Revised Information for Investigational COVID-19 Convalescent Plasma

A licensed physician must participate in one of the IND pathways described below and obtain the COVID-19 convalescent plasma from a blood center. FDA does **not** provide COVID-19 convalescent plasma.

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The Food and Drug Administration (FDA or Agency) plays a critical role in protecting the United States from public health threats including the Coronavirus Disease 2019 (COVID-19) pandemic. FDA is committed to doing everything we can to provide timely response efforts to this pandemic and facilitate access to investigational drugs for use in patients with serious or immediately life-threatening COVID-19 infections.

One investigational treatment being explored for COVID-19 is the use of convalescent plasma collected from individuals who have recovered from COVID-19. It is possible that convalescent plasma that contains antibodies to SARS-CoV-2 (the virus that causes COVID-19) might be effective against the infection. Use of convalescent plasma has been studied in outbreaks of other respiratory infections, including the 2009-2010 H1N1 influenza virus pandemic, 2003 SARS-CoV-1 epidemic, and the 2012 MERS-CoV epidemic.

Although promising, convalescent plasma has not yet been shown to be effective in COVID-19. It is therefore important to determine through clinical trials, before routinely administering convalescent plasma to patients with COVID-19, that it is safe and effective to do so. The following pathways are available for administering or studying the use of COVID-19 convalescent plasma:

Clinical Trials: Investigators wishing to study the use of convalescent plasma are encouraged to submit requests to FDA for investigational use under the traditional IND regulatory pathway (21 CFR 312).

Expanded Access: FDA has worked with multiple federal partners and academia to open an expanded access protocol to facilitate access to COVID-19 convalescent plasma. For patients with, or at risk of, severe or life-threatening COVID-19 disease who are not eligible or who are unable to participate in randomized clinical trials, access may be available through participation

of acute care facilities in an investigational expanded access protocol under an IND already in place ("National Expanded Access Treatment Protocol (https://www.uscovidplasma.org/) (http://www.fda.gov/about-fda/website-policies/website-disclaimer)").

Single Patient Emergency IND: Although participation in clinical trials or an expanded access program are ways for patients to obtain access to convalescent plasma, for various reasons these may not be readily available to all patients in potential need. Therefore, given the public health emergency that the expanding COVID-19 outbreak presents, while clinical trials are being conducted and an expanded access protocol is available, FDA also is facilitating access to COVID-19 convalescent plasma for use in patients with serious or immediately life-threatening COVID-19 infections through the process of the patient's physician requesting a single patient emergency Investigational New Drug Application (eINDs) for the individual patient under 21 CFR 312.310. This process allows the use of an investigational drug for the treatment of an individual patient by a licensed physician upon FDA authorization. This eIND process is not for the use of COVID-19 convalescent plasma for the prevention of infection.

Investigational COVID-19 Convalescent Plasma - Emergency INDs Frequently Asked Questions (/media/136470/download)

Considerations for healthcare providers interested in obtaining COVID-19 Convalescent Plasma for Use under IND: COVID-19 convalescent plasma must only be collected from recovered individuals if they are eligible to donate blood (21 CFR 630.10, 21 CFR 630.15). Required testing must be performed (21 CFR 610.40) and the donation must be found suitable (21 CFR 630.30).

Considerations for eligibility of plasma donors:

- Evidence of COVID-19 documented by a laboratory test
    - either by:
        - a diagnostic test (e.g., nasopharyngeal swab) at the time of illness, OR
        - a positive serological test for SARS-CoV-2 antibodies after recovery, if prior diagnostic testing was not performed at the time COVID-19 was suspected.

- Either one of the following:
    - Complete resolution of symptoms at least 28 days prior to donation

      OR
    - Complete resolution of symptoms at least 14 days prior to donation, AND

  - Negative results for COVID-19 either from one or more nasopharyngeal swab specimens or by a molecular diagnostic test from blood. A partial list of available tests can be accessed at https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations (https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations).
- Male donors, female donors who have not been pregnant or female donors who have been tested since their most recent pregnancy and results interpreted as negative for HLA antibodies.
- Defined SARS-CoV-2 neutralizing antibody titers (e.g., greater than 1:80)
  - If neutralizing antibody titers cannot be obtained in advance, consider storing a retention sample from the convalescent plasma donation for determining antibody titers at a later date.

The container label of COVID-19 convalescent plasma units must include the following statement, “Caution: New Drug--Limited by Federal (or United States) law to investigational use." (21 CFR 312.6 (a)

To facilitate requests for emergency INDs for use of COVID-19 convalescent plasma to treat patients, health care providers seeking an emergency IND may want to consider the eligibility criteria used for the National Expanded Access Treatment Protocol. These criteria include:

- Laboratory confirmed COVID-19
- Severe or immediately life-threatening COVID-19, for example:[1]
  - Severe disease is defined as one or more of the following:
    - dyspnea,
    - respiratory frequency ≥ 30/min,
    - blood oxygen saturation ≤ 93%,
    - partial pressure of arterial oxygen to fraction of inspired oxygen ratio < 300, and/or
    - lung infiltrates > 50% within 24 to 48 hours
  - Life-threatening disease is defined as one or more of the following:
    - respiratory failure,
    - septic shock, and/or
    - multiple organ dysfunction or failure

- Provide informed consent

How to obtain authorization for use of COVID-19 convalescent plasma to treat patients using an emergency IND

- For requests that are not highly time sensitive (response from FDA provided within 4 to 8 hours), the requesting physician may contact FDA by completing form 3926 (https://www.fda.gov/media/98616/download (/media/98616/download)) and submitting the form by email to CBER_eIND_Covid-19@FDA.HHS.gov. (mailto:CBER_eIND_Covid-19@FDA.HHS.gov)
    - **If you have problems opening the PDF form in your browser,** try downloading it instead:
      1. Right-click the form link.
      2. Click the Save option. (On most browsers, this is the Save Link As option.)

      You may also need to upgrade your version of Adobe Reader (http://get.adobe.com/reader/) (http://www.fda.gov/about-fda/website-policies/website-disclaimer).
    - The completed form should include a brief clinical history of the patient, including: diagnosis, current therapy, and rationale for requesting the proposed investigational treatment in order to meet the expanded access use requirements of 21 CFR 312.305 and 312.310.
    - The form should include information regarding where the COVID-19 convalescent plasma will be obtained.
    - Providers should complete the form to the extent possible, and FDA will work with the provider if additional information is required.
    - FDA will review the request and, upon approval, FDA will send the requesting physician a confirmatory email that includes the emergency IND number.
- In the event of an emergency that is highly time sensitive (response required in less than 4 hours) or where the provider is unable to complete and submit form 3926 due to extenuating circumstances, the provider may contact FDA's Office of Emergency Operations at 1-866-300-4374 to seek verbal authorization.
    - If verbal authorization is given, the requestor must agree to submit an expanded access application (e.g., form 3926) within 15 working days of FDA's authorization of the use.

[1] *Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. JAMA. Published online February 24, 2020. doi:10.1001/jama.2020.2648*