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

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U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
April 2020

Contains Nonbinding Recommendations

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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 revised 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. We are revising or removing our prior recommendations to screen blood donors for: 1) geographic risk of possible exposure to bovine spongiform encephalopathy, including time spent on United States (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. These changes are summarized in the Appendix of this guidance.

This guidance finalizes the draft guidance of the same title dated January 2020, and supersedes the document entitled "Revised Preventive Measures to Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob Disease and Variant Creutzfeldt-Jakob Disease by Blood and Blood Products, Guidance for Industry" dated May 2010 and updated January 2016 (2016 guidance).

In general, FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the 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

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). TSEs are believed to be caused by an abnormal isoform of a cellular glycoprotein known as the prion protein (Refs. 1-4). The general term CJD comprises sporadic (classic) CJD (sCJD), iatrogenic CJD (iCJD), and genetic CJD. 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). Genetic forms of CJD account for about 5-15% of CJD cases inherited as mutations in the prion protein gene (PRNP), including familial CJD (fCJD), Gerstmann-Sträussler-Scheinker (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 human cadaveric pituitary-derived growth hormone (hGH) from contaminated preparations (Refs. 6-8). Thirty-three cases of iCJD were reported among the nearly 7,700 people in the U.S. who received hGH prior to 1977 (Ref. 7). Clinical latency for iCJD following exposure to infectious material is typically 5-15 years, but it has also exceeded 30 years in case reports (Ref. 8). 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 United Kingdom (U.K.) reported a previously unrecognized TSE, now designated as vCJD (Refs. 9-11). Distinct from CJD, vCJD is a prion disease related to bovine spongiform encephalophy (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 and 12). Although definitive diagnosis requires neuropathologic examination of brain tissue, the following notable 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):

1. Current age or age at death <55 years.
2. Psychiatric symptoms at illness onset and/or persistent painful sensory symptoms (frank pain and/or dysesthesia).

3. Dementia and development ≥4 months after illness onset of at least two of the following five neurologic signs: poor coordination, myoclonus, chorea, hyperreflexia, or visual signs.
4. A normal or an abnormal EEG, but not the diagnostic EEG changes often seen in classic CJD.
5. Duration of illness of over 6 months.
6. Routine investigations of the patient do not suggest an alternative, non-CJD diagnosis.
7. No history of iatrogenic exposure to CJD, such as receipt of cadaveric human pituitary growth hormone or an allogeneic dura mater graft.
8. No history of CJD in a first degree relative or prion protein gene mutation in the patient.

The incidence of vCJD in the U.K. peaked at 29 cases in 1999 and has decreased each year since (Refs. 13 and 14). The last two reported deaths from vCJD in the U.K. were in 2013 and 2016 (Refs. 13 and 14). To date, there is no evidence of a second wave of vCJD cases in the U.K. (Ref. 15). As of October 8, 2019, 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 U.S., and 18 cases in eight other countries (Refs. 13 and 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 cases in this cohort that were likely transfusion transmitted. 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, plasma derivatives have not been implicated in vCJD transmission in any country other than the U.K. To date, no U.S.-licensed plasma-derived products have been manufactured from a donor known to have developed vCJD and no cases of vCJD have been reported from use of a U.S.-licensed plasma derivative.

In contrast to vCJD, no transfusion-transmitted cases of CJD have been described to date, 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 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 have concluded that there have been no cases of any type of CJD identified among the transfusion recipients to date.

Differences between CJD and vCJD are also apparent in experimental studies with respect to prion protein detection in blood, the extent of replication in lymphoid tissues and infectivity through blood exposure in animal studies (Refs. 30 and 31). Abnormal prion protein accumulates in lymphoid tissues in persons with vCJD, but generally not in persons with sCJD or genetic CJD, possibly reflecting the different propensity for detection of the agent in blood and transmission of vCJD by blood transfusion (Ref. 16). Correspondingly, a recent study demonstrated that the prion protein was detected in the blood of all 14 patients with vCJD tested, but not in any of the 16 patients with sCJD or in 137 controls who were either healthy or had other neurological diseases (Ref. 31).

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.

III. DISCUSSION

A. Rationale for Revised CJD Recommendations

Based on the available scientific data and on public comments, FDA is revising its recommendations on reducing the possible risk of transmission of CJD and vCJD by blood and blood components.

There is currently no donor screening measure that can identify individuals who will later develop CJD. 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. Standard procedures are already 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)

In the 2016 guidance, we recommended that individuals who report having received hGH should be permanently deferred from blood donation. Human cadaveric pituitary-derived hGH was available in the U.S. from 1958 to 1985. All associated cases of iCJD in the U.S. resulted from exposure to hGH prior to 1977 (Ref. 7). The national program to communicate annually with hGH recipients ended in June 1999, although surveillance activities continue (Ref. 7). The average incubation period for iCJD from hGH treatment is 15 years, although there have been case reports of incubation periods longer than 30 years (Ref. 6). Because the risk exposures to hGH occurred prior to 1977, it is unlikely that any additional cases of iCJD will occur in this cohort. Therefore, we recommend that establishments may remove hGH from their medication deferral lists used in donor screening.

We recommend that donors previously deferred for receiving hGH are not eligible for reentry as a precaution, because of the remote possibility of long incubation periods. (Ref. 6).

2. Donor Deferral for Having a Blood Relative with CJD

In the 2016 guidance, we recommended that prospective blood donors should be indefinitely deferred if they report having a blood relative with CJD. However, almost all cases reported are sCJD, not a genetic form of CJD. Blood relatives of individuals with sCJD are not at increased risk of developing the disease. The rare genetic forms of CJD (e.g., fCJD, GSS, or FFI) share pathophysiological features with sCJD, and the transmission risk by blood components remains

theoretical. Consequently, we recommend that establishments may stop asking prospective donors about having blood relatives with CJD.

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

We recommend that donors who volunteer that they have one or more blood relatives with genetic CJD (e.g., fCJD, GSS, or FFI) are not eligible for reentry.

3. Donor Deferral for Receipt of a Dura Mater Transplant

The recommendation to defer donors who receive human (cadaveric) dura mater allografts remains unchanged 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 the findings of our risk assessment that the revised recommendations will achieve a similar reduction of vCJD risk exposure while simplifying the donor screening process and potentially allowing more donors to donate.

1. Donor Deferral for Geographic Risk of BSE Exposure

FDA developed a quantitative risk assessment based on a global geographic risk-ranking model (Ref. 32) that estimated the contributions of donors potentially exposed to BSE in various countries. The model evaluated both risk reduction and donor loss resulting from the current geographic donor deferral policy compared with alternative deferral options. The model also evaluated the potential additional risk reduction afforded by leukocyte reduction of RBC. The model indicated that U.K., Ireland, and France, the three countries with the most attributed vCJD cases and BSE-related risk, contributed 95% of the total risk exposure in the U.S. Estimating that about 95% of RBC currently transfused in the U.S. are leukocyte reduced, the model predicted that deferring donors only for time spent in the U.K., Ireland, and France would maintain a predicted level of blood safety similar to that achieved with the current policy (Ref. 32). Based on these results, we recommend indefinite deferral only of donors who spent time in the U.K., Ireland, and France.

We maintain the recommendation in the 2016 guidance to defer prospective donors who report receiving a blood transfusion in France or the U.K. We also recommend deferral for transfusion in Ireland from 1980-present to align the

deferrals for blood transfusion with the geographic deferrals for time spent in the U.K., France, and Ireland (Ref. 32).

We recommend that donors previously deferred for geographic risk for time spent in other European countries can be assessed for requalification using the revised recommendations for vCJD geographic deferrals and may be eligible for reentry.

2. Donor Deferral for Potential Exposure to U.K.-Sourced Beef on U.S. Military Bases

In the 2016 guidance, we recommended that prospective donors should be deferred based on cumulative time spent on U.S. military bases in Europe from 1980-1996. The deferrals were first recommended in 2001 because some U.S. military bases in Northern Europe sourced beef from the U.K. between 1980 and 1990 and military bases elsewhere in Europe between 1980 to 1996 (Ref. 33). During this time, over 4.4 million military personnel and civilians might have ingested beef obtained from the U.K. on military bases in Europe; however, there have been no reported cases of vCJD in the intervening 20 years. This observation supports that the risk associated with time spent on U.S. military bases in Europe is different from the country-based risk calculations for time spent in the U.K., France, and Ireland that was based on the number of BSE-related vCJD cases in those countries. Therefore, we no longer recommend deferral of individuals for time spent on U.S. military bases in Europe.

We recommend that donors previously deferred for time spent on military bases in Europe can be assessed for requalification and may be eligible for reentry.

3. Donor Deferral for Injection of Bovine Insulin Since 1980

In the 2016 guidance, we recommended that prospective donors should be deferred if they report injecting bovine insulin, which may have been manufactured after 1980 from cattle in the U.K. However, no cases of transmission of vCJD have been reported in recipients of bovine insulin manufactured in BSE-affected countries. Therefore, establishments may remove bovine insulin from their medication deferral lists used in donor screening.

We recommend that donors previously deferred for injecting bovine insulin can be assessed for requalification and may be eligible for reentry.

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 elements:

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

b. Assess donors for cumulative time spent in the U.K. (i.e., England, Northern Ireland, Scotland, Wales, the Isle of Man, the Channel Islands, Gibraltar, or the Falkland Islands) between 1980 to 1996.

c. Assess donors for cumulative time spent in France[1] or Ireland from 1980 to 2001. Note that this assessment does not include time spent in the U.K, which is evaluated separately in section IV.A.1.b. of this guidance.

d. Assess donors for a history of ever receiving a blood transfusion in the U.K. (i.e., England, Northern Ireland, Scotland, Wales, the Isle of Man, the Channel Islands, Gibraltar, or the Falkland Islands), France[1], or Ireland from 1980 to the present.

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 genetic CJD (e.g., fCJD, GSS, or FFI).[2]

[1] This assessment does not include time spent in French overseas departments (e.g., Martinique, French Guiana, Guadeloupe, Mayotte, and Réunion).

[2] We do not recommend asking donors for a history of vCJD, CJD or any TSE or for family history of genetic CJD (e.g., fCJD, GSS, FFI). However, donors that volunteer such information should be permanently deferred.

b. Defer permanently a donor who has received a human cadaveric (allogeneic) dura mater transplant.

c. Defer indefinitely a donor who has spent three months or more cumulatively in the U.K. (i.e., England, Northern Ireland, Scotland, Wales, the Isle of Man, the Channel Islands, Gibraltar, or the Falkland Islands) from 1980 to 1996.

d. Defer indefinitely a donor who has spent five years or more cumulatively in France[1] or Ireland from 1980 to 2001. Note that this assessment does not include time spent in the U.K, which is evaluated separately in section IV.A.1.b. of this guidance.

e. Defer indefinitely a donor with a history of blood transfusion in the U.K. (i.e., England, Northern Ireland, Scotland, Wales, the Isle of Man, the Channel Islands, Gibraltar, or the Falkland Islands), France[1], or Ireland from 1980 to the present.

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).

Accordingly, donors who were previously deferred for certain risk factors for vCJD and CJD may now be eligible based on the revised recommendations in section IV of this guidance, except as follows:

- Donors previously deferred for receiving hGH are not eligible for reentry.

- Donors that have one or more blood relatives with genetic CJD (e.g., fCJD, GSS, or FFI) are not eligible for reentry.

Donors previously deferred for having a blood relative with CJD can be reentered if the blood relative was not diagnosed with genetic CJD (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, or Geographic Risk Factors for vCJD

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 genetic CJD (e.g., fCJD, GSS, or FFI), or who should have been deferred for risk factors for CJD or geographic risk factors for vCJD 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.

Quarantined blood components from donors with CJD, or from donors with risk factors for CJD or geographic risk factors for vCJD 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;" or "Collected from a donor with potential risk of exposure to variant 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[3] 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

[3] 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.

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:

- "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 BLA to FDA in accordance with 21 CFR 601.12.

1. Licensed blood establishments that revise their DHQs and accompanying material must report the change to FDA in a Changes Being Effected (CBE) Supplement under 21 CFR 601.12(c)(5) (see 21 CFR 601.12(a)(3)). The blood and blood components collected using the change may be distributed immediately upon receipt of the supplement by FDA. Include the following information in your CBE Supplement:

    a. Form FDA 356h "Application to Market a New or Abbreviated New Drug, or Biologic for Human Use."
    b. Cover letter describing the request and contents of the supplement.
    c. The DHQ and accompanying document(s). Please highlight the modifications.

2. Licensed blood establishments that 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) found acceptable by FDA must report the changes to FDA in an annual report under 21 CFR 601.12(d), noting the date the process was implemented.

3. Unlicensed establishments are not required to report this change to FDA.

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APPENDIX

Table 1: Comparison of Recommendations in 2016 Guidance and 2020 Guidance

2016 Guidance		**2020 Guidance**	
Section	**Recommendations**	**Section**	**Recommendations**
IV.A.1.	Defer permanently donors who have been diagnosed with vCJD or any other form of CJD.	IV.A.2.a.	Defer permanently a donor who has been diagnosed with vCJD, CJD or any other transmissible spongiform encephalopathy **or who has a blood relative diagnosed with genetic CJD (e.g fCJD, GSS, or FFI).** Note: We do not recommend questioning donors for vCJD, CJD, or any other TSE or for blood relatives with genetic CJD (e.g., fCJD, GSS, or FFI) because of the inability to identify asymptomatic individuals harboring TSEs, the rarity of the conditions, and the available evidence from lookback studies that have not identified a case among recipients of blood from infected donors. However, individuals that volunteer such information should be permanently deferred.
IV.A.2.	Defer permanently donors if they have received: • A dura mater transplant.	IV.A.2.b.	Revised to clarify the source of tissue that is a cause for deferral: • Defer permanently a donor who has received a **human cadaveric (allogeneic)** dura mater transplant.
	• an injection of human cadaveric pituitary-derived growth hormone (hGH).	**N/A**	**Deleted**
	Defer indefinitely donors with one or more blood relatives diagnosed with CJD.	**N/A**	**Revised (see IV.A.2.a.).**
IV.A.3.	Defer indefinitely donors who have spent 3 months or more in U.K. from 1980-1996.	IV.A.2.c.	No change

2016 Guidance		**2020 Guidance**	
Section	**Recommendations**	**Section**	**Recommendations**
IV.A.4.	Defer indefinitely donors who have spent 5 years or more cumulatively in France from 1980 – present.	IV.A.2.d.	Defer indefinitely a donor who has spent 5 or more years cumulatively in France **or Ireland** from the beginning of 1980 **to the end of 2001.** Note that this assessment does not include time spent in the U.K., which is assessed separately in IV.A.1.b. This assessment also does not apply to French overseas departments (e.g. Martinique, French Guiana, Guadeloupe, Mayotte, and Réunion).
IV.A.5.	Defer indefinitely former or current U.S. military personnel, civilian military personnel, and their dependents, for residence on: • U.S. military bases in Northern Europe (Germany, U.K., Belgium, and the Netherlands) for 6 months or more from 1980 through 1990, or • U.S. military bases elsewhere in Europe (Greece, Turkey, Spain, Portugal, and Italy) for 6 months or more from 1980 through 1996.	**N/A**	**Deleted**
IV.A.6.	Defer indefinitely donors with a history of transfusion in the U.K. or France from 1980 – present.	IV.A.2. e.	Defer indefinitely a donor with a history of transfusion in U.K. (i.e., England, Northern Ireland, Scotland, the Isle of Man, the Channel Islands, Gibraltar, or the Falkland Islands), France, **or Ireland** from the beginning of 1980 to present.

2016 Guidance		**2020 Guidance**	
Section	**Recommendations**	**Section**	**Recommendations**
IV.A.7.	Defer indefinitely donors who have injected bovine insulin since 1980, unless you can confirm that the product was not manufactured after 1980 from U.K. cattle.	**N/A**	**Deleted**
IV.A.8.	Defer indefinitely donors who have spent 5 years or more in Europe from 1980-present.	**N/A**	**Deleted**