

Toolkit for COVID-19 Convalescent Plasma (CCP) Under Emergency Use Authorization Issued 02 25 21

The Toolkit has been updated to reflect the new information from:

- FDA’s February 4, 2021 and February 23, 2021 [Revised EUA for Use of COVID-19 Convalescent Plasma](#)
- FDA’s February 11, 2021 [Investigational CCP Guidance for Industry](#),
- FDA’s webpage, updated February 11, 2021 [Recommendations for Investigational COVID-19 Convalescent Plasma](#)

This Toolkit (dated 02/25/21) is intended to:

- supplement but not replace your review of the three documents listed above,
- provide an update on blood donor deferral following COVID-19 vaccine and transfusion,
- help you identify new information in guidance.

TABLE OF CONTENTS

PAGE

1- FDA’s February 11, 2021 CCP Guidance and the Impact of the February 4 and 23, 2021 CCP EUA	2
2- FDA’S RESPONSES TO QUESTIONS - Hot Topic Discussion: FDA Updates EUA for CCP in Response to New Data	6
3- AABB Summary: Donation Of CCP, Blood Components And HCT/Ps Following COVID-19 Vaccines or Treatment With CCP or Monoclonals	6
4- EXAMPLE FLOWCHART: ELIGIBILITY FOR CCP DONATION AFTER COVID-19 VACCINATION/MONOCLONAL ANTIBODY THERAPY	6

1- FDA's February 11, 2021 Guidance: [Investigational COVID-19 Convalescent Plasma and the Impact of the February 4 and 23, 2021 CCP EUA](#)

Changes are identified:

- ✓ Updated information in the February 11, 2021 Guidance
- ✓ Recommendations impacted by the revised [CCP EUA \(February 23, 2021\)](#) requiring updated policies

[February 11, 2021 CCP Guidance](#)

- Key changes in the [revised CCP EUA \(Feb 4, 2021\)](#) - FDA recommendations impacted by the EUA are **highlighted** at left.
- **Additional test authorized in the revised Feb 23, 2021 EUA. No additional significant changes.**

I. INTRODUCTION

Updated information is highlighted below

Page 1:

On August 23, 2020, FDA issued an Emergency Use Authorization (EUA) for COVID-19 convalescent plasma for the treatment of hospitalized patients with COVID-19. FDA has subsequently reissued this EUA with revisions.

...

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. We also describe FDA's interim compliance and enforcement policy regarding the IND requirements for the use of investigational convalescent plasma. **This document supersedes the guidance of the same title issued in January 2021** (previous versions November 2020, September 2020, May 2020, and April 2020). We have revised the recommendations in section III.B.1 of this guidance pertaining to convalescent plasma donors. The revisions address when individuals who **have 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**, qualify as convalescent plasma donors. We also revised the recommendations in section III.B.2 and 3 of the guidance pertaining to the **qualification and labeling of high titer COVID-19 convalescent plasma** under the EUA. In addition, we updated section IV of the guidance to note that FDA intends to exercise

Revised CCP EUA page 1-2:

Having concluded that revising this EUA is appropriate to protect the public health or safety under Section 564(g)(2)(C) of the Act (21 U.S.C. § 360bbb-3(g)(2)(C)), FDA is again reissuing the Letter of Authorization in its entirety with revisions to: (1) include updates based on data from additional clinical trials; (2) **clarify that the authorization is limited to use of only high titer COVID-19 convalescent plasma in hospitalized patients early in the course of disease and those hospitalized with impaired humoral immunity;**

Following the August 23, 2020 authorization, additional studies, including randomized, controlled trials, have provided data to further inform the safety and efficacy of COVID-19 convalescent plasma, and further characterize product attributes and patient populations for its use. Based on assessment of these data, potential clinical benefit of transfusion of COVID-19 convalescent plasma **in hospitalized patients with COVID-19 is associated with high titer units administered early in the course of disease.**⁶

⁶Based on what is known about the typical course of illness and kinetics of the humoral immune response in COVID-19, for most hospitalized patients, early in the course of disease likely represents **prior to respiratory failure requiring intubation and mechanical ventilation**. The therapeutic window may be longer when CCP is administered to patients with clinical or laboratory evidence of impaired humoral immunity.



<p>enforcement discretion related to the investigational new drug requirements for use of convalescent plasma including when, among other circumstances, the donor meets the qualifications for individuals who have received a COVID-19 vaccine or COVID-19 monoclonal antibody therapy in accordance with section III.B.1 of this guidance.</p>	
<p>III. RECOMMENDATIONS</p> <p>A. Pathways for Use of Investigational Convalescent Plasma</p> <p>1. Emergency Use Authorization, page 4</p> <p>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.</p> <p>2. Clinical Trials</p> <p>3. Expanded Access</p>	<p>Refer to the Revised CCP EUA page 1-2 (above)</p>
<p>B. Collection of COVID-19 Convalescent Plasma under the EUA</p> <p>1. Donor Eligibility, page 7</p> <p>New information is highlighted below</p> <p>NOTE: III.B.1.d was added to address CCP donor eligibility criteria after COVID-19 vaccination and a new 3-month deferral recommendation following monoclonal antibody therapy:</p> <p>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:</p> <p>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:</p> <ol style="list-style-type: none"> 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 above), AND 2) received the COVID-19 vaccine after diagnosis of COVID-19, AND 3) 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 page 8

- b. Plasma units that meet the specific testing requirements for SARS-CoV-2 antibodies described in the EUA qualify as high titer COVID-19 convalescent plasma. (See section III.B.3 of this guidance for labeling requirements.)

Revised CCP EUA page 2:

Therefore, this EUA is being revised to authorize only the use of high titer COVID-19 convalescent plasma, for the treatment of hospitalized patients with COVID-19, early in the disease course. The related fact sheets are revised accordingly. **The use of low titer COVID-19 convalescent plasma is no longer authorized under this EUA.**

Tests Acceptable for Use in the Manufacture of High Titer COVID-19 Convalescent Plasma

Manufacturer (listed alphabetically)	Assay	Qualifying Result
Abbott	SARS-CoV-2 IgG (ARCHITECT and Alinityi)	Index (S/C) ≥ 4.5
Beckman Coulter	Access SARS-CoV-2 IgG	S/CO ≥ 3.3
EUROIMMUN	Anti-SARS-CoV-2 ELISA (IgG)	Ratio ≥ 3.5
GenScript	cPass SARS-CoV-2 Neutralization Antibody Detection Kit	Inhibition ≥ 68%
Kantaro	COVID-SeroKlir, Kantaro Semi-Quantitative SARS-CoV-2 IgG Antibody Kit	Spike ELISA > 47 AU/mL
Mount Sinai	COVID-19 ELISA IgG	Spike ELISA titer ≥ 1:2880

Ortho	VITROS Anti-SARS-CoV-2 IgG	S/C ≥ 9.5
Roche	Elecsys Anti-SARS-CoV-2	COI ≥ 109
Roche	Elecsys Anti-SARS-CoV-2 S	≥ 132 U/mL
Siemens	ADVIA Centaur SARS-CoV-2 IgG (COV2G)	Index ≥ 4.8

3. Labeling page 8

- 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.

Revised CCP EUA page 5:

To be labeled as COVID-19 convalescent plasma under this EUA, units containing anti-SARS-CoV-2 antibodies must be labeled as high titer according to the results of the tests described above. Low titer units are no longer authorized for use under the conditions of this EUA.

C. Collection of Convalescent Plasma Under an IND

No change to this section.

IV. COMPLIANCE AND ENFORCEMENT POLICY REGARDING INVESTIGATIONAL NEW DRUG REQUIREMENTS FOR USE OF CONVALESCENT PLASMA

Reference to “qualifying the unit as low titer” has been removed.

New information is highlighted below

...

FDA intends to exercise this temporary enforcement discretion provided the following circumstances are present:

- 3) The investigational convalescent plasma is collected by registered blood establishments from donors who meet
 - a) all eligibility requirements and qualifications in accordance with section III.C.1 of this guidance, and b) the qualifications for individuals who have received a COVID-19 vaccine or COVID-19 monoclonal antibody therapy, in accordance with section III.B.1 of this guidance.

NOTE: FDA HAS INDICATED THAT THE AGENCY DOES NOT PLAN TO EXTEND THIS DEADLINE:

FDA intends to exercise this discretion with respect to the IND requirements for the collection, shipment, and administration of investigational convalescent plasma through May 31, 2021.

Revised CCP EUA page 2:

Therefore, this EUA is being revised to authorize only the use of high titer COVID-19 convalescent plasma, for the treatment of hospitalized patients with COVID-19, early in the disease course. The related fact sheets are revised accordingly. The use of low titer COVID-19 convalescent plasma is no longer authorized under this EUA.

2- FDA’s RESPONSES TO YOUR QUESTIONS-Hot Topic Discussion: FDA Updates EUA for CCP in Response to New Data

Officials from the Food and Drug Administration answered a series of questions from the blood community during AABB’s 02/09/21 [Hot Topic Discussion](#) on the [updated emergency use authorization](#) for CCP. In the hour-long event, Peter Marks, MD, PhD, director of the Center for Biologics Evaluation and Research CBER; and Nicole Verdun, MD, director of CBER’s Office of Blood Research and Review, clarified questions on implementation of the EUA, use of high-titer CCP and the eligibility of CCP donors following vaccination for COVID-19. **This session is available [ON-DEMAND](#). FDA’s responses can also be found in the [slide presentation](#).**

3-UPDATED INFORMATION ON DONATION OF CCP, BLOOD COMPONENTS and HCT/Ps During the COVID-19 Pandemic Updated 02 12 2021, includes:

- 1) HCT/P DONOR ELIGIBILITY
- 2) CCP and ROUTINE BLOOD DONOR ELIGIBILITY
 - 2-1. Blood donor eligibility following COVID-19 vaccine
 - 2-2. Blood donor eligibility following CCP transfusion
 - 2-3. CCP donor eligibility following vaccination if never infected
 - 2-4. CCP donor eligibility if recovered patient later receives a COVID-19 vaccine
 - 2-5. CCP donor eligibility after treatment with monoclonals

4-EXAMPLE FLOWCHART: ELIGIBILITY FOR CCP DONATION AFTER COVID-19 VACCINATION/MONOCLONAL ANTIBODY THERAPY based on recommendation III.B.1.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:

