The University of Chicago may make an exception to the standard policy of requiring full indemnification from the company funding and/or providing drug/device for a clinical study in cases of investigator-initiated studies. This document summarizes the procedure required to request waiver of the University standard indemnification policy. The determination of exception is based on an institutional risk/benefit analysis of the investigator-initiated clinical research protocol. This analysis is conducted by the Associate Dean for Clinical Research who reviews documents submitted by the PI (with sectional (when appropriate) and departmental endorsement) and formulates a recommendation as to whether the University should assume all or substantial liability related to an investigator-initiated protocol. The Associate Dean for Clinical Research makes his/her recommendation to the Associate Vice President for Research Administration, who reviews the recommendation and forwards the assessment and endorsements for review by the General Counsel (or designee). The ultimate determination is made by the Vice President for Research who may request consultation with the Office of the Provost.

The process will be used when full indemnification is not offered or made available in the clinical trial or sponsored study agreement by the study pharmaceutical company (i.e. for injuries (or death) or when the study pharmaceutical company requires the University to indemnify them, sustained during participation in a study, for product liability, and/or payment for subject.

Based on past policy and practice, the University accepts that some types of investigator-initiated studies do NOT need to undergo the assessment process describe in this document:

- Protocols that have been reviewed via a peer review process, e.g. federally funded studies or studies supported by most voluntary health or large foundation grants;
- Studies that are not categorized as greater than minimal risk by the BSD Institutional Review Board (IRB).

The specific procedures that must be followed in developing the risk-benefit assessment are:

1. The Principal Investigator (PI) should have already submitted the protocol and consent form to the BSD IRB and the clinical trial agreement to the Office of Clinical Research and University Research Administration.
2. URA will review the clinical study agreement for the level of institutional risk as presented by the company’s indemnification (or lack of) provisions. The BSD IRB will review the protocol and determine whether the study is categorized as greater than minimal risk and thus will require full IRB review.
3. All protocols and consent forms must be approved by the IRB prior to initiating the institutional risk assessment.
4. After the IRB review and approval, the Principal Investigator is responsible for submitting the following documents to the Associate Dean for Clinical Research:
   a. Copy of the IRB application
   b. Copy of IRB approval letter
   c. The complete IRB-approved protocol
   d. Approved consent form (describes the risks that the IRB has determined were important to disclose to the subjects)
   e. The date that the risk/benefit analysis completion is requested
   f. Any comments/concerns about the sponsor study agreement arising from the review of URA
   g. Clear statement of level of indemnification offered by the company
   h. A document that will form the basis of the institutional risk-assessment to be completed by the Associate Dean for Clinical Research. See below for Institutional Risk Assessment

The Institutional Risk Assessment is initiated by the PI who may also consult with departmental resources, the Clinical Research Office, and the Associate Dean for Clinical Research. The Risk Assessment document should include:
a. Assessment of the risks to the study subject. This should include information about the number of subjects proposed for the study; a description that quantifies risks such as the likelihood of untoward effects of the device or drug(s) which could lead to damages, claims, or payment of protocol related expenses. If the study involves a combination of FDA approved drugs with investigational drugs, the assessment should include this information clearly designating which drugs (devices) are FDA approved and which are the study drugs, the likelihood of side effects from the combination therapies – whether offsetting or enhancing, if known;

b. Brief assessment of the benefits to study subjects, the faculty, the Medical Center, and to scientific knowledge.

c. If company requires University to indemnify company, a description of the company (small business, corporation, assets, etc.) must be included - specific language in proposed sponsored agreement regarding indemnification request must be included.

d. If PI or other co-investigator(s) has real or perceived financial conflict of interest with sponsor, a full disclosure of this outside interest must be included in the documentation provided to the Associate Dean.

e. The Risk Assessment document must be signed off by the PI, section chief (if appropriate) and the Department Chair.

f. The PI should review the “Consideration for Institutional Risk Assessment” guidance document to assure that all aspects necessary for divisional and University review have been addressed.

g. **The PI should bear in mind that the institutional review will be carried out by nonclinical personnel; the descriptions and discussions must be in language understandable by a reasonably knowledgeable but not medically trained layperson.**

5. The Associate Dean for Clinical Research reviews the materials provided by the PI and provides an assessment from the BSD perspective. In making the assessment, the Associate Dean may consult with Medical Center legal staff to discuss the liability risk in light of the identified medical risks to the subjects, the limited (if any) indemnification offered by the sponsor, the University’s compensation obligation as expressed in the consent form. The Associate Dean’s review is expected to have considered and addressed all applicable Risk Factors, Risk Modifiers, and Benefits described on the Consideration for Institutional Risk Assessment. Materials should be returned to the PI if these considerations have not been appropriately addressed or the Associate Dean may consult informally with the PI to include these considerations in the Associate Dean’s recommendation. The Associate Dean forwards all materials to the Associate Vice President for Research Administration, with a copy to the PI. The PI may not share this document with the sponsor without the prior written consent of URA.

6. The Associate Vice President for Research Administration (AVPRA) reviews the documents, in conjunction with any additional documentation about the negotiations with the sponsor regarding indemnification. The AVPRA consults with Risk Management at the University to determine if the University’s insurance coverage provides any financial assistance in the absence of sponsor indemnification. The AVPRA consults with University General Counsel (or designee) for an opinion regarding the risk-benefit assessment, and forwards the documentation to the Vice President for Research with the endorsement and recommendation of the URA and the opinion of General Counsel.

7. The Vice President for Research evaluates the materials forwarded by URA and makes the final determination about the exception to the standard policy of requiring full indemnification from the clinical study sponsor.

**The judgment may be rebutted and/or appealed by the PI to the Vice President for Research. The judgment may be reversed by provision of additional information on risk or benefit not provided previously.**

If the study proceeds, the judgment will be kept on file in URA and the Associate Dean’s office for the life of the protocol/sponsored agreement.
Considerations for Institutional Risk Assessment

**Risk Factors**
- Risk of subject injury or death due to the underlying medical condition considering especially the nature of the study population and nature of the underlying medical condition
- Risk of subject injury or death given standard treatment for the underlying medical condition
- Risk that effects of the illness could be attributed to the intervention under study
- Severity and frequency of known or suspected adverse events associated with all arms of the study, considering especially the nature of the study population
- Availability of alternative treatments
- Probability and ramifications of subject non-compliance
- Cost of care to treat subjects for injuries caused by adverse events
- Possibility of a legal obligation to indemnify subjects for care
- Cost of litigation related to liability claims
- Likelihood of losing a lawsuit regarding a liability claim
- Likelihood of the subject’s medical insurance would not cover cost of care up front
- Likelihood that an insurer paying for the care would seek to recover cost from the University
- Company/sponsor providing funds and/or drug, device, etc requires University to indemnify company/sponsor
- PI has financial conflict of interest with company/sponsor

**Risk Modifiers**
- Number of subjects
- Characteristics of subjects, such as age, member of vulnerable populations
- Skill and experience of the investigator
- Risk monitoring and control plans in protocol (such as frequency and thoroughness of monitoring for adverse events, plans for subject care in case of adverse events, plans to monitor and assure subjects compliance, etc.)
- Experience with study intervention in previous studies
- Presence of DSMB

**Benefits**
- Free Treatment made available to study subjects, especially in the case of a Phase IV trial where subject would have to pay
- Availability of a potentially beneficial treatment in cases where no other treatment is available or where available treatments are extremely risky or carry a poor prognosis
- Availability of protocol to patients who wish to volunteer for research
- Potential benefits to study subjects if intervention is beneficial
- Benefits to investigator’s career or reputation
- Initiation, continuation or enhancement of a research program at this institution
- Possibility of increasing the number of patient visits related to a particular disorder
- Enhanced reputation of the institution as a place to do excellent research
- Possibility of increasing the number of patient visits related to a particular disorder
- Enhanced reputation of the institution as an advanced provider of care
- Possibility of intellectual property benefits to the institution (may need to discuss research protocol with UChicagoTech)
- Potential benefits to society that might result if the intervention is proven effective