SACRAMENTO MEDICAL FOUNDATION | Blood Centers



July 21, 1999

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

Re: **Docket Number 98D-0814**

Dear Sir:

Thank you for the opportunity to comment on the Draft Guidance for Industry entitled, *"Current Good Manufacturing Practice for Blood and Blood Components: (1) Quarantine and Disposition of Prior Collections from Donors with Repeatedly Reactive Screening Tests for Hepatitis C Virus (HCV); (2) Supplemental Testing, and the Notification of Consignees and Transfusion Recipients of Donor Test Results for Antibody to HCV (Anti-HCV)."* I trust that the following comments and suggestions are of use to you as you finalize this Draft Guidance Document which extends Lookback for Hepatitis C, which may have been acquired by transfusion recipients.

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In the Introduction, Section I, on page 4, and in Section II. Background, on page 5, it is stated that ***"...the search of records of prior donations from donors with repeatedly reactive screening tests for HCV extend back indefinitely to the extent that electronic or other readily retrievable records exist."*** Why is this lookback to extend back indefinitely, i.e., not as in the prior Guidance Document that limits the lookback to January 1, 1988? Second, what is the definition of ***"readily retrievable records"***? Without the prior limitation to 1988, and a clear definition of the retrievability of records, a great deal of wasted effort and time could be spent in trying to identify recipients transfused prior to 1988. The vast majority of these recipients will have died of their underlying disease, for which they were transfused, and/or it could be extremely difficult to locate them because of the mobility of the American population. Thus, I suggest that the HCV lookback envisaged here also be limited to January 1, 1988, and a clear definition is provided for what is meant by ***"readily retrievable records."***

In III., Recommendations, Section 1., A., under Current Testing, it specifies that ***"donor's in-date (screened or unscreened) prior collections in inventory..."*** should be identified and quarantined. This already appears to be the case under the current (September 1998) set of recommendations. But, the difference here is, the previously collected units identified with testing by the First Generation 1.0 anti-HCV assay would, essentially, no longer be in-date. Further, 3 calendar days is insufficient, in most cases, to enable confirmatory testing of repeatedly reactive EIA samples to be performed. It should be changed to at least 10 days, or seven

working days, to enable the testing of EIA repeatedly reactive samples for verification that they are, indeed, true positives and not false positives, since notification for false positive results would serve no useful purpose save to alarm the recipient, who would then have to be renotified if the follow-up (confirmatory) test is found to be falsely reactive, and told not to be concerned about the prior notification.

Under Item (4) of the Exceptions, a nucleic acid technology (NAT) test, e.g., polymerase chain reaction (PCR), or transcription mediated amplification (TMA), should serve as a "confirmatory" test on the repeatedly reactive EIA donation! If so, and the result were negative with a NAT test, prior quarantine would not be necessary; and the previously affected blood and blood components could be released on this basis without waiting for a serologic confirmatory test for anti-HCV, e.g., the RIBA. Since NAT testing is pervasive now, and it does indicate, in all likelihood, that a donor is infectious, it would seem appropriate to use the NAT result to define whether or not the repeatedly reactive EIA result is a true or false positive. Even though the NAT testing is being performed under an IND, it would likely be done within days of the collection, although this, too, should be extended to at least 10 calendar days, or 7 working days.

Regarding Section B., under III. Recommendations, the first paragraph on page 7, again address additional testing on the donor's EIA repeatedly reactive sample. Once again, would NAT testing be considered sufficient if performed within 45 days and found to be negative to enable release of prior collections?

Further, regarding Section C., entitled, ***"Supplemental Testing and Notification of Consignees and Transfusion Recipients,"*** on page 7, under this same section, if nucleic acid testing is negative, would this not obviate the notification process? Also, wouldn't supplemental testing, even using an appropriate, licensed multiantigen test be unnecessary? I think both would be appropriate, especially since the polymerase chain reaction (PCR) is noted in discussing RIBA results on page 8, under Sections ii and iii, among other places.

Section II, Previous Testing Using EIA 1.0 or EIA 3.0, Section A., Exception (3). Once again, 3 calendar days is far too short a period. This should be extended to at least 10 calendar days, or 7 working days.

Page 12, under Section B., Notification of Consignees and Transfusion Recipients, the last two paragraphs appear to be in conflict with one another. Why are there two dates regarding lookback – January 1, 1988, and the other indefinite – with two different time periods for notification – March 23, 2000 for the former, and September 30, 2000 for the latter? These are inconsistent; they should be the same, in both cases: January 1, 1988 re lookback and September 30, 2000 for notification.

Section D., Additional Testing Following an Indeterminate RIBA 2.0 Test Result, re item 2 on page 14: Since the results on Abbott's PRISM for anti-HCV, while nominally a 2.0 test, appear to be at least equivalent to, if not superior to, the licensed HCV EIA 3.0, would this not satisfy this requirement? I suggest that this possibility be addressed, and that results on the PRISM, one way or another, be considered essentially equivalent to the EIA 3.0.

On page 17, 3. Previous Testing Using EIA 1.0, Section A., Review of Records and Quarantine of Prior Collections: This paragraph, again, addresses the issue of having only 3 calendar days for identification of prior units for the repeatedly reactive donation (given in 1990 to 1992) to identify and quarantine all previously distributed in-date prior donations. First, the testing with EIA 1.0 was stopped at least 7 years ago, so it is not clear why only 3 days now are allowed to do identification and quarantine. Second, only frozen red cells would still be in-date, if anything. Thus, a more appropriate approach would be to suggest that frozen red cells should be checked for but all other components would no longer be in-date, so do not attempt to find them.

Section B., Notification of Consignees and Transfusion Recipients, on page 17: Once again, the possibility of using NAT as a supplemental test should be permitted. A reactive NAT for HCV RNA would be considered equivalent to a supplemental serologic test and would require notification, whereas a non-reactive test would not.

Page 19, under the same section, re the statement that ***"Prior collections should be released only if there is a record of a negative EIA 2.0, EIA 3.0, RIBA 2.0, or RIBA 3.0,"*** should also permit release if the NAT test is non-reactive on the current sample, or on a properly frozen, storage sample.

Regarding Section 2., on page 19, it would appear that the establishment should look to see what is in the freezer regarding red cells, as it is not likely that any other components would still be in-date. This would be an appropriate way to search for potential components which could be quarantined and prevented from transfusion.

Under Section 4., Notification of Transfusion Recipients, item A., on page 22, the word "insure" should be "ensure." Under Section C. on the same page, how would the transfusion service or hospital know that a physician made only a single attempt at notification? I am pleased to see on this page, and on the following one, that, if a patient is deceased, the notification process may be discontinued

It should be noted that extending the lookback to EIA 1.0 repeatedly reactive donations would be even less efficient, in terms of identifying a few people at risk of HCV infection, than the current notification process. A minority of individuals infected with HCV, even via transfusions, will be so notified; a more appropriate approach would be a blanket notification of all individuals at risk of HCV, not just from transfusions. If the goal were to identify, and possibly treat, individuals infected with HCV, this would be much more effective. A widespread notification of all individuals at risk of HCV would probably identify more individuals with this infection and, thereby, accomplish more good for America, as compared to the labor-intensive, inefficient, lookback process recommended in this Guidance Document.

Once again, thank you for the opportunity to comment on the draft Guidance Document. I trust that my comments and suggestions will enable the finalization of a more practical and useful set of recommendations.

Sincerely,

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