

COALITION FOR BLOOD SAFETY

American Association of Blood Banks - America's Blood Centers -
American Blood Resources Association

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March 30, 2000

Dockets Management Branch
HFA-305
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Docket No 99D-5046

Re: Guidance for Industry Changes to an Approved Application: Biological Products: Human Blood and Blood Components Intended for Transfusion or For Further Manufacture

The Coalition For Blood Safety (CFBS), formerly known as the Coalition for Regulatory Reform appreciates the opportunity to comment on the Draft Guidance, Guidance for Industry Changes to an Approved Application: Biological Products: Human Blood and Blood Components Intended for Transfusion or For Further Manufacture which was issued for comment only. CFBS is composed of the American Association of Blood Banks (AABB), including the American Red Cross (ARC) and the Armed Services Blood Program, America's Blood Centers (ABC), and the American Blood Resources Association (ABRA). CFBS was formed in 1994 after the Food and Drug Administration (FDA) invited the blood banking industry to develop and explore ideas with FDA for a more efficient regulatory system for blood and plasma products. The coalition represents the entire spectrum of blood and plasma collection and transfusion interests.

CFBS is particularly appreciative that the FDA has responded to our concerns that we needed a guidance that was more specific to blood as noted in our comments of September 17, 1997 to Docket No 95-D-0052 Changes to an Approved Application: Biological Products and September 9, 1999, to Docket No 99-N-0193 Supplements and Other Changes to an Approved Application. We are pleased to see that definitions have been included and that examples cited throughout the guidance are specific to blood banks. Detailed explanations of anticipated agency response, if the supplement for a Changes Being Effected (CBE) and/or CBE30 is determined by the agency to be filed in an incorrect category, are informative and should permit our members to carefully consider using this option. The description of the expected content of an Annual Report, including examples of both what to include and what not to include, as well as samples included in Appendix A, B and C are very helpful. We also note the added information and attention to detail in the Comparability Protocol. Appendix D makes it much easier to identify the FDA definitions of types of facilities based on manufacturing steps performed.

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We still remained concerned about the number of submissions which are judged to require preapproval (PAS). It would be helpful if the FDA were to provide information about the process and/or risk analysis, which resulted in the three reporting categories and assignment of "changes" to each category.

We request that CBER consider developing reasonable time frames into the managed review process for review of PAS and CBE30 changes. Review times for PAS should not exceed 6 months and should not exceed 3 months for review of an approval request for a comparability protocol or alternative procedure. Review times for changes must not be excessive and must not have an undesirable impact on availability of new products and facilities.

Specific comments

Section III A 2 The SOP areas are too broadly defined, and will likely result in many trivial SOP changes being sent to FDA for review. Manufacturers now prepare more restrictive SOPs that address many international requirements that are not addressed by published guidance documents. Specific examples of the categories might be beneficial.

We request deletion of Reference 7, Workshop for Licensing Blood Establishments. This publication is not an FDA guidance document; the policies and reviewer checklists were not developed with industry input or through good guidance practices and should not be used as inflexible criteria for restricting changes in blood establishments.

Section III A 2 SOP changes states that addition or revision of SOPs (for categories like donor suitability) that are less restrictive than previously approved OR that is not addressed in published FDA guidance should be submitted as PAS. Other citations in the guidance, Section III A.3. and Section VI.A.5. state that addition of procedures or tests that are not required or recommended by FDA should be reported in the annual report. These sections are not consistent. For example, If donors with red hair were to be deferred, would this change be submitted as a PAS or an annual report? **We request that these subsections be reviewed for consistency.**

Section III A 2 We suggest that that you reconsider the language stating "Addition or revision of SOP for the following categories if the change is less restrictive than previously approved or is not addressed in published FDA guidance documents". **We suggest that this should read "AND" is not addressed in published FDA guidance documents rather than "OR" is not addressed in published FDA guidance documents.**

Section III A 2 The intent of **NOTES** bullet point 3 is not clear. Does this mean that **any** SOP revised as a result of FDA inspection findings must be submitted as a PAS? We do not believe that is necessary and note that such a submission will result in long delays in closing the inspection. **A definition of post approval FDA inspection may be warranted.**

Section III A 3 We initially found the language of the last sentence to be slightly confusing We suggest that it would be easier to understand if the reference to the appropriate section is moved so that the sentence would read CBE30 (see section IV.A.1.) or in the annual report (see section VI.A.).

Section III A 5 includes Plasma Cryoprecipitate Reduced as an example of a request to manufacture additional products that require a PAS. **We request that Plasma Cryoprecipitate Reduced be CBE30 if the facility licensed for Cryoprecipitate.** Since Plasma Cryoprecipitate Reduced is a byproduct of production of Cryoprecipitate, the manufacturing process will already have been approved.

Section III A 10 The example of computer crossmatch may not be a good example to use in this guidance. It is our understanding that the intent of the proposed Direct Final Rule, Revisions to the Requirements Applicable to Blood, Blood Components, and Source Plasma, proposed on August 19, 1999, Docket No 98N-0673 is to allow computer crossmatching without filing a request for alternative procedures (21 CFR 640.120). If this Direct Final rule is approved, or the proposed rule is substituted and approved, then a different example would be more appropriate. We are unable to suggest an alternative example, so perhaps A10 is unnecessary.

Section III B 2 requires that changes or upgrades in automated apheresis equipment that affects the purity, potency or quality of the product be submitted as PAS. **We request that a reduction in donation time be included in the annual report.** This change does not have significant potential to affect safety, purity, or potency unless accompanied by other device changes. In addition, **we continue to request that FDA permit changes in plateletpheresis, especially those in which equipment has been upgraded and the manufacturer has obtained 510k clearance, be categorized as a CBE30.**

Section III C 2 discusses changes in contractors that perform manufacturing steps. We have some concern about requiring a PAS to change contractors who are providers of personnel responsible for blood collection. We believe this would limit contract negotiations because the contract could not be finalized until FDA approved the contractor change. If the contract staff will be operating under the SOPs and License of the collecting facility, **this should be reportable as a CBE or in an annual report.** We do not believe that replacing contractor-supplied employees is significantly different from replacing blood bank employees.

Section IV A 1 discusses changes that are more restrictive than previously approved. **We request that such changes should be reported in the annual report.** Manufacturers now prepare more restrictive SOPs that address international requirements that are not addressed by published FDA guidance documents. Specific examples of categories might be beneficial.

Section VI A 2 Implementation of a change in the Uniform Donor History Questionnaire (UDHQ) would always generate a change in SOP. However, SOP changes are to be reported as CBE30 or PAS. **We suggest that the two changes should always be reported at the same time, preferably in the annual report.**

Section VI D 3 requires that openings, moves, and closures of auxiliary facilities are reported in the annual report. **We request that this be deleted.** As stated in the guidance, a facility registration form (Form FDA 2830) must be completed within five days of an opening, move, or closure of the center. Thus the FDA has already been notified of these actions, and including this information in the annual report is redundant and unnecessary.

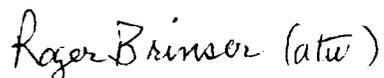
Section VIII A addresses labeling changes requiring PAS. **We request that the requirement to submit the current circular of information be deleted.** FDA approves the content of the circular of information prior to its publication. The change request should be able to just list and reference the current circular.

Section VIII A 3 We note the requirement that an approved SOP must state that the donor must weigh at least 110 lb. **We request that this be deleted.** This has never been an FDA stated requirement, and it is inappropriate to put it in writing for the first time in this particular guidance. If this is to be a requirement, it should be stated in a document addressing requirements for donor suitability or collection volumes. However, we believe that this requirement is outdated. Although we are aware that *AABB Standards for Blood Banks and Transfusion Services* previously had a statement about 110 lb., the 19th edition, published in 1999 deleted this requirement. Standard B1.200 now states that donors shall donate no more than 10.5 ML per kilogram of body weight. The amount drawn shall include samples, and the volume collected shall be appropriate for the blood collection container. **Should the FDA wish to state a requirement in an appropriate document, we request that they adopt the AABB language.**

Section VIII A 6 requires a PAS submission for conversion from Codabar to ISBT 128 labels. This appears to be a contradiction to Section VIII B 2, which states that "Labels consistent with an FDA-approved uniform labeling guidance may be submitted as CBE or CBE30 supplement." In November 1998 FDA published, for comment, US Industry Consensus Standard for the Uniform Labeling of Blood and Blood Components Using ISBT 128, Docket 98-D-0965. When finalized, this document will constitute an FDA approved uniform labeling guideline for ISBT 128.

In summary, CFBS appreciates the opportunity to comment on this draft guidance, and looks forward to continued cooperation with the FDA in finalizing the guidance. Questions concerning these comments should be directed to Kay Gregory by email kayg@aabb.org or telephone 301-215-6522.

Yours truly,



Roger Brinser
Chair, CFBS

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