3 March 2023

EUROPEAN BLOOD ALLIANCE

Summary report EID Monitor - vCJD survey

During the European Blood Alliance (EBA) Emerging Infectious Diseases (EID) Monitor meeting on June 28th 2022 it was agreed to launch a short survey about the current strategy for blood donor selection to reduce the risk for transfusion-transmitted (TT) variant Creutzfeldt Jakob disease (vCJD). The survey was prompted by several recent publications relating to the risk assessment of TT vCJD performed by SaBTO (1), the ECDC (2), Australian colleagues (3), the FDA (4) as well as recent changes to donor selection criteria implemented in several countries. The purpose of the survey was to gather information about the current policies of donor deferral for vCJD risk on request for the preparation of a dedicated session about vCJD in the IPFA/PEI 28th International Workshop on Surveillance and Screening of Blood-borne Pathogens.
The survey questionnaire was circulated to EID Monitor members on July 5th and a reminder was sent on August 4th. The questions that were asked are found in the Appendix.
The results of the questionnaire were shared with EID Monitor members. The preliminary anonymized results were used for the IPFA/PEI 28th International Workshop on Surveillance and Screening of Blood-borne Pathogens for the session about vCJD and prion diseases on 21 September 2022.

As of 25th October 2022, 21 answers from 21 countries, including 3 non-European countries, were received. The following countries responded: Australia, Austria, Belgium, Canada, Denmark, Estonia, France, Germany, Ireland, Italy, Luxemburg, Malta, Netherlands, Portugal, Slovenia, Spain, Sweden, Switzerland, UK, USA and XXXX[1].

Permanent deferral of blood donors due to the risk of transfusion exposure to vCJD
Implementing the permanent deferral of blood donors due to the risk of transfusion exposure to vCJD depends on the period when the blood transfusion was given (before, during, or after the BSE/vCJD outbreak, with the risk period considered to be approximately 1980–1996). Countries who have a permanent deferral for blood transfusion apply this either regardless of the country where the transfusion was received or only in specific countries that are considered at risk. The overall results are depicted in figure 1 and table 1.

No countries have a permanent deferral of donors who had received a blood transfusion before the BSE/vCJD outbreak as a measure to mitigate the risk of TT vCJD. There are reasons other than vCJD risk for which donors are deferred permanently due to the history of blood transfusion for all or specific donation types. Examples are blood transfusion in countries endemic for Chagas disease unless negative tested with a validated *T. cruzi* test or the presence of irregular erythrocyte antibodies after transfusion. In Malta, a general rule of permanent deferral is applied for donors who had received a blood transfusion outside the Maltese islands, any time in life. This measure is not exclusively for vCJD risk, but in consideration of the lack of traceability, and therefore unknown level of safety, of the transfusion.

[1] XXXX – A country that did not provide consent to sharing non-anonymized data

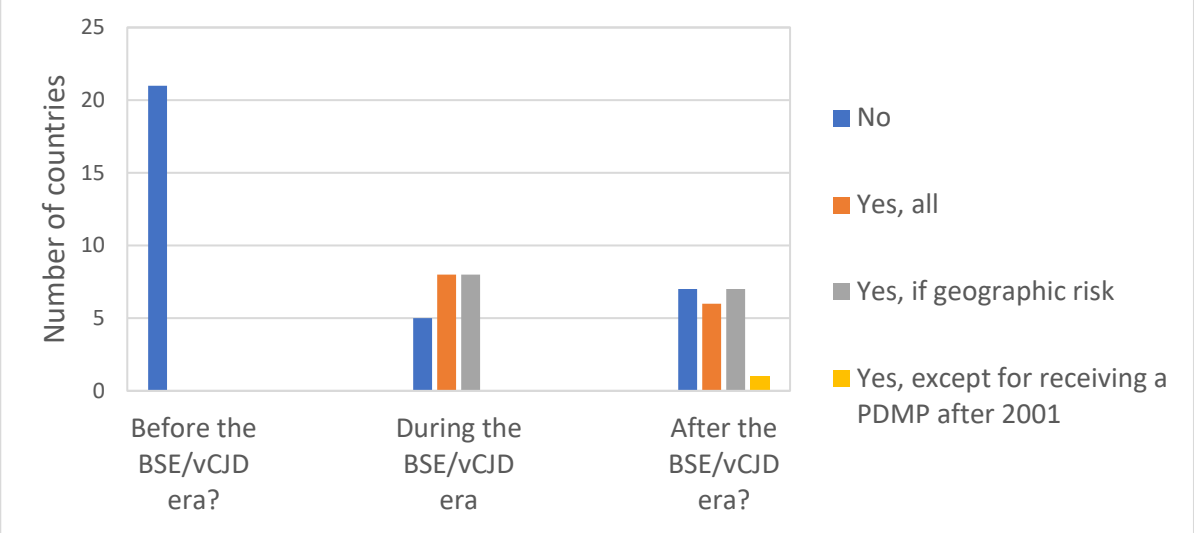

Figure 1. Permanent deferral of blood donors due to the risk of transfusion exposure to vCJD

For donors who had received a blood transfusion during the BSE/vCJD outbreak, 16 countries defer these donors permanently. Eight of these countries have a geographically restricted deferral i.e. if the blood donations occurred in certain countries (i.e. France, Ireland or the UK). The five countries without a permanent deferral included Denmark, Sweden (except plasma for the manufacturing of plasma-derived medicinal products (PDMP), XXXX and finally the USA who recently reviewed and lifted this ban (4). As mentioned above, in Malta a permanent deferral is applied for blood transfusion outside Maltese islands. Of note the survey did not include a specific question on the year the deferral commenced.

Table 1. Permanent deferral of blood donors due to the risk transfusion exposure to vCJD

Country	before the BSE/vCJD era?	during the BSE/vCJD era	after the BSE/vCJD era?
Australia	No	Yes	Yes, except for receiving a PDMP after 2001
Austria	No	Yes	No
Belgium	No	Yes, if geographic risk	Yes, if geographic risk
Canada	No	Yes, if geographic risk	Yes, if geographic risk
Denmark	No	No	No
Estonia	No	Yes, if geographic risk	Yes, if geographic risk
France	No	Yes	Yes
Germany	No	Yes, if geographic risk	Yes, if geographic risk
Ireland	No	Yes	Yes
Italy	No	Yes, if geographic risk	Yes, if geographic risk
Luxembourg	No	Yes, if geographic risk	Yes, if geographic risk
Malta	No	No	No
Netherlands	No	Yes	Yes
Portugal	No	Yes	Yes
Slovenia	No	Yes, if geographic risk	No
Spain	No	Yes, if geographic risk	Yes, if geographic risk
Sweden	No, plasma for PDMP not used	No, plasma for PDMP not used	No, plasma for PDMP not used
Switzerland	No	Yes	Yes
UK	No	Yes	Yes
USA	No	No	No
XXXX	No	No	No

For blood transfusion receipt after the BSE/vCJD outbreak a permanent deferral of donors is in place in 14 countries. In seven of these 14 countries the deferral applies to blood transfusion in regions considered to have a vCJD risk. In Australia, blood or PDMP recipients are permanently deferred unless they only received a PDMP after 2001. There is no deferral for those who received blood transfusions in Austria, Denmark and XXXX. In Sweden recipients of a transfusion may donate blood (after six months if the transfusion was in the UK) but their plasma may not be used for PDMP manufacture.

Noteworthy is that for blood transfusions during or after the vCJD outbreak, countries applying permanent donor deferral can make exceptions for donors donating specific blood or blood components for certain patients (rare blood type erythrocytes, HLA-matched thrombocytes, lymphocytes for donor lymphocyte infusions).

Permanent deferral of blood donors due to the "geographic vCJD risk[2] "

Four countries currently have no deferral for time spent in countries considered at risk of BSE (the UK plus recent changes in policies in Australia, USA, and Ireland). Seventeen countries have a deferral applied for variable cumulative periods of time spent in the UK; including timeframes of 3, 6 and 12 months. Canada also applies a deferral for time spent in Ireland or France for a cumulative period of 5 years. The results are shown in table 2.

Table 2. Permanent deferral of blood donors due to the "geographic vCJD risk"

Deferral	Policy in country
No deferral	Australia, UK, USA, Ireland
Yes, 3 months UK (1980-1996), 5 years France/Ireland (1980-2001)	Canada
Yes, 6 months UK (1980-1996)	Austria, Belgium, Estonia, Germany, Italy, Malta, Netherlands, Switzerland
Yes, 6 months UK (1980-1996), only for plasma for PDMP	Sweden
Yes, 12 months UK (1980-1996)	Denmark, France, Luxembourg, Portugal, Slovenia, Spain, XXXX

Reconsidering donor selection criteria for vCJD risk and recent changes

The overall results are shown in figure 3.

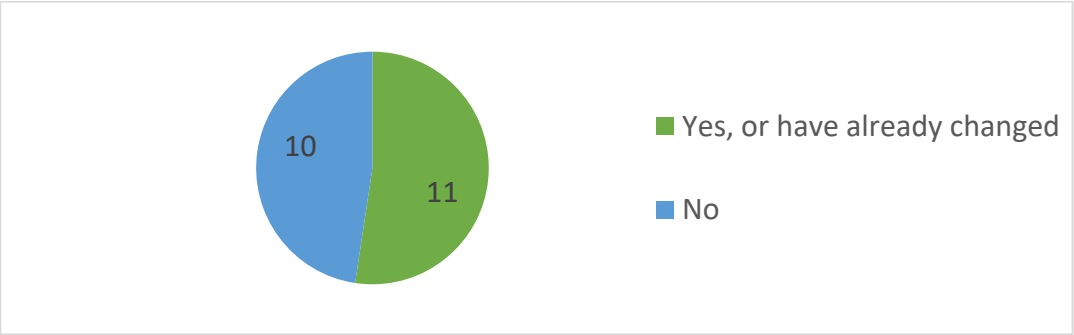

Figure 3 – Countries reconsidering donor selection criteria for vCJD risk

[2] "geographic vCJD risk" = risk of dietary exposure to BSE according to the length of stay in certain countries

Eleven countries responded that they have recently made changes or are considering changes to their guidelines. Ten countries responded that they have not reconsidered and are not currently reconsidering their policy at the moment (Austria, Belgium, Denmark, Estonia, France, Germany, Malta, Portugal, Sweden, XXXX). Relatively recently, Ireland, Australia and the USA have already reconsidered and changed their donor selection policies (see below).

In 2019 the deferral for UK residency was removed in Ireland. Australia responded that they also changed recently to accept donors who have lived in the UK during the BSE/vCJD outbreak. They are reconsidering their current policy on donors who had a blood transfusion in the UK and those who had a cornea transplant. For the USA the FDA removed the recommendation for deferral of individuals who spent time in the UK (from 1980-1996) Ireland and France (from 1980-2001) and the recommendation for indefinite deferral of individuals who received a blood transfusion in the U.K., France or Ireland from 1980-present.

Eight countries are considering changing their donor selection criteria. Four of them did not provide the details. The other four countries are reconsidering criteria related to blood transfusion exposure (three countries), the geographic vCJD risk (two countries); cornea transplant (one country) and dental/ surgical procedures in BSE/vCJD risk countries (one country).

Conclusion

This survey shows the significant variability among EBA members in the donor selection criteria applied to mitigate vCJD risk. There is some consistency for permanent donor deferral due to the risk of transfusion exposure during BSE/vCJD outbreak, but some countries only defer those who were transfused in a country that is considered to be at higher risk for vCJD.

The cumulative period of time deemed to be associated with a risk of possible exposure to BSE includes 3, 6 or 12 months. For the geographic deferral the UK was considered to be the main country of risk but France and Ireland were also mentioned.

According to the EU directive 2004/33 for vCJD, further precautionary measures may be recommended (see below).

- *Directive 2004/33/EC has a legislative requirement that "persons who have a family history which places them at risk of developing a TSE, or persons who have received a corneal or dura mater graft, or who have been treated in the past with medicines made from human pituitary glands" are permanently excluded from donation; and*
- *"For variant Creutzfeldt Jacob disease, further precautionary measures may be recommended".*

The 20th edition of the Council of Europe (CE) Guide to the preparation, use and quality assurance of blood components does not recommend one unique approach to donor selection criteria for vCJD risk.

- *"Deferral of donors as a preventative measure for vCJD must be based on appropriate risk assessment." and noting that*
- *"Endogenous risk of vCJD differs between countries. Therefore, different measures to reduce risk will be appropriate depending on each country's own risk assessment, balancing risk with sufficiency of supply."*

The EU directive and CE Guide allow countries to perform their own risk assessment for blood safety to reduce vCJD risk which may explain the variety of blood safety measures and definition between countries.
It would appear there is now a significant shift towards removing the geographic deferrals applied to those previously considered to have been at risk of BSE exposure between 1980 and 1996. This is evident in the recent changes introduced in Australia, the USA and the Republic of Ireland such that those considered to be at risk previously can now donate blood. Several other countries who responded to this survey indicated similar intentions.

Why some countries are hesitant to change their measures was not investigated in this survey, It can be speculated that some of them are cautious due to a) 2010 predictions of a second wave of vCJD in those with prion protein gene heterozygosity (5) although a second wave has not been seen, and b) the outcomes of the UK appendix studies although the interpretation of these are now in question (6). It also may be that some countries do not have the necessary resources to perform risk assessments and evaluate if all criteria for the implementation of their precautionary measures are valid, or that this is considered to be futile if European-wide guidelines are not changed. Epidemiological data and modelling studies would suggest the tranfusion-transmitted risk of vCJD is very low and the incidence of BSE worldwide is negligible.

DISCLAIMER
Australian Governments fund Australian Red Cross Lifeblood for the provision of blood, blood products and services to the Australian community.

References

1. Advisory Committee on the safety of Blood, Tissues and Organs. Importation of plasma and use of apheresis platelets as risk reduction measures for variant Creutzfeldt-Jakob Disease. London: SaBTO; 2019. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/829906/SaBTO_PC_report.pdf
2. European Centre for Disease Prevention and Control (ECDC). The risk of variant Creutzfeldt-Jakob disease transmission via blood and plasma-derived medicinal products manufactured from donations obtained in the United Kingdom – 3 August 2021. ECDC: Stockholm; 2021. Available at: https://www.ecdc.europa.eu/sites/default/files/documents/vCJD-blood-plasma-amended-version-July-2022-JD.pdf
3. Seed CR, Hewitt PE, Dodd RY, Houston F, Cervenakova L. Creutzfeldt-Jakob disease and blood transfusion safety. Vox Sang. 2018 Apr;113(3):220-231. doi: 10.1111/vox.12631.
4. Food and Drug Administration. Recommendations to reduce the possible risk of transmission of Creutzfeldt-Jakob Disease and variant Creutzfeldt-Jakob Disease by blood and blood components. Guidance for Industry. May 2022. Available at: https://www.fda.gov/media/124156/download
5. Garske T, Ghani AC. Uncertainty in the tail of the variant Creutzfeldt-Jakob disease epidemic in the UK. PLoS One. 2010 Dec 23;5(12):e15626. doi: 10.1371/journal.pone.0015626.
6. Salamat MKF, Stewart P, Brown H, Tan KBC, Smith A, de Wolf C, et al. Subclinical infection occurs frequently following low dose exposure to prions by blood transfusion. Sci Rep. 2022;12:10923

Appendix. Questions of survey

Do you defer donors who received a blood transfusion:

a) before the BSE/vCJD era?
b) during the BSE/vCJD era
c) after the BSE/vCJD era?

If yes, please specify additional criteria if applicable (e.g. only transfusions in certain regions)

Do you have a deferral for donors for geographic risk of possible exposure to bovine spongiform encephalopathy for time spent in specific countries?

If yes, please specify (e.g. for which countries and for which period of stay)

Do you have other selection criteria, not mentioned above, to exclude donors at risk for vCJD?

If yes, please specify

Are you currently reconsidering your policy on donor selection criteria for vCJD risk; do you expect a change; or have you changed your policy recently?

If yes, please specify