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October 15, 2001

Docket's Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockwell, MD 20852

Re: Docket No. 97 D – 0318
Revised Preventive Measures to Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob Disease (CJD) and Variant Creutzfeldt-Jakob Disease (vCJD) by Blood and Blood Products

Dear Sir:

Please consider the following comments on the recently issued Draft Guidance concerning measures to prevent the risk of transmission of CJD and vCJD by blood and blood products issued in August of 2001. I trust that these comments are of use to you in finalizing the guidance for "industry" regarding means to prevent the transmission of these agents, even though transmission by blood and plasma products is still theoretical.

Overall, the Guidance is complex, confusing, and difficult to comprehend. The Guidance should be markedly simplified to make it easier to implement, and follow, with less risk of an error in carrying out the suggested precautionary measures. As written, not only would these recommendations be difficult to follow, they would likely detract from the more important deferrals we attempt by our other donor questions to reduce the risk of real transfusion transmissible infections, as opposed to this potential one. Simpler, more straightforward guidance with one date for implementation would be easier to follow.

From data presented in the draft, it appears that the theoretical risk of transmission of vCJD will be reduced by an additional 3%, from the 87% expected with the current deferral criteria to 90% with the new deferral criteria. This miniscule change in reduction of a theoretical risk does not seem worthwhile for the large donor (and donation) losses that will result. Further, reducing a theoretical risk, which is zero, by 3% means that, functionally, nothing has been done; a percentage of zero is still zero.

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As noted on page 4, part of the rationale for the need to further restrict individuals from donating blood, who might be at risk of carrying vCJD, is the transfusion experiment reported in a single sheep (Reference 26). This experiment is suspect, as discussed at the recent ISBT meeting in Paris, in that blood samples collected from that same sheep before and after the single transfusion experiment which appeared to show transfusion transmission have not been found to transmit BSE.

It is noted on page 8 that transmissible spongiform encephalopathy (TSE) agents may result in low levels of infectivity in the blood of animals with these agents. Further, it is stated that such agents, including BSE, may be transmitted by transfusions in some experimental models. Finally, the risk of transmission of vCJD by human blood components and plasma derivatives is considered a theoretical possibility. Having made these statements, it is not clear why chronic wasting disease (CWD) of deer and elk is not similarly considered in this theoretical possibility realm. Using the same logic, individuals who have consumed venison or elk, especially that which came from Western states such as Utah, Wyoming, Colorado and Nebraska, have a theoretical possibility of transmitting CWD in their blood and blood components. Thus, we should consider deferring all individuals as blood and plasma sources who've consumed venison in the last 22 years and/or all individuals who reside or have resided in at least those four states where CWD is endemic. My point is, once we start making these geographic or other ill-founded deferrals for one disease, there is no way to stop because it's all theoretical and there is no way to prove or disprove a theoretical risk or possibility. I note also on page 8 that one of the reasons for <u>not</u> deferring individuals who provide Source Plasma, who've lived or traveled in Europe for five years or more, is that the risk for transmission of vCJD by plasma derivatives has not been established. <u>The risk for vCJD transmission by human blood and blood components has not been established either!</u> It also appears that since the potential loss of regular blood donors has been established, but not established for those who provide Source Plasma, this is one of the rationales for proceeding to implement just the former's deferral. This distinction is illogical. The potential loss of individuals who provide Source Plasma who might qualify for the revised deferral criteria should be established so the impact can be measured. If it is no more than that for the loss of whole blood and blood component donors, it should similarly be implemented for those providing Source Plasma, or neither should be implemented.

As noted on page 9, individuals may provide Source Plasma who would be deferred as blood donors; if so, these deferred individuals who do provide blood should be able to have their Recovered Plasma used for further manufacture. Blood centers are capable of segregating the Recovered Plasma from such whole blood deferred donors, but they, in general, are not able to collect Source Plasma for further manufacture. Therefore, the recommendation that "you defer whole

blood but not Source Plasma donors who have resided in Europe for a cumulative period of five years or more between 1980 and the present" should not be made for any material to be made into plasma derivatives.

On page 10, a big issue is made about exposure to bovine insulin from the United Kingdom, while the whole document presumes that individuals who acquired vCJD have developed this disease because of ingestion of beef from animals infected with BSE. In fact, in the United Kingdom, 90% of the BSE-infected cattle were dairy cattle. Therefore, what about individuals who have consumed milk or milk products like cheese from the U.K., and their risk of vCJD? It seems to me that there is a theoretical possibility that consuming dairy products from cattle such as those in the U.K. with BSE might result in vCJD in humans.

Regarding Item IV.A.2, it is noted that "you should indefinitely defer, and appropriately counsel, donors at increased risk for CJD..." What appropriate counsel is suggested? It does not seem appropriate to tell individuals that they are at increased risk of developing a fatal, degenerative disease with no treatment and no risk of transmission to their family members or contacts. How would it help to tell them that the only way to know for sure would be to have a brain biopsy after they have died or already have their neurological disease?

Re IV.A.4. and 6: These two sections appear inconsistent. I believe France is in Europe, so why have both Item 4 and Item 6; number 6 seems to take care of Item 4. In addition, Item 5 is really confusing. Why not just say "6 months in Europe from 1980 to 1996." This would be simpler and more encompassing, plus easier to follow.

Re IV.B. and D: Under B it says "...Plasma donors at the first donation and at each annual physical examination thereafter..." should be questioned, while in Item D it says that such individuals should be questioned at no greater than 3 months. These, clearly, should be the same, but probably should be made identical to that for whole blood donors, i.e., questions are to be asked at each donation or collection. The wording of the questions is complex and lengthy so may confuse many donors.

Page 13. Differentiation is made between US military personnel and dependents stationed in different parts of Europe regarding their risk between 1980 and 1990 versus the time period of 1980 and 1996. Without providing more on the difference, why not just be consistent and pick the over-riding time, 1980-1996? Further, as noted above, why not just be simple and make it clear that there is one rule, that of 3 months in the U.K. and 6 months or, preferably, 5 years in Europe for everybody regardless of whether or not they were in the military? Countries in Europe without known BSE are being lumped with those that do, yet people

who have spent time in Canada, where a case of BSE was found in 1993, or Japan, where a case of BSE was found this year, are not to be deferred. This appears inconsistent!

Section V.B. If individuals who have resided 5 years or more in Europe may continue to supply Source Plasma, why should Recovered Plasma from such individuals be retrieved and quarantined? This is illogical. Further, it seems that separating out France, even for Source Plasma providers, is not warranted. Providing an exception is, again, confusing. Either there's no risk, or we're not worried about the negligible risk until some point in time in the future. Further, it's noted under D, on Page 15, that once these units are made into a pool, intermediates or plasma derivatives, that they do not have to be retrieved or withdrawn.

Item V.D.3.a. and b. In the large NIH series of individuals studied there with CJD, approximately 5% had plaques in their brains and about 5% were less than 55 years of age. The records on these individuals should be carefully checked for any events or possibility that they may really have had vCJD and not classical CJD. Further, risk factors for those with the florid plaques and/or who were under age 55 should be sought to make sure that we don't already have vCJD in this country, and have had it here for awhile, albeit at a low level or an inapparent level.

Item V.E. Do we need to arrange for special disposal of material from a confirmed case?

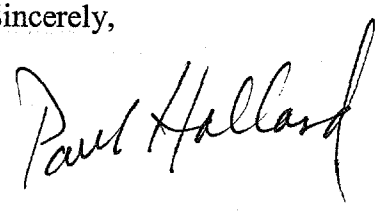
Item VI. Please define "suspected." Who will make this determination? Is additional wording to be added to the Circular of Information (COI) re this? If so, this adds nothing to the safety of transfusions.

In sum, for a theoretical risk, we are making life very complex for blood and plasma centers and, potentially, putting patients at risk of not receiving blood and plasma products. It appears that we are already doing more than enough to reduce vCJD and CJD risks, which are still theoretical. If additional deferral criteria are to be implemented, then at least they should be as simple as possible and consistent. Without simple, straightforward criteria, which also should be implemented at a uniform time by all, there will be confusion, errors, and also the potential of causing a real increase in risks which are not theoretical, e.g., HIV and Viral Hepatitis. A major impact of the new guidelines will not only be the loss of many donors in America, but the end of the Euroblood program. The combination of the two actually presents more risk to patients who may need a transfusion, which may now be unavailable, than the theoretical risk of vCJD. Adequate time should be permitted to phase in the new guidelines. The October

2002 deadline may be too short and it is clearly arbitrary for the theoretical risk it is preventing. It would seem more time should be permitted to ensure that an adequate supply of replacement plasma and blood donors will be available to prevent any real loss of life in American patients who need transfusions and plasma derivatives.

Thank you for your consideration of these comments on the new draft guidance to reduce the theoretical risk of CJD and vCJD.

Sincerely,



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SACRAMENTO
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