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.

Assumption used in the model: US Source Plasma 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.

APPENDIX A

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:

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

A-IV. C. 1. a. iii. US plasma donors with a history of travel to the UK: Adjustment of relative risk to account for variations in BSE risk by specific year and travel duration

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 the BSE epidemic in UK cattle and exposure of the human population to the BSE agent in the UK was greater than 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. 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 (TSEAC 2004). BSE was first diagnosed in the United Kingdom in 1986 and the epidemic peaked in 1992, a year when the risk of exposure to the BSE agent would have likely been highest for residents and visitors to the UK. Human exposure risk to the BSE agent would likely have decreased dramatically in 1996 with the culling of animals over 30 months of age from the food production system and the institution of food chain controls to prevent high risk tissues that might contain BSE agent from entering the food and animal food supplies. Presumably there were dramatic variations in the BSE exposure risk, and hence, the human vCJD infection risk that occurred from year to year. Therefore, the model adjusted the vCJD risk for US plasma donors with a history of extended travel or residence in the UK by multiplying by the proportional BSE risk per year (e.g., the BSE exposure risk in a given year compared to the total BSE risk since 1980). Additionally, the model included calculations on the estimated duration of UK travel or residence by US plasma donors based on US donor survey data (TSEAC 2000) to generate a more accurate vCJD risk estimate.

A-IV. C. 1. a. iii. a. Variant CJD risk for individual UK residents from 1980 through 1996

Variable: R_{UK}- The accumulated vCJD risk per UK resident from 1980 through 1996.

Assumption used in the model: The UK population has the highest risk of exposure to BSE or vCJD, we assumed the average accumulated risk per UK individual is 1. Also, the relative risk for UK residents is 1, which is equivalent to the UK vCJD prevalence.

A-IV. C. 1. a. iii. b. US plasma donors with a history of travel to the UK: Adjustment for the proportional individual BSE exposure risk for the UK population per year between 1980 to 1996.

The model calculates the risk and potential magnitude of BSE exposure for donors, in any given year in the UK since 1980, as a function of the number of BSE cases in a specific year divided by the total of all BSE cases since 1980.

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

Variable: BSE_{UKy}- The annual number of reported BSE cases in the UK since 1986 (OIE, 2005).

Variable: R_{UKy}- Proportional BSE exposure risk in the UK by specific year from 1980 to 1996.

Assumptions used in the model:

- The BSE exposure risk, and hence, most of the vCJD risk in the UK occurred largely between 1980 and 1996.
- The vCJD risk in the UK was assumed to be negligible after 1996, when stringent food chain controls were put in place to prevent contamination of beef with high risk tissue.
- The yearly rate of the human exposure risk to the BSE agent in the UK is proportional to the number of reported BSE annual cases in the UK
- The vCJD risk is additive for each year of residency during the specific time period.
- A person residing for five or more years during the time period between 1980 and 1996 in the UK is assumed to have a relative risk of 1 (or 100%), i.e., a probability of vCJD infection that is the same as that of the entire UK population.

The proportional BSE risk in the UK per specific year prior to 1997 is represented by the equation:

$$R_{UKy} = R_{UK} \times BSE_{UKy} / \sum_{y=1980}^{1996} BSE_{UKy} \qquad \text{(IV.C.1.a-15)}$$

A-IV. C. 1. a. iii. c. US plasma donors with a history of travel to the UK: BSE exposure risk and vCJD risk in year *y* for a period of *i*, during the period from 1980 to 1996.

Variable: $R_{DR\text{-}UKy,i}$- The potential vCJD risk of an individual US donor who traveled to the UK in specific year during the period 1980-1996 for a specific duration.

The potential vCJD risk for the US plasma donor subpopulation that traveled to the UK in a specific year for a specific duration was calculated using a pro-rated monthly rate, which was calculated based on the proportional BSE exposure risk in the UK in the specific year. The blood donor travel survey conducted by the American Red Cross (TSEAC 2000) collected data on the accumulated stay of donors in the UK from 1980 through 1996, which, for simplicity, was assumed to be the duration of a single, consecutive stay, when calculating the risk.

Assumptions used in the model:

- Risk of vCJD infection is proportional to the duration of the stay in the UK during the period 1980-1996
- All travelers evaluated completed a single, consecutive stay

As mentioned earlier, any US plasma donor with 5 years or more of accumulated stay in the UK is assumed to have average risk of 1, a risk equal to the average risk of an UK resident and equal to the UK vCJD prevalence.

The BSE exposure risk for US plasma donors with a stay less than or equal to one year – is represented by the equation:

$$R_{DR-UKy,i} = (R_{UKy} / 12) \times D_i \qquad \text{(IV.C.1.a-16)}$$

for $i_{upper} \leq 1$ years;

The BSE exposure risk for US plasma donors with a stay less than five years but greater than or equal to one year is represented by the equation:

$$R_{DR-UKy,i} = (Average(R_{UKy} : R_{UK(y+Roundup(i_{upper},0)})/12) \times D_i \quad \text{(IV.C.1.a-17)}$$

for 5 years $< i_{upper} \geq 1$ year;

The BSE exposure risk for US plasma donors with a stay greater than or equal to five – is represented by the equation:

$$R_{DR-UKy,i} = 1 \quad \text{(IV.C.1.a-18)}$$

for $i_{upper} \geq 5$ years

A-IV. C. 1. a. iv. US plasma donors with a history of travel to the UK: Probability of potential infection with vCJD based on duration of travel to the UK and age

This section describes the portion of the model that estimates the probability that a US plasma donor in a specific age group, who traveled to the UK for a specific duration during the time-span of 1980 through 1996, was infected with vCJD.

Variable: $Pr_{vCJD-UK(age)}$ – the probability of vCJD infection per individual UK resident of a specific age group

Variable: $Prev_{Asym-vCJD(age)}$- Prevalence of asymptomatic vCJD infection in the UK for each age groups in five-year increments (e.g., 20-24 yrs, etc.) and the 18-19yr old group (calculated in A-IV.A.3.b.).

$$Pr_{vCJD-UK(age)} = Prev_{Asym-vCJD(age)}/1000000 \quad \text{(IV.C.1.a-19)}$$

Variable: $Pr_{vCJD-DR-UK(age)y,i}$ – The probability of infection for individual US plasma donor of a specific age group who had traveled to the UK in a specific year for a specific duration

Assumption used in the model: Probability of infection is proportional to the risk of exposure

$$Pr_{vCJD-DR-UK(age)y,i} = Pr_{vCJD-UK(age)} \times R_{DR-UKy,i} \quad \text{(IV.C.1.a-20)}$$

A-IV. C. 1. a. v. Number of all US pdFVIII plasma donors with history of travel to the UK and potentially infected with vCJD

This section of the model estimates the total number of all US plasma donors potentially infected with vCJD during travel to the UK from 1980 through 1996. To derive the total number of donors the model separately estimates the number of potentially infected Source Plasma donors and potentially infected recovered plasma donors (described in the subsequent sections below) and sums the two.

APPENDIX A

A-IV. C. 1. a. v. a. Number US Source Plasma donors with history of travel to the UK and potentially infected with vCJD during travel to the UK

Plasma is collected from Source Plasma donors in a process called plasmapheresis in which an average of approximately 700 milliliters of plasma are collected. Source Plasma donors donate an average of 14 times per year, but can donate up to 48 times per year.

This component of the model estimates the number of US Source Plasma donors potentially infected with vCJD during travel to the UK from 1980 through 1996.

Variable: $DR_{vCJD\text{-}S\text{-}UK(age)y,i}$- Number of Source Plasma donors potentially infected with vCJD during travel to the UK during 1980-1996 by age, year and duration of travel.

$$DR_{vCJD-S-UK(age)y,i} = Bionomial(DR_{S-UK(age)y,i}, \Pr_{vCJD-DR-UK(age)y,i}) \quad \text{(IV.C.1.a-21)}$$

Variable: $DR_{vCJD\text{-}S\text{-}UKy}$ - Number of Source Plasma donors potentially infected with vCJD in year y during travel/residency in the UK.

$$DR_{vCJD-S-UK} = \sum_{Age=18-19yrs}^{50-54yrs} \sum_{i=1day-3months}^{>=5years} DR_{vCJD-S-UK(age)y,i} \quad \text{(IV.C.1.a-22)}$$

Variable: $DR_{vCJD\text{-}S\text{-}UK\text{-}Defy}$- Number of Source Plasma donors potentially infected with vCJD in year y and not deferred by current policy.

$$DR_{vCJD-S-UK-defy} = \sum_{Age=18-19yrs}^{50-45yrs} \sum_{i=3-5months}^{>=5years} DR_{vCJD-S-UK(age)y,i} \quad \text{(IV.C.1.a-23)}$$

Current deferral policy (FDA 2002) defers individuals who have history of travel to the UK from 1980 through 1996 for an accumulated residence of 3 months or more from donating blood and plasma. The number of potentially infected donors who meet deferral criteria was calculated by equation:

Variable: $DR_{vCJD\text{-}S\text{-}UK\text{-}Res}$- Residual risk due to the number of Source Plasma donors potentially infected with vCJD not deferred by current policy

$$DR_{vCJD-S-UK-Resy} = \sum_{Age=18-19}^{50-54yrs} DR_{vCJD-S-UK(age)y,i=1day-3months} \quad \text{(IV.C.1.a-24)}$$

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

Perhaps 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 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.

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 disease is in the last half incubation period of the disease (and donor is prionemic), if infected in year y

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

$$T_{Inf-2002y} = 2002 - y \qquad \text{(IV.C.1.a-25)}$$

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 greater than the half of incubation period of the disease.

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 the time between events, in this case the time from infection to the occurrence of symptomatic disease. The distribution is defined by two parameters, one that produces the shape of the curve and a second that generates the scale between events, which in this case is the mean incubation period of 14 years.

Variable: $Pr_{LH\text{-}y}$ -The probability an individual has vCJD agent present in their blood and plasma in year 2002 (the baseline year of the model) was calculated by the expression:

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

Variable: $DR_{vCJD\text{-}S\text{-}UKy}$ - Total number of Source Plasma donors potentially infected with vCJD in year y during travel/residency in the UK.

Variable: $DR_{vCJD\text{-}S\text{-}UK\text{-}LHy}$ - Total number of Source Plasma donors potentially infected with vCJD in year y during travel/residency in the UK and were in the last half incubation period of the disease in 2002 at the time of donation.

$$DR_{vCJD-S-UK-LHy} = Binomial(DR_{vCJD-S-UKy}, \Pr_{LH-y}) \qquad \text{(IV.C.1.a-26)}$$

Variable: $DR_{vCJD\text{-}S\text{-}UK\text{-}defy}$- Total number of Source Plasma donors potentially infected with vCJD in year y during travel/residency in the UK and met deferral criteria

Variable: $DR_{vCJD\text{-}S\text{-}UK\text{-}def\text{-}LHy}$ - Total number of Source Plasma donors in the last half incubation period of the disease (prionemic) and met current deferral criteria (FDA 2002).

$$DR_{vCJD-S-UK-Def-LHy} = Binomial(DR_{vCJD-S-UK-Defy}, \Pr_{LH-y}) \quad \text{(IV.C.1.a-27)}$$

Variable: $DR_{vCJD\text{-}S\text{-}UK\text{-}Resy}$- Total number of Source Plasma donors potentially infected with vCJD in year y during travel/residency in the UK and did not meet deferral criteria

Variable: $DR_{vCJD\text{-}S\text{-}UK\text{-}Res\text{-}LHy}$ - Total number of Source Plasma donors in the last half of the incubation period of the disease who did not meet current deferral criteria (FDA 2002).

$$DR_{vCJD-S-UK-Res-LHy} = Binomial(DR_{vCJD-S-UK-Resy}, \Pr_{LH-y}) \quad \text{(IV.C.1.a-28)}$$

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

Recovered plasma donors donate whole blood from which the plasma is separated out (or recovered). Like blood donors recovered plasma donors donate an average of 1.7 times per year but can donate up to 6 times per year. The model assumes the average amount of plasma in a recovered plasma unit is approximately 200 milliliters.

This component of the model estimates the number of US recovered plasma donors potentially infected with vCJD during travel to the UK from 1980 through 1996.

Variable: $DR_{vCJD\text{-}R\text{-}UK(age)y,i}$ - Number of recovered plasma donors potentially infected with vCJD during travel to the UK during 1980-1996 by age, year and duration of travel

$$DR_{vCJD-R-UK(age)y,i} = Bionomial(DR_{R-UK(age)y,i}, \Pr_{vCJD-DR-UK(age)y,i}) \quad \text{(IV.C.1.a-29)}$$

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

$$DR_{vCJD-R-UKy} = \sum_{Age=18-19}^{50-54} \sum_{i=1day-3months}^{>=5years} DR_{vCJD-R-UK(age)y,i} \quad \text{(IV.C.1.a-30)}$$

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

$$DR_{vCJD-R-UK-Defy} = \sum_{Age=18-19}^{50-54} \sum_{i=3-5months}^{>=5years} DR_{vCJD-R-UK(age)y,i} \quad \text{(IV.C.1.a-31)}$$

Variable: $DR_{vCJDS\text{-}UK\text{-}Resy}$ - Residual risk due to the number of recovered plasma donors potentially infected with vCJD not deferred by current policy and represented by the equation:

$$DR_{vCJD-R-UK-resy} = \sum_{Age=18-19}^{50-54} DR_{vCJD-R-UK(age)y,i=1day-3months} \quad \text{(IV.C.1.a-32)}$$

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

As discussed in the sections above the most critical determinant in the model of whether exposure occurs is the estimation of whether a plasma donation was collected from a vCJD infected donor who had infectious vCJD agent in their blood (e.g., 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 have infectious vCJD agent in their blood at the time of donation.

Variable: $Pr_{LH\text{-}y}$ -The probability an individual will have vCJD agent in blood and plasma (prionemic) in year 2002

Variable: $DR_{vCJD\text{-}R\text{-}UKy}$- Total number of recovered plasma donors potentially infected with vCJD in year y during travel/residency in the UK (calculated in A-IV. C. 1. a. v. b)

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

$$DR_{vCJD-R-UK-LHy} = Binomial(DR_{vCJD-R-UKy}, \Pr_{LH-y}) \quad \text{(IV.C.1.a-33)}$$

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

Variable: $DR_{vCJD\text{-}R\text{-}UK\text{-}def\text{-}LHy}$ - Total number of recovered plasma donors in the last half incubation period of the disease who met deferral criteria.

$$DR_{vCJD-R-UK-Def-LHy} = Binomial(DR_{vCJD-R-UK-Defy}, \Pr_{LH-y}) \quad \text{(IV.C.1.a-34)}$$