plasma fractionation process (Foster, 1999). Studies with blood from endogenously infected animals (Brown *et al*, 1998; Foster, 2004) and blood spiked with high-titre brain homogenates (Foster *et al*, 2000, 2004; Tateishi *et al*, 2001; Reichl *et al*, 2002; Stenland *et al*, 2002; Vey *et al*, 2002), suggest that a number of steps in existing plasma fractionation processes should contribute individually to reduction in infectivity, including cryoprecipitation and cold ethanol fractionation, depth filtration, adsorption chromatography and nanofiltration. Some of these steps have also been studied in sequence, where it has been shown that, in general, the overall degree of prion removal exceeds that of any one individual step but is less than the sum of the individual steps (Foster, 2004).

Other measures

For the past 5 years the UK Transfusion Services have had an active policy of trying to optimise the use of all blood and blood products. An important component of this policy has been to ensure the appropriate use of red cell concentrates. The aim has been to prevent unnecessary red cell use as exemplified by Sirchia *et al* (1994). Such a policy not only reduces the risk of all transfusion-transmitted infections to each individual patient but it allows more patients to be treated with a scarce red cell resource.

Non-blood transfusion related strategies to prevent secondary spread of variant CJD horizontally in population

Between 1996 and 2004 several attempts were made to assess the risk of horizontal spread of variant CJD transmission by mechanisms other than blood products and make rational recommendations on appropriate safety measures (Bird, 2004). There has been concern about transmission in health care settings by invasive medical and surgical procedures. The second 2004 DNV risk assessment was informed by animal studies, which provided some measure of risk related to prion load in the inoculum. The aim was to try and identify the patients and procedures for which specific safety precautions should be instituted. Clearly some level of precaution was appropriate for patients who had clinical variant CJD, but for what other groups of individuals should precautions be taken? It was proposed that precautions should be taken for individuals who could be identified as having more than a 1% risk of exposure to an infectious dose of variant CJD prions (two ID_{50} extrapolated from experimental rodent studies).

The UK CJD Incidents Panel and Health Protection Agency offered advice based on the 2004 DNV risk assessment in relation to recipients of blood components and plasma products. Precautions were to be taken with all identified recipients of fresh blood components from donors who went on to develop variant CJD. For those who received fractionated plasma products, the risk from each was calculated on a product-by-product basis, dependent on the size of the donor pool, detail of the manufacturing process, and the dose of product that would give a 1% risk of exposure to an infectious dose (as defined above) was estimated. The products were divided into three groups based on the assessed risk. Those that were considered to pose a high risk were factors VIII/IX and antithrombin concentrates, where less than one injection of a therapeutic dose for an adult would exceed the risk threshold. Products in the medium risk group were those where the risk threshold would be exceeded if several or more treatments were given and included intravenous immunoglobulin and high doses of albumin. The low risk group consisted of products where very high doses, far in excess of those used in normal medical practice would be required to exceed the risk threshold, e.g. albumin used as an excipient in other products, intramuscular immunoglobulin.

Having defined the threshold dose of 'implicated' product it was necessary to identify which patients were likely to have received such a dose. For those with haemophilia and antithrombin deficiency, it would have been possible in principle to have identified all those patients known to have received implicated concentrates. But this was likely to represent a significant proportion of all UK haemophiliacs as, by September 2004, 16 batches of factor VIII and eight batches of factor IX were implicated and furthermore, it is likely that more batches used in treatment several years ago will become implicated as further former blood donors develop variant CJD in the future. It was therefore decided to use a 'population' approach and consider all haemophiliacs who had received clotting factor concentrate manufactured from UK plasma between 1980 (the beginning of the BSE epidemic) and 2001 (the expiry date of the last batch of product prepared from UK plasma) as being 'at risk of variant CJD for public health purposes'. Such a policy strongly, advocated by UKHCDO, was seen as the simplest and least threatening way to categorise those for whom extra precautions would need to be taken for certain invasive procedures. For other groups, e.g. those with immunodeficiency, patients are being reviewed individually and a decision made as to whether they would fall into the 'at additional risk of exposure to variant CJD for public health purposes' category (Hewitt, 2004).

For those considered to in the 'at additional risk of exposure to variant CJD for public health measures' group, either on the basis of population or individual assessment, the arrangements to prevent horizontal transmission have been laid out by the Advisory Committee on Dangerous Pathogens (http://www.hpa.org.uk/infections/topics_az/cjd/blood_products.htm). In such individuals CNS tissue constitutes a high risk of tissue infectivity and therefore potential contamination of surgical instruments. Surgery on lymphoid tissue or olfactory epithelium and the anterior chamber of the eye, e.g. cataract surgery, involved tissue of medium risk infectivity. Instruments for all these procedures should either be disposable or 'quarantined' after surgery and not reused. It has been suggested that some of these could profitably be used for research studies into decontamination techniques. All other surgeries, including dental and orthopaedic, were not considered to pose a significant risk of contaminating instruments with prions as the tissues were considered at low risk of infectivity and therefore no special precautions were advised.

With the publication of the primate study (Herzog *et al*, 2004), in which, following infection of Macaques with BSE prion both orally and intravenously, PrP^{Sc} was clearly demonstrated in the gut subepithelial neural plexuses as well as Payer's patches, it became clear that endoscopic biopsies of the gut mucosa could potentially contaminate the biopsy forceps and its channel in the instrument with PrP^{Sc}. Whilst the current recommendation is that endoscopes used for non-invasive procedures be cleaned and reused in the normal way, those used for invasive procedures, e.g. colonic biopsies, should be 'quarantined' and not reused. This has had major financial implications for hospitals.

Concluding remarks

Management of the risk of transmission of variant CJD and indeed, other prion diseases by blood and plasma products remains highly problematic (Wilson & Ricketts, 2004a,b). Although the relatively small and falling number of clinical cases in the UK is reassuring, data indicating that up to 90% of infected individuals may sustain long-term preclinical or subclinical disease and that most such individuals are likely to be currently in the 20–40 years age group suggests a significant pool of potentially infectious blood donors. Blood donor selection criteria are a blunt instrument for risk management and current measures, such as universal leucodepletion, seem likely to be only of limited efficacy. Blood donor screening assays and prion reduction filters offer a better chance of control, but much of the validation will need to be based on animal experimentation, the extrapolation of which to the human setting is problematic. Most new risk reduction measures are likely to be highly expensive and engender the possibility of alternative risks, including critical blood shortages. In this context, it is of increasing importance that health services work to ensure prescription of blood products only where they are required (Hart *et al*, 2004; McClelland & Contreras, 2005).

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Vaccines, Blood & Biologics

Questions and Answers on "Guida... Revised Preventive Measures ... Risk of Transmission of Creutzfeldt-... (CJD) and Variant Creutzfeldt-... Blood and Blood Products"

Why do we recommend new blood ... exposure to BSE and vCJD?

FDA is taking this step as a prudent m... supply by further reducing the theoretical ... recommended the first donor deferral ... to the vCJD agent, which is believed to be ... spongiform encephalopathy (BSE, or "mad c... deferral of donors who resided in the United Kingdom ... more between 1980 and 1996. At this time, we are ... donor deferrals for possible exposure to BSE and vCJD ... reasons:

1. Since 1999, the rate of vCJD cases in the U.K. ...
2. Significant exposures to potentially co... France and cases of vCJD have appe...
3. Significant exposures to potentially ... U.S. military bases in Europe
4. In Europe, outside the U.K., the BSE ...
5. Particularly in the U.K., transfusion ... to donors already infected with vCJD

What are the new donor deferrals ...

1. Residence in the U.K. for 3 months ...

Rationale: The U.K. has experienced the ... has the largest number of cases of vCJD ... U.K. instituted and enforced rules to prevent ... entering the human food chain (www.defra.... health/public-health-index.html). Due to these effective food protections, the risk of exposure to the BSE agent has been ... For this reason, the donor deferral extends only through 19...

2. Military personnel (current and former), and their d... spent time in military bases in northern Europe 198... 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 deferral for 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 will be deferred. However, in some locations, such as in large coastal cities where more people travel, up to 10% of donors may be deferred.

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

1. We have recommended two separate phases of deferral implementation, 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 the U.K. for 6 months or more, 1980-1996), in the rest (1980-present) of Europe and military bases (as described above), and 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 77% 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 of the additional risk reduction accomplished by the revised deferral policy and 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 level of loss of donors can be tolerated without causing local blood shortages.
3. The Department of Health and Human Services has established a system for monitoring the blood supply, nationwide, in an effort to detect supply shortages.
4. We continue to encourage more blood donations, and encourage among blood banks to assist each other in cases of local shortages.

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

Because it is still uncertain whether blood can transmit vCJD, and because it is possible that donor screening tests may be developed to identify blood carrying the disease, it is possible that you will be able to donate 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, 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 (PDF) (PDF - 93KB)

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Health Canada / Santé Canada

(19)

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

UNITED **KINGDOM, FRANCE &** ***WESTERN EUROPE***

Canada

1. PURPOSE

The purpose of this Directive is to advise all licensed Canadian blood establishments of [illegible] 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 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 5 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 other Western Europe(WE) consisting of Germany, Italy, Netherlands, Switzerland, Belgium, Spain, Republic of Ireland, Portugal, Denmark, Luxembourg, Liechtenstein, Andorra between the years 1980 and ongoing; or
- have received a transfusion of whole blood or labile blood components in the UK, France or WE 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 WE countries considers 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 is five years or more .

2. BACKGROUND

Variant Creutzfeldt-Jakob disease (vCJD), first described in 1996, is a "new" disease associated 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 substantive [illegible] limited knowledge available on certain biological effects associated with this infectious agent, lack of information on the concentration and infectivity of the vCJD prion in blood to allow for conclusion that it can not occur. In addition, a report that TSE in sheep can be transmitted within that species through blood transfusion, suggests that these diseases have the potential to spread through human blood [illegible] the Transmissible Spongiform Encephalopathies (TSE) can be transmitted [illegible] incubation period of the known TSE infections [illegible] vCJD and BSE [illegible] diagnostic procedures available for early detection. Consequently, Health Canada [illegible] to mitigate the risks of potential human to human transmission of vCJD with [illegible] 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 [illegible] that one must seek to apply measures which will reduce the targeted risk without [illegible] 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 [illegible]

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:

- 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;
- The number of observed BSE cases is increasing steadily in West European countries once thought to be free of the disease;
- Brain tissue from BSE-infected primates, injected intravenously into other primates, has been shown to transmit disease;
- 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 REQU[illegible]

Blood establishments are requir[illegible] Tissues Division of the Biologic[illegible]

An attachment must be included [illegible] the donor base and plans to miti[illegible] materials to be used in explaini[illegible] appropriate understanding of th[illegible]

Regarding the withdrawal of pri[illegible] that all available components co[illegible] or pooled for further manufactur[illegible]

5. COMPLIANCE DATE

The exclusion is to be introduce[illegible] months from the date of this Dir[illegible]

6. ADDITIONAL INFOR[illegible]

Blood operators will be required [illegible] donor bases and the supply of bl[illegible]

On an ongoing basis, Health Can[illegible] knowledge. If other cases of vC[illegible] carried out to determine specific [illegible]

The Directive, with a list of sup[illegible] an HC website.

Questions concerning the " Don[illegible] variant CJD through the Blood [illegible]
Biologics and Genetic Therapies [illegible]
Blood and Tissues Division
3rd Floor LCDC Building #6
Postal Locator 0603C
Tunney's Pasture
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KIA 0L2

7. REFERENCES

Scientific references used in the [illegible]

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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/
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and Office International des Epizooties - Number of reported cases of BSE worldwide
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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

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 that fabricate blood and blood components for transfusion of the requirement to implement measures to reduce the potential risk of transmission of vCJD through the blood supply to be accomplished by screening and excluding from donating blood, all persons who 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 outlined 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 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 5 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, 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 knowledg[illegible] establishments that are licenced to fabricate [illegible] further reduce the risk of vCJD transmissi[illegible] exclusion of donors who received a blood transfusion [illegible] ongoing, to include France and WE. These [illegible] Licence Amendment Submission to the Biologics and [illegible] review.

An attachment must be included which indicates [illegible] the donor base and plans to mitigate any such effects. [illegible] develop materials to be used in explaining these deferr[illegible] foster an appropriate understanding of these precaut[illegible]

Regarding the withdrawal of prior donations by defer[illegible] that all available components collected from these do[illegible] or pooled for further manufacture, be retrieved.

4. SCOPE

This Directive applies to all Canadian blood establ[illegible] and blood components for transfusion. Products [illegible] components for transfusion with the exception of [illegible] cells collected for transplants, and rare blood types.

It is recommended that Canadian and non-Canadian [illegible] follow the donor exclusion requirements outlined in [illegible]

5. CONSULTATIONS

The scientific finding have been discussed and advised by the Canadian Advisory Committee on Blood Regulation as well as the Canadian Public Advisory Committee. Also, Canadian blood [illegible] been consulted in the development of this Directive.

The blood donor loss as a result of this new [illegible]

6. COMPLIANCE DATE

The exclusion is to be introduced as soon as [illegible]

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/bgtd-dpbtg/blooddeferral_uk_france_we_e.html

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http://www.pnas.org/cgi/doi/10.1073/pnas.041490898

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

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http://www.eurocjd.ed.ac.uk/

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http://www.cjd.ed.ac.uk/figures.htm

13. Number of cases of vCJD in France
http://www.invs.sante.fr/publications/mal_transm/vcjd.htm