Guidance for Industry

Amendment (Donor Deferral for Transfusion in France Since 1980) to "Guidance for Industry: 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"

DRAFT GUIDANCE

This guidance is for comment purposes only.

Submit comments on this draft guidance by the date provided in the *Federal Register* notice announcing the availability of the draft guidance. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to http:www.fda.gov/dockets/ecomments. You should identify all comments with the docket number listed in the notice of availability that publishes in the *Federal Register.*

Additional copies of this draft guidance are available from the Office of Communication, Training and Manufacturers Assistance (HFM-40), 1401 Rockville Pike, Suite 200N, Rockville, MD 20852-1448 or by calling 1-800-835-4709 or 301-827-1800, or from the Internet at http://www.fda.gov/cber/guidelines.htm.

For questions on the content of this guidance, contact Dr. Sharyn Orton, Division of Blood Applications at 301-827-3524.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
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Contains Nonbinding Recommendations

Draft – Not for Implementation

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I. INTRODUCTION

This draft guidance, which we are issuing as a level I guidance, is intended to amend the "Guidance for Industry: Revised Preventive Measures to Reduce the Possible Risk of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" (CJD/vCJD guidance), dated January 2002 (Ref. 1), by adding a donor deferral recommendation for donors who have received a transfusion of blood or blood components in France since 1980. After we review comments received on this draft guidance, we will amend the CJD/vCJD guidance by incorporating this donor deferral recommendation, update any outdated information, and reissue the revised CJD/vCJD guidance as a level II guidance document for immediate implementation.

This draft guidance applies to Whole Blood and blood components intended for transfusion, and blood components intended for use in further manufacturing into injectable products, including recovered plasma, Source Leukocytes and Source Plasma. Special provisions apply to donors of blood components intended solely for manufacturing of non-injectable products (see section III). Within this document, "donors" refers to donors of Whole Blood and blood components and "you" refers to blood collecting establishments.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe FDA's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in FDA's guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

Since the publication of the CJD/vCJD guidance, we have learned of additional information warranting revision to the guidance to address a possible increased risk of vCJD transmission from individuals who have been transfused in France since 1980. This revision is based on (1) the likelihood of exposure to the Bovine Spongiform Encephalopathy (BSE) agent in that country and (2) the recent documentation of three presumptive cases of transfusion-transmitted vCJD infection in the United Kingdom (U.K). As of August 1, 2005, 14 definite or probable cases of vCJD have been reported in France (Ref. 2).

Available data suggest that large amounts of U.K. beef exported to France during the peak years of the U.K. BSE epidemic constituted a substantial source of exposure in France to the BSE agent. An estimated 60% of U.K. bovine carcasses were exported to France (Ref. 3) accounting for approximately 6% of French consumption of beef products (Ref. 4). It is believed that the first recognized vCJD cases in France were infected by consuming imported U.K. beef because: 1) none of the individuals had lived in the U.K.; 2) the indigenous French BSE epidemic is relatively small and more recent than that in the U.K.; and 3) travels to the U.K. accounted for only 2% of the French total exposure to the BSE agent (Ref 3).

There have been a total of three presumptive cases of transfusion-transmitted vCJD, and all have been in the U.K. The first presumptive transfusion-transmitted case of vCJD by red blood cells was reported to the U.K. Parliament on December 17, 2003 (Ref. 5). A second presumptive case was reported in the U.K. in 2004 (Ref. 6). A third presumptive case was publicly announced by authorities in the U.K. in 2006 (Ref. 7).

On February 8, 2005, the Transmissible Spongiform Encephalopathies Advisory Committee (TSEAC) discussed the available data and recommendations for deferral of U.S. donors transfused since 1980 in France and in other European countries. The TSEAC voted for deferral of blood donors who have received a transfusion of blood or blood components in France since 1980 but against deferral of Source Plasma donors with that same history. The TSEAC did not support deferral of blood donors or Source Plasma donors with history of transfusion in other European countries since 1980 (Ref. 8).

The incubation period for classical CJD may be as long as 38.5 years. Accumulating evidence suggests that the asymptomatic incubation periods of vCJD may be very long as well (sometimes exceeding 12 years from the time of exposure to the BSE agent), and blood collected as long as three years before otherwise healthy blood donors showed any sign of illness is presumed to have transmitted vCJD infection to recipients (Refs. 5 and 6). While the risk of dietary exposure to the BSE agent in France, as in the U.K. and other European countries, has almost certainly decreased in recent years thanks to successful efforts to control the BSE epidemic in cattle and to protect food from contamination with the BSE agent, an unknown but possibly significant number of blood donors might have already been infected in France during the peak years of the BSE outbreak in Europe. These considerations led FDA, consistent with the recommendations of the TSEAC, to conclude that it would be a prudent

preventive measure to indefinitely defer blood donors who have received transfusions of blood or blood components in France since 1980. Laboratory studies using model TSE agents have demonstrated that TSE infectivity may be reduced by certain plasma fractionation manufacturing steps (Ref. 9). While experimental studies are reassuring, not all products have been thoroughly studied. In addition, it remains uncertain whether the models accurately reflect the form of infectivity in blood, which has not been characterized. Therefore, as an added safeguard and prudent preventive measure, we also recommend that Source Plasma donors who have received a transfusion of blood or blood components in France since 1980 be indefinitely deferred. However, we believe that blood components collected solely for manufacturing into non-injectable products (e.g., materials used in in vitro diagnostic test kits) need not be deferred. We will continue to monitor the BSE epidemic and re-evaluate the necessity of deferring donors transfused in other European countries.

III. RECOMMENDATIONS

You should indefinitely defer all donors who have received a transfusion of blood or blood components in France since 1980.

NOTE: Donors who are otherwise deferred based upon this recommendation should continue to donate if they are participating in a CBER-approved program that allows collection of blood components solely for use in manufacturing of non-injectable products. We recommend special labeling for products obtained from such donors (see section VII.A of the CJD/vCJD guidance).

All other recommendations from the CJD/vCJD guidance remain unchanged.

IV. IMPLEMENTATION

We recommend that you implement this donor deferral recommendation within six months of the date that we finalize this draft guidance amendment. This draft guidance amendment will be finalized by reissuing the CJD/vCJD guidance inclusive of the amended language.

V. REFERENCES

1. FDA "Guidance for Industry: 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," January 2002; http://www.fda.gov/cber/gdlns/cjdvcjd.htm.
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