APPENDIX A

Variable: $Prev_{Asym\text{-}vCJD(age)}$- Prevalence of asymptomatic vCJD infected individuals in the UK by age groups (cases/million).

The prevalence of asymptomatic vCJD cases in the UK by age group is estimated using the equation:

$$Prev_{Asym\text{-}vCJD(age)} = Asym\text{-}_{vCJD(age)} / Pop_{UK(age)} \qquad \text{(IV.A.2-5)}$$

A-IV. A. 3. b. Estimating the UK vCJD prevalence derived from tissue surveillance for each age group

For the risk assessment model we converted the 3 in 12,674 presumptive positive rate to an average rate of vCJD in the UK population of 1 in 4,225 (and used the 1 / 20,300 to 1 / 1,450 at 95% CI; proportions were converted from the 95% CI reported by Hilton et al (2004)). Demographic information of reported vCJD cases **(Table A-4.3)** indicated that the younger population (20 -29 yrs of age) that was deliberately oversampled in this study may have been more susceptible to the disease. The vCJD prevalence among UK donors might, therefore, be over-represented by the prevalence of 20-29 years age group derived from the surveillance study. Assuming the sensitivity and specificity of the testing method is 100%, the estimated rate of 1 in 4,225 translates roughly to a vCJD prevalence of 237 cases per million (95% CI: 49 – 692 cases per million) for all age groups. The authors (Hilton et al 2005) indicated that approximately 60% of the samples tested (from 7,600 patients) came from patients 20-29 years of age. Among the 20-29 year old group we calculated a vCJD prevalence of approximately 400 cases per million for which we assumed a 95% CI of 100-1200 cases per million.

We then derived the prevalences for the remainder of the UK donor population by determining the proportional difference between the vCJD prevalence from the tissue study group and the number of actual reported vCJD cases for donors in the 20-29 years age group. This proportion was then applied to the remaining age groups in the distribution of reported vCJD cases to determine the prevalence for each age group. By multiplying our extrapolated vCJD prevalence for incubating cases by the total donor population we were able to estimate the number of possible incubating vCJD cases in each US donor age group. We assumed that a plasma pool used to manufacture pdFVIII product in the US in the year 2002 consisted 6,000 to 360,000 donations, and several donations in the pool likely came from the same donor. The estimated prevalence was then used to generate variables and parameters representing the potential number of vCJD donors or donations that might be present in a plasma pool.

Variable: $Prev_{Asym\text{-}vCJD(20\text{-}30)}$. Prevalence of asymptomatic vCJD infected individuals in the UK 20-30 year old age group (cases/million)

Assumptions used in the model: The vCJD infectious agent is present in the blood of the individual when the the accumulation of prion protein can be detected in lymphoreticular tissue. Prevalence of vCJD asymptomatic individuals in the UK 20-30 year old age group is likely to be 400 cases/million, 95% CI=100-1200 cases/million. The values for this variable were estimated from the Hilton *et al* studies (2000, 2002, 2004).

Variable: $Pop_{UK(age)}$- Population in the UK by age groups (Thousands).

Data used in the model: The data for UK population were sourced from UK government statistics (UK National Statistics, 2005). Where UK data were organized in broader categories of 10 to 15 years we allocated population equally among smaller 5 year age groups.

Variable: $Asym\text{-}vCJD_{(20\text{-}30)}$ - The number of asymptomatic vCJD infected individuals in the 20-30 yr-old UK age group. This variable is represented by the equation:

$$Asym\text{-}vCJD_{(20\text{-}30)} = Prev_{vCJD(20\text{-}30)} \times Pop_{UK(20\text{-}30)} \quad \text{(IV.A.2-1)}$$

Variable: $Asym\text{-}vCJD_{(age)}$ - Number of asymptomatic vCJD infected individuals in the UK by age groups

Assumptions used in the model: Number of asymptomatic vCJD infected individuals from an age group is proportional to the percentage of reported vCJD cases from that age group. The age distribution of asymptomatic vCJD cases was assumed to be the same as that of symptomatic cases.

The number of asymptomatic vCJD individuals in the UK per age group was estimated using the following equation:

$$Asym\text{-}vCJD_{(age)} = Asym\text{-}vCJD_{(20\text{-}30)} \times (Perc_{vCJD(age)} / Perc_{vCJD(20\text{-}30)}) \quad \text{(IV.A.2-2)}$$

Variable: $Prev_{Asym\text{-}vCJD(age)}$- Prevalence of asymptomatic vCJD infected individuals in the UK by age groups (cases/million).

The prevalence of asymptomatic vCJD cases in the UK by age group is estimated by the equation:

$$Prev_{Asym\text{-}vCJD(age)} = Asym\text{-}_{vCJD(age)} / Pop_{UK(age)} \quad \text{(IV.A.2-3)}$$

A-IV. B. Estimation of vCJD Prevalence in US Plasma Donors and Plasma Pools (Module 2)

A-IV. B. 1. a. Annual US plasma donors and characterization by age

A-IV. B. 1. b. Source Plasma collection in the United States: characterized by donor age

Variable: DN_S– Annual number of Source Plasma units used to make pdFVIII .

Assumption used in the model: It was assumed that, on average, 3.3 million units of Source Plasma were used in each year to make pdVIII. It was further assumed that there is a 10% standard deviation in the number of Source Plasma units used to make pdFVIII for any given year.

Data used in the model: The annual number of Source Plasma units was back calculated based on annual units of pdVIII product made from Source Plasma, the average yield of pdFVIII (187 units per liter

plasma) and average volume of single unit of Source Plasma (700 ml per unit). The information on annual units of pdFVIII made from plasma collected in the US, yield of factor VIII and unit volume of plasma were collected from pdFVIII manufacturers.

Variable: DR_S–Annual number of donors who contribute Source Plasma for manufacture of pdFVIII.

Assumption used in the model: It was assumed that there are approximately 1 million Source Plasma donors in the US each year. It was further assumed that Source Plasma from any individual donor may be used to make pdFVIII. Therefore, we calculated that there were approximately 1 million donors who contributed Source Plasma for the manufacture of pdFVIII. It was further assumed that there could be a 10% standard deviation in the number of donors in any given year.

Variable: *Age* – Age information for US plasma donors was grouped in a two year increment for 18-19 years old because the model assumed that 18 was the minimum age of donation. The remaining population was grouped by 5-year increments – including 20- 24yrs old, 25-29yrs old, and so on

Variable: $DR_{S\text{-}perc(age)}$ - The percentage of Source Plasma donors from a given age group.

Data used in the model: Distribution of US Source Plasma donors by age was obtained from the Plasma Protein Therapeutics Association (2005). Where data (PPTA, 2005) were organized in broader age groups of 10 years or 15 years, we generated 5-year age subgroups by allocating the percentage equally among each subgroup.

Variable: $DR_{S(age)}$ – The annual Source Plasma donors by age groups who contribute plasma for pdFVIII manufacturing is represented by the equation:

$$DR_{S(age)} = DR_S \times DR_{S-perc(age)} \qquad \text{(IV.B.1-1)}$$

A-IV. B. 1. c. Recovered plasma collection in the United States: Characterized by donor age

Variable: DN_R - Annual units of recovered plasma used to make pdFVIII.

Assumption used in the model: It was assumed that approximately 1,800,000 units of recovered plasma are used to make pdFVIII annually. This estimation was generated by backcalculation beginning with the total quantity of pdFVIII manufactured in the US. It was further assumed that there was a 10% standard deviation in the number of units for any given year.

Data used in the model: The annual number of total units of pdFVIII manufactured from recovered plasma collected in the US was estimated by back calculation. The calculation was based on the total quantity of annual units of pdVIII product made from recovered plasma collected in the US. We can further estimate the number of donations used to make the pdFVIII from recovered plasma using estimates in the literature for the average yield of pdFVIII 187 units per liter of plasma (WFH, 2004) and average volume of single unit of recovered plasma (200 ml per unit). The information on annual units of pdFVIII made from plasma collected in the US was collected from pdVIII manufacturers.

Variable: $DN_{Bl\text{-}perc(age)}$ – The percentage of blood units donated by a given age group.

Data used in the model: Distribution of blood units by donor age group was obtained from Westat data provided to FDA in 2002 (Data shown in A-4.3).

Variable: $DN_{R(age)}$ – Annual units of recovered plasma used to make pdFVIII by donor age group

$$DN_{R(age)} = DN_R \times DN_{Bl-perc(age)} \quad \text{(IV.B.2-1)}$$

Variable: $DR_{R(age)}$ – Annual number of donors by age group who contribute recovered plasma that is used for manufacture of pdFVIII

Assumption used in the model: Each unit of recovered plasma used to make pdFVIII comes from different donors. Therefore, number of donors from an age group equals the number of donations from that age group.

The annual number of recovered plasma donors by age group was calculated using the equation:

$$DR_{R(age)} = DN_{R(age)} \quad \text{(IV.B.2-2)}$$

Variable: DR_R - The annual total of potential recovered plasma donors who contribute the plasma that is used for manufacture of pdFVIII, which was estimated in the model using the summation function:

$$DR_R = \sum_{age=12-19}^{70-74} DR_{R(age)} \quad \text{(IV.B.2-3)}$$

A-IV. B. 2. Total plasma donors and donations- for manufacture of pdFVIII in the US

Variable: DR_{Tot} - The annual total of potential plasma donors who contribute plasma for pdFVIII manufacturing is estimated by summing the number of Source Plasma donors and recovered plasma donors and is represented by the equation:

$$DR_{Tot} = DR_S + DR_R \quad \text{(IV.B.3-1)}$$

Variable: DN_{Tot} - The annual total of potential plasma units used to make pdFVIII is estimated by summing the number of Source Plasma donations and recovered plasma donations and is represented by the equation:

$$DN_{Tot} = DN_S + DN_R \quad \text{(IV.B.3-2)}$$

A-IV. C: Estimation of the probability that a plasma pool may contain a donation from an infected donor that contains vCJD agent

IV.C. 1. US plasma donors with history of travel to the UK, France or other Countries in Europe: Annual number potentially infected and vCJD agent is present in the blood

A-IV. C. 1. a. US plasma donors with history of travel to the UK: Number of donors potentially infected and vCJD agent is present in the blood

A-IV. C. 1. a. i. US plasma donors with history of travel to the UK: Percentage of donors and duration of travel

The risk of vCJD infection in US plasma donors is a function of the intensity of exposure to the BSE agent. The intensity of exposure is assumed to be proportional to the amount of time spent, or duration of travel, in the UK and the prevalence of BSE in UK cattle during the period from 1980 – 1996. The FDA model used data from the National Blood Donor Travel Survey 1980-1996 (TSEAC 2000) to derive estimates of the percentages of US donors with a history of extended travel or residence ($\geq$ 3 months) in the UK during 1980-1996, and to derive the frequencies for various durations of travel for 3 months or more. The period of 3 months or more corresponds to the length of time in the current policy that defers donors that traveled to or resided in the UK. The travel survey data on blood donors pose a limitation because the survey was conducted on whole blood donors and may not exactly reflect the travel histories of plasma donors. Unfortunately, to our knowledge there is not travel data available on plasma donors. Therefore, we assumed that plasma donor travel characteristics to the UK and other countries in Europe since 1980 are similar to those of whole blood donors and used this information in the FDA risk assessment. Some may argue that plasma donors travel less frequently than their blood donor counterparts so use of data on blood donors may overestimate the risk.

Data used in the model: National Blood Donor Travel Survey 1980-1996 was conducted by the American Red Cross and presented at the Transmissible Spongiform Encephalopathies Advisory Committee (TSEAC 2000).

Variable: i - The duration interval used to group donors who traveled to the UK from 1980-1996 based on the quantity of time spent in the UK during the period from 1980 – 1996.

Variable: D_i - The average duration of time (in months) for interval i representing the duration of travel or residence by US donors in the UK during the period from 1980 – 1996.

Variable: $CumPerc_{BIDR\text{-}UKi}$ – The cumulative percentage of blood donors who traveled to the UK within duration interval i or longer.

Variable: $Perc_{BIDR\text{-}UKi}$ - Percentage of blood donors who traveled to the UK within duration interval i. This variable was converted from $CumPerc_{BIDR\text{-}UKi}$

Variable: $Perc_{BIDR\text{-}UKi/UK}$ - The percentage of blood donors who traveled for a specific duration interval *i* among all donors who have ever traveled to the UK is represented by the equation:

$$Perc_{BIDR-UKi/UK} = (Perc_{BIDR-UKi} / CumPerc_{BIDR-UK,i>1day-1month}) \times 100\% \quad \text{(IV.C.1.a-1)}$$

A-IV.C.1.a.ii. All US plasma donors with a history of travel to the UK: Percentage and number of donors in each age group by year and duration of travel

For the purposes of our analyses we grouped all donors and donors who traveled to the UK between 1980 and 1996 into age groups of five year increments (20 – 24yrs, 25 – 29 yrs, etc). Because the minimum age of donation is 18, the model also included the donor group 18 & 19 years of age. The percentage of donors in each age group who traveled to the UK between 1980 and 1996 was calculated based on the total annual number donors who traveled to the UK between 1980 and 1996 compared to (or divided by) the total number of donors, and the age specific odds ratio for travel.

As mentioned earlier, data are lacking on the travel characteristics of plasma donors, so the FDA used travel survey data collected from blood donors to estimate past travel history. Because plasma donors are less likely to travel use of these data may yield an overestimate of the actual risk. Characteristics of blood donors on travel including the percentage of donors from each age group who traveled to the UK during period between 1980 and 1996, and distribution of donor travel by duration were applied to plasma donors for estimation of the number of plasma donors from each age group who have traveled or resided in the UK from 1980 to 1996 for specific periods of time ranging from less than 3 months to greater than 5 years duration. Furthermore, the model used data that detailed the number of annual visits of US travelers to the UK to allocate donor travel specifically to an individual calendar year.

- **Calculation of the annual number of blood donors who traveled to the UK from 1980 through 1996**

Blood donors donate whole blood and soon after the liquid plasma portion of whole blood is separated and plasma is called recovered plasma. The model assumes that approximately 200 mls of recovered plasma are produced from a unit of whole blood.

Variable : DR_{BI}-The annual total number of potential blood donors in the US per year

Data used in the model: There are approximately 8 million individuals who donate blood each year in the United States (Westat, 2002).

Variable: $Perc_{BIDR\text{-}UK}$ - Percentage of US blood donors who traveled to the UK during the period from 1980 through 1996.

Data used in the model: Approximately, 22.5% of US blood donors have a history of travel to the UK any time during the period from 1980 through 1996, according to data contained in the National Blood Donor Travel Survey (TSEAC 2000).

Variable: $DR_{BI\text{-}UK}$ -Total number of blood donors estimated to have traveled to the UK from 1980 through 1996

$$DR_{BI-UK} = DR_{BI} \times Perc_{BIDR-UK} \quad \text{(IV.C.1.a-2)}$$

- **Calculation of the percentage of blood donors for each specific age group**

Variable: *Age*- Age of donors grouped in 5 year increments (e.g., 20 – 24 yrs, 25 – 29yrs, etc.) per year and 18-19 yr old age cohort.

Variable: $Perc_{BIDR(age)}$ Percentage blood donors in a specific age group.

Variable: ***BLDR(age)***- Annual number of blood donors in a specific age group

$$Perc_{BLDR(age)} = BLDR(age) / \sum_{age=18-19}^{65-69} BLDR(age) \quad \text{(IV.C.1.a-3)}$$

Variable: ***BLDN***-Annual total number of blood donations in the US.

Variable: $Perc_{BIDN(age)}$- Percentage of blood donations in each specific age group of US donors.

Data used in the model: Percentage of blood donations by age group was obtained from Westat (2002).

Variable: $Freq_{BIDN(age)}$-Average annual number of blood donations from a donor in a specific age group

Data used in the model: Information on the average annual number of donations bydonors in each specific age group was obtained from Westat (2002).

$$BLDR(age) = BLDN \times Perc_{BLDN(age)} / Freq_{DN(age)} \quad \text{(IV.C.1.a-4)}$$

Replace *BLDR(age)* in equation IV.C.1.a-3 with equation IV.C.1.a.-4, resulting in the expression:

$$Perc_{BIDR(age)} = (Perc_{BIDN(age)} / Freq_{BIDN(age)}) / \sum_{age=18-19}^{65-69} (Perc_{BIDN(age)} / Freq_{BIDN(age)}) \quad \text{(IV.C.1.a-5)}$$

Variable : DR_{BI}-The annual total number of blood donors in the US, which is assumed to be 8 million.

Variable: $DR_{BI(age)}$- The annual number of blood donors in each five-year age group and the18-19 yr old age cohort.

$$DR_{BI(age)} = DR_{BI} \times Perc_{BIDR(age)} \quad \text{(IV.C.1.a-6)}$$

Variable: $DR_{BI\text{-}UK}$ -Total number of US blood donors who have traveled to the UK during the period 1980 - 1996

Variable: $Perc_{BIDR\text{-}UK(age)}$ - The percentage of US blood donors in an age group who traveled to the UK during the period 1980 - 1996.

$$DR_{BI-UK} = \sum_{age=18-19}^{65-69} (Perc_{BIDR-UK(age)} \times DR_{BI(age)}) \qquad \text{(IV.C.1.a-7)}$$

Variable: $Odd_{T(age)}$- Age specific odd ratios for travel compared to the age group 18-19 years.

Data used in the model: The odds ratios for likelihood of travel for each age group were derived from the travel data obtained from 1980-1996 blood donor travel survey. An odds ratio of 1 was assigned to the donor group aged 18-19 years. The odds ratios for other age groups is a function of the travel frequency of those age groups compared to the travel frequency of the age group of 18-19 years

$$Perc_{BIDR-UK(age)} = Odd_{T(age)} \times Perc_{BIDR-UK(18-19)} \qquad \text{(IV.C.1.a-8)}$$

Replacing the variable, $Perc_{BIDR\text{-}UK(age)}$, in equation IV.C.1.a-7 with equation IV.C.1.a-8 the percentage of blood donors in the age group of 18-19 years of age who traveled to the UK was calculated using the following equation:

$$Perc_{BIDR-UK(18-19)} = DR_{BI-UK} / \sum_{age=18-19}^{65-69} (Odd_{T(age)} \times DR_{BI(age)}) \qquad \text{(IV.C.1.a-9)}$$

A-IV. C. 1. a. ii. a. Number of US Source Plasma donors who traveled to the UK in a specific year from 1980 to 1996 and by age group

Variable: *age* - Age of US plasma donors in groups by 5-year increments and 18-19 yr old age cohort.

Variable: $DR_{S(age)}$ (calculated in section A-IV.B. 1.) - The annual number of donors by age group who contribute Source Plasma to make pdFVIII.

Variable: $Perc_{BIDR\text{-}UK(age)}$ (calculated in section A-IV.C.1.a.i.b.) - the percentage of blood donors in each age group who traveled to the UK between 1980-1996.

Variable: $DR_{S\text{-}UK(age)}$ - Number of Source Plasma donors who traveled to the UK from 1980 through 1996 by age groups.

Assumptions used in the model: The percentage of Source Plasma donors who traveled to the UK is the same as the percentage of blood donors of the same age group.

The number of Source Plasma donors who traveled to the UK from 1980 to 1996 by age group is represented by:

$$DR_{S-UK(age)} = DR_{S(age)} \times Perc_{BIDR-UK} \quad \text{(IV.C.1.a-8)}$$

The risk of vCJD infection in US donors who traveled to the UK was assumed proportional to the relative level of exposure to the BSE agent in each year through the UK food supply. The proportional risk was derived based on the number of BSE-reported cattle in a given year from 1980 through 1996 divided by the total number of BSE cases to date. The model generates categories (or bins) for Source Plasma donors by year of travel and estimates the risk more accurately by incorporating the information about proportional risk due to the BSE epidemic in the UK

In 1996 after the emergence of human vCJD cases the UK government implemented stringent food chain controls that decreased the number of high risk animals and high risk tissues containing BSE agent from entering the human food supply. In the early 1980s human exposure may have begun at a low level as BSE spread among the UK cattle population. The BSE epidemic expanded throughout the 1980s and peaked in 1992, then risk started to decrease as animal feed measures were implemented and more stringent human food chain controls were implemented in 1996. Today, a few hundred cases of BSE are identified in the UK annually – but it is unlikely that the animals or products from BSE-infected animals in the UK enter the human food supply. The model incorporates the changing dynamics of the BSE epidemic since 1980 and accounts for relative changes in the levels of human, specifically US plasma donors, exposure to the BSE agent and possible vCJD infection.

Variable: y - Calendar year of travel.

Variable: V_y - Number of visits by year to the UK by US travelers (in thousands)

Data used in the model: Number of visits by year to the UK by US travelers (UK Government Statistics, 2005).

The yearly distribution of travel visits by each age group was adjusted to account for the minimum age of 18 when a donor can donate plasma or blood. Therefore, in calculating the US donor risk for vCJD the yearly distribution of travel visits by each age group was adjusted to account for this requirement. The model adjusted the potential vCJD exposure for younger donors who were born during the period from 1980 to 1986 and would have essentially a zero chance of being exposed to the BSE agent in the years prior to their birth. Therefore, donors 18 years of age in 2002 were assumed to have zero exposure to the BSE agent prior to 1985, those 19 years of age in 2002 were assumed to have zero exposure prior to 1984, those 20 years of age in 2002 were assumed to have zero exposure prior to 1983, those 21 years of age in 2002 were assumed to have zero exposure prior to 1982, those 22 years of age in 2002 were assumed to have zero exposure prior to 1981. The model assumed that there was zero exposure of all donors prior to 1980.

<u>Assumption used in the model</u>: US <u>Source Plasma</u> donors have similar travel patterns to the US blood donor population, which is assumed to be similar for the larger US population.

Assumption used in the model: It was assumed that no US traveler visited the UK more than once per year. This may potentially overestimate the vCJD risk for US plasma donors (because repeat travel by the

same donor is not addressed) and underestimate it in certain other cases (travelers who visit multiple times per year). FDA found no data that quantified the numbers of multiple visits or repeat visits by the same traveler that likely occurred for US donors with a history of UK travel.

Variable: $V_{y/1996}$ - The number of visits to the UK by US travelers in year y compared to the number of visits in 1996 is represented by the equation:

$$V_{y/1996} = V_y / V_{1996} \qquad \text{(IV.C.1.a-9)}$$

Variable: ***age*** - Age of US plasma donors in groups of 5-year increments (e.g., 20-24 yrs, etc.) and 18-19 yr old age cohort..

Variable: $DR_{S(age)}$ (calculated in section A-IV.B. 1.) - the annual Source Plasma donations by age groups.

Variable: $DR_{S\text{-}UK(age)}$ - Number of Source Plasma donors who traveled to the UK from 1980 through 1996 by age group in five-year increments and 18-19 yr old age cohort.

Assumptions used in the model:

- The same percentage of Source Plasma donors traveled to UK as blood donors
- Frequencies of travels are similar among the donors of different age groups.
- Travel rates for the general US population are the same as the travel rate for blood and plasma donors.

The number of Source Plasma donors who traveled to the UK from 1980 to 1996 by age group is represented by:

$$DR_{S\text{-}UK(age)} = DR_{S(age)} \times Perc_{DR\text{-}UK} \qquad \text{(IV.C.1.a-5)}$$

Variable: $DR_{S\text{-}UK(age),y}$ - the number of Source Plasma donors who traveled to the UK in year y by age group

Source Plasma donors with a history of travel to the UK among each age group ($DR_{S\text{-}UK(age)}$) was allocated to individual travel years based on the yearly distribution of visits to the UK by US travelers (UK National Statistics, 2005). The yearly distribution of travel visits by each age group was adjusted to account for the minimum age of 18 when a donor can donate plasma or blood. Therefore, in calculating the US donor risk for vCJD the yearly distribution of travel visits by each age group was adjusted to account for this requirement. The model adjusted the potential vCJD exposure for younger donors who were born during the period from 1980 to 1986 and would have essentially a zero chance of being exposed to the BSE agent in the years prior to their birth. Therefore, donors 18 years of age in 2002 were assumed to have zero exposure to the BSE agent prior to 1985, those 19 years of age in 2002 were assumed to have zero exposure prior to 1984, those 20 years of age in 2002 were assumed to have zero exposure prior to 1983, those 21 years of age in 2002 were assumed to have zero exposure prior to 1982, those 22 years of age in 2002 were assumed to have zero exposure prior to 1981. The model assumed that there was zero exposure of all donors prior to 1980.

<u>Assumption used in the model</u>: US Source Plasma donors have similar travel patterns as the general US population and US blood donors.

The number of US Source Plasma donors who have traveled to the UK in year y between 1980-1996 is represented by the equation:

$$DR_{S-UK(age)y} = DR_{S-UK(age)} \times V_{y/1996} / \sum_{y=1980}^{1996} V_{y/1996} \quad \text{(IV.C.1.a-10)}$$

A-IV. C. 1. a. ii. b. US Source Plasma donors with history of travel to the UK: Duration of travel by age group

There were no data that we are aware of that details the travel histories of Source Plasma donors in the US. Travel data for US blood donors was used to estimate travel patterns for Source Plasma donors after an adjustment for the frequency of travel based on the age of Source Plasma donors and the age-specific odds ratios for travel, which was obtained from 1980-1996 Blood Donor Travel Survey (TSEAC, 2000). The model used the data on the number of Source Plasma donors who have traveled to the UK in a specific year and subdivided those individuals into additional categories based on estimated duration of stay. The categories of duration of stay was estimated based on the Blood Donor Travel Survey (TSEAC, 2000). Use of blood donor travel data in the model implicitly assumes that travel rates are similar for both blood and plasma donors. However, it is thought that plasma donors likely travel less and are therefore at lower risk for vCJD, therefore the model results may overestimate the potential vCJD risk for plasma donors.

Variable: i - The duration interval used to group blood donors who had traveled to UK from 1980-1996 based on the time they spent in the UK (same variable used above in section A-IV. C. 1. a. i.).

Variable: D_i - The average duration of time for interval i (months) (same variable used above in section A-IV. C. 1. i.).

Variable: $DR_{S-UK(age),y}$ - the number of Source Plasma donors who traveled to the UK in year y by age group (calculated in A-IV. C. 1. a. ii. (a))

Variable: $Perc_{BIDR-UKi/UK}$ - The percentage of blood donors who traveled for a specific duration interval i among all donors who have ever traveled to the UK (calculated in A-IV. C. 1. a. i. a)

Variable: $DR_{S-UK(age)y,i}$ - Number of Source Plasma donors within a specific age group that traveled to the UK in year y for a duration of i and is represented by the equation:

$$DR_{S-UK(age)y,i} = DR_{S-UK(age)y} \times Perc_{DR-UKi/UK} \quad \text{(IV.C.1.a-11)}$$

A-IV. C. 1. a. ii. c. Number of US recovered plasma donors with a history of travel to the UK in a specific year from 1980 – 1996 by age group

Recovered plasma is plasma that is separated or "recovered" from a unit of whole blood soon after the blood is collected. As expected, recovered plasma donor donation characteristics mirror those of whole blood donors. A recovered plasma donor can donate plasma a maximum of six times per year (or once every 54 days)– and on average we assumed a recovered donation is approximately 200 milliliters (versus an average of 700 milliliters for a Source Plasma donation).

Variable: y – year of travel (same variable used above in section A-IV. C. 1. a. ii. a) to the UK during the period 1980 - 1996 by US plasma donors.

Variable: age – age groups of the population in five-year increments (same variable used above in section A-IV. B. 1.).

Variable: $DR_{R(age)}$ - number of potential recovered plasma donors per year by age group (described in section A-IV. B. 2).

Variable: $Perc_{BIDR\text{-}UK(age)}$ (calculated in section A-IV.C.1.a.i.b.) - the percentage blood donors in each specific age group who have traveled to the UK between 1980-1996.

Variable: $DR_{R\text{-}UK(age)}$ – The number of recovered plasma donors who have traveled to the UK from 1980 through 1996 by age group and is represented by the equation:

$$DR_{R-UK(age)} = DR_{R(age)} \times Perc_{BIDR-UK(age)} \qquad \text{(IV.C.1.a-12)}$$

The model categorizes US recovered plasma donors by year of travel in order to estimate the potential vCJD risk more accurately by incorporating the information about BSE epidemic in the UK. The number of beef cattle affected each year by the BSE epidemic in the UK changed throughout the epidemic. Donors who visited the UK at the height of the BSE epidemic in 1992, we assumed, were more likely to be exposed to BSE agent (and vCJD risk) than a donor who visited in 1996 after food chain controls were implemented. The model accounts for this changing exposure potential by analyzing US donors who may have traveled to the UK for each year from 1980 through 1996. The number of recovered plasma donors who traveled to the UK was allocated to individual travel year based on the yearly distribution of visits to the UK by US travelers determined from UK travel data.

Variable: $DR_{R\text{-}UK(age)}$ - Number of recovered plasma donors traveled to the UK from 1980 through 1996 by age groups (calculated above).

Variable: $V_{y/1996}$ - The number of visits to the UK by US travelers in year y compared to the number of visits in 1996 (calculated in A-IV.C.1.a. ii. a.).

Data used in the model: Number of visits by year to the UK by US travelers was determined using UK Government Statistics (2005).

Assumption about variable: US recovered plasma donors have a similar travel pattern as the US total population. The yearly distribution of travel visits by each age group was adjusted to account for the minimum age of 18 when a donor can donate plasma or blood. Therefore, in calculating the US donor risk for vCJD the yearly distribution of travel visits by each age group was adjusted to account for this requirement. The model adjusted the potential vCJD exposure for younger donors who were born during

the period from 1980 to 1986 and would have essentially a zero chance of being exposed to the BSE agent in the years prior to their birth. Therefore, donors 18 years of age in 2002 were assumed to have zero exposure to the BSE agent prior to 1985, those 19 years of age in 2002 were assumed to have zero exposure prior to 1984, those 20 years of age in 2002 were assumed to have zero exposure prior to 1983, those 21 years of age in 2002 were assumed to have zero exposure prior to 1982, those 22 years of age in 2002 were assumed to have zero exposure prior to 1981. The model assumed that there was zero exposure of all donors prior to 1980.

The number of recovered plasma donors who traveled to the UK in year *y* by age groups during the period from 1980-1996 is represented by the equation:

$$DR_{R-UK(age)y} = DR_{R-UK(age)} \times V_{y/1996} / \sum_{y=1980}^{1996} V_{y/1996} \qquad \text{(IV.C.1.a-13)}$$

A-IV. C. 1. a. ii. d. US recovered plasma donors with history of travel to the UK: Duration of travel by age group

Recovered plasma donors who traveled to the UK in a specific year ($DR_{R-UK(age)y}$) in the years 1980-1996 were further partitioned in the model into subgroups or "bins" based on travel duration and by 5-year age groups and 18-19 yr old age cohort. Data on the percentage of blood donors who traveled to the UK since 1980 for a certain duration(s) (TSEAC 2000) was used in this risk assessment.

Variable: i - The duration interval used to group blood donors who had traveled to the UK from 1980-1996 based on the time they spent in the UK (same variable used above in section A-IV. C. 1.)

Variable: D_I - The average duration of time for interval i (months) (same variable used above in section A-IV. C. 1.)

Variable: $DR_{R-UK(age)y}$ - The number of recovered plasma donors who traveled to the UK in year *y* by age group (calculated in A-IV. C. 1. a. ii. c)

Variable: $Perc_{BIDR-UKi/UK}$ - The percentage of blood donors who traveled for a specific duration interval i among all donors who have ever traveled to the UK (calculated in A-IV. C. 1. a. i. a)

Variable: $DR_{R-UK(age)y,i}$ - The number of recovered plasma donors among an age group who have traveled to the UK in year, *y* ,for duration of i and represented by the expression:

$$DR_{R-UK(age)y,i} = DR_{R-UK(age)y} \times Perc_{DR-UKi/UK} \qquad \text{(IV.C.1.a-14)}$$