**Background**

CTTI has recommended[[1]](#footnote-1) the use of a single IRB of record[[2]](#footnote-2) for multi-center clinical trials. To facilitate adoption of this model, CTTI has developed tools and resources for sponsors, institutions, and organizations that serve as a central IRB. This template IRB Authorization Agreement (IAA) is intended to address an administrative concern about using a single central IRB for multicenter clinical trials.

**How was the template IRB Authorization Agreement drafted?**

This template IAA is the work product of the CTTI Advancing the Use of Central IRBs for Multicenter Clinical Trials project team and an additional 46 experts from the Human Research Protection Program community who came together during a 2-day expert meeting held June 12-13, 2014 in Rockville, MD.

Prior to the expert meeting, a request was made on the IRB Forum Listserv in July 2013 asking for members of the Institutional Review Board (IRB) community who allow reliance on or who serve as a central IRBs to share their template agreements with the CTTI project team. Twenty institutions and organizations agreed to be part of the initial data collection process where template IRB agreements were reviewed to determine domains, the kinds of clauses included in each domain, and the frequency that those clauses appeared. Once common domains and clauses were established, the CTTI Central IRB Advancement project team reviewed example clauses and created a working draft which was then further evaluated during an expert meeting and finally validated by attendees post meeting.

What kinds of IRBs submitted their template agreements for review?

Note: total is greater than 100% as IRBs may have been associated with more than one role.

* Institutional IRBs: 56%
* Commercial/Independent IRBs: 31%
* IRBs associated with a federal sponsor: 30%
* IRBs associated with a clinical trial network: 30%

This template IAA may be used as a tool to help organizations move forward with centralized IRB review where appropriate. It represents the consensus of meeting attendees and should not be construed as the opinion of any one individual attendee nor does it represent an explicit endorsement by the federal agencies in attendance.

**Name of Organization Providing IRB Review** (hereinafter, “Central IRB”):

|  |  |
| --- | --- |
| IRB Registration Number |  |
| Street Address |  |
| City |  |
| State (if US) |  |
| Zip/Postal Code |  |
| Country |  |

|  |  |
| --- | --- |
| Name of Individual Responsible for  Administration of the IAA |  |
| Title of Individual |  |
| Phone Number |  |
| Email address |  |

**Name of Institution Relying on the Reviewing IRB** (hereinafter, “Institution”):

|  |  |
| --- | --- |
| Institution’s OHRP Federalwide Assurance  (FWA) #, if applicable |  |
| Name of Institutional Official |  |
| Street Address |  |
| City |  |
| State (if US) |  |
| Zip/Postal Code |  |
| Country |  |

|  |  |
| --- | --- |
| Name of Individual Responsible for  Administration of the IAA |  |
| Title of Individual |  |
| Phone Number |  |
| Email address |  |

1. ***Scope of the Agreement****:* 
   1. The Officials signing below agree that Institution shall rely on Central IRB for review and continuing oversight of human subject research covered by the Institution’s FWA, if applicable.

OR, if project specific

The Officials signing below agree that Institution shall rely on Central IRB for review and continuing oversight of the following human subject research covered by the Institution’s FWA:

|  |  |
| --- | --- |
| Title of Research Project |  |
| Name of Principal Investigator |  |
| Name of Sponsor |  |
| Name of Funding Agency |  |
| Award Number, if any |  |

* 1. This Agreement does not preclude any party from participating in any other IRB authorization agreements that it may have or enter with other entities for human subject research other than the study for which review is ceded to the Central IRB under this Agreement. This document must be kept on file by all parties and provided to FDA, OHRP, and/or other applicable regulatory agencies upon request. This Agreement may be executed in any number of counterparts, either in original, emailed or faxed form.
  2. The Central IRB will follow Institution/Central IRB (pick one)’s policies and procedures pertaining to documentation and review. For the purposes of conducting the IRB review, Institution/ Central IRB (pick one) will identify and interpret the requirements of applicable state or local laws, and regulations. Institution shall have the ability to discuss these interpretations with the Central IRB

1. ***Responsibilities of the Central IRB***
   1. The review performed by Central IRB will meet the human subject protection requirements of the Common Rule (e.g., 45 CFR 46) and applicable FDA regulations (e.g., 21 CFR Parts 50, 56, 312, 812). Central IRB will follow written procedures for reporting its findings and actions to the PI, Sponsor, and appropriate officials at the Institution and federal agencies as appropriate. Relevant minutes of IRB meetings may be made available to the Institution by Central IRB upon request.
   2. Central IRB services shall include, but not be limited to:
      * review and approval or disapproval of new protocols;
      * review and approval, disapproval or modification of consent forms or waivers of informed consent;
      * review and approval of modifications to protocols;
      * review and approval or disapproval of the investigator(s) and changes in research;
      * collection of reports of unanticipated problems and serious or continuing noncompliance;
      * maintenance of required IRB records pursuant to applicable federal regulations.
      * continuing review of certain new research studies appropriate to the degree of risk in such studies. Central IRB agrees to conduct at least an annual review of each non exempt study.
   3. Central IRB shall promptly notify the Principal Investigator (PI) of the study as designated on the IRB protocol submission of all IRB decisions and shall make available to the PI all applicable study related documents including but not limited to approved protocols, consent forms, surveys, and decision letters.
   4. CentralIRB shall notify the institution promptly
      * if there is ever a suspension or restriction of the IRB’s authorization to review studies;
      * of any changes in Central IRB operating procedures or practices that might affect the institution’s reliance on CentralIRB reviews;
      * of complaints from human subjects enrolled in studies at the institution;
      * of unanticipated problems involving injury or risks to subjects or others in the study;
      * if the Central IRB determines that serious or continuing non-compliance has occurred, and any steps the Central IRB deems necessary for remediation of non-compliance;
      * of suspension or termination of IRB approval;
      * of any communication with the FDA, OHRP or funding agency of matters relevant to human subject protections and relating to the institution’s studies; or
      * changes in accreditation status, if applicable.
   5. ***HIPAA If applicable (optional)***Central IRB will perform those determinations required by the Health Insurance Portability and Accountability Act of 1996 and its implementing regulations (collectively, “HIPAA”) with respect to the use and disclosure of Protected Health Information (“PHI”) for the research protocol in this Agreement, including authorization and waivers of authorization for use and disclosure of PHI. If it becomes necessary for the parties to use or disclose PHI in any way not covered by the existing authorization or waiver of authorization, then the parties will work together to determine any additional steps necessary to ensure that the required information is used or disclosed in a HIPAA-compliant manner
2. ***Responsibilities of the Institution***
   1. The Institution shall ensure investigator compliance withthe protocol, IRB determinations, applicable federal and state regulations, sponsor requirements, and if applicable with the terms of its OHRP-approved FWA.
   2. The institution shall ensure prompt reporting to the IRB of proposed changes in a research activity, and ensure that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject.
   3. Institution shall provide all information reasonably required by Central IRB in order to conduct its reviews and will facilitate Central IRB access to Institution expertise when needed. Institution cannot approve any research study that has been disapproved by the Central IRB. Institution may, however, disapprove any study approved by the Central IRB. Institution agrees to abide by the decisions of the Central IRB and shall use its best efforts to ensure that the human subject research performed by Institution shall be conducted in accordance with those decisions.
   4. Institution shall ensure that investigators and other study personnel at the institution are qualified and have appropriate resources to conduct the research, including but not limited to education and training in human research protection regulations. The institution shall provide documentation of training and education, as requested by the Central IRB.
   5. Institution shall ensure an institutional process exists by which complaints about the study can be made by local study participants or others. Complaints that meet criteria as a potential unanticipated problem involving risks to subjects or others or serious or continuing noncompliance must be reported to the Central IRB in accordance with the timeframe specified by the Central IRB.
   6. Institution shall cooperate with any Central IRB investigation regarding serious or continuing noncompliance or an unanticipated problem involving risk to subjects or others related to the study at the institution. Nothing in this Agreement shall prevent either party from conducting its own investigation. However, Central IRB shall have primary authority to determine whether serious or continuing noncompliance or unanticipated problems involving risks to subjects or others have occurred.
   7. Institution shall notify the Central IRB promptly:
      * if there is ever a suspension or restriction of the Institution’s authorization or ability to conduct studies;
      * of any changes in institutional operating procedures or practices that might affect the Central IRB’s ability to review for the institution;
      * of complaints from human subjects enrolled in studies reviewed by the Central IRB which involve potential unanticipated problems involving risks to subjects or others;
      * of unanticipated problems involving injury or risks to subjects or others in a study reviewed by the Central IRB;
      * if the Institution believes that serious or continuing non-compliance has occurred in a study reviewed by the Central IRB, and any steps the Institution deems necessary for remediation of non-compliance;
      * of suspension or termination of Institutional approval;
      * of any communication with the FDA, OHRP or funding agency relating to the institution’s studies being reviewed by the Central IRB;
      * changes in accreditation status, if applicable.
   8. ***Federally Funded Studies (optional, if applicable):*** *Institution will maintain a current, approved Federalwide Assurance (FWA) with OHRP for the duration of this Agreement. The Institution will notify the Central IRB promptly in writing if its FWA is suspended or expires for any reason.*
3. ***Joint Responsibilities***
   1. **Confidentiality** Each party is authorized to exchange information pursuant to this Agreement and agrees to treat such information as confidential (Confidential Information). No Party shall disclose Confidential Information received pursuant to this Agreement to any individual or entity other than another Party without prior written approval of all Parties. Notwithstanding the foregoing, nothing in this Agreement shall be construed to restrict a Party from disclosing Confidential Information as required by law, subpoena, court order, or other governmental order or request. Institution shall cause Principal Investigator and all other research personnel to comply with the terms and conditions of this section in the same manner as such terms and conditions apply to Institution. This section shall survive the termination of this Agreement.
   2. **Protected Health Information (Optional, if applicable)** The parties shall hold in confidence the identity of the participants in any Studies and shall comply with applicable laws regarding confidentiality of individually-identifiable subject information and the requirements of any authorization executed by subjects for a given study. . Each party shall comply with all applicable laws and regulations, including, but not limited to, HIPAA, relating to the use and disclosure and privacy and security of individually identifiable health information of human subjects (“**Subject Health Information**”). Each party shall use and disclose Subject Health Information only as authorized by the subject or legally-authorized representative pursuant to subjects’ written authorization and informed consent forms. Each party shall notify the other party orally and in writing within twenty-four (24) hours of its discovery of any Subject Health Information in its possession, which is improperly used or disclosed in violation of HIPAA or the applicable subject authorization, and serious or continuing noncompliance. The parties shall cooperate with each other in taking such steps as are deemed appropriate, to enjoin misuse, regain possession of the data, and otherwise protect each parties’ rights and subjects’ privacy. It is expressly understood that, by providing review services as described herein, Central IRB shall not be regarded as a “Business Associate” of Institution
   3. **Record Keeping** Central IRB and Institution agree to maintain records in compliance with all applicable federal, state, and local regulations regarding record retention and agree to make to records available when and as required by law.
   4. **Federal Regulatory Agency Review** Central IRB and Institution agree to notify the other party when a federal regulatory agency has or will conduct an audit or review of a study applicable to this authorization agreement and will notify each party of the outcome of the review.
   5. **Inspection** CentralIRB or its authorized representatives shall be permitted upon request to: (1) examine and inspect Institution’s facilities used for the performance of its research, including storage and use of any investigational products; (2) observe the conduct of the research performed at the Institution; (3) inspect and copy all documents relating to its studies, including study records and informed consent documents, investigational product logs, required licenses, certificates and accreditations; and (4) interview all necessary personnel involved in the research conduct of its studies.

Likewise the Institution shall be permitted upon request to (1) obtain copies of all applicable IRB correspondence pertaining to activities hereunder; (2) review Central IRB’s policies, procedures, roster and other information pertinent to board functions; and (3) inspect and copy all documents relating to its studies, including but not limited to protocols and informed consent documents, investigational drug brochures, reports, unanticipated problems, reports of noncompliance, required licenses, certificates and accreditations.

* 1. **Reporting to Sponsor, Federal Agencies, or other oversight entities** If the Central IRB or Institution determines that it must report the findings of an investigation to sponsor, OHRP, the FDA and/or other oversight entities, it will notify the Institution in advance. The party making the report will share the report with the other party before it is sent to the sponsor/oversight authority, and will copy the other parties’ institutional official(s) and designees. Nothing in this Agreement shall be construed to prevent prompt reporting, or an Institution or Central IRB from making its own report to OHRP, the FDA, in accordance with its written procedures, or from taking additional remediation steps.
  2. **Conflict of Interest Review** The Institution may perform its own investigator conflict of interest analysis under its relevant policies. Any applicable conflict of interest and associated management plan shall be communicated to the Central IRB. The Central IRB will apply its standard policies regarding confidentiality of review of information and disclosures submitted to it regarding potential investigator conflicts of interest. Central IRB will implement institutional conflict of interest management plans to the extent that they involve human subject protection considerations, such as mandated language in informed consent forms once this information is communicated to the Central IRB. If the Central IRB determines the management plan is not acceptable, the Central IRB will promptly inform the PI and the institution’s responsible individual.
  3. ***Clinical Trial Agreements and Compensation for Research Related Injury (Optional, if applicable)*** The Central IRB shall, unless a waiver of informed consent is issued, approve an informed consent form for use at the Institution. Institution shall ensure that the Clinical Trial Agreement (CTA) and the approved consent form do not conflict with each other with regard to provisions regarding the availability of compensation for research-related injury regarding the compensation for injury clause. In the event of a conflict between the CTA and the consent form, the research will not be approved until the conflict is resolved in a way acceptable to Institution and Central IRB.

1. ***General Terms and Conditions***
   1. ***Term and Termination*[[3]](#footnote-3)**The term of this Agreement shall commence upon execution of this Agreement by both parties, and shall continue until [DATE] or until such time as either party gives       days written notice of termination, whichever comes first. Notwithstanding the foregoing, in the event that either party is in default in the performance of any of its obligations under this Agreement, and the default has not been remedied within       days after the date of notice in writing of such default, the party not in default may terminate this Agreement immediately by written notice.

Notwithstanding the immediately preceding paragraph, the parties specifically recognize that 45 CFR 46.109(e) and 21 CFR § 56.109(f) requires that, “An IRB shall conduct continuing review of research . . . not less than once per year, and shall have authority to observe or have a third party observe the consent process and the research.” Therefore, termination of this Agreement shall not affect the Central IRB’s obligations of continuing review for studies approved hereunder or Institution’s payment responsibilities until such studies are appropriately transferred to a new IRB.

* 1. ***Assignment:*** This Agreement may not be assigned or transferred by either party without the prior written consent of the other party.
  2. ***Notices:*** All notices relating to this Agreement shall be delivered personally, by facsimile, by e-mail, by registered or certified first class mail, or by overnight courier service to the contact addresses set forth below. Notice shall be effective upon receipt if personally delivered, delivered by e-mail or delivered by facsimile; upon the third business day following the date of mailing by registered or certified first class mail; or on the first business day following the date of delivery to the overnight courier. All notices hereunder shall be directed as follows

If to Institution: [include information here]

If to Central IRB: [include information here]

* 1. ***IRB Review Fee:*[[4]](#footnote-4)** Central IRB will charge for services in accordance with its published fees. Central IRB will provide notice of changes to its fee structure prior to implementation. For new studies, Central IRB shall bill Institution, investigators or sponsors, or their agents, for services rendered as directed upon the applicable submission form(s); the Compensation provisions of this Agreement will survive termination of this Agreement.
  2. ***Relationship of the Parties:*** Each party’s relationship with the other is and shall be that of an independent contractor, and no partnership, joint venture, co-venture, employer/employee, principal/agent, master/servant, business associate or other similar relationship is created, or intended to be created, hereby. Neither party is nor shall be the agent or employee of the other, and neither party has authority to act on behalf of the other in any matter except to the extent expressly agreed upon in writing.
  3. ***Indemnification*[[5]](#footnote-5)** Institution shall indemnify and hold Central IRB, its officers, directors, employees and agents, harmless from liability resulting from the negligent acts or omissions of Institution, its agents or employees pertaining to the activities to be carried out pursuant to the obligations of this Agreement; provided, however, that Institution shall not hold Central IRB harmless from claims arising out of the negligence or willful malfeasance of Central IRB, its officers, agents, or employees, or any person or entity not subject to Institution’s supervision or control.

Central IRB shall indemnify and hold Institution, their officers, agents and employees harmless from any liability or loss resulting from judgments or claims against them arising out of the activities to be carried out pursuant to the obligations of this Agreement; provided, however, that the following is excluded from Central IRB’s obligation to indemnify and hold harmless:

* the negligent failure of Institution to substantially comply with any applicable governmental requirements; or
* the negligence or willful malfeasance by an, officer, agent, or employee of Institution.

This section shall survive the termination of this Agreement

* 1. ***Insurance*[[6]](#footnote-6) *Institution*** agrees that it shall maintain, or cause to be maintained, during the performance of this Agreement, insurance covering Institution, Principal Investigators and all other research personnel for bodily injury, death and professional liability, each with liability limits of not less than       per occurrence and       in the annual aggregate. The amount of Institution’s insurance coverage shall not be construed as creating a limitation on Institution’s indemnification obligations assumed herein. Institution will provide evidence of its insurance or self-insurance to Central IRB upon request. This section shall survive the termination of this Agreement. Central IRB will provide at its expense, and maintain throughout the term of this Agreement; general liability coverage in an amount no less than       each claim/     annual aggregate, and officer and director liability coverage in an amount no less than       each claim/     annual aggregate. Upon request, Central IRB agrees to provide Institution with Certificates of Insurance demonstrating this coverage.
  2. ***Amendment/Modification t***his Agreement shall not be subject to any change or modification unless such modification is signed by both parties and specifically states that it is an amendment to this Agreement.
  3. ***Governing Law*** This agreement shall be governed by the substantive law of the jurisdiction in which the reviews occur, without reference to that jurisdiction’s conflicts-of-law rules.

IN WITNESS WHEREOF, each party accepts the terms herein as evidenced by their authorized signatures below.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| [Institution] | |  | [Central IRB] | |
|  | |  |  | |
|  | |  |  | |
| (Authorized Signature) | |  | (Authorized Signature) | |
|  | |  |  | |
| Name: |  |  | Name: |  |
|  |  |  |  |  |
| Title: |  |  | Title: |  |
|  |  |  |  |  |
| Date: |  |  | Date: |  |

1. Flynn KE, Hahn CL, Kramer JM et al. Using central IRBs for multicenter clinical trials in the United States.

   PLoS One 2013; 8 (1): e54999.

   http://www.ctti-clinicaltrials.org/what-we-do/study-start/central-irb/products [↑](#footnote-ref-1)
2. Definition **of Central IRB:** A single IRB of record for all sites involved in a multi-center protocol. This is a properly constituted IRB to which sites cede all regulatory responsibility for scientific oversight and integrity of the protocol from initial review to termination of the research, including review of informed consent. A range of entities may serve as a central IRB (e.g. another institution’s IRB, a federal IRB, an independent IRB). [↑](#footnote-ref-2)
3. Institution and Central IRB should determine time periods for acceptable notification; the workgroup recommends periods no greater than 60 days. [↑](#footnote-ref-3)
4. Institution and Central IRB should determine fee schedule and time periods for payment in keeping with organizational policies. [↑](#footnote-ref-4)
5. The workgroup believes a section on indemnification may be important for agreements, which govern complex or large engagements. Note, the language provided is meant to simply serve as an example, should not be used without evaluation and may need to be altered based on state laws, organizational policies, or degree of risk to Institution or Central IRB [↑](#footnote-ref-5)
6. The workgroup believes a section on Insurance may be important for agreements which govern complex or large engagements. Note, the language provided is meant to simply serve as an example, should not be used without evaluation and may need to be altered based on state laws, organizational policies, or degree of risk to Institution or Central IRB [↑](#footnote-ref-6)