Research Funding Opportunities through the FDA Broad Agency Announcement (FDABAA-23-00123) to Facilitate Systemic and Inhaled Antifungal Drug Development and Address Antifungal Drug Resistance

FDA Broad Agency Announcement (FDABAA-23-00123)

The FDA Broad Agency Announcement (FDABAA-23-00123) is an open solicitation for research and development to support regulatory science and innovation. The BAA solicitation can be viewed at: https://sam.gov/opp/52766923970840219c29d0ba2f0f4711/view#attachments-links

In fiscal year 2023, the following research area under FDABAA-23-00123 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 Area of Interest: **B. Antimicrobial Resistance**
- FDA-Regulated Areas: **1. Drugs**
    - **1b - Advance the science of in vitro, animal model, pharmacokinetic studies, and/or real- world evidence studies to facilitate drug development, including studies focused on antifungal and antibacterial resistance and drug development for special populations such as patients with unmet need, children and patients with renal or hepatic dysfunction**

Specifically, research proposals focused on advancing the development of animal models of serious infections caused by rare, emerging, and drug-resistant fungal pathogens associated with invasive systemic disease will be prioritized.

Depending on the scientific merit of Full Proposals, the Agency anticipates awarding 2 research contracts on or before September 30, 2023, to address this priority area**.** The total funding for this priority area will not exceed $1,300,000 ($650,000/contract).

Information regarding proposal preparation and submission is available at the link above. **To ensure consideration for awarding of research contracts by September 30, 2023, please submit the Quad Chart and White Paper by January 23, 2023.**

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

There is an urgent need for antifungal drugs, as monotherapy or in combination, that are active against rare, emerging, and drug-resistant fungal pathogens associated with poor clinical outcomes. In April 2020, the World Health Organization (WHO) convened a meeting of experts to identify priority fungal

pathogens of public health importance and to define research priorities[1] and is creating a fungal priority pathogen list along with an analysis of the antifungal development pipeline[2,3].

The Centers for Disease Control and Prevention (CDC) has listed some of the fungal pathogens that are urgent and serious threats to human health[4].
Some systemic and inhaled drugs may be active against several species of rare, emerging, and drug-resistant fungi while others may be active against only a single species. Performing clinical trials for these drugs are challenging as the target species may be a relatively infrequent cause of human disease and utilization of pre-study and concomitant antifungal drug therapy is likely. These challenges were discussed at the following three FDA Public Workshops:

1. Development Considerations of Antifungal Drugs to Address Unmet Medical Need - August 4, 2020[5].
2. Coccidioidomycosis (Valley Fever): Considerations for Development of Antifungal Drugs - August 5, 2020[6].
3. Addressing Challenges in Inhaled Antifungal Drug Development - September 25, 2020[7].

These Workshops included an overview of the challenges associated with development of new antifungal drugs targeting rare, emerging and drug-resistant fungi, lessons learned from existing animal models of fungal infection, drug development efforts, and discussion of next steps and research priorities.

Development and refinement of animal models of rare and emerging invasive fungal diseases are helpful for the development of antifungal drugs and allow for the evaluation of the natural history and pathogenesis of the disease, clinically relevant endpoints/biomarkers, and pharmacokinetics/pharmacodynamic (PK/PD) targets that could inform the design of clinical trials. They are also critical to exploration of the activity of a candidate systemic and/or inhaled antifungal drug(s), administered as monotherapy or in combination, targeting a single or multiple fungal species and help to predict whether the drug will be efficacious in humans. Adaptation and/or refinement of an existing model to other fungal pathogens is also of great importance.

Research Proposal Objectives

FDA is interested in developing or refining animal models of invasive fungal diseases due to yeast, molds, and dimorphic fungi to study the efficacy of FDA-approved antifungal drugs, as monotherapy and/or in combination, for the human fungal disease of interest, including emerging, rare and resistant pathogens as well as those causing endemic mycoses and/or those associated with pulmonary and CNS involvement. Research objectives could encompass:

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[1] https://www.who.int/publications/i/item/9789240006355
[2] Support the development of the WHO fungal priority pathogens list of public health importance (ungm.org)
[3] Antimicrobial resistance (who.int)
[4] https://www.cdc.gov/drugresistance/biggest-threats.html
[5] https://www.fda.gov/news-events/fda-meetings-conferences-and-workshops/development-considerations-antifungal-drugs-address-unmet-medical-need-08042020-08042020
[6] https://www.fda.gov/news-events/fda-meetings-conferences-and-workshops/coccidioidomycosis-valley-fever-considerations-development-antifungal-drugs-08052020-08052020
[7] https://www.fda.gov/drugs/news-events-human-drugs/addressing-challenges-inhaled-antifungal-drug-development-09252020-09252020

a) Understanding the pathophysiology of invasive fungal disease in an animal species following challenge with the infectious agent including median lethal and/or infectious dose determination, natural history of infection, and pathogenesis studies.
b) Significant improvement of an existing animal model of fungal disease, including optimization of its ability to support evaluation of an antifungal drug, as monotherapy or in combination, for systemic and/or inhalational use following challenge with the fungal pathogen.
c) Adaptation and/or refinement of an existing animal model of disease caused by one fungal pathogen to a different fungal pathogen.
d) Establishment of relevant PK/PD parameters to inform PK/PD analyses of antifungal drugs.

Research Proposal Preparation Considerations

FDA will prioritize White Papers and Full Proposals based on program relevance to achieve the objectives outlined above, overall scientific and technical merit, and offeror's capability.

Proposed activities should include:

- A scientific literature review and description of research previously conducted to justify the specific animal model development/refinement research being proposed.
- Description of how the proposed research would be expected to advance the development of animal models of serious infections caused by rare and emerging fungal pathogens.
- Specifics of the fungal species and strains being proposed for testing along with supporting rationale, animal species being proposed for use in the model and supporting rationale, and animal challenge methods including route of infection, route of drug administration, biomarkers and endpoints. It is expected that the methods proposed will be clinically relevant for human disease caused by the pathogens under study.
- Methods to assess the capacity of the model(s) to evaluate the activity of an antifungal drug including appropriate negative and positive controls
- Justification of the model relevance to human disease and clinical response.

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, and compliance should be included.

The contractor will also be responsible for subcontracting with institutions and other collaborators. Proposals also must include a plan to make research findings publicly available.

Further information on how to submit the quad chart and white paper by the **January 23, 2023, deadline** can be found at (starting on pg. 39 of the PDF):
https://sam.gov/opp/52766923970840219c29d0ba2f0f4711/view#attachments-links

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Office of Infectious Diseases' Research Webpage Link:
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