

FY2025 Office of Infectious Diseases Funding Announcement to Facilitate Development of Susceptibility Test Interpretive Criteria (STIC or Breakpoints) for Enterococci through the FDA Broad Agency Announcement

The FDA Broad Agency Announcement (FDABAA-25-00123) is an open solicitation for research and development to support regulatory science and innovation. The FY25 FDA BAA solicitation, including detailed information regarding proposal preparation and submission, can be viewed here:

<https://sam.gov/opp/c3e35e83134c40e5b96dde9c65f5c23a/view>

In fiscal year 2025, the following research area has been identified as a priority area by the Office of Infectious Diseases in FDA's Center for Drug Evaluation and Research.

- Charge Area: III. Invigorate public health preparedness and response of the FDA, patients, and consumers.
- Regulatory Science Topic of Interest: B. Antimicrobial Resistance
- FDA-Regulated Areas: 1. Drugs
 - **1a - 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.**

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 one research contract to address charge area IIIb1a. The total funding for this priority area will not exceed **\$325,000** (direct and indirect cost).

Background

Informing appropriate selection of antibacterial drugs is critical to individual patient care and public health. The selection of an appropriate antibacterial drug is guided by breakpoints, the criteria to interpret antimicrobial susceptibility testing (AST) results. Enterococci are important clinical pathogens with limited treatment options, especially for infections resistant to first line therapies such as ampicillin and vancomycin. While nonclinical pharmacokinetic-pharmacodynamic (PK-PD) data relying on animal models of infection are instrumental in establishing breakpoints, existing animal models of enterococcal infection are limited. In the frequently used murine thigh infection model, Enterococci exhibiting poor growth characteristics may confound the interpretability of a drug's antibacterial activity. As a result, reliable nonclinical PK-PD data for antibacterial drugs used to treat resistant enterococcal infections, such as daptomycin, are limited.¹

Research Proposal Objectives

FDA has previously awarded the following proposal:

- Development of Modernized Susceptibility Guidance for Ampicillin and Vancomycin for Enterococcus Species Using Pharmacometric Approaches

FDA is interested in advancing the science of antibacterial drug susceptibility testing for daptomycin in the treatment of enterococcal infection. Proposals are requested to develop and evaluate, among other

¹ Kidd JM, Abdelraouf K, Asempa TE, Humphries RM, Nicolau DP. Pharmacodynamics of Daptomycin against Enterococcus faecium and Enterococcus faecalis in the Murine Thigh Infection Model. Antimicrob Agents Chemother. 2018 Sep 24;62(10):e00506-18.

characteristics, the following:

- Develop an *in vivo* model demonstrating predictable and reproducible growth characteristics of *E. faecium* and *E. faecalis*
- Test dose ranges equivalent to daptomycin human doses of 6, 8, 10, and 12 mg/kg/day

Research Proposal Preparation Considerations

Concept 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 combination and any relevant information available regarding clinical response.

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

- Providing daptomycin MIC against enterococcal surveillance isolates collected in the preceding 3 years including isolates with various known resistance phenotypes and details on specific strains (i.e., ATCC or CDC) used in experiments, e.g., susceptibility and virulence factors (presence of known resistance genes)
- Nonclinical infection models to characterize PK/PD efficacy and emergence of resistance relationships, identify the PK/PD index, and select target values to be used to bridge this information to humans. Relevant information may include:
 - *In vivo* PK/PD animal infection model findings including confirmatory assessments of bacterial growth of the selected strains under no treatment
 - *In vivo* animal infection model findings utilizing human-simulated antimicrobial exposures at the infection site
 - Human pharmacokinetic data of the drugs in plasma
- PK/PD modeling, Monte Carlo simulations, and probability of target attainment analyses

Offerors should include a description of their qualifications, capabilities, related experience, and past performance, and 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 breakpoints². The contractor will also be responsible for subcontracting with institutions and other collaborators.

It's anticipated that research contract awards will be made through the FY25 FDA BAA.

Submission Deadlines:

- Early Concept Papers - **November 8, 2024**
- Stage I Package (Concept Paper and Full Proposal) - **February 24, 2025**

² <https://www.regulations.gov/docket?D=FDA-2017-N-5925>

It's recommended that potential Offerors attend the upcoming FDA BAA Day on **November 14, 2024**, to learn about the BAA submission process:

<https://www.fda.gov/science-research/advancing-regulatory-science/2024-fda-broad-agency-announcement-day-11142024>

Office of Infectious Diseases Research Webpage:

<https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/office-infectious-diseases-research-activities>

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