

Research Funding Opportunity to Facilitate Development or Refinement of Rabbit Animal Models of Ventilator-Associated Bacterial Pneumonia through the FDA Broad Agency Announcement (FDABAA-20-00123N)

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The FDA Broad Agency Announcement (FDABAA-20-00123N) 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/2313b4c8ab7a967d880cf16dee4ec116/view?keywords=fdabaa-20-00123&sort=-relevance&index=&is_active=true&page=1

In fiscal year 2020, research area 2.4.2 (advance the science of *in vitro*, animal model, and/or pharmacokinetic studies to facilitate antibacterial drug development, including studies focused on drug development for special populations) has been identified as a priority area by the Office of Infectious Diseases in FDA's Center for Drug Evaluation and Research. To address this priority area, research proposals focused on the development or advancement of large animal models (i.e. rabbits of ventilator-associated bacterial pneumonia caused by carbapenem-resistant strains of *Pseudomonas aeruginosa* or *Acinetobacter baumannii*) will be prioritized for funding consideration.

Depending on scientific merit of Full Proposals, the Agency anticipates awarding 1 research contract on or before September 30, 2020 to address priority area 2.4.2. The funding for this priority area will not exceed \$1,000,000.

Information regarding proposal preparation and submission is available at the link above. **To ensure consideration for awarding of research contracts by September 30, 2020, please submit the Quad Chart and White Paper no later than February 28, 2020.**

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 a Full Proposal be submitted. The date for submission of the Full Proposal will be provided in the invitation letter.

Background

A significant concern to public health has been the emergence of antibiotic-resistant bacteria. To continue to advance the development and validation of ventilator-associated rabbit pneumonia infection models as a translational approach for testing new drug candidates, the predictive power of an animal model against resistant organisms needs to be examined. Specific interest lies in the treatment of serious infections, including ventilator-associated pneumonia, caused by *Pseudomonas aeruginosa* or *Acinetobacter baumannii* carbapenem resistant strains in humans. There is particular interest in development of models with the long term goal of a model that would utilize meropenem treatment as a control and could be used in the development of a new antibacterial drug that retains activity in the presence of certain carbapenem resistance mechanisms.

On March 1, 2017, FDA held a Public Workshop entitled, “Current State and Further Development of Animal Models of Serious Infections Caused by *Acinetobacter baumannii* and *Pseudomonas aeruginosa*.” The Public Workshop included an overview of the challenges with development of a new antibacterial drug targeting a single species, lessons learned from past and current animal models of infection development efforts, and discussion of next steps and research priorities. Meeting materials can be reviewed at: <https://www.fda.gov/Drugs/NewsEvents/ucm534031.htm>.

While every effort should be made to perform human clinical trials, animal models of serious bacterial infection are useful to explore the activity of a candidate antibacterial drug targeting a single species and may be further developed to help to predict whether the drug will be efficacious in humans.

Research Proposal Objectives

FDA is interested in advancing regulatory science to facilitate the development of novel antibiotics against carbapenem-resistant strains. As one may anticipate some uncertainties in a clinical trial specifically targeting carbapenem-resistant strains, such as prior antibiotic treatment or concomitant antibiotic treatment, data from animal models may provide informative data. Validating the predictive ability of animal models of ventilator-associated pneumonia against susceptible and resistant strains would increase the utility of animal models in predicting a human clinical response.

FDA will prioritize White Papers submitted in response to the FDA Broad Agency Announcement by the February 28, 2020 deadline that propose efforts focused on developing or refining rabbit animal models of ventilator-associated pneumonia utilizing a carbapenem-resistant strain of *Pseudomonas aeruginosa* or *Acinetobacter baumannii*. Proposed efforts may include a systematic approach to reproduce the pathophysiology of human disease in an animal species following challenge with the infectious agent and may include median lethal and/or infectious dose determination, natural history of infection, serial pathogenesis studies, and determination or validation of a humanized dosing regimen. Efforts should include a systematic approach to develop/adapt or refine an existing animal infection model with consideration of similarities and differences between animal and human disease.

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 refinement research being proposed. Specifically, describe how the proposed research would be expected to advance the development of animal models of serious infections caused by carbapenem-resistant *Pseudomonas aeruginosa* or *Acinetobacter baumannii*. Please include information regarding bacterial strains being proposed for testing and rationale, animal species being proposed for use in the model and rationale, animal challenge method, biomarkers that will be studied, antibiotics utilized and the rationale behind their selection, and endpoints that will be assessed.

The Full Proposal should include plans to assess the capacity of the model(s) to evaluate the activity of an antibacterial drug and predict the human clinical response including use of appropriate negative and positive controls.

For example, research plans could include a development of a new model or validation of an existing model, determination of a lethal dose, natural history of bacterial strains, and efficacy studies.

Proposals should either include work to determine the humanized dosing for animal infection model of all antibiotics proposed or background to support the proposed dosing. Humanized dosing in animal infection model is expected to attain a study drug's exposure that matches to the exposure in patients following routinely used clinical dosing for that drug.

Offerors should include a description of their qualifications, capabilities, related experience, and past performance. Information regarding the facilities, GLP capability, animal care and use accreditation, licensing, bioanalytical instruments and capability for PK sample analysis, and compliance should be included.

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>