Study Startup

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Study Startup Steps

1st Step

• Confidentiality Agreement (CDA)
• Feasibility

2nd Step

• Contract to DSP via UIRIS
• Create internal and external budget

3rd Step done concurrently w/2nd Step

• Start IRB application
• Submit to committees

4th Step done concurrently w/2nd Step

• Consent/Record of Consent
• Financial disclosures
• I-Cart application (Epic, CRU, Redcap)
• FDA 1572
• Clinicaltrials.gov

Steps 2, 3 and 4 can be done at the same time!
Step 1

• Confidentiality Agreement (CDA)
• Feasibility

*These steps will only be done for an industry study.

**NIH studies have a letter of support that they submit with the grant if they are collaborating with another academic center.
Confidentiality Agreement (CDA): This is a legal agreement between the University of Iowa and the study sponsor that outlines what information the parties wish to share with one another, but wish to restrict from wider use.

A CDA protects you, your PI and the university from future litigation, thus it is imperative that it be routed through the proper channels for review.
Step 1 part A: CDA (continued)

- A CDA MUST be completed before any study start up activities occur.
- NIH studies typically will not have this.
- Also sometimes referred to as a Non-Disclosure Agreement (NDA)

NEVER HAVE YOUR PI SIGN THIS FORM AND SEND IT BACK TO THE SPONSOR!

Always route the form to DSP
Step 1 part A: CDA (continued)

- CDAs are routed to the Division of Sponsored Programs (DSP) through the UIRIS system on a Non-Monetary routing form.
- To create and route a form, go to: https://uiris.uiowa.edu and log in with your HawkID and password.
- The form will be routed to the PI and Division of Sponsored Programs (DSP) at minimum. Allow at least 5 business days for this process to be completed.
The Division of Sponsored Programs offers a range of services for faculty, staff, and students seeking external funding for research, training, service, and other scholarly and creative endeavors that enrich The University and its broad and far-reaching communities. DSP assists with the search for external funding sources; reviews and approves grant applications; negotiates award stipulations; facilitates post-award project management; and monitors and advises on issues of regulatory compliance.

Learn more about DSP here: http://dsp.research.uiowa.edu/

UI Routing Policy: https://dsp.research.uiowa.edu/ui-routing-policy-procedure
Step 1 part B: Feasibility

- The sponsor will also assess the feasibility of conducting the study at our site. This may be done concurrently with the CDA.

- Sponsors often ask us to complete a feasibility questionnaire. This gives them an idea if our site has access to a population that will yield the enrollment they desire, and if we have adequate facilities, equipment and personnel to complete the study.
Your team must carefully study the protocol and other materials provided by the sponsor at this point to determine whether you are capable of meeting the study’s requirements. There should be clear, honest communication between the PI and study team members about what they are able to do.
Step 1 part B (continued): Feasibility

Feasibility visit: Frequently, study sponsors or their representatives will visit our site to meet the study team and view our facilities and equipment.

- This is our opportunity to make a positive impression, as the sponsor is still determining whether they want to fund the research at this site.

- Normally, sponsors or their representative will want to see any areas that this study will utilize. This could include the Clinical Research Unit, Investigational Drug Service, and any other areas such as x-ray or MRI. You may need to make appointments to see these specific areas.

- If the sponsor knows our site and/or the PI/study team well, a feasibility visit may not be required.
As a recap....

What form do you submit through UIRIS?

Confidentiality agreement (CDA)

How long does that form take to complete?

Minimum 5 days

Will you need to communicate to your sponsor this time frame?

YES!
Congratulations!
Your site has been selected!
First: Get Organized!

- Study startup is a long, labor-intensive process that can take months.
- You will be filling out many, many different forms and working with many different people.

Before you start, create the following:

- A checklist of forms to be completed
- A list of contact info for everyone involved with the study
- Electronic and hard copy folders for study documents
- Gather the study information you will need for the IRB application (recruiting, where study procedures will take place, study team members, etc)
- If this is an industry study, you will need specific documents from the sponsor (IDE, IND, NCT, lab manuals, G-12, etc)
Save...save...save!!!

Make sure to save electronic copies of **EVERYTHING** in a secure location.

- Shared drive folders
- Organize your folders so you and others can find things easily!
- You will also need paper copies of many of these forms for your reg binder. Some coordinators prefer to keep copies of all forms.
- **DO NOT** save any study forms on your desktop!!
Step 2, 3 and 4 can be done at the same time!

2nd Step
- Route the contract to DSP via UIRIS
- Create internal and external budget

Step 3 done concurrently w/2nd Step
- Start IRB application
- Submit to committees
- I-Cart application

Step 4 done concurrently w/2nd Step
- Consent/Record of Consent
- Financial disclosures
- FDA 1572
- ClinicalTrials.gov
The sponsor will send you a study contract or Clinical Trial Agreement (CTA).

A Clinical Trial Agreement (CTA) is a legally binding agreement that manages the relationship between the sponsor that may be providing the study drug or device, the financial support and/or proprietary information and the institution that may be providing data and/or results, publication, input into further intellectual property.

It is important to have a CTA for allocation of risk, responsibility, funds, obligations, and the protection of academic, legal, intellectual property and integrity.
This Clinical Study Agreement is made and entered into as the date signed by both parties below (the “Effective Date” (“Sponsor”) and University of Iowa 200 Hawkins Drive Iowa City, IA 52242, (“Institution”) and PI., a physician licensed to practice medicine in the state of Iowa (“Investigator”), have agreed to the following terms and conditions (“Agreement”) with respect to the conduct of the clinical research study identified below.

Whereas, Institution employs or provides study staff and facilities or other services to conduct clinical research studies; and

Whereas, Sponsor is engaged in the research and development, manufacture and marketing of medical devices, software, firmware and other intellectual property defined herein; and is developing the (“Study Device”) to provide a general direction for further standard of care evaluation and testing of patients with or without symptoms

Whereas, Principal Investigator is qualified by training and experience to conduct clinical studies;

Whereas, Institution, Principal Investigator and Sponsor desire to enter into this Agreement to provide the terms and conditions upon which Sponsor may engage Institution and Principal Investigator to conduct research pursuant to this Clinical Study Agreement and Protocol (as defined below) specifying the details of the research services described herein and the related terms and conditions; and

Whereas, the Clinical Study (as defined below) contemplated by this Agreement is of mutual interest and benefit to Institution and Sponsor, and will further Institution's instructional, basic science, clinical science and fundamental research objectives and missions.
Step 2: Contract and budget

- The contract must be routed to DSP through UIRIS.
- The contract negotiation process can be lengthy, taking weeks or even months. It is very important to route the contract as soon as you receive it to minimize delays.
- Use a Monetary Routing Form
- To create and route a form, go to: https://uiris.uiowa.edu and log in with your HawkID and password.

https://dsp.research.uiowa.edu/
Step 2: Contract and budget

- The sponsor will send you a proposed budget, usually at the same time as the contract.
- Review the budget VERY carefully as it is in the sponsor’s best interest to offer us as little as possible, and their offer may not cover our costs.
- Use UIHC standard research pricing to help you determine how much you should ask the sponsor to pay for services.
- If you are using the Clinical Research Unit, you can submit your I-CART request to help with your budget.
Step 2: Budget

- **Research Pricing**
  - Research pricing and coding tools for radiology, cardiology, laboratory procedures and other hospital services can be found here:
    - [https://thepoint.healthcare.uiowa.edu/sites/Compliance/researchbilling/default.aspx](https://thepoint.healthcare.uiowa.edu/sites/Compliance/researchbilling/default.aspx)
  - CRU I-CART information and log in can be found here:
    - [https://icts.uiowa.edu/investigators/i-cart-information](https://icts.uiowa.edu/investigators/i-cart-information)
Step 3: IRB application and submission to committees

- Start IRB application
- Submit to committees
- I-CART request
Step 3: IRB application and submission to committees

- Determine which **IRB** is best or required for your study
  - IRB-01 Biomedical
  - IRB-02 Behavioral/Social Science
  - IRB-03 VAHCS
  - IRB-04 Department of Defense funded studies (being developed)
  - External IRB such as WIRB, StrokeNet, Great Plains Collaborative etc.
  - sIRB model
Step 3: IRB application and submission to committees

- Begin your HawkIRB application.
  - You must submit the study first to HawkIRB even if you are using WIRB or another external IRB.
  - The HawkIRB application will automatically determine which committee approvals are required for your study.

https://hso.research.uiowa.edu/hawkirb-1
Step 3: IRB application and submission to committees

- Most committee applications are incorporated in the HawkIRB application.
  - The CRU will require a separate I-CART application
    https://icts.uiowa.edu/investigators/i-cart-information
  - Pathology will require a separate application.
    http://www.path.uiowa.edu/forms/RA_Path.pdf
Step 3: IRB application and submission to committees

Research Billing

- Reviews all new studies to determine whether the study involves tests, medications, procedures, office visits or hospitalizations at UIHC.

- Research Billing will create a billing plan to make sure the subject’s care is billed to the study when appropriate.

- Research Billing will send the billing plan for approval. The PI must sign and date the billing plan and the signed copy must be returned to Research Billing.

- Research Billing must approve or determine a study is exempt before IRB review can be scheduled.

https://hso.research.uiowa.edu/research-billing-compliance
The P&T Subcommittee must review a research protocol if it involves:

- the administration of investigational new drugs or drugs that are given "off-label"

- FDA approved drugs that are given as a component of a research protocol

- any other substance that is ingested (with the exception of enteral feedings such as baby formulas, unless they contain a non-Generally Regarded As Safe [GRAS] ingredient)

- any other substance that is injected, inhaled, or applied to the body.
IDS is required to dispense study medications and must approve studies prior to UI IRB approval being granted.

IDS pharmacy is located at elevator M, lower level.

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**Investigational Drug Service (IDS)**

**Investigational Drug Study Standard Charge Worksheet FY 2015-2016**

Submit completed worksheet electronically to the Investigational Drug Service with the IRB application. Please note worksheet contains 2 pages.

NOTE: The fees below are effective July 1, 2015. It is anticipated that fees will be adjusted again on July 1, 2016. If the protocol will extend for more than one year, please include at least a 5% increase in your budget for administrative and dispensing fees, and at least 10% for drugs or supplies not provided by sponsors. For questions or clarifications, please contact the Investigational Drug Service at (319) 356-2577, Theresa-Hobbs@uiowa.edu, Kristine-Johnson@uiowa.edu, or Angela-Merriss@uiowa.edu. Thank you.

<table>
<thead>
<tr>
<th>ACTIVITY</th>
<th>RATE</th>
<th>SUBTOTAL</th>
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<tbody>
<tr>
<td>I Study Set-Up and Close-Out Activities, includes:</td>
<td>$1200 / Protocol / Initial year</td>
<td>$</td>
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<tr>
<td>Review of study design, identification of pharmacy issues</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initiate search and inventory of investigational agent(s)</td>
<td></td>
<td></td>
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<tr>
<td>Preparation of Drug Accountability Record/Notebooks</td>
<td></td>
<td></td>
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<tr>
<td>Studies requiring electronic drug accountability and/or electronic case report completion will be charged an additional fee of $100/year</td>
<td>$100 / Initial year</td>
<td>$</td>
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<tr>
<td>Development and distribution of dispensing guidelines</td>
<td></td>
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<tr>
<td>Randomization and double blinding if requested</td>
<td></td>
<td></td>
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<tr>
<td>Training of staff</td>
<td></td>
<td></td>
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<tr>
<td>Epic Build</td>
<td></td>
<td></td>
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<tr>
<td>Set up supplies, storage</td>
<td></td>
<td></td>
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<tr>
<td>(Drug Destruction, Temperature Monitoring etc)</td>
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<tr>
<td>Staff in-services</td>
<td></td>
<td></td>
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<tr>
<td>Site initiation meetings with investigators and study monitors</td>
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<td></td>
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<tr>
<td>Reconciliation of drug accountability records at end of study</td>
<td></td>
<td></td>
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<tr>
<td>Pharmacying, losses at drug, maintenance of discontinued study files</td>
<td></td>
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<tr>
<td>Temperature Logs</td>
<td></td>
<td></td>
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<tr>
<td>Study close-out</td>
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</tbody>
</table>

| II Study Maintenance [just assessed for the 1st year] | $600 / Subsequent year | $ |
| Inventory Control/Accountability (monthly) | | |
| Studies requiring electronic drug accountability and/or electronic case report completion will be charged an additional fee of $100/year | $100 / Subsequent year | $ |
| Ordering, and maintaining, appropriate stock of drug | | |
| Drug Receipts | | |
| Checking for expired drugs, data extension and relabeling of drugs | | |
| Monitor visits | | |
| Internal QM audits | | |
| • Temperature Reports | | |
| • Copying, drug accountability forms, and shipping reports | | |
| • Making scripts, printing copies | | |

Complete preparation/dispensing costs and estimated total charge on page 2.

Per UIHC policy N-A-12.001, NRC must approve any research that will involve:

- Participation of nursing staff, patients or supplies
- Procedures not standard of care in the nursing unit or clinic
- Development of instruments or procedures

https://workflow.uiowa.edu/entry/new/2642
Medical Radiation Protection Committee (MRPC)

- MRPC must review studies that involve radiation exposure for subjects and/or study personnel.
- Any study that involves X-Rays, CT scans, PET scans, Nuclear Medicine or radioactive drugs such as MRI contrast, must be reviewed.
  - MRI scans without contrast do not emit radiation and do not need to be reviewed.
- Note that there is a long form and a short form.
- The long form must be used if the study involves procedures with an effective dose equivalent greater than 100 mrem, or radiation exposure to minors or pregnant women; radiation procedures performed outside UIHC, UI College of Dentistry, or VAMC facilities.

https://hso.research.uiowa.edu/medical-radiation-protection-committee
Institutional Biosafety Committee (IBC)

- If the study has any recombinant DNA (rDNA) activities, the study must be reviewed and approved by the Institutional Biosafety Committee (IBC).
- The IBC is required to approve the study and ensure that the study’s activities comply with the National Institutes of Health (NIH) Guidelines.
- The PI is required to submit a rDNA registration document for all recombinant DNA experiments that are not exempted from the NIH Guidelines.
- This document must be reviewed and approved by the IBC prior to the initiation of any research activities.

https://hso.research.uiowa.edu/institutional-biosafety-committee
Pathology

- Any study that uses pathology services must be reviewed
- Labs that are processed by specimen control or another UIHC lab (except CRU) must be reviewed
- Pathology application is not built in to the HawkIRB application
- You do not need to have pathology approval prior to submitting to IRB, but submit to pathology as soon as possible.
- More info, instructions and application can be found here: https://www.medicine.uiowa.edu/pathology/research/pathology-clinical-trials-support-core

- To find pricing for research pathology tests, use the research pricing link in the budgeting section.
I-CART for Clinical Research Unit (CRU)

- Any protocol that utilizes CRU services must be reviewed by CRU.
- You do not have to have CRU approval to submit to IRB, but submit to CRU as soon as possible.
  - It can take several weeks from submitting your application to finalizing a CRU cost analysis, orders and nurses notes.
  - New study team members must also attend a 45-minute CRU orientation prior to using CRU in any capacity.

- You will want to get a CRU cost analysis before your study budget is finalized, so you can ask the sponsor for the appropriate amount to cover CRU fees.

https://icts.uiowa.edu/investigators/i-cart-information
I-CART for Clinical Research Unit (CRU)

- Apply for CRU services through I-Cart:
  http://icts.uiowa.edu/pages/i-cart-view-and-order-services

- Please contact the CRU directly for assistance with completing an I-Cart application.

- More information on the CRU:
  http://www.icts.uiowa.edu/pages/clinical-research-unit
I-CART for Epic Study Creation

- I-CART will be used to request that a study be built in Epic for associating subjects.
- Following the request, the requestor will receive a REDCap survey that will ask a few study specifics.
- After the survey is completed, the study will be created in Epic (IRB number is required).
- All subjects that are consented for a study, are required to be associated to that study within a timely manner and following the subjects completion, the subject will need to have their status changed to completed in a timely manner.
I-CART for REDCap Creation

REDCap (Research Electric Data Capture) is a tool that provides a secure multi-user web based interface for storing study information.

There is no charge to use REDCap.

A request will need to be made, through I-CART, to create a study in REDCap.
Step 4: Documents

Consent/Record of Consent
Financial disclosures
FDA 1572
ClinicalTrials.gov
Step 4: Informed Consent Form (ICF)

- Industry sponsors will send you a template consent form.
- Download the HawkIRB consent from your application.
- UI has required language that must be included, unaltered, in any consent form. Use the HawkIRB template to incorporate that language.
- The other committees may have required language to include.
- Negotiate the consent language with the sponsor prior to submitting to IRB.
- A consent summary will also need to be completed for clinical trials.
Step 4: Record of Consent

- A Record of Consent (ROC) will be created when you complete the HawkIRB application if the research related activities meet the registration requirements under the University of Iowa Health Care Policy IM-MR-06.21.

- The ROC will appear in the subject’s Epic record after you have associated the subject to the research study.

- The ROC is important because it will alert medical staff that are caring for the subject outside of the research staff of any medication or procedure that the subject may have been exposed to.
Submit to IRB!

How long will it take to receive approval?

Once submitted to HawkIRB, allow at least 8-12 weeks to receive approval from all committees, a finalized contract, and IRB approval.

- Can be longer or shorter, but this is a good estimate to give to your sponsor when they ask.
- If several weeks go by and you haven’t received any approvals, do not hesitate to follow up directly with the committees!
- If submitting to HawkIRB, Research Billing will have to approve the study prior to having the IRB meeting scheduled.
- If submitting to WIRB or another external IRB, P & T, IDS, and MRPC will need to approve prior to the submission to WIRB or another external IRB.
- All committees will need to approve prior to receiving final IRB approval.
The Food and Drug Administration (FDA) is issuing regulations requiring the sponsor of any drug, including a biological product, or device marketing application (applicant), to submit certain information concerning the compensation to, and financial interests of, any clinical investigator conducting certain clinical studies. This requirement will apply to any covered clinical study of a drug or device submitted in a marketing application that the applicant or FDA relies on to establish that the product is effective, including studies that show equivalence to an effective product, or that make a significant contribution to the demonstration of safety. This final rule requires applicants to certify to the absence of certain financial interests of clinical investigators and/or disclose those financial interests, as required, when covered clinical studies are submitted to FDA in support of product marketing.

Source: https://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/ucm119145.htm
Step 4: Financial Disclosure Forms (FDF)

Financial Disclosure Form

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

The following information concerning [Name of clinical investigator], who participated as a clinical investigator in the submitted study [Name of clinical study], is submitted in accordance with 21 CFR part 54. The named individual has participated in financial arrangements or holds financial interests that are required to be disclosed as follows:

Please mark the applicable check boxes:

- any financial arrangement entered into between the sponsor of the covered study and the clinical investigator involved in the conduct of the covered study, whereby the value of the compensation to the clinical investigator for conducting the study could be influenced by the outcome of the study;

- any significant payments of other sorts made on or after February 2, 1999, from the sponsor of the covered study, such as a grant to fund ongoing research, compensation in the form of equipment, retainer for ongoing consultation, or honoraria;
Step 4: 1572

A form that must be filed by an investigator running a clinical trial to study a new drug or agent. The investigator agrees to follow the U.S. Food and Drug Administration (FDA) Code of Federal Regulations for the clinical trial. The investigator verifies that he or she has the experience and background needed to conduct the trial and that it will be done in a way that is ethical and scientifically sound. Also called 1572 form.
Step 4: ClinicalTrials.gov

- ClinicalTrials.gov is a public database containing information about clinical trials.
- Clinical trials registration and results reporting is required by law for all clinical trials funded by the NIH and for investigators who wish to publish in an ICMJE journal.
- Most industry-sponsored trials will be registered by the sponsor.
- You may need to register a PI-initiated or a study from a startup/smaller sponsor yourself.
- Contact: ct-gov@uiowa.edu for questions or applying for an account.

https://hso.research.uiowa.edu/clinicaltrialsgov#1a

https://clinicaltrials.gov/
Startup of NIH Studies

- NIH and other public grant-funded studies usually come with pre-determined, non-negotiable budgets and contracts.
- Usually there is no CDA.
- Most of the time, you can start with Step 3
- If your PI is submitting a NIH grant and there will be other academic centers participating, it is IMPARATIVE that you start the sIRB process as soon as possible before the grant is submitted!

Contact: uirb-external@uiowa.edu for more information on sIRB submission

What happens after IRB approval?

- Sponsor will schedule a site initiation visit (SIV) with you.
- Your sponsor will tell you when you are approved to begin enrolling—usually only after SIV occurs.
Questions??

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