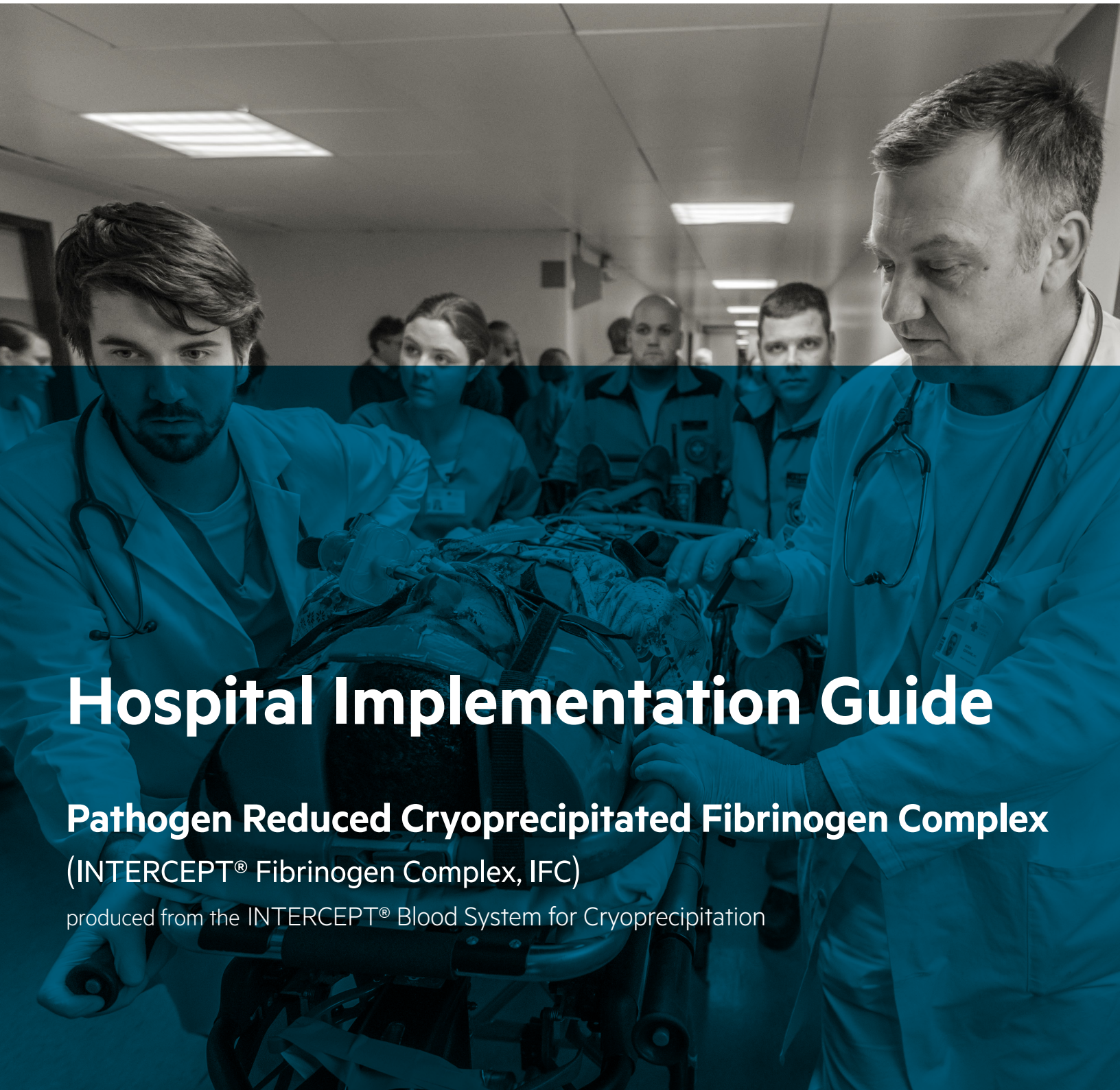
cerus



Hospital Implementation Guide

Pathogen Reduced Cryoprecipitated Fibrinogen Complex

(INTERCEPT® Fibrinogen Complex, IFC)

produced from the INTERCEPT® Blood System for Cryoprecipitation

Welcome to the INTERCEPT® Blood System Family!

The following sections will guide you through the implementation steps for ordering, receiving, distributing, and billing for Pathogen Reduced Cryoprecipitated Fibrinogen Complex, also referred to as INTERCEPT® Fibrinogen Complex (IFC).

The sections within this document are as follows:

If you have any questions, please contact us at hospitalsupport@cerus.com.

1 IFC Implementation Checklist

Getting IT Systems Ready

- ☐ Build products with new ISBT codes as applicable into your blood bank information system
- ☐ Update Hospital information system bedside scanning software to accept IFC
- ☐ Update billing system with inpatient and outpatient coding and billing rates
- ☐ Confirm key stakeholders have received education regarding ordering, policy, and procedure updates

IFC Policy and Procedure Updates

- ☐ Confirm your start date with Cerus and/or your blood provider
- ☐ Confirm your timeline to 100% (or desired inventory level) with Cerus and/or your blood provider
- ☐ Update all relevant policies and procedures per your plan
- ☐ Design your education and communication plan to properly reflect your ordering processes

IFC Logistics - Receiving, Handling & Storage

- ☐ Confirm key stakeholders have received education regarding receiving, bag handling and storage recommendations

Hospital Staff Education

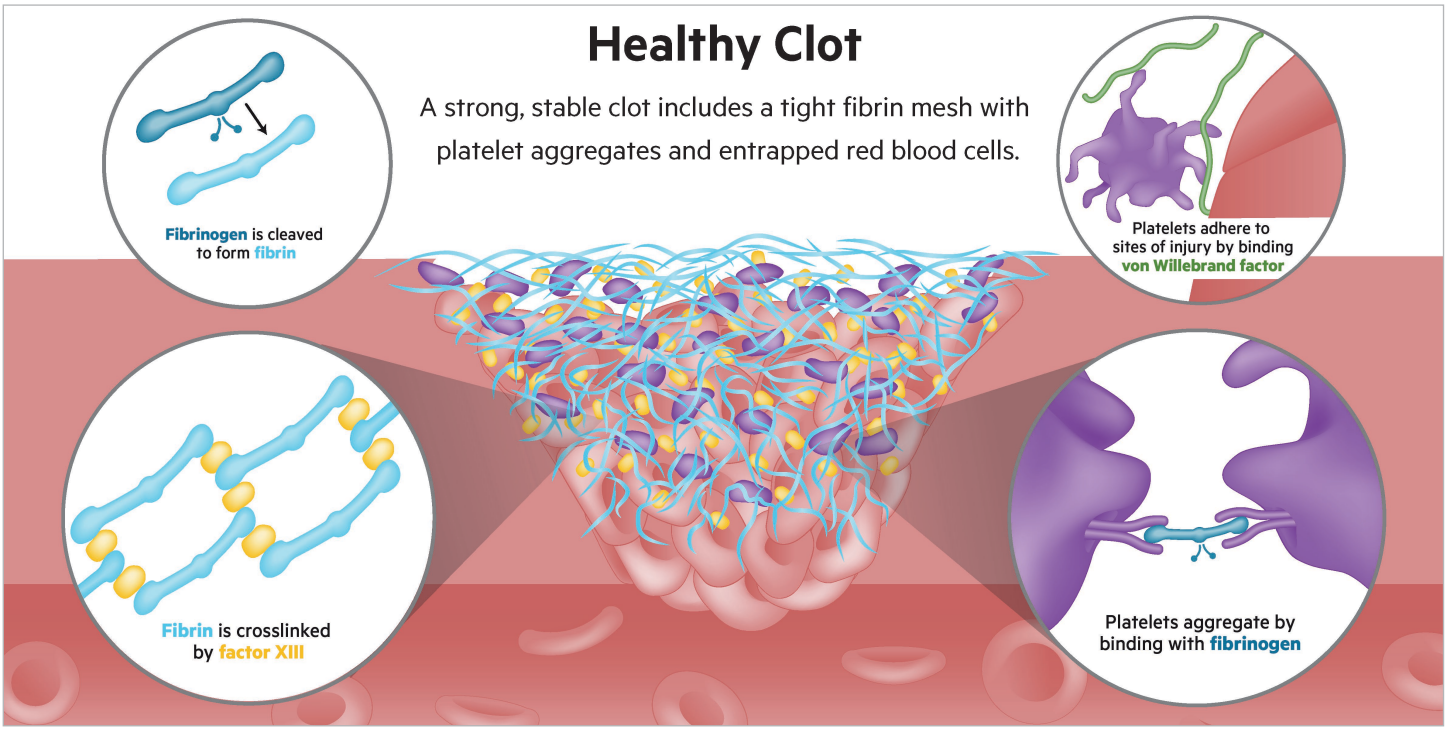
- ☐ Educate key hospital staff regarding the operational and clinical updates for IFC

2 Pathogen Reduced Cryoprecipitated Fibrinogen Complex

Pathogen Reduced Cryoprecipitated Fibrinogen Complex, also referred to as INTERCEPT® Fibrinogen Complex (IFC), serves as an enriched source of fibrinogen, factor XIII, von Willebrand factor (vWF), and other key clotting factors for the treatment and control of bleeding, including massive hemorrhage, associated with fibrinogen deficiency. Fibrinogen, vWF, and factor XIII are key constituents in effective hemostasis and functional levels correlate with risk of bleeding, morbidity and mortality.[1-3]

Early fibrinogen supplementation restores clot strength, reduces blood loss, and decreases mortality.[1]

Unlike other fibrinogen sources which must be thawed or reconstituted on demand due to short post-preparation shelf life, IFC can be stored post-thaw at room temperature for up to 5 days after thawing. This enables IFC to be an immediately available coagulopathy treatment for hemorrhaging patients with fibrinogen deficiency, while also minimizing wastage and improving turnaround times (reducing wait times).



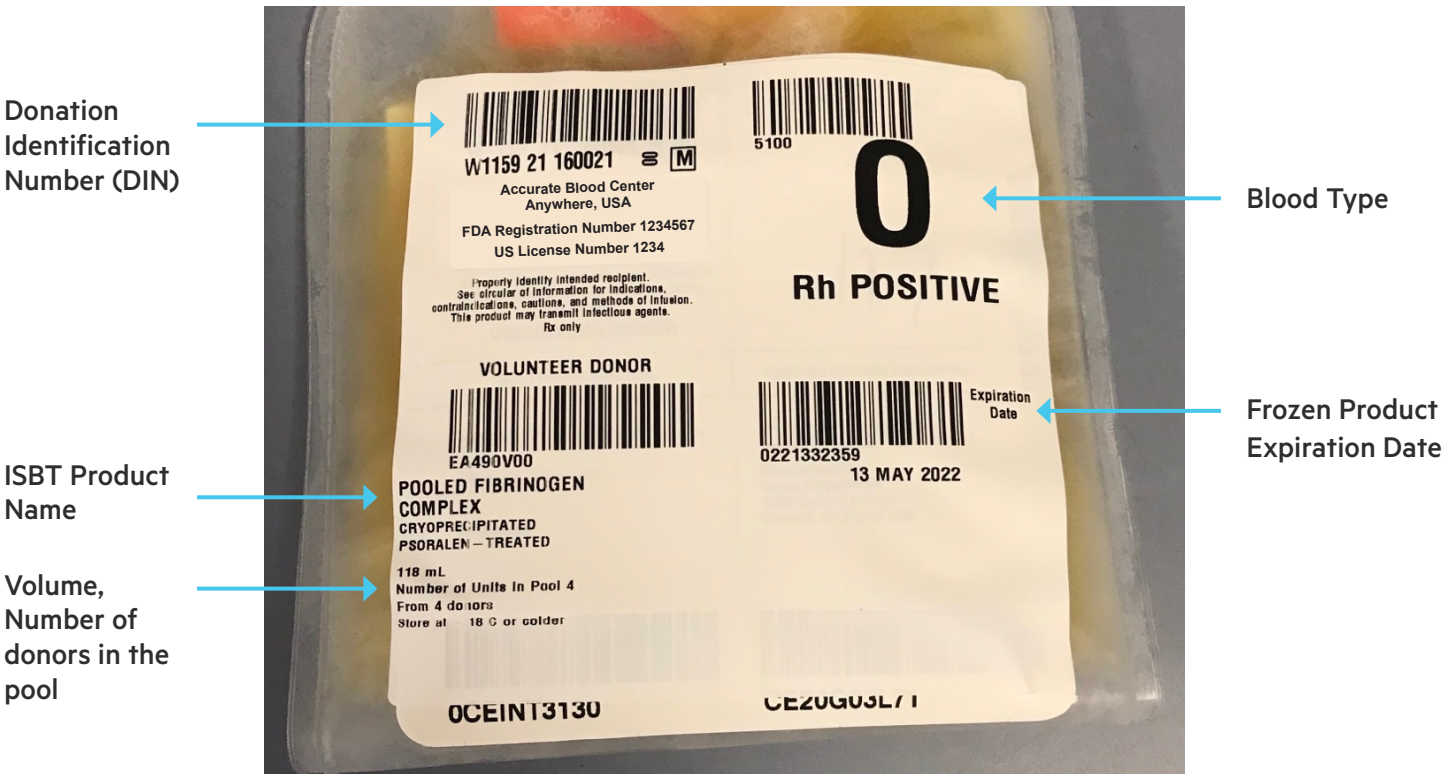
Fibrinogen, **factor XIII** and **von Willebrand factor** add the clotting strength needed to achieve stable clot formation and restore hemostasis.[2]

1. Rourke C et al. Journal of thrombosis and haemostasis : JTH 2012;10:1342-51.
2. Chapin JC, Hajjar KA. Fibrinolysis and the control of blood coagulation. Blood Reviews 2015;29:17-24.
3. Levy JH et al. Fibrinogen and hemostasis: a primary hemostatic target for the management of acquired bleeding. Anesthesia and analgesia 2012;114:261-74.

3 ISBT Nomenclature for IFC

IFC is labeled "**Pooled Fibrinogen Complex, Cryoprecipitated, Psoralen-Treated**" using ISBT nomenclature. "Psoralen-Treated" refers to the psoralen/UVA light treatment for pathogen reduction used in the INTERCEPT Blood System process. The specific psoralen is known as amotosalen. IFC is produced from pathogen reduced plasma treated by the INTERCEPT Blood System. The INTERCEPT Blood System for Cryoprecipitation is the only FDA approved system for producing Pathogen Reduced Cryoprecipitated Fibrinogen Complex.

Sample Label



4 Implementation Considerations

It is recommended that your implementation plan be developed based on a mutually agreed upon start date for receiving IFC from Cerus and/or your blood provider.

- Updating Hospital and Laboratory IT systems will take the greatest amount of time – establish the estimated timelines in the implementation plan.
- Expectations for how both parties will manage ordering and inventory during the conversion to IFC should be included.
- Plans for increasing the number of units to reach your target use and inventory of IFC should include timelines and a usage strategy for the units you will be receiving.
- IFC comes in various sizes (Table 1). If your Transfusion Committee has decided to use IFC either for specific patient populations, or for all patients, consider the number of IFC units needed in each configuration.

Table 1: IFC Catalog Numbers and Descriptions

Catalog #	Description	Average Fibrinogen (mg)*	# of Donors†	Estimated Volume (mL)
FC10	Pooled Fibrinogen Complex 1.0, Cryoprecipitated, Psoralen Treated	740	2	60
FC15	Pooled Fibrinogen Complex 1.5, Cryoprecipitated, Psoralen Treated	1,556	4	120
FC20	Pooled Fibrinogen Complex 2.0, Cryoprecipitated, Psoralen Treated	2,220**	6	180
FC30	Pooled Fibrinogen Complex 3.0, Cryoprecipitated, Psoralen Treated	2,845	8	240
FC40	Pooled Fibrinogen Complex 4.0, Cryoprecipitated, Psoralen Treated	3,700**	10	300

*Mean fibrinogen content (per package insert). Fibrinogen content depends on donor plasma fibrinogen levels.
**Calculated based on pooling of FC10.
†Number of donors based on whole blood donors.

5 Getting Your IT System Ready

This section will guide you through the necessary updates to your laboratory and hospital IT systems. If your facility uses a manual documentation system, this section provides considerations to keep in mind as you are updating the manual system.

When considering the scope of the IT changes required to effectively use IFC in your hospital, it is appropriate to segment the changes into three processes:

1. Inventory and Dispensing related IT
2. Transfusion related IT
3. Billing and Reimbursement related IT

Inventory and Dispensing Related IT

The following two technical tasks must be considered:

1. Building the products in your system
2. Adjusting your system to identify IFC as an alternative to cryo AHF for treatment of bleeding associated with fibrinogen deficiency, if approved by your medical director or current transfusion policy

The Laboratory Blood Bank/Transfusion Service Information System includes the ISBT (EA-code) product build. Hospital Transfusion staff should be encouraged to build all codes so that they are prepared to receive any configuration of IFC. This step typically takes the longest during any implementation. It is extremely advantageous to begin this process as early as possible.

Table 2 lists IFC's catalog numbers and ISBT product codes, with their corresponding "thawed" codes. IFC is labeled "**Pooled Fibrinogen Complex, Cryoprecipitated, Psoralen-Treated**" using ISBT nomenclature.

The IFC ISBT codes are identified as either being derived from whole blood or an apheresis collection, and are based on the number of donors. Here is an example for FC15:

- The first two codes for each IFC catalog number represent the product in the frozen state.
  - EA485V00 is the code for frozen apheresis derived pooled fibrinogen complex
  - EA490V00 is the code for frozen whole blood derived pooled fibrinogen complex
- The next two codes for each IFC catalog number represent the product after it is thawed.
  - EA496V00 is the modified code for the thawed whole blood derived pooled fibrinogen complex
  - EA500V00 is the modified code for the thawed apheresis derived pooled fibrinogen complex

Table 2. ISBT/ICCBBA Coding

Catalog #	Product Code	Description
INTERCEPT Fibrinogen Complex		
FC10	EA484V00	Apheresis FIBRINOGEN COMPLEX | None/XX/<=-18C | Cryoprecipitated | Psoralen-treated
	EA489V00	POOLED FIBRINOGEN COMPLEX | None/XX/<=-18C | Cryoprecipitated | Psoralen-treated | From 2 donors
	EA494V00	Thawed Apheresis FIBRINOGEN COMPLEX | None/XX/rt | Cryoprecipitated | Psoralen-treated
	EA495V00	Thawed POOLED FIBRINOGEN COMPLEX | None/XX/rt | Cryoprecipitated | Psoralen-treated From 2 donors
FC15	EA485V00	Apheresis POOLED FIBRINOGEN COMPLEX | None/XX/<=-18C | Cryoprecipitated | Psoralen-treated | From 2 donors
	EA490V00	POOLED FIBRINOGEN COMPLEX | None/XX/<=-18C | Cryoprecipitated | Psoralen-treated | From 4 donors
	EA496V00	Thawed POOLED FIBRINOGEN COMPLEX | None/XX/rt | Cryoprecipitated | Psoralen-treated | From 4 donors
	EA500V00	Thawed Apheresis POOLED FIBRINOGEN COMPLEX | None/XX/rt | Cryoprecipitated | Psoralen-treated | From 2 donors
FC20	EA486V00	Apheresis POOLED FIBRINOGEN COMPLEX | None/XX/<=-18C | Cryoprecipitated | Psoralen-treated | From 3 donors
	EA491V00	POOLED FIBRINOGEN COMPLEX | None/XX/<=-18C | Cryoprecipitated | Psoralen-treated | From 6 donors
	EA497V00	Thawed POOLED FIBRINOGEN COMPLEX | None/XX/rt | Cryoprecipitated | Psoralen-treated | From 6 donors
	EA501V00	Thawed Apheresis POOLED FIBRINOGEN COMPLEX | None/XX/rt | Cryoprecipitated | Psoralen-treated | From 3 donors
FC30	EA487V00	Apheresis POOLED FIBRINOGEN COMPLEX | None/XX/<=-18C | Cryoprecipitated | Psoralen-treated | From 4 donors
	EA492V00	POOLED FIBRINOGEN COMPLEX | None/XX/<=-18C | Cryoprecipitated | Psoralen-treated | From 8 donors
	EA498V00	Thawed POOLED FIBRINOGEN COMPLEX | None/XX/rt | Cryoprecipitated | Psoralen-treated | From 8 donors
	EA502V00	Thawed Apheresis POOLED FIBRINOGEN COMPLEX | None/XX/rt | Cryoprecipitated | Psoralen-treated | From 4 donors
FC40	EA488V00	Apheresis POOLED FIBRINOGEN COMPLEX | None/XX/<=-18C | Cryoprecipitated | Psoralen-treated | From 5 donors
	EA493V00	POOLED FIBRINOGEN COMPLEX | None/XX/<=-18C | Cryoprecipitated | Psoralen-treated | From 10 donors
	EA499V00	Thawed POOLED FIBRINOGEN COMPLEX | None/XX/rt | Cryoprecipitated | Psoralen-treated | From 10 donors
	EA503V00	Thawed Apheresis POOLED FIBRINOGEN COMPLEX | None/XX/rt | Cryoprecipitated | Psoralen-treated | From 5 donors

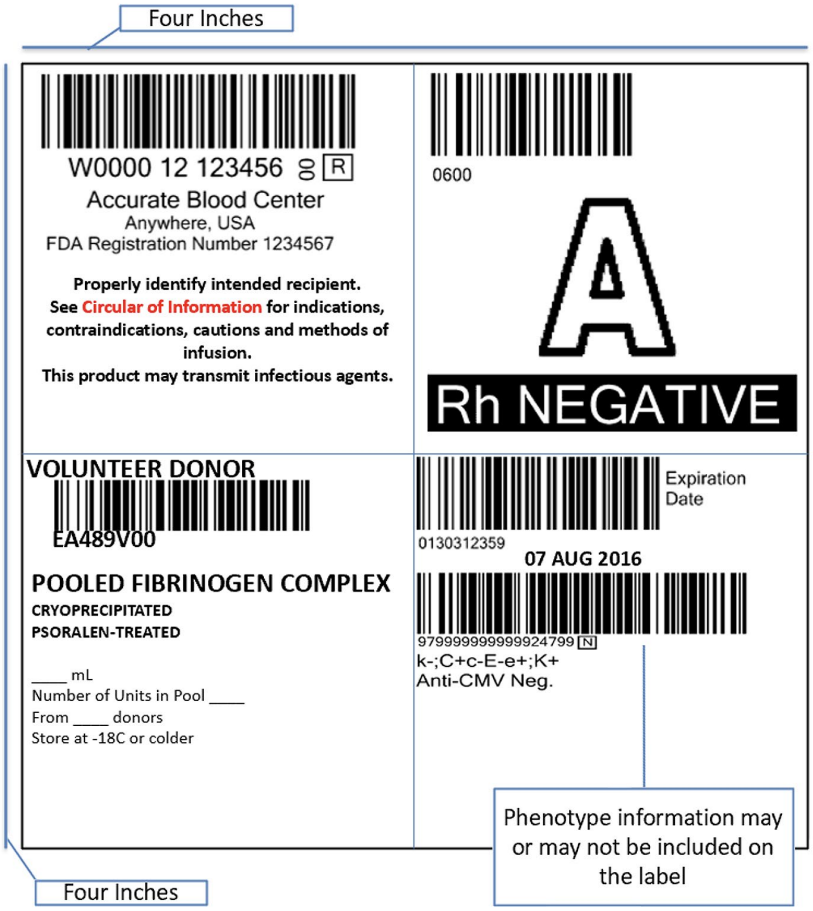
In the event you cannot find an ISBT code for a specific product configuration that is used in your facility, you can request a new ISBT code from the ICCBBA website.

Transfusion Related IT

While building and validating the products into your system, it may be helpful to verify that:

1. Blood Bank IT and Hospital IT can accept ISBT codes that begin with “EA”
2. Product label printers can print the product description as the character length is longer
3. Barcode readers are compatible
4. Transfusion tags print the accurate product/attribute description

Barcodes on this label are for example only



Sample IFC Label

If approved by your medical director or current transfusion policy, the hospital IT system may require updates to notify ordering physicians that IFC may be dispensed as an alternative to cryo AHF in patients with fibrinogen deficiency.

Additional updates include:

- Update Computerized Physician Order Entry (CPOE) to include notification that IFC may be dispensed as an alternative to cryo AHF in patients with fibrinogen deficiency.
- If implemented, update bedside Hospital Information System (HIS) blood product administration system (i.e., eTAR, BPAM) to read new product barcode.

To avoid delays in IFC use once approved, address required hospital IT updates as early as possible.

Billing and Reimbursement IT

It is extremely important that the appropriate charges for IFC are built in the hospital billing system, as the Centers for Medicare and Medicaid Services (CMS) use hospital claims data to set future payment rates.

Set up a meeting between the Hospital Transfusion department and Billing department in advance of IFC use to ensure all the billing codes and reimbursement, coding and billing processes are built and validated to ensure appropriate reimbursement for IFC.

Please refer to the IFC Medicare Coding and Payment Guide, for additional Inpatient and Outpatient coding information.

6 Policy and Procedure Updates

Policies, procedures, and order sets (if required) will need to be updated to include IFC. Please review your institution's policies and procedures to determine the documents that will be impacted by adding IFC to your inventory. This may include, but is not limited to, the following policies and/or procedures:

1. Product receipt and frozen storage at -18°C or colder
2. Selection of IFC for transfusion
3. Preparation of IFC for transfusion
   a. Thawing
   b. Labeling
   c. Storage of thawed product at room temperature for up to 5 days
4. Dispensing IFC
5. Transporting IFC
6. Returning IFC to the transfusion service for reissue
7. Massive Transfusion Protocol(s)
8. Post-Partum Hemorrhage Safety Protocol

Depending on the size of your facility, an educational plan may be helpful to inform key personnel about the benefits and potential changes associated with IFC. The best communication pathway for your education plan is what works best for your hospital culture.

7 IFC Logistics

Ordering IFC

IFC orders can be placed via Cerus' website, Bloodbuy or your local blood center. Please work with Cerus and/or your blood provider to determine which option is best for your institution. Software training for ordering IFC will be provided by the Cerus team during the implementation process, as appropriate.

Receiving IFC

When the shipment arrives at your facility, open the shipping container, and accept into your inventory following proper procedures for the receipt and storage of frozen blood products. If there is any issue at receipt, notify Cerus and/or your blood provider immediately.

- The average shipping container dimensions are 16.5" x 15" x 14".
- The average weight for 15 FC15s is 35lbs.

Since IFC is shipped frozen, be sure to use appropriate safety precautions when handling the product, such as wearing thermally insulated gloves.

Storing IFC

Frozen IFC

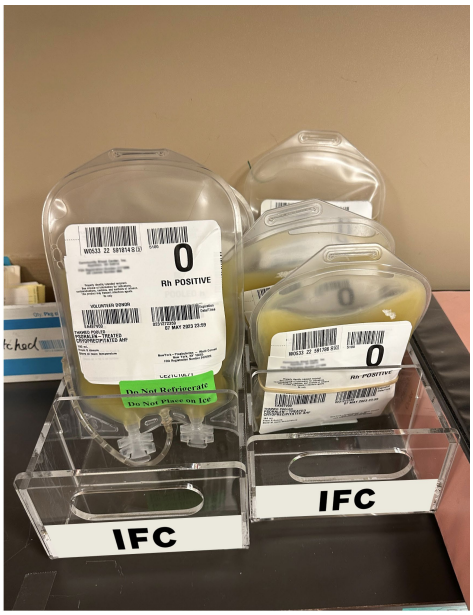
- IFC may be stored at -18°C (-0.4°F) or colder for up to 12 months.
- Store frozen IFC according to institutional procedures for frozen blood components.
- Thaw frozen IFC according to institutional procedures.

Frozen Storage

Thawed IFC

- IFC may be stored at room temperature for up to 5 days post thaw.
- The product must be stored without agitation.
- Place thawed IFC on a shelf, within a drawer or anywhere that is institutionally validated for room temperature storage without agitation.

Post-Thaw Storage



Please refer to the IFC Hospital Handling Recommendations for best practices in the care and handling of final storage containers in the hospital environment, for distribution within the hospital and transportation between hospitals.

If any damage has occurred that has compromised the integrity of the units:

- Do not administer if there is evidence of container breakage.
- Retain the product, if possible.
- Take a picture of the damaged area.
- Contact your blood provider or Cerus Customer Service at Customercare.usa@cerus.com.

8 Hospital Staff Education

An educational plan to facilitate your implementation of IFC is recommended. This section will walk you through the educational resources available for your nursing, blood bank / lab generalist, and physician staff. As nursing and lab staff typically handle the products more than any other departments, it is recommended to meet with their education leaders early in the implementation to notify them of the upcoming product change.

In hospitals that have already implemented other Cerus products, hospital staff education has typically occurred two weeks before the first pathogen reduced products have been distributed from the blood bank.

Education Template

The handout below can be used in live in-service sessions, as an email attachment, or posted in nursing stations, to announce the adoption of IFC. Some blood banks have also included the handout with each unit of IFC distributed for the first few weeks of routine use in the hospital.

This sample document contains information that hospital staff should know about IFC.

Key takeaways are:

- Sample product labels: The label has the name "**Pooled Fibrinogen Complex**" with "**Cryoprecipitated**" and "**Psoralen-Treated**" as attribute descriptions.
- If approved by your medical director and consistent with approved institutional transfusion policy, this handout will notify hospital staff that IFC can be transfused as an alternative to cryo AHF in patients with fibrinogen deficiency.
- There are no differences in the tubing used, transfusion time, or the ordering process for IFC compared to cryo AHF.
- Informs hospital staff that if the product is unused, it should be returned to the blood bank or transfusion service to minimize outdating.

The sections highlighted in yellow should be customized to your hospital's transfusion service policies.

Hospital Staff Education Template

<Insert Hospital logo>

The <Hospital Name> Blood Bank will be introducing Pathogen Reduced Cryoprecipitated Fibrinogen Complex, also referred to as INTERCEPT® Fibrinogen Complex (IFC), in <enter month, date>. The following points supported the <Hospital Name> Transfusion Service to adopt IFC. The <Transfusion or other Committee> has reviewed the contraindications and warnings and has determined that this new product may be issued for the treatment and control of bleeding, including massive hemorrhage, associated with fibrinogen deficiency.

Faster is Better in Hemorrhage Control

- Every effort should be made to decrease the time to administration of the first blood products in a hemorrhaging patient.[1]
- Massive Transfusion Protocols (MTPs) improve hemorrhage outcomes by delivering blood products quickly.
- Every minute of delay between the activation of MTP and the arrival of the first blood products results in a 5% increase in the odds of mortality.[1]
- Fibrinogen decreases rapidly and significantly during hemorrhage.[2,3] Fibrinogen is the most critical protein needed for stable clot formation and hemostasis.[2,4] Factor XIII adds strength and stability to clot formation.[5,6]
- Early fibrinogen supplementation restores clot strength, reduces blood loss, and lowers mortality.[2]
- Cryoprecipitated (cryo) AHF takes time to thaw and has a short shelf life (4 to 6 hours after thawing), resulting in high wastage rates.[7-10]

INTERCEPT Fibrinogen Complex (IFC)[11]

- IFC is produced from pathogen reduced plasma treated by the INTERCEPT Blood System. The INTERCEPT Blood System for Cryoprecipitation was awarded "Breakthrough Device Designation" by the FDA.
- The INTERCEPT pathogen reduction process includes a psoralen/UVA light treatment process. An extensive preclinical toxicology program was conducted per FDA product safety standards on the specific psoralen.
- IFC is an immediate, enriched source of key factors in effective hemostasis, including fibrinogen, factor XIII and von Willebrand Factor.
- IFC is approved specifically for the treatment and control of bleeding, including massive hemorrhage, associated with fibrinogen deficiency.
  - IFC should not be used for the replacement of factor VIII.
- The INTERCEPT Blood System for Cryoprecipitation for the manufacture of IFC was approved by the FDA in November 2020, and is approved for empirical use.
- A transfusion-ready product, IFC may be stored at room temperature for up to 5 days post thaw. Unused IFC should be returned to the blood bank where it can be placed back into inventory.

Administration of IFC

- IFC should be transfused in the same manner as you would normally transfuse cryoprecipitated AHF.
- IFC comes in multiple configurations to meet patient specific needs.

Catalog #	Description	Average Fibrinogen (mg)*	# of Donors†	Estimated Volume (mL)
FC10	Pooled Fibrinogen Complex 1.0, Cryoprecipitated, Psoralen Treated	740	2	60
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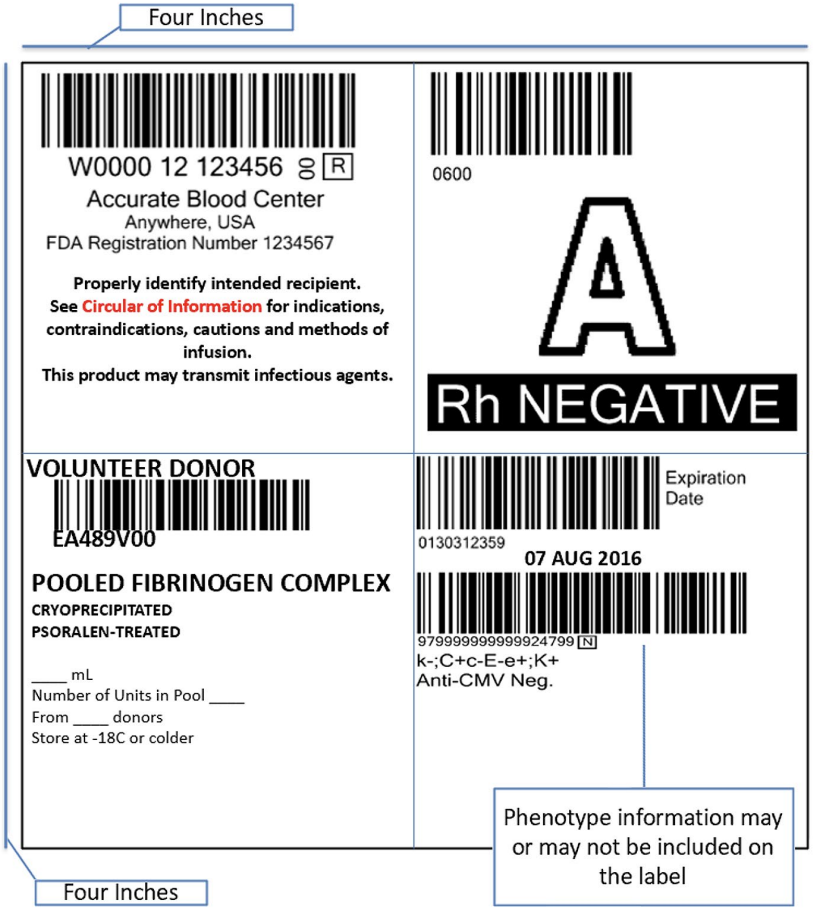
FC20	Pooled Fibrinogen Complex 2.0, Cryoprecipitated, Psoralen Treated	2,220**	6	180
FC30	Pooled Fibrinogen Complex 3.0, Cryoprecipitated, Psoralen Treated	2,845	8	240
FC40	Pooled Fibrinogen Complex 4.0, Cryoprecipitated, Psoralen Treated	3,700**	10	300

*Mean fibrinogen content (per package insert). Fibrinogen content depends on donor plasma fibrinogen levels. **Calculated based on pooling of FC10. †Number of donors based on whole blood donors.

- Key words to look for on the new product labels - **PSORALEN TREATED** which indicates that this product has undergone the psoralen + UVA light treatment process to reduce the risk of pathogens.

Barcodes on this label are for example only



Sample IFC Label

References:

1. Meyer DE et al.. J Trauma Acute Care Surg. 2017;83(1):19-24.
2. Rourke C et al. Journal of thrombosis and haemostasis : JTH 2012;10:1342-51.
3. Hiippala ST et al. Anesthesia and analgesia 1995;81:360-5.
4. Levy JH et al. Anesthesia and analgesia. 2012;114:261-74.
5. von Rappard et al. Transfus Med Hemother 2017;44:85-92.
6. Rijken DC et al. Biomed Res Int 2017;2017:1209676.
7. Holcomb JB et al. The journal of trauma and acute care surgery 2013;75:S31-S39.
8. AABB. Circular of Information for the Use of Human Blood and Blood Components. Bethesda, MD: AABB; 2021.
9. Dunbar NM et al. Transfusion 2017;57:45-52.
10. Wagner SJ et al. Transfusion 2019;59:3549-50.
11. INTERCEPT Blood System for Cryoprecipitation for the manufacturing of Pathogen Reduced Cryoprecipitated Fibrinogen Complex Package Insert.

Indications For Use

- Treatment and control of bleeding, including massive hemorrhage, associated with fibrinogen deficiency.
- Control of bleeding when recombinant and/or specific virally inactivated preparations of factor XIII or von Willebrand factor (vWF) are not available.
- Second-line therapy for von Willebrand disease (vWD).
- Control of uremic bleeding after other treatment modalities have failed.

Limitations of Use: Should not be used for replacement of factor VIII.

Contraindications

- Contraindicated for preparation of blood components intended for patients with a history of hypersensitivity reaction to amotosalen or other psoralens.
- Contraindicated for preparation of blood components intended for neonatal patients treated with phototherapy devices that emit a peak energy wavelength less than 425 nm, or have a lower bound of the emission bandwidth <375 nm, due to the potential for erythema resulting from interaction between ultraviolet light and amotosalen.

Warnings and Precautions

- Only the INTERCEPT Blood System for Cryoprecipitation is approved for use to produce Pathogen Reduced Cryoprecipitated Fibrinogen Complex.
- For management of patients with vWD or factor XIII deficiency, Pathogen Reduced Cryoprecipitated Fibrinogen Complex should not be used if recombinant or specific virally-inactivated factor preparations are available. In emergent situations, if recombinant or specific virally-inactivated factor preparations are not available, Pathogen Reduced Cryoprecipitated Fibrinogen Complex may be administered.

Rx Only. See package inserts for full prescribing information.

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