**AMENDMENT OF SOLICITATION/MODIFICATION OF CONTRACT**

1. CONTRACT ID CODE
   - N/A

2. AMENDMENT/MODIFICATION NO.
   - 01 (one)

3. EFFECTIVE DATE
   - 1/24/2018

4. REQUISITION/PURCHASE REQ. NO.
   - N/A

5. PROJECT NO. (If applicable)
   - N/A

6. ISSUED BY
   - National Institutes of Health
   - Eunice Kennedy Shriver National Institute of Child Health and Human Development
   - Contracts Management Branch
   - 6710B Rockledge Drive
   - Bethesda, MD 20892

7. ADMINISTERED BY (If other than Item 6)
   - CODE
   - N/A

8. NAME AND ADDRESS OF CONTRACTOR
   - TO THE PROSPECTIVE OFFEROR

9. AMENDMENT OF SOLICITATION NO.
   - NIH-NICHD-OPPTB-2018-2

10. MODIFICATION OF CONTRACT/ORDER NO.
    - CODE
    - FACILITY CODE

11. THIS ITEM ONLY APPLIES TO AMENDMENTS OF SOLICITATIONS
   - ✗ The above numbered solicitation is amended as set forth in Item 14. The hour and date specified for receipt of Offers is extended, ✗ is not extended. Offers must acknowledge receipt of this amendment prior to the hour and date specified in the solicitation or as amended, by one of the following methods:
     (a) By completing Items 8 and 15, and returning one (1) copy of the amendment;
     (b) By acknowledging receipt of this amendment on each copy of the offer submitted;
     or (c) By separate letter or telegram which includes a reference to the solicitation and amendment numbers. FAILURE OF YOUR ACKNOWLEDGMENT TO BE RECEIVED AT THE PLACE DESIGNATED FOR THE RECEIPT OF OFFERS PRIOR TO THE HOUR AND DATA SPECIFIED MAY RESULT IN REJECTION OF YOUR OFFER.

12. ACCOUNTING AND APPROPRIATION DATA (If required)
   - N/A

13. THIS ITEM APPLIES ONLY TO MODIFICATIONS OF CONTRACTS/ORDERS, IT MODIFIES THE CONTRACT/ORDER NO. AS DESCRIBED IN ITEM 14.

   A. THIS CHANGE ORDER IS ISSUED PURSUANT TO: (Specify authority) THE CHANGES SET FORTH IN ITEM 14 ARE MADE IN THE CONTRACT ORDER NO. IN ITEM 10A.

   B. THE ABOVE NUMBERED CONTRACT/ORDER IS MODIFIED TO REFLECT THE ADMINISTRATIVE CHANGES (such as changes in paying office, appropriation date, etc.) SET FORTH IN ITEM 14, PURSUANT TO THE AUTHORITY OF FAR 43.103(b).

   C. THIS SUPPLEMENTAL AGREEMENT IS ENTERED INTO PURSUANT TO AUTHORITY OF:
      - D. OTHER (Specify type of modification and authority)

   E. IMPORTANT: Contractor ✗ is not, ✗ is required to sign this document and return 1 copy.

14. DESCRIPTION OF AMENDMENT/MODIFICATION (Organized by UCF section headings, including solicitation/contract subject matter where feasible.)

**PURPOSE:** To amend RFP NIH-NICHD-OPPTB-2018-2, entitled, “Best Pharmaceuticals for Children Act Pediatric Trials Network” and to respond to inquiries received.

**DUE DATE:** Until February 21, 2018, 4:00 PM Local Time (Eastern Standard Time (EST) (Unchanged). Questions must be submitted in writing via e-mail by January 31, 2018 (Unchanged).
A. As a result of this Amendment the RFP is revised as follows:

1. Page 47, PART III – SECTION J – INFORMATIONAL ATTACHMENTS is modified to add the following new Attachment:

   ATTACHMENT 25 Additional Technical and Business Proposal Information

2. PART III – SECTION J LIST OF ATTACHMENTS, Attachment 1 – Packaging and Delivery is hereby deleted and replaced to reflect the changes specified below. See revised Attachment 1 - Packaging and Delivery included with this Amendment.

II. Formatting and Page Limitation, subparagraph B. Page Limitations is revised as follows:

   B. Page Limitations

   **TECHNICAL PROPOSAL**
   The offeror must submit one (1) electronic PDF file for the Technical Proposal including the following:
   1. *IDIQ – Not to exceed 50 pages*
   2. *Task Order 1 – Not to exceed 25 pages*
   3. Sample Task Order 2 – Not to exceed 25 pages

   The proposal should not exceed 100 pages.

   * Offerors have the option to combine Task Order 1 and the IDIQ.

   **BUSINESS PROPOSAL**
   The offeror must submit one 1) electronic PDF file for the Business Proposal (including budget narrative) with **two (2) sections:**
   1. Task Order 1
   2. Sample Task Order 2

   NO PAGE LIMITS ON BUSINESS PROPOSALS

   In addition, the Offeror must include the Excel Spreadsheet with the Breakdown of the Proposed Estimated Costs

3. Page 54, PART IV – SECTION L, subparagraph d. ESTIMATE OF EFFORT, the last paragraph is revised as follows:

   The above information is provided for guidance only and is not to be considered restrictive (see **Attachment 25** “Additional Technical and Business Proposal Information” for more details).

B. This Amendment provides answers to questions received regarding this RFP, please note that individual questions may have been combined or reworded.

**Question 1:** Do we need to submit 3 separate budget Excel files for IDIQ contract, Task Order 1 and Sample Task Order 2?

**Answer:** No, Offerors are only required to submit two separate budget Excel files: one for Task Order 1 and one for Sample Task Order 2. Attachment 1 – Packaging and Delivery was revised to reflect the change in the number of separate budgets required.

**Question 2:** Is it correct that the main clinical trial work should be listed in the IDIQ contract section while the Task Order 1 is to assemble the team and infrastructure (Core Function Activities)?

**Answer:** Yes. See Attachment 1 - Packaging and Delivery included with this Amendment.
**Question 3:** Is it correct that the Contractor should present the “Draft Work Plan” in the IDIQ contract technical proposal and it will be revised after the Initial Kick-Off Meeting with the comments from NICHD?

**Answer:** Yes, Offerors must submit an initial work plan with the proposal submission and it will be reviewed by NICHD after the Initial Kick-Off Meeting. See Attachment 25 – Additional Technical and Business Proposal Information included with this Amendment.

**Question 4:** Is it correct that a nomination package of potential experts for each Network Steering Committee (NSC) should be included in both the IDIQ base Technical Proposal and Task Order 1 Technical proposal?

**Answer:** Offerors may choose to include the NSC nomination packages with the IDIQ and/or Task Order 1. See revised Attachment 1 - Packaging and Delivery included with this Amendment.

**Question 5:** Since the Protocol Development Teams (PDT) will be assembled only after the Initial Kick-Off Meeting, clinical protocols will not be finalized before the Effective Date of the Task Order (EDOTO). Should the Contractor still propose potential clinical sites?

**Answer:** Yes, an initial core of clinical sites based on the areas of consideration listed in the IDIQ SOW should be proposed. See Attachment 3a, page 3 of the IDIQ SOW.

**Question 6:** Can an NIH biosketch be used in place of a CV?

**Answer:** Yes.

**Question 7:** The RFP requests the inclusion of a Base Contract section in the Business Proposal. Should this section include a summary budget that reflects the maximum reimbursement amount ($96M)?

**Answer:** No, Offerors are required to submit only one electronic PDF file for the Business Proposal (including budget narrative) with two (2) sections: Task Order 1 and Sample Task Order 2. See the revised Attachment 1 – Packaging and Delivery included with this Amendment.

**Question 8:** The Statement of Work for Sample Task Order 2 lists the requirements as 1) providing a summary of literature and 2) developing a draft protocol. However, the technical requirements list trial implementation and close-out tasks. Should the Business Proposal, Cost Proposal, and Technical Proposal reflect literature review, protocol development, and trial implementation (to include close-out) or should the proposals only reflect literature review and protocol development?

**Answer:** For evaluation purposes, offerors are required to develop a protocol that includes the requirements listed on Attachment 3c – Sample Task Order 2 SOW (page 1) for submission with their Technical Proposal. In addition, the Technical Proposal must also address the technical requirements listed on pages 2-4 of Attachment 3c – SOW Sample Task Order 2 (preparation for implementation, implementation and close-down).

The Business/Cost Proposal should only include technical requirements listed on pages 2-4 of Attachment 3c – SOW Sample Task Order 2 (preparation for implementation, implementation and close-down).
Additional Technical and Business Proposal Information

In addition to the format requirements for the Business Proposal that are contained in Section L of the solicitation, the information presented here is to assist with proposal preparation.

A. General Contract Information

1. Most clinical testing will be conducted on four (4) age groups for the clinical studies.
2. Phase 3 studies (large scale efficacy trials) are unlikely, but possible.
3. For studies conducted in the European Union (EU), the Contractor must have experience in regulatory standards for international trials, in line with the International Conference on Harmonisation (ICH), the EU and the European Medicines Agency (EMEA) guidelines.
4. Formulations:
   a. A new research formulation of a commercially available drug, likely a liquid formulation for the pediatric clinical trials, may be required in some instances for the pediatric clinical trials conducted under the PTN.
   b. The formulation must be produced according to FDA’s Good Manufacturing Practice (GMP) standards.

B. Task Order 1 (Core Function Activities)

1. Draft Work Plan – Offerors must submit an initial work plan with the proposal submission.
2. Estimate of Effort: The Government considers the effort to be approximately 3,640 labor hours per year for Task Order 1. The information is provided for guidance only and is not to be considered restrictive.
3. Travel Assumptions: Assume one trip per year for four people to attend a one-day meeting in Bethesda, MD.
4. Offerors should assume the following tasks will be initiated during the life of Task Order No. 1:
   Types of Clinical Studies – NICHD anticipates that individual TOs for Clinical Studies will be written for one of the following types of trials during performance of this Contract:

   a. Phase 1 studies
      1) Phase 1 studies may need to be performed prior to the Phase 2 study to determine the correct dose for the larger Phase 2 study.
      2) The Phase 1 studies will be designed with either a sparse or dense PK sampling, and with pertinent safety data collection.

   b. Phase 2 studies
      1) Phase 2 studies are small efficacy and safety studies, and may include PK data collection.
      2) The Phase 2 studies may use the dose determined from the Phase 1 PK/dose-ranging study.
C. Sample Task Order 2 (Pharmacokinetics and Safety of Ciprofloxacin in Obese Children)

**NOTE:** The purpose of Sample Task Order 2 is to assess the Offerors’ capabilities to conduct and fulfill the requirements of the Statement of Work for projects of similar scope and size to be issued under contracts awarded in response to this solicitation. Although Sample Task Order 2 will NOT be executed nor, will an award be made, Offerors are to include in their proposals a response that specifies the methods by which the Sample Task Order 2 will be accomplished.

For evaluation purposes, offerors are required to develop a protocol for the Sample Task Order 2 study and submit it with their proposal. This requirement includes the following:

1. The Offeror must provide a summary of literature of successful and failed pediatric PK/Safety clinical trials (as well as FDA label review) for ciprofloxacin involving obese children and relevant comparator studies.
2. A draft protocol shall be developed including the following:
   a. Assume that the number of patients 1 – 18 years of age needed to achieve statistical significance is 50. To ensure adequate representation across the pediatric age spectrum, the study population will contain a minimum of 6 children in each of the following age cohorts: 1-< 6 years, 6-<12 years, and 12-<18 years.
   b. Determine the number of sites required for adequate recruitment.
   c. Develop a screening process for site recruitment.
   d. Develop inclusion/exclusion criteria for the study.
   e. Develop a drug-specific PK study design, employing a timed sampling scheme to determine the PK.
   f. Present draft statistical analysis plan including PK modeling to determine correct dosing for protocol purposes.
   g. The impact of all covariates on ciprofloxacin systemic exposure and apparent plasma clearance (e.g., demographic determinants of extent of obesity such as the waist: hip ratio, genotype, body mass index (BMI), and resting energy expenditure (REE) shall be explored using validated population-based PK methods (NONMEM).
   h. As part of the protocol describe what steps will be taken to ensure clinical and laboratory Quality Control.
   i. Develop clinical and laboratory criteria for safety and tolerability.
   j. Draft/revise the informed consent and assent forms (ICF).
PACKAGING AND DELIVERY OF PROPOSAL FOR USE WITH THE NIH ELECTRONIC CONTRACT PROPOSAL SUBMISSION (eCPS) WEBSITE

I. PROPOSAL SUBMISSION

A. eCPS:

2. Proposals submitted by facsimile or e-mail will not be accepted.
3. Follow the “How to Submit an Electronic Proposal” instructions provided on the eCPS website at: https://ecps.nih.gov/home/howto. Please note that creating an account to submit may take up to three (3) business days. Please apply for a new account early to allow enough time for the registration process.
4. Offerors are solely responsible for submitting proposals and any modifications or revisions so as to reach the Government office designated above by the date and time specified in the solicitation. If your proposal is not received by the date and time specified in the solicitation, it will be considered a “late proposal,” in accordance with HHSAR 352.215-070, Late Proposals and Revisions (December 18, 2015).

B. Creating and Naming Files:

1. Create one PDF file of your Technical Proposal, including all attachments. The Technical Proposal should be created in a PDF format that enables word searches to the maximum extent practicable. Forms and/or documents requiring signature(s) may be scanned, but must be merged into the Technical Proposal PDF file.
2. Create one PDF file of your Business Proposal, including all attachments: The Business Proposal should be created in a PDF format that enables word searches to the maximum extent practicable. Forms and/or documents requiring signature(s) may be scanned, but must be merged into the Business Proposal PDF file. Additionally, the “Breakdown of Proposed Estimated Costs (plus Fee) with Excel Spreadsheet” (http://oamp.od.nih.gov/sites/default/files/DGS/contracting-forms/spshexcl_dec2012.xlsx) must be included in the Business Proposal.
3. Create your Business Document Excel. The Excel file should be the “Breakdown of Proposed Estimated Costs (plus Fee) with Excel Spreadsheet” (http://oamp.od.nih.gov/sites/default/files/DGS/contracting-forms/spshexcl_dec2012.xlsx) included in the Business Proposal in its original Excel format, not PDF. Multiple Excel files may be included, as necessary.
4. File naming convention: It is requested that the filenames for your Technical Proposal, Business Proposal, and Excel Workbook include the name of the offeror, the solicitation number and the type of proposal (i.e., Technical, Business, or Excel Workbook).

Examples:
Excel Workbook: XYZ Company_ NIH-NICHD-OPPTB-2018-2_Business.xlsx
II. FORMATTING AND PAGE LIMITATIONS

A. Proposal Formatting:

1. The PDF files should be created in a format that enables word searches to the maximum extent practicable.
2. Each of the proposals, Technical and Business, must be separate and complete, so that evaluation of one may be accomplished independently of, and concurrently with, evaluation of the other.
3. Proposals shall not include links to internet website addresses (URLs) or otherwise direct readers to alternate sources of information.
4. Font size must be 10 to 12 points
5. Spacing should be no more than 15 characters per inch. Within a vertical inch, there must be no more than six lines of text.
6. Print margins must be at least one-inch on each edge of the paper.
7. Signatures may be electronic, or scanned, but must be merged into the respective file

Failure to adhere to the formatting requirements above may impact whether your proposal is reviewed in its entirety.

B. Page Limitations

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The proposal should not exceed 100 pages.

In addition, the Offeror must include the Excel Spreadsheet with the Breakdown of the Proposed Estimated Costs

The page limitation is inclusive of all attachments, but does not include: bio sketches/resumes, references, Summary of Related Activities, NIST 800 53 Self-Assessment, Proposal Cover Sheet, Section Dividers that do not contain information other than title of Section, Technical Proposal Direct Cost Summary Sheets, Title and Back Page and Table of Contents. (Please note that the Draft Information Security Plan should be included in the business proposal). **Pages in excess of this limitation will be removed from the proposal and will not be considered.**