CSSC- Summary of Changes for the Investigational Product SOP Manual

The purpose of this document is to record the history of IP SOP version numbers, publication dates, approval signatures, and revision records.

Versions:

Version 9: July 10, 2020
Version 10: August 26, 2020
Version 11: November 23, 2020
Version 12: August 05, 2021

Significant Changes in SOP version 12

Version 12 of the SOP involves an entire rewrite of the document, which includes multiple new sections, definitions, and structure. To get a full picture of all the changes, please refer to the SOP. The major, significant changes are highlighted in the table below.

Investigational Product Qualification:

The FDA approved a new definition of high titer plasma on March 26, 2021. The new definition involves a range of high titer definitions, including but not limited to Euroimmun > 3.5, Ortho-Vitros > 9.6; and Mt. Sinai titer > 1:2880. This replaced the old definition of > 1:320 and was effectively implemented on August 1, 2021.

IP Transfer Process:

A request for the transfer of IP from one protocol to another protocol must be from a study protocol for which IPs are no longer needed to an active protocol. A detailed procedure is listed in the SOP version 12 & LOCATOR- Data Entry Manual (Attachment to version 12).

IP Close out activities:

Closeout IP procedures are included in the SOP manual v 12, including discarding the IP product or returning to the Sponsor with the Sponsor approval.

IP team changes:

The Sponsor IP team had changed to new team members between versions 11 and 12 of the SOP. **Melanie Morabito** and **Sonja Cooper** joined the study on **January 19, 2021,** as unblinded CRA/monitors. On **May 14, 2021,** Sonja Cooper left the study. On **September 1, 2021,** Preeti Khanal joined the study as a Research Assistant (IP coordinator), and Craig Ou joined as a Data manager. On September 17, 2021, Aaron Ye (Data Manager) will leave the study.

LOCATOR data Entry Manual:

The Data Entry SOP manual was created and attached to version 12 of the SOP. This manual has instructions on LOCATOR and steps to entering data. This manual aims to ensure data integrity and provide clear procedural steps to site blood bank staff on the Locator Data entry.

Changes from Version 11 to 12:

Page(s)	Section	Used to read	Now reads	Reason
3	4. Investigational Study Product	The investigational product, HCIP, is anti-SARS-CoV-2 convalescent plasma. HCIP will be collected by apheresis from healthy adults identified as having recovered from COVID-19. Healthy adult donors with SARS-CoV-2 antibody titers ≥ 1:320 by an FDA approved test will donate plasma to be used in the study.	Healthy adult donors with SARS-CoV-2 antibody titers ≥ 1:320 dilution by an FDA approved test will donate plasma to be used in the trial. After July 2021 the new March 9 EUA for high titer hospital plasma may be used to qualify plasma for study use including Euroimmun ration >3.5; Ortho-Vitros >9.6; and Mt. Sinai titer greater than 1:2880.	The definition of high titer convalescent plasma has been changed for the study. After July, it is required to utilize only units that fall under this new definition.
4	4. Investigational Study Product	Blood Bank of Delmarva (NYBC) or another qualified center	Blood Bank of Delmarva (NYBC) Evanston Hospital The United States Department of Defense Vitalant Impact Life (Mississippi Valley Regional Blood Center).	With the addition of a new central supplier, Impact Life, it was decided to be more specific in terms of suppliers that provide CCP for the study.
9, 10, 11	D. Transfer of the Investigational Product	N/A	See SOP.	A new form in LOCATOR allows the transfer of plasma units between sites in the study.
13	Segment/Tail Collection	For every locally acquired convalescent plasma unit that is tested locally and not sent to JHU for titer testing, a 1mL sample must obtained at the time of donation and sent to JHU. If it is not obtained at the time of donation, collect and ship a 1mL segment/tail at the time of transfusion instead.	The blood bank staff should collect and save a tail or 1 ml segment for **Impact Life© (Mississippi Valley Regional Blood Center) units**. The **Impact Life© units begin with DIN # W0383.**	The new central supplier, Impact Life, requires a tail for each unit to be sent to JHU's laboratory. Meanwhile, sites that locally collect and locally test their units have been closed, so those tails no longer need to be sent in.

13, 17	Manifest for Shipping Plasma Units	Once a tracking number has been obtained, an email should be sent to Yolanda Eby (yeby1@jh.edu) to announce the delivery for the next day	Once a tracking number has been obtained, an email should be sent to Yolanda Eby (yeby1@jh.edu). Copy the Sponsor IP team Anusha Yarava (ayarava1@jh.edu), Preeti Khanal (pkhanal2@jhmi.edu), Sonya Griffin sgriff48@jhu.edu to announce the delivery for the next day.	Updated contacts to include the central IP team.
14, 18	IP Reorder Forms	Blood bank staff will be required to order replacement units weekly or twice a week in order to maintain the ideal minimum stock requirements. Forms will be emailed to our unblinded IP coordinator Aaron Ye (aye4@jhu.edu)or Sonya Griffin (sgriff48@jhu.edu). Blinded individuals must not be copied to prevent accidental unblinding.	Blood bank staff will be required to order replacement units weekly or twice a week in order to maintain the ideal minimum stock requirements. IP reorder Forms will be emailed to Central Investigational Product team. **Point of Contacts:** CSSC - IP Pharmacist, Anusha Yarava ayarava1@jh.edu CSSC - IP Coordinator Preeti Khanal pkhanal2@jhmi.edu Please note, blinded individuals must not be copied to prevent accidental unblinding	Removed Aaron Ye and Sonya Griffin. Added Anusha Yarava and Preeti Khanal.
16	Contacts List	See table.	See table.	Added Preeti Khanal and Craig Ou.
19, 20, 26, 33	Various	N/A	3-month extension of the expiry of the qualified study convalescent plasma units.	FDA approval on July 12, 2021 allowed CCP units in the study to extend its expiration dates by 3 months.

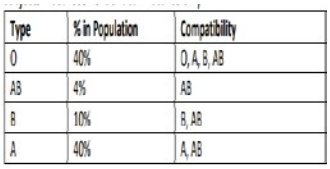
19-28	Letters of Communication	N/A	See SOP.	Included email letters of communication with the active sites and the FDA, regarding plasma expiration extension and new Euroimmun >35 and high titer definitions.
29-53	Instructions – LOCATOR Data Entry	N/A	See SOP.	Multiple instructions regarding how to enter data into the LOCATOR database has been added, to provide detailed instructions to site blood bank staff.
47	Data Entry SOP – Site Level Documents: Site	N/A	Blood bank personnel must also upload packing slips for both local and centrally acquired plasma for the study.	Included packing slips from locally sourced plasma, which must also be entered into LOCATOR.
50	Form Completion and Query Process	N/A	Form completion is a process to monitor data entry and query process is for communication.	Form completion helps track data entry and monitoring process in the study. The query process helps track communications between the blood bank staff and monitors.

Changes from Version 10 to 11:

Page(s)	Section	Used to read	Now reads	Reason
3, 4	Investigational Product (Control Plasma - definition)	SARS-CoV-2 Non-Immune Plasma collected prior to December 31, 2019.	SARS-CoV-2 NonImmune Plasma collected prior to December 31, 2019 or confirmed as seronegative.	Added definition of control plasma to include seronegative confirmed units.
8	11. Reordering Forms	Blood bank staff will be required to order replacement units weekly or twice a week in order to maintain the ideal minimum stock requirements. Forms will be emailed directly to the supplier. The coordinating center must not be copied to prevent accidental unblinding.	Blood bank staff will be required to order replacement units weekly or twice a week in order to maintain the ideal minimum stock requirements. Forms will be emailed to our unblinded IP managers Aaron Ye (aye4@jhu.edu) or Sonya Griffin (sgriff48@jhu.edu). Blinded individuals must not be copied to prevent accidental unblinding.	Due to a shortage of central supply, orders are now managed by Aaron Ye and Sonya Griffin, to ensure a proper distribution of study plasma.
8	10. Segment/Tail Collection	For every locally acquired convalescent plasma unit, a 1mL sample must obtained at the time of donation and sent to JHU. If it is not obtained at the time of donation, collect and ship a 1mL segment/tail at the time of transfusion instead. For centrally acquired convalescent plasma, a 1mL segment may be required to be shipped to JHU, but only if it is sourced from Sinai. Blood banks should hold onto a segment from units with DIN numbers starting with W0470, until further determination on if this segment is needed.	For every locally acquired convalescent plasma unit that is tested locally and not sent to JHU for titer testing, a 1mL sample must obtained at the time of donation and sent to JHU. If it is not obtained at the time of donation, collect and ship a 1mL segment/tail at the time of transfusion instead.	Updated section on tails/segments to remove Mount Sinai units.
10	15. Contacts List	See contacts table.	See contacts table.	Change in study staff. Added Sonya Griffin and Anusha Yarava. Removed David Reichert.

12	Reorder Form	See the 2 reorder forms, at the end of the document.	See the 1 new reorder form, at the end of the document.	Orders are now being managed through the central team, so only 1 reorder form is required. It is updated with new contact information.

Changes from Version 9 to 10:

Page(s)	Section	Used to read	Now reads	Reason
4	4. IP Shipment and Receipt	N/A	It is essential to have 24/7 blood bank availability. Available staff must receive the IP as soon as it arrives so that it can be transferred into the freezer immediately for storage.	To encourage blood banks to be available 24/7 to receive plasma, since some central supply shipment could arrive during off-hours.
5	4. IP Shipment and Receipt	N/A		Providing blood bank staff with a reference to blood type compatibility and rarity in the population.
5	5. IP Storage	N/A	Each unit will have a unique trial number, used to track units to subjects and units to blood samples sent to Hopkins for testing.	Inform blood bank staff that the database automatically assigns a unique number to each unit for tracking.
8	10. Segment/Tail Collection	N/A	See new section 10.	Provide detailed instructions on how to send tails from locally acquired segments to JHU's laboratory.
8	11. Reordering Forms	N/A	Blood bank staff will be required to order replacement units weekly or twice a week in order to maintain the ideal minimum stock requirements. Forms will be emailed directly to the supplier. The coordinating center must not be copied to prevent accidental unblinding.	Provide instructions on how to reorder plasma from central suppliers. The form is essential to keeping track of plasma orders.
9	12. IP Management	AABB Accreditation (or acceptable alternative accreditation)	AABB Accreditation (or acceptable alternative accreditation, such as CAP or CLIA)	Emphasize that CAP or CLIA accreditation is acceptable as an alternative to AABB.
10	15. Contacts List	N/A	See contacts list.	Provide a list of contacts for blood bank staff, in case they need to communicate with the central team.
10	16. FedEx Number	N/A	Use this number to charge directly to JHU for FedEx deliveries: 706936335 Place "JHU DOD" in the internal billing line.	To bill shipments to the study account, a FedEx number is provided to the blood bank staff, to cover shipment costs.

11	Manifest	N/A	See Manifest form attachment.	Included the manifest form that sites have to fill out when sending tails to Yolanda Eby.
12, 13	Reorder Forms	N/A	See reorder forms attached.	Included the reorder forms, so sites can directly use it. There is one for Blood Bank of Delmarva (New York Blood Center) and one for the American National Red Cross.

Report Author: Aaron Ye (IP coordinator)
Reviewed & Approved: Anusha Yarava (IP Pharmacist Manager)

CSSC Central Pharmacist: Anusha Yarava Signature: Date:

Anusha Yarava Digitally signed by Anusha Yarava Date: 2021.09.20 09:20:08 -04'00' 9/20/21

Blood Bank Director: Signature: Date:

Site Principal Investigator: Signature: Date: