

## Legal Agreements and Confidentiality Agreements

This worksheet provides an overview of the various types of legal agreements utilized in the clinical research setting. These agreements include Confidentiality Agreements, Material Transfer Agreements (MTA) Clinical Trial Agreements (CTA) and Cooperative Research and Development Agreements (CRADA)

### Confidentiality Agreement

<b>DEFINITION</b>	<ul style="list-style-type: none"> <li>IT IS AN AGREEMENT THAT BINDS THE SIGNATORY TO KEEPING ALL PATIENT, EMPLOYEE, RESEARCH, AND PROPRIETARY INFORMATION CONFIDENTIAL AND KEPT FOR THE PURPOSES OF ITS INTENDED USE</li> </ul>
<b>Purpose</b>	<ul style="list-style-type: none"> <li>It commits the individual to an ethical and legal obligation of protecting the information and authorizes the disclosure of information to managers, and those on a need- to – know basis only as part of healthcare delivery, education, or research. It protects the patients from media and unauthorized use of confidential information</li> </ul>

### Material Transfer Agreement (MTA)

<b>Definition</b>	<ul style="list-style-type: none"> <li>A material transfer agreement (MTA) is the free exchange of proprietary information for the receiving party to use it for his/her own research purposes</li> <li>There is no collaboration between scientists and involves scientists of various institutions (both for profit or non-profit institutions).</li> </ul>
<b>Intellectual Property Rights and Rights for Commercial Purposes</b>	<ul style="list-style-type: none"> <li>In this type of agreement, neither intellectual property rights nor rights for commercial purposes are granted.</li> </ul>
<b>Typical Terms and Conditions of MTA</b>	<ul style="list-style-type: none"> <li>Specific MTAs define the terms and conditions under which the recipients may use the materials granted</li> <li>Each specific agreement agreements lists the specific requirements that the materials be used for research purposes only and that they cannot be used in human subjects</li> </ul>
<b>Material of Human Origin</b>	<ul style="list-style-type: none"> <li>Any material that is of human origin must be given the proper Assurance Number and is subject to the provisions of 45 CFR Section 46, entitled Protection of Human Subjects</li> <li>All human samples or materials derived form human samples must also be approved by the Institutional Review Board</li> </ul>
<b>MTA Application Process</b>	<ul style="list-style-type: none"> <li>In order to undertake a transfer, an interested party must contact the owner of the material of interest, then negotiate an acceptable MTA with the NIH Technology Transfer Office or other authorized NIH Office, create an appropriate agreement, and have the proper representative sign to legally bind the other party</li> </ul>

## Clinical Trial Agreement (CTA)

<b>Definition</b>	<ul style="list-style-type: none"> <li>• <b>A Clinical Trial Agreement consists of a written agreement, a signature page, and any appendices referenced in the agreement, and serves to document the conditions, aims, background, parties, protocol, adverse events, compound information, etc. about a clinical trial</b></li> </ul>
<b>Typical Information included in the CTA</b>	<p>The CTA:</p> <ul style="list-style-type: none"> <li>• Describes the party involved as well as the participant who is collaborating in the study</li> <li>• Describes the clinical study, the treatment used, and the disease</li> <li>• Describes what the parties agree to</li> <li>• Lists the meanings of the words involved</li> </ul>
<b>Investigational New Drug (IND) Application</b>	<ul style="list-style-type: none"> <li>• Collaborator must submit an Investigational New Drug (IND) Application, which includes background data and information of the treatment involved</li> </ul>
<b>Institutional Review Board (IRB) Review</b>	<ul style="list-style-type: none"> <li>• Before the start of the study, the Investigator must have evidence of review and approval of the study and the patient informed consent form to be used</li> <li>• The Principal Investigator must have records of the protocols that were approved by the IRB protocols and all finalized patient consent forms</li> </ul>
<b>Protocol Conduct of Study</b>	<ul style="list-style-type: none"> <li>• The study must be conducted in accordance with the protocol with the number of patients and a number of years involved</li> <li>• The protocol for the study must be in agreement with all federal laws, regulations, and guidelines</li> <li>• The location of where the study is to be conducted must be included</li> </ul>
<b>Adverse Event Reactions, Annual Reports, and INDs</b>	<ul style="list-style-type: none"> <li>• The collaborator must include copies of all adverse event reactions that may possibly occur</li> <li>• Copies of annual reports and other pertinent IND data should be provided to the FDA, reviewed, and distributed among the collaborators.</li> </ul>
<b>Drug Information and Supply</b>	<ul style="list-style-type: none"> <li>• The collaborator must supply the sufficient amount of the compound or placebo involved in the study</li> <li>• The Principal Investigator cannot charge the third party for the drug involved in the study</li> <li>• The collaborator must also provide the Investigational Drug Brochure describing all known contraindications, warnings, precautions, and adverse reactions associated with the administered compound</li> </ul>
<b>Data and Data Rights</b>	<ul style="list-style-type: none"> <li>• Data generated by the respective organization is the property of the organization and the Principal Investigator involved</li> <li>• The Principal Investigator is responsible for releasing annual copies of all final summary data reports</li> <li>• The Principal Investigator is also responsible for releasing an annual patient accrual status reports which includes the site ID, investigator, patients, enrollment status, total screened, in screening, failed screening, total enrolled, enrolled failure, active, complete, and dropped</li> <li>• An annual overview of study progress is also released with proposed timelines for the start-up and completion of the study</li> </ul>

<b>Proprietary Information and Confidential Information</b>	<ul style="list-style-type: none"> <li>• Upon completion or early termination of the agreement, each party will return all other party all written confidential information supplied by or which incorporated confidential information of the other Party</li> <li>• 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</li> <li>• 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 or as otherwise required by law</li> </ul>
<b>Publications</b>	<ul style="list-style-type: none"> <li>• Neither party shall issue a press release that uses the other party's name trademarks with the express written consent of the other party</li> <li>• Before either party submits a paper or abstract for publication or otherwise intends to publicly disclose information about the agreement, the other party shall be provided time to review the proposed publication and time before the abstract presentation for review and comments or disclosure to assured that Proprietary/ Confidential information is protected</li> </ul>
<b>Patents</b>	<ul style="list-style-type: none"> <li>• The agreement shall have no effect on the parties' rights in the existing inventions and technologies</li> </ul>
<b>Indemnification</b>	<ul style="list-style-type: none"> <li>• No indemnification for any loss, claim, damage, or liability is intended or provided by any party under this agreement</li> <li>• 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</li> </ul>
<b>Governing Law</b>	<ul style="list-style-type: none"> <li>• The agreement shall be governed by and construed in accordance with Federal laws as construed by the Federal Courts of the District of Columbia</li> </ul>
<b>Period of Agreement</b>	<ul style="list-style-type: none"> <li>• The agreement will be effective upon the execution of this document by all parties and shall be in effect for a certain period of time</li> </ul>
<b>Notices</b>	<ul style="list-style-type: none"> <li>• Any additional notifications that may be of concern for the clinical trials</li> </ul>
<b>Modifications</b>	<ul style="list-style-type: none"> <li>• This agreement and the study shall not be altered or amended except pursuant to an instrument in writing signed by each of the parties</li> </ul>
<b>Debarment Clause</b>	<ul style="list-style-type: none"> <li>• Each party represents that to the best of its knowledge that it does not use in any capacity the services of any person debarred in connection with any of the services performed by the party</li> </ul>
<b>Disclaimer of Warranty</b>	<ul style="list-style-type: none"> <li>• The collaborator makes no warranty regarding the use of the compound in the study</li> </ul>
<b>Compliance with the Law</b>	<ul style="list-style-type: none"> <li>• The study shall be conducted in accordance with all rules and regulations by the FDA, federal, state, and local laws, rules and regulations</li> </ul>
<b>Termination</b>	<ul style="list-style-type: none"> <li>• The agreement can be terminated at any time by the mutual written consent of the parties</li> </ul>
<b>Alternative Sources for Compound</b>	<ul style="list-style-type: none"> <li>• The parties must specify alternative options if the primary source of the compound can no longer supply funding and supplies for the development of the compound</li> </ul>
<b>Survivability</b>	<ul style="list-style-type: none"> <li>• The provisions of this agreement as they relate to confidential information and drug supply shall survive the expiration of early termination of this agreement</li> </ul>
<b>Acceptance of Agreement</b>	<ul style="list-style-type: none"> <li>• Name, date, title, and address of collaborator</li> <li>• Name, date, title, and address of organization</li> </ul>

## Cooperative Research and Development Agreement (CRADA)

<b>Definition</b>	<ul style="list-style-type: none"> <li>• A CRADA is a formal research and development agreement of collaboration between a Public Health Service (PHS) laboratory (federal party) and a non-federal party such as a pharmaceutical or biotechnology company</li> <li>• Research can cover basic, preclinical, or clinical areas, a combination of any, or even a nontraditional project like developing software</li> <li>• This partnership encourages work between federal laboratories, state and local governments, universities, and the private sector</li> <li>• It is the only mechanism available to NIH or any government agency to promise licensing rights to future inventions to a company or collaborator</li> </ul>
<b>Purpose</b>	<ul style="list-style-type: none"> <li>• The purpose of this agreement is to encourage national technological competition and rapid transfer of innovation to the marketplace by sharing resources and research</li> </ul>
<b>Types of CRADAs</b>	<ul style="list-style-type: none"> <li>• Standard CRADAs</li> <li>• Material CRADAs (M-CRADAs)</li> <li>• Clinical Trials CRADAs (CT- CRADAs)</li> </ul>
<b>Contribution of each party</b>	<ul style="list-style-type: none"> <li>• Under this agreement the PHS laboratories contribute personnel, services, facilities, equipment, or other resources with or without reimbursement</li> <li>• The non-federal parties provide funds, personnel, services, facilities, equipment, or other resources toward a specified research or development project</li> </ul>
<b>Intellectual Property</b>	<ul style="list-style-type: none"> <li>• For pre-CRADA intellectual property, whatever intellectual property rights the non-federal party or federal party owns before the CRADA agreement was established still completely remains theirs. Neither party cannot expect rights to the other's party's previously owned intellectual property</li> <li>• The federal or non-federal party can license any needed background rights to conduct the CRADA research</li> <li>• New inventions discovered during the CRADA term, what is joint is joint to all parties involved and what was previously agreed to belong to each party, still belongs to each party</li> </ul>
<b>Licensing</b>	<ul style="list-style-type: none"> <li>• The CRADA collaborator does not get an automatic license to all CRADA subject inventions.</li> <li>• The CRADA collaborator only receives an option to negotiate an exclusive or non-exclusive license for the NIH inventions discovered while the CRADA was active</li> <li>• Licensing is expected to be royalty-bearing</li> <li>• The fields of use will be consistent with the scope of the CRADA research plan</li> </ul>
<b>Time period</b>	<ul style="list-style-type: none"> <li>• The exchange of material, research, and development occurs in a specific field over an agreed upon period of time which is specific in the CRADA agreement</li> </ul>
<b>Funding in CRADA</b>	<ul style="list-style-type: none"> <li>• CRADA is not intended to be a general funding mechanism</li> <li>• They are to be used to settle the costs of the project of a specified project</li> <li>• Therefore, the sole justification for a CRADA cannot be for a PHS laboratory to conduct research or tests for the collaborator, support post-doctoral fellows, technicians, obtain funds, or purchase equipment</li> </ul>
<b>Situations for creation of CRADA</b>	<ul style="list-style-type: none"> <li>• There is not always a clear definition of what the CRADA encompasses; however it is necessary when:             <ul style="list-style-type: none"> <li>○ there is an exchange of material and or research and development over a substantial period of time,</li> <li>○ when staff or equipment is to be supplied by one or more parties,</li> <li>○ when the industrial partner contributes funding or requests the granting of intellectual property rights, and</li> <li>○ when an industrial partner is providing otherwise non-available material to PHS and requests the transfer of intellectual property rights</li> </ul> </li> </ul>
<b>Topics for CRADA</b>	<ul style="list-style-type: none"> <li>• There is no restriction on the scope of topics that CRADA encompasses; PHS investigators are free to choose the subject matter</li> <li>• However, all CRADA research projects must be highly focused, defined, and explained</li> </ul>

<b>Assessment Criteria for Receiving a CRADA</b>	<ul style="list-style-type: none"> <li>• Each CRADA will be assessed for its research objectives</li> <li>• The proposed CRADA are considered by PHS components in order to determine CRADA appropriateness compared to procurement contracts, material transfer agreements, cooperative agreements or other contractual mechanisms</li> </ul>
<b>Involvement of Parties</b>	<ul style="list-style-type: none"> <li>• CRADA agreements are only appropriate with investigators who will make large contributions to the research project</li> <li>• Sponsored research involving routine or conventional research is not suitable for CRADA</li> <li>• There must be an intellectual contribution from all parties in order to meet the standards of a CRADA. CRADA research results must be published and discussed in order to fulfill the mission of PHS</li> <li>• Thus, if any CRADA agreement unreasonably restricts scientific interaction or dissemination of research it will not be approved</li> </ul>
<b>CRADA Process</b>	<ul style="list-style-type: none"> <li>• The collaborator is selected             <ul style="list-style-type: none"> <li>– Fair access to all parties is established                 <ul style="list-style-type: none"> <li>○ By law special consideration is given to small business firms and businesses located outside the United States</li> <li>○ In accordance with this, fair access for collaborative opportunities is provided to all outside organizations</li> </ul> </li> <li>– Conflicts of Interest are addressed                 <ul style="list-style-type: none"> <li>○ No Principal Investigators in either party involved in the CRADA owns stock above threshold amount in the prospective collaborating company</li> <li>○ No Principal Investigator can be a paid consultant with the collaborating company</li> <li>○ No Principal Investigator is on the Board of Scientific Advisors at the collaborating company</li> <li>○ No negotiating official or signatory at the prospective collaborating company is a former NIH employee within the past 12 months</li> </ul> </li> </ul> </li> <li>• The agreement is arranged             <ul style="list-style-type: none"> <li>– Appendix A: The Research Plan                 <ul style="list-style-type: none"> <li>○ Specific goals</li> <li>○ Introduction, background, and expertise of the parties</li> <li>○ A workscope which includes the responsibilities of the parties and a detailed description of the scope of the research</li> <li>○ A list of publications, patents, patient applications, and prior agreements</li> </ul> </li> <li>– Appendix B: Financial and Staffing Contributions                 <ul style="list-style-type: none"> <li>○ The contribution of materials, facilities, equipment, and staff that is committed by each party</li> <li>○ Any funds provided by the collaborating parties</li> </ul> </li> <li>– Appendix C: Modifications to the CRADA Template                 <ul style="list-style-type: none"> <li>○ Certain terms in the agreement which restate statutory law and regulations cannot be modified</li> <li>○ Certain terms which reflect NIH policy can be modified</li> <li>○ All other terms are to be negotiated to accommodate each collaborator's needs.</li> </ul> </li> </ul> </li> <li>• NIH reviews the CRADAs</li> <li>• The various parties execute your tasks as established in the agreement</li> </ul>
<b>Oversight of CRADA</b>	<ul style="list-style-type: none"> <li>• Within NIH, the CRADA Subcommittee meets monthly to review new and existing CRADAs</li> <li>• Within each specific NIH institute representatives include:             <ul style="list-style-type: none"> <li>– Technology development</li> <li>– Director of Technology Transfer and Development</li> <li>– Principal Investigator and Lab Chief</li> <li>– Ethics coordinator</li> <li>– Scientific Director</li> </ul> </li> <li>• This committee includes representatives from             <ul style="list-style-type: none"> <li>– NIH Office of Technology Transfer</li> <li>– NIH Office of the General Counsel</li> <li>– NIH Scientists</li> <li>– Office of the Director</li> </ul> </li> </ul>

Non-CRADAs versus CRADAs

MTAs, CTAs, RCAs, etc	CRADAs
<ul style="list-style-type: none"> <li>• No funds to NIH</li> <li>• No license options or IP rights</li> <li>• Purpose is transfer materials (MTAs) and/ or conduct research (RCAs), clinical studies (CTAs)</li> <li>• Does not and usually is not collaborative but can be esp. in case of RCAs and CTAs</li> </ul>	<ul style="list-style-type: none"> <li>• Funds can flow to NIH form collaborators</li> <li>• Company gets license option to yet to be discovered CRADA inventions</li> <li>• Purpose is to conduct research (of any kind)</li> <li>• Must be a true collaborative effort with intellectual input from all parties</li> </ul>

Sources

1. NIH OTT: <http://www.ott.nih.gov/cradas/crada.html>
2. NIAID: [http://www3.niaid.nih.gov/about/organization/odoffices/omo/otd/When\\_to\\_use\\_MTA\\_CRADA.htm](http://www3.niaid.nih.gov/about/organization/odoffices/omo/otd/When_to_use_MTA_CRADA.htm)
3. NCI: <http://ttc.nci.nih.gov/resources/brochures/sec6c.php>
4. NIH Clinical Center: <http://cris.cc.nih.gov/accounts/pdf/CCConfidentialityAgreement.pdf>