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Vaccines, Blood & Biologics

Questions and Answers on "Guidelines for Donor Deferrals: Revised Preventive Measures to Minimize the Risk of Transmission of Creutzfeldt-Jakob Disease (CJD) and Variant Creutzfeldt-Jakob Disease (vCJD) from Blood and Blood Products"

Why do we recommend new blood donor deferrals for exposure to BSE and vCJD?

FDA is taking this step as a prudent measure to protect the blood supply by further reducing the direct and indirect exposure to the vCJD agent, which is believed to be a strain of the same agent that causes spongiform encephalopathy (BSE, or "mad cow" disease). The deferral of donors who resided in the United Kingdom (U.K.) from more between 1980 and 1996. At this time, we are recommending donor deferrals for possible exposure to BSE and vCJD for the following reasons:

1. Since 1999, the rate of vCJD cases in the U.K. has increased.
2. Significant exposures to potentially contaminated blood in France and cases of vCJD have appeared in France.
3. Significant exposures to potentially contaminated blood in U.S. military bases in Europe.
4. In Europe, outside the U.K., the BSE epidemic peaked in 1992.
5. Particularly in the U.K., transfusion recipients were exposed to donors already infected with vCJD.

What are the new donor deferrals for exposure to BSE and vCJD?

1. Residence in the U.K. for 6 months or more between 1980 and 1996.

Rationale: The U.K. has experienced the highest reported number of cases of vCJD (over 100 cases). In 1996, the U.K. instituted and enforced rules to prevent contaminated blood from entering the human food chain (www.defra.gov.uk/food/fda/health/public-health-index.html). Due to these effective food protections, the risk of exposure to the BSE agent has been greatly reduced. For this reason, the donor deferral extends only through 1996.

2. Military personnel (current and formerly), and their dependents, who spent time in military bases in northern Europe, 1980–1996, for 6 months or more.

Rationale: British beef was eaten at military bases during these time periods. The maximum amount of U.K. beef eaten was about 35% of the total beef diet.

3. Donors who lived in France for 5 years or more, between 1980 and the present.

Rationale: The French imported at least 5% of their beef supply from the U.K. before 1996. There are also 5 cases of vCJD in France. This deferral will go into place before the European deferral (# 5., below).

4. Donors who received a transfusion in the U.K. between 1980 and the present.

Rationale: Although there are no known cases of transfusion of vCJD, it is too early to rule out this possibility. Since the U.K. has the highest number of vCJD cases, and is likely to also have the highest number of people incubating vCJD, we recommend deferral of people who have received blood products from U.K. donors.

5. Blood donors who lived in Europe for 5 years or more, between 1980 and the present.

Rationale: Most European countries now have reported BSE, although in fewer cattle than in the U.K. However, methods to prevent BSE from getting into human food are not completely in place in all European countries, so we recommend deferral up to the present time.

How effective are the new donor deferrals at reducing risk of vCJD from transfusion?

Combined with the effect of our previous recommendations, our new recommendations, added to the previous U.K. deferral, eliminate an estimated total 90% of overall risk (calculated by "risk-weighted" person-days of exposure to infected beef), and may decrease the number of donors an average of an additional 5% nationwide. The new deferrals reflect an attempt to minimize the theoretical risk of transmission of vCJD, while maintaining critical supplies of blood products.

Why can people who have lived in Europe for 5 years or more, give Source Plasma, but not blood?

Blood donors are deferred, but donors of "Source Plasma," who have lived in Europe (except France and the U.K. as above), may continue to donate. Unlike blood, Source Plasma undergoes manufacturing into highly processed products ("plasma derivatives"), several of which have been in short supply. Donors who have lived in Europe have a low likelihood of incubating vCJD, compared to people who lived in France or the U.K. Furthermore, published studies show that some of the steps used in plasma derivative manufacturing remove agents which are similar to the vCJD agent, thus adding a potential

margin of safety. Thus we consider the risks and benefits of deferring Source Plasma donors, as opposed to blood donors, for residence in Europe, to be different.

How will the new deferrals affect the blood supply?

Based upon a 1999 survey, we estimate that about 8% of blood donors may be deferred. However, in some locations, such as in large coastal areas where more people travel, up to 10% of donors may be deferred.

What measures are being taken to attenuate the impact of donor deferrals?

1. We have recommended two separate phases of donor deferral to spread out the potential impact on supplies over time. Phase I will start on May 31, 2002, and includes deferral of people who lived in France for 5 months or more, 1980-1996, in France (1980-present) on military bases (as described above), or who had a transfusion in the U.K. Phase I will provide 82% of the additional risk reduction accomplished by the revised deferral policy and is estimated to eliminate approximately 82% of current potential vCJD risk.

For blood donors who lived in Europe for 5 years or more, deferral will start on October 31, 2002. Phase II will provide the balance (18%) of additional risk reduction accomplished by the revised deferral policy. It is estimated to eliminate an additional 13% of current potential risk.

2. We have asked blood banks that choose to have broader deferrals than those we recommend, to implement pilot studies, to see what kind of loss of donors can be tolerated without causing local blood shortages.
3. The Department of Health and Human Services has initiated a plan for monitoring the blood supply, nationwide, in an effort to detect and prevent supply shortages.
4. We continue to encourage more blood donations, and will continue to work among blood banks to assist each other in cases of local shortages.

If I am deferred, will I ever be asked to donate again?

Because it is still uncertain whether blood can transmit vCJD, and even if it is possible that donor screening tests may be developed to identify people carrying the disease, it is possible that you will be able to donate again in the future. Along with our expert Transmissible Spongiform Encephalopathy Advisory Committee (TSEAC), we are continuing to monitor the BSE epidemic, human exposure to BSE, possible testing methods for blood, and scientific advances which will help us understand whether or not human blood components are able to transmit vCJD. New advances in science and epidemiology may enable you to donate again in the future.

What will happen when new countries, not now on the blood donor deferral list, are discovered to have BSE?

Since the publication of our draft guidance in August 2001, BSE was diagnosed in Japan, which is not on the blood donor deferral list. The source of this outbreak is believed to be contaminated material from BSE cattle, which was imported and fed to Japanese cows. The news media has reported that other countries may also have received potential BSE-contaminated material which they could have fed to their own cows. We may consider additional deferrals based upon possible exposure to BSE in Asia or elsewhere, but only after additional information about the potential level of BSE exposure and food chain controls in these other countries is acquired and, preferably, would anticipate doing so after the currently recommended deferrals have been implemented and their impact is assessed.

How is FDA monitoring the risk of vCJD transmission by blood?

We monitor the risk by keeping up to date with new published, and unpublished scientific work from academia and industry. Much of this material is made publicly available at meetings of the TSEAC. We maintain close contacts, and consult with experts in other agencies that are also involved in BSE and vCJD, such as the U.S. Department of Agriculture and the Centers for Disease Control and Prevention, as well as with international government agencies. FDA also maintains its own pool of scientific experts in these diseases who perform active research to address questions of transmission of spongiform encephalopathies, such as BSE and vCJD by blood.

Where can I obtain more information?

1. Previous TSEAC transcripts, containing discussion and information about many of the issues and decisions, above:
 - TSEAC Transcripts, December 18, 1998
 - TSEAC Transcripts June 1-2, 2000
 - TSEAC Transcripts, January 18-19, 2001
 - TSEAC Transcripts June 28, 2001

Referenced Guidance

- [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 \(PDE\) \(PDE - 93KB\)](#)

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**Donor Exclusion to Address Theoretical Risk of Transmission
of variant Creutzfeldt-Jakob Disease (vCJD) through the Blood Supply**

**UNITED KINGDOM, FRANCE &
WESTERN EUROPE**

1. PURPOSE

The purpose of this Directive is to advise all licensed Canadian blood establishments to take further measures to reduce the theoretical risks of transmission of vCJD through the blood supply. This is to be accomplished by excluding from donating blood all persons who:

- have spent a cumulative period of time of 7 months or more in the United Kingdom (UK) consisting of England, Scotland, Wales, Northern Ireland, Isle of Man, the Channel Islands between the years 1980 to 1996; or
- have spent a cumulative period of time of 3 months or more in France between 1980 to 1996; or
- have spent a cumulative period of time of 3 years or more in Western Europe (WE) consisting of Germany, Italy, Netherlands, Switzerland, Austria, Belgium, Spain, Republic of Ireland, Portugal, Denmark, Luxembourg, Liechtenstein, between the years 1980 and ongoing; or
- have received a transfusion of whole blood or blood components in the UK or France between the years 1980 and ongoing.

The period of time of three months or more spent in the UK or France is not based on a combination of time in either country. The period spent in the above noted countries is considered either the time spent individually in each country or any combination of time spent in the various countries so that cumulatively, the residence period requiring deferral amounts to 3 months or more.

2. BACKGROUND

Variant Creutzfeldt-Jakob disease (vCJD), first described in 1996, is a "new" variant of disease with the outbreak of Bovine Spongiform Encephalopathy (BSE) in cattle.

While there have been no cases of vCJD attributable to the use of human blood or plasma derivatives to date, lack of experience with this condition and the cumulative uncertainties with limited knowledge available on certain biological effects associated with this infection, the lack of information on the concentration and infectivity of the vCJD prion in blood, and the lack of information on the concentration and infectivity of the vCJD prion in blood, do not allow for conclusion that it can not occur. In addition, a report that BSE in cattle can be transmitted within that species through blood transfusion suggests that there is a possibility that vCJD have the potential to spread through human blood. Blood derivatives used in the treatment of the Transmissible Spongiform Encephalopathies (TSE) have been implicated in the transmission of the disease. The incubation period of the known TSE infections is approximately 10-20 years. The current diagnostic procedures available for early detection of vCJD are not sufficient to allow for donor deferral for persons who have spent time in the UK, or France or WE.

In considering this potential risk and measures to deal with it, the principle has been adopted that one must seek to apply measures which will reduce the targeted risk without jeopardizing the safety of the blood system in other ways. Using this rationale, Health Canada issued Directives on August 17, 1999 and August 20, 2000 requiring the exclusion from blood donation of all persons who had spent time amounting cumulatively to a period of 6 months or more in the UK, or France or WE.

the UK or France between the years 1980 to 1996, inclusive. Based on recent scientific knowledge available since the issuance of the 1999 and 2000 Directives, Health Canada, in consultation with stakeholders including Canadian Blood Services(CBS) and Héma-Québec(HQ), is directing industry to tighten the blood donor deferral for the UK and France to 3 months or more and to add a deferral based on 5 years or more spent in the above-noted countries of WE.

This new Directive is based on recent scientific knowledge available since the issuance of the 1999 and 2000 Directives and the following new information:

- e.g. The total number of cases of vCJD is increasing, with a cumulative total that reached 110 in August, 2001, with 106 in the UK, France reporting 3 cases and one case in the Republic of Ireland;
- e.g. The number of observed BSE cases is increasing steadily in West European countries once thought to be free of the disease;
- e.g. Brain tissue from BSE-infected primates, injected intravenously into other primates, has been shown to transmit disease;
- e.g. Recent research has shown experimental sheep-to-sheep transmission of the BSE agent by blood transfusion.

Recent surveys conducted by CBS and HQ indicate that reducing the deferral period to three months or more for either France or the UK and the addition, of a deferral based on 5 years or more time spent in the above-noted countries of WE, will not jeopardize the blood supply. Health Canada's Population and Public Health Branch has carried out a number of modeling studies to estimate the theoretical risk of acquiring vCJD for those persons who have spent time in the UK. Similar modeling studies have been done to estimate vCJD risk for persons spending time in France and the above noted countries of WE. These risks are not identical and consequently, HC would not require a deferral based on a combination of time in the UK with time spent in France; or a combination of times spent between the above-noted WE countries and either the UK or France. However, WE deferral does allow for a combination of times spent among the above-noted WE countries.

A theoretical risk reduction of 72% is achieved under the 1999 and 2000 Directives. With the implementation of the current Directive, there is expected to be an additional 16-18% reduction of the theoretical risk for an estimated overall risk reduction value of 88-90%. A blood donor loss of around 3% or less is estimated under the current Directive.

3. SCOPE

This Directive applies to all Canadian blood establishments that are licensed to fabricate blood and blood components for transfusion or for further manufacture. Products affected by the Directive include all blood components for transfusion with the exception of: autologous donations, peripheral blood stem cells collected for autologous transplants, rare blood types and products derived from USA-sourced plasma.

4. REGULATORY REQUIREMENTS

Blood establishments are required to submit a Letter of Implementation, detailing to the Blood and Tissues Division of the Biologics and Genetic Therapies Directorate (BGTD) the relevant

An attachment must be included which indicates the impact of this Directive on the donor base and plans to mitigate any such effect. Operators are also encouraged to develop materials to be used in explaining these deferral policies to deferred donors in order to develop an appropriate understanding of the regulatory rationale.

Regarding the withdrawal of prior donations by deferred donors, Health Canada wishes to ensure that all available components collected from these deferred donors, that have not been released or pooled for further manufacture, be retrieved.

5. COMPLIANCE DATE

The exclusion is to be introduced as soon as operationally feasible, but not later than six months from the date of this Directive.

6. ADDITIONAL INFORMATION

Blood operators will be required to report semi-annually on the impact of this policy on donor bases and the supply of blood.

On an ongoing basis, Health Canada may update its guidance in response to new scientific knowledge. If other cases of vCJD are confirmed in the future, an ongoing research program will be carried out to determine specifically what deferral periods will be required.

The Directive, with a list of supporting references, is available for download from the HC website.

Questions concerning the "Donor Exclusion Policy" or the theoretical risk of acquiring variant CJD through the Blood Supply may be directed to:
Biologics and Genetic Therapies Directorate
Blood and Tissues Division
3rd Floor LCDC Building #6
Postal Locator 0603C
Tunney's Pasture
Ottawa, Ontario
K1A 0L2

7. REFERENCES

Scientific references used in the development of the Directive's implementation strategy:

1. Monthly statistics on the United Kingdom's CJD and vCJD

- and <http://www.doh.gov.uk/cjd/stats/aug01.htm>
EUROCID and NEUROCID: The European and Allied Countries Collaborative Study Group of CJD(EUROCJD) plus the Extended European Collaborative Study Group of CJD(NEUROCJD)
<http://www.eurocjd.ed.ac.uk/>
2. Monthly statistics on the cases of BSE determined through testing in the European countries. Monthly BSE testing - Cumulative table from January to May 2001 http://europa.eu.int/comm/food/fs/bse/testing/bse_test06_en.pdf - BSE testing - May 2001
- and Office International des Epizooties - Number of reported cases of BSE worldwide
http://www.oie.int/eng/info/en_esbmonde.htm
3. Corinne Ida Lasmézas et al. PNAS, March 27, 2001, vol.98(7),4142-4147 "Adaptation of the bovine spongiform encephalopathy agent to primates and comparison with Creutzfeldt-Jakob disease: Implications for human health"
<http://www.pnas.org/cgi/doi/10.1073/pnas.041490898>
4. Houston F, Foster J.D., Chong A, et al. Transmission of BSE by blood transfusion in sheep. Lancet 2000; 356:999-1000

The modelling studies carried out by Health Canada's Population and Public Health Branch to estimate the theoretical risk of acquiring vCJD under the conditions of the Directive can be found on the Health Canada website with URL:
http://www.hc-sc.gc.ca/sab-ccs/sep2000_BSE_vCJD_slide11_e.html



April 22, 2005

Additional Donor Exclusion Measures to Address the Potential for Transmission of variant Creutzfeldt-Jakob Disease (vCJD) through the Blood Supply

1. PURPOSE

The purpose of this new Directive is to advise all Canadian blood establishments that in order to fabricate blood and blood components for transfusion of the requirement to implement exclusion measures to reduce the potential risk of transmission of vCJD through the blood supply must be accomplished by screening and excluding from donating blood, all persons who have received a transfusion of whole blood or blood components in France or Western Europe between the years 1980 and ongoing. These new requirements are in addition to those already found in Health Canada's Directive *Donor Exclusion to Address Theoretical Risk of Transmission of variant Creutzfeldt-Jakob Disease (vCJD) through the Blood Supply UNITED KINGDOM, FRANCE & WESTERN EUROPE* dated August 30, 2001¹.

To summarize the current requirements, risk reduction is to be achieved by excluding from donating blood, all persons who:

- have spent a cumulative period of time of 5 months or more in the United Kingdom consisting of England, Scotland, Wales, Northern Ireland, Isle of Man, the Channel Islands between the years 1980 to 1996; or
- have spent a cumulative period of time of 3 months or more in France between the years 1980 to 1996; or
- have spent a cumulative period of time of 5 years or more in countries of Western Europe of Germany, Italy, Netherlands, Switzerland, Austria, Belgium, Spain, Portugal, Ireland, Portugal, Denmark, Luxembourg, and Liechtenstein between the years 1980 and ongoing; or
- have received a transfusion of whole blood or blood components in the United Kingdom or WE between the years 1980 and ongoing.

2. BACKGROUND

Variant Creutzfeldt-Jakob disease (vCJD), first described in 1996, is a fatal disease linked with the outbreak of Bovine Spongiform Encephalopathy (BSE) in cattle and the consumption of beef and beef products from cattle infected with BSE².

Scientific knowledge of the Transmissible Spongiform Encephalopathies (TSEs) has been hampered by the long incubation period of the known TSE infectious agents (e.g. vCJD and BSE) and the lack of diagnostic procedures available for early detection. Consequently, Health Canada (HC) wishes to mitigate the risks of potential human to human transmission of vCJD with policies on blood donor deferral for persons who have spent time or received transfusion of blood or blood components, in the UK, or France or WE.

In considering this potential risk and measures to deal with it, the principle has been adopted that one must seek to apply measures which will reduce the targeted risk without jeopardizing the availability or safety of blood in Canada. Using this rationale, Health Canada issued Directives based on the scientific knowledge available at the time, on August 17, 1999³, August 20, 2000⁴ and August 30, 2001⁵. The first two directives required the exclusion from blood donation of all persons who had spent time amounting cumulatively, to a period of 6 months or more in the UK or France between the years 1980 to 1996, inclusive, based on the BSE epidemic and the occurrences of vCJD in the UK and France. The August 30, 2001 Directive was issued to tighten the blood donor deferral for the UK and France to 3 months or more, to add a deferral based on 5 years or more spent in the above-noted countries of WE, and to add a deferral for donors who received a blood transfusion in the UK, between the years 1980 and ongoing.

The scientific knowledge related to vCJD since the issuance of the 2001 Directive has increased, including the following:

- A study in 2002 demonstrating that scrapie infected asymptomatic sheep could transmit the disease to other sheep by transfusion⁶.
- Research indicates that the intravenous route of transmission of BSE is highly efficient⁶.
- There have been two recent reports of potential human to human transmission of vCJD by blood transfusion^{7,8}. The two blood donors involved did not develop symptoms of vCJD until 40 and 18 months after the donation. One of two recipients of the suspected blood component was a methionine-valine heterozygote (MV) at codon 129 of the prion protein gene (PRNP), contrary to previous data suggesting that susceptibility to vCJD was restricted to the methionine homozygous (MM) PRNP genotype⁷.
- There has been an increase in BSE and vCJD cases reported worldwide^{9,10,11}. The total number of definite and probable cases of vCJD has reached 168 as of February 7, 2005, with 154 cases in the UK, 9 in France, and one case each in the Republic of Ireland, Canada, Italy and United States^{12,13}.

3. REGULATORY REQUIREMENTS

Based on the current scientific knowledge, Health Canada will require all Canadian blood establishments that are licenced to fabricate blood components to take measures to further reduce the risk of vCJD transmission through blood components. This includes the exclusion of donors who received a blood transfusion in the UK, France or WE, and ongoing, to include France and WE. These blood establishments are required to submit a Licence Amendment Submission to the Biologicals and Veterinary Division for review.

An attachment must be included which indicates how the blood establishment will maintain the donor base and plans to mitigate any such effects, such as the development of educational materials to be used in explaining these deferral requirements to donors, and to foster an appropriate understanding of these precautionary measures.

Regarding the withdrawal of prior donations by donors who have been excluded, it is required that all available components collected from these donors, whether they are frozen, stored, or pooled for further manufacture, be retrieved.

4. SCOPE

This Directive applies to all Canadian blood establishments that collect blood and blood components for transfusion. Products are not included in the scope of this Directive, with the exception of donations for transfusion with the exception of donations for transfusion, and rare blood types.

It is recommended that Canadian and non-Canadian blood establishments follow the donor exclusion requirements outlined in this Directive.

5. CONSULTATIONS

The scientific findings have been discussed and addressed by the Canadian Blood Component Advisory Committee on Blood Regulation as well as the Canadian Blood Component Public Advisory Committee. Also, Canadian Medical Association and the Canadian Nurses Association have been consulted in the development of this Directive.

The blood donor loss as a result of this new exclusion is estimated to be minimal.

6. COMPLIANCE DATE

The exclusion is to be introduced as soon as possible, but no later than 2006.

months from the date of this Directive.

7. ADDITIONAL INFORMATION

Blood operators will be required to report semi-annually on the impact of this policy on their donor bases and the supply of blood.

On an ongoing basis, Health Canada may update its guidance in response to new scientific knowledge.

Questions concerning the "Donor Exclusion to Address Theoretical Risk of Transmission of variant CJD through the Blood Supply" should be directed to:

Biologics and Genetic Therapies Directorate

Centre for Biologics Evaluation

Director's Office

3rd Floor LCDC Building #6

Postal Locator 0603D

Tunney's Pasture

Ottawa, Ontario

K1A 0L2

8. REFERENCES

1. Donor exclusion to address theoretical risk of transmission of variant Creutzfeldt-Jakob disease (vCJD) through the blood supply. Health Canada Directive, 2001
http://www.hc-sc.gc.ca/hpfb-dgpsa/bgt-dpbtg/blooddeferral_uk_france_we_e.html
2. Corinne Ida Lasmézas et al. PNAS, March 27, 2001, vol.98(7),4142-4147 "Adaptation of the bovine spongiform encephalopathy agent to primates and comparison with Creutzfeldt-Jakob disease: Implications for human health"
<http://www.pnas.org/cgi/doi/10.1073/pnas.041490898>
3. Directive 99-01: Donor Exclusion to Address Theoretical Risk of Transmission of Variant CJD through the Blood Supply.
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5. Hunter, N., et al. Transmission of prion diseases by blood transfusion. J. Gen. Virol., 83: 2897- 2905, 2002.
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8. Peden, Alexander, et al. "Preclinical vCJD after blood transfusion in a PRNP transgenic heterozygous patient." The Lancet (2004) 363: 527-528.
9. Monthly statistics on the cases of BSE determined through surveillance in the EU member countries.
http://europa.eu.int/comm/food/food/safety/bse/monthly_statistics_e2004_en.htm
10. Office International des Epizooties - Number of reported cases of BSE worldwide
http://www.oie.int/eng/info/en_esbmndb.htm
11. EUROCID and NEUROCID: The European and Allied Countries' Guidance Full Group of CID (EUROCID) plus the Extended European Collaborative Study of CID (NEUROCID)
<http://www.eurocid.ed.ac.uk/>
12. Statistics on the United Kingdom's CID cases
<http://www.cid.ed.ac.uk/figures.htm>
13. Number of cases of vCJD in France
http://www.invs.sante.fr/publications/mel_h_mpsas_mn2/