied, the acronym is automatically displayed in parentheses following the brief title. (Limit: 14 characters)
Example:
Brief Title: Women's Health Initiative
Acronym: WHI
Displayed on ClinicalTrials.gov as: Women's Health Initiative (WHI)

**Official Title**

Definition: Official name of the protocol provided by the study principal investigator or sponsor.
Example: Phase 1 Study of Recombinant Vaccinia Virus That Expresses Prostate Specific Antigen in Metastatic Adenocarcinoma of the Prostate (Limit: 600 characters)

**Study Type**

Definition: Nature of the investigation. Select one.

- **Interventional**: studies in human beings in which individuals are assigned by an investigator based on a protocol to receive specific interventions. Subjects may receive diagnostic, therapeutic or other types of interventions. The assignment of the intervention may or may not be random. The individuals are then followed and biomedical and/or health outcomes are assessed.

- **Observational**: studies in human beings in which biomedical and/or health outcomes are assessed in pre-defined groups of individuals. Subjects in the study may receive diagnostic, therapeutic, or other interventions, but the investigator does not assign specific interventions to the subjects of the study.

- **Patient Registry**
  Definition: For observational studies only, check the Patient Registry box if this record describes a study that is also considered to be a Patient Registry. This type of study should only be registered once in the PRS, by the sponsor responsible for the primary data collection and analysis.

The Agency for Healthcare Research and Quality (AHRO) defines a Patient Registry as including an organized system that uses observational methods to collect uniform data (clinical and other) prospectively for a population defined by a particular disorder/disease, condition (including susceptibility to a disorder), or exposure (including products, health care services, and/or procedures) and that serves a predetermined scientific, clinical, or policy
purpose. Patient registries may be single purpose or on-going data collection programs that address one or more questions.

- Expanded Access: records describing the procedure for obtaining an experimental drug or device for patients who are not adequately treated by existing therapy, who do not meet the eligibility criteria for enrollment, or who are otherwise unable to participate in a controlled clinical study. Expanded Access records are used to register all types of non-protocol access to experimental treatments, including protocol exception, single-patient IND, treatment IND, compassionate use, emergency use, continued access and parallel track.

2. US Food and Drug Administration (FDA) Information

Applicable Clinical Trial

FDA Regulated Intervention? *(FDAAA)*
Definition: Indicate whether this trial includes an intervention subject to US Food and Drug Administration regulation under section 351 of the Public Health Service Act or any of the following sections of the Federal Food, Drug and Cosmetic Act: 505, 510(k), 515, 520(m), and 522. Select Yes/No.

Section 801 Clinical Trial? *(FDAAA)*
Definition: If this trial includes an FDA regulated intervention, indicate whether this is an "applicable clinical trial" as defined in US Public Law 110-85, Title VIII, Section 801. Briefly, applicable drug trials include controlled clinical investigations, other than Phase I investigations, of a drug or biologic subject to US FDA regulation. Applicable device clinical trials are controlled trials with health outcomes of devices subject to FDA regulation, other than small feasibility studies, and pediatric postmarket surveillance. Select Yes/No.

Delayed Posting? *(FDAAA)*
Definition: If this is a Section 801 applicable clinical trial, indicate whether this trial includes a device NOT previously approved or cleared by the US FDA for any use, as specified in US Public Law 110-85, Title VIII, Section 801. Select Yes/No. If "Yes" is selected, full posting of the trial information on ClinicalTrials.gov will be delayed until after the device has been approved or cleared. **At that time, it is the registrant's responsibility to change this selection to "No" and release the record for full publication.**

Investigational New Drug Application (IND)/Investigational Device Exemption (IDE) Information:
Complete the following only if the protocol involves an Investigational New Drug Application (IND) or Investigational Device Exemption (IDE) under US Food and Drug Administration regulations.

IND/IDE Protocol? * *(FDAAA)*
Definition: Indicate if the protocol involves an Investigational New Drug Application (IND) or
Investigational Device Exemption (IDE) under US Food and Drug Administration regulations (Will not be made public - for administrative purposes only.)

IND/IDE Grantor *
Definition: FDA center to which the IND or IDE was submitted, i.e., Center for Drug Evaluation and Research (CDER) or Center for Biologics Evaluation and Research (CBER) for INDs; Center for Devices and Radiological Health (CDRH) for IDEs. Select one. (Will not be made public - for administrative purposes only.)

IND/IDE Number *
Definition: Number assigned to an Investigational New Drug Application (IND) or Investigational Device Exemption (IDE). (Will not be made public - for administrative purposes only.)
Examples: 22,333; BB1234

IND/IDE Serial Number
Definition: Use the serial number from the first submission of the protocol to the IND or IDE. (Will not be made public - for administrative purposes only.)

Has Expanded Access? 
Definition: Indicate whether any non-protocol access is to be provided for the investigational drug or device. If so, an Expanded Access record should also be created for this IND/IDE.

Expanded Access Record
Definition: The ClinicalTrials.gov identifier (NCT number) for the Expanded Access record associated with this study, specified if and only if "Yes" is specified for Has Expanded Access.

3. Human Subjects Review
Submitted studies must have approval from a human subjects review board prior to the recruitment of the first patient. Appropriate review boards include an Institutional Review Board, an ethics committee or an equivalent group that is responsible for review and monitoring of this protocol to protect the rights and welfare of human research subjects. A study may be submitted for registration prior to approval of the review board so long as the study is not yet recruiting patients.

Review board information is desired but not required for trials associated with U.S. FDA Investigational New Drug (IND) or Investigational Device Exemption (IDE) applications.

Review board information is required for internal administrative use and is not revealed to the public.

Board Approval *
- provide information for only one review board, even for studies involving multiple boards

Board Approval Status *
Definition: Human subjects review board approval status. Select one.

- Request not yet submitted: review board approval is required but has not yet been requested
- Submitted, pending: review board approval has been requested but not yet granted
- Submitted, approved: review board approval has been requested and obtained
- Submitted, exempt: review board has granted an exemption in response to the approval request
- Submitted, denied: review board has denied the approval request
- Submission not required: the study does not require human subjects review

**Board Approval Number** *(required only if status is "Submitted, approved")*
Definition: Number assigned by the human subjects review board upon approval of the protocol. May be omitted if status is anything other than approved. If the human subjects review board does not assign numbers, please enter the date of approval in mm/dd/yyyy format.

**Board Name** *(required unless status is "Submission not required")*
Definition: Full name of the approving human subjects review board.
Example: National Institutes of Health - NCI - IRB #1

**Board Affiliation** *(required only if status is "Submitted, approved" or "Submitted, exempt")*
Definition: Official name of organizational affiliation of the approving human subjects review board.
(Limit: 255 characters)
Example: US National Institutes of Health

**Board Contact** *(required only if status is "Submitted, approved" or "Submitted, exempt")*
Definition: Contact information for the human subjects review board.
- Phone (or Email required): * Use the format 123-456-7890 within the United States and Canada. Otherwise, provide the country code.
- Ext: Phone extension, if needed
- Email (or Phone required): * Electronic mail address.
- Address: Mailing address for the board, including street address, city, state or province, postal code, and country.

**Data Monitoring Committee?**
Definition: Indicate whether a data monitoring committee has been appointed for this study. The data monitoring committee (board) is a group of independent scientists who are appointed to monitor the safety and scientific integrity of a human research intervention, and to make recommendations to the sponsor regarding the stopping of the trial for efficacy, for harms or for futility. The composition of the committee is dependent upon the scientific skills and knowledge required for monitoring the particular study.
**Oversight authority information is displayed on ClinicalTrials.gov.** For IND/IDE protocols, Oversight Authority is filled in automatically with "United States: Food and Drug Administration."

**Oversight Authorities* **
Definition: The name of each national or international health organization with authority over the protocol. Use the following format for each authority:

country: organization name

Examples:
United States: Institutional Review Board
United States: Food and Drug Administration
Germany: Federal Institute for Drugs and Medical Devices
Australia: Therapeutic Goods Administration

4. Sponsors

**Responsible Party** \(^{FDAAA}\) [* Required by ClinicalTrials.gov for records first released on or after December 1, 2012]*
Definition: As defined in US Public Law 110-85, Title VIII, Section 801, the term "responsible party," with respect to a clinical trial, means

1. the sponsor of the clinical trial (as defined in 21 CFR 50.3) or

2. the principal investigator of such clinical trial if so designated by a sponsor, grantee, contractor, or awardee, so long as the principal investigator is responsible for conducting the trial, has access to and control over the data from the clinical trial, has the right to publish the results of the trial, and has the ability to meet all of the requirements for the submission of clinical trial information.

Select one:

- Sponsor: the entity (e.g., corporation or agency) that initiates the study

- Principal Investigator: the individual who serves as the principal investigator and is designated as responsible party, consistent with the conditions described in the statute

- Sponsor-Investigator: the individual who both initiates and conducts the study

**Investigator Information**
If either **Principal Investigator** or **Sponsor-Investigator** is selected, the following is required:
- **Investigator Name**: select from the list of PRS users/administrators; if the investigator does not have an account, one must be created. The Full Name for the selected PRS account must be the name of a person and include first and last name, and may include any relevant degrees.

- **Investigator Official Title**: title of the investigator, at the primary organizational affiliation (Limit: 254 characters)

- **Investigator Affiliation**: primary organizational affiliation of the investigator; typically will be the same as sponsor’s full name, as recorded in the PRS (Limit: 160 characters)

**Sponsor *FDAAA**

Definition: Name of primary organization that oversees implementation of study and is responsible for data analysis. For applicable clinical trials, sponsor is defined in 21 CFR 50.3. (Limit: 160 characters)

Examples: National Institute of Allergy and Infectious Diseases, Bristol-Myers Squibb

**Collaborators**

Definition: Other organizations (if any) providing support, including funding, design, implementation, data analysis and reporting. The data provider is responsible for confirming all collaborators before listing them. Provide up to 10 full names of collaborating organizations. (Limit: 160 characters per name)

### 5. Study Description

**Brief Summary *FDAAA**

Definition: Short description of the protocol intended for the lay public. Include a brief statement of the study hypothesis. (Limit: 5000 characters)

Example: The purpose of this study is to determine whether prednisone, methotrexate, and cyclophosphamide are effective in the treatment of rapidly progressive hearing loss in both ears due to autoimmune inner ear disease (AIED).

**Detailed Description**

Definition: Extended description of the protocol, including more technical information (as compared to the Brief Summary) if desired. Do not include the entire protocol; do not duplicate information recorded in other data elements, such as eligibility criteria or outcome measures. (Limit: 32,000 characters)

For Patient Registries: Also describe the applicable (1) registry procedures and (2) other quality factors (e.g., third party certification, on-site audit). In particular, summarize any procedures implemented as part of the patient registry, including, but not limited to the following:

- Quality assurance plan that addresses data validation and registry procedures, including any plans for site monitoring and auditing.
- Data checks to compare data entered into the registry against predefined rules for range or consistency with other data fields in the registry.

- Source data verification to assess the accuracy, completeness, or representativeness of registry data by comparing the data to external data sources (e.g., medical records, paper or electronic case report forms, or interactive voice response systems).

- Data dictionary that contains detailed descriptions of each variable used by the registry, including the source of the variable, coding information if used (e.g., World Health Organization Drug Dictionary, MedDRA), and normal ranges if relevant.

- Standard Operating Procedures to address registry operations and analysis activities, such as patient recruitment, data collection, data management, data analysis, reporting for adverse events, and change management.

- Sample size assessment to specify the number of participants or participant years necessary to demonstrate an effect.

- Plan for missing data to address situations where variables are reported as missing, unavailable, "non-reported," uninterpretable, or considered missing because of data inconsistency or out-of-range results.

- Statistical analysis plan describing the analytical principles and statistical techniques to be employed in order to address the primary and secondary objectives, as specified in the study protocol or plan.

### 6. Status

**Record Verification Date**

- Definition: Date the protocol information was last verified. Verification date is shown along with organization name on ClinicalTrials.gov to indicate to the public whether the information is being kept current, particularly recruiting status and contact information. **Update verification date when reviewing the record for accuracy and completeness, even if no other changes are made.**

**Overall Recruitment Status** [Required when Study Type is "Interventional" or "Observational"].

- Not yet recruiting: participants are not yet being recruited
- Recruiting: participants are currently being recruited
- Enrolling by invitation: participants are being (or will be) selected from a predetermined population
- Active, not recruiting: study is ongoing (i.e., patients are being treated or examined), but participants are not currently being recruited or enrolled
- Completed: the study has concluded normally; participants are no longer being examined or treated (i.e., last patient's last visit has occurred)
- Suspended: recruiting or enrolling participants has halted prematurely but potentially will resume
- Terminated: recruiting or enrolling participants has halted prematurely and will not resume; participants are no longer being examined or treated
- Withdrawn: study halted prematurely, prior to enrollment of first participant

NOTE: Contact information is shown on ClinicalTrials.gov only when overall status is "Recruiting" or "Not yet recruiting".

**Why Study Stopped?**
Definition: For suspended, terminated or withdrawn studies, provide a brief explanation of why the study has been halted or terminated. If desired, use brief summary or detailed description to provide additional information. (Limit: 160 characters)

**Study Start Date**
Definition: Date that enrollment to the protocol begins.

**Primary Completion Date** [*Required by ClinicalTrials.gov for records first released on or after December 1, 2012]*
Definition: As specified in US Public Law 110-85, Title VIII, Section 801, with respect to an applicable clinical trial, the date that the final subject was examined or received an intervention for the purposes of final collection of data for the primary outcome, whether the clinical trial concluded according to the prespecified protocol or was terminated. A "Type" menu is also included, with options Anticipated and Actual. For active studies, set Type to Anticipated and specify the expected completion date, updating the date as needed over the course of the study. Upon study completion, change Type to Actual and update the date if necessary.

**Study Completion Date**
Definition: Final date on which data was (or is expected to be) collected. Use the Type menu (Anticipated/Actual) as described above.

**Expanded Access Status**
Definition: Status indicating availability of an experimental drug or device outside any clinical trial protocol. This data element is only applicable for Expanded Access records (see Expanded Access under Study Type). Select one.
- Available: expanded access is currently available for this treatment.
- No longer available: expanded access was available for this treatment previously but is not currently available and will not be available in the future.
• Temporarily not available: expanded access is not currently available for this treatment, but is expected to be available in the future.

• Approved for marketing: this treatment has been approved for sale to the public.

7. Study Design

Interventional Study Design * (FDAAA)
Definition: Primary investigative techniques used in the protocol. Select the most appropriate term describing the protocol from each of the following data elements.

Primary Purpose FDAAA - reason for the protocol

• Treatment: protocol designed to evaluate one or more interventions for treating a disease, syndrome or condition

• Prevention: protocol designed to assess one or more interventions aimed at preventing the development of a specific disease or health condition

• Diagnostic: protocol designed to evaluate one or more interventions aimed at identifying a disease or health condition

• Supportive Care: protocol designed to evaluate one or more interventions where the primary intent is to maximize comfort, minimize side effects or mitigate against a decline in the subject's health or function. In general, supportive care interventions are not intended to cure a disease.

• Screening: protocol designed to assess or examine methods of identifying a condition (or risk factors for a condition) in people who are not yet known to have the condition (or risk factor).

• Health Services Research: protocol designed to evaluate the delivery, processes, management, organization or financing of health care.

• Basic Science: protocol designed to examine the basic mechanism of action (e.g., physiology, biomechanics) of an intervention.

• Other: describe in Detailed Description.

Study Phase * (FDAAA)
Definition: Phase of investigation, as defined by the US FDA for trials involving investigational new drugs. Use "N/A" for trials that do not involve drug or biologic products. Select only one.

N/A: for trials without phases (e.g., trials of devices or behavioral interventions)
Phase 0: exploratory trials, involving very limited human exposure, with no therapeutic or diagnostic intent (e.g., screening studies, microdose studies). See [FDA guidance on exploratory IND studies](https://www.fda.gov/medical-devices/investigational-device-exemption-ind-studies) for more information.

Phase 1: includes initial studies to determine the metabolism and pharmacologic actions of drugs in humans, the side effects associated with increasing doses, and to gain early evidence of effectiveness; may include healthy participants and/or patients

Phase 1/Phase 2: for trials that are a combination of phases 1 and 2

Phase 2: includes controlled clinical studies conducted to evaluate the effectiveness of the drug for a particular indication or indications in patients with the disease or condition under study and to determine the common short-term side effects and risks

Phase 2/Phase 3: for trials that are a combination of phases 2 and 3

Phase 3: includes expanded controlled and uncontrolled trials after preliminary evidence suggesting effectiveness of the drug has been obtained, and are intended to gather additional information to evaluate the overall benefit-risk relationship of the drug and provide an adequate basis for physician labeling

Phase 4: studies of FDA-approved drugs to delineate additional information including the drug's risks, benefits, and optimal use

**Intervention Model**(FDAAA) (at least one of the following required: Intervention Model, Masking, Allocation. All may be required as part of Study Design under PL 110-85, Section 801) - intervention assignments

- Single Group: single arm study
- Parallel: participants are assigned to one of two or more groups in parallel for the duration of the study
- Cross-over: participants receive one of two alternative interventions during the initial phase of the study and receive the other intervention during the second phase of the study
- Factorial: two or more interventions, each alone and in combination, are evaluated in parallel against a control group

**Number of Arms**(FDAAA)
Definition: Number of intervention groups (enter 1 for single-arm study).

**Masking**(FDAAA) (at least one of the following required: Intervention Model, Masking, Allocation. All may be required as part of Study Design under PL 110-85, Section 801) - knowledge of intervention assignments
- **Open**: no masking is used. All involved know the identity of the intervention assignment.

- **Single Blind**: one party, either the investigator or participant, is unaware of the intervention assignment; also called single-masked study.

- **Double Blind**: two or more parties are unaware of the intervention assignment

If Single Blind or Double Blind is selected, check the role(s) that are to be masked: Subject, Caregiver, Investigator or Outcomes Assessor.

**Allocation (FDAAA)** (at least one of the following required: Intervention Model, Masking, Allocation. All may be required as part of Study Design under PL 110-85, Section 801) - participant assignment to intervention group

- **N/A**: single arm study

- **Randomized Controlled Trial**: participants are assigned to intervention groups by chance

- **Nonrandomized Trial**: participants are expressly assigned to intervention groups through a non-random method, such as physician choice

**Study Classification** (formerly Endpoint) - type of primary outcome or endpoint that the protocol is designed to evaluate. Select one.

- **N/A**: not applicable

- **Safety**: show if the drug is safe under conditions of proposed use

- **Efficacy**: measure of an intervention’s influence on a disease or health condition

- **Safety/Efficacy**

- **Bio-equivalence**: scientific basis for comparing generic and brand name drugs

- **Bio-availability**: rate and extent to which a drug is absorbed or otherwise available to the treatment site in the body

- **Pharmacokinetics**: the action of a drug in the body over a period of time including the process of absorption, distribution and localization in tissue, biotransformation, and excretion of the compound

- **Pharmacodynamics**: action of drugs in living systems

- **Pharmacokinetics/dynamics**
Enrollment (Target or Actual Number of Subjects)

Definition: Number of subjects in the trial. A "Type" menu is also included, with options Anticipated and Actual. For active studies, set Type to Anticipated and specify the expected enrollment, updating the number as needed over the course of the study. Upon study completion, change Type to Actual and update the enrollment if necessary.

Observational Study Design

Observational Study Model * - primary strategy for subject identification and follow-up. Select one.

- Cohort: group of individuals, initially defined and composed, with common characteristics (e.g., condition, birth year), who are examined or traced over a given time period
- Case-control: group of individuals with specific characteristics (e.g., conditions or exposures) compared to group(s) with different characteristics, but otherwise similar
- Case-only: single group of individuals with specific characteristics
- Case-crossover: characteristics of case immediately prior to disease onset (sometimes called the hazard period) compared to characteristics of same case at a prior time (i.e., control period)
- Ecologic or community studies: geographically defined populations, such as countries or regions within a country, compared on a variety of environmental (e.g., air pollution intensity, hours of sunlight) and/or global measures not reducible to individual level characteristics (e.g., health care system, laws or policies median income, average fat intake, disease rate)
- Family-based: studies conducted among family members, such as genetic studies within families or twin studies and studies of family environment
- Other - explain in Detailed Description

Time Perspective * - temporal relationship of observation period to time of subject enrollment. Select one.

- Prospective: look forward using periodic observations collected predominantly following subject enrollment
- Retrospective: look back using observations collected predominantly prior to subject selection and enrollment
- Cross-sectional: observations or measurements made at a single point in time, usually at subject enrollment
- Other - explain in Detailed Description

**Biospecimen Retention** - select one

- None Retained - no samples retained
- Samples With DNA - samples retained, with potential for extraction of DNA from at least one of the types of samples retained (e.g., frozen tissue, whole blood)
- Samples Without DNA - samples retained, with no potential for DNA extraction from any retained samples (e.g., fixed tissue, plasma)

**Biospecimen Description**
Definition: Specify all types of biospecimens to be retained (e.g., whole blood, serum, white cells, urine, tissue). (Limit: 1000 characters)

**Enrollment** *
Definition: (see above)

**Target Follow-Up Duration** *
Definition: For Patient Registries, the anticipated time period over which each participant is to be followed. Provide a number and select a unit of time (years, months, weeks, days).

**Number of Groups/Cohorts** *
Definition: Number of study groups/cohorts. Enter 1 for a single-group study. Many observational studies have one group/cohort; case control studies typically have two.

**Outcome Measures**
NOTE: When Results are added to a record, outcome measures are transferred from the protocol section to the results section.

**Primary Outcome Measure** FDAAA [* Required by ClinicalTrials.gov for records first released on or after December 1, 2012]
Definition: Specific key measurement(s) or observation(s) used to measure the effect of experimental variables in a study, or for observational studies, to describe patterns of diseases or traits or associations with exposures, risk factors or treatment.

- **Title** * - A concise name for the specific measure that will be used to determine the effect of the intervention(s) or, for observational studies, related to core objectives of the study and receiving the most emphasis in assessment. (Limit: 254 characters)

- **Time Frame** FDAAA [* Required by ClinicalTrials.gov for records first released on or after December 1, 2012] - Time point(s) at which outcome measure is assessed. (Limit: 254 characters)
• **Description** - Additional information about the outcome measure, if needed for clarification. (Limit: 999 characters)

• **Safety Issue?** (FDAAA) - Is this outcome measure assessing a safety issue? Select: Yes/No

Examples:

Title: all cause mortality
Time Frame: one year
Safety Issue: No

Title: Evidence of clinically definite ischemic stroke (focal neurological deficits persisting for more than 24 hours) confirmed by non-investigational CT or MRI
Time Frame: within the first 30 days (plus or minus 3 days) after surgery
Safety Issue: Yes

**Secondary Outcome Measures** (FDAAA)
Definition: Secondary measurements that will be used to evaluate the intervention(s) or, for observational studies, that are a focus of the study. Specify Title, Time Frame, Description (if needed) and Safety Issue as described above.

**Other Pre-specified Outcome Measures**
Definition: Any other measurements, excluding post-hoc measures, that will be used to evaluate the intervention(s) or, for observational studies, that are a focus of the study. Specify Title, Time Frame, Description (if needed) and Safety Issue.

8. **Arms, Groups and Interventions**

For interventional studies specify the arms, corresponding to Number of Arms specified under Study Design (for single-arm studies, the following data elements are optional).

**Arm Label** (FDAAA) - the short name used to identify the arm. (Limit: 62 characters)
Examples:

- Metformin
- Lifestyle counseling
- Sugar pill

**Arm Type** (FDAAA) - select one

- Experimental
- Active Comparator
- Placebo Comparator
- Sham Comparator
- No intervention
- Other

**Arm Description** *(FDAAA)* - brief description of the arm. This element may not be necessary if the associated intervention descriptions contain sufficient information to describe the arm. (Limit: 999 characters)

For observational studies specify the predefined participant groups (cohorts) to be studied, corresponding to Number of Groups specified under Study Design (for single-group studies, the following data elements are optional). Do not use this section to specify strata (Detailed Description can be used for that purpose, if desired).

**Group/Cohort Label** * - the short name used to identify the group. (Limit: 62 characters)
Examples:

- Statin dose titration
- Chronic kidney disease, no anemia
- No treatment

**Group/Cohort Description** Definition: Explanation of the nature of the study group (e.g., those with a condition and those without a condition; those with an exposure and those without an exposure). Note that the overall study population should be described under Eligibility. (Limit: 1000 characters)

For all studies, and for expanded access records, specify the associated intervention(s). For interventional studies, at least one intervention must be specified. For observational studies, specify the intervention(s)/exposure(s) of interest, if any.

**Intervention Type** *(FDAAA)* - select one per intervention

- Drug (including placebo)
- Device (including sham)
- Biological/Vaccine
- Procedure/Surgery
- Radiation
- Behavioral (e.g., Psychotherapy, Lifestyle Counseling)
- Genetic (including gene transfer, stem cell and recombinant DNA)
- Dietary Supplement (e.g., vitamins, minerals)
- Other

**Intervention Name** *(FDAAA)* - for drugs use generic name; for other types of interventions provide a brief descriptive name. (Limit: 160 characters)

For investigational new drugs that do not yet have a generic name, a chemical name, company code or serial number may be used on a temporary basis. As soon as the generic name has been established, update the associated protocol records accordingly.

For non-drug intervention types, provide an intervention name with sufficient detail so that it can be distinguished from other similar interventions.

**Intervention Description** *(FDAAA)* - cover key details of the intervention. Must be sufficiently detailed to distinguish between arms of a study (e.g., comparison of different dosages of drug) and/or among similar interventions (e.g., comparison of multiple implantable cardiac defibrillators). For example, interventions involving drugs may include dosage form, dosage, frequency and duration. (Limit: 1000 characters)

Example:
50 mg/m2, IV (in the vein) on day 5 of each 28 day cycle. Number of Cycles: until progression or unacceptable toxicity develops.

**Other Names** - list other names used to identify the intervention, past or present (e.g., brand name for a drug). These names will be used to improve search results in ClinicalTrials.gov. (Limit: 160 characters per name)

**Arms/Groups** *(FDAAA)* - if multiple Arms/Groups have been specified for the study, edit the Cross-Reference, checking boxes to indicate which of the Interventions are to be administered under each Arm/Group of the study.

9. Conditions and Keywords

**Conditions or Focus of Study** *(FDAAA)*
Definition: Primary disease or condition being studied, or focus of the study. Diseases or conditions should use the National Library of Medicine’s Medical Subject Headings (MeSH) controlled vocabulary when possible.

**Keywords**
Definition: Words or phrases that best describe the protocol. Keywords help users find studies in the database. Use NLM’s Medical Subject Heading (MeSH) controlled vocabulary terms where appropriate. Be as specific and precise as possible. Avoid acronyms and abbreviations.

10. Eligibility
Study Population Description *
Definition: For observational studies only, a description of the population from which the groups or cohorts will be selected (e.g., primary care clinic, community sample, residents of a certain town). (Limit: 1000 characters)

Sampling Method * - For observational studies only, select one and explain in Detailed Description.
- Probability Sample: exclusively random process to guarantee that each participant or population has specified chance of selection, such as simple random sampling, systematic sampling, stratified random sampling, cluster sampling, and consecutive patient sampling
- Non-Probability Sample: any of a variety of other sampling processes, such as convenience sampling or invitation to volunteer

Eligibility Criteria *
FDAAA
Definition: Summary criteria for participant selection. The preferred format includes lists of inclusion and exclusion criteria as shown below. (Limit: 15,000 characters)
Example:

Inclusion Criteria:
- Clinical diagnosis of Alzheimer's Disease
- Must be able to swallow tablets

Exclusion Criteria:
- Insulin dependent diabetes
- Thyroid disease

Gender *
FDAAA
Definition: Physical gender of individuals who may participate in the protocol. Select one.
- Both: both female and male participants are being studied
- Female: only female participants are being studied
- Male: only male participants are being studied

Age Limits *
FDAAA
Minimum Age
Definition: Minimum age of participants. Provide a number and select a unit of time (years, months, weeks, days, hours or minutes). Select "N/A (No limit)" if no minimum age is indicated.
Maximum Age
Definition: Maximum age of participants. Provide a number and a unit of time (years, months, weeks, days, hours or minutes). Select "N/A (No limit)" if no maximum age is indicated.

Accepts Healthy Volunteers? FDAAA
Definition: Indicate if persons who have not had the condition(s) being studied or otherwise related conditions or symptoms, as specified in the eligibility requirements, may participate in the study. Select Yes/No.

11. Protocol Location, Contact and Investigator Information

Multiple locations may be specified. Location is composed of the following fields.

Facility *(FDAAA)*

- Name: Full name of the organization where the protocol is being conducted. (Limit: 254 characters)
  Examples: UCLA Eye Institute; Springfield Memorial Hospital
- City *(FDAAA)*
- State/Province *(FDAAA)*
- Postal Code
- Country *(FDAAA)*

Recruitment Status *(FDAAA)* - protocol accrual activity at a facility. Select one.

- Not yet recruiting: participants are not yet being recruited
- Recruiting: participants are currently being recruited
- Enrolling by invitation: participants are being (or will be) selected from a predetermined population
- Active, not recruiting: study is ongoing (i.e., patients are being treated or examined), but participants are not currently being recruited or enrolled
- Completed: the study has concluded normally; participants are no longer being examined or treated (i.e., last patient's last visit has occurred)
- Suspended: recruiting or enrolling participants has halted prematurely but potentially will resume
- Terminated: recruiting or enrolling participants has halted prematurely and will not resume; participants are no longer being examined or treated
Withdrawn: study halted prematurely, prior to enrollment of first participant

NOTE: Contact information is shown on ClinicalTrials.gov only for locations with status set to "Recruiting" or "Not yet recruiting".

Tip: When a trial's overall status changes to "Active, not recruiting," it is not necessary to change recruitment status for each location. Location recruitment status is only shown on ClinicalTrials.gov when Overall Status is "Recruiting".

**Facility Contact** *(FDAAA) (or Central Contact required)*

- First Name
- Middle Initial
- Last Name *(FDAAA)*
- Degree
- Phone *(FDAAA)*: (or Email required) office phone of the facility contact person. Use the format 123-456-7890 within the United States and Canada. Otherwise, provide the country code.
- Ext: phone extension, if needed
- Email *(FDAAA)*: (or Phone required) electronic mail address of the facility contact person

**Facility Contact Backup**
Person to contact if Facility Contact is not available (i.e., a second contact person).

**Investigators** (at the protocol location)

- First Name
- Middle Initial
- Last Name
- Degrees
- Role: Site Principal Investigator or Site Sub-Investigator (pick one)

**Central Contact** *(FDAAA) (or Facility Contact required)*
Definition: Person providing centralized, coordinated recruitment information for the entire study.

- First Name
- Middle Initial
• Last Name * (FDAAA)

• Degree

• Phone * (FDAAA): Toll free phone number of the central contact person. Use the format 800-555-5555 within the United States and Canada. Otherwise, provide the country code.

• Ext: phone extension, if needed

• Email * (FDAAA): electronic mail address of the central contact person

Central Contact Backup
Person to contact if Central Contact is not available.

Overall Study Officials
Definition: Person(s) responsible for the overall scientific leadership of the protocol, including study principal investigator.

• First Name

• Middle Initial

• Last Name

• Degree

• Official's Role: Position or function of the official. Select one (Study Chair/Study Director/Study Principal Investigator).

• Organizational Affiliation: Full name of the official's organization. If none, specify Unaffiliated.
  (Limit: 255 characters)

If Overall Status is "Recruiting":

• At least one location must be specified.

• At least one location must have status set to "Recruiting".

• All locations must have status specified.

• Either any location that is recruiting must have Contact specified, or Overall Contact must be specified.

Contact information limits:

• First Name: 62 characters
12. Related Information

References
Definition: Citations to publications related to the protocol: background and/or results. Provide either the unique PubMed Identifier (PMID) of an article or enter the full bibliographic citation.

MEDLINE Identifier
Definition: unique PubMed Identifier (PMID) for the citation in MEDLINE
Example: PMID: 10987815

Citation
Definition: bibliographic reference in NLM's MEDLINE format (Limit: 2000 characters)
Example: Barza M; Pavan PR; Doft BH; Wisniewski SR; Wilson LA; Han DP; Kelsey SF. Evaluation of microbiological diagnostic techniques in postoperative endophthalmitis in the Endophthalmitis Vitrectomy Study. Arch Ophthalmol 1997 Sep;115(9):1142-50

Results Reference?
Definition: Indicate if the reference provided reports on results from this clinical research study.

Links
Definition: A Web site directly relevant to the protocol may be entered, if desired. Do not include sites whose primary goal is to advertise or sell commercial products or services. Links to educational, research, government, and other non-profit Web pages are acceptable. All submitted links are subject to review by ClinicalTrials.gov.

URL
Definition: complete URL, including http:// (Limit: 254 characters)
Example: http://www.alzheimers.org/

Description
Definition: title or brief description of the linked page. If the page being linked is the protocol's homepage on the sponsor's Web site, include the words "Click here for more information about this study:"
Examples:
Updates and Submitting Results

xxiv) Required Registration Updates

(1) Responsible Parties should update their records within 30 days of a change to any of the following:
   (a) Recruitment Status and Overall Recruitment Status
   
   (b) Completion Date (Primary Completion Date data element in ClinicalTrials.gov)

(2) Other changes or updates to the record must be made at least every 12 months.

(3) It is recommended that the Record Verification Date be updated at least every 6 months for studies that are not yet completed, even if there were no changes to the record.

xxv) Submitting Results

(1) For certain trials subject to FDAAA 801, Responsible Parties should submit summary results no later than 12 months after the date of final data collection for the prespecified primary outcome measure (Primary Completion Date data element in ClinicalTrials.gov).

Why Should I Register and Submit Results?
Registering clinical trials when they begin, providing timely updates, submitting summary results, and making this information publicly available fulfills a number of purposes and benefits a variety of people.

1) Trial Registry Purposes for Various Groups

<table>
<thead>
<tr>
<th>Registry Purpose</th>
<th>Group That Benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fulfill ethical obligations to participants and community</td>
<td>Patients, general public, research community</td>
</tr>
<tr>
<td>Provide information to potential participants and referring clinicians</td>
<td>Patients, clinicians</td>
</tr>
<tr>
<td>Reduce publication bias</td>
<td>Users of the medical literature</td>
</tr>
<tr>
<td>Help editors and others understand the context of study results</td>
<td>Journal editors, users of the medical literature</td>
</tr>
<tr>
<td>---------------------------------------------------------------</td>
<td>--------------------------------------------------</td>
</tr>
<tr>
<td>Promote more efficient allocation of research funds</td>
<td>Granting agencies, research community</td>
</tr>
<tr>
<td>Help institutional review boards (IRBs) determine appropriateness of a research study</td>
<td>IRBs, ethicists</td>
</tr>
</tbody>
</table>

[Full Text]

2) Results Database Purposes for Various Groups

<table>
<thead>
<tr>
<th>Results Database Purpose</th>
<th>Group That Benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Provide public record of basic study results in a standardized format</td>
<td>Researchers, journal editors, institutional review boards, and ethicists</td>
</tr>
<tr>
<td>Promote fulfilling of ethical responsibility to participants; use of research results to contribute to medical knowledge</td>
<td>Patients, general public, and research community</td>
</tr>
<tr>
<td>Mitigate &quot;publication&quot; and &quot;outcome reporting&quot; biases</td>
<td>Users of medical literature</td>
</tr>
<tr>
<td>Facilitate systematic reviews and other analyses of the research literature</td>
<td>Researchers and policymakers</td>
</tr>
</tbody>
</table>

[Full Text]

3) Required by Law

Section 801 of the Food and Drug Administration Amendments Act (FDAAA 801) (PDF) requires Responsible Parties to register and submit summary results of clinical trials with ClinicalTrials.gov. The law applies to certain clinical trials of drugs (including biological products) and medical devices. For more information:

- See [FDAAA 801 Requirements](#) to learn about Responsible Party, Applicable Clinical Trials, and deadlines for registration and results submission
- See the [Protocol Data Element Definitions](#) and [Basic Results Data Element Definitions](#) to learn about the specific data elements
- See [History, Policies, and Laws](#) to learn about other relevant laws, including the Food and Drug Administration Modernization Act
- View the online presentation:

  **Key FDAAA Issues** (9:23) Deborah A. Zarin, M.D., Director, ClinicalTrials.gov, NLM:
  
  o Discusses key issues in the Food and Drug Administration Amendments Act related to registering trials and submitting results.

4) **Required for Journal Publication**

The [International Committee of Medical Journal Editors (ICMJE) requires trial registration](#) as a condition for the publication of research results generated by a clinical trial. ClinicalTrials.gov is a registry where organizations and individuals can provide the [World Health Organization (WHO) Trial Registration Data Set](#) required by ICMJE.

See [ICMJE section of Support Materials](#) or visit [http://www.icmje.org](http://www.icmje.org).

5) **Selected Trial Registration Laws and Policies**

A summary of key laws and policies requiring clinical trial registration are shown in the table below:

<table>
<thead>
<tr>
<th>Name</th>
<th>Type</th>
<th>Intervention Type</th>
<th>Registration Policy Scope</th>
<th>Results Submission Policy Scope</th>
</tr>
</thead>
<tbody>
<tr>
<td>Section 801 of the Food and Drug Administration Amendments Act (FDAAA 801) (PDF)</td>
<td>U.S. Federal law enacted in 2007</td>
<td>Drugs, biologics, and devices</td>
<td>Controlled clinical investigations of an FDA-regulated drug, biologic, or device, other than Phase 1 (drugs/biologics) or small feasibility studies</td>
<td>Same scope as registration, but interventional studies of FDA approved drugs, biologics, or devices</td>
</tr>
<tr>
<td>2013 Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects</td>
<td>International policy initially adopted by the World Medical Association (WMA) General Assembly in 1964; last amended in</td>
<td>Any (includes drugs, biologics, devices, surgical procedures, and behavioral treatments)</td>
<td>&quot;Every research study involving human subjects must be registered in a publicly accessible database before recruitment of the first subject.&quot; (Para 35)</td>
<td>&quot;Researchers have a duty to make publicly available the results of their research on human subjects... Negative and inconclusive as well as positive results should be published or...&quot;</td>
</tr>
<tr>
<td><strong>Regulatory Basis</strong></td>
<td><strong>Year</strong></td>
<td><strong>Target</strong></td>
<td><strong>Scope</strong></td>
<td><strong>Regulatory Text</strong></td>
</tr>
<tr>
<td>-----------------------------------------------------------------------------------</td>
<td>----------</td>
<td>------------------------------------------</td>
<td>---------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Clinical Trials Directive (2001/20/EC), Article 11 (and associated Regulations and Guidelines)</td>
<td>2001</td>
<td>Drugs and biologics</td>
<td>Phase 2–4 adult trials and Phase 1–4 pediatric trials</td>
<td>Same scope as registration (includes products without marketing authorization applications)</td>
</tr>
<tr>
<td>European Union directive adopted in 2001</td>
<td>2001</td>
<td>Drugs and biologics</td>
<td>Phase 2–4 adult trials and Phase 1–4 pediatric trials</td>
<td>Same scope as registration (includes products without marketing authorization applications)</td>
</tr>
<tr>
<td>WHO International Clinical Trials Registry Platform</td>
<td>2006</td>
<td>Any (includes drugs, biologics, devices, surgical procedures, and behavioral treatments)</td>
<td>&quot;The registration of all interventional trials is a scientific, ethical and moral responsibility.&quot;</td>
<td>N/A</td>
</tr>
<tr>
<td>ICMJE Statement</td>
<td>2004</td>
<td>Any (includes drugs, biologics, devices, surgical procedures, and behavioral treatments)</td>
<td>All interventional studies, including Phase 1 studies; defines criteria for &quot;acceptable registries&quot;</td>
<td>N/A</td>
</tr>
<tr>
<td>Section 113 of the Food and Drug Administration Modernization Act</td>
<td>1997</td>
<td>Drugs and biologics</td>
<td>Efficacy trials for &quot;serious or life threatening diseases or conditions&quot; regulated by FDA</td>
<td>N/A</td>
</tr>
</tbody>
</table>


For more information see *History, Policies, and Laws*
Clinical Translational Science Institute Resources

Study Development

Research Project Navigators

CTSI Research Project Navigators advise research teams on available resources and help them navigate research-related processes. They serve as a central resource through which researcher inquiries and requests for assistance are managed and supported; information is available through personalized consultation and the CTSI portal. The navigators continuously improve their methods to address changing needs, the changing environment and user feedback.

Resources Consultation

Navigators can advise investigators on available resources across the CTSI and help them access these resources.

Study Implementation

CTSI Research Project Navigators are well versed in IRB application preparation, protocol development, Good Clinical Practice (GCP) guidelines, and NIH research rules and standards for the design, conduct, performance, monitoring, data collection, management and analysis, and reporting of clinical trials. Through consultation, we help investigators assemble research teams to conduct studies, oversee study management, and aid in the timely completion of the study.

Contacts

Teresa d’Angelo, RN, BSN, CCRC (teresadangelo@ufl.edu) – (352) 294-5881

H. Robert Kolb, RN, BS, CCRC (kolbhr@ufl.edu) – (352) 273-8882

Informatics Consulting

The UF CTSI provides free informatics consulting to all faculty, staff and students of the University of Florida and its affiliated health care partners.

What is informatics? Informatics is the science of information representation and processing. Informaticists study knowledge representation and management and are often involved in the design and construction of information systems. Biomedical informaticians focus on informatics problems related to health care and health research.

If you are writing a grant, or considering work in quality assurance, the relation of Epic to research, the improvement of clinical care through information technology, or just have questions about the direction the academic health center is taking in its information infrastructure in support of research and care, please feel free to set up an appointment to speak with one of the faculty involved with our informatics activities.
CTSI-supported informatics resources include the UF Health Integrated Data Repository for clinical and research data and a study registry for all clinical research studies at UF.

To set up an appointment to speak with an informatician regarding your interests in information use and management, please call 352-273-8700.

**IRB, RAC and ClinicalTrials.gov Support Services**

The UF Clinical and Translational Science Institute’s Regulatory Knowledge and Research Support (RKRS) Program offers tiered support services to help investigators navigate the complexities of preparing submissions for UF Institutional Review Boards and the College of Medicine’s Research Administration and Compliance (RAC) office. The program can also advise investigators on compliance with ClinicalTrials.gov requirements.

Support is available to anyone, from the novice researcher to the experienced investigator, for any step of the process—whether writing an informed consent or preparing the RAC billing grid. Initial consultations are always free, and hands-on support for any component of the IRB or RAC submission processes is available on a fee-for-service basis. Contact Wajeeh Bajwa, Ph.D., at bajwa@ufl.edu or (352) 273-8702 or any of the specialists listed below with questions about IRB, RAC, or ClinicalTrials.gov submission preparation.

**Contacts**

Wajeeh Bajwa, Ph.D. (352-273-8702, bajwa@ufl.edu)  
Director, CTSI Regulatory Knowledge and Research Support Program  
Office 3218, 3rd floor, North Wing  
Clinical and Translational Research Building  
2004 Mowry Road  
Gainesville, FL 32610

Rebecca Wichman, M.S.  
Research Program Coordinator  
rwichman@ufl.edu, (352) 273-5132

H. Robert Kolb, RN, BS, CCRC  
Research Project Navigator  
kolbhr@ufl.edu, 352-273-8882

**RAC Billing Compliance Review Assistance**

How can CTSI RKRS help me with my RAC submission?

When it is time for an investigator to prepare a RAC Billing Compliance Review submission, it is an ideal opportunity to schedule a free hour of time to discuss RAC documents with a CTSI RAC submission
specialist. This specialist has been trained by RAC staff and regularly attends RAC meetings in order to stay up-to-date on all RAC Billing Compliance Review requirements. This free hour can be used as:

- A consultation where the RAC specialist will show the investigator what is missing or needs revision from the study’s RAC documentation and how to complete it.
- An opportunity for the investigator to have the RAC specialist review the study to provide a quote for the preparation of a complete RAC Package that is ready for submission to RAC.

For more information or to schedule your free consultation, please contact Rebecca Wichman for details at rwichman@ufl.edu or (352) 273-5132.

**How should I prepare for my consultation with the CTSI RAC specialist?**

No preparation is required for investigators to consult with the CTSI RAC specialist. Our RAC specialist will show investigators how they should move forward in preparing for the RAC Billing Compliance Review at any point in the process, even if the investigator only has a proposal.

**What is the RAC Research Billing Compliance Review?**

Before submitting to an IRB, a study must undergo a RAC Research Billing Compliance Review. Just as the IRB considers the ethics of proposed studies, the RAC ensures that all billing related aspects of studies are planned correctly. To learn more about RAC requirements and the submission process to the RAC Office, please visit: [http://rac.med.ufl.edu/preparation/rac_dsr_irb/rac/](http://rac.med.ufl.edu/preparation/rac_dsr_irb/rac/)

**Literature Searches**

The Health Science Center Libraries (HSCL) at the University of Florida offer specialized expertise in searching and critical appraisal of the literature to researchers developing clinical and translational studies. Based on a personalized consultation, a librarian can develop search strategies, deliver curated bibliographies, provide summarized or tabulated review of the literature, or collaborate on conducting and writing systematic reviews/meta-analyses. The HSCL representative to the CTSI is always available for confidential discussion with investigators, can provide training for all research study personnel, and can match the project with the most qualified librarian.

**Contact**

Jennifer Ann Lyon (jalyon@ufl.edu) – (352) 273-8441 or (352) 273-8408, or submit your request electronically at [http://library.health.ufl.edu/help/literature-search/](http://library.health.ufl.edu/help/literature-search/)

**Qualitative Research Collaboration**

The [CTSI Research Design and Analysis Program](http://library.health.ufl.edu/help/literature-search/) (RDAP) is developing a Qualitative Research Collaboration to link researchers conducting health-related research with experienced qualitative researchers from across the UF campus when study designs (including mixed methods) call for qualitative research components.
Faculty with expertise in qualitative research from several disciplines welcome the opportunity to discuss and develop collaborative partnerships with both novice and experienced health-related researchers and contribute to the development and implementation of qualitative research methods during the project design phase.

The goal is to develop collaborative partnerships between health-related researchers and those with qualitative expertise in the design and implementation of research projects by being actively involved in the project from conception to conclusion.

**Qualitative Research Design and Grant Proposal Collaborations**

Rigorous qualitative research requires expertise in qualitative theory, research design, and methods including data collection and analysis. Faculty are available for collaboration on projects employing qualitative study design and can assist in defining study aims and research questions, choosing the appropriate method(s), and developing a rigorous plan for data collection and analysis.

Grant proposals must include appropriate funding for implementation, training, and data collection and analysis. The percent FTE will be negotiated during proposal development and consultation stages of the collaboration.

**Suggested role assignment by FTE on a grant:**

- 30%+ PI or Co-PI
- 10% – 29.9% Key Investigator (Co-PI or Co-I)
- 5% – 9.9% Co-Investigator (limited involvement)
- <5% Consultant

For grant submissions with a qualitative research component, please be sure to contact possible collaborators as soon as possible. An updated list of UF faculty with qualitative research expertise is under development.

**Qualitative Research Resources**

Selected Qualitative Research Courses at UF

- EDF 6475: Qualitative Foundations of Educational Research
- EDF 7483: Qualitative Data Collection
- EDF 7479: Qualitative Data Analysis
- NGR 6815: Foundations of Qualitative Research in Health
- NGR 7814: Qualitative Field Methods for Health-Related Research
- PHC 6937: Special Topics: Qualitative Data Analysis

**UF Qualitative Research Community**
http://education.ufl.edu/international-institute-qualitative-inquiry/.

Other Resources

- **e-Source: Behavioral & Social Sciences Research**, a Web-based interactive anthology with the latest research methods and tools to address emerging challenges in public health (launched in 2012 by the NIH Office of Behavioral and Social Sciences Research and the New England Research Institutes)

- **NIH Best Practices for Mixed Methods Research in the Health Sciences, 2011**

- **Robert Wood Johnson Foundation, Qualitative Research Guidelines, 2008**

- **NIH Qualitative Methods in Health Research: Opportunities and Considerations in Application and Review, 2001**

- **Qualitative data management software:**
  - Atlas.ti
  - MaxQDA
  - NVivo

- **Software training**: Queri, Inc., Kristi Jackson

- **Transcription**: Landmark Associates

Contact

For more information about the opportunities and resources described on this page, please contact:

Mary Ellen Young, Ph.D.
Clinical Associate Professor
Department of Behavioral Science and Community Health
College of Public Health and Health Professions
Telephone: (352) 273-6745
Fax: (352) 273-6048

Physical address:
HPNP 4160 Suite, Room 4156
1225 Center Drive
University of Florida
Gainesville, FL, 32610

Mailing address:
P.O. Box 100175
Gainesville, FL 32610-0175
**Study Design**

The [CTSI Research Design and Analysis Program](#) offers study design services for all proposed clinical and translational work, including grant applications. This is primarily a joint effort of the Department of Health Outcomes and Policy and the Department of Biostatistics, in association with the CTSI and the Departments of Epidemiology and Statistics.

We can help you set up your study in terms of refining your objectives into testable hypotheses, choosing a study design, providing you with a data analysis plan, and completing a sample size/power analysis. Although we do not get directly involved in data management, we work closely with you to ensure that your data will be compatible with the analytic needs of the study.

The primary goal of the CTSI Research Design and Analysis Program is research collaboration, not merely technical consultation. We welcome the opportunity to forge long-term collaborative arrangements with clinical and translational researchers where ultimately, we can contribute to research questions and develop new methodologies in your field. We are especially interested in helping promote research careers for young investigators.

**Important Information**

1. For grant submissions involving the CTSI, be sure to contact Dr. Shuster at least four weeks before your planned internal submission to the Division of Sponsored Research (usually six weeks before the due date at the agency). In exceptional circumstances, where this deadline cannot be met, we shall evaluate our participation on a case by case basis.
2. For investigator initiated Clinical Research Center protocols: Unless your project has faculty support from one of the following – Department of Biostatistics, Department of Epidemiology, Department of Statistics, or Department of Health Outcomes and Policy – you must contact Dr. Shuster prior to submitting your protocol to the CTSI for review and ultimate submission to the Scientific Advisory Committee. In some situations, this might be as simple as providing a biosketch and contact information for the individual who wrote the analytic research plan.

**Studios**

RDAP has initiated monthly studios where up to ten researches can join three RDAP members for individualized discussion about upcoming research projects. These are normally held the third Wednesday of a month from 11:30 to 1:00 p.m. with lunch provided. One need not attend the entire session, but an RSVP should be made on a first-come, first-served basis to April Barnes, abarnes27319@ufl.edu.

**Charges for Study Design**

With the exception of analyzing data from preliminary studies (which is charged under the rubric of [Data Analysis](#)), there are no upfront charges for study design.
Grant work

If there is a substantial analytical component to the grant that involves biostatistical or epidemiological work, the PI’s grant must include appropriate funding for the data monitoring and analytical work. If the assigned analyst is not in one of the four participating departments, an NIH biosketch of the person assigned to do this work needs to be forwarded to Dr. Shuster. Where RDAP members are listed investigators on a grant, a support letter to the granting agency is available on request.

Role Assignment by FTE on the grant

- 30%+ PI or Co-PI
- 10%-29.9% Key Investigator or Co-PI
- 5%-9.9% Co-Investigator of Key Investigator
- <5% Consultant

Budget Note: There are modest surcharges that apply to participation in grants that vary from department to department. Contact the analytic investigator for more details.

Contact

Dr. Jonathan Shuster
shusterj@ufl.edu
352-294-5968
Room 2247
Clinical and Translational Research Building
2004 Mowry Road
Gainesville, FL 32610

Participant Recruitment

The UF CTSI supports several resources to help facilitate cohort identification and the recruitment of research participants:

- UF Health Integrated Data Repository’s i2b2 – cohort discovery tool for querying a HIPAA-compliant and IRB-approved “Limited Data Set” from the UF Health IDR, which aggregates data from the university’s various clinical, administrative and research information systems, including the Epic electronic medical record system
- HealthStreet – a team of community health workers who connect northeast Florida residents to opportunities to participate in research as well as medical and social services
- UF StudyConnect – a central resource that helps interested individuals learn about and search for UF Health research studies that are enrolling participants
- Research Subject Advocate – guidance and education on ethical principles, regulations and guidelines
• **ResearchMatch.org** – a national registry of volunteers willing to learn about opportunities to participate in research

**Related CTSI Research Services**

• **Community Advisory Board** – feedback on all aspects of community-based projects, including participant recruitment and retention strategies

• **Research Ethics Consulting** – expert consultations on issues including recruitment and informed consent

**Future Resources**

The UF CTSI is collaborating with numerous partners across UF Health to develop additional resources to help facilitate the recruitment and retention of research participants. Related projects underway:

• **UF Consent2Share**

**Community Advisory Board**

The **Community Engagement and Research Program** (CERP) provides consultation to faculty, students and affiliated health care partners and community organizations on designing and conducting health-focused studies and outreach in community settings. The CERP works closely with a Community Advisory Board (CAB) to ensure the perspective of different community stakeholders is considered and incorporated into all community-based research projects.

CAB members represent a wide range of community members including health care providers, school-based representatives and community service groups from Jacksonville and Gainesville. Faculty, students and affiliated health care partners and community organizations can submit protocols to the CERP, which will be shared with CAB members for review and comment.

The CAB, with support from CERP faculty advisors, provides feedback on all aspects of community-based projects including study design, pilot studies, participant recruitment and retention strategies, data collection strategies, interpretation of study findings, and dissemination of findings to the community. The CAB members also can recommend potential research partners in the community.

CTSI Community Research Associates (CRAs) work closely with the CAB along with other community advisors, as needed, to be sure that a community perspective is incorporated into CERP-affiliated studies and projects. The CRAs along with CERP faculty advisors will work with faculty and students to obtain the important perspective and input of CAB members on their projects.

**Contact**

Linda Cottler – lbcottler@ufl.edu; 352-273-5468
Mobeen Rathore – mobeen.rathore@jax.ufl.edu; 904-244-3739
HealthStreet

Through the efforts of our Community Health Workers, we can directly contact individuals in the community and link them to your study based on their primary health concern, medical history, and eligibility criteria. If HealthStreet staff meet community members who fit the eligibility criteria for your study, they will be referred to your coordinator for screening. We will also routinely check our population database for persons who may fit your general criteria and refer them accordingly.

Recruitment through HealthStreet is free, and provides opportunities for University of Florida researchers to learn from and improve the health of diverse and underrepresented populations in North Central Florida. All we ask is that you keep us abreast of the status of each person referred. Were they enrolled in your study? If not, why not? This helps to inform future HealthStreet practices.

Contact Us

http://epidemiology.phhp.ufl.edu/healthstreet/contact-us-3/

ResearchMatch

ResearchMatch is a national volunteer research registry that brings together researchers and willing volunteers who want to get involved in research studies. This national registry, developed by institutions
affiliated with the Clinical and Translational Science Awards (CTSA) program, provides a secure, web-based approach to address a key barrier to advancing research: finding research participants.

**Volunteers**
Volunteers can register for ResearchMatch at researchmatch.org – it only takes 5 to 10 minutes to register. Volunteers of any age, race, ethnicity and health status are invited to join. By registering in ResearchMatch individuals are not registering to participate in any study. They are showing interest to be contacted about studies that may be a good ‘match’ for them. The goal of ResearchMatch is to better connect volunteers with potential study opportunities.

**Researchers**
Researchers interested in using ResearchMatch to do a feasibility analysis for a study or as a possible, complementary recruitment tool for an IRB-approved study can submit a Researcher Interest Form or contact H. Robert Kolb, UF’s institutional liaison for ResearchMatch, at kolbhr@ufl.edu or 352-273-8882.

**Contact**
H. Robert Kolb – kolbhr@ufl.edu, 352-273-8882

**Research Subject Advocate**

The mission of the RSA is to pursue risk reduction and enhancement of health and safety of volunteers in medical research, while seeking to improve the reliability of research outcomes at the University of Florida.

The goal is to promote the safety of individuals who participate in research studies supported by the CTSI, promoting subjects’ understanding of research, and ensuring professional integrity of research teams through education.

**The RSA:** 1) assists investigators to plan for protection of the validity and integrity of their research data, 2) educates all who are involved in research (including investigators, research staff, trainees, and human subjects) about applicable ethical principles, regulations and guidelines related to research, and 3) assists them to apply those principles and regulations during their studies. The RSA is available to answer questions for subjects and for research staff members.

The RSA reviews studies considered by the Scientific Advisory Committee ensuring regulatory and ethical principles for human subject protections, with inclusion of prospective strategies to evaluate each study’s progress, protecting the validity and integrity of the data. The RSA also plays important part in protecting the welfare and safety of research participants by ensuring that Data and Safety Monitoring Plan exists for each study.

**Contact**
H. Robert Kolb (kolbhr@ufl.edu) – (352) 273-8882
UF StudyConnect

In collaboration with the four UF IRBs, UF Health and UF research teams, the UF CTSI maintains and promotes UF StudyConnect as a central resource for listing UF clinical research studies that are seeking volunteers. In addition to being displayed on UF StudyConnect, the study listings appear on UFHealth.org Research Studies & Clinical Trials.

How Studies Get Listed on the Site

As part of its ongoing Study Registry project, the UF CTSI has a team of trained individuals collecting data about human research studies approved by the four UF IRBs since 2008. This team identifies studies that may be enrolling participants for inclusion on StudyConnect. In addition, UF research teams can easily request that listings for IRB-approved studies be added, modified or removed from the site at any time.

The CTSI Study Registry Team gathers the data required for the listings and provides investigators an opportunity to review their study information before publishing it on the site. All that’s required of research teams is to notify the CTSI when they have an actively enrolling study and/ or when enrollment for a study has ended. The CTSI Study Registry Team will update the site accordingly.

To see if your studies are already listed or need to be updated, search for the PI’s last name at http://studyconnect.ctsi.ufl.edu.

How to Add, Modify or Remove Study Listings

UF research teams can easily request that listings for IRB-approved studies be added, modified or removed at any time.

Following are links to the online “add a study” form and one-page guides illustrating how to add and modify or remove study listings and what’s included on UF StudyConnect:

- “ADD A STUDY” form
- How to Add Study Listings
- How to Find and Modify or Remove Study Listings
- UF StudyConnect: An Overview

Additional Resources

- CTSI Participant Recruitment Resources

Contact

To learn more about UF StudyConnect or the CTSI Study Registry project, email the CTSI Study Registry Team at ctsi-ufstudyconnect-l@lists.ufl.edu, and we will respond to your inquiry promptly.
Research Support

Data Analysis

The CTSI Research Design and Analysis Program (RDAP) offers data analysis services for clinical and translational science studies. The service is provided as a collaborative effort among the RDAP and Biostatistics faculty.

Data analysis is available for:

1. Funded grants where the budget includes a component for data analysis by a faculty member who is listed at a level of 10% FTE or higher
2. Other analytic needs for projects that have not made a commitment for RDAP faculty to do the analysis as a Co-Investigator. The presumption is that the data management will have been done in cooperation with RDAP, and that the analysts will receive the data in a form ready for analysis.

Grant work

Depending upon the role, faculty involvement will vary. Faculty appointed to grants at 10% FTE or higher will have major participation in the analyses. Faculty appointed below 10% FTE will have oversight of the RDAP or PI’s Master’s-level biostatistician.

Charges

Senior Consultant Analyst: Advanced statistical consulting services requiring a Ph.D.-level statistician, including experimental design, power and sample-size calculations, specialized analysis, interpretation of results and manuscript review. $150/hr

Consultant Analyst: (Currently not available.) Services requiring a Master’s-level statistician, including experimental design, power and sample-size calculations, interpretation of results, statistical analyses for inclusion into reports and manuscript review. Other services may include Programming: SAS, STATA, SPSS and other programming for data analysis and generation of graphics for reports, and conversion of databases to SAS or SPSS. $80/hr

Before beginning work, the RDAP will provide a cost estimate and verify funding with the principal investigator of the study. RDAP biostatisticians and CTSI staff will be responsible for managing work flow to ensure timely delivery of services, drafting invoices to collect payment for those services and following up to ensure payment is received.

Note: There will be no charge for the first hour of consultation.

Students, post-docs and other young faculty can apply for a voucher covering up to eight hours of consulting support if they have no other support to pay for the charges. APPCI, TL1 and KL2 scholars are especially encouraged to contact Dr. Shuster.
Integrated Data Repository

Supported by the UF CTSI and Shands HealthCare, the Integrated Data Repository (IDR) is a large-scale database that collects and organizes information from across the UF Academic Health Center’s clinical and research enterprises. The IDR enables new research discoveries as well as improvements in the quality and safety of patient care.

**Accessing IDR Data for Research**

- Access to IDR data is provided through the NIH-funded i2b2 tool, which provides researchers access to a HIPAA-compliant and IRB-approved “Limited Data Set.” Faculty researchers can query the i2b2 Limited Data Set to identify cohort counts as they prepare grant proposals, plan clinical trials, and write IRB protocols.
  - [i2b2 Overview](#)
  - [i2b2 10-minute Online Training](#)
  - [i2b2 Registration](#)
Faculty researchers can also apply for IRB approval to obtain more detailed data from the IDR for further research analysis.

Learn More

- CTSI Resource Spotlight: Integrated Data Repository
- IDR Website
- Background on Creation of the IDR

Contact

Email the IDR Team at i2b2support@ahc.ufl.edu.

Quality Assurance Services

Quality Assurance (QA) is the systematic monitoring and evaluation of the various aspects of a project, service or facility to maximize the probability that minimum standards of quality are being attained by the given process.

CTSI Quality Assurance Services was set up in 2009 and specializes in providing Good Manufacturing Practice (GMP) and Good Laboratory Practice (GLP) Quality Assurance services to investigators. Services include:

- Consultation: General advice and assistance with GMP and GLP compliance issues.
- Auditing: Quality system audits.
- SOP Development: Assistance in development of Standard Operation Procedures (SOP) to meet regulatory and project-specific requirements.
- Batch Releases: Audit of batch manufacturing records and batch disposition for clinical trial materials.
- Training: Introductory presentations about GLP and GMP regulations.

Contact

Corinne R. Abernathy (cabernat@ufl.edu) – (352) 273-5133
Rebecca L. Wichman (rwichman@ufl.edu) – (352) 273-5132

REDCap

REDCap (Research Electronic Data Capture) is a secure, Web-based application designed to support traditional case report form data capture for your research studies. It is provided at no cost for use with
any research project. For those with funding, fee-based configuration services are also available to jump-start a given project.

REDCap was originally developed at Vanderbilt University. The University of Florida and more than 195 other partners now comprise the REDCap Consortium that continues to develop and support the software. Read more about REDCap’s features at the consortium Web site at http://project-redcap.org/.

Using REDCap’s streamlined process for rapidly developing databases, users create a project, define and organize the data they wish to capture, build the related forms and associate them with study events. Other features include automated export procedures for seamless data downloads to Excel and common statistical packages (SPSS, SAS, Stata, R), as well as a built-in project calendar, a scheduling module, ad hoc reporting tools, and advanced features, such as branching logic, file uploading, and calculated fields.

Login to or register for REDCap

Is REDCap right for my study?

This is a question we frequently receive. REDCap supports prospective and retrospective studies and multicenter clinical trials very well. It has been used across a broad spectrum of research, from bench studies to community-based research. It works best for research projects that have a limited number of well defined time points; it is not optimized for use in creating registries.

REDCap Support Services provides free consultation for investigators with mature projects. We will help you determine if REDCap is a ‘good fit’ for your project and can explain in detail the support and configuration services that are available. For a no-cost consultation, contact the REDCap Support Services Team at CTSI-REDCAP-SUPPORT-L@lists.ufl.edu.

Training

Training is available through a variety of mechanisms here at the University of Florida; trainings are announced through the REDCap-all Listserv that all registered users are subscribed to.

On-line Training Videos are provided by the REDCap Consortium and available to all. These videos provide users the necessary information to get started as well as a standing reference library to refer to while creating your project.

REDCap 101, Introductory Class Monthly overview of REDCap project creation basics, this hands-off class covers the essentials of REDCap project creation: Defining data elements and timepoints, building forms and using data validation, previewing and revising the project, assigning user rights, and moving the project to production. We will also look at the calendar feature, creating reports, and the file repository and data export functions.

Registration for REDCap training is available through HSC Training.

Configuration Service
REDCap software and end-user support are provided at no-cost to UF investigators. Investigators have no-cost access to REDCap, training and end-user support, but must learn details of project development and build their own projects.

While this model serves many investigators very well — especially young investigators with pilot studies — early on we identified the need to provide a more complete service for funded investigators. To that end, we offer a REDCap configuration service that can develop and deliver a fully operational REDCap project to you based on your protocol, case report forms and/or time and events schedule.

Collectively, the REDCap Support Services team has more than 39 years experience in research support, clinical trials management and informatics. Use of our configuration service saves investigators time, reduces the learning curve, and ensures that best practices are applied during the development of their project. Costs for the configuration are very competitive for both the UF community and external clients, and inquiries are encouraged. With two weeks notice, quotes can be provided for grant submissions. For more details, contact the REDCap Support Services Team at CTSI-REDCAP-SUPPORT-L@lists.ufl.edu.

Support Services

The REDCap Support Services Team provides end-user support, project configuration and training for both University of Florida Investigators and their staff as well as external clients. E-mail and phone support is available M-F from 8-5PM, excluding holidays, with 48 hour response time for inquires at other times.

Support Contacts

REDCap Support Services Team Listserv (CTSI-REDCAP-SUPPORT-L@lists.ufl.edu)
Corinne Abernathy (cabernat@ufl.edu) – 352-273-5133
Taryn Stoffs (tls@ufl.edu) – 352-294-5206

Regulatory Assistance

Regulatory assistance is available to help researchers understand and meet the many regulatory and compliance requirements. Assistance is available for:

- Determination of product classification (i.e., drug, device, combination product, biologic).
- Applicability of an IND or IDE.
- Assistance with submission of an IND or IDE application.
- Preparation, coordination, facilitation, and attendance at FDA meetings.
- Preparation for regulatory support during FDA inspections of investigator sponsored clinical trials.
- Provide information about new guidance documents, inspection trends, inspection actions and new regulatory actions taken by FDA relating to clinical trials.

We work closely with the Research Project Navigators to identify projects that may need IND or IDE assistance; to clarify and provide support the FDA mandated obligations of sponsor/investigators.

We also work with with sponsor/investigators to facilitate pre-IND, IND or IDE meetings with the FDA. RAP provides guidance to the investigator during the preparation process (slides and document preparation, proper inquiry format and process, subject matter preparation and communication) and will attend FDA meetings as facilitator, when requested.

Contact

Wajeeh Bajwa (bajwa@ufl.edu) – (352) 273-8702

Research Ethics Consulting

The CTSI Research Ethics Consult Service provides investigators and other research personnel with expert consultation on ethical issues in the design and conduct of biomedical research. Research ethics consultation services are available for the following issues or others that may arise:

- Ethical factors in protocol design (clinical equipoise, randomization, placebo controls, blinding, inclusion / exclusion criteria, endpoints, stopping rules, etc.)
- Participant selection, recruitment, retention, withdrawal and follow-up
- Informed consent, refusal, and waivers of informed consent
- Therapeutic misconception
- Studies involving vulnerable populations
- Research in emergency settings
- Conflicts of interest
- Data safety and monitoring
- Research participant privacy and confidentiality issues
- Barriers and motivations to participate in research protocols
- Research subject advocacy
- Special issues in genetics research
- Research integrity
• Research in cultures, communities, or groups
• Disclosure of results
• Disclosure and reporting of findings unrelated to study questions

The best time to ask for research ethics consultation is early in the conception of the project, rather than as an afterthought before submission of a grant or for IRB review. Of course, unexpected issues may arise at any point in the process in a protocol, and ethical issues may arise as a consequence of new information during its execution.

Contact

H. Robert Kolb (kolbhr@ufl.edu) – (352) 273-8882
Wajeeh Bajwa (bajwa@ufl.edu) – (352) 273-8702

UF CTSI Info Hub

Download fliers about the resources and activities of CTSI programs. Each flier includes contact information.

Can’t find what you’re looking for? Give us a call at 352-273-8700 or email us at info@ctsi.ufl.edu.

Biomedical Informatics Program

Program Fliers:

• Program Overview
• Clinical and Translational Science-IT
• UF Health Integrated Data Repository
• UF StudyConnect Overview
• UF StudyConnect: How to Add Study Listings
• UF StudyConnect: How to Find and Modify or Remove Study Listings
• VIVO

Also see: Program Webpage, UF StudyConnect, VIVO at UF

Communications Research Program

Program Flier:

• Program Overview
Also see: Program Webpage

Community Engagement and Research Program

Program Fliers:

- Program Overview
- North Florida Pediatric Community Research Network

Also see: Program Webpage, HealthStreet Webpage

Implementation Science Program

- Program Overview
- Program Webpage
- Health IMPACTS for Florida Webpage

Participant and Clinical Interactions Program

Program Fliers:

- Program Overview
- UF Clinical Research Center
- Dental CRU
- Pain CRU

Also see: Program Webpage, 12 CRU Webpages

Personalized Medicine Program

Program Flier:

- Program Overview

Also see: Program Webpage

Pilot and Collaborative Projects Program

Program Resources:

- CTSI Seminar Series Video Archive

Also see: Program Webpage
Regulatory Knowledge and Research Support Program

Program Fliers:

- Program Overview
- REDCap

Also see: Program Webpage

Research Design and Analysis Program

Program Fliers:

- Program Overview
- Study Design
- Data Analysis
- Qualitative Research Collaboration

Also see: Program Webpage

Training and Professional Development Program

Program Fliers:

- Program Overview
- Training and Research Academy for Clinical and Translational Science
- KL2 Multidisciplinary Program for Junior Faculty
- Opportunities for Ph.D. Students
- CTSI Academy of Research Excellence Master Certificate Program
- CTSI Academy of Research Excellence Research Coordinator Program

Also see: Program Webpage

Translational Technologies and Resources Program

Program Fliers:

- Program Overview
- Biobehavioral Core
• Biomedical Mass Spectrometry Core
• CTSI Biorepository
• CTSI Human Imaging Core
• Genotyping Core
• Metabolomics Core/ SECIM

Also see: Program Webpage