

Increasing Efficiency for Investigator Initiated Trials

The [UC BRAID Contracting Network](#) wanted to simplify the contracting process for Investigator Initiated Trials (IIT), so we developed this Toolkit. These webpages are intended to provide guidance on the information needed when starting an IIT to facilitate efficient contracting and move the trial forward as quickly as possible.

Each page highlights information about elements of the study, questions that the contracting office will need answered, or checklist items for the PI to accomplish.

This Toolkit for Investigators was created by the [BRAID Contracting Work Group](#).

IIT Toolkit Web Resource

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Study Plan

Information to Gather

- What are the projected start and end dates for the study?
- Are there any study specific deadlines related to execution of the agreement?
- Where will the work be performed? Provide specific addresses.
- What is the study material being investigated?
- Will University staff be in control of the performance for the entire study (i.e. will any portion of the treatment be done by the patient at the patient's home, by a home health care service, or by an outside institution)?
- Will the sponsor provide the study material, will the University purchase study material, or will insurance pay for the study material?
- What is the status of the study material? For example, is it on the market or approved in other countries but not in the US? Is this a new use?
- Are there other treatments available for the condition under study?
- Are the other parties requesting access to identifiable patient information?
- Did the University -- or anyone performing the study -- contribute to the development of the study material or procedures (either as part of University or otherwise)?
- Are the proposed publication provisions acceptable to the PI and the University, and consistent with the anticipated publication plan?
- Is there a time requirement for completing data entry in the case report form and/or adverse event reporting (e.g., 24 hours from visit, 3 days from visit vs. 3 business days)? Can you meet the timelines?

Reminders

- The 'pre-proposal' process is generally managed by the PI and department to secure funding for IITs.
- The contracts office does not review proposals for clinical trials.
- The PI or department should consult with their Contracts and Compliance Offices, or Conflict of Interest Committee if they have any concern that the funding entity is requiring intellectual property, confidentiality or other rights, or creating obligations that may interfere with the study in a pre-proposal.

Protocol Design

Key Considerations

- It's important that the study team reach out early to determine which office will handle the research contract review.
- The contract will supersede specific legal terms in the protocol ONLY if the topic is addressed in both documents.
- A well-defined protocol is essential for all projects, but particularly when there are:
 - Multiple funding entities
 - Subcontractors
 - Publication as a deliverable
 - Multiple arms
 - Correlative studies

Information to Gather

- Do the procedures required by the protocol provide a unique emergency or urgent medical intervention?
- Will any third parties receive data or information as part of the study? Will this involve PHI?
- Is a Confidential Disclosure Agreement or Non-Disclosure Agreement needed with the third parties?
- Is the third party's participation detailed in the protocol or will it require separate IRB review

Reminders

- Provide the final protocol to your appropriate clinical trials contracts office.
- Ensure the title of the protocol conforms with the protocol in the agreement.
- Identify whether any portion of the protocol that will not be performed by the University to the contracts analyst. This may include external services, correlative studies, subcontracts or separate research projects entirely.
- Submit the protocol and informed consent to the IRB promptly and ensure the IRB approves the protocol and informed consent form

Budgets

Information to Gather

- Is the proposed payment schedule acceptable to all parties (or, if there is no payment schedule, do you wish to include one)
- Have you identified sufficient activities to allow recovery of partial payments if a subject does not complete the full study?
- Is the language with respect to the number of patients expected acceptable to you? For example, do they include a minimum number of patients that may eliminate their obligation to pay if not met?
- Is there a written or implied obligation to amend the agreement for increases in enrollment past a certain number of patients? Is this acceptable to you?
- Have you distinguished department IRB preparation costs from IRB fees that will be charged by the IRB?
- Is there a holdback of more than 10% of the amounts payable reserved for the end of the study? Is a higher holdback value acceptable?
- Are there multiple holdbacks (i.e. 10% upon final report and 10% upon submission of a publication)?
- Does your budget include applicable indirect costs?

Reminders

- Include sufficient startup funding to break even in the event no patients are involved.
- Ensure that all of your costs are covered, including indirect, start-up, per patient and close-out, and that IRB fees are included in the correct amounts.
- Complete coverage analysis, if required.
- Ensure it is sufficiently clear that the project is fee for service vs. cost reimbursement. A statement to that effect in the budget is ideal.
- Include applicable indirect costs and reference them appropriately.
- Provide a payment remittance or invoicing address.

Funding

Information to Gather

- Is the study material manufactured by the funding entity?
- Will we be providing study material to the subcontractors or will it be through the funding entity or a third party?
- Is there any expected positive conflict of interest disclosure with the funding entities? Check with your institution to determine whether the federal, state, or both conflict of interest forms are required to be completed.
- Who is funding the study or providing materials.
- Did the sponsor receive a Small Business Innovation Research or Small Business Technology Transfer grant to conduct the research?

Reminders

- Make sure to indicate to the contract office if there is more than one funding source, or if any portion of the funding is not industry.
- Confirm that the funding entity has sent an indemnity letter or indemnity agreement along with the contract if a CRO is the contracting party. If they haven't, check with the CRO to see if one is available.
- Consult with your institution's contracts office for review of any budget and other relevant documentation, and allow time for negotiation of the agreement.

Multiple Funding Entities

Please note: Clinical trials are significantly more complex with multiple funding entities. Make sure to reach out to the contracting office early to avoid delays.

Key Considerations

- Be aware of competing funding entity interests.
- Funding entities rarely respect competing interests.
- The University cannot have overlapping obligations to other parties.
- You may want to discuss at an early stage whether the sponsors are willing to engage in a three (or more) party agreement rather than separate negotiations. This can save time and effort, particularly if a multi-party template is agreed to by the funding entities.
- Is there a mix of non-profit and for-profit funds?

Reminders

- Clearly delineate each party's responsibilities in the protocol.
- Consider using a template such as the "Multi-Party Investigator-Initiated Clinical Trial Agreement" if the project meets all the requirements of a clinical trial. It is best to confer briefly with your contracts office before sending out a template agreement to make sure that the provisions are appropriate to the type of study you are doing

Modifications and Changes

Key Considerations

- Compared to sponsor initiated studies, IITs more frequently have modifications to the protocol, additional arms, additional subcontractors, and additional correlative studies after initiation of contract negotiation.

Reminders

- Communicate any changes (even anticipated changes) to the contracts office as soon as possible. Please follow campus policies and federal rules.
- Be aware that while it may make sense to wait and amend the IIT agreement to accommodate changes, in many cases it is critical to make the changes prior to execution of the contract. Make sure to discuss this with your contracts office in advance, rather than delaying submission of the changes..

Correlative Studies

Correlative studies may include:

- Additional samples from existing subjects
- Expanded testing of study samples
- A full additional arm of the study
- A new funding entity
- A new PI
- New patient pool
- A full, separate research project or service agreement
- A reference to a separate protocol without clear separation from the current protocol

Key Considerations

- Forcing a separate project (that would not by itself be considered a clinical trial) into an IIT protocol does not make it a clinical trial and will result in significant delays. It is often necessary to remove the separate project from the protocol at a later time, which can result in major budget, contract and compliance issues.
- You should describe the correlative study in the protocol if the project is part of the clinical trial and if the correlative project uses all of the same:
 - Funding as the clinical trial
 - Funding entity as the clinical trial
 - PI as the clinical trial
 - Study subjects as the clinical trial
 - Study team as the clinical trial
- The following types of correlative projects should NOT be described in the protocol:
 - Independent research projects that involve different patients, a different PI or different funding (even partially).
 - Projects that will be done off site by other entities (i.e. services or subcontracts)
 - Projects that are sponsor initiated (under a sponsor written protocol)
- If you must reference a separate correlative project in an IIT protocol that will use other funding, staff, patients or facilities, the IIT protocol should reference, but not describe, the correlative activity clearly. For example:
 - “Correlative Study: The de-identified samples will be analyzed along with samples from similar studies under a separate, state-funded grant. The results of the correlative study will be published, and all rights, payments and services will be handled, exclusively in accordance with the terms of that grant.”

Reminders

- Describe a correlative study in the protocol if you want incorporated into the protocol. Merely referring to a correlative study does not mean that it is part of the protocol.
- Funding for correlative studies may require separate grant terms, agreements, or protocol. This should be made clear to the funding entity in communications, and included in the budget and the contract to ensure that there are no conflicting commitments.

Subcontracts

Key Considerations

- Subcontracts can add numerous twists to a negotiation.
- Subcontractors may not agree with exceptions University attains to move the project forward (or even the University standard language).
- Funding entities may try to insist that University be liable for sub-sites. The University can agree to be responsible for monitoring the sub-sites or collecting data, but not for their specific performance.
- It should be clear if the experimental treatment is being provided through the University or to the sub-sites directly.
- Subcontracts to unusual entities (e.g., the VA) should be discussed with the contracts office in advance.

Reminders

- Consider whether subcontractors will be performing the same protocol as the University study, or perform a subset of the protocol.
- Promptly advise the contracts office if a material transfer agreement is necessary.

Consortium Agreements

Key Considerations

- The PI or department should consult with the contracts office or the appropriate compliance office if they have any concern that the funding entity is requiring intellectual property, confidentiality or other rights or creating obligations that may interfere with the study.
- The contracts office is generally not privy to any of the discussions or documents that pre-date the IIT agreement and relies on the PI and department to identify any concerns about obligations or commitments in these external documents that may interfere with the study.
- The University is not a party to and not subject to the terms and conditions of any documents signed solely by the PI or the department.
- There can also be outside confidentiality, outside consulting or outside consortium agreements that may impact the trial and the trial agreement.