

Fact Sheet for Health Care Professionals or Authorized Providers

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of Centre de Transfusion Sanguine des Armées Leukocyte-Depleted Freeze Dried Plasma (French FDP) for U.S. military forces for the treatment of hemorrhage or coagulopathy during an emergency involving agents of military combat (e.g., firearms, projectiles, and explosive devices) when plasma is not available for use or when the use of plasma is not practical. The EUA also permits use of French FDP if needed to treat other individuals, such as allied military personnel operating with Department of Defense.

What is French FDP and why is it needed at this time?

French FDP is a lyophilized, leukocyte-depleted, pooled apheresis Fresh Frozen Plasma product collected from volunteer donors and manufactured by the Centre de Transfusion Sanguine des Armées. French FDP may be manufactured from either pooled French-sourced, pathogen-reduced (INTERCEPT™ -treated) apheresis plasma or pooled United States-sourced, FDA-licensed apheresis plasma. U.S.-sourced plasma has been subjected to standard donor screening and tested for relevant transfusion-transmitted infections in accordance with U.S. federal regulations. The source of plasma will be identified in the labeling of the final product. Following reconstitution with water for injection, French FDP can be administered intravenously. The Department of Defense (DoD) determined that agents of military combat (e.g., firearms, projectiles, and explosive devices) may cause, or are otherwise associated with, an imminently life-threatening and specific risk to U.S. military forces, in this case, hemorrhage or coagulopathy. French FDP is anticipated to be used for U.S. military forces for the treatment of individuals with hemorrhage or coagulopathy during an emergency involving agents of military combat (e.g., firearms, projectiles, and explosive devices) when plasma is not available for use or when the use of plasma is not practical. French FDP does not require refrigeration and is supplied in a form compatible with the logistical constraints of a military operational environment.

Based on this determination, the U.S. Department of Health and Human Services (HHS) has declared that circumstances exist to justify the emergency use of French FDP for the treatment of hemorrhage or coagulopathy during an emergency involving agents of military combat (e.g., firearms, projectiles, and explosive devices) when plasma is not available for use or when the use of plasma is not practical. The EUA will terminate when the HHS Secretary's declaration terminates unless FDA revokes it sooner. French FDP is not an FDA-licensed product. Therefore, FDA has issued this EUA to allow access to and use of French FDP. This EUA Fact Sheet provides information about the significant known and potential risks and benefits of the emergency use of French FDP.

Operational Setting and Management of Product

The product and standard Tactical Combat Casualty Care will be administered by U.S. military medical personnel specifically trained on use of French FDP. All hemorrhage will be controlled when possible and as early as tactically feasible in accordance with Tactical

Combat Casualty Care guidelines and U.S. Military Forces standard operating procedures with adjunct measures, to include approved tourniquets, compression, and hemostatic dressings, before treatment with French FDP. Pre- and post-product administration vital signs (heart rate [HR], blood pressure [BP], respiratory rate [RR], and temperature [T]) will be obtained if tactical circumstances permit, or at the first safe opportunity.

If a patient is determined to be in a life-threatening situation requiring intervention and the likelihood of death is high, use of this product would be justified. When practicable, in view of the circumstances of the imminently life-threatening combat casualties and the patient's capacity to make a knowledgeable decision, the patient will be given an option to accept or refuse administration of French FDP. When it is not practicable to do so because of the circumstances, the health care provider will act in the best interest of the patient.

Prior to deployment, an allotment of French FDP units, based on projected mission need, will be issued to each participating military medical unit, which will be responsible for product storage, accountability, and use documentation. Upon return, the military health care provider will return unused French FDP to the Logistic Warehouse for final disposition. Logs of product distribution, turn-in, and use will be maintained in the EUA file, which will be sent to the sponsor's representative at the U.S. Army Medical Research and Development Command annually and at the termination of the EUA. All French FDP units lost during contingency operations will be reported in accordance with standard procedures for sensitive/controlled items.

Data Collection

This EUA requires minimal data collection. The data collected under this EUA is intended to support the safety of the use of French FDP in combat settings. The following data will be collected by the health care provider who administers the product and subsequent health care providers to the extent feasible given the emergency circumstances:

- Patient survival until transfer of care
- Patient survival at Day 30 following treatment with French FDP
- Adverse events related to French FDP administration until transfer of care

Storage Conditions and Expiry Dating

French FDP can be stored for 2 years from the date of manufacture at temperatures between +2°C (36°F) and +25°C (77°F). When possible, the product should be stored at 2°C (36°F) to 8°C (46°F). During an emergency, the French FDP may require transportation or temporary storage for rapid administration without the capacity to maintain labeled storage conditions during the response. Significant excursions from the labeled storage conditions should be documented to the extent practicable given the circumstances of an emergency.

Product Description

The current formulations of the authorized French FDP are:

- A lyophilized, Leukocyte-Depleted, pathogen-reduced (Intercept-treated), pooled apheresis FFP product collected from French volunteer donors

OR

- A lyophilized, Leukocyte Depleted, pooled apheresis FFP product collected from U.S. volunteer donors.

French FDP is a packaged unit that includes:

- One (1) bottle of freeze dried plasma,
- One (1) bottle containing 200 mL or 250 mL water for injection; CAUTION: The plasma bottle must be reconstituted with the volume of water indicated on the plasma bottle label
- One (1) transfer set
- One (1) transfuseur pour sang et derives (transfuser for blood and derivatives); the transfuser is a sterile tubing set that contains: a toggle, an in-line 200 μ filter, a vent, and a needle for product administration

Instructions for Product Reconstitution

It is recommended to have all the French FDP used to treat an individual patient come from the same batch to limit the number of donors involved in the treatment of an individual patient. French FDP is supplied as a powder and is reconstituted with water for injection immediately before use to form an injectable preparation. Reconstitution should be completed at room temperature in less than 5 minutes, and the solution in most cases is a cloudy liquid. Sometimes the solution will have visible particles. These do not constitute signs of degradation. When reconstituted, the volume of French FDP is equivalent to about 210 - 270 mL of human plasma.

French FDP is reconstituted in the following manner:

- Bring the 2 flasks (powder and solvent) to room temperature (+20°C to +25°C) (68°F- 77°F) if necessary.
- Remove the protective capsules from the 2 flasks.
- Disinfect the surface of each lid.
- Pierce the lid of the flask containing the water first with one of the bevels of the transfer set. **Be sure that you spike the water first. If you accidentally spike the powder first, you will lose the vacuum and then be unable to transfer the water to the bottle of powder using the transfer set.**

- Use the other bevel to pierce the lid of the flask containing the powder.
- Pour the entire contents of the water flask into the flask containing the powder via the transfer set.
- Gently agitate the flask making horizontal rotations without generating a foam (do not shake) to homogenize the mixture.
- Wait 3 to 5 minutes for the product to dissolve entirely before injecting.

Instructions for Product Administration:

- Before infusion, check that the glass flask is intact. Do not use the contents of a damaged flask under any circumstances.
- Obtain a set of pre-infusion vital signs if tactical conditions permit.
- Prior to infusion, you must open the vent on the sterile tubing set. Using the intravenous infusion set provided, immediately administer the entire preparation intravenously.
- Obtain a set of post-infusion vital signs if tactical conditions permit.
- Closely monitor the patient for signs of an adverse reaction (e.g., fever, rash, hives, difficulty breathing, flank pain, darkening urine) and for adequacy of resuscitation (return of radial pulse or improvement in systolic blood pressure to approximately 90 mm Hg, improvement in mental status, improved hemorrhage control).

Repeated administration may be necessary until evacuation to a higher capability of care where more sophisticated treatment can be rendered. Following administration of French FDP, patients should be monitored as closely as circumstances permit. Ideally, vital signs will be checked and recorded 15 minutes after the first infusion, and this will be repeated in 15 minutes, then every 30 minutes (twice), and then hourly or until transfer of care occurs. Patients need to be observed for signs and symptoms of reaction to blood products including chills, back or chest pain, hives, rash, fever, shortness of breath, and/or wheezing.

Risks and Adverse Events and Emergency Measures

As with transfusion of standard blood plasma, the use of French FDP carries infectious risks. French FDP may contain viruses and other infectious agents that cause hepatitis and other diseases (e.g., HIV and variant Creutzfeldt-Jakob disease (vCJD), a transmissible spongiform encephalitis). However, the risk of infection is very low.

Other potential risks of French FDP transfusion include: over-transfusion, which is unlikely to occur since French FDP will be given only to treat hemorrhage or coagulopathy; system dysfunction; severe hypocalcemia; acute shortness of breath after transfusion (due to transfusion-associated circulatory overload or transfusion-related acute lung injury); hemolytic transfusion reactions; and non-hemolytic febrile transfusion reactions due to the presence of inflammatory mediators in French FDP. There also is the possibility of risks that are unknown or that cannot be foreseen based on current data. Anyone receiving this product may not be able to donate blood or blood products, such as plasma, in the future.

In the case of an adverse reaction to French FDP, the infusion should be stopped immediately, venous access should be maintained, and treatment appropriate for the severity of the symptoms should be initiated. A US Pharmacopeial (USP)-grade calcium solution (approved for parenteral administration) should be administered after 4 units of French FDP have been infused to avoid hypocalcemia secondary to citrate administration and if signs and symptoms of hypocalcemia develop. Signs and symptoms of hypocalcemia include seizures and other neuropsychiatric symptoms, increased neuromuscular irritability, cardiovascular symptoms, and autonomic symptoms.

Risk and Benefit Statement

The known and potential benefits of French FDP, when used to treat hemorrhage or coagulopathy during an emergency involving agents of military combat (e.g., firearms, projectiles, and explosive devices) when plasma is not available for use or when the use of plasma is not practical, outweigh the known and potential risks. Treatment of hemorrhage or coagulopathy should be instituted immediately. In instances when plasma is not available and treatment with French FDP is needed, the potential risk of developing serious treatment-related adverse events must be weighed against the risk of death due to hemorrhage or coagulopathy. The expected benefit of treatment with French FDP is to increase human survival by mitigating the consequences of hemorrhage or coagulopathy during an emergency involving agents of military combat (e.g., firearms, projectiles, and explosive devices) when plasma is not available for use or when the use of plasma is not practical.

Contraindications

Hypersensitivity to the active substance or one of the excipients. History of hypersensitivity to FFP or to plasma-derived products.

Adverse Event Reporting and Additional Product Information

Report adverse events to your service component coordinator and the U.S. Army Medical Research and Development Command. Reports should state that French FDP was used under an EUA.

For additional information about French FDP and this EUA, contact the U.S. Army Medical Research and Development Command:

US Army Medical Research and Development Command
ATTN: FCMR-ORA
1430 Veterans Drive
Fort Detrick, MD 21702-5009 Fax: 301-619-0197
Telephone: 301-619-0317
Email: usarmy.detrick.medcom-usamrdc.mbx.sae-reporting@health.mil

To the extent feasible given emergency circumstances, U.S. military personnel receiving French FDP under this EUA should receive the authorized *Fact Sheet for Recipients* about this product. However, given operational conditions under which French FDP may need to be administered under this EUA, in an emergency some patients may not be able to read a fact sheet due to life-threatening medical conditions or U.S. military medical personnel might not be able to provide the fact sheet. Therefore, the fact sheet information may also be provided to U.S. military forces prior to or during deployment (e.g., in training).