

Additional Technical Proposal Instructions

The following Additional Technical Proposal Instructions are meant to provide additional instructions as well as a uniform format for technical proposals. The information requested in these instructions should be used as a guide for formatting and preparing the proposal. Offerors should follow the instructions in Section L of the solicitation, plus include the information requested in this Attachment.

Offerors are advised to give careful consideration to the Statement of Work (SOW), all reference material, and attachments, the technical evaluation criteria, and the RFP as a whole, in the development of their Technical Proposal.

Offerors who propose subcontracts to perform portions of the Statement of Work should clearly identify the specific sections for which they plan to utilize subcontractors, as well as the method and level of integration between the prime and subcontractor(s), and the expected advantages of such an approach.

The Government encourages the offerors to be complete but succinct in the presentation and to limit the total number of pages for the entire proposal to **150 pages**.

TOTAL PAGE COUNT DOES INCLUDE: Principal Investigator's (PI's) Resume/*Curriculum Vitae* (CV), with highlights of any items that are directly related to the subject project, indicated by preceding them with a double asterisk (**).

TOTAL PAGE COUNT DOES NOT INCLUDE (some of which may be added as appendices): Table of Contents; Section Dividers that do not contain information other than title of Section; Resumes/CVs of other key personnel (same information and format as used for the PI); certificates and licensures, examples of protocols, Standard Operating Procedures (SOP), Health and Safety Manual, letters of commitment by proposed consultants and subcontractors.

FORMATTING AND LAYOUT:

Use your usual word processing and spreadsheet programs to prepare and format the technical and business proposals.

Documents submitted using Adobe .pdf shall be submitted using a .pdf searchable format.

- Type size must be a minimum of font of Arial 10.
- Type spacing should be no more than 15 characters per inch. Within a vertical inch, there must be no more than six lines of text.
- Print margins must be at least one inch on the left and .075 inch margins on the remaining sides.
- Print setup should be single-sided on standard letter size paper (8.5 x 11").
- Offerors shall **NOT** use 8.5 x 14 legal size paper.
- Proposals shall **NOT** include links to Internet Web site addresses (URLs) or otherwise direct readers/reviewers to alternate sources of information.
- Additional appendices may be added as needed.

- The proposal with pagination, including appendices, shall be formatted sections, cross referenced, and include a detailed Table of Contents with page references.

Please provide a CD with the electronic copy of the Technical Proposals in .pdf readable format.

TECHNICAL PROPOSAL – TABLE OF CONTENTS

General Instructions

SECTION 1

- A. PROPOSAL TITLE PAGE. Include RFP title and number, name of organization, DUNS number, proposal part, and identify if the proposal is an original or a copy.
- B. PROJECT OBJECTIVES (NIH FORM 1688-1)
- C. GOVERNMENT NOTICE FOR HANDLING PROPOSALS
- D. PROPOSAL SUMMARY AND DATA RECORD (NIH-2043)
- E. TABLE OF CONTENTS

Section L of the RFP specifies the minimum documentation requirements for cost data and all cost related support. All related documentation should be included in the proposal in a clearly marked section. Cost and Pricing support should be provided for all proposed subcontractors.

SECTION 2: MANDATORY QUALIFICATION CRITERIA

The offeror should include all information that documents and/or supports the mandatory qualification criterion in one clearly marked section of its technical proposal.

This section related to the Mandatory Qualification Criteria must be listed in the Table of Contents with a page reference.

SECTION 3 TECHNICAL DISCUSSIONS

The technical discussion included in the technical proposal should respond to the items set forth below:

a) Personnel and Experience

General:

The offeror shall document staff experience to conduct this work. Documentation shall include education, training and experience of the offeror's proposed staff. Demonstrate training and experience by providing specific examples of projects in staff resumes indicating level of involvement and outcomes.

Describe the experience and qualifications of all personnel who shall be assigned for direct work on this project. Information is required which shows the composition of the task or work group, its general qualifications and recent experience with similar programs. Each area of the Statement of Work should be addressed in sufficient detail to permit evaluation of the proposal in terms of the adequacy and availability, as needed, of all staff to be assigned to the project. Indicate the approximate percentage of total time each could be made available for this contract and specifically to which tasks each employee would be assigned. Also demonstrate that contractor employees will be available on short notice, operations during inclement weather and under conditions of multiple and competing tasks.

Provide complete detailed resumes of the Project Manager and all other senior level personnel that indicate their educational background, recent research experience associated with biomedical research, and scientific accomplishments. A minimum of a Master's Degree in biology, biomedical or health related field or equivalent is considered appropriate for this position.

Include dates, places and names of previous employers, and any related training. State the estimated time to be spent on the project. Senior level personnel include: Co-Project Manager, Safety Team Leader(s), InSight[®] template and publishing lead, Clinical Research Team Leader and the IND regulatory support team leader.

Because of the complex and detailed nature of the information involved, employees shall require considerable instruction and orientation to function efficiently. A stable workforce is therefore necessary. Indicate the employment stability of all personnel assigned to this project by evidence of CVs or resumes noting continued service with this or another organization.

Key personnel shall not be consultants or subcontractors. For proposed consultant relationships to be acceptable, the prospective contractor shall provide signed agreements between itself and the consultant clearly stating the availability for assignment and the priority of this project's needs in relation to the needs of the consultant's employer, if any, and/or other projects in which the consultant may be involved. Please note that subcontractor staff may not be proposed for the Project Manager/Principal Investigator position.

OFFERORS SHOULD ASSURE THAT THE PROJECT MANAGER AND ALL OTHER PERSONNEL PROPOSED SHALL NOT BE COMMITTED ON FEDERAL GRANTS AND OTHER CONTRACTS FOR MORE THAN A TOTAL OF 100% OF THEIR TIME. IF THE SITUATION ARISES WHERE IT IS DETERMINED THAT A PROPOSED EMPLOYEE IS COMMITTED FOR MORE THAN 100% OF HIS/HER TIME, THE GOVERNMENT WILL REQUIRE ACTION ON THE PART OF THE OFFEROR TO CORRECT THE TIME COMMITMENT.

Key Personnel

List the names of the individuals who shall be responsible for overall implementation and management of the contract. This includes the offeror's key contact for technical aspects of the program and those individuals responsible for supervision and management of staff. It is expected that Project Management would consist of at least one individual responsible for overall project management and additional team leaders for the management of Clinical Research, IND Support staff and Adverse Event Reporting. The lead Project Management personnel will be named as Key Personnel in the contract.

The Project Manager(s) should possess at minimum a Master's Degree in a biomedical or health related field or equivalent with relevant experience in meeting FDA (CDER and CBER) Regulations and medical writing. The individual responsible for overall management of the contract should document experience in directing a project with multiple tasks and shifting priorities and experience in managing a multi-disciplinary team of individuals with a primary focus of the team management being maintenance and enhancement of data management systems and databases for clinical research. The individual should have experience managing a workforce of similar size, scope and complexity as required for this contract. The proposal should document this individual's knowledge and experience in development of a quality control program, the use of database systems, and the management of employees who use computers to work with Microsoft Office, SharePoint and InSight.

It is expected that other personnel responsible for the management of the Clinical Research Support team and IND Regulatory support staff will possess either a Master's Degree or equivalent in a biomedical or health related field with experience supervising efforts similar to those to be conducted under the contract, particularly the supervision of activities involving the collection and processing of medical research data. Also, extensive experience with information technology and database utilization should be documented.

It is expected that Adverse Event Reporting management will require a sound understanding of medical terminology, CTCAE, MedDRA, organ system terminology and medical case management. The Adverse Event Reporting Team Leader must demonstrate experience in leading an AE Reporting team and possess a minimum of a Master's Degree or equivalent in a biomedical or health related field. The AE reporting team should comprise of a minimum of one physician with experience and one nurse with experience in the assessment of oncology AE reports. These staff should demonstrate experience with computerized databases, biomedical research record-keeping or biomedical research abstraction.

As part of the presentation of Key Personnel, describe which management personnel will be responsible for:

- being the primary key contact for technical aspects of the contract
- staffing of the contract and monitoring hours and expenses charged to the contract
- authorizing purchases within the scope of the contract

- overall personnel management
- supervision of Clinical Research and IND Regulatory Support staff
- secondary key contact for technical aspects of the contract
- supervision and management of the Adverse Event Reporting
- supervision of electronic InSight[®] software IND publishing and FDA gateway submissions

Other Professional Support

i) Clinical Research Support

The proposal should document the personnel that will be responsible for preparation of FDA Annual Reports and assisting in the maintenance of an up to date project management plan for each agent. In conjunction with the IDB physician responsible for a clinical agent or portfolio of agents, these personnel are expected to develop a thorough familiarity with the agents, update Investigator's Brochures, and prepare FDA Annual Reports and other summary data reports and manuscripts. This staff shall perform literature searches and maintain and regularly update literature searches and bibliographies. These individuals also obtain and maintain files of publications related to the agent. This staff attends IDB and BRC meetings, drafts Project Team Application announcements and prepares responses to LOIs. The preparation of reports relevant to drug/biologics development is performed by Clinical Research Support staff, as is in the analyses of data. These personnel are expected to have a Master's or higher degree (or equivalent experience) in relevant sciences (Immunology, Chemistry, Microbiology, Toxicology, Pharmacology, etc.) and excellent writing skills. Familiarity with information technology and database utilization is also desirable.

ii) IND Preparation Support

These individuals write organize and assemble Investigational New Drug Applications (INDs) from materials supplied by RAB. The format, organization and content of the INDs shall be specified by RAB and a model IND shall be supplied. The IND shall contain all elements required to meet FDA regulations for an IND (21 CFR 312). Manufacturing information, preclinical data, pharmacokinetics, and toxicology data will in most cases be supplied by various Divisions of the NCI and clinical investigators. Draft pre-IND meeting requests and briefing packages. These individuals may be required to interact with the appropriate parties to obtain additional information. These individuals will acquire appropriate publications using PubMed or Grateful Med/Loansome Doc online computer programs to obtain relevant publications for incorporation into the IND. These staff should have experience in preparing IND sections in

electronic CTD IND compatible format with understanding of InSight[®] IND electronic publishing and submission software. These individuals will attend relevant NCI and pharmaceutical company meetings. A minimum of two individuals should have experience with the development and requirements of electronic IND templates for InSight[®] publishing and submitting documents through the FDA electronic gateway. It is expected that the personnel assigned to this work will possess at least a Master's Degree in relevant sciences (Immunology, Chemistry, Microbiology, Toxicology, Pharmacology, etc.) and excellent writing skills.

iii) IDE/CDRH Pre-sub Preparation Support

These individuals write organize and assemble Investigational Device Exemptions (IDEs)/Pre-sub from materials supplied by RAB. The format, organization and content of the IDEs/Pre-sub shall be specified by RAB and a model IDE shall be supplied. The IND IDE shall contain all elements required to meet FDA regulations for an IND IDE/Pre-sub (21 CFR 3812). Manufacturing information, preclinical data, pharmacokinetics, and toxicology data will in most cases be supplied by various Divisions of the NCI and clinical investigators. These individuals may be required to interact with the appropriate parties to obtain additional information. These individuals will order appropriate publications using PubMed or Grateful Med/Loansome Doc, on line computer programs to obtain relevant publications for incorporation into the IND IDE/Pre-sub. These individuals will attend relevant NCI and pharmaceutical company meetings. It is expected that personnel assigned to this work will possess at least a Master's Degree in relevant sciences and excellent writing skills.

iv) Adverse Event Reporting

Adverse Event (AE) reporting requires staff that will be responsible for processing all adverse events transmitted to the NCI for DCTD, NCI-sponsored therapeutic clinical trials as outlined in Section 2 (A-H) of the Statement of Work. Individuals proposed for this work should demonstrate knowledge of Common Toxicity Criteria for Adverse Events (CTCAE), MedDRA terminology and usage, and electronic AE reporting systems. The AE staff should be aware of differences between versions of CTC and CTCAE. The composition of the Adverse Event team shall have a minimum of one physician and one nurse. They must demonstrate their experience with safety reporting for oncology agents, be familiar with the conduct of cancer clinical trials and have prior work experience in AE reporting. In addition, personnel should have documented knowledge of medical terminology, the requirements of AE reporting, data entry and database access experience.

v) Information Technology

Information technology staff will be responsible for maintaining on-site computer hardware and software used to support CTEP designated tasks. Staff shall be involved in the upgrade and maintenance of on-site IT systems to ensure that they are current with evolving technology and operational requirements. This should be demonstrated by providing resumes of IT staff with examples of past experience noting staff's extent of involvement. This staff will maintain a reliable high speed-high capacity data link that meets NIH security clearance standards. These individuals will collaborate with IT and operational staff from the NCI or NCI contractors to troubleshoot application and identify system improvements.

General and Administrative Support

- i) Research and Development Agreement Support (Sections 1.E. 1-6 of the Statement of Work). Experience and familiarity with database software, presentation software, organizational charts and project management software is expected by personnel proposed for this support.
- ii) IND and MF Processing as specified in Sections 1.A, 1.B, 1.C., 1.D of the Statement of Work Personnel proposed for this activity are expected to demonstrate familiarity with computers, database and project management software.
- iii) Data entry activities. Familiarity with medical terminology and experience with high level data entry pertaining to Sections 1.A, 1.C, 1.E.iv and 4.A-E of the Statement of Work.
- iv) Literature Search Activities. This includes searching and retrieving publications for inclusion into INDs and DMFs and distribution to IDB and RAB staff. This necessitates that computer searches be performed on specific topics. Older publications and non-electronic journals and texts may still require someone to physically go to the library.
- v) Administrative Support. Documentation of experience with medical terminology, RABITS, Insight[®], Word, Excel, and MS Office Suite (including PowerPoint), PDF files, SharePoint, and database entry and retrieval should be provided (paragraphs 4.A-F. of the Statement of Work).

b) Technical Approach

The proposal should include: (1) a statement of the overall objectives of the project, as envisaged by the offeror; and (2) an outline of the technical approach that would be used to achieve the objectives.

Proposals should address each area of the Statement of Work in a manner which describes the offeror's approach to the particular task and methods of quality assurance. The offeror should demonstrate a clear understanding of the needs of the program and an understanding of the potential problems involved with these types of projects.

Specifically, the offeror should discuss its technical understanding of the requirements for investigational agent development including INDs, the contents and format of INDs, FDA Annual Reports, Investigator's Brochures, drug related scientific manuscripts, adverse event tracking, computerized databases and approach to clinical research information management. The offeror should discuss its understanding of the scientific needs of the project and understanding of the regulatory and information needs and requirements related to sponsoring clinical research with a large number of investigational agents. The offeror should demonstrate a clear understanding of the technical aspects of investigational agent development, adverse event tracking, clinical research information management, and regulatory and legal requirements associated with sponsoring clinical research with investigational agents. The offeror should discuss the approach to addressing changing FDA regulations. The offeror should also demonstrate a technical understanding of the information needs in tracking a large number of clinical trials, the specific information needs of the National Cancer Institute related to its mission, and an understanding of the potential problems involved with these types of projects.

The offeror must explain the methods for accomplishing the various tasks including methods of assuring quality performance, quality control and flexibility to meet shifting priorities.

The offeror should discuss overall project approaches and approaches to special problems in regulatory affairs and clinical research. The proposal must demonstrate an understanding of the needs of the project and an understanding of the FDA and the Center for Biologics Evaluation and Research (CBER) and the Office of Division of Oncology Drug Products, CDER in particular. The proposal must demonstrate knowledge of the organization of the Division of Cancer Treatment and Diagnosis, NCI.

In most cases the Government will provide the necessary proprietary information such as preclinical screening, animal toxicology, chemistry/manufacturing/control information, pharmacology, investigator's brochure, clinical research and protocol

as well as instructions on how to prepare the IND. IND preparation requires significant scientific and technical writing. Drafting an IND and requires literature searches and acquiring appropriate reference information and organization of the IND into the appropriate format. [21 CFR 312, 600, 700 and 800; 45 CFR part 46, 21 CFR parts 50, 56].

The offeror will need to demonstrate expertise and ability to comply with the FDA requirements for electronic submission of INDs and IND amendments through the e-sub gateway. NCI utilizes InSight Software for electronic eCTD IND submission preparation. Until NCI fully transitions to fully electronic submissions, paper IND amendments will be submitted to the FDA, there will be a transition period in which some submissions will be paper and others electronic. NCI expects that submissions will be fully electronic by April 1, 2018. For the purposes of estimating costs, offerors should assume that the average number of paper copies of INDs required will be four (4) per IND. Additionally, the assumption should be that one (1) copy shall remain at the contractor site, three (3) copies shall be delivered to the FDA, and electronic files shall be delivered to collaborative drug manufacturers as well as filed in the RAB database.

The offeror shall demonstrate the expertise and ability to be involved in the upgrade and maintenance of on-site IT systems to ensure that they are current with evolving technology and operational requirements. This staff will maintain a reliable high speed, high capacity data link that meets NIH security clearance standards.

The offeror will be responsible for maintaining all new, current, inactivated, withdrawn and transferred IND paper and electronic files in addition to those cited in 1A. There are currently approximately 120 active INDs.

Approximately twelve IDB physicians are responsible for the medical and scientific development of a large number of individual anti-cancer agents which are assigned to them. These physicians are assigned portfolios of agents based on agent mechanism, such as cell signaling, angiogenesis inhibitors, monoclonal antibodies, cancer vaccines, as well as a number of additional unrelated agents which may be assigned to them. They are responsible for assuring that the development plans for the agents are appropriate and for monitoring the safety and activity of the agents in development. They are also responsible for insuring the accuracy of and approving regulatory and scientific documents, such as clinical brochures, annual reports, scientific manuscripts, and adverse event reports that are prepared for agents in their portfolios. Adequate discharge of these responsibilities requires detailed and current knowledge of the relevant medical/scientific literature and close and timely collaboration and communication between the responsible IDB physician the clinical research support staff who will also develop an in-depth knowledge of the agents, perform the necessary literature searches, and draft these relevant documents. The offeror should describe a structure that will facilitate this close collaboration and communication and insure timely interactions. The offeror should describe how they will resolve computer problems and will be responsible

for the installation of new computers and software that is compatible with CTEP computer systems.

The Contractor shall maintain a backup personnel system for key personnel and key positions. Provide a succession plan for key personnel and a detailed description of how the contract performance will be maintained during fluctuations in the personnel needs as a result of high or low levels of work, etc. Also explain in detail the plan for maintaining performance during periods of extended absences by personnel (defined as greater than 10 consecutive working days). For personnel proposed as "backup" personnel to key positions, Curriculum Vitae or resumes should be provided. Back-ups named must be thoroughly familiar with the position that they are supporting.

c) **Corporate Experience**

Offerors should describe in detail prior experience of the organization in furnishing services similar to each area described in the Statement of Work. The proposal should include sufficient information to demonstrate the previous effectiveness of the firm in similar or related work and the ability to smoothly coordinate all aspects of the Statement of Work. Include documentation with specific reference to applicable contract numbers, dates of agreements and dollar volume. This documentation should include clear and concise description of these project(s) and should indicate the project sponsors (e.g., pharmaceutical company, Government contract or grant, etc.). For each of the described projects, references (including phone numbers) should be provided. Please note that organizational experience is defined as accomplishment of work, either past or ongoing that is comparable or related to the effort required by this RFP. This includes overall offeror or corporate experience, but not the experience and/or past performance of individuals who are proposed as personnel involved with the Statement of Work in the RFP. The relationship of the proposed working group within the offeror's organizational structure should be described as well as how this relationship may facilitate performance on this project. Describe the hierarchal organization of the proposed staff and the approach to supervision and management. Information should be provided on how staff training needs shall be met.

If the proposal includes the use of a subcontractor, please describe the supervision and management of subcontract staff. Please provide information that demonstrates that the prime and subcontractor can work together in a seamless and effective manner to accomplish coordinated tasks.

Include a statement on the priority your organization would place on this work effort as compared to other commitments now or reasonably expected during the proposed period of performance of the contract. Provide documentation of how the corporate office and expertise shall provide support to this project and the organization would support the Project manager in resolving problems or special situations.

d) **Facilities and Equipment**

The offeror should provide detailed information regarding the office facilities, storage facilities, and equipment available for use on this project, or clearly describe how they will be available at the start of the project. Detailed information regarding a fire suppression room available to hold regulatory documents should be provided. Documentation of a minimum of 2000 cubic feet of secure fire suppression space available to store NCI files. Include documentation of a non-water based fire suppression measures with a minimum of NFPA 2001 standards, secure room access and the system maintenance plan in use.

Performance of the Statement of Work will be conducted in other than NCI facilities and the contractor will be required to provide suitable office space and equipment to permit their staff to perform file maintenance and storage, managerial and report preparation, copying and distribution, and record-keeping functions. The offeror should provide a list of the computer and printer equipment designated for routine use by contract staff with descriptors such as processor speed, memory, operating system and printer speed information. The offeror should provide a plan for upgrading this equipment and discuss the frequency and benchmark by which the upgrades shall occur. The offeror must provide detailed information on a fully installed and reliable high speed, high capacity data link with access to NCI servers that meets NIH security clearance standards. The offeror must demonstrate how it will assure that the stored files will be maintained in their original condition and in electronic files. The offeror must have the ability to readily transfer paper files upon request and to transfer other information rapidly via electronic means (E-mail). The offeror should have the ability to access databases such as the CTEP-ESYS, Medline, Cancerlit, PubMed, Grateful Med, Loansome Doc and PDQ or similar databases. The offeror should submit a floor plan showing space which would be dedicated to this project. Due to the nature of the described work, location of all project staff in consolidated office space is preferable in order to enhance communications and accessibility. However, if the work is to be performed in more than one location, describe the interrelationships, organization and personnel of the respective organizations. In addition, describe and demonstrate efficient integration of the locations and provide a contingency plan for when phone and computer systems are down.

OTHER CONSIDERATIONS

Record and discuss specific factors not included elsewhere which support your proposal. Using specifically titled subparagraphs, items may include:

- a) Unique arrangements, equipment, etc., which none or very few organizations are likely to have which is advantageous for effective implementation of this project.

- b) Equipment and unusual operating procedures established to protect personnel from hazards associated with this project.
- c) Other factors you feel are important and support your proposed research.
- d) Recommendations for changing reporting requirements if such changes would be more compatible with the offeror's proposed schedules.
- e) Regarding subcontracts: In the event that the offeror does not have facilities, equipment, or personnel for performing any component of the described in each section, then the offeror shall be prepared to implement the work through a suitable subcontractor(s). The proposal shall include the sub-contractors prior experience with projects of similar size and scope to those which they are assigned. Letters of commitment from and qualifications of all proposed subcontractors shall be included in the proposal. The offeror shall describe any previous working relationship with proposed subcontractors. Furthermore, the offeror shall address how they will handle privacy of contract issues, i.e., the offeror should explain how information will flow between the NCI, the prime contractor (offeror), and any subcontractors since the prime contractor's presence is required for any discussions.