PUBLIC HEALTH SERVICE

EXAMPLE INTRAMURAL
CLINICAL TRIAL AGREEMENT

This Clinical Trial Agreement, hereinafter referred to as the "Agreement," consists of this Agreement, a Signature Page and various Appendices referenced in the Agreement. The Parties to this Agreement are:

(1) The **National Institute of Diabetes and Digestive and Kidney Diseases** hereinafter referred to as **"NIDDK"**; and

(2) _____ hereinafter referred to as "**Collaborator**".

Background

The NIDDK recognizes the importance of the pharmaceutical industry in the clinical development of new methods of treatment of many diseases and conditions and wishes to foster collaboration with industry whenever possible. As part of its mission to improve the treatment of *[insert disease]*, NIDDK shares with industry the important goal of defining the contribution of pharmacologic agents in the treatment of [insert disease]. The NIDDK, therefore, recognizes and supports the need of private Sponsors to focus at the appropriate time on clinical trials focused on the treatment of *[insert disease]*.

Thus, the NIDDK considers it appropriate for the investigators funded by the NIDDK to conduct a clinical trial that, in part, is supported by pharmaceutical firms, provided that the trial has scientific merit and is consistent with the overall goals of the funded investigators and the NIDDK.

The pharmaceutical firms recognize that participation in clinical trials developed by NIDDK funded investigators can lead to further insights into the indications for utilization of their drugs in the treatment of *[insert disease]*. The pharmaceutical firms also recognize the necessity of preserving the spirit of free and open inquiry among clinical investigators.

Collaborator is considered to be exempt from 45 CFR Part 46 and consequently Collaborator does not need an Assurance number from the Office of Human Research Protections, at the NIH for the following reasons:

1. Collaborator employees or agents neither interact or intervene with living individuals nor obtain, receive, or possess Identifiable Private Information about living individuals (e.g., Collaborator employees will receive and/or analyze data that cannot be linked to individual subjects, either directly or indirectly through codes).
2. Collaborator employees or agents access or review of Identifiable Private Information will be solely for purposes of on-site quality auditing. This Agreement unequivocally prohibits use or release of such information for other purposes.

WHEREAS, NIDDK, through its Principal Investigator *[name]*, wishes to conduct a clinical study utilizing *[insert compound]* supplied by COLLABORATOR, upon terms and conditions set forth in this Agreement;

NOW, THEREFORE, the parties agree to the following:

Article 1. Definitions

As used in this Agreement, the following terms shall have the indicated meanings:

1.1 "**Adverse Event Reaction**" or AER means an adverse clinical experience as defined under 21 CFR § 310.305 "Records and Reports Concerning Adverse Drug Experience", and other applicable Federal Regulations. Specific guidelines and policies for reporting adverse drug reactions, as well as common toxicity criteria have been developed.

1.2 "**Annual Report**" means a brief report of the progress of an IND associated investigation which the IND sponsor is required to submit to the FDA within 60 days of the anniversary date that the IND went into effect (pursuant to 21 C.F.R. § 312.33). If NIDDK is the drug sponsor, NIDDK shall provide COLLABORATOR a copy of the Annual Report simultaneously with the submission of the Annual Report to the FDA. In accordance with NIDDK procedures, Annual Reports will not be made public.

1.3 "**Clinical Center**" means the *[insert lab or section]* of NIDDK located at the Warren Grant Magnuson Clinical Center at NIH, which will conduct or perform experimental, developmental, or research work.

1.4 "**Compound**" shall mean Collaborator's *[insert compound name]*. Collaborator represents and agrees that the Compound supplied to NIDDK and Principal Investigator will be appropriately formulated pursuant to the United States Food and Drug Administration ("FDA") standards for investigational compounds.

1.5 "**Confidential Information**" means data or information related to the uses of Compound disclosed by either Party to the other Party. All such Confidential Information shall be owned solely by the providing Party. Confidential Information shall not include:

a) data or information that is in the public domain or subsequently enters the public domain through no fault of the receiving Party; or
b) data or information that is presently known or becomes known to the receiving Party from its own independent sources from a person having the legal right to disclose data; or
c) data or information that is developed independently by individuals who have not had access to Confidential Information; or
d) data or information that is required to be disclosed by law.

1.6 **"Drug Master Files"** or **"(DMFs)"** means reference files submitted to FDA that are used in the review of investigational and marketing applications for human drugs. Drug Master Files are submitted to the FDA to allow another party to reference this material without disclosing to that party the contents of the file.

1.7 "**FDA**" means the Food and Drug Administration, PHS.

1.8 **"Human Subjects"** means individuals whose physiologic or behavioral characteristics and responses are the object of study in a research project. Under the federal regulations for the protection of human subjects, human subjects are defined as living individuals about whom an investigator conducting research obtains: (1) data through intervention or interaction with the individual; or (2) identifiable private information (45 CFR §46.102(f)).

1.9 **"Identifiable Private Information"** means patient-identifying data from medical records or attached to patient specimens, to be obtained prospectively or from stored medical records or specimens, that can be linked to individual human subjects, either directly or indirectly through codes.

1.10 "**IND**" means an Investigational New Drug Application that is the legal mechanism under which experimental new-drug research is performed in the United States and is submitted to the FDA to receive approval to conduct experimental clinical trials. The FDA regulations require continual updates to the IND including, but not limited to, Annual Reports, Adverse Event Reaction reports, new protocols, protocol amendments and pharmaceutical data.

1.11 **"Investigational Drug Brochure" or "IDB"** means a document containing all the relevant information about the drug, including animal screening, preclinical toxicology, and detailed pharmaceutical data. Also included, if available is a summary of current knowledge about pharmacology and mechanism of action and a full description of the clinical toxicities.

1.12 "**Investigator**" means any physician who assumes full responsibility for the treatment and evaluation of patients on research protocols as well as the integrity of the research data.

1.13 **"IRB"** means the NIDDK Institutional Review Board.

1.14 **"Parties"** means Collaborator and NIDDK.

1.15 "**Principal Investigator**" or "**PI**" means the physician who has organizational and fiscal responsibility for its Party's use of federal funds to conduct a plan of research.

1.16 **"Protocol"** means the document describing how the clinical trial is to be performed.

1.17 "**Study**" means the specific clinical trial for which this Agreement is prepared. Clinical Protocol No. *[insert Protocol No.]* is attached as Appendix A.

1.18 **"Raw Data"** means the primary quantitative and empirical data first collected by an Investigator from experiments and clinical trials conducted under the scope of this Agreement.

1.19 **"Summary Data"** means a summary of the Raw Data used to prepare an Annual Report to the FDA. Summary Data shall specifically exclude Identifiable Private Information.

Article 2. Investigational New Drug Applications

Generally, the needs of both NIDDK and the Collaborator are best served when each sponsors an IND. It is expected, therefore, that either NIDDK or Collaborator will submit an IND that may cross-reference an IND, Drug Master File, or New Drug Application held by the other. In the event NIDDK elects to file its own IND, the Collaborator agrees to provide NIDDK background data and information and agrees to execute such documents as may be reasonably required to effect such cross-reference. Collaborator's employees will be reasonably available to respond to inquiries from the FDA regarding information or data contained in NIDDK's IND, Drug Master File, New Drug Application, or other information and data provided to NIDDK by Collaborator pursuant to this Article 2. Nothing herein shall require Collaborator to undertake additional studies of any kind or to prepare and submit any additional data to the FDA that are not already included in NIDDK's IND, Drug Master File, or New Drug Applications. In the event that either Party supplies CONFIDENTIAL information directly to the other Party in support of an IND, such information will be protected in accordance with the corresponding Confidentiality provisions of Article 10 of this Agreement. All information will be fully shared from each IND including, but not limited to, Investigation Drug Brochures, Adverse Event Reactions, and formulation and pre-clinical data, including toxicology findings. However, certain Collaborator proprietary information pertaining to manufacturing processes that is not required for the conduct of the Study may be held in confidence by Collaborator and not disclosed to NIDDK.

Collaborator may sponsor its own clinical trials and hold its own IND for studies performed outside the scope of this Study from which all data is proprietary Collaborator for purposes of this Agreement.

Article 3. Institutional Review Board Review

Before the Study is initiated, the NIDDK shall obtain, from the Institutional Review Board (IRB) of the NIDDK at the Clinical Center of the NIH, evidence of review and approval of the Study and the patient informed consent form to be used at that Center. The NIDDK PI will serve as a repository for IRB approved protocols and patient consent forms, including the yearly renewals. The NIDDK PI will monitor the receipt and quality of informed consent from all Study participants.

Article 4. Protocol

The Study will be conducted in accordance with the Protocol and all amendments as established by the PI for the trial. The Study is projected to enroll and treat approximately *[insert number]* patients in the United States for a minimum of *[insert number (#)]* years and a maximum of *[insert number (#)]* years.

Article 5. Conduct of Study

The Study shall be conducted in accordance with the terms of this Agreement, the Protocol(s), and all applicable federal laws, regulations, and guidelines. The location(s) where the Study is to be conducted and the number of patients to be enrolled in the Study are set forth in the Protocol(s).

Article 6. Adverse Event Reactions, Annual Reports, Other IND Data

NIDDK will provide COLLABORATOR with copies of all Adverse Event Reactions that may be possibly, probably, or definitely related to the use of the Compound used in this Study concurrently with their submission to FDA. In addition, copies of the Annual Reports and other pertinent IND data will be provided to COLLABORATOR by NIDDK as they become available. Collaborator in turn will provide the PI and NIDDK with relevant Adverse Event Reaction information from their on-going trials of *[insert compound]* during the course of this Agreement.

Article 7. Drug Information and Supply

For the performance of this Study, COLLABORATOR shall supply, without charge the Compound. Such Compound shall be supplied on such schedule as specified in the Protocol. Further, neither NIDDK nor Principal Investigator shall charge any third party payer or patient enrolled in the Study for the Compound, nor shall NIDDK or Principal Investigator include the cost of such drug in any cost report to third party payers.

(a) COLLABORATOR will provide sufficient Compound and placebo to complete the Study in accordance with the Protocol.

(b) COLLABORATOR will provide starter kits, drug maintenance and placebo in sufficient quantity for the patients participating in the Study.

(c) All COLLABORATOR drug supplies will be packaged and shipped by COLLABORATOR to the Clinical Center. The Clinical Center pharmacy will dispense the assigned drugs to the Study participants in accordance with FDA regulations and the Study Protocol. The Clinical Center pharmacy will return unused Compound to COLLABORATOR, or dispose of same at COLLABORATOR'S option. Unused Compound shall be accounted for and disposed of in accordance with 21 CFR 312.59 and other applicable regulations.

(d) The Compound will not, under any circumstances, be used other than as specified in the Protocol.

Collaborator agrees to provide the NIDDK Principal Investigator with an Investigational Drug Brochure describing all known contraindications, warnings, precautions, and adverse reactions associated with the administration of the Compound. If such information is revised while the Study is in progress, the latest revisions will also be sent to the NIDDK Principal Investigator at that time.

For inquiries related to Compound, the contact person for Collaborator will be *[insert Collaborator contact information]* and the NIDDK contact will be *[insert NIDDK contact information]*.

Article 8. Data Rights

The Raw Data generated under this Agreement are considered the property of the Party that generates the data. Analysis of the Raw Data will be conducted by NIDDK in accordance to the statistical methods delineated in the Protocol. In addition to any other reports or data made available to them hereunder, COLLABORATOR shall be provided on a timely basis:

(a) Annual copies of all final Summary Data reports;
(b) Annual patient accrual status report (Site ID, Investigator, patients: enrollment status, total screened, in screening, failed screening, total enrolled, enrolled failure, active, complete, dropped); and
(c) Annual overview of study progress (Proposed timelines for start-up and completion of the Study).

The data generated in trials conducted by NIDDK are the property of NIDDK. Collaborator shall have complete access to all Summary Data and results generated under this Agreement that are in the possession and control of NIDDK. Summary Data will be made fully available to Collaborator for its own analyses and for its application for FDA approval.

Collaborator's access to and review of Identifiable Private Information shall only be for on-site quality auditing. Collaborator will receive Identifiable Private Information only if necessary for purposes of satisfying FDA or health authorities' reporting requirements, and for internal research purposes directly related to obtaining regulatory approval of Compound.

Article 9. FDA Meeting

All meetings with FDA concerning this Study will be discussed by the Parties in advance and will be held on mutually agreed upon dates. Each Party will have the opportunity to suggest topics for the agenda for such a meeting and attend such meeting.

Article 10. Proprietary Data and Confidential Information

Upon completion or early termination of the Agreement, each Party will promptly return to the other Party all written Confidential Information supplied by or which incorporates Confidential Information of the other Party. Each Party will maintain one copy of the written Confidential Information supplied by or which incorporate Confidential Information from the other Party for archival purposes.
Neither Party will use any Confidential Information supplied by the other Party for its own benefit or for the benefit of any third party, and will not furnish to any third party any materials which incorporate any Confidential Information supplied by the other Party except as required under court order or the Freedom of Information Act (5 U.S.C. §552), or as otherwise required by law. The Parties shall immediately notify the other, in writing, of such required disclosure. All obligations of confidentiality and non-disclosure set forth in this Agreement will survive until the third (3rd) anniversary of the date on which this Agreement executed, unless extended by mutual written agreement.

Article 11. Publications

Neither Party shall issue a press release that uses the other Party's name or trademarks without the express written consent of the other Party. Collaborator issued press releases that reference or rely upon the work of NIDDK under this Agreement shall be made available to NIDDK at least fourteen (14) days prior to publication for review and comments. Collaborator shall not in any way state or imply that this Agreement is in an endorsement of any product or service by the U.S. Government or any of its organizations units or employees.

Before either Party submits a paper or abstract for publication or otherwise intends to publicly disclose information about this Agreement, the other Party shall be provided thirty (30) days to review the proposed publication and ten (10) days prior to an abstract presentation, for review and comments or disclosure to assure that Proprietary/Confidential Information is protected.

The publication or other disclosure shall be delayed for up to thirty (30) additional days for publications and five (5) days for abstracts, upon written request by any Party as necessary to preserve U.S. or foreign patent or other IP rights.

Article 12. Patents

This Agreement shall have no effect on the Parties' rights in the existing inventions and technologies of each including, but not limited to, the Compounds, and information and technology relating to the Protocol. Nothing in this Agreement will be construed as granting any license or obligation to license any intellectual property owned by Collaborator to NIDDK with respect to compound other than the limited right to use Compound for the performance of the protocol in accordance with the terms of this Agreement.

This Agreement does not represent a Cooperative Research and Development Agreement (CRADA) under the Federal Technology Transfer Act, 15 U.S.C. 3701 et seq). Neither Party is authorized to promise rights in advance for inventions developed under this Agreement.

Article 13. Indemnification

No indemnification for any loss, claim, damage, or liability is intended or provided by any Party under this Agreement. Each Party shall be liable for any loss, claim, damage, or liability that said Party incurs as a result of its activities under this Agreement, except that the NIDDK, as an agency of the United States, assumes liability only to the extent as provided under the Federal Tort Claims Act (28 U.S.C. Chapter 171).

Article 14. Governing Law

This Agreement shall be governed by and construed in accordance with Federal law as construed by the Federal Courts of the District of Columbia. Federal law and regulations will preempt any conflicting or inconsistent provisions in this Agreement. NIDDK and Collaborator, if Collaborator is sponsoring trials at the NIH under this Agreement, shall comply with all Department of Health and Human Services regulations relating to Human Subject use.

Article 15. Period of Agreement

The Agreement will be effective upon the execution of this document by all Parties and shall be in effect for ten (10) years from execution or five (5) years from enrollment of the last patient, whichever occurs first.

Article 16. Notices

If any Party is required, or wishes to give any notice hereunder, such notice shall be deemed to be duly given when delivered via traceable courier to the address given by the addressee in this Article or by subsequent written notice to all Parties. The primary executive contacts responsible for the coordination and communication of any written notices of this Agreement are listed below:

For the NIDDK:

Name:
Title:
Address:

Telephone:
Fax:

For Collaborator:

Name:
Title:
Address:

Telephone:
Fax:

Article 17. Modifications

This Agreement and the Study shall not be altered or otherwise amended except pursuant to an instrument in writing signed by each of the Parties hereto, except that either Party to this Agreement and the Study may waive any obligation owed to it (and only to it) by the other Party under this Agreement and Study. The waiver by either Party hereto of a breach of any provision of this Agreement or Study shall not operate or be construed as a waiver of any subsequent breach.

Article 18. Debarment Clause

Each Party represents that to the best of its knowledge that it does not use in any capacity the services of any person debarred under subsections 306(A) or 306(B) of the Generic Drug Enforcement Act of 1992 (the "Act") in connection with any of the services performed by the Party hereunder. Each Party to the best of its knowledge will not use in any capacity the services of any person debarred under such subsection of the Act and will immediately disclose in writing to the other Party if any person who is performing services hereunder is debarred or if any action, suit, claim, investigation or legal or administrative proceeding is pending or, to the best of the Party's knowledge, threatened, relating to the debarment of the Party or any person performing services hereunder. Upon receipt of such written disclosure, or if the Party becomes aware of such debarment or threatened debarment, then the Party shall have the right to immediately terminate this Agreement.

Article 19. Disclaimer of Warranty

NIDDK UNDERSTANDS AND AGREES THAT COLLABORATOR MAKES NO WARRANTY, EITHER EXPRESSED OR IMPLIED, REGARDING THE USE OF THE COMPOUND IN THE STUDY. WITHOUT LIMITING THE FOREGOING, COLLABORATOR EXPRESSLY DISCLAIMS ANY WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE.

Article 20. Compliance with the Law

NIDDK shall conduct the Study in accordance with all rules and regulations promulgated by the FDA, including 21 CFR Part 312, and all other applicable federal, state and local laws, rules and regulations.

Article 21. Termination

A. This Agreement may be terminated at any time by the mutual written consent of the Parties.
B. Either Party may unilaterally terminate this Agreement at any time by giving written notice to the other Party at least ninety (90) days prior to the desired termination date subject to Article 22.
C. Collaborator may terminate this Agreement immediately for safety reasons.

Article 22. Alternative Sources of Compound in the Event Collaborator Terminates Development of the Compound

A. In the event Collaborator elects to terminate its development of Compound for reasons other than safety, without the transfer of its development efforts and obligations under this Agreement to another party acceptable to NIDDK within ninety (90) days of discontinuation then Collaborator will provide NIDDK with Compound for all then-enrolled patients sufficient to complete the Study in the manner described in the Protocol.

B. Collaborator hereby grants to NIDDK a nonexclusive, nontransferable, irrevocable, paid-up license to practice or have practiced for or on behalf of the United States any invention which Collaborator may have or obtain on Compound, its manufacture, or on the process for use of Compound, throughout the world, for medical research purposes related to *[insert scope of use]*. This license shall only become effective in the event Collaborator terminates its development of Compound for reasons other than safety, without the transfer of its development efforts to another party within ninety (90) days of termination, and NIDDK elects to continue the development of Compound. This provision shall become null and void upon FDA approval of the Compound indications and marketing of the Compound by Collaborator.

Article 23. Survivability

The provisions of this Agreement as they relate to Confidential Information and Drug Supply shall survive the expiration or early termination of this Agreement.

ACCEPTED AND AGREED

FOR NIDDK:

_____ _____

Name: Date
Title:

Address
National Institute of Diabetes and Digestive and Kidney Diseases
National Institutes of Health
9000 Rockville Pike
Bethesda, MD 20892

FOR COLLABORATOR:

_____ _____

Title:
Name: Date

Address