U.S. FOOD & DRUG ADMINISTRATION

Guidance Snapshot

Master Protocols for Drug and Biological Product Development

Revised Draft Guidance (June 2026)

What Is Recommended in This Guidance?

This guidance provides recommendations on the design and analysis of trials conducted under a master protocol. It focuses on randomized trials using a master protocol intended to contribute to evidence of safety and effectiveness of drugs. The document also provides guidance on the submission of master protocol documents for FDA review.

Why Is This Guidance Important?

Compared with traditional stand-alone trials under separate protocols, trials conducted under master protocols can share control arms, protocol elements, infrastructure, and oversight, thereby maximizing the amount of information obtained from a research effort. This document provides guidance to support well-designed, well-conducted trials using master protocols to accelerate drug development, particularly in certain settings, such as where subject recruitment is challenging.

What Is a Master Protocol?

A protocol designed with multiple substudies:

- These substudies may have different objectives
- These substudies are coordinated within an overall study structure to evaluate:
  - One or more drugs
  - One or more diseases or conditions

Guidance Snapshots are a communication tool and are not a substitute for the guidance document. To learn more about master protocols, **read the draft guidance**. To see additional Guidance Snapshots, check out the **pilot program**.

Examples of Trial Types That Could Utilize a Master Protocol

Umbrella Trial

Evaluates multiple drugs at the same time for a single disease or condition

Platform Trial

Evaluates multiple drugs for one or more diseases, conditions, or disease subtypes, and drugs can enter or leave the platform in an ongoing manner

Basket Trial

Evaluates a drug for multiple diseases, conditions, or disease subtypes

Trial Design Considerations

Randomization

Randomization is recommended to remove systematic imbalances between treatment arms and ensure reliable inference. The choice of randomization scheme can be informed by multiple factors, including efficiency and operational considerations.

Control Group

Platform trials in which drugs enter and exit should generally only use concurrent control subjects who meet drug-specific eligibility criteria for primary comparisons.

Blinding to Treatment Assignment

Blinding is critical to avoid bias, but complex strategies may be needed as the number of drugs, routes of administration, and dosing schedules increases.

Multiplicity

In master protocols, FDA generally does not recommend controlling for multiplicity across comparisons of different drugs to the control, or across comparisons of drug to control in different diseases. However, it remains important to control for multiplicity across different analyses (e.g., of different endpoints) for a given drug in a given disease.

Comparison Between Drugs

Comparisons between drugs are not required but may be useful. If conducted, they should be prespecified in the statistical analysis plan. Sponsors should consider entering into data-sharing agreements to allow for leveraging of information across drugs.

Evaluating Drug Effects in Basket Trials

Sponsors should prespecify and justify the approach for evaluating drug effects in multiple diseases, conditions, or disease subtypes, including any proposals to leverage information across substudies in related populations.

Independent, External Data Monitoring Committee (DMC)

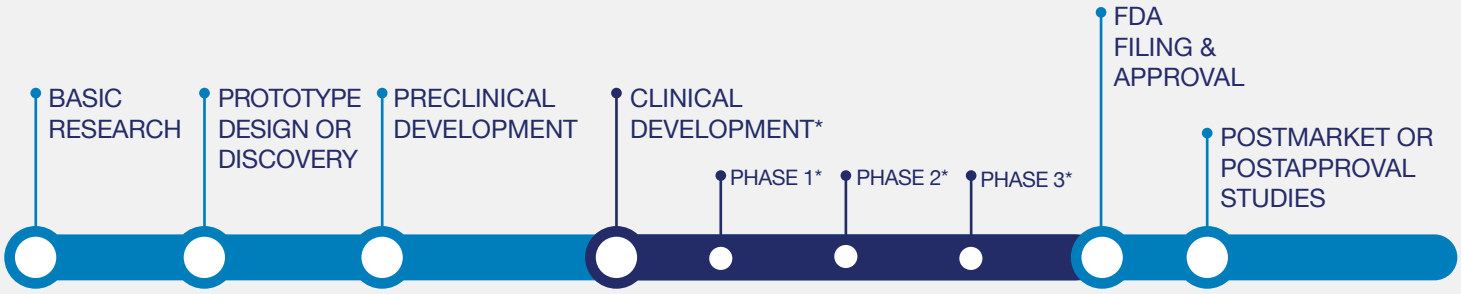
Establishing a DMC is recommended to oversee data access plans, analyses, and communication of results while maintaining trial integrity and preventing inadvertent dissemination of information when multiple drugs are being studied.

Background About the Guidance

This draft guidance revises and replaces the previous draft guidance for industry of the same name issued on December 21, 2023, and reflects FDA's consideration of public comments on the draft guidance. This revision provides additional recommendations on basket trials and minor changes for clarity on topics such as randomization, choice of control, and informed consent.

Drug Development Timeline

***When to Apply the Guidance Recommendations**



Recommendations from the Guidance Apply to Clinical Development

The regulatory considerations for a master protocol have increased complexity compared to those for a protocol for a stand-alone trial given the involvement of additional interested parties, the potential for frequent changes, and the quantity of documentation. Because of these complexities, each master protocol should be submitted in a new investigational new drug application (IND) to FDA, and a master protocol sponsor should request a pre-IND meeting to discuss the protocol and submission details.

Guidance Recap Podcast

Hear highlights from FDA staff

Speaker: *Gregory Levin, PhD, Associate Director for Statistical Science and Policy, Office of Biostatistics, Office of Translational Sciences, Center for Drug Evaluation and Research*

Click here to listen

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Continue the Conversation

Share your thoughts on the draft guidance

(docket opens on 06/24/2026)

Click here to provide official comments to the FDA Docket

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