A-IV. C. 1. b. v. b. Number of US Source Plasma donors with history of travel to France and potentially infected and vCJD agent is present in the blood

Perhaps the most critical component of the model is the estimation of whether a plasma donation was collected from a vCJD infected donor who had infectious vCJD agent in their blood (i.e., was prionemic at the time of donation). Based on data from animal studies, the model assumes that vCJD infectious individuals have infectious vCJD agent present in the blood during the last half of the incubation period. This portion of the model calculates the number of Source Plasma donors who may potentially contain infectious vCJD agent in their blood at the time of donation.

Variable: *y*-The calendar year in which a plasma donor traveled and infected with vCJD

Assumption used in the model: This risk assessment assesses the risk for pdFVIII product made in 2002 (but risk is assumed to be similar up to the year 2006).

Variable: $T_{Inf\text{-}2002y}$-Time Period between infection/travel and year of 2002 when the plasma was collected

Variable: $Pr\text{-}LH_y$-Probability the individual is in the last half incubation period of the disease, if infected in year y

Variable: $T_{Inf\text{-}2002y}$-Time period between infection and travel and 2002 when the plasma was collected

$$T_{Inf-2002y} = 2002 - y \qquad \text{(IV.C.1.b-22)}$$

For an individual to have vCJD agent present in their blood and plasma (prionemic) in 2002, the elapsed period of time since infection up to 2002 ($I_{Inf\text{-}2002y}$) should be equal to or less than the remaining half of incubation period of the disease; in another words, the incubation period of the disease should be equal to or less than twice as much as $I_{Inf\text{-}2002y}$.

Assumption used in the model The variability and uncertainty of the incubation period of vCJD is represented mathematically by a gamma distribution, specifically Gamma (4.7, 3.6). A gamma distribution is usually used to represent processes that occur sequentially, in this case infection, incubation period of the disease, etc. The distribution is defined by two parameters (or arguments) that produce the shape of the curve and generates a mean incubation period of 14 years and a median incubation period of 13 years.

Variable: $Pr_{LH\text{-}y}$ -The probability an individual will be prionemic in the year 2002, was determined using the distribution:

Cumulative frequency of Gamma (4.7, 3.6), at x=2×(1997-y)

Variable: $DR_{vCJD\text{-}S\text{-}FR_y}$- Total number of Source Plasma donors potentially infected with vCJD in year y during travel/residency in France (calculated in A-IV. C. 1. b. v. a.)

Variable: $DR_{vCJD\text{-}S\text{-}FR\text{-}LHy}$ - Total number of Source Plasma donors potentially infected with vCJD in year y during travel/residency in France and in the last half incubation period of the disease.

$$DR_{vCJD-S-FR-LHy} = Binomial(DR_{vCJD-S-FRy,}\ \Pr_{LH-y}) \quad \text{(IV.C.1.b-23)}$$

Variable: $DR_{vCJD\text{-}S\text{-}FR\text{-}defy}$- Total number of Source Plasma donors potentially infected with vCJD in year y during travel/residency in France and met deferral criteria (calculated in A-IV. C. 1. b. v. a)

Variable: $DR_{vCJD\text{-}S\text{-}FR\text{-}def\text{-}LHy}$ - Total number of Source Plasma donors in the last-half of the incubation period of the disease who met deferral criteria.

$$DR_{vCJD-S-FR-Def-LHy} = Binomial(DR_{vCJD-S-FR-Defy,}\ \Pr_{LH-y}) \quad \text{(IV.C.1.b-24)}$$

Variable: $DR_{vCJD\text{-}S\text{-}FR\text{-}Resy}$- Total number of Source Plasma donors potentially infected with vCJD in year y during travel/residency in France and did not met deferral criteria (calculated in A-IV. C. 1. b. v. a)

Variable: $DR_{vCJD\text{-}S\text{-}FR\text{-}Res\text{-}LHy}$ - Total number of Source Plasma donors in the last half incubation period of the disease who did not met deferral criteria or were not deferred is represented by the equation:

$$DR_{vCJD-S-FR-Res-LHy} = Binomial(DR_{vCJD-S-FR-Resy,}\ \Pr_{LH-y}) \quad \text{(IV.C.1.b-25)}$$

A-IV.C. 1. b. v. c. Number of US recovered plasma donors with a history of travel to France and potentially infected with vCJD

Variable: $DR_{vCJD\text{-}R\text{-}FR(age)y,i}$ - Number of recovered plasma donors potentially infected with vCJD during travel to France since 1980 by age, year and duration of travel

$$DR_{vCJD-R-FR(age)y,i} = Bionomial(DR_{R-FR(age)y,i}, \Pr_{vCJD-DR-FR(age)y,i}) \quad \text{(IV.C.1.b-26)}$$

Variable: $DR_{vCJD\text{-}R\text{-}FRy}$ - Total number of recovered plasma donors potentially infected with vCJD in year y:

$$DR_{vCJD-R-FRy} = \sum_{Age=18-19}^{50-54} \sum_{i=1day-3months}^{>=5years} DR_{vCJD-R-FR(age)y,i} \quad \text{(IV.C.1.b-27)}$$

Current deferral policy defers individuals who have history of travel to France since 1980 for an accumulated residence of 5 years or more from donating blood and plasma. The number of potentially infected donors who meet the deferral criteria was calculated by equation:

$$DR_{vCJD-R-FR-Defy} = \sum_{Age=18-19}^{50-54\,yrs} DR_{vCJD-R-FR(age)y,i>=5\,years} \quad \text{(IV.C.1.b-28)}$$

Variable: $DR_{vCJD-S-FR-Resy}$- The residual risk due to the number of recovered plasma donors potentially infected with vCJD in year y and not deferred by current policy

$$DR_{vCJD-R-FR-Resy} = \sum_{Age=18-19\,yrs}^{50-54\,yrs} \sum_{t=1-30\,days}^{>3-5\,years} DR_{vCJD-R-FR(age)y,i} \quad \text{(IV.C.1.b-29)}$$

A-IV. C. 1. b. v. d. Number of US recovered plasma donors with history of travel to France and potentially infected and vCJD agent is present in the blood

As discussed in the sections on Source Plasma (above) the most critical component of the model is the estimation of whether a plasma donation was collected from a vCJD infected donor who had infectious vCJD agent in their blood (i.e., was prionemic at the time of donation). Based on data from animal studies, the model assumes that vCJD infectious individuals have infectious vCJD agent present in the blood during the last half of the incubation period. This portion of the model calculates the number of recovered plasma donors who may potentially contain infectious vCJD agent in their blood at the time of donation.

Variable: Pr_{LH-y} -The probability an individual will have vCJD agent present in their blood or present (prionemic) at the time of donation in the year 2002 (calculated in A-IV.C.1.a.v. b.)

Variable: $DR_{vCJD-R-FRy}$- Total number of recovered plasma donors potentially infected with vCJD in year y during travel/residence in France (calculated in A-IV. C. 1. b. v. c.)

Variable: $DR_{vCJD-R-FR-LHy}$ - Total number of recovered plasma donors potentially infected with vCJD in year y during travel/residence in France and in the last half incubation period of the disease.

$$DR_{vCJD-R-FR-LHy} = Binomial(DR_{vCJD-R-FRy,}\ \Pr_{LH-y}) \quad \text{(IV.C.1.b-30)}$$

Variable: $DR_{vCJD-R-FR-defy}$- Total number of recovered plasma donors potentially infected with vCJD in year y during travel/residency in France and met deferral criteria (calculated in A-IV. C. 1. b. v. c)

Variable: $DR_{vCJD-R-FR-def-LHy}$ - Total number of recovered plasma donors in the last half incubation period of the disease who met deferral criteria and presumably were deferred from donation.

$$DR_{vCJD-R-FR-Def-LHy} = Binomial(DR_{vCJD-R-FR-Defy,}\ \Pr_{LH-y}) \quad \text{(IV.C.1.b-31)}$$

Variable: $DR_{vCJD\text{-}R\text{-}FR\text{-}Resy}$ - Total number of recovered plasma donors potentially infected with vCJD in year y during travel/residency in France and did not met deferral criteria and were likely not deferred from donation (calculated in A-IV. C. 1. b. v. c.)

Variable: $DR_{vCJD\text{-}R\text{-}FR\text{-}Res\text{-}LHy}$ - Total number of recovered plasma donors in the last half incubation period of the disease who did not meet deferral criteria and were likely not deferred from donation.

$$DR_{vCJD-R-FR-Res-LHy} = Binomial(DR_{vCJD-R-FR-Resy}, \Pr_{LH-y}) \quad \text{(IV.C.1.b-32)}$$

A-IV. C. 1. b. v. e. Number of all US plasma donors with history of travel to France and potentially infected with vCJD

This section sums the number of all US plasma donors, predicted by the model to donate to plasma pools used in manufacturing pdFVIII made from plasma collected in the US. This includes recovered plasma donors and Source Plasma donors, and generates an estimate for the total number of donors potentially infected with vCJD during extended travel to France since 1980.

Variable: $DR_{vCJD\text{-}FR}$ - Total number of plasma donors potentially infected with vCJD during travel/residence in France

$$DR_{vCJD-FR} = \sum_{y=1980}^{1996} DR_{vCJD-S-FRy} + \sum_{y=1980}^{1996} DR_{vCJD-R-FRy} \quad \text{(IV.C.1.b-33)}$$

Variable: $DR_{vCJD\text{-}FR\text{-}Def}$ - Total number of plasma donors potentially infected with vCJD during travel/residence in France and meet deferral criteria

$$DR_{vCJD-FR-Def} = \sum_{y=1980}^{2002} DR_{vCJD-S-FR-Defy} + \sum_{y=1980}^{2002} DR_{vCJD-R-FR-Defy} \quad \text{(IV.C.1.b-34)}$$

Variable: $DR_{vCJD\text{-}FR\text{-}Res}$ - Total number of plasma donors potentially infected with vCJD during travel/residence in the UK and did not meet deferral criteria

$$DR_{vCJD-FR-Res} = \sum_{y=1980}^{2002} DR_{vCJD-S-FR-Resy} + \sum_{y=1980}^{2002} DR_{vCJD-R-FR-Resy} \quad \text{(IV.C.1.b-35)}$$

A-IV. C. 1. b. v. f. Total number of US plasma donors with history of travel to France and are potentially infected and vCJD agent is present in the blood

Again, whether a donor contains vCJD agent in their blood is a pivotal calculation in the model since a donation from such an individual would contain vCJD agent that may find its way into a large plasma pool of thousands of donations that are used to manufacture pdFVIII. This section sums the number of

US Source Plasma donors and recovered plasma donors predicted by the model to be infected with vCJD and contain vCJD agent in their blood and arrives at an estimate of the total number of US donors potentially infected with vCJD and who are prionemic.

Variable: $DR_{vCJD\text{-}FR\text{-}LH}$ - Total number of plasma donors in the last half incubation period of the disease

$$DR_{vCJD-FR-LH} = \sum_{y=1980}^{2002} DR_{vCJD-S-FR-LHy} + \sum_{y=1980}^{2002} DR_{vCJD-S-FR-LHy} \quad \text{(IV.C.1.b-36)}$$

Variable: $DR_{vCJD\text{-}FR\text{-}Def\text{-}LH}$ - Total number of plasma donors in the last half incubation period of the disease and met deferral criteria

$$DR_{vCJD-FR-Def-LH} = \sum_{y=1980}^{2002} DR_{vCJD-S-FR-Def-LHy} + \sum_{y=1980}^{2002} DR_{vCJD-R-FR-Def-LHy} \quad \text{(IV.C.1.b-37)}$$

Variable: $DR_{vCJD\text{-}FR\text{-}Res\text{-}LH}$- Total number of plasma donors in the last half incubation period of the disease and did not met deferral criteria

$$DR_{vCJD-FR-Res-LH} = \sum_{y=1980}^{2002} DR_{vCJD-S-FR-Res-LHy} + \sum_{y=1980}^{2002} DR_{vCJD-R-FR-Res-LHy} \quad \text{(IV.C.1.b-38)}$$

A-IV.C. 1. c. Number of US plasma donors with a history of travel to countries in Europe (other than the UK and France) potentially infected and vCJD agent is present in the blood

A-IV.C.1.c.i. US recovered plasma donors with a history of travel to countries in Europe: Percentage of US donors and travel duration

In this portion of the FDA risk assessment, US blood (recovered plasma) donors are characterized by frequency and duration of travel to countries in Europe (other than the UK) during the period 1980-1996. The risk of vCJD infection is a function of exposure to the BSE agent and is assumed to be proportional to the amount of time spent, or duration of travel, in countries in Europe (other than the UK) since 1980. 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 ($\geq$ 5 years) in other countries in Europe (other than the UK and France) since 1980, and to derive the frequencies for various durations of travel for 5 years or more. The period of 5 years or more corresponds to the length of time in the current policy that defers blood (recovered plasma) donors who traveled to or resided in European countries (other than the UK).

Data used in the model: National Blood Donor Travel Survey 1980-1996 was conducted by the American Red Cross and presented at the TSEAC in 2000.

Variable: i - The duration interval used to group donors who had traveled to countries in Europe from 1980-1996 based on the quantity of time spent in Europe (other than the UK and France) 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 countries in Europe (other than the UK and France) during the period from 1980 – 1996.

Variable: $CumPerc_{BIDR\text{-}EUi}$ – The cumulative percentage of blood donors who traveled to countries in Europe (other than the UK and France) within duration interval i or longer.

Data used in the model: Travel data for US blood donors was obtained from a blood donor survey conducted by the American Red Cross and presented at the TSEAC in 2000.

Variable: $Perc_{BIDR\text{-}EUi}$ - Percentage of blood donors who traveled to countries in Europe (other than the UK and France) within duration interval i. This variable was converted from $CumPerc_{BIDR\text{-}EUi}$

Variable: $Perc_{BIDR\text{-}EUi/EU}$ - The percentage of blood donors who traveled for a specific duration interval i among all donors who have ever traveled to countries in Europe (other than the UK and France) is represented by the equation:

$$Perc_{BIDR\text{-}EUi/EU} = (Perc_{BIDR\text{-}EUi} / CumPerc_{BIDR\text{-}EU,i>1day\text{-}1month}) \times 100\% \qquad \text{(IV.C.1.c-1)}$$

The following portion of the risk assessment estimated the frequency of travel for each recovered plasma donor by age group based on travel data of blood donors. First, estimates for blood donors who traveled to countries in Europe (other than the UK and France) between 1980 and 1996 was calculated to generate the total number of US blood donors and percentages of donors who traveled. For the purposes of our analyses we grouped all donors and donors who traveled to countries in Europe since 1980 into age groups of five-year increments (20 – 24yrs, 25 – 29 yrs, etc) and for the 18 – 19 year old cohort. The percentage of donors in each age group that traveled to countries in Europe since 1980 was calculated based on the total annual number donors who traveled to Europe since 1980 compared to (or divided by) the total number of donors, and the age specific odds ratio for travel.

- **Calculation of the annual number of blood donors who traveled to countries in Europe (other than the UK and France) from 1980 through 1996**

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

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

Variable: $Perc_{BIDR\text{-}EU}$ - The total percentage of US blood donors who traveled to countries in Europe (other than the UK and France) during the period from 1980 through 1996.

Data used in the model: Approximately, 15.6% of US blood donors have histories of travel to countries in Europe (other than the UK and France) during the period from 1980 through 1996, based on the travel data of US blood donors (TSEAC, 2000).

Variable: $DR_{BI\text{-}EU}$ -Total number of blood donors who have traveled to countries in Europe (other than the UK and France) during the period 1980 - 1996.

$$DR_{BI-EU} = DR_{BI} \times Perc_{BIDR-EU} \qquad \text{(IV.C.1.c-2)}$$

Then, the percentage of donors in each age group who traveled to countries in Europe (other than the UK and France) between 1980 and 1996 was calculated based on the total number donors who traveled to countries in Europe, the number of donors from each age group, and the odds ratio of travel for each age group.

Variable: $DR_{BI(age)}$- Annual number of blood donors from each age group (calculated IV.C.1.a)

Variable: $Perc_{BIDR\text{-}EU(age)}$ - Annual percentage of US blood donors of an age group who traveled to countries in Europe during the period from 1980 through 1996.

Total number of blood donor who traveled to countries in Europe (other than the UK and France) equals to the sum of donors from all age groups who have ever traveled to Europe:

$$DR_{BI-EU} = \sum_{age=18-19}^{65-69} (Perc_{BIDR-EU(age)} \times DR_{BI(age)}) \qquad \text{(IV.C.1.c-3)}$$

Variable: $Odd_{T(age)}$- The odds ratio for each five-year age group (e.g. 20-24 yrs, etc.) of travelers was compared to the group of age 18-19 yr olds.

Data used in the model: The odds ratios of travel to countries in Europe (other than the UK and France) for each age group was derived from the travel data obtained from 1980-1996 blood donor travel survey. An odds ratio of 1 was assigned to the donor group of age 18-19 yr olds. The odds ratios for the other age groups were generated by comparing the frequency of travel for those age groups to the group of age 18-19 yr-olds.

$$Perc_{BIDR-EU(age)} = Odd_{T(age)} \times Perc_{BIDR-EU(18-19)} \qquad \text{(IV.C.1.c-4)}$$

The percentage of blood donors from the age group of 18-19 yr olds who have traveled to countries in Europe (other than the UK and France) can be calculated by the following equation:

$$Perc_{BIDR-EU(18-19)} = DR_{BI-EU} / \sum_{age=18-19}^{65-69} (Odd_{T(age)} \times DR_{BI(age)}) \qquad \text{(IV.C.1.c-5)}$$

Then, the percentage blood donors from other age groups who traveled to Europe (other than the UK and France) can be calculated using the equation (A-IV.C.1.c-4).

A-IV. C. 1. c. ii. US recovered plasma donors who traveled to countries in Europe: Total number by year of travel, duration of travel and by age group

This part of the risk assessment calculates the annual number of US recovered plasma donors who traveled to countries in Europe (other than the UK and France) since 1980. The number of donors from an age group who traveled was calculated by year and duration of travel. The risk of a US donor acquiring vCJD is a function of duration of the stay, as well as the year(s) (since 1980) they resided in Europe.

A-IV. C. 1. c. ii.a. Number of US recovered plasma donors who traveled to Europe in a specific year between 1980 and 1996 by age group

This portion of the model estimates the potential vCJD risk for US recovered plasma donors with a history of travel to countries in Europe (other than the UK and France). Recovered plasma is derived from single units of Whole Blood as a by-product in the preparation of blood components from whole blood collection and is intended for further manufacturing. 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 – and on average 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. b. ii. a.) to a country in Europe (other than the UK or France) since 1980 by US plasma donors.

Variable: age – Age groups of the population by five-year increments (same variable used above in section A-IV. B. 1.) and the two year cohort for 18 and 19 year olds for US recovered plasma donors who traveled to countries in Europe (other than the UK and France).

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

Variable: $Perc_{BIDR\text{-}EU(age)}$ (calculated in section A-IV.C.1.b.ii.b.)- The percentage US blood donors by age group who have traveled to countries in Europe (other than the UK and France) between 1980-1996.

Variable: $DR_{R\text{-}EU(age)}$ - Number of recovered plasma donors who traveled to countries in Europe (other than the UK and France). from 1980 through 1996 by age group and is represented by the equation:

$$DR_{R-EU(age)} = DR_{R(age)} \times Perc_{BIDR-EU(age)} \qquad \text{(IV.C.1.c-10)}$$

The risk a traveler was exposed to BSE in Europe is proportional to the magnitude of the BSE epidemic in the UK in the year of travel. Because the major exposure risk in Europe was assumed to be from consumption of beef contaminated with BSE agent imported from the UK. The model groups recovered plasma donors by year of travel. This provides a more precise estimate of the risk by incorporating the (age and year) specific information and details that better capture the dynamics of the BSE epidemic in the UK on a year by year basis. Travel for the years not covered by the UK National Survey 1997 to 2002 relied on extrapolation of trends from 1996 and before to estimate travel characteristics up to the baseline year of 2002 in the model (see equation A-IV.C.1.c-12 (below)).

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.)

Variable: $DR_{R\text{-}EU(age),y}$ - Number of recovered plasma donors who traveled to Europe in year y by age groups.

The number of recovered plasma donors who have traveled to countries in Europe (other than the UK and France) was allocated to individual travel year based on the yearly distribution of visits to the UK by US travelers.

$$DR_{R\text{-}EU(age)y} = DR_{R\text{-}EU(age)} \times V_{y/1996} / \sum_{y=1980}^{1996} V_{y/1996} \qquad \text{(IV.C.1.c-11)}$$

for travel during 1980-1996;

$$DR_{R\text{-}EU(age)y} = DR_{R} \times V_{y/1996} \qquad \text{(IV.C.1.c-12)}$$

for travel after 1996.

Assumption used in the model: The yearly distribution of travel to countries in Europe (other than the UK and France) by US recovered plasma donors is similar to the yearly distribution of travel to the UK by US travelers. 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.

A-IV. C. 1. c. ii. b. Number of US recovered plasma donors who traveled to countries in Europe by specific year of travel and duration of travel by age group

Recovered plasma donors who traveled to countries in Europe (other than the UK and France) in a specific year ($DR_{R\text{-}EU(age)y}$) since 1980 were further partitioned into the subgroups in the model based on travel duration and by 5-year age groups and also the two year cohort of donors 18 and 19 years of age. Data on the percentage of blood donors who traveled to countries in Europe (other than the UK and France) since 1980 for a certain duration(s) (TSEAC, 2000) were used in this risk assessment.

Variable: i - The duration interval used to group blood donors who had traveled to countries in Europe (other than the UK and France) from 1980-1996 based on the time spent (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: $DR_{R\text{-}EU(age),y}$ - The number of recovered plasma donors who traveled to countries in Europe (other than the UK and France) in year *y* by age group

Variable: $Perc_{BIDR\text{-}EU/FEU}$- The percentage of blood donors who traveled for a specific duration interval *i* among all donors who have ever traveled to countries in Europe (other than the UK and France) (calculated in A-IV. C. 1. c. i).

Variable: $DR_{R\text{-}EU(age)y,i}$- Number of recovered plasma donors within a specific age group who have traveled to countries in Europe (other than the UK and France) in year, *y* ,for duration of *i*.

$$DR_{R-EU(age)y,i} = DR_{R-EU(age)y} \times Perc_{DR-EU/EU} \qquad \text{(IV.C.1.c-13)}$$

A-IV.C. 1. c. iii. US recovered plasma donors who traveled to countries in Europe: Adjustment of relative risk for the proportion of exposure to the BSE agent per year and by duration of travel and by age group

As indicated in previous sections the FDA model assumed that the relative vCJD risk for UK residents residing for any five-year period or longer from 1980 through 1996 is assumed to have a value of 1, because exposure to BSE in the UK was greater than that of any other country. The relative risk value of 1 equates to 100% of the UK asymptomatic and symptomatic vCJD prevalence, which is difficult to estimate. Again, based on information in FDA guidance (2002), the relative risk value for France was assumed to be 0.05 (or 5% of the UK risk). The relative risk value is assigned based on factors such as domestic UK beef consumption, and the rate and number of vCJD cases, and indigenous BSE cases that may have occurred (FDA 2002). Countries in Europe (other than the UK and France) received meat and bone meal from the UK during the BSE epidemic and approximately 1.5% of their beef was imported from the UK. Additionally, the model included calculations on the estimated duration of travel or residence in Europe by US plasma donors to generate a more accurate vCJD risk estimate. Current US vCJD geographic deferral policy defers blood donors with a history of residence in countries in Europe (other than the UK and France) for a period of 5 years or more since 1980; this policy does not include Source Plasma donors.

A-IV. C. 1. c. iii. a. Number of US recovered plasma donors with a history of travel to countries in Europe: Average accumulated vCJD risk for donors since 1980, assuming that the average accumulated risk for a UK individual since 1980 is 1

This section calculates the number of US plasma donors with a history of travel to countries in Europe (other than the UK and France) and their average accumulated vCJD risk since 1980, assuming that the average accumulated risk for a UK individual since 1980 is 1.

Variable: R_{EU} - Ac– The cumulative vCJD risk of an individual resident of countries in Europe (other than the UK and France) from 1980 till now; assuming the accumulated risk of a UK individual from 1980 through 1996 is 1.

Assumption used in the model: The average accumulated vCJD risk for travel to countries in Europe (other than the UK and France) by an individual resident since 1980 was assumed to be 0.015 relative to 1, the average accumulated risk of UK individual since 1980, based on UK. It was assumed that approximately 1.5% or less of the beef imports, imported into many countries since 1980 was imported from the UK. The 0.015 relative risk value also considers the number of human vCJD cases present and the presence of indigenous BSE in European countries (other than the UK and France) since 1980.

A-IV. C. 1. c. iii. b. US plasma donors with a history of travel to countries in Europe: Proportional risk per individual resident per year since 1980

Variable: Y_{epi} –*y* Years of BSE epidemic in countries in Europe (other than the UK and France).

Variable: BSE_{UKy} Annual numbers of reported BSE cases in the UK.

Variable: BSE_{EUy} - Annual numbers of reported BSE cases in European countries other than the UK and France.

Data used in the model: Data on the annual number of reported cases of BSE in cattle in European countries was obtained from the Orgainization Internationale de Epizootics (OIE) (2005).

Variable: R_{EUy} - Proportional vCJD risk for European countries (other than the UK and France) in a specific year

Assumptions used in the model:

- The risk of vCJD and BSE in European countries (other than the UK and France) has been present since 1980 and continues to present day. As of August 2006, very few cases of BSE continue to be reported in European countries (other than the UK and France)..
- The vCJD risk is assumed to be additive, and can be prorated on a yearly or monthly basis.
- The yearly rate of the vCJD risk in European countries (other than the UK and France) is proportional to the reported BSE annual cases in Europe (including indigenous and imported cases)

A-IV. C. 1. c. iii. b. US recovered plasma donors with a history of travel to countries in Europe: Potential vCJD risk for an individual in year y for a period of i since 1980

Variable: $R_{DR\text{-}EUy_{w}i}$ - Risk for individual US donors who traveled to countries in Europe other than the UK and France in a specific year for a specific duration, assuming the accumulative risk of a UK person resident in the years 1980 through 1996 is 1.

The vCJD risk for the US plasma donors with less than 5 years accumulated stay in Europe was calculated based on travel to European countries other than the UK and France in a specific year for a specific duration of travel. Potential exposure risk was calculated using a prorated monthly rate, which was calculated based on the yearly rate of the risk (1 month = 1/12 x yearly risk) in Europe during the year of travel. US plasma donors with a total accumulated stay in countries in Europe (other than the UK or France) of 5 years or more is assumed to have average risk of 0.015, which is the same as the risk of an individual citizen or long-term resident of a country in Europe (other than the UK or France). Information on duration of accumulated stays was collected in the blood donor travel survey; however, for simplicity we assumed all travel was consecutive. The blood donor travel survey (TSEAC 2000) collected information on the accumulated stay of US donors who stayed in Europe (other than the UK or France) from 1980 through 1996. For simplicity, these data were used to estimate the duration of consecutive stay, which was used to calculate the potential vCJD risk for recovered plasma donors.

Assumptions used in the model:

- Risk is proportional to the duration of the stay
- All the travelers' stays were assumed to be single and consecutive stays.
- US plasma donor subpopulation having 5 or more years accumulated stay in countries in Europe (other than the UK or France) have an average risk of 0.015, which is the same as the average risk of individual European resident.

For < 1 year;

$$R_{DR-EUy,i} = (Average(R_{EUy} : R_{EU(y+i)})/12) \times D_i \qquad \text{(IV. C. 1. c-14)}$$

for 5 years <i>=1 year;

$$R_{DR-EUy,i} = 0.015 \qquad \text{(IV. C. 1. c-15)}$$

for i>= 5 years

A-IV. C. 1. c. iv. US recovered plasma donors with a history of travel to countries in Europe: Probability of vCJD infection for a donor of a specific age group, who traveled in a specific year for a specific duration, i

This section describes the portion of the model that estimates the potential probability that a US plasma donor in a specific age group, who traveled to countries in Europe (other than the UK or France) for a specific duration since 1980 was infected with vCJD.

Variable: $\mathbf{Pr_{vCJD\text{-}UK(age)}}$ – the probability of infection for an individual UK resident of a specific age group (calculated in A-IV. C. 1. a. iv.).

Variable: $Pr_{vCJD\text{-}DR\text{-}EU(age)y,i}$ - Probability of infection for an individual US plasma donor of a specific age group who have traveled to countries in Europe other than the UK and France in a specific year with specific duration.

Assumption used in the model: The probability of vCJD infection is proportional to the risk of exposure

$$\Pr_{vCJD-DR-EU(age)y,i} = \Pr_{vCJD-UK(age)} \times R_{DR-EUy,i} \quad \text{(IV.C.1.c-16)}$$

A-IV.C. 1. c. v. Number of US recovered plasma donors with a history of travel to countries in Europe: Number potentially infected with vCJD.

Variable: $DR_{vCJD\text{-}R\text{-}EU(age)y,i}$ - Number of recovered plasma donors potentially infected with vCJD during travel to countries in Europe (other than the UK and France) since 1980 by age, year and duration of travel

$$DR_{vCJD-R-EU(age)y,i} = Bionomial(DR_{R-EU(age)y,i}, \Pr_{vCJD-DR-EU(age)y,i}) \quad \text{(IV.C.1.c-26)}$$

Variable: $DR_{vCJD\text{-}R\text{-}EUy}$ - Total number of recovered plasma donors potentially infected with vCJD in year y

$$DR_{vCJD-R-FRy} = \sum_{Age=18-19}^{50-54} \sum_{i=1day-3months}^{>=5years} DR_{vCJD-R-FR(age)y,i} \quad \text{(IV.C.1.c-27)}$$

Variable: $DR_{vCJD\text{-}R\text{-}EU\text{-}Defy}$- Number of recovered plasma donors potentially infected with vCJD in year y and deferred by current policy

Current FDA guidance (FDA 2002) recommends deferral of individuals who have history of travel to countries in Europe (other than the UK or France) since 1980 for an accumulated stay of 5 years or more from donating blood. The number of potential vCJD-infected recovered plasma donors who meet current deferral criteria (FDA 2002) was calculated by the equation:

$$DR_{vCJD-R-EU-Defy} = \sum_{Age=18-19}^{50-54} DR_{vCJD-R-EU(age)y,i>=5years} \quad \text{(IV.C.1.c-28)}$$

Variable: $DR_{vCJDS\text{-}EU\text{-}Resy}$ – The residual risk associated with recovered plasma donors potentially infected with vCJD that meet deferral criteria but because of limitations in the donor screening process and are not deferred by current policy; is represented by the equation:

$$DR_{vCJD-R-EU-Resy} = \sum_{Age=18-19}^{50-54} \sum_{i=1-30days}^{>=3-5years} DR_{vCJD-R-EU(age)y,i} \quad \text{(IV.C.1.c-29)}$$

A-IV. C. 1. c. vi. Number of US recovered plasma donors who traveled to countries in Europe: Number potentially infected and vCJD agent is present in the blood

The most critical component of the model is the estimation of whether a plasma donation was collected from a vCJD infected donor that contained infectious vCJD agent in their blood (or was prionemic) at the time of donation. Based on data from animal studies, the model assumes that vCJD infectious individuals have infectious vCJD agent present in the blood during the last half of the incubation period. This portion of the model calculates the number of recovered plasma donors who may potentially contain infectious vCJD agent in their blood at the time of donation.

Variable: Pr_{LH-y} -The probability an individual was prionemic in year 2002.

Variable: $DR_{vCJD\text{-}R\text{-}EUy}$- Total number of recovered plasma donors potentially infected with vCJD in year y during travel/residence in European countries (other than France).

Variable: $DR_{vCJD\text{-}R\text{-}EU\text{-}LHy}$ - Total number of recovered plasma donors potentially infected with vCJD in year y during travel/residence in a country in Europe (other than the UK or France) and are in the last half incubation period of the disease (and has vCJD agent present in their blood).

$$DR_{vCJD-R-EU-LHy} = Binomial(DR_{vCJD-R-EUy,}\ \Pr_{LH-y}) \qquad \text{(IV.C.1.c-30)}$$

Variable: $DR_{vCJD\text{-}R\text{-}EU\text{-}defy}$- Total number of recovered plasma donors potentially infected with vCJD in year y during travel/residency in European countries (other than the UK or France) and met deferral criteria and were presumably deferred from donation .

Variable: $DR_{vCJD\text{-}R\text{-}EU\text{-}def\text{-}LHy}$ - Total number of recovered plasma donors in the last half incubation period of the disease (and presumably has vCJD agent present in their blood) who met deferral criteria and were presumably deferred from donation.

$$DR_{vCJD-R-EU-Def-LHy} = Binomial(DR_{vCJD-R-EU-Defy,}\ \Pr_{LH-y}) \qquad \text{(IV.C.1.c-31)}$$

Variable: $DR_{vCJD\text{-}R\text{-}EU\text{-}Resy}$- Total number of recovered plasma donors potentially infected with vCJD in year y during travel/residency in countries in Europe (other than the UK or France) and did not meet the deferral criteria and were likely not deferred .

Variable: $DR_{vCJD\text{-}R\text{-}EU\text{-}Res\text{-}LHy}$ - Total number of recovered plasma donors in the last half of the incubation period of the disease who did not met the deferral criteria and were likely not deferred from donation:

$$DR_{vCJD-R-EU-Res-LHy} = Binomial(DR_{vCJD-R-EU-Resy}, \Pr_{LH-y}) \quad \text{(IV.C.1.c-32)}$$

A-IV. C. 1. d. Number of US plasma donors deployed by the military in the UK or other countries in Europe and potentially infected with vCJD

A-IV. C. 1. d. i. Percentage of US plasma donors deployed at US military bases in the UK or other countries in Europe during the years 1980 through 1996

Variable: $Perc_{DR\text{-}DOD}$ - Percentage of US blood donors who were military residents in countries in Europe for ≥ 6 months from 1980 through 1996.

Assumption used in the model: Approximately 2% of US blood donors have been military residents in European countries between 1980-1996 (TSEAC 2002). There were no data for plasma donors, therefore, data for US blood donors was used to estimate the number of US donors stationed in US military facilities during the period 1980-1996

- The FDA model assumed that the same percentage of plasma donors have been in the military and deployed in European countries as blood donors.

A-IV. C. 1. d. ii. Number of US plasma donors deployed by Military in the UK or other countries in Europe by year of deployment since 1980

A-IV. C. 1. d. ii. a. Number of US Source Plasma donors stationed at US military facilities in the UK or countries in Europe during the period from 1980 -1996 by year of deployment

Variable: ***y*** - Calendar year of deployment

Variable: ***DODy*** - Number of US military residents, their family and dependents who resided on US military facilities in Europe by year from 1980 through 1996.

Assumption used in the model: The risk of BSE exposure and vCJD infection for donors previously deployed to US military facilities in the UK or countries in Europe after 1996 was assumed to be negligible, because it is assumed that most of the risk was associated with imported UK beef. Food chain controls put in place in the UK after 1996 were assumed to reduce the BSE exposure risk to negligible levels (TSEAC, 2002) and shipment of UK beef to US military facilities had stopped in 1996 or earlier.

Variable: ***age*** - age of donors in grouped by five-year increments (e.g., 20-24, etc.) and the 18-29 year old group (same variable used above in section A-IV.C.1.a.ii.)

$$Perc_{DR-DODy} = (DOD_y / \sum_{y=1980}^{1996} DOD_y) \times 100\% \quad \text{(IV.C.1.d-1)}$$