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 5% of blood donors may 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 new donor deferrals?

1. We have recommended two separate phases of donor deferrals, to spread out the potential impact on supplies over time. Phase I will start May 31, 2002, and includes deferral of people who lived in the U.K. (3 months or more, 1980-1996), in France (1980-present), or 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 59% of current potential vCJD risk.

For blood donors who lived in Europe for 5 years or more, deferrals will start on October 31, 2002. Phase II will provide the balance (18%) 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 whether the loss of donors can be tolerated without causing local blood shortages.
3. The Department of Health and Human Services has instituted a system for monitoring the blood supply, nationwide, in an effort to detect blood supply shortages.
4. We continue to encourage more blood donations, as well as cooperation 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 exclude anyone 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 blood or 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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(19)

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 licenced 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 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 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 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 amounts to 5 years or more .

2. BACKGROUND

Variant Creutzfeldt-Jakob disease (vCJD), first described in 1996, is a "new" disease, linked 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 causative agent, together with limited knowledge available on certain biological effects associated with this infection (e.g. 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 sheep can be transmitted within that species through blood transfusion, suggests that theoretically, vCJD may have the potential to spread through human blood or blood derivatives. 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 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 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.