Research Funding Opportunity to Optimize Dosing Strategies for Antimicrobial Drugs through the FDA Broad Agency Announcement (FDABAA-22-00123)

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The FDA Broad Agency Announcement (FDABAA-22-00123) is an open solicitation for research and development to support regulatory science and innovation. The BAA link can be viewed at: https://sam.gov/opp/c00c56895d2c45b1895ea60d0e4e4747/view

In fiscal year 2022, research area **2.4.2** (Advance the science of in vitro, animal model, pharmacokinetic studies, and/or real world evidence studies to facilitate drug development, including studies focused on antimicrobial resistance and drug development for special populations such as patients with unmet need, children, and patients with renal or hepatic dysfunction) 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 evaluating appropriate dosing strategies for certain specific populations at high risk for treatment failure or adverse events will be prioritized.

Depending on scientific merit of Full Proposals, the Agency anticipates awarding 2-3 research contracts on or before September 30, 2022, to address priority area 2.4.2. The funding for this priority area will not exceed $1,200,000 ($400,000/contract).

Information regarding proposal preparation and submission is available at the link above. **To ensure consideration for awarding of research contracts by September 30, 2022, please submit the Quad Chart and White Paper no later than January 21, 2022.**

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

The success or failure of antimicrobial therapy results from a combination of factors related to the patient, the microbe, and the drug. Appropriate evaluation of the combination of these factors is essential for dose selection for the full range of the intended patient population. As such, drug developers should consider the needs of particularly vulnerable populations and determine strategies for optimal dose selection. Two vulnerable populations are obese patients and patients who are receiving continuous renal replacement therapy (CRRT).

Obesity and related comorbidities can complicate the treatment of infectious diseases. For example, there are no clear instructions for determining when and how to alter dosing of antimicrobial drugs for patients with larger body sizes. Orally administered drugs are typically administered as a fixed dose in adult patients, an approach that may underdose obese patients. Many parenterally administered drugs are dosed on a body-weight scaled dose, such as mg/kg, which for some parenteral drugs may lead to excess drug concentrations in obese patients. In both situations clinicians may want to use a different

dosing approach, which would require them to select a dose that is not consistent with FDA approved labeling. Approaches to determine appropriate antimicrobial dosing in obese patients are needed, including evaluation of various methodologies to assess body size or composition.

CRRT is the predominant form of renal replacement therapy in the intensive care unit (ICU). Severe infections are a common contributing factor to acute kidney injury (AKI) in critically ill patients and account for many AKI cases in ICUs. Elimination of drugs administered in patients receiving CRRT may be substantially different from drug elimination in patients receiving traditional hemodialysis; however, there is little guidance for the dosing of antimicrobials in patients receiving CRRT. It is possible to narrow the number of antimicrobial drugs that need to be evaluated in the setting of CRRT, based on drug attributes such as molecular weight and plasma protein binding. However, a standardized approach for evaluation of the impact of CRRT on dosing is needed for antimicrobial drugs used in the ICU whose attributes indicate their pharmacokinetics may be affected by CRRT. Although considerations for approaches to evaluate the effect of various CRRT modalities on drug dosing have been described, clinical studies are rare.

Research Proposal Objectives

FDA is interested in advancing methods that optimize dosing strategies for antimicrobial drugs.

FDA will prioritize White Papers submitted in response to the FDA Broad Agency Announcement by the **January 21, 2022** deadline that provide a rationale and study design to assess methods to optimize dosing strategies for antimicrobial drugs to treat populations at high risk for treatment failure or adverse events, specifically obese patients and patients who are receiving CRRT.

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 of optimizing antimicrobial drug dosing in obese patients and patients undergoing CRRT.

The Full Proposal should include sufficient detail regarding planned studies including a description of the population of patients and the selected antimicrobial drugs for evaluation. Sufficient detail should be provided including evaluations needed prior to conduct of a clinical study, the specific infection(s) to be studied, the specific antimicrobial drug(s) to be studied, the proposed methods for approaching dose selection, the feasibility of obtaining data for individual patient dosing regimens, clinical outcomes (both effectiveness and safety) to be evaluated, and other patient characteristics that may be associated with outcome. Proposed activities could include:

- Cohort identification and site agreements
- IRB/EC review and approval
- Development of the statistical analysis plan

- Database development
- Data acquisition and input
- Data analyses
- Preparation of reports of findings

Offerors should include a description of their 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 21, 2022 deadline** can be found at (page 33):
https://sam.gov/opp/c00c56895d2c45b1895ea60d0e4e4747/view

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Office of Infectious Disease Research Webpage Link:

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