Important Prescribing Information

October 20, 2000

Dear Doctor/Healthcare Provider:

This letter is to advise you of a reported cluster of serious adverse events occurring at a single institution in patients receiving **PLAS+®SD** (Pooled Plasma, (Human) Solvent Detergent Treated) during orthotopic liver transplantation and to provide information on the handling and storage of **PLAS+®SD**.

REPORTED SERIOUS ADVERSE EVENTS IN LIVER TRANSPLANT PATIENTS

We have received reports of serious adverse events occurring in a cluster of six patients, who underwent orthotopic liver transplantation for end stage liver disease due to a variety of underlying disease processes. All six patients died due to thrombotic events or excessive bleeding during the transplant procedure. All patients received intra-operative **PLAS+®SD** along with multiple other blood components. The possible relationship between the use of **PLAS+®SD** and these reported adverse events is currently under investigation. Until the investigation has concluded, we ask that caution be exercised when using **PLAS+®SD** during liver transplant procedures. If **PLAS+®SD** is to be used during liver transplant, the coagulation status of the patients should be carefully monitored for evidence of thrombosis, excessive bleeding or exacerbation of disseminated intravascular coagulation (DIC).

VITEX is continuing to monitor and investigate the occurrence of thrombotic events and determine if there is a relationship between the use of **PLAS+®SD** and the occurrence of thrombotic events.

Healthcare professionals should report adverse events associated with or possibly associated with the use of **PLAS+®SD** to INFOTRAC® at 1-800-535-5053. Alternatively, this information may be reported to FDA's MedWatch Reporting System by phone (1-800-FDA-1088), fax (1-800-FDA-0178), via the MedWatch website at www.fda.gov/medwatch, or by mail (using postage paid form) to MedWatch, HF-2, 5600 Fisher's lane, Rockville, MD 20852-9787. Health professionals and consumers should use the Form 3500 for adverse event reporting.

STORAGE AND HANDLING OF PLAS+®SD

There have also been reports of particulates of various types in thawed **PLAS+®SD**. The reported particulates include strands of proteinaceous material, large, opaque protein aggregates, and translucent clots. The formation of particulates may be related to improper handling or storage of **PLAS+®SD**. The storage and handling information provided below should minimize the potential for the formation of particulates in thawed **PLAS+®SD**. This information is being incorporated into the labeling for **PLAS+®SD** as follows:

1. **Always store PLAS+®SD at -18°C or colder during transport and prior to thawing. Do not use a bag of PLAS+®SD if the "freeze bar" indentation is not clearly visible.**

   ALWAYS INSPECT THE BACK OF THE FROZEN **PLAS+®SD** PLASTIC BAG FOR THE PRESENCE OF AN INDENTED "FREEZE BAR" PRIOR TO THAWING. The

"freeze bar" indentation is part of the freezing operation in the manufacturing process. If it is not clearly visible, it may be that thawing or partial thawing has taken place. Storage stability studies reveal maintenance of product coagulation factors when stored for 24 months at -18°C.

2. **Always thaw PLASMA SD® at 30-37°C.**

   It is preferable to thaw product in a 30-37°C water bath with very gentle shaking. Prior to submerging in a water bath, the frozen bag of **PLASMA SD®** should be inserted into an outer plastic protective bag. Only thaw the number of **PLASMA SD®** bags that can adequately be accommodated by the bath and still maintain the 30-37°C water temperature throughout the thawing process. Time to thaw is dependent upon the number of bags to be thawed and the size of the water bath.

3. **Once thawed, only store PLASMA SD® at room temperature, not in the cold or on ice.**

   PLASMA SD® may be used up to 24 hours after thawing. However, it is important that product be kept at room temperature and not stored in the cold (not in a refrigerator or on ice).

Healthcare professionals should report medication errors and product complaints associated (either actual or probable) with the use of **PLASMA SD®** to INFOTRAC® at 1-800-535-5053. Alternatively, this information may be reported to FDA's MedWatch Reporting System by phone (1-800-FDA-1088), fax (1-800-FDA-0178), via the MedWatch website at www.fda.gov/medwatch, or by mail (using postage paid form) to MedWatch, HF-2, 5600 Fisher's lane, Rockville, MD 20852-9787. Health professionals and consumers should use the Form 3500 for product problem reporting.

Please refer to the amended full prescribing information.

Sincerely,

Kathleen J. Beach, M.D.
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PLASMA SD® is distributed by the American National Red Cross, Blood Services
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