# European Union to Halt Commercialization of Hydroxyethyl Starch Products; FFF First Raised Safety Concerns in 2002

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Temecula, Calif.

European drug regulators have announced the suspension of marketing authorizations for all hydroxyethyl starch (HES) plasma volume replacement solutions across the European Union, citing continued administration of hydroxyethyl starch products in critically ill and septic patients despite 2013 labeling restrictions intended to reduce the risk of kidney injury and death in these patient populations.

In relation to this development, FFF Enterprises is particularly proud of its initiative, 15 years ago, to raise U.S. Food & Drug Administration (FDA) awareness about evidence of serious patient safety issues with HES products. This input directly led to the first warning by any major regulatory agency worldwide against the commercial use of hydroxyethyl starch products in a specified patient population.

In a public meeting held by FDA and its Blood Products Advisory Committee in June 2002, medical and market research consultants supported by FFF Enterprises presented evidence of excessive bleeding, increased transfusion requirements and increased reoperation rates in open heart surgery patients administered HES as a colloid substitute in place of human albumin. Our consultants urged a thorough going review of the safety of HES in this particular high-risk patient population. Acting on its advisory panel's recommendation, FDA shortly thereafter added warning statements to the labeling of all HES products cautioning against its use during or immediately after cardiopulmonary bypass surgeries.

In the wake of FDA's early 2003 regulatory action, numerous investigations have been conducted to evaluate the safety issues of hydroxyethyl starch both in open heart surgery and in other clinical settings where it has been widely used in lieu of albumin or crystalloid solutions.

Following review of a meta-analysis of open heart surgery studies published a decade later in 2012, FDA included an additional warning about excessive bleeding associated with HES use in cardiopulmonary bypass surgeries. A year later, a review of data from newer patient studies and meta-analyses documenting increased risks of mortality and renal injury in critically ill adults, including adult patients with sepsis, prompted FDA to require a Boxed Warning, instructing providers not to use HES products in those patientpopula tions as well. The European Medicines Agency (EMA) included similar labeling restricting use of HES in critically ill and septic patients in 2013. Last month, EMA's Pharmacovigilance Risk Assessment Committee (PRAC) concluded that these restrictions have not been sufficiently effective and suspension of all hydroxyethyl starch marketing authorizations is necessary to protect patient health, which prompted its recommendation to suspend marketing authorizations for all hydroxyethyl starch products.

**About FFF Enterprises, Inc.**

FFF Enterprises is the largest and most trusted distributor of plasma products, vaccines, biosimilars and other specialty pharmaceuticals and biopharmaceuticals. Founded in 1988, FFF, a multi-billion dollar organization, celebrates 30 years of business and a flawless safety track record for product distribution. FFF has taken a leadership position in regard to supply chain safety and innovation, setting new standards and pioneering industry firsts. FFF's commitment to Guaranteed Channel Integrity™ ensures that products are purchased only from the manufacturer and shipped only to licensed healthcare providers, with additional steps taken to safely store, handle and ship products to ensure patient safety is never compromised. FFF's proprietary systems — Verified Inventory Program-Consignment (VIPc™) and Lot-Track® — provide verification of this secure channel, BioSupply® online ordering system offers an easy-to-use and convenient platform to order products, and MyFluVaccine™ is an unprecedented vaccination program that has added a new level of safety, convenience and reliability to both healthcare providers and patients. Stay tuned to learn more about Costparency™, a new initiative aimed to strengthen the level of trust provided to healthcare providers, pharmaceutical manufacturers and customers. FFF Enterprises works diligently each day to fulfill its mission of Helping Healthcare Care™, knowing that there is always a patient at the end of every transaction. Wherever and whenever future opportunities are identified, FFF will continue to advocate for the advancement of patient health and safety.

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