REQUEST FOR PROPOSAL

Cognitive Interview Study and Preparation of Initial Briefing Package

Critical Path Institute (C-Path) is seeking proposals, including timelines and budget, to conduct a cognitive interview study and prepare an Initial Briefing Package ready for submission to FDA. This is to support the continued development of two clinical outcome assessments (COAs), a patient-reported outcome (PRO) measure and an observer-reported outcome (ObsRO) measure, that can be qualified by the FDA for use as secondary endpoints in clinical trials to document treatment benefit in pediatric patients ages four to 11 years old with asthma, for the purposes of labeling.

The purpose of this Request for Proposal (RFP) is to facilitate selection of the most appropriate organization to complete this project. The project will be completed in conjunction with C-Path’s PRO Consortium (https://c-path.org/programs/pro/). C-Path, in cooperation with the FDA and the medical products industry, formed the PRO Consortium for the purpose of developing, evaluating, and qualifying COA tools for use in clinical trials designed to evaluate the safety and effectiveness of medical products.

Information contained in your proposal will be evaluated by the members of the PRO Consortium’s Pediatric Asthma Working Group and will be considered confidential.

Clarifying questions must be received no later than November 9, 2018; a conference call may be convened if deemed necessary. Proposals must be received by November 21, 2018. Both are to be sent to:

Stephen Joel Coons, PhD
Executive Director, PRO Consortium
sjcoons@c-path.org

I. RFP Provisions

The proposal is a firm offer that will be considered valid for 180 calendar days from the due date. Please provide the contact information of the person responsible for submitting the proposal. C-Path shall not be responsible for any errors or omissions on the part of the Bidder in preparing this proposal. Bidder shall bear all costs associated with preparing this proposal.
This RFP is being distributed to numerous organizations and is posted on the C-Path website, www.c-path.org. The project will be awarded based on organizational qualifications and experience, proposal content, schedule, and cost. We will be unable to provide any verbal or written feedback on any individual proposals.

Please prepare your proposed strategy to address the objectives and scope of the cognitive interview study and development of an Initial Briefing Package (IBP) ready for submission to FDA. You must demonstrate a knowledge base consistent with the objectives and requirements of this RFP and describe your cognitive interview strategy and rationale of the qualitative methods (e.g., site identification, patient/caregiver recruitment, number of patient/caregiver interviews, number of rounds of interviews) that will be used to confirm the content of the PRO and ObsRO measures. All of the required elements (i.e., methods, deliverables, milestones, experience, timelines, and costs) should be clearly explained in 30 pages or less.

II. Background

The U.S. Food and Drug Administration (FDA) has identified pediatric asthma as an area in need of novel COA tools for evaluating treatment benefit in clinical trials for a broader range of asthma patients (i.e., < 12 years old).

Merck Sharpe & Dohme Corp., a member of the PRO Consortium, contributed draft versions of a PRO measure (for completion by children ages 8 to 11 years old) and an observer-reported outcome (ObsRO) measure (for completion by parents or caregivers of children ages 4 to 11 years old) developed for use in pediatric asthma trials. The PRO Consortium’s Pediatric Asthma WG was formed to examine Merck’s research and assess the adequacy of the two draft measures as candidates for qualification. The draft measures cannot be shared currently due to confidentiality agreements in place. A summary of work completed to date is provided in the attached poster (Appendix A) that was presented at the Ninth Annual Patient-Reported Outcome Consortium Workshop in April 2018.

Merck completed the qualitative phase of development of the two COA measures including concept elicitation and cognitive interviews with the respective target populations. Merck also received feedback from FDA on the draft COA measures.

The two COA measures initially developed by Merck have been modified by the Pediatric Asthma WG in response to additional FDA feedback obtained within the past year. The child measure is now called the Pediatric Asthma Diary-Child (PAD-C) and consists of a morning diary with 7 items and an evening diary with 12 items. The observer diary is now called the Pediatric Asthma Diary-Observer (PAD-O) and consists of a morning diary with 9 items and an evening diary with 12 items. Both measures are ready to be evaluated in cognitive interviews to determine if the modifications to wording, response options, and instructions are well understood by the respective target populations. It is expected that a study of approximately 45 participants will be adequate at this stage of measure development to confirm the content of the measures.
III. Project Objective

The goal of the Pediatric Asthma WG is to pursue FDA qualification of the two COA measures for the assessment of asthma signs and symptoms in pediatric patients; the primary measure would be the ObsRO measure for parents or caregivers of children aged 4 to 11 years old. The observer would also consider input from other informants (e.g., siblings, teachers, babysitters, spouses) regarding observable asthma signs or impacts. The PRO measure for children aged 8 to 11 years old would be a supportive measure. To achieve this goal, additional qualitative research is necessary to test the recent revisions to the two measures and an Initial Briefing Package must be developed for submission to FDA.

IV. Expected Statement of Work

A. Review all relevant background material related to the two draft COA measures.
   Approximately 500 pages of background information to be provided by C-Path to successful bidder.

B. Conduct study and document results
   1. Develop protocol, interview guide and analysis plan
      a. Include in interview guide a question to evaluate the PRO Consortium’s proposed wording for one Patient Global Impression of Change (PGIC) item and a question regarding meaningful change for the observer sample. Both questions to be provided by C-Path.
   2. Obtain feedback from expert panel members, C-Path, and Pediatric Asthma Working Group on the protocol, interview guide, and analysis plan
   3. Conduct translatability assessment of both measures. Review and feedback on translatability assessment is expected between rounds of cognitive interviews if changes are made to the measures. NOTE: An electronic implementation assessment will be conducted concurrently by members of the ePRO Consortium.
   4. Select study sites and negotiate budget with sites
   5. Obtain institutional review board (IRB) approval
   6. Recruit participants for study, consisting of approximately 45 participants and conduct interviews in waves, which should be as follows:
      a. PAD-C: 12 to 15 children 8 to 11 years of age equally distributed by age
      b. PAD-O: 12 to 15 parents/caregivers of children 4 to 7 years of age
      c. PAD-O: 12 to 15 parents/caregivers of children 8 to 11 years of age (likely to include parent or caregiver of child in PAD-C interview; do not want parent or caregiver intervening; recommend having parent interviewed prior to child interview)
      d. NOTE: Recruitment for the study must meet standard diversity requirements (i.e., geographic, age, race, ethnicity, education) as well as diversity in terms of marital and employment status of the observers.
7. Revise the two draft measures, PAD-C and PAD-O, as needed, following completion of the cognitive interview study and expert panel consultation. Revised measures are to be ready for quantitative testing.

8. Develop an item tracking matrix and item definition table for each measure.

9. Develop one user manual to address both measures and include the proposed scoring function, patient/observer training materials, and other supporting documentation.

10. Refine training material that has been developed for each measure.

11. Manage expert panel activity
   a. Work with the PRO Consortium’s Pediatric Asthma Working Group to form and manage an expert panel of up to four clinicians. The expert panel should include clinicians who are familiar with pediatric asthma as well as two representatives of a patient group (i.e., Allergy & Asthma Network [AAN]), one for each observer age range described above.
   b. Manage contracting with the expert panelists, as well as coordinate meetings and seek feedback at various stages.
   c. Obtain the expert panel’s feedback following its review of the cognitive interview study protocol, study results, and proposed PRO and ObsRO measures so that these can be finalized for submission to FDA.
   d. Conduct up to two expert panel meetings via teleconference/WebEx (the second meeting and associated deliverables can be shown in proposal as an optional task).
   e. Work with PRO Consortium staff and the Pediatric Asthma Working Group to develop expert panel meeting agendas and content, including slides.
   f. Prepare meeting minutes of expert panel meetings.
   g. Track expert panel member’s expenses to comply with the Physician Payment Sunshine Provision of the Patient Protection and Affordable Care Act of 2009 and vendor must complete quarterly reporting to the PRO Consortium using the PRO Consortium’s HCP reporting template provided as separate file.

**Deliverables**
1. Study documents including: cognitive interview protocol, interview guide, and qualitative analysis plan; plan for three iterations of each:
   a. Draft 1 for PRO Consortium staff review
   b. Draft 2, incorporates revisions requested in draft 1, delivered for WG and expert panel review
   c. Final, incorporates all revisions requested from prior reviews

2. Documentation of IRB approval of study documents

3. Translatability report, plan for three iterations:
   a. Draft 1 for PRO Consortium staff review
   b. Draft 2, incorporates revisions requested in draft 1, delivered for WG and expert panel review
   c. Final, incorporates all revisions requested from prior reviews

4. Coding dictionary
5. Cognitive interview report; three iterations expected:
   a. Draft 1 for PRO Consortium staff review
   b. Draft 2, incorporates revisions requested in draft 1, delivered for WG and expert panel review
   c. Final, incorporates all revisions requested from prior reviews.

6. Item tracking matrices for each measure documenting changes made leading up to and during study

7. Item definition tables, one for each measure; plan for three iterations of each:
   a. Draft 1 for PRO Consortium staff review
   b. Draft 2, incorporates revisions requested in draft 1, delivered for WG and expert panel review
   c. Final, incorporates all revisions requested from prior reviews

8. User manual; plan for three iterations:
   a. Draft 1 for PRO Consortium staff review
   b. Draft 2, incorporates revisions requested in draft 1, delivered for WG and expert panel review
   c. Final, incorporates all revisions requested from prior reviews

9. Expert panel meeting agendas and meeting slides; three iterations expected:
   a. Draft 1 for PRO Consortium staff review
   b. Draft 2, incorporates revisions requested in draft 1, delivered for WG and expert panel review
   c. Final, incorporates all revisions requested from prior reviews

10. Expert panel meeting minutes; three iterations expected:
    a. Draft 1 for PRO Consortium staff review
    b. Draft 2, incorporates revisions requested in draft 1, delivered for WG and expert panel review
    c. Final, incorporates all revisions requested from prior reviews

11. Interview recordings and transcripts; to be held by vendor in de-identified format and made available to C-Path upon request

12. Revised PRO and ObsRO measures incorporating changes recommended by the Expert Panel after review of study results in form ready for quantitative testing. To include final items, response options, instructions, and appropriate recall period.

13. Quarterly HCP report due to C-Path within one week of quarter close

C. Develop and deliver Initial Briefing Package

1. Prepare an Initial Briefing Package (IBP) that summarizes all work completed to date to obtain agreement that the content validity evidence is sufficient to move the measures forward to the quantitative testing stage. The documentation that will be submitted as part of this package will include: concept elicitation report from Merck, saturation grid from Merck, item generation report from Merck, item tracking matrices, conceptual framework, cognitive interview study report, and the revised draft PRO and ObsRO measures. Outline of IBP is attached as Appendix B.
2. Participate in at least one teleconference with QRT and Pediatric Asthma WG to discuss feedback on the IBP.

**Deliverables**

1. Initial Briefing Package document (Word format); three iterations expected:
   a. Draft 1 for PRO Consortium staff review
   b. Draft 2 incorporates revisions requested in draft 1, delivered for WG and expert panel review
   c. Final incorporates all revisions requested from prior reviews and is in form ready to be put into PDF format for submission to FDA

2. Initial Briefing Package (PDF format); this document will be a fully linked PDF and will contain all appendices and attachments referenced in the IBP

**D. Manuscript development**

In addition, although the PRO Consortium will not pay for the preparation of abstracts or manuscripts, the selected vendor is welcome to participate with a writing team from the Pediatric Asthma Working Group in the preparation of abstracts and/or manuscripts that will be submitted to peer-reviewed journals. Hence, costs associated with participation in the preparation of abstracts or manuscripts should not be included in submitted budgets.

**V. Review Meetings and Overall Project Management**

It is anticipated that the Bidder will participate in regularly designated Pediatric Asthma WG teleconferences (held on the second and fourth Monday of the month from 1:00 to 2:00 pm Eastern (US). Bidder will be expected to provide a weekly project status report throughout recruitment and an update each time the WG teleconference is cancelled to keep the WG apprised of current status. The Bidder will formally report (via WebEx or face-to-face) to the Pediatric Asthma WG at the following checkpoints (at a minimum):

1. Project kickoff to present overall project plan and timeline
2. Review of the cognitive interview study protocol and interview guide, along with other documents to be submitted to IRB
3. Review of the translatability assessment report and incorporation of changes prior to subsequent round of cognitive interviews
4. Review of the cognitive interview summaries in waves along with developmental versions of the PRO and ObsRO measures if changes are proposed
5. Review of the draft cognitive interview study report
6. Review of the draft Initial Briefing Package

**VI. Previous Experience**

Please define your organization’s capabilities and any previous experience in the pediatric asthma area as it relates to PRO and ObsRO measure development and validation. Describe any unique insight or relationships that would facilitate the identification and recruitment of the target population.
Describe the roles and responsibilities of key personnel on this proposed project. Please include brief descriptions (300 words or less) of all key personnel who will be involved in the project. If necessary, CVs of key personnel and a list of their publications relevant to either pediatric asthma or COA instrument development should be provided as an Appendix. In addition, please provide a brief description (300 words or less) of your overall organization (e.g., size, locations, and primary business units).

VII. Timelines
Organizations responding to this RFP are required to provide a detailed timeline including anticipated completion dates for the deliverables and milestones described above. Projected timelines for completion of the project will be an element of the proposal evaluation criteria.

VIII. Costs
Costs associated with the qualitative research are to be broken out and identified per task and deliverable. Third party expenses (e.g., subcontractor, honoraria, out-of-pocket, and travel) must be identified and totaled separately from your direct service costs in relation to all tasks of this project. Management and contracting with third parties, including key opinion leaders (KOLs), is the responsibility of the vendor. Please provide your proposed budget using the templates for direct, pass-through, and optional task costs provided below. The budget template is attached in Excel format to assist in creating the table shown below. Also, please provide proposed payment terms.
**BUDGET TEMPLATE**

**Note:** Below entries are required at a minimum; additional details will be appreciated.

### Direct Costs

<table>
<thead>
<tr>
<th>Task Name</th>
<th>Time to Completion from Kick-off (in weeks)</th>
<th>Total Hours for all Staff</th>
<th>Blended Hourly Rate</th>
<th>Total</th>
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<td>Project Kick-off and Project Management (e.g., including twice monthly WG telecons, prepare and deliver quarterly HCP report)</td>
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<td>Review of Work Done to Date* (e.g., review of previously collected qualitative data)</td>
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<td>Expert Panel Management (e.g., managing KOL involvement)</td>
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<td>Conduct Translatability Assessment and Prepare Report</td>
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<td>Prepare for Cognitive Interviewing (e.g., develop or update protocol, interview guide, analysis plan)</td>
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<td>Conduct Cognitive Interviews</td>
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<td>Perform Analysis and Document Results of Cognitive Interviews (e.g., Cognitive Interview Report)</td>
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<td>Update/Complete Measure Documents based on Results of Study (e.g., user manual, training material, item definition tables)</td>
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<td>Develop Initial Briefing Package for submission to FDA</td>
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<td>Additional Tasks (Please specify any additional tasks)</td>
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<td><strong>Total Direct Costs</strong></td>
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Pass-through Expenses
Pass-through expenses are included as estimated costs. Actual pass-through expenses are to be billed monthly as incurred.

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<td>Vendor Travel for Face-to-Face Meetings</td>
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<td>Facility Costs (including rental fees, refreshments)</td>
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<td>Telephone, Photocopies, other office services</td>
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<td><strong>Total Pass-Through Costs</strong></td>
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**Total Budget (Direct and Pass-through)**
(excluding optional tasks) $ 

Optional Tasks

*Note: The PRO Consortium will not pay for the preparation of abstracts or manuscripts.*

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<th>Task Name</th>
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<th>Total Hours for all Staff</th>
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