4. REGULATORY REQUIREMENTS

Blood establishments are required to submit a Licence Amendment Submission to the Blood and Tissues Division of the Biologics and Genetic Therapies Directorate (BGTD) for review.

An attachment must be included which indicates both the impacts that this measure will have on the donor base and plans to mitigate any such effects. Operators are also encouraged to develop materials to be used in explaining these deferral actions to affected donors in order to foster an appropriate understanding of these precautionary actions.

Regarding the withdrawal of prior donations by deferred donors, Health Canada, will require that all available components collected from these deferred donors, that have not been transfused 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 three 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 their 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 a specific country, a risk assessment will be carried out to determine specifically what deferral measures will be required.

The Directive, with a list of supporting references on the Background science, will be posted on an HC website.

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
Blood and Tissues Division
3rd Floor LCDC Building #6
Postal Locator 0603C
Tunney's Pasture
Ottawa, Ontario
KIA 0L2

7. REFERENCES

Scientific references used in the development of the Directive's "Background"Section:

1. Monthly statistics on the United Kingdom's CJD cases

http://www.doh.gov.uk/cjd/stats/aug01.htm

and EUROCJD and NEUROCJD: 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

(20)

Health Canada Santé Canada

April 22, 2005

Additional Donor Exclusion Measures to Address the Potential Risk of 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 licenced to fabricate blood and blood components for transfusion of the requirement to implement further measures to reduce the potential risk of transmission of vCJD through the blood supply. This is to 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 (WE) between the years 1980 and ongoing. These new requirements are in addition to those detailed 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, 2001[1].

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 3 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 the years 1980 to 1996; or
- have spent a cumulative period of time of 5 years or more in countries of WE consisting of Germany, Italy, Netherlands, Switzerland, Austria, Belgium, Spain, Republic of 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 UK, **France 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 BSE[2].

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, 1999[3], August 20, 2000[4] and August 30, 2001[1]. 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 transfusion[5].
- Research indicates that the intravenous route of transmission of BSE is highly efficient[6]
- 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 genotype[7].
- 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 is directing all Canadian blood establishments that are licenced to fabricate blood and blood components for transfusion to further reduce the risk of vCJD transmission through the blood supply by expanding the exclusion of donors who received a blood transfusion in the UK between the years 1980 and ongoing, to include France and WE. These blood establishments are required to submit a Licence Amendment Submission to the Biologics and Genetic Therapies Directorate (BGTD) for review.

An attachment must be included which indicates both the impacts that this measure will have on the donor base and plans to mitigate any such effects. Establishments are also encouraged to develop materials to be used in explaining these deferral actions to affected donors in order to foster an appropriate understanding of these precautionary actions.

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

4. SCOPE

This Directive applies to all Canadian blood establishments that are licenced to fabricate blood and blood components for transfusion. Products affected by the Directive include all blood components for transfusion with the exception of: autologous donations, peripheral blood stem cells collected for transplants, and rare blood types.

It is recommended that Canadian and non-Canadian manufacturers of plasma-derived products follow the donor exclusion requirements outlined in this directive.

5. CONSULTATIONS

The scientific finding have been discussed and advised upon by Health Canada's Expert Advisory Committee on Blood Regulation as well as the Health Products and Food Branch Public Advisory Committee. Also, Canadian Blood Services, Cangene, and Héma-Québec have been consulted in the development of this Directive.

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

6. COMPLIANCE DATE

The exclusion is to be introduced as soon as operationally feasible, but not later than three

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
KIA 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/bgtd-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. http://www.hc-sc.gc.ca/hpfb-dgpsa/bgtd-dpbtg/d99-01_e.html

4. Directive D2000-01: Donor Exclusion to Address Theorerical Risk of Transmission of Variant CJD Through the Blood Supply http://www.hc-sc.gc.ca/hpfb-dgpsa/bgtd-dpbtg/d2000-01_0830_e.html

5. Hunter, N., et al. Transmission of prion diseases by blood transfusion. J. Gen. Virol., 83: 2897- 2905, 2002.

6. Herzog, C., et al. Tissue distribution of bovine spongiform encephalopathy agent in primates after intravenous or oral infection. Lancet, 363: 422-428, 2004.

7. Llewelyn, C A, et al. "Possible Transmission of variant Creutzfeldt-Jakob disease by blood transfusion." The Lancet (2004) 363:417-421.

8. Peden, Alexander, et al. "Preclinical vCJD after blood transfusion in a PRNP codon 129 heterozygous patient." The Lancet (2004) 364:527-528.

9. Monthly statistics on the cases of BSE determined through testing in the European countries.
http://europa.eu.int/comm/food/food/biosafety/bse/mthly_reps_bse2004_en.htm

10. Office International des Epizooties - Number of reported cases of BSE worldwide
http://www.oie.int/eng/info/en_esbmonde.htm

11. EUROCJD and NEUROCJD: 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/

12. Statistics on the United Kingdom's CJD cases
http://www.cjd.ed.ac.uk/figures.htm

13. Number of cases of vCJD in France
http://www.invs.sante.fr/publications/mcj/donnees_mcj.html