Research Funding Opportunity to Develop Patient Reported Outcome Tools for Use in Pulmonary Non-tuberculous Mycobacterial (NTM) Infections, Coccidioidomycosis, or Allergic Bronchopulmonary Aspergillosis through the FDA Broad Agency Announcement (FDABAA-21-00123)

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The FDA Broad Agency Announcement (FDABAA-21-00123) is an open solicitation for research and development to support regulatory science and innovation. The BAA link can be viewed at: https://beta.sam.gov/opp/80543862ddf14b65a8eb2fa0072de138/view?keywords=fdabaa-21-00123&sort=-relevance&index=&is_active=true&page=1&watch=false

In fiscal year 2021, research area **2.4.1** (Evaluate potential innovations in clinical trial design for new drugs such as enrollment strategies, data collection streamlining, drug development tools, clinical endpoints, and new statistical analytic approaches) has been identified as a priority area by the Office of Infectious Diseases in FDA's Center for Drug Evaluation and Research. Specifically, research proposals focused on developing patient reported outcome (PRO) instruments for evaluating results of clinical trials in pulmonary non-tuberculous mycobacterial (NTM) infections, coccidioidomycosis, or allergic bronchopulmonary aspergillosis (ABPA) will be prioritized.

Depending on scientific merit of Full Proposals, the Agency anticipates awarding 3 research contracts (1 contract for each disease area) on or before September 30, 2021, to address priority area 2.4.1. The funding for this priority area will not exceed $1,290,000 ($430,000 per study).

Information regarding proposal preparation and submission is available at the link above. **To ensure consideration for awarding of research contracts by September 30, 2021, please submit the Quad Chart and White Paper no later than January 28, 2021.**

Following a successful review of the Quad Chart and White Paper, the Offeror may be invited to submit a Full Proposal. FDA's Office of Acquisitions & Grants Services (OAGS) will send invitation letters requesting that Full Proposals be submitted. The date for submission of the Full Proposal will be provided in the invitation letter.

Background

Recent interest and public discussions have highlighted the need for the development of PRO instruments for use in clinical trials of new drugs for the treatment of pulmonary NTM infections, coccidioidomycosis, and ABPA*.

In pulmonary NTM infections clinical trials and drug approval have relied upon a surrogate endpoint of sputum culture conversion, which does not allow assessing clinical benefit of the drug studied and necessitates conducting confirmatory trials to demonstrate meaningful clinical outcomes for the patients. However, no clinical outcome assessment instruments have been universally accepted and validated for pulmonary NTM clinical trials.

For coccidioidomycosis, clinical trials outcomes have been measured with endpoints based on scoring systems, which include laboratory, microbiological, radiological, and clinical components. These scoring

systems have not been validated as clinical outcome assessment tools, and their ability to measure how a patient feels and functions is uncertain.

Similarly, assessment of treatment outcomes in ABPA involves clinical, radiological, and serological evaluations, and tools measuring patient experiences are lacking. Thus, the development of PRO instruments is urgently needed to facilitate patient-focused development of new therapies for these difficult to treat diseases.

Research Proposal Objectives

FDA is interested in the development, evaluation and qualification of PRO instruments for use in trials in patients with pulmonary NTM infections (including MAC and *M. abscessus* infections), coccidioidomycosis, and ABPA to facilitate evaluation of new therapies for these conditions. The studies to develop and assess a candidate PRO instrument should be well-designed to include plans for the qualitative phase of instrument development including: 1) hypothesize the conceptual framework, 2) adjust the conceptual framework and draft the instrument, and 3) confirm the conceptual framework and assess other measurement properties. No intervention studies involving the use of an investigational drug product will be funded through this RFP.

Studies to evaluate the PRO instrument under development in patients longitudinally would generally not be expected to be proposed under these research contracts but may be requested in a future funding opportunity.

FDA will prioritize White Papers submitted in response to the FDA Broad Agency Announcement by the **January 28, 2021** deadline that provide a rationale for why development of a PRO for pulmonary NTM infections, coccidioidomycosis, or ABPA is a high priority.

Proposals also must include a plan to make research findings publicly available for consideration by the FDA and standards development organizations.

Research Proposal Preparation Considerations

White Papers and Full Proposals will be evaluated based on program relevance to new drug development and regulatory review, overall scientific and technical merit, and offeror capability.

Offerors should provide a scientific literature review and description of research previously conducted to justify the specific research being proposed including the public health priority regarding pulmonary NTM infections, coccidioidomycosis, or ABPA.

Proposed activities to develop a PRO instrument that will ultimately be fit for use in future clinical trials should include milestones such as conceptual framework development, pilot testing of the draft instrument, and assessment of score reliability and construct validity. For studies aimed at developing a PRO instrument that is qualified by the FDA for use in clinical trials, milestones should be based on the advice provided by the FDA in response to consultations.

Applicants should include milestones for the qualitative phase of PRO development in their applications. The milestones will be used by FDA to facilitate monitoring of progress and assessing the

feasibility for completing the study. Thus, the applicant should provide a Gantt chart that outlines all the milestones and timelines related to the qualification of the PRO. Note that "go/no go decision points," PRO instrument content validity, and other measurement properties (e.g., sensitivity, reliability, and responsiveness) should be incorporated into each goal/milestone. Funding of the contract is contingent upon unique milestones accomplished and subsequent years will be based on availability of funds.

During the technical review, FDA staff may recommend changes to the research plan or suggestions from peer reviewers, and the plan may be revised as appropriate prior to the award. The deliverables for the award will include recruitment milestones expected to be met by specific time periods and other milestones specific to the research project.

Examples of studies to be supported through this RFP include, but are not limited to the following:

- Studies aimed at obtaining patient input such as cognitive interviewing
- Studies to pilot test the draft instrument
- Studies to assess score reliability, construct validity, and ability to detect change

The Full Proposal should include sufficient detail regarding:

PRO Development: Hypothesize the conceptual framework to identify the relevant concepts, adjust the conceptual framework and draft instrument, and confirm the conceptual framework and assess other measurement properties.

a. Start-up activities (i.e., literature review, expert interviews)
b. Development of study protocol (i.e., case report forms, patient interview materials)
c. Site and patient recruitment (i.e. site contracting/training/monitoring/IRB approval)
d. Communication plan outlining how changes to any prespecified parameters or instrument modifications will be communicated to FDA.
e. Concept elicitation and cognitive interviews with patients and other/or caregivers
f. Qualitative analysis and draft PRO instrument
g. Data collection
h. Development of statistical analysis plan, development of all instrument administration modes (i.e., electronic/other, including associated instructions) and translatability assessment plan
i. Submit FDA Letter of Intent (LOI) and Qualification Plan for draft PRO instrument

The FDA provides additional information about the Drug Development Tools Qualification Program on its website: 1) Patient-Focused Drug Development: Methods to Identify What Is Important to Patients Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders 2) Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims; 3) Drug Development Tools; 4) FDA Clinical Outcome Assessment Qualification Program, 5) Qualification Process for Drug Development Tools; Guidance for Industry.

Utilizing existing resources, including ongoing communications with FDA staff, will ensure widespread acceptance and understanding of a potentially qualified PRO instrument for use by all stakeholders. It is the expectation that applicants will initiate formal communications with FDA staff early in the

development process and prior to submission of the Letter of Intent (LOI) through the Drug Development Qualification Program, beginning with plans to develop the conceptual framework. For PRO instruments that are already in development, applicants should also engage the FDA staff early for input regarding the further development of an existing instrument such as plans for conducting psychometric evaluation.

Applicants should demonstrate any prior experience in the disease area, their resourcing capability (e.g., established connections with patient advocacy groups, clinical experts, access to patients), recruitment strategies, project management expertise, and milestones including a specified recruitment forecast and timeline for both patients and clinical experts.

Applicants are encouraged to collect the clinical data early in the research study. Prior advice from the FDA regarding the development of the PRO should be stated in the application, if applicable.

The FDA provides additional information about the Drug Development Tools Qualification Program on its website as noted above.

Offerors should include a description of their scientific qualifications, capabilities, related experience, and past performance. The contractor will also be responsible for subcontracting with institutions and other collaborators.

Further information on how to submit the quad chart and white paper by the January 28, 2021 deadline can be found at (on page 35 of the BAA document):
https://beta.sam.gov/opp/80543862ddf14b65a8eb2fa0072de138/view?keywords=fdabaa-21-00123&sort=-relevance&index=&is_active=true&page=1&watch=false

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Office of Infectious Disease Research Webpage Link:

https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm536676.htm

*FDA Workshops:

Addressing Challenges in Inhaled Antifungal Drug Development (9/25/20): (https://www.fda.gov/drugs/news-events-human-drugs/addressing-challenges-inhaled-antifungal-drug-development-09252020-09252020).

Coccidioidomycosis (Valley Fever): Considerations for Development of Antifungal Drugs (8/5/20): https://www.fda.gov/news-events/fda-meetings-conferences-and-workshops/coccidioidomycosis-valley-fever-considerations-development-antifungal-drugs-08052020-08052020

Development of Antibacterial Drugs for the Treatment of Nontuberculous Mycobacterial Disease (4/18/19): (https://www.fda.gov/drugs/development-antibacterial-drugs-treatment-nontuberculous-mycobacterial-disease-04082019-04082019