FY2026 Office of Infectious Diseases Funding Announcement to Advance the Development of External Controls for Invasive Fungal Infection Trials through the FDA Broad Agency Announcement

The FDA Broad Agency Announcement (FDABAA-26-00123) is an open solicitation for research and development to support regulatory science and innovation. The FY26 FDA BAA solicitation, including detailed information regarding proposal preparation and submission, can be viewed here: https://sam.gov/workspace/contract/opp/5622acb8db634d37b3b55d607e6ba561/view

In fiscal year 2026, 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
    - 1b. Advance the science of non-clinical studies, pharmacokinetic studies, and/or real-world evidence studies, such as studies assessing antifungal and antibacterial resistance, and studies to address areas of unmet medical need.

Specifically, research proposals focused on construction of external control cohorts for invasive fungal infections (IFI), including invasive mold infections, using open-source, deidentified real-world patient data either through databases such as the Observational Medical Outcomes Partnership (OMOP) using the Common Data Model (CDM), electronic health records (EHR) or other publicly-available data, e.g., patient/disease registries, will be prioritized.

Depending on the 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 **$300,000** (direct and indirect cost).

Background

Clinical trials of drugs for the treatment of IFI are challenging to conduct due to small numbers of patients with uncommon or rare IFI, significant morbidity and mortality associated with these infections, heterogeneity of presentation, prolonged duration of treatment, difficulty in determination of appropriate endpoints and choice of controls. Given these challenges, the use of external controls could be an option in clinical trials for rare IFI infections. In this type of trial design, patients with the IFI under evaluation would be assigned to study treatment with comparison of efficacy to external controls to support the effectiveness of the proposed study treatment. External controls can be a group of patients, treated or untreated, at an earlier time-point (historical control) or a contemporaneous treated group.[1] Real-world data (RWD) on the latter group of patients may be found in EHRs[2], databases such as OMOP and others, and patient/disease registries[3].

Given that externally controlled trials do not involve randomization of the study population to the treatments being compared, the treatment and control arm populations should be as similar as

[1] FDA Guidance for Industry: Demonstrating Substantial Evidence of Effectiveness for Human Drug and Biological Products. https://www.fda.gov/media/133660/download

[2] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/real-world-data-assessing-electronic-health-records-and-medical-claims-data-support-regulatory

[3] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/real-world-data-assessing-registries-support-regulatory-decision-making-drug-and-biological-products

possible regarding known factors that can affect the outcome being measured. Factors that could impact comparability of data include time frames between the study and external control cohorts resulting in differences in standard of care, geographic region, criteria for diagnosis, prognostic indicators, treatments, concomitant medications, follow-up periods, intercurrent events, outcomes and missing data.[4]

Despite their limitations, external controls can provide support for effectiveness when a) the natural history of the disease is well defined; b) the external control population is very similar to the treatment group; c) concomitant treatments that affect the primary endpoint are not substantially different between the external control and trial populations; and d) the results provide compelling evidence of a change in the established progression of disease. Lack of appropriate external controls represents a significant barrier to feasible trial design for uncommon or rare IFI.

Research Proposal Objectives

FDA is interested in advancing the development of external controls for IFI clinical trials. Research objectives could encompass:

a) Establishing a definition of, and requirements for optimal external controls for at least two specific IFI including invasive mold infections.
b) Exploring the feasibility of real-world data (RWD) accessed through the modalities listed above, or others, to establish an external control cohort for each selected IFI, including an assessment of fungal registries.
c) Develop an electronic case report form (eCRF) for external sources to evaluate similarity of external control populations and ensure collection of data needed for regulatory purposes.

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 relevant background to justify the proposal.

The Full Proposal should include sufficient detail regarding planned analyses including:

- Detailed evaluation of the strengths and limitations of existing sources of RWD for development of an external control cohort for each IFI specified.
- Determination of the appropriate source of, and methodology to identify appropriate external cohorts, including algorithms using structured data, large language models, machine learning and other modalities.
- Establishment of criteria and development of a CRF to establish an appropriate external cohort for each specified IFI.
- Evaluation of the capability of the developed methodology to fulfil desired design considerations in externally controlled trials using RWD, such as a) reduction of statistical bias; b) baseline eligibility criteria, including characteristics of the study population; c) attributes of treatment; d) appropriate exposure definitions and windows, including establishment of index date (time zero); e) well-defined and clinically meaningful endpoints and assessment of outcomes; f) appropriate analytic plans and g) approaches to minimize missing data.

[4] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/considerations-design-and-conduct-externally-controlled-trials-drug-and-biological-products

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 breakpoints[5]. The contractor will also be responsible for subcontracting with institutions and other collaborators.

It is anticipated that research contract awards will be made through the FY26 FDA BAA.

Submission Deadlines:

- Stage I Package (Concept Paper and Full Proposal) – **February 24, 2026**

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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