CANADIAN BLOOD SERVICES
SOCIÉTÉ CANADIENNE DU SANG

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CBS Control: # CBS2689

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

Dear Sir or Madam:

Re: Proposed Rule – Revisions to Labeling and Storage Requirements For Blood and Blood Components, Including Source Plasma. 21CFR 600, 606, 610,640, Docket #2003N-0211

Canadian Blood Services has reviewed the Federal Register Notice concerning the subject Proposed Rule and wishes to offer comments on the proposal to change storage temperatures for frozen blood components.

From 1996 until 2003, CBS was required to adhere to the temperature standards now proposed by the FDA. During that period, we encountered approximately 1% of breakage of the bags in which plasma or cryoprecipitate was made and stored. Our investigation of this problem established that the glass transition temperature of the polymer film (P.V.C. plasticized with DEHP or TEHTM) used to manufacture the bags is between -20°C and -25°C. Below this temperature, the film becomes as brittle as glass and is highly likely to shatter upon impact.

The situation is exacerbated by the fact that, to maintain the temperature of most walk-in freezers below -30°C, they must be set at -40°C or colder. If this is not done, the temperature will exceed the required limit for a brief period four to six times per day when the automatic defrost function of the freezer control system engages. This is true even if the temperature recorder probe is placed in a container of glycerol as recommended in the (14th edition, 2002) AABB Technical Manual. We perceive one goal of the proposed changes to be international harmonization, since the new standards are identical to those in force in Europe for several years (Ref. Guide to the preparation, use and quality assurance of blood components, 8th edition, Council of Europe Publishing, 2002). We recommend caution in using the European experience as validation of the proposed requirements, since on the basis of anecdotal information it is our understanding that European Regulators are willing to "filter out" brief, recurring temperature excursions (10-15°C for 30 to 60 minutes, like those described above) when reviewing a temperature recording. It has been our experience that North American inspectors do not share this European view.

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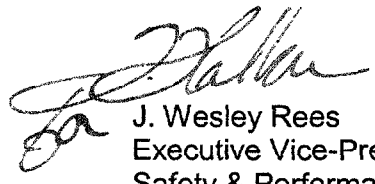
It was also our experience that many Canadian hospitals were unable to maintain the -30°C temperature limit, rendering our efforts to satisfy this requirement, futile. Under the auspices of the Canadian Standards Association and with the sponsorship of Health Canada, a Technical Committee with balanced representation from all constituencies with an interest in blood transfusion (including a representative of the AABB), has **drafted** a National Standard for Blood and Blood Components. This sets the storage temperature for frozen components at -18^{0}C and the shelf life at one year.

Since, for transfusable components, the rationale for temperature/shelf life conditions is related to product efficacy, not product safety. We recommend that the storage temperature be maintained at the values currently stated in 21 CFR subject for BPAC and that the shelf life be reduced below two years based on an assessment of whether product quality at expiry meets clinical needs.

For components to be used for further manufacture, the storage temperature of the plasma has no bearing on the efficacy of the final product. The issue is the yield of the final product achieved by the manufacturer who purchases the plasma. This is a commercial concern and the issue of storage conditions can be dealt with by the buyer and seller in determining the price of the plasma, according to current industry practice. There is no need that standards for storage conditions be enshrined in regulations.

If you require clarification or further information, please do not hesitate to contact the undersigned. **Please reference the above CBS control number in any correspondence.**

Sincerely,



J. Wesley Rees
Executive Vice-President
Safety & Performance Management

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