



17 October 2003

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Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm.1061
Rockville, MD 20852

RE: Docket No. 2003N-0211

Dear Sir or Madam:

Alpha Therapeutic Corporation is providing the following comments relative to the proposed rule entitled, "Revisions to Labeling and Storage Requirements for Blood and Blood Components, Including Source Plasma" published in the Federal Register/Vol.68, No. 146/Wednesday, July 30, 2003.

The agency states that the proposed regulations reflect current industry practice and do not impose an additional burden. Alpha Therapeutic Corporation disagrees with the FDA's Analysis of Impacts statement in regards to the proposed rule amendments for storage temperatures and labeling of Source Plasma.

Storage Requirements

1. As a manufacturer involved in the collection of Source Plasma, the majority of Alpha Therapeutic Corporation's plasma collection facilities adhere to the current US standard for freezing and storage of Source Plasma at temperatures of -20°C or colder. Source Plasma collected for only a few non-US customers is maintained at colder temperatures.
 - The equipment in the majority of Alpha collection facilities was designed to provide cooling capacity to meet current US requirements. Should a lower temperature requirement be adopted, the majority of facilities will require major modifications to the freezing equipment to meet the revised regulation. The freezer replacement or upgrade costs will be at least \$3,402,020, an additional \$252,000 in validation costs, and approximately \$10,000 to update procedures and conduct training. It will cost an additional \$2,000,000 to upgrade the freezer warehouse facility where the plasma is centrally stored pending distribution.
 - Lowering the storage temperature will result in additional energy consumption that will result in additional utility costs.

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- Lowering the storage temperature also has worker safety issues. The colder temperatures will require more protective equipment, reduced times that the employee can remain in the freezer, and affects the employees' health in increased risk of respiratory illnesses.
2. The proposed amendment for storage of Source Plasma at $-30\text{ }^{\circ}\text{C}$ is not consistent with European requirements. The 8th edition of the "Guide to the preparation, use and quality assurance of blood components" published by the Council of Europe has distinct criteria for storage of fresh frozen plasma at $-25\text{ }^{\circ}\text{C}$.
 - In addition to the potential impact on Source Plasma manufacturers currently following US standards of $-20\text{ }^{\circ}\text{C}$, other manufacturers following European guidelines may employ a two-step freezing/storage process, using two freezers or flash freeze equipment, that does not require storage of frozen plasma at $-30\text{ }^{\circ}\text{C}$. By recommending a uniform $-30\text{ }^{\circ}\text{C}$ temperature for both freezing and storage, the proposal exceeds current European requirements and imposes further requirements on these manufacturers.
 3. In the background discussion for the proposed regulation, the FDA states that they have determined that the current requirements for storage and shipping temperatures should be updated to ensure potency of the blood components over time and to provide more flexibility in inventory management. The FDA further states that the proposed changes are consistent with published data.

The reference given is to a published study, "Stability of Fresh Frozen Plasma: Results of the 36-Month Storage at $-20\text{ }^{\circ}\text{C}$, $-25\text{ }^{\circ}\text{C}$, $-30\text{ }^{\circ}\text{C}$, and $-40\text{ }^{\circ}\text{C}$ ". The results of this study indicate that, with the exception of one analyte (Factor IX) in one of the three plasma pools stored at $-20\text{ }^{\circ}\text{C}$, there was no discernible difference in the preservation of the labile clotting factors. There was no statistically significant difference in Factor IX concentration in two other plasma pools stored at $-20\text{ }^{\circ}\text{C}$. The conclusion of the investigator is that Fresh Frozen Plasma may be stored at $-20\text{ }^{\circ}\text{C}$ for 2 years or at $-25\text{ }^{\circ}\text{C}$, $-30\text{ }^{\circ}\text{C}$, and $-40\text{ }^{\circ}\text{C}$ for 3 years, without any detectable changes in the sensitive plasma proteins.

- This reference does not support the FDA's proposal to lower storage temperatures, particularly in light of the potential burden placed on the Source Plasma industry.
- In addition, Source Plasma, unlike Fresh Frozen Plasma, is required to be placed into the freezer within 30 minutes of collection. This difference in time from collection to time placed in freezer (≤ 30 minutes) has more potential to protect the labile proteins in Source Plasma.

Labelling

4. The proposed amendment to 606.121(c)(2) which replaces “registration number” with “unique facility identifier” imposes an additional requirement on collectors of Source Plasma operating multiple sites under a single license. Under current regulations, these manufacturers are required to list the name, address, and license number on the container label.
 - Alpha Therapeutic Corporation’s current approved label does not contain a unique, site specific identifier that was assigned by FDA, other than the license number. Unit traceability is assured under our current procedures and approved labels. However, should this amendment be adopted, the effective date should reasonably anticipate timelines for implementation, to include label design, acquisition, procedural changes, and depletion of available stock to minimize transition costs.
 - Changes to our current FDA approved labels will cost approximately \$40,000 annually in registration and licensing fees if ISBT or a similar system is utilized. A substantial additional cost will be involved in the purchase of printers, scanners, bar code readers, validation and training.
5. Proposed amendment 606.121(c)(11) requires labels of products intended for further manufacturing use to list the names and results for communicable disease agents for which the donation has been tested and found to be negative.

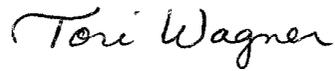
In a Final Rule published in the June 11, 2001 *Federal Register*, the FDA concluded that there was insufficient data to justify eliminating the requirement for a serological test for syphilis. This requirement is retained under 610.40(i) with reference to 640.65(b)(2) for Source Plasma.

- Source Plasma is unique in that a serological test for syphilis is performed at intervals of no more than four months, rather than at each individual donation. Further clarification is needed for Source Plasma labeling requirements for syphilis, since each donation is not tested.
- Should syphilis be considered a “communicable disease agent” for which labeling is required, an individual “donation” may require additional labeling for syphilis testing. This is not consistent with the intent of uniform labeling, since other donations that were not individually tested would not carry the same testing statement.

- Labeling all Source Plasma donations as “tested and found negative” for syphilis would constitute misbranding for those donations not individually tested.
- Currently, labels are not generated at each collection site. Rather, the collection is pre-labeled with the required tests that will be performed upon the donation. If a syphilis testing statement is required to be placed on each Source Plasma unit that is tested, this would be very burdensome for industry. Non-tested syphilis units would have to be segregated from units tested for syphilis.

We ask that the Food and Drug Administration not include Source Plasma in these proposed changes and prefer that Source Plasma is kept separate from the transfusion requirements in the Code of Federal Regulations. We believe that the proposed regulations do not reflect current industry practice and would impose an additional burden upon the industry. Alpha Therapeutic Corporation appreciates the opportunity to comment on these proposed rules.

Respectfully,



Tori Wagner
Director, Regulatory Affairs and Quality Assurance