

Elements of the IRB Process



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College of Research

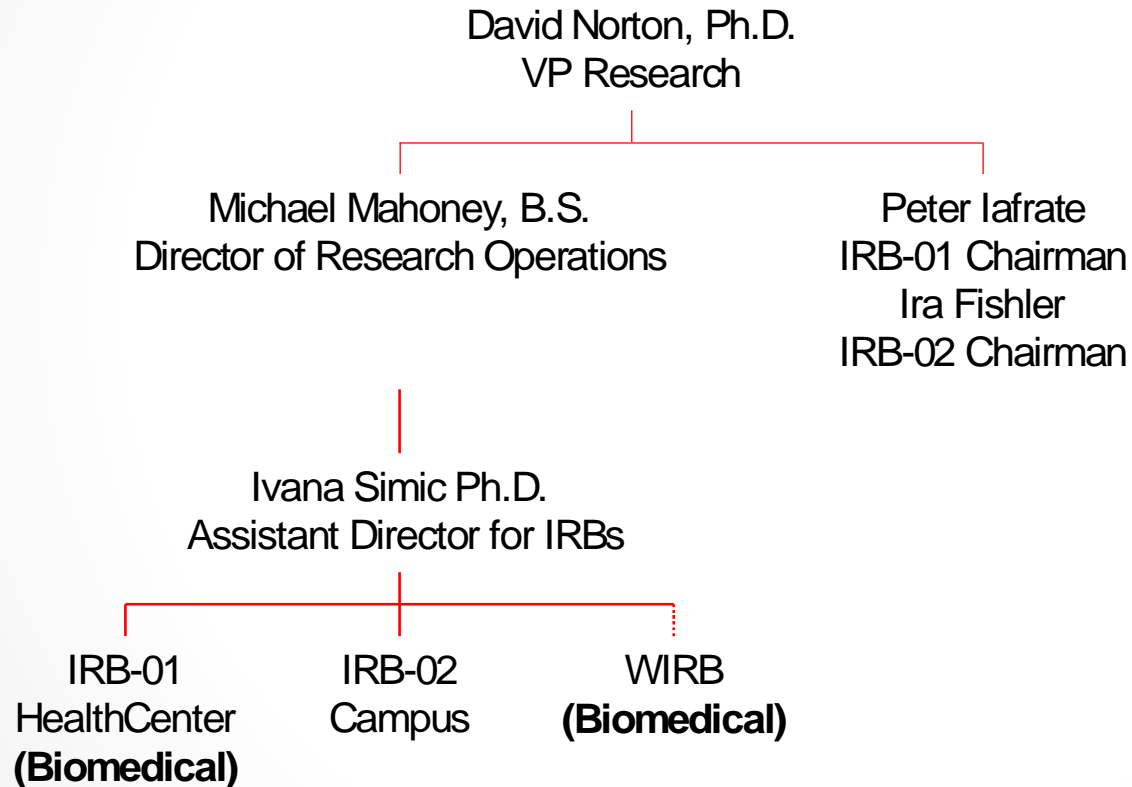
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Objectives

- Research at UF (IRB, ancillary committees/offices)
- Why is Research Regulated and Regulatory Frameworks
- What Does It Mean to be Engaged in Research
- Exemptions
- Single IRB/Collaborative Research

College of Research Structure



UF IRBs

- **IRB-01:** (Biomedical) Health Science Center, Shands, (Gainesville and Jacksonville), VAMC, affiliates (Sacred Heart, Halifax)
 - IRB-01 also serves as the Privacy Board to ensure HIPAA compliance when it comes to approving alternations and/or waivers of HIPAA authorization.
- **IRB-02:** (Social/Behavioral)
 - No PHI
 - No VA
 - No tissue
 - No nurses
 - No medical devices/drugs

Commercial IRBs

- Western Institutional Review Board (WIRB) (Biomedical)
 - Industry authored, FDA regulated, multicenter clinical trials, with a PI from COM, must submit to WIRB (PI submits directly to WIRB)
 - Federally funded studies that use WIRB must be ceded* to WIRB via a local myIRB submission.
- Advarra
 - Funded studies (federal, industry, foundations) and must be ceded* to Advarra via a local myIRB submission.

Regulations

- Federal Regulations – multiple regulatory frameworks that sometimes apply simultaneously
 - HSS
 - FDA
 - HIPAA, etc.
- State Laws: FL Statutes
- University Policies
- IRB Policies
- ❖ Among other things, **Federal Regulations** define **research** and **human subject**, structure of IRBs, categories of **exemption**, regulatory oversight for collaborative research, criteria for approval, and much more.
- ❖ **Local rules** govern implementation of regulations in a specific research context.

Layers of Responsibility

Institution

- Federalwide assurance (FWA: Any institution engaged in Federally-supported human subjects research must commit itself in writing to the protection of those subjects.
 - As a matter of institutional policy UF applies its FWA to all human subject research, regardless of funding.
- UF is responsible for meeting the conditions of its FWA -IO is the signatory official on our FWA.

IRB

- Implementing protection of human research subjects by reviewing, approving, and monitoring research according to regulations.
 - IRB's mission is protection of rights and welfare of human research subjects

Investigator

- Responsible for complying with all Federal, State and Local regulations.
- The best way to meet this responsibility is to be knowledgeable about the rules at your institution and to be very involved in running of the study.

Criteria for IRB Approval

- (1) Risks to subjects are minimized
- (2) Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result.
- (3) Selection of subjects is equitable.
- (4) Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by, [§46.116](#).
- (5) Informed consent will be appropriately documented or appropriately waived in accordance with [§46.117](#).
- (6) When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.
- (7) When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

Research Definition

- *Research* means a **systematic** investigation, including research development, testing, and evaluation, designed to develop or contribute to **generalizable** knowledge. 45CFR46 102 (I)

Human Subject Definition

- *Human subject* means a living individual about whom an investigator (whether professional or student) conducting research:
 - (i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or
 - (ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens. 45CFR46 102 e(1)

What does engagement in human subject research mean?

When an institution is *engaged* in non-exempt human subjects research that is conducted or supported by the US Department of Health and Human Services (HHS), it must satisfy HHS regulatory requirements related to holding an assurance of compliance and certifying institutional review board (IRB) review and approval

The screenshot shows the HHS.gov website for the Office for Human Research Protections. The page title is "Engagement of Institutions in Human Subjects Research (2008)". A navigation menu includes "About OHRP", "Regulations, Policy & Guidance", "Education & Outreach", "Compliance & Reporting", "News", "Register IRBs & Obtain FWAs", "SACHRP Committee", and "International". The main content area features a sidebar with "Belmont Report", "Regulations", "Decision Charts", and "Guidance". The "Guidance" section is expanded to show "OHRP Guidance on COVID-19", "OHRP Guidance on Elimination of IRB Review of Research Applications and Proposals", and "OHRP Guidance on Maintaining Consistency Regarding the". The main text area contains a "NOTE: This guidance document replaces two previous OHRP guidance documents: (1) 'Engagement of Institutions in Research' (January 26, 1999); and (2) 'Engagement of Pharmaceutical Companies in HHS-Supported Research (PDF)' (December 23, 1999)." and a paragraph explaining that the guidance represents OHRP's current thinking and should be viewed as recommendations unless specific regulatory requirements are cited.

Examples of activities that engage institutions in human subjects research

Being the primary awardee for a federal grant that supports human subjects research

Intervening for research purposes with any human subjects of the research by performing invasive or noninvasive procedures or manipulating the environment

Interacting for research purposes with any human subject of the research

Obtaining the informed consent of human subjects for the research

Obtaining for research purposes identifiable private information or identifiable biological specimens from any source for the research

Examples of activities that do not engage institutions in research

Institutions

- Whose employees or agents
 - perform commercial or other services for investigators
 - inform prospective subjects about the availability of the research
 - provide prospective subjects with information about the research but do not obtain subjects' consent for the research or act as representatives of the investigators;
 - provide prospective subjects with information about contacting investigators for information or enrollment
 - seek or obtain the prospective subjects' permission for investigators to contact them
 - release to investigators at another institution identifiable private information or identifiable biological specimens pertaining to the subjects of the research
 - obtain coded private information or human biological specimens from another institution involved in the research that retains a link to individually identifying information (such as name or social security number); and are **unable** to readily ascertain the identity of the subjects to whom the coded information or specimens
- That permit use of their facilities for intervention or interaction with subjects by investigators from another institution

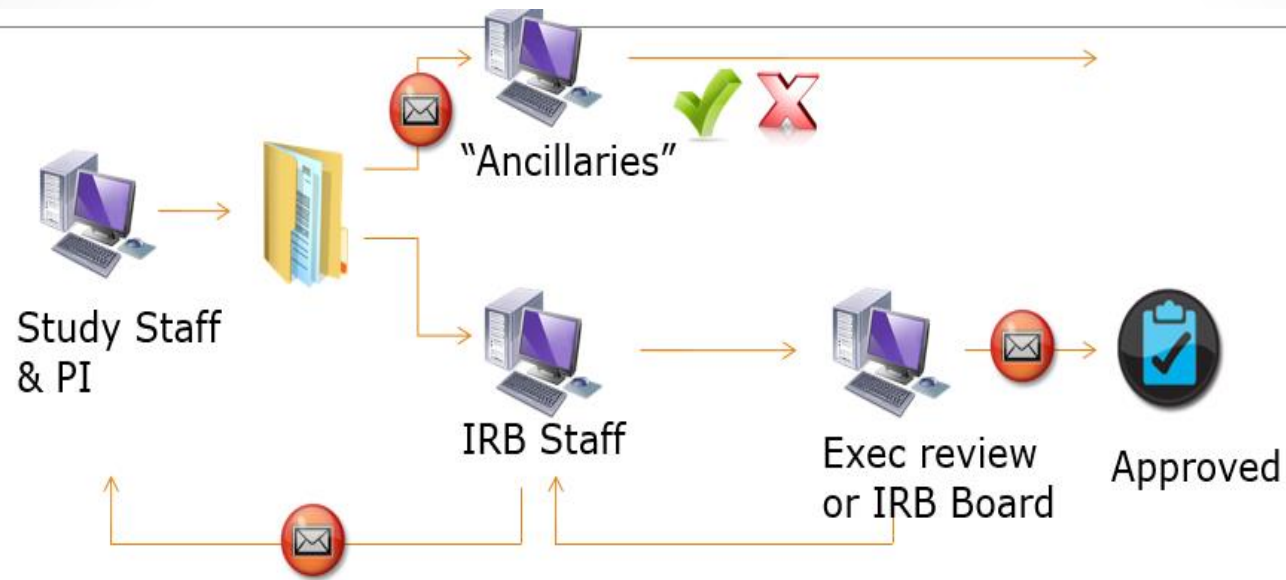
IRB Submission Process

- myIRB registration
- Training IRB803
 - Training exception for non-human research
- Completion of myIRB electronic application

Review Types

- Non-Human
- Data/Chart Review
- Banking Only
- Exempt
- Expedited
- Full Board

Workflow



Ancillary Committees/Reviews

- myIRB is the hub for ancillary reviews (OCR coverage analysis, radiation safety, conflict of interest (personal and **institutional**), institutional **biosafety**, **SRMC**, **COVID-19**, EH&S, International, etc).
 - **Hard stop** vs. Concurrent review
- Of note: Even if criteria for IRB approval are met per 45CFR46, a study can't be approved until all relevant ancillary reviews are complete and submitted.
 - **Investigators must follow up directly with the relevant ancillary offices about the status of the review.**

Exemptions from the Regs: What Are Exemptions and Who Makes Exempt Determinations?

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Varieties of Exemptions

- Exempt because a study does not meet the definition of '**Research**' -- **Quality Improvement**
- Exempt because a study does not meet the definition of '**Human Subject**' research – **Non-Human**
- Exempt because a study it falls under one of the **exempt categories** described in the Common Rule.

Who Makes Exemptions?

- Per the university policy, **UF IRBs make exempt determinations, not the PI** (non-human and exempt based on a category)
 - The policy is grounded in OHRP guidance on non-human research involving coded and de-identified tissue and pragmatic considerations regarding expertise required to assign exempt categories.

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Who Should Determine Whether Human Subjects are Involved in Research

OHRP recommends that institutions have policies in place that designate the individual or entity authorized to determine whether research involving coded private information or specimens constitutes human subjects research. The person(s) authorized to make the determination should be knowledgeable about the human subject protection regulations. In addition, the institution should ensure the appropriate communication of such a policy to all investigators. OHRP recommends that investigators not be given the authority to make an independent determination that research involving coded private information or specimens does not involve human subjects.

Who Makes Exemptions?

- At UF, a trained Board Member makes exempt/non-human determinations
- Median approval time for exempt 12 days (77% of that time the study is with the study staff)

Non-Human

- NO interventions or interactions with a living person
 - Anonymous or coded samples or data only; if data/samples are coded, a Confidentiality Agreement needs to be in place between a recipient and supplier.
 - The study does NOT involve an investigational device that uses human specimens
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- Approval: 1 time

Exempt

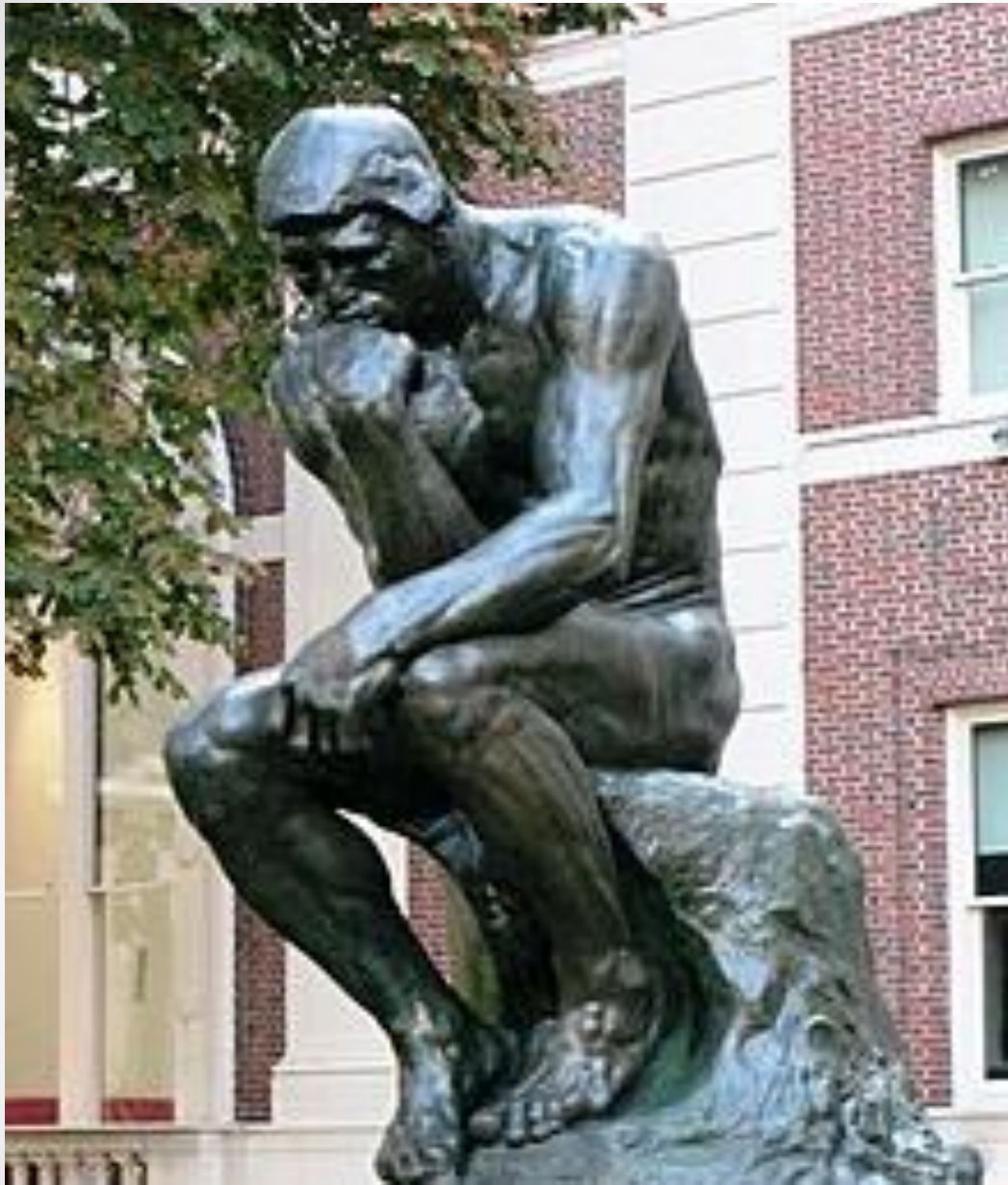
- Survey studies, educational studies, or benign behavioral interventions
- Other studies that fits one of the 8 exempt categories (6 at UF since categories 7 and 8 (Broad consent) are not implemented)
- **Exempt Data/Chart Reviews:** secondary research, from medical records (or research records).
- Approval: 1 time

How to Submit a Chart Review?

- Choose this review type if you are looking at data from medical records, or specimens or for any secondary research.
- Can be retrospective or prospective
- Can involve PHI
- Approved as exempt unless review involves **identifiable tissue, then expedited**
- See mechanics and the content of submission
 - <https://irb.ufl.edu/wp-content/uploads/Chart-Review-Submission-Guide.pdf>
 - <https://irb.ufl.edu/wp-content/uploads/Data-Chart-Review-Brown-Bag-slides-11.18.20.pdf>

Typical Issues with Chart Reviews

- Indicating the time frame for data abstraction
 - The need for and justifying HIPAA waiver for prospective chart reviews when one sees the patients whose records are under study
- De-identification plan (de-identified means de-identified)
- Clinical Relationship requirement to access medical records (Privacy requirement)
- Consistency between the forms indicating data collected and HIPAA waiver scope (PHI indicated as collected under the waiver)
- Don't submit quality only projects as chart reviews.



Questions

Resources

- [Investigator Guidelines](#)
- [MyIRB](#)
- [Researcher Manual](#)
- [Research Roles at UF/PI Qualifications](#)
- [Training](#)
- [IRB Website](#)
- [Contact us](#)

sIRB, Ceding Review, Reliance

- **Ceding** of a study – an institution's relying on a **single IRB of record** for regulatory oversight of a study.
 - Institutions still review local context matters by leveraging local IRB offices
- Regulations require documenting reliance
- **IRB Authorization Agreement (IAA)** is a legal document between institutions that have an FWA that documents and specifies the terms of reliance between institutions.

NIH Single IRB Policy

- In effect since January 25th 2018
- Applies to **domestic** sites of **NIH funded** multisite studies where each site conducts the **same protocol** involving **non-exempt** human subjects research.
- Does not apply to approved projects before 1/25/2018 (but it does affect competitive renewals)

Revised Common Rule

- In effect since January 20th 2020
- Any institution **located in the United States** that is **engaged** in **cooperative research** must rely upon approval by a single IRB for that portion of the research that is conducted in the United States.
- Does not apply to studies approved by an IRB before January 20th 2020.
 - Common rule exceptions are specified in 45 CFR 46.114(b)(2)(ii) which allows Federal departments and agencies supporting or conducting the research to determine and document that the use of a single IRB is not appropriate for the particular context

SMART IRB IAA

- SMART IRB IAA – a common non-negotiable master agreement.
 - SMART Joinder – a document the signing of which by an Institutional Official evidences that the institution accepts the terms specified in the Master Agreement
 - Study specific checklists, flexibility agreements
- UF uses SMART Master Reliance Agreement, along with 900 other institutions, but **we are not using the SMART Tracking system**. We use myIRB for this purpose.
- The sIRB determines which IAA will be used. When UF is sIRB, we use SMART IAA.

Ceding Review to a sIRB: UF Process

What research is eligible for ceding to a sIRB?

- Studies for which use of an sIRB is a requirement of the sponsor or funding agency for participation in the study
- Domestic Multisite or collaborative, non-exempt research studies.
 - UF will consider ceding review to a sIRB for a study meeting the above criteria, provided that the IRB in question **has sufficient standards of review**

Eligible For Ceding to a sIRB?

- **Exempt studies (including chart reviews and non-human research)**
- Industry or other non-federally funded studies where sponsor does not require sIRB review.
- Research on UF's Student Athletes
- Research involving the Alachua County School System
- Research involving fetal tissue, and embryonic stem cells
- Review of proposed community consultation plan for studies involving exception from informed consent (EFIC)
- Research studies proposing to defer IRB oversight to an IRB that is not sufficiently qualified (AAHRPP accredited or having equivalent standards to accredited organizations)

Commercial IRBs

- WIRB
- Advarra
- Institutional policy on using commercial IRBs
 - **Industry** authored/sponsored, FDA regulated trials from COM faculty submitted directly to WIRB under the Master Service Agreement
 - **Federally** funded studies ceded to WIRB or Advarra by using SMART IAA (local IRB submission required)
 - Sponsor required sIRB review -- ceded to WIRB or Advarra by using SMART IAA (documentation about sponsor requirement must be submitted with the CED submission in myIRB)

UF Ceding Process - Overview

- When the overall protocol is approved by sIRB create New Ceded Study in myIRB
 - Notice a different nomenclature CED00000xx
 - SmartForms (SF) have rudimentary branching (enough to assess local context issues and trigger relevant ancillaries)
 - If the main study is not approved and IAA needs to be negotiated submitting a CED study is a way to put IAA through the system
- New SmartForm sIRB: IRB of Record Site for Ceded Review
 - The name of the Institution, Overall PI and Coordinator, and IRB Contact information.
 - Upload study specific document(s) requiring institutional sign off to the effect that the institution is willing to cede review
 - If an IAA other than SMART is used, upload executed copy here.
 - The approval letter for the overall study at the institution providing regulatory oversight

Process

- sIRB determines the consent template to be used.
- Local UF information is either captured in the editable portions of the consent (which is usually highlighted or tracked), or there is a consent addendum, or there is a checklist with the local language that the IRB of record used to produce final consent.
 - Local information includes subject cost/injury language, HURRC, HSP, etc, any applicable state laws.
- The study team will work with all the ancillaries (which get myIRB notifications prompting them to review), and insert all necessary language in the consent form.
 - Unlike our regular practice, we'll not be entering the ancillary language into the consent for you as we are not finalizing documents.

- When local context review is done and all ancillaries are approved, **the study is acknowledged** and in the state of **Awaiting Site Materials**.
- PI submits Acknowledgement Letter to the overall PI who initiates a revision at the IRB of record to add UF as a site.
- Once the revision is approved, a coordinator/PI submits the letter of approval with the approved documents to UF IRB via 'Submit IRB of Record Correspondence'.
- The UF IRB approves ceding of the study.
 - OR if the IRB of record has concerns about local context issues, they might request changes which are also submitted by using 'Submit IRB of Record Correspondence'.
 - The study team addresses issues and the study is acknowledged again, after which UF PI sends the acknowledgment letter to the overall PI who follows up on the submitted revision to the IRB of record.

Q: What are the relying PI responsibilities?

- UF PI has increased responsibilities
- Staying up-to-date with the IRB of record's determinations/communications.
- Communicating institutional determinations to the overall PI.
- Being knowledgeable about the IRB of record's policies and procedures (especially regarding event reporting).
- Ensuring that local institutional rules are observed (e.g. recruitment)

Post Approval

- Revisions
 - Only changes in the local context

6.0 * Please indicate if your revision includes any of the following (choose all that apply):

- Change in PI
- Change in location where study procedures will be performed
- Change in frequency or addition or removal of study procedures
- Changes in the use or location of radiographic procedures, radiation or radioactive materials
- Addition or removal of conflict of interest involving study staff or the institution
- Addition or change to NCT registration for ClinicalTrials.gov
- Addition or changes involving gene therapy or use of Recombinant DNA molecules
- Addition of CTSI resources
- Changes to funding
- None of the above**

8.0 Does this revision involve changes to any of the following:

- Pregnancy testing for minors that is not standard of care
- Research on UF athletes
- Collection of SSN**
- The collection of information pertaining to abuse (e.g., abuse involving children, the elderly, or the disabled)
- Consenting minors
- Use of social media advertising
- Enrolling pregnant minors
- HIV Testing
- Use of an LAR
- Use of cold calls to recruit subjects
- Research on fetuses, fetal tissue, or embryonic stem cells

- CRs: (Current Protocol, ICF, and Approval letter from the IRB of record)
- Reportable Events:
 - Serious or continuing local non-compliance
 - Local Unanticipated problems and AEs that are serious, unexpected, and related/more likely than not caused by study intervention/participation

UF serving as a sIRB

UF process
UFResearch

The Initial Process

- PI and staff meet with the IRB Reliance Team in the study planning phase
 - [sIRB Intake Form on the IRB Website](#)
- IAA status (SMART, UF Master Agreement)
- The Reliance Team sets parameters.
 - Study team is the link between the IRB and all the sites. The team must be experienced and highly organized and have systems in place for reporting events and ensuring that CR is submitted in time. Implications of study expiring affect all sites.
 - PI responsibilities – PI responsible for all sites

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Approval

- Study is approved as sIRB but without any sites; sites are added with revisions (this is done via exec review)
 - Study Title and Staff SF declares that the submission is sIRB (UF serves as IRB of Record label is on Study Workspace)
 - Nomenclature the same as other IRB studies (IRBYEARNUMBER)
 - **UF core consent** is used with site addenda.
 - Each **site addendum** has the local institution's logo and captures the local context items; initially only UF addendum is submitted.

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Revisions to Add pSites

- Revisions to add sites new project type
 - can exist concurrently with other revisions to the main study.
 - *Information needed*
 - *Site information (PI, Coordinator, local IRB Contact Info)*
 - *Attach Exhibit Cs/Smart Acknowledgments (signed by the institutional official or his designee)*
 - *Local Site ICF Addendum*

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Revisions CRs, AEs

- As Revisions and Continuing Reviews are approved by the UF IRB, the overall PI is responsible for providing a copy of the UF IRB approval letter and any applicable documents (i.e. stamped consent, protocol, etc.) to the local PI(s) at the relying site(s).
 - Plan CRs so they do not interfere with Revisions and vice versa (revisions and CRs can't be in the system at the same time)
- The main PI, submits reportable events received by the relying site(s) to the UF IRB per UF reporting policy.
- Acknowledged AEs have to be communicated to the local sites by the main PI.

Questions

sIRB – different kind of work.



UF Research