



**Boston University
Office of Sponsored Programs**

Negotiation of Clinical Trial Agreements: Standard Operating Procedures

I. Background and Purpose

Investigators at Boston University/Boston Medical Center (the “Institution”) are often approached by pharmaceutical and medical device companies to participate in clinical trials (“Trials” or “Studies”) in order to test the safety and efficacy of drugs, devices and medical treatments in human subjects. These Investigators are willing to take part in these Studies for a variety of reasons, including: a desire to advance the state of medicine and understanding of disease; the opportunity to help develop new treatment options; and the possibility of providing patients with access to treatment that is not otherwise available, and which may be more effective than standard treatments and/or may improve such patients’ quality of life.

The purpose of a Clinical Trial Agreement (“CTA”) is to set forth the terms and conditions under which an Investigator will recruit and engage subjects to participate in a Trial, and will thereafter perform such Trial at Boston Medical Center. The CTA will include provisions governing conduct of the Trial, confidentiality, publication, intellectual property, compensation by the sponsor of the Trial (the “Sponsor”) to the Institution, regulatory compliance, and allocation of liability, among others.

The goal of the Contracts & Agreements group within the Office of Sponsored Programs (“C&A”) is to accommodate the desire of the Sponsor and the Investigator to finalize each CTA as efficiently as possible, while ensuring, through negotiation with the Sponsor (or contract research organization (“CRO”) engaged by the Sponsor to handle administration of the Trial), that the CTA comports with the policies of the Institution and does not expose the Institution to undue burdens or risk.

Note: A critical component of each CTA is the budget and accompanying compensation terms, which are addressed in a separate SOP.

II. Process; Required Documentation and Approvals

CDA: Often, the first indication to C&A that an Investigator is contemplating participating in a Trial is execution of a Confidential Disclosure Agreement (“CDA”), pursuant to which a potential

Sponsor will disclose information relating to the Trial to the Investigator so that the Investigator can decide whether or not to take part in the Study. The Institution's preference is that such CDAs be executed by the Investigator, rather than the Institution. However, this is not always acceptable to the Sponsor, and if necessary, the CDA will be signed by an authorized representative of the Institution in order to move the evaluation process forward.

Documentation; Negotiation Process. Once an Investigator has made a decision to participate in a Trial, he/she, directly or through a member of his/her team, will forward the initial draft of the CTA, budget and any ancillary documents received from the Sponsor or CRO to C&A for review. C&A then enters the agreement into its internal log for tracking purposes, and sends a set of forms to the Investigator for completion, including a Proposal Summary Form ("PSF"), Checklist for Industry-Sponsored Research Studies ("Checklist"), and Financial Interest Disclosure Form ("FID"). The purpose of the forms is to provide C&A with certain factual information that is necessary for (a) internal record-keeping, (b) account set-up once the CTA has been executed, and (c) ensuring that participation in the trial complies with institutional requirements. The Checklist must be returned to C&A, and the FID to the Office of Research Compliance (coi@bu.edu or via fax at 617.414.4738) immediately; the PSF may be submitted at any time prior to account set-up, and need not include final budgetary information. Concurrently, C&A commences review of the CTA and budget, which are processed in tandem in order to maximize efficiency. Primary responsibility for review and negotiation of CTAs lies with Anne Clark, Associate Director, Contracts & Agreements, and Elizabeth Alcock, Senior Research Administrator, negotiates budgets and other compensation terms. Negotiation of the CTA and budget may occur directly between C&A and the Sponsor, or may be effected through a CRO. In the course of negotiations, multiple rounds of comments are typically exchanged; however, the process is greatly expedited if the Institution has a Master Clinical Trial/Study Agreement in place with the Sponsor, in which case the only requirement is that a pre-negotiated Work Order, or similar form document, be executed between the parties.

Note: Investigator-initiated Studies are handled in the same manner as set forth above, except that, on occasion, the Institution will have the opportunity to provide its template CTA for Sponsor review, instead of starting with the Sponsor's form.

IRB Approval: It is important to note that while approval of an Institutional Review Board (either local, or Western Institutional Review Board ("WIRB")) must be obtained before Study activities may commence, the negotiation, finalization and execution of the CTA and budget are not dependent on prior IRB approval. Thus, the Investigator and the Institution may recover start-up costs from the Sponsor even if IRB approval is not ultimately obtained or if the Trial is abandoned for some other reason. C&A is largely uninvolved in submission to or approval by the IRB, with one exception: If a Sponsor rejects the Institution's preferred subject injury language for the informed consent form ("ICF") to be executed by Study subjects, initial negotiation of the language will be handled by Anne Clark. The goal of these negotiations is to persuade the Sponsor to accept the preferred language, so that the Trial may be submitted to WIRB for

approval. If the preferred language is rejected, the Trial must be approved by the Institution's local IRB. C&A does not have authority to accept any changes to the template language on behalf of the IRB, but these negotiations are often effective in terms of convincing the Sponsor to either accept the preferred language or at least limit the requested changes to those that are more likely to be approved by the local IRB, necessitating fewer deferrals, rejections and resubmissions and thereby shortening the time until the Investigator may start treating subjects.

Execution: Once all terms have been finalized, the Sponsor will provide either an execution version of the agreement, or a partially executed copy, to C&A, and the CTA is signed by Michael Collins, Assistant Vice President, Sponsored Programs, and Thomas Moore, Director, Clinical Research, on behalf of the Institution, as well as by the Investigator, if necessary. When a fully executed copy of the CTA has been obtained, a copy is sent to the Investigator for his/her records. A copy of the fully executed agreement is also sent to Boston Medical Center for its records. Promptly following final execution, C&A submits a copy of the signed CTA, along with an Award Checklist and Budget Worksheet, to the Sponsored Research Information Management group within OSP for account set-up. Concurrently, the fully executed agreement, PSF and PSD are uploaded onto OSP's shared drive (the "Y Drive"). When notification of the I/O number for the Study and evidence of IRB approval are received by C&A, such corresponding documentation is also uploaded. The Y Drive is organized by Investigator name, followed by Study identifier, for ease of future location. All such paperwork is also included in the paper file for the relevant CTA, which is kept in OSP offices on the 8th Floor of the Fuller Building at 85 E. Newton Street.

III. Negotiation of Specific Terms

Some of the terms most commonly included in a CTA are set forth below. This list is not intended to be comprehensive and does not capture every provision that may be found in a CTA, which will depend on the form provided by the individual Sponsor. The Institution's preferred position with respect to the following areas is outlined below:

- Data/Results;
- Intellectual Property;
- Publication;
- Confidential Information;
- Indemnification/Insurance;
- Warranties/Limitation of Liability;
- Subject Injury; and
- Termination

Ownership and Use of Data/Results: The Sponsor owns Study results/data, but the Institution owns subject medical records and other original source documentation (other than case report

forms). The Institution always reserves the right to use the results/data for internal research and teaching purposes.

Intellectual Property (“IP”):

- Sponsor-initiated Trials: The Sponsor owns IP generated in performance of the Trial relating directly to the study drug/device, its confidential information, and the protocol; the Institution should own everything else. The Sponsor is entitled to a non-commercial, non-exclusive, royalty-free license, plus the option to negotiate an exclusive commercial license.
- Investigator-initiated Trials: The Institution should own all resulting IP and offer the Sponsor the same license terms as set forth in the previous paragraph.
- The Institution and the Investigator will provide reasonable assistance to the Sponsor to secure the Sponsor’s IP rights, with reimbursement for time spent and expenses incurred.

Publication: As in other research agreements, the Institution must retain right to publish the results of the Study; however, in a multi-site trial, independent publication is generally prohibited until the earlier of (a) the multi-site publication and (b) 18 months following completion of the Study at all sites. The Institution may not have right to publish independently at all if data from a single site is not considered adequate from scientific/statistical perspective. Generally, the Sponsor has thirty (30) days prior to submission for publication to review a proposed publication and request removal of its confidential information. The Institution will agree to remove such confidential information, but will not agree to remove Study results or any basic information about the Study drug or device or its properties and functions, or about the protocol, that the Investigator deems to be reasonably necessary to meaningfully convey the study results and their significance to their intended scientific audience. The Sponsor may also request that publication be delayed for an additional period, not to exceed ninety (90) days, in order to file patent applications on any inventions described in the publication.

Confidential Information: “Confidential Information” generally includes all information provided by the Sponsor to the Institution pursuant to the CTA. The Institution prefers that Confidential Information be marked as such, but this is rarely agreed to by Sponsors (only 4 out of 21 Master CTAs contain a marking requirement). The Institution will maintain the confidentiality of such information using the same effort it uses to protect its own confidential information of a similar nature, but no less than a reasonable degree of care. The obligation of confidentiality generally survives for between five (5) and ten (10) years, with a shorter time period being preferable.

Indemnification/Insurance:

- Sponsor:

- Indemnification: The Sponsor must indemnify the Institution for losses resulting from: the proper performance by the Institution of the Study; the design, production, manufacture, sale, use in commerce, lease, or promotion by the Sponsor or sublicensee of the Sponsor of any product, process or service relating in whole or in part to the subject matter of the CTA; or the use, nonuse, interpretation or publication by the Sponsor or its agents of the Study results or any invention made in the course of the Trial.
- Insurance: The Institution's template CTA sets forth the preferred insurance coverage for Sponsors. Deviations from this must be approved by Paul Clancy in the Risk Management department. The Sponsor's policy should name the Institution as an additional insured.
- Institution:
 - Indemnification: The Institution prefers not to offer indemnification to the Sponsor, but will if necessary indemnify the Sponsor for Institution's negligence or willful misconduct, failure to conduct the Trial in accordance with protocol or applicable laws, breach of representations and warranties, and similar. Fifty percent (50%) of the Institution's Master CTAs provide for indemnification of the Sponsor.
 - Insurance: The Institution will agree to the following: "The Institution shall carry liability insurance in the type and amount, and for such period, as is appropriate and customary for the conduct of clinical trials (or maintain a comparable program of self-insurance). In accordance with Massachusetts law, the Investigator shall maintain medical professional liability insurance with limits of at least \$1,000,000 per incident and \$3,000,000 aggregate." If requested, the Institution will agree to specific limits of \$1,000,000 per incident and \$3,000,000 annual aggregate.
- The indemnification obligations of each party are limited to the extent the loss results from the negligence or willful misconduct of the other party.

Warranties/Limitation of Liability: As with any research agreement executed by the Institution, the CTA must include language stating that, other than expressly set forth in the agreement, the Institution makes no warranties, express or implied, with respect to the conduct of the Trial or the results thereof. In addition, it is advisable to limit the Institution's liability to direct, rather than consequential/indirect/special, damages.

Subject Injury: It is not necessary that the subject injury language in the CTA track the ICF exactly. The CTA may provide that the Sponsor will not be obligated to reimburse subjects for expenses incurred in connection with a Study-related injury if such injury was caused by the negligence of the Institution, including failure to abide by protocol, despite the fact that the IRB might not approve such language for the ICF. However, the Institution will not accept a carve-out to the Sponsor's obligation for subject negligence or failure to follow instructions.

Termination:

Typically, only the Sponsor may terminate a CTA at will. The Institution should retain the right to terminate upon any breach by the Sponsor that remains uncured thirty (30) days following notification thereof. It is very important that in the event of any early termination of the CTA, the Institution be explicitly entitled to recover costs and non-cancelable commitments incurred through the termination date. In addition, it is optimal to provide for continued treatment of subjects, at the Sponsor's expense, to the extent medically necessary or prudent in opinion of the Investigator.

Miscellaneous: A few of the other standard provisions that are frequently seen in CTAs and which typically do not require extensive negotiation include, among others:

- Requirement on the part of the Institution to abide by Good Clinical Practice (FDA regulations)
- Requirement to obtain ICF/HIPAA authorization from subjects (required by Privacy Rule established by HHS under HIPAA)
- Debarment of, or other sanctions imposed on, Study personnel
- Inspection/audit of the Trial by the Sponsor
- Governmental inspections
- Notification of adverse events
- Retention of Study records
- Publicity restrictions
- Registration on clinicaltrials.gov

For more information, please contact the Associate Director, Contracts & Agreements, in the Office of Sponsored Programs: (617) 638-4600.