

Investigational COVID-19 Convalescent Plasma

Guidance for Industry

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**This document supersedes the guidance of the same title issued on
February 11, 2021.**

**U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
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Preface

Public Comment

This guidance is being issued to address the Coronavirus Disease 2019 (COVID-19) public health emergency. This guidance is being implemented without prior public comment because the Food and Drug Administration (FDA or Agency) has determined that prior public participation for this guidance is not feasible or appropriate (see section 701(h)(1)(C) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 371(h)(1)(C)) and 21 CFR 10.115(g)(2)). This guidance document is being implemented immediately, but it remains subject to comment in accordance with the Agency's good guidance practices.

Comments may be submitted at any time for Agency consideration. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. Submit electronic comments to <https://www.regulations.gov>. All comments should be identified with the docket number FDA-2020-D-1825 and complete title of the guidance in the request.

Additional Copies

Additional copies are available from the FDA webpage titled "COVID-19-Related Guidance Documents for Industry, FDA Staff, and Other Stakeholder," available at <https://www.fda.gov/emergency-preparedness-and-response/mcm-issues/covid-19-related-guidance-documents-industry-fda-staff-and-other-stakeholders>, and from the FDA webpage titled "Search for FDA Guidance Documents" available at <https://www.fda.gov/regulatory-information/search-fda-guidance-documents>.

Additional copies of this guidance are also available from the Office of Communication, Outreach and Development (OCOD), 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, Silver Spring, MD 20993-0002, or by calling 1-800-835-4709 or 240-402-8010, or email ocod@fda.hhs.gov, or from the Internet at <https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances>.

Questions

For questions on the content of this guidance, contact OCOD at the phone numbers or email address listed above.

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Investigational COVID-19 Convalescent Plasma

Guidance for Industry

This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

I. INTRODUCTION

FDA plays a critical role in protecting the United States (U.S.) from threats such as emerging infectious diseases, including the Coronavirus Disease 2019 (COVID-19) pandemic. FDA is committed to providing timely guidance to support response efforts to this pandemic.

On August 23, 2020, FDA issued an Emergency Use Authorization (EUA)¹ for COVID-19 convalescent plasma for the treatment of hospitalized patients with COVID-19. FDA has subsequently reissued this EUA with revisions. Most recently, FDA revised the EUA to limit authorization to the use of COVID-19 convalescent plasma with high titers of anti-SARS-CoV-2 antibodies for the treatment of COVID-19 in patients with immunosuppressive disease or receiving immunosuppressive treatment in either the outpatient or inpatient setting.² FDA recognizes that while COVID-19 convalescent plasma may be used under an EUA consistent with the authorization, COVID-19 convalescent plasma may also be used under an

¹ On February 4, 2020, pursuant to section 564(b)(1)(C) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 360bbb-3), the Secretary of Health and Human Services (HHS) determined that there is a public health emergency that has a significant potential to affect national security or the health and security of U.S. citizens living abroad, and that involves the virus that causes COVID-19. On the basis of such determination, the Secretary then declared, on March 27, 2020, that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic, pursuant to section 564 of the FD&C Act. Under section 564 of the FD&C Act, the Commissioner of Food and Drugs may authorize unapproved medical products or unapproved uses of approved medical products to be used in an emergency to diagnose, treat, or prevent serious or life-threatening diseases or conditions caused by chemical, biological, radiological, and nuclear agents, including emerging infectious disease threats when the product may be effective for its intended use, the known and potential benefits of the product outweigh the known and potential risks, and there are no adequate, approved, and available alternatives to the product. Additional information on Emergency Use Authorization and a list of all current EUAs are available at <https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization>.

² Denise M. Hinton, U.S. Food & Drug Admin., U.S. Dep't of Health & Human Servs., Emergency Use Authorization for COVID-19 Convalescent Plasma (originally issued Aug. 23, 2020, and subsequently reissued with revisions) available at <https://www.fda.gov/media/141477/download>.

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investigational new drug application (IND). For the purposes of this guidance, the term “COVID-19 convalescent plasma” refers to the convalescent plasma authorized under the EUA, while the term “investigational convalescent plasma” refers to convalescent plasma that does not meet all the conditions of the EUA and/or is being used under an IND.

FDA is issuing this guidance to provide recommendations to health care providers and investigators on the use of COVID-19 convalescent plasma or investigational convalescent plasma during the public health emergency. The guidance also provides recommendations to blood establishments on collection. This document supersedes the guidance of the same title issued in February 2021 (previous versions January 2021, November 2020, September 2020, May 2020, and April 2020). We have revised the guidance to reflect that the EUA authorizes COVID-19 convalescent plasma with high titers of anti-SARS-CoV-2 antibodies for the treatment of COVID-19 in patients with immunosuppressive disease or receiving immunosuppressive treatment in either the outpatient or inpatient setting.³ In addition, we have revised certain recommendations pertaining to COVID-19 convalescent plasma donors. In sections III.B.1 and III.C.1, we now recommend that individuals qualify as COVID-19 convalescent plasma donors 10 days following complete resolution of symptoms. We also have revised the recommendations in section III.B.1 that address when individuals who have received an investigational COVID-19 vaccine as a participant in a clinical trial or received an authorized or licensed COVID-19 vaccine, qualify as convalescent plasma donors. Also, the section on FDA’s interim compliance and enforcement policy regarding the IND requirements for the use of investigational convalescent plasma has been removed because the period of enforcement discretion ended on May 31, 2021.

This policy is intended to remain in effect only for the duration of the public health emergency related to COVID-19 declared by HHS on January 31, 2020, effective January 27, 2020, including any renewals made by the HHS Secretary in accordance with section 319(a)(2) of the Public Health Service Act (PHS Act) (42 U.S.C. 247d(a)(2)).

Given this public health emergency, and as discussed in the Notice published in the *Federal Register* of March 25, 2020, titled “Process for Making Available Guidance Documents Related to Coronavirus Disease 2019,” available at <https://www.govinfo.gov/content/pkg/FR-2020-03-25/pdf/2020-06222.pdf>, this guidance is being implemented without prior public comment because FDA has determined that prior public participation for this guidance is not feasible or appropriate (see section 701(h)(1)(C) of the FD&C Act (21 U.S.C. 371(h)(1)(C)) and Title 21 of the Code of Federal Regulations (CFR) 21 CFR 10.115(g)(2)). This guidance document is being implemented immediately, but it remains subject to comment in accordance with the Agency’s good guidance practices.

The contents of this document do not have the force and effect of law and are not meant to bind the public in any way, unless specifically incorporated into a contract. This document is intended only to provide clarity to the public regarding existing requirements under the law. FDA guidance documents, including this guidance, should be viewed only as recommendations,

³ Denise M. Hinton, U.S. Food & Drug Admin., U.S. Dep’t of Health & Human Servs., Emergency Use Authorization for COVID-19 Convalescent Plasma (originally issued Aug. 23, 2020, and subsequently reissued with revisions) available at <https://www.fda.gov/media/141477/download>.

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unless specific regulatory or statutory requirements are cited. The use of the word *should* in FDA guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

There is currently an outbreak of respiratory disease caused by a novel coronavirus. The virus has been named “SARS-CoV-2” and the disease it causes has been named “Coronavirus Disease 2019” (COVID-19). On January 31, 2020, HHS issued a declaration of a public health emergency related to COVID-19 and mobilized the Operating Divisions of HHS.⁴ In addition, on March 13, 2020, there was a Presidential declaration of a national emergency in response to COVID-19.⁵

One investigational treatment for COVID-19 is convalescent plasma collected from individuals who have recovered from COVID-19, which contains antibodies to SARS-CoV-2 (Refs. 1-4). Use of convalescent plasma has been studied in other respiratory viral infections, including SARS-CoV-1, H1N1 influenza, and MERS-CoV (Refs. 5-7).

On August 23, 2020, FDA issued an EUA for COVID-19 convalescent plasma for the treatment of hospitalized patients with COVID-19. FDA has subsequently reissued the EUA with revisions. Most recently, FDA revised the EUA to limit authorization to the use of COVID-19 convalescent plasma with high titers of anti-SARS-CoV-2 antibodies for the treatment of COVID-19 in patients with immunosuppressive disease or receiving immunosuppressive treatment in either the outpatient or inpatient setting. Given that the clinical evidence in patients with immunosuppressive disease or receiving immunosuppressive treatment remains limited, data from additional adequate and well-controlled randomized trials remain necessary for a definitive demonstration of COVID-19 convalescent plasma efficacy and to determine the optimal product attributes.

III. RECOMMENDATIONS

A. Pathways for Use of Investigational Convalescent Plasma

Because convalescent plasma for the treatment of COVID-19 has not yet been approved for use by FDA,⁶ it is an investigational product. As such its administration must be

⁴ Secretary of Health and Human Services, Determination that a Public Health Emergency Exists (originally issued Jan. 31, 2020, and subsequently renewed), available at <https://www.phe.gov/emergency/news/healthactions/phe/Pages/default.aspx>.

⁵ Proclamation on Declaring a National Emergency Concerning the Novel Coronavirus Disease (COVID-19) (Mar. 13, 2020), available at <https://trumpwhitehouse.archives.gov/presidential-actions/proclamation-declaring-national-emergency-concerning-novel-coronavirus-disease-covid-19-outbreak/>. On February 24, 2021, there was a Presidential Declaration continuing the national emergency concerning the COVID-19 pandemic beyond March 1, 2021. See Continuation of the National Emergency Concerning the Coronavirus Disease 2019 (COVID-19) Pandemic (February 24, 2021), available at <https://www.federalregister.gov/documents/2021/02/26/2021-04173/continuation-of-the-national-emergency-concerning-the-coronavirus-disease-2019-covid-19-pandemic>.

⁶ Convalescent plasma is a biological product subject to the licensure requirement under section 351 of the PHS Act. 42 U.S.C. 262(a).

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under the EUA or an IND. The emergency use of COVID-19 convalescent plasma is not authorized under the EUA unless it is consistent with, and does not exceed, the terms of the Letter of Authorization, including the Scope of Authorization and Conditions of Authorization.⁷ Alternatively, investigational convalescent plasma may be administered under the traditional IND regulatory pathway, a single-patient IND for emergency use, or an intermediate-size population expanded access IND (section 351(a)(3) of the PHS Act (42 U.S.C. 262(a)(3)); section 505(i) of the FD&C Act (21 U.S.C. 355(i)); 21 CFR 601.21; and 21 CFR Part 312).

FDA does not collect convalescent plasma or provide convalescent plasma. Health care providers or acute care facilities should obtain convalescent plasma from an FDA-registered or licensed blood establishment.

The following pathways are available for administering or studying the use of convalescent plasma:

1. Emergency Use Authorization

On August 23, 2020, FDA issued an EUA for COVID-19 convalescent plasma for the treatment of hospitalized patients with COVID-19. FDA has subsequently reissued the EUA with revisions. Most recently, FDA revised the EUA to limit authorization to the use COVID-19 convalescent plasma with high titers of anti-SARS-CoV-2 antibodies for the treatment of COVID-19 in patients with immunosuppressive disease or receiving immunosuppressive treatment in either the outpatient or inpatient setting.

Health care providers intending to administer COVID-19 convalescent plasma under the EUA are not required to report its use to FDA. Providers should refer to the Fact Sheet for Health Care Providers⁸ for information on the intended use and known and potential risks and benefits of COVID-19 convalescent plasma. The Fact Sheet also provides a description of the product, information on the dosage, administration and storage of COVID-19 convalescent plasma, use in specific populations, and instructions for communicating with recipients.

As described in the Fact Sheet, health care providers must maintain records and conduct a thorough investigation of adverse reactions after transfusion of COVID-19 convalescent plasma and must report fatalities to FDA as required in 21 CFR 606.170. Refer to FDA's guidance entitled "Notifying FDA of Fatalities Related to Blood Collection or Transfusion" for recommendations on reporting fatalities related to blood transfusion to FDA (Ref. 8).

⁷ See <https://www.fda.gov/media/141477/download>.

⁸ See <https://www.fda.gov/media/141478/download>.

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2. Clinical Trials

The EUA is not intended to replace clinical trials that are critically important for the definitive demonstration of safety and efficacy of investigational convalescent plasma. Ongoing clinical trials of investigational convalescent plasma should not be amended based on the issuance of the EUA. Healthcare providers are encouraged to enroll patients in those trials and complete clinical trials to fully answer the questions about the effectiveness of convalescent plasma for the treatment of COVID-19.

Investigators wishing to study the use of convalescent plasma in a clinical trial should submit requests to FDA for investigational use under the traditional IND regulatory pathway (21 CFR Part 312). The Center for Biologics Evaluation and Research (CBER) Office of Blood Research and Review (OBRR) is committed to engaging with sponsors and reviewing such requests expeditiously. During the COVID-19 pandemic, INDs may be submitted via email to CBERDCC_eMailSub@fda.hhs.gov.

3. Expanded Access

An IND application for expanded access is an alternative for use of investigational convalescent plasma for patients with serious or immediately life-threatening COVID-19 disease who are not eligible or who are unable to participate in randomized clinical trials (21 CFR 312.305). During the COVID-19 pandemic, INDs for expanded access, that are not single patient INDs, may be submitted via email to CBERDCC_eMailSub@fda.hhs.gov.

a. Single Patient IND for Emergency Use

Given the public health emergency that the COVID-19 pandemic presents, FDA is continuing to facilitate access to investigational convalescent plasma through the process of a physician requesting a single patient IND for an individual patient with serious or life-threatening COVID-19 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, if the applicable regulatory criteria are met. Note, in such cases, a licensed physician seeking to administer investigational convalescent plasma to an individual patient must request the IND (21 CFR 312.310(b)).

Note: Given that the intended use of COVID-19 convalescent plasma under the EUA is for treatment of COVID-19 in patients with immunosuppressive disease or receiving immunosuppressive treatment in either the outpatient or inpatient setting, and COVID-19 convalescent plasma is not authorized for the treatment of COVID-19 in immunocompetent patients, FDA expects few requests for single patient INDs. FDA recommends that physicians seeking to use convalescent plasma for treatment of COVID-19 in patients with immunosuppressive disease or receiving immunosuppressive treatment should

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do so under the EUA and not under single patient INDs. Other options for the use of investigational convalescent plasma are listed above.

To obtain a single patient IND for emergency use, the requesting physician may contact FDA by completing **Form FDA 3926** (<https://www.fda.gov/media/98616/download>) and submitting the form by email to CBER_eIND_Covid-19@FDA.HHS.gov. CBER requests that all forms be filled out electronically to facilitate rapid review. Handwritten forms are often hard to read and may delay the processing of the request. For more detailed instructions see the Form FDA 3926 Instructions (<https://www.fda.gov/media/98627/download>).

For requests when the provider is unable to complete and submit **Form FDA 3926** due to extenuating circumstances, or in the case of a medical emergency between the hours of 8pm and 8am Eastern Time (ET), i.e., when authorization and issuance of an IND number is needed before 8am ET the next morning, the provider should contact FDA's Office of Emergency Operations at 1-866-300-4374 to be routed to the appropriate clinical review staff for assistance with submitting the request and issuance of an IND number.

B. Collection of COVID-19 Convalescent Plasma under the EUA

Blood establishments collecting authorized COVID-19 convalescent plasma must comply with the Conditions for Authorization in the EUA. Please refer to the Letter of Authorization for the Conditions of Authorization for registered and licensed blood establishments.⁹

Note: Registered and licensed blood establishments do not need to contact FDA or request a supplement to their license, respectively, to collect and manufacture COVID-19 convalescent plasma for the authorized use under the EUA provided they 1) follow their standard operating procedures for plasma collection and all applicable regulations, and 2) collect plasma from individuals who meet the donor qualifications specified below. Once manufactured, COVID-19 convalescent plasma may be distributed for use under the EUA. Blood establishments do not need to request an alternative procedure or exception under 21 CFR 640.120(a) to collect and distribute COVID-19 convalescent plasma.

1. Donor Eligibility

As described in the authorization letter, COVID-19 convalescent plasma is human plasma collected from individuals whose plasma contains high titers of anti-SARS-CoV-2 antibodies and who meet all donor eligibility requirements (21 CFR 630.10 and 21 CFR 630.15) and qualifications. Under the EUA, authorized COVID-19

⁹ See <https://www.fda.gov/media/141477/download>.

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convalescent plasma must be collected by registered or licensed blood establishments from donors in the U.S. or its territories in accordance with applicable regulations, policies, and procedures. Testing for relevant transfusion-transmitted infections (21 CFR 610.40) must be performed and the donation must be found suitable (21 CFR 630.30).

COVID-19 convalescent plasma is collected from individuals who meet the following qualifications:

- a. Evidence of COVID-19 documented by laboratory testing in either:
 1. Individuals who had symptoms of COVID-19 and a positive test result from a diagnostic test approved, cleared, or authorized by FDA.

OR

2. Individuals who did not have a prior positive diagnostic test and/or never had symptoms of COVID-19 may be qualified to donate if they have had reactive (positive) results in two different tests approved, cleared, or authorized by FDA to detect SARS-CoV-2 antibodies.

A list of all current EUA COVID-19 in vitro diagnostics is available at: <https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#covidinvitrodev>.

- b. Complete resolution of symptoms at least 10 days before the donation. A negative result for COVID-19 by a diagnostic test is not necessary to qualify the donor.
- c. Male donors, female donors who have never been pregnant, or female donors who have been tested since their most recent pregnancy and results interpreted as negative for HLA antibodies.
- d. To ensure that COVID-19 convalescent plasma collected from donors contains antibodies directly related to their immune responses to SARS-CoV-2 infection, you should not collect COVID-19 convalescent plasma from:
 - i. Individuals who have received an investigational COVID-19 vaccine as a participant in a clinical trial, or received an authorized or licensed COVID-19 vaccine, unless they:
 - 1) had symptoms of COVID-19 and a positive test result from a diagnostic test approved, cleared, or authorized by FDA (i.e., individuals who meet the qualification for evidence of COVID-19 described in section III.B.1.a.1 of this guidance), AND

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- 2) are within 6 months after complete resolution of COVID-19 symptoms.

Administration of COVID-19 vaccines for the purpose of boosting immunity of convalescent plasma donors would need to be conducted within a clinical trial under IND (21 CFR Part 312).

or

- ii. Individuals who received an investigational COVID-19 monoclonal antibody therapy as a participant in a clinical trial or received an authorized or licensed COVID-19 monoclonal antibody therapy, until at least three months after receipt of the therapy.

2. Testing for anti-SARS-CoV2 Antibodies

- a. Under the EUA, all plasma donations must be tested by registered or licensed blood establishments for high titers of anti-SARS-CoV-2 antibodies as a manufacturing step to determine suitability before release, using one of the tests and qualifying results referenced in the EUA Letter of Authorization.¹⁰
- b. Plasma units that meet the specific testing requirements for SARS-CoV-2 antibodies described in the EUA qualify as COVID-19 convalescent plasma with high titers of anti-SARS-CoV-2 antibodies.¹¹ (See section III.B.3 of this guidance for labeling requirements.)
- c. Blood establishments considering the use of a test not referenced in the EUA to qualify COVID-19 convalescent plasma should have the test developer contact CBER OBRR to determine acceptability of the proposed test, which if accepted, would require an amendment to the EUA. FDA will consider data submitted to support such use in assessing the acceptability of other tests.

Requests should be submitted to CBER-EUA-CCP-Assays@fda.hhs.gov.

3. Labeling

COVID-19 convalescent plasma must be appropriately labeled.

- a. The requirements in 21 CFR 606.121 for the container label apply, including the requirement to include a reference to the circular of information.

¹⁰ See <https://www.fda.gov/media/141477/download>.

¹¹ Plasma units that do not qualify as COVID-19 convalescent plasma with high titers of anti-SARS-CoV-2 antibodies under the EUA may qualify for investigational use under an applicable IND or may be relabeled as Fresh Frozen Plasma or other plasma type, as applicable, depending on the manufacturing process.

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FDA recognizes that the current circular of information does not contain specific information about COVID-19 convalescent plasma regarding indications for use, dosage information, contraindications, or cautions, but it provides information on the use of plasma.

- b. COVID-19 convalescent plasma is not an approved product. The container label must not indicate a license number.
- c. COVID-19 convalescent plasma units must be clearly labeled as high titer COVID-19 convalescent plasma based on the results of the SARS-CoV-2 antibody test used as part of manufacturing. This information may be placed on the container label or on a tie tag.
- d. We recommend the use of a uniform container label for COVID-19 convalescent plasma. In particular, we recommend the use of the International Society of Blood Transfusion (ISBT) format specified in the U.S. Industry Consensus Standard for the Uniform Labeling of Blood and Blood Components Using ISBT 128.
- e. The manufacturing process used and the expiration date on the label for COVID-19 convalescent plasma should be the same as for other plasma products that are of the same type. For example, COVID-19 Convalescent Plasma, Fresh Frozen, should be frozen within 8 hours after collection, stored at -18°C or colder and have an expiration date of one year from the date of collection.

C. Collection of Convalescent Plasma Under an IND

Under FDA's IND regulations, an IND (including an intermediate-size population expanded access or single patient IND) must provide information with respect to the investigational drug, chemistry, manufacturing, and controls adequate to ensure the proper identification, quality, purity, and strength of the investigational drug (21 CFR 312.23(a)(7) and 21 CFR 312.305(b)(2)(vi)). For INDs for use of investigational convalescent plasma, the IND should contain, among other things, adequate information to demonstrate that the plasma will contain SARS-CoV-2 neutralizing antibody titers, if available. Accordingly, health care providers or acute care facilities should include information in the IND submission that the investigational convalescent plasma will be obtained from an FDA-registered blood establishment that follows the donor eligibility criteria and donor qualifications described in section III.C.1 of this guidance in collecting plasma from donors.

1. Donor Eligibility

- a. Investigational convalescent plasma must only be collected from individuals who meet all donor eligibility requirements (21 CFR 630.10 and 21 CFR 630.15). Donation testing for relevant transfusion-transmitted infections must

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be performed (21 CFR 610.40) and the donation must be found suitable (21 CFR 630.30).

- b. We recommend investigational convalescent plasma is collected from individuals who meet the following qualifications:
 - i. Evidence of COVID-19 documented by laboratory testing in either:
 - 1. Individuals who had symptoms of COVID-19 and a positive test result from a diagnostic test approved, cleared, or authorized by FDA.

OR

- 2. Individuals who did not have a prior positive diagnostic test and/or never had symptoms of COVID-19 may be qualified to donate if they have had reactive (positive) results in two different tests approved, cleared, or authorized by FDA to detect SARS-CoV-2 antibodies.

A list of all current EUA COVID-19 in vitro diagnostics is available at: <https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#covidinvitrodev>.

- ii. Complete resolution of symptoms at least 10 days before the donation. A negative result for COVID-19 by a diagnostic test is not necessary to qualify the donor.
 - iii. Male donors, female donors who have never been pregnant, or female donors who have been tested since their most recent pregnancy and results interpreted as negative for HLA antibodies.

2. Testing for anti-SARS-CoV2 Antibodies

Plasma donations should be tested for anti-SARS-CoV-2 antibodies to determine suitability before release in accordance with an applicable IND.

Note: Plasma units that do not qualify as COVID-19 convalescent plasma under the EUA may qualify for investigational use under an applicable IND. The units should be labeled as described in section III.C.3 of this guidance.

Registered and licensed blood establishments that collect plasma intended for transfusion do not need to contact FDA or request a supplement to their license, respectively, or obtain their own IND to collect and manufacture convalescent plasma for investigational use provided they 1) follow their standard operating procedures for plasma collection and all applicable regulations, and 2) collect plasma from individuals who meet the donor qualifications specified in this guidance, which

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would be included in the applicable IND(s) held by a health care provider or other sponsor.

Once manufactured, the convalescent plasma may be distributed for investigational use.

Blood establishments do not need to request an alternative procedure or exception under 21 CFR 640.120(a) to collect and distribute investigational convalescent plasma.

3. Labeling

Investigational convalescent plasma must be appropriately labeled.

- a. The container label of investigational 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)).
- b. In addition, the requirements in 21 CFR 606.121 for the container label apply, including the requirement to include a reference to the circular of information.

FDA recognizes that the current circular of information does not contain specific information about investigational convalescent plasma regarding indications for use, dosage information, contraindications or cautions, but it provides information on the use of plasma.

- c. The investigational convalescent plasma container label must not indicate a license number.
- d. We recommend the use of a uniform container label for investigational convalescent plasma. In particular, we recommend the use of the ISBT format specified in the U.S. Industry Consensus Standard for the Uniform Labeling of Blood and Blood Components Using ISBT 128.
- e. The manufacturing process used and the expiration date on the label for investigational convalescent plasma should be the same as for other plasma products that are of the same type. For example, Convalescent Plasma, Fresh Frozen, should be frozen within 8 hours after collection, stored at -18°C or colder and have an expiration date of one year from the date of collection.
- f. Investigational convalescent plasma units may be labeled for anti-SARS-CoV2 antibodies based on the test results as specified under the applicable IND. This information may be placed on the container label or on a tie tag.

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D. Recordkeeping

A health care provider who is participating in an IND, including an expanded access IND or single patient IND for emergency use, must maintain records for the investigational convalescent plasma unit(s) administered to the COVID-19 patient (21 CFR 312.62). Such records should include the unique identification number(s) (e.g., the ISBT donation identification number(s) of the unit(s)).

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IV. REFERENCES

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