

# Recommendations to Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob Disease and Variant Creutzfeldt-Jakob Disease by Blood and Blood Components

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## Guidance for Industry

**This guidance is for immediate implementation.**

This guidance is being implemented in accordance with 21 CFR 10.115(g)(2) without prior public comment because the Food and Drug Administration has determined that prior public participation for this guidance is not feasible or appropriate. This guidance document is being implemented immediately, but it remains subject to comment in accordance with the Agency's good guidance practices.

Comments may be submitted at any time for Agency consideration. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. Submit electronic comments to <https://www.regulations.gov>. All comments should be identified with the docket number listed in the notice of availability that publishes in the Federal Register.

Additional copies of this guidance are available from the Office of Communication, Outreach and Development (OCOD), 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, Silver Spring, MD 20993-0002, or by calling 1-800-835-4709 or 240-402-8010, or email [ocod@fda.hhs.gov](mailto:ocod@fda.hhs.gov), or from the Internet at <https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances>.

For questions on the content of this guidance, contact OCOD at the phone numbers or email address listed above.

**U.S. Department of Health and Human Services  
Food and Drug Administration  
Center for Biologics Evaluation and Research  
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### Table of Contents

<b>I.</b>	<b>INTRODUCTION.....</b>	<b>1</b>
<b>II.</b>	<b>BACKGROUND .....</b>	<b>2</b>
	<b>A. CJD and vCJD.....</b>	<b>2</b>
	<b>B. TSE Agents and Blood.....</b>	<b>3</b>
	<b>C. FDA Regulatory History on CJD and vCJD and Blood Donation.....</b>	<b>4</b>
<b>III.</b>	<b>DISCUSSION .....</b>	<b>5</b>
	<b>A. Rationale for CJD Recommendations.....</b>	<b>5</b>
	1. Donor Deferral for Receipt of Human Growth Hormone (hGH) .....	5
	2. Donor Deferral for Having a Blood Relative with CJD .....	6
	3. Donor Deferral for Receipt of a Dura Mater Transplant .....	6
	<b>B. Rationale for Revised vCJD Recommendations .....</b>	<b>6</b>
	1. Removal of Donor Deferral for Geographic Risk of BSE Exposure.....	6
<b>IV.</b>	<b>RECOMMENDATIONS.....</b>	<b>8</b>
	<b>A. Blood Donor Screening and Management.....</b>	<b>8</b>
	1. Donor History Questionnaire .....	8
	2. Donor Deferral .....	8
	3. Donor Requalification.....	8
	<b>B. Product Retrieval and Quarantine; Notification of Consignees of Blood and Blood Components .....</b>	<b>9</b>
	1. Blood and Blood Components Collected from Donors with CJD, Risk Factors Related to CJD .....	9
	2. Blood and Blood Components Collected from Donors with vCJD, Donors Suspected of Having vCJD, or Under Investigation for vCJD .....	10
	<b>C. Circular of Information.....</b>	<b>11</b>
<b>V.</b>	<b>IMPLEMENTATION .....</b>	<b>11</b>
<b>VI.</b>	<b>REFERENCES.....</b>	<b>12</b>

# Recommendations to Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob Disease and Variant Creutzfeldt-Jakob Disease by Blood and Blood Components

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## Guidance for Industry

*This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.*

### I. INTRODUCTION

We, FDA, are issuing this guidance document to provide you, blood establishments that collect blood and blood components, with recommendations intended to reduce the possible risk of transmission of Creutzfeldt-Jakob disease (CJD) and variant Creutzfeldt-Jakob disease (vCJD) by blood and blood components. The recommendations in this guidance apply to the collection of Whole Blood and blood components intended for transfusion or for use in further manufacturing, including Source Plasma.

This guidance supersedes the guidance of the same title dated April 2020 and updated August 2020 (2020 guidance). We removed the recommendations to defer indefinitely blood donors for: 1) geographic risk of possible exposure to bovine spongiform encephalopathy for time spent in the United Kingdom (U.K.) from 1980-1996 and for time spent in France and Ireland from 1980-2001, and 2) receipt of a blood transfusion in the U.K., France, and Ireland from 1980-present. We also provide recommendations for requalification of individuals previously deferred for these geographic risk factors, provided they meet all other eligibility requirements.

The contents of this document do not have the force and effect of law and are not meant to bind the public in any way, unless specifically incorporated into a contract. This document is intended only to provide clarity to the public regarding existing requirements under the law. FDA guidance documents, including this guidance, should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in FDA guidances means that something is suggested or recommended, but not required.

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### II. BACKGROUND

#### A. CJD and vCJD

CJD is a rare, but invariably fatal degenerative disease of the central nervous system, belonging to a group of diseases called transmissible spongiform encephalopathies (TSEs) or prion diseases (Refs. 1-8). Most authorities believe TSEs are caused by an abnormal isoform of a cellular glycoprotein known as the prion protein (Refs. 1-4). The general term CJD comprises sporadic CJD (sCJD), iatrogenic CJD (iCJD), and familial CJD (fCJD). The most common form, sCJD, accounts for about 85-95% of CJD cases, with an estimated annual incidence of one case per million population worldwide (Ref. 1). Familial prion diseases account for about 5-15% of CJD cases associated with mutations in the prion protein gene (PRNP), including fCJD; and other, even rarer, familial prion diseases include Gerstmann-Sträussler-Scheinker syndrome (GSS) and fatal familial insomnia (FFI) (Ref. 5). There are an estimated 56 GSS families and 27 FFI families worldwide (Ref. 2). Finally, a small percentage (less than 1%) of CJD cases are iatrogenic (iCJD) and are acquired through transplantation of dura mater from donors with CJD or through injections of cadaveric pituitary human growth hormone (hGH) from contaminated preparations (Refs. 6-8). Among the nearly 7,700 people exposed to cadaveric pituitary hGH in the National Hormone and Pituitary Program (NHPP) in the United States (U.S.), 33 cases of iCJD have been reported (Ref. 7). All the NHPP iCJD cases to date have occurred among about 2,600 people who began cadaveric pituitary hGH treatment prior to 1977, with an average treatment duration of 8.2 years (Ref. 7). The average incubation period between the start of NHPP cadaveric pituitary hGH exposure and onset of CJD symptoms is 28 years and the time between the start of NHPP cadaveric pituitary hGH treatment and the first sign of CJD symptoms ranges from 14 to 45 years (Ref. 7). CJD is rapidly progressive, with a median duration of illness of 4-5 months from onset of symptoms (Ref. 1). Clinically, CJD is usually suspected on the basis of rapidly progressive dementia, neuropsychiatric signs, and death usually within a year of symptom onset; however, definitive diagnosis requires neuropathologic examination of brain tissue (Ref. 1).

In 1996, the U.K. reported a previously unrecognized TSE, now designated as vCJD (Refs. 9-11). Distinct from CJD, vCJD is a prion disease attributed to human infection with the agent of bovine spongiform encephalopathy (BSE, sometimes referred to as “mad cow disease”), that is likely acquired from consuming contaminated beef products (Ref. 10). BSE was first recognized in the U.K. in 1985 and subsequently spread to many European countries and worldwide. Cases of BSE in the U.K. peaked in 1992 but subsequently fell to low levels by 1996 as a result of control measures.

vCJD is distinguished from CJD by differences in clinical presentation, cerebral imaging, and neuropathological changes (Refs. 1, 12). Definitive diagnosis requires neuropathologic examination of brain tissue; however, several features distinguish vCJD from CJD and form the basis of a clinical diagnosis of suspected vCJD (<https://www.cdc.gov/prions/vcjd/diagnostic-criteria.html>). In contrast to CJD, vCJD typically affects younger individuals (i.e., onset or death in individuals younger than 55

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years), presents with psychiatric symptoms at illness onset and/or persistent painful sensory symptoms, and has a duration of illness lasting more than 6 months.

The incidence of vCJD in the U.K. peaked at 28 cases in 2000 and has decreased each year since (Refs. 13, 14). The last two reported deaths from vCJD in the U.K. were in 2013 and 2016 (Refs. 13, 14). To date, there is no evidence of a second wave of vCJD cases in the U.K. (Ref. 15). As of April 2021, there has been a total of 232 cases of vCJD worldwide, with 178 in the U.K., 28 in France, four in Ireland, four in the United States (U.S.), and 18 cases in eight other countries (Refs. 13, 14).

Of the four cases of vCJD in the U.S., two were reported in former residents of the U.K.; one in a former resident of Saudi Arabia; and one in a former resident of Kuwait, Russia and Lebanon (Ref. 12). None of these patients had donated blood in the U.S.

### **B. TSE Agents and Blood**

Among the 178 vCJD cases in the U.K., 18 were individuals who donated blood components that were traced to 67 transfusion recipients (Ref. 16). There have been four documented vCJD infections in this cohort that were likely transfusion transmitted (Refs. 16-19). Of these cases, three deaths from vCJD were linked to blood transfusions between 1996-1999 of non-leukocyte reduced red blood cells (RBC) collected from two blood donors who died from vCJD within 1-3 years of their donations (Refs. 16-19). The fourth possible case was a latent transmission to a patient who died five years after the implicated transfusion without symptoms of vCJD, but who had abnormal prion accumulation in the spleen at autopsy (Ref. 18). The U.K. has also reported one possible latent transmission of vCJD by plasma-derived Factor VIII to an asymptomatic 73-year-old patient with hemophilia, based on postmortem findings (Ref. 20). At this time, blood and blood components and plasma derivatives have not been implicated in vCJD transmission in any country other than the U.K. The last reported case of transfusion-transmitted vCJD in the U.K. occurred in 2006 and implicated a non-leukocyte reduced red cell unit.

To date, no U.S.-licensed plasma-derived products have been manufactured from blood collected from a donor known to have developed vCJD and no cases of vCJD have been reported in persons treated with U.S.-licensed plasma derivative.

In contrast to the 4 reported cases of vCJD transmitted by blood transfusion in the U.K., there have been no transfusion-transmitted cases of CJD described to date worldwide, and the risk remains theoretical (Refs. 16, 21-29). The evidence base supporting the improbability of transfusion transmission includes five case-control studies of over 600 CJD cases, two autopsy studies of patients with hemophilia, a large binational cohort study, and two ongoing lookback studies tracing recipients of components collected from donors later found to have CJD (Refs. 16, 21-29). The U.K. lookback study includes 29 sCJD blood donors with transfusions to 211 recipients, and four fCJD blood donors with transfusions to 15 recipients (Ref. 16). The U.S. lookback study includes 63 sCJD blood donors with transfusions to 817 recipients; one iCJD donor linked to eight recipients; and

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one fCJD donor linked to one recipient (Ref. 28). These studies have investigated the reported causes of death and have continued the surveillance of surviving transfusion recipients. Many recipients lived five or more years after transfusion (76 recipients in the U.K. study; 264 recipients in the U.S. study), which likely would allow sufficient time to recognize cases should they occur (Refs. 16, 28). The U.S. study also describes 414 recipients who received transfusion within five years of the donors' CJD diagnosis or symptom onset, of which 105 of those recipients survived more than five years (Ref. 28). Both studies concluded that there have been no cases of any type of CJD identified among the transfusion recipients to date.

### C. FDA Regulatory History on CJD and vCJD and Blood Donation

In 1987, FDA first issued recommendations in a memorandum to blood establishments for deferral of individuals who received human cadaveric pituitary growth hormone injections to reduce the possible risk of transmission of CJD by blood and blood products. In 1999, FDA issued the first guidance with recommendations for CJD and vCJD. FDA held several Transmissible Spongiform Encephalopathies Advisory Committee (TSEAC) meetings between 1995 and 2015 to review the available scientific evidence and the risk assessment of geographic donor deferrals and transfusion-transmitted vCJD. As the number of issues requiring Committee advice declined, the Committee meetings occurred infrequently and, in 2016, FDA terminated TSEAC.

FDA updated the 1999 guidance several times. Most recently, in 2020, we revised or removed our prior recommendations to screen blood donors for: 1) geographic risk of possible exposure to bovine spongiform encephalopathy in most European countries, including time spent on U.S. military bases in Europe; 2) receipt of a blood transfusion in certain vCJD risk countries; 3) risk factors for iatrogenic CJD (i.e., a history of taking human cadaveric pituitary-derived growth hormone (hGH)); 4) having blood relatives with CJD; and 5) a history of injecting bovine insulin. FDA did not change the recommendation for deferral based on time spent or transfusion in the UK, France, or Ireland at that time.

FDA's decision in 2020 to remove certain geographic-based deferrals was based on the risk-ranking model that estimated the country-specific, relative risk of possible exposure to vCJD (Ref. 30). The model determined that the U.K., Ireland, and France had the most attributed cases and thereby accounted for most of the potential risk of exposure to vCJD. The model also considered the extent of leukocyte reduction of the U.S. blood supply at the time and the associated risk reduction contributed by leukocyte reduction. Notably, leukocyte reduction of blood and blood products is almost universally implemented in the U.S. today. In the U.S., most whole blood/red blood cell units (97%) and platelet units (97%) are leukocyte reduced, which further reduces the risk of transfusion transmission of vCJD (Ref. 31).

However, FDA's risk-ranking model did not estimate the absolute risk of transmitting vCJD through blood transfusion, in terms of the expected number of transfusion-transmitted vCJD cases in the U.S. and the contribution of the deferral policy as a risk

## Contains Nonbinding Recommendations

reduction measure. Since publication of FDA's risk-ranking model, U.K.'s Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO) (Ref. 32) and Medicines and Healthcare Products Regulatory Agency (MHRA) (Ref. 33) have conducted risk assessments that mathematically model the risk of vCJD infection through blood transfusion or immunoglobulin administration in the U.K., the country with the highest number of vCJD cases worldwide.) In light of the new information, FDA has evaluated these new data and mathematical models, to assess the relevance of donor deferral for geographic risk in the UK, France, and Ireland to blood safety. As described further below, based on this evaluation, FDA has determined that it is appropriate to update this guidance.

### III. DISCUSSION

#### A. Rationale for CJD Recommendations

The recommendations on reducing the possible risk of transmission of CJD are unchanged from the 2020 guidance. Exposure of transfusion recipients to blood from asymptomatic CJD donors has been demonstrated; however, no transfusion-transmitted cases of CJD have been reported, and the risk of such transmission remains theoretical (Refs. 16, 21-29). Standard procedures are in place to assure that donors are healthy at the time of donation and serve as an effective safeguard against collecting blood or blood components from a donor after the onset of clinical symptoms of CJD. As a precaution, we recommend that any donor suspected of having CJD or any other TSE is permanently deferred. In addition, we recommend that establishments quarantine and retrieve blood and blood components collected from donors with CJD based on post-donation information.

##### 1. Donor Deferral for Receipt of Human Growth Hormone (hGH)

Human cadaveric pituitary hGH was available in the U.S. from 1958 to 1985 (starting in 1986, all U.S.-produced hGH was recombinant). Thirty-five cases of iCJD in the U.S. occurred among about 2,600 patients who began NHPP cadaveric pituitary hGH treatment prior to 1977 (Ref. 7). The average incubation period for iCJD from the start of NHPP hGH treatment to the onset of CJD symptoms is 28 years, and the time between the start of NHPP hGH treatment and the first sign of CJD symptoms ranges from 14 to 45 years (Refs. 6, 7). The prevalence of individuals who might have been treated with cadaveric pituitary hGH prior to 1977 is very low among blood donors, and the transmission risk of CJD by blood components remains theoretical (Ref. 28). Consequently, we do not recommend inclusion of hGH in medication deferral lists used in donor screening educational materials.

As a precaution, however, we recommend that individuals who volunteer that they received cadaveric pituitary hGH should be permanently deferred.

## **Contains Nonbinding Recommendations**

Donors previously deferred for receiving cadaveric pituitary hGH are not eligible for requalification under 21 CFR 630.35(b) (Refs. 6, 7).

### **2. Donor Deferral for Having a Blood Relative with CJD**

Familial prion disease is extremely uncommon, and most cases reported by donors are sCJD, and not familial prion disease. Blood relatives of individuals with sCJD are not at increased risk of developing the disease. Familial CJD shares pathophysiological features with sCJD, and the transmission risk by blood components remains theoretical for both types.

As a precaution, we recommend that individuals who volunteer that they have blood relatives known to have a familial prion disease (e.g., fCJD, GSS, or FFI) should be permanently deferred. Establishments should also quarantine and retrieve in-date blood and blood components upon receipt of post-donation information about blood relatives with CJD.

Donors who volunteer that they have one or more blood relatives with familial prion disease (e.g., fCJD, GSS, or FFI) are not eligible for requalification under 21 CFR 630.35(b).

### **3. Donor Deferral for Receipt of a Dura Mater Transplant**

We recommend that blood establishments defer donors who receive human cadaveric dura mater allografts because such transplantation is still performed in the U.S. and presents a remote risk of iCJD.

## **B. Rationale for Revised vCJD Recommendations**

We are changing the geographic deferral recommendations for vCJD risk based on new information in the risk assessments published by U.K.'s SaBTO (Ref. 32) and MHRA (Ref. 33). These risk assessment models, which FDA has independently evaluated, demonstrate that, in the UK, the current risk of vCJD transmission by blood and blood components would expose transfusion recipients to no or minimal additional risk of vCJD in the future, and, for blood components that are leukocyte reduced, the possible risk is even further reduced (Refs. 32, 33).

We have determined that our recommendations will simplify the donor screening process and increase the number of eligible donors while maintaining the safety of blood and blood components.

### **1. Removal of Donor Deferral for Geographic Risk of BSE Exposure**

The U.K. SaBTO recently updated their risk assessment for transfusion of plasma collected in the U.K. Since 2004, plasma has been imported from outside the U.K., for transfusion to individuals born after 1995 or with thrombotic



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thrombocytopenic purpura. The model predicted that if the risk reduction measures were not in place, an additional 1 or 2 clinical cases of vCJD from plasma transfusion may occur in the U.K. over the next 50 years. Based on this risk assessment, the U.K. eliminated their risk reduction measures in 2021, and stopped importing plasma from outside the U.K. for transfusion (Ref. 32). Further, the MHRA risk assessment demonstrated that the risk from the use of U.K.-sourced plasma for the manufacture of immunoglobulin products was negligible and led to the conclusion that U.K.-sourced plasma is now acceptable for the manufacture of immunoglobulins in the U.K. (Ref. 33). As noted above, FDA has reviewed the methods and modeling data in these U.K. assessments and believes they are valid estimates of risk. Thus, FDA has concluded that these new data support removing the recommendation for deferral of individuals for geographic risk for time spent in the U.K.

Additionally, based on the smaller number of vCJD cases in France and Ireland, FDA expects the risk of vCJD transmission by blood and blood components in France and Ireland would be even lower than what was modeled in the risk assessments for the U.K. (Refs. 32, 33). Consequently, we are removing the recommendation for deferral of individuals who spent time in the U.K. (from 1980-1996) and Ireland and France (from 1980-2001).

Finally, the U.K. assessment of the risk of transfusion-transmitted vCJD in the U.K. predicted a small number of cases might be associated with plasma or platelet transfusion over the next 50 years (Ref. 32). By extrapolation, we believe there would be an even lower risk of transfusion-transmitted vCJD in France and Ireland. Consequently, we are removing the recommendation for indefinite deferral of individuals who have received a blood transfusion in the U.K., France or Ireland from 1980-present.

Donors previously deferred for geographic risk for time spent in the U.K., France, and Ireland - or for receipt of a blood transfusion in the U.K., France, or Ireland - can be assessed for requalification under 21 CFR 630.35(b) and may be eligible for reentry, provided they meet all other eligibility requirements.

In the 2020 guidance, we removed the recommendation for indefinite deferrals for time spent in other European countries, time spent on U.S. military bases, and receipt of bovine insulin since 1980. Donors previously deferred for these reasons can be assessed for requalification under 21 CFR 630.35(b), provided they meet all other eligibility requirements.

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### IV. RECOMMENDATIONS

#### A. Blood Donor Screening and Management

The following recommendations apply to the collection of Whole Blood and blood components intended for transfusion or for use in further manufacturing, including Source Plasma.

##### 1. Donor History Questionnaire

We recommend that blood collection establishments update their donor history questionnaires (DHQ), including full-length and abbreviated DHQ and accompanying materials (e.g., flow chart, medication deferral list), and processes to incorporate the revised recommendations provided in this guidance.

We recommend that the updated DHQ and accompanying materials include the following:

- a. Assess donors for a history of ever receiving a human cadaveric (allogeneic) dura mater transplant.

##### 2. Donor Deferral

- a. Defer permanently a donor who has been diagnosed with vCJD, CJD or any other TSE or who has a blood relative diagnosed with familial prion disease (e.g., fCJD, GSS, or FFI) or who received cadaveric pituitary hGH treatment.<sup>1</sup>
- b. Defer permanently a donor who has received a human cadaveric (allogeneic) dura mater transplant.

##### 3. Donor Requalification

Under 21 CFR 630.35, you may determine a deferred donor to be eligible if, at the time of the current collection, the criteria that were the basis for the previous deferral are no longer applicable. For donors deferred for reasons other than reactive screening test results for relevant transfusion-transmitted infections under 21 CFR 610.41(a), you must determine that the donor has met the criteria for requalification by a method or process found acceptable for such purposes by FDA under 21 CFR 630.35(b).

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<sup>1</sup> We do not recommend asking donors about a history of vCJD, CJD or any TSE, or about blood relatives with familial prion disease (e.g., fCJD, GSS, FFI) or about receipt of cadaveric pituitary hGH because of the inability to identify asymptomatic individuals harboring TSEs and the rarity of the conditions. However, donors that volunteer such information should be permanently deferred.

## Contains Nonbinding Recommendations

Accordingly, donors who were previously deferred for geographic risk factors for vCJD or receipt of a blood transfusion in the U.K., France or Ireland, may now be eligible provided they meet all other eligibility requirements.

The following are not eligible for requalification and the recommendation for deferral remains in place:

- Donors previously deferred for receiving cadaveric pituitary hGH.
- Donors that have one or more blood relatives with familial prion disease (e.g., fCJD, GSS, or FFI).

Donors previously deferred for having a blood relative with CJD can be reentered if the blood relative was not diagnosed with familial prion disease (e.g., fCJD, GSS, or FFI). If the donor does not know these terms, the donor is eligible for reentry.

### **B. Product Retrieval and Quarantine; Notification of Consignees of Blood and Blood Components**

#### 1. Blood and Blood Components Collected from Donors with CJD, Risk Factors Related to CJD

If you collected blood or blood components intended for transfusion or further manufacture from a donor who has been diagnosed with CJD, who has a blood relative diagnosed with familial prion disease (e.g., fCJD, GSS, or FFI), or who should have been deferred for risk factors for CJD (i.e., receipt of cadaveric pituitary hGH treatment or human cadaveric (allogeneic) dura mater transplant) as described in section IV.A.2. of this guidance, we recommend the following:

- a. Quarantine all undistributed in-date blood and blood components from such a donor.
- b. If you distributed blood or blood components intended for transfusion or for further manufacture from such a donor, we recommend that you notify consignees to retrieve and quarantine the in-date blood and blood components.

If the blood components were transfused, we do not recommend tracing and notification of recipients of prior donations.

- c. We do not recommend retrieval or quarantine of plasma components that have been pooled for further manufacture or plasma derivatives manufactured from the plasma of such a donor.

## Contains Nonbinding Recommendations

Quarantined blood components from donors with CJD, who have a blood relative diagnosed with familial prion disease (e.g., fCJD, GSS, or FFI), or with risk factors for CJD (i.e., receipt of cadaveric pituitary hGH treatment or human cadaveric (allogeneic) dura mater transplant) may be used in laboratory research. You should relabel these products with the following statements:

- “Biohazard;”
- “Collected from a donor determined to be at risk for CJD;” or “Collected from a donor diagnosed with CJD;” and
- “Caution: For laboratory research use only.”

### 2. Blood and Blood Components Collected from Donors with vCJD, Donors Suspected of Having vCJD, or Under Investigation for vCJD

We recommend that you contact FDA<sup>2</sup> as soon as possible upon learning that you collected blood or blood components from a donor later determined to have vCJD, a donor suspected of having vCJD or under investigation for vCJD (i.e., CJD diagnosis and age younger than 55 years). In addition, you should consider notifying state and local public health authorities.

- a. If you collected blood or blood components from such a donor, you should immediately quarantine all undistributed in-date blood and blood components held at your establishments and notify consignees to retrieve and quarantine all in-date components from that donor.

If such blood components were transfused, you should consider identifying the transfusion recipient’s physician of record, so that notification and counseling may be performed as appropriate.

- b. You should immediately retrieve and quarantine plasma components that have been pooled for further manufacture and plasma derivatives manufactured from such a donor.

We recommend that you contact FDA regarding a donor’s diagnosis of vCJD or suspected vCJD. Our recommendations regarding product disposition of plasma derivatives from such donors will depend upon results of the investigation.

Quarantined blood components from donors with vCJD or suspected vCJD may be used in laboratory research on vCJD by qualified laboratories. You should relabel these products with the following statements:

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<sup>2</sup> Contact CBER’s Office of Communication, Outreach and Development (OCOD) by calling 1-800-835-4709 or 240-402-8010. After regular business hours and on weekends, call the FDA emergency number: 1-866-300-4374.

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- “Biohazard;”
- “Collected from a donor with variant CJD” or “Collected from a donor with suspected variant CJD;” and
- “Caution: Only for laboratory research on variant CJD.”

### **C. Circular of Information**

For Whole Blood and blood components intended for transfusion, the circular of information should include the following warning statement:

“Because Whole Blood and blood components are made from human blood, they may carry a risk of transmitting infectious agents (e.g., viruses, bacteria, parasites, the variant Creutzfeldt-Jakob disease (vCJD) agent, and theoretically, the Creutzfeldt-Jakob disease agent (CJD).”

## **V. IMPLEMENTATION**

You may implement the recommendations once you have revised your DHQ, including the full-length and abbreviated DHQ, and accompanying materials to reflect the new donor deferral recommendations.

Licensed blood establishments must report changes to their approved Biologics License Application (BLA) to FDA in accordance with 21 CFR 601.12.

1. Licensed blood establishments that revise their DHQs and accompanying material or implement a revised version of the DHQ and accompanying materials prepared by the AABB Donor History Task Force or the Plasma Proteins Therapeutic Association (PPTA) must report the change to FDA in an annual report under 21 CFR 601.12(d), noting the date the process was implemented.
2. Unlicensed establishments are not required to report this change to FDA.

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