Research Funding Opportunity to Facilitate Updating Susceptibility Test Interpretive Criteria (Breakpoints) through the FDA Broad Agency Announcement (FDABAA-21-00123)

FDA Broad Agency Announcement (FDABAA-21-00123)

The FDA Broad Agency Announcement (FDABAA-21-00123N) 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 **2.4.4** (Advance the science of antibacterial drug susceptibility testing to ensure that up to date susceptibility testing criteria (breakpoints) are available for patient care and antimicrobial stewardship) 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 microbiologic and pharmacokinetic data that could be utilized by standards development organizations and the FDA to update susceptibility testing criteria (breakpoints) will be prioritized.

Depending on scientific merit of Full Proposals, the Agency anticipates awarding 4 research contracts on or before September 30, 2021 to address priority area 2.4.4. The funding for this priority area will not exceed $1,000,000 ($250,000 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

Enabling physicians to select appropriate antibacterial drugs is critical to individual patient care and public health. Generally, physicians rely on antimicrobial susceptibility testing (AST) performed by clinical microbiology laboratories to help choose an appropriate treatment. Breakpoints are the criteria used to interpret AST results. Breakpoints identify whether bacteria are considered susceptible or resistant to a particular antibacterial drug. Bacteria can change over time. When bacteria change in a way that affects their susceptibility to antimicrobial drugs, breakpoints need to be updated. Laboratories and AST device manufacturers need to be able to use up-to-date breakpoints for the reports provided to physicians to inform appropriate treatment choices. Identification of patients who have certain types of resistant bacteria is also essential to infection control practices. Up-to-date AST results are an important component in addressing the problem of antimicrobial resistance.

The data considered in determining whether or not a breakpoint for a particular drug-bacteria combination should be updated includes Minimum Inhibitory Concentration (MIC) distribution of the particular bacteria using contemporary surveillance data, pharmacokinetic-pharmacodynamic modeling to determine if the dose recommended in humans is adequate to attain drug exposures that can cover

the breakpoint, and clinical response in patients with respect to the MIC of the particular bacteria. Obtaining these data for older antibacterial drugs, particularly those no longer marketed by the innovator, has been challenging.

Research Proposal Objectives

FDA is interested in advancing the science of antibacterial drug susceptibility testing to ensure that up-to- date breakpoints are available for patient care and antimicrobial stewardship by supporting high quality proposals to obtain needed microbiologic and pharmacologic data needed to consider updating breakpoints for high priority drug-bacteria combinations.

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 data to support updating of breakpoints for a particular drug-bacteria combination is a high priority, propose to synthesize or obtain relevant microbiologic data, propose to utilize relevant human pharmacokinetic data and animal model studies to conduct probability of target attainment analyses, incorporate any clinical response data available in the public literature or other sources to justify any proposal for updating of breakpoints based on the research findings. Proposals to obtain data for older antibacterial drugs are encouraged.

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 breakpoints for the proposed drug-bacteria and any relevant information available regarding clinical response.

The Full Proposal should include sufficient detail regarding planned microbiologic and pharmacokinetic studies. Proposed activities could include:

- MIC and zone diameter distributions (if relevant) against the bacteria of interest from isolates collected in the preceding 3 years, categorical agreement between MIC and zone diameter breakpoints (if relevant),
- Plans for pharmacokinetic-pharmacodynamic (PK-PD) modeling including sources of pharmacokinetic data that will be utilized
- PK-PD index and target values that will be utilized along with the relevant supportive information that may include:
    - Static and/or dynamic in vitro infection model findings
    - In vivo animal infection model findings
    - Human pharmacokinetic data of the drugs in plasma, ELF (pulmonary) and/or other body sites

Offerors should include a description of their qualifications, capabilities, related experience, and past performance.

Offerors should describe their plan to make research findings publicly available for consideration by the FDA and standards development organizations. For example, FDA has opened a public docket for information and data relevant to updating breakpoints (https://www.regulations.gov/docket?D=FDA-2017-N-5925).

The contractor will also be responsible for subcontracting with institutions and other collaborators.

Contact Information for Questions:

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Office of Infectious Disease Research Webpage Link:

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