# FDA Issues New Guidance to Developers of COVID-19 Drugs and Biological

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On May 11, the U.S. Food and Drug Administration (FDA) released two guidance documents to provide recommendations for sponsors "to accelerate development" of drugs and biologics designed to prevent or treat COVID-19. According to FDA, "more than 130 clinical trials of potential COVID-19 related drugs and biological products are underway with FDA oversight and additional development programs for other agents are in the planning stages."[1]

**Meeting Requests for COVID-19 Related Drugs and Biological Products**

The first guidance document provides a process for developers to receive **early agency feedback** regarding their supporting data, which could potentially provide a head start to related clinical trials.[2] The guidance explains how to prepare and submit a pre-investigational new drug application (pre-IND) meeting request for COVID-19-related drugs or biological products during the public health emergency. The guidance provides a list of information that sponsors should include in a pre-IND meeting request, including nonclinical and clinical data and information expected and general product quality considerations.

- FDA recommends initiating a **development discussion with a pre-IND meeting request** rather than a pre-Emergency Use Authorization (pre-EUA) request, since many drugs proposed for use under EUAs will more appropriately be the subject of INDs due to the lack of available data to support an EUA.
- FDA "strongly recommends" that **sponsors propose a randomized, placebo-controlled double-blind clinical trial using a superiority design**, given the variable clinical course of COVID-19 and the incomplete scientific understanding of the disease.Proposed clinical endpoints should reflect an improvement in how a trial subject feels, functions, or survives.
- A pre-IND submission should include a **detailed safety monitoring plan**, and the use of an independent data monitoring committee (DMC) is recommended.
- Sponsors should also consider whether **dosage forms and instructions for use** would need to be adjusted for use with severe cases, such as the administration of oral dosage forms to patients who are intubated.Other recommendations and considerations are provided for developers of antiviral drugs and inhalational drugs.

**Developing Drugs and Biological Products for COVID-19 Treatment or Prevention**

The second guidance provides FDA's recommendations on the design of **later stage clinical trials** intended to establish safety or efficacy of COVID-19 drug or biologic products other than preventative vaccines and convalescent plasma.[3] The focus of the guidance is on the development of drugs with direct antiviral activity or immunomodulatory activity but the guidance can be applied to drug with other mechanisms of action. The guidance provides a number of recommendations on clinical design topics such as patient selection, population size, study duration, efficacy assessment, and safety monitoring.

Key takeaways include:

- FDA encourages sponsors to include a **range of populations**, and the inclusion of high-risk patients, racial and ethnic minorities, patients with renal or hepatic impairment, and patients in various clinical settings should be considered.If appropriate, pregnant and lactating women should be included, and children should not be categorically excluded from clinical trials if there is a prospect for direct benefit. Sponsors considering including children in their studies should discuss this with FDA.
- The guidance expands upon the recommendation that COVID-19 drugs should be evaluated in **randomized, placebo-controlled,**

**double-blind clinical trials using a superiority design**.

- If feasible, sponsors should **limit in-person data collection activities** to those measurements that are intended to ensure safety and establish effectiveness or to impact the benefit-risk assessment due to infection control concerns.
- A trial should be **sufficiently long in duration to evaluate safety and effectiveness** reliably. For mechanically ventilated patients, a 4-week duration "would likely be sufficient to capture most important outcomes (e.g. mortality)" while longer durations may be appropriate for patients who are not as ill at baseline or for studies of preventative treatments.
- **Prospectively planned stop criteria** should be incorporated to ensure a high probability of halting the trial if the drug is harmful or shown not to be effective.
- **Possible endpoints to consider** include the need for invasive mechanical ventilation, the necessity for intensive care unit level care, hospitalization, the proportion of patients alive and free of respiratory failure, the length of time for symptoms to resolve, etc.The choice, time frame, and interpretation of efficacy endpoints may differ depending on the population of the trial. Virologic measures may be appropriate as a primary endpoint in a phase 2 treatment study but not for phase 3 trials.
- The **primary endpoint for prevention trials** should be the occurrence of laboratory-confirmed SARS-CoV-2 infection or infection with symptoms through a pre-specified time point.
- The guidance provided an **appendix with baseline severity categories**, ranging from infection without symptoms to critical COVID-19. Sponsors should include a subgroup analysis by baseline severity if a treatment trial enrolls a mixture of patients with different severity levels.

**Foley Hoag has formed a firm-wide, multi-disciplinary task force dedicated to client matters related to the novel coronavirus (COVID-19). For more guidance on your COVID-19 issues, visit our Resource Portal or contact your Foley Hoag attorney.**

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[1] FDA, Coronavirus (COVID-19) Update: FDA Takes New Actions to Accelerate Development of Novel Prevention, Treatment Options for COVID-19, May 11, 2020.

[2] FDA Guidance, *COVID-19 Public Health Emergency: General Considerations for Pre-IND Meeting Requests for COVID-19 Related Drugs and Biological Products* (May 2020), available at https://www.fda.gov/media/137927/download

[3] FDA Guidance, *COVID-19: Developing Drugs and Biological Products for Treatment or Prevention* (May 2020), available at https://www.fda.gov/media/137926/download

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