APPENDIX A

$$DR_{vCJD-S-DOD} = \sum_{y=1980}^{1996} \sum_{age=16-19}^{70-74} DR_{vCJD-S-DOD(age)y} \qquad \text{(IV.C.1.d-11)}$$

A-IV. C. 1. d. iv. b. Potential number of Source Plasma donors with a history of deployment to a US military facility in the UK or other countries of Europe from 1980 to 1996 in the last half incubation period of the disease

This section estimates the number of Source Plasma donors that may potentially be infected with vCJD who may have vCJD agent in their blood (or be prionemic) at the time of donation.

Variable: *y*-The calendar year in which a plasma donor was deployed to a US military base in Europe.

Assumption used in the model: This risk assessment assesses the vCJD risk for pdFVIII product made in 2002 but it is assumed that the potential vCJD risk is similar to the present day risk in 2006.

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

Variable: $Pr\text{-}LH_y$- Probability that the vCJD disease is in the last half of the incubation period of the disease, if infected in year y and the individual has infectious vCJD agent present in their blood and plasma (or was prionemic).

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

$$T_{Inf-2002y} = 2002 - y \qquad \text{(IV.C.1.d-12)}$$

For an individual to be prionemic in 2002, the remaining period of time since infection up to 2002 ($I_{Inf\text{-}2002y}$) should be equal to or less 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 processes that occur sequentially or the time between events. In this case it would be the time from infection to the time until the appearance of clinical disease (incubation period of the disease). The distribution is defined by two parameters: one that produces the shape of the curve; and a second generates the scale for the distribution, which in this case is represented by the mean incubation period of 14 years.

Variable: $Pr_{LH\text{-}y}$ -The probability an individual was prionemic in year 2002-was calculated by using the cumulative frequency of Gamma (4.7, 3.6), at x=2×(1997-y)

Variable: $DR_{vCJD\text{-}S\text{-}DODy}$- Total number of Source Plasma donors potentially infected with vCJD in year y during military deployment on European bases (calculated in A-IV. C. 1. d. v. a.).

Variable: $DR_{vCJD\text{-}S\text{-}DOD\text{-}LHy}$ - Total number of Source Plasma donors potentially infected with vCJD in year y during military deployment to US military bases in European countries and in the last half incubation period of the disease.

$$DR_{vCJD\text{-}S\text{-}DOD\text{-}LHy} = Binomial(DR_{vCJD\text{-}S\text{-}DODy}, \Pr_{LH-y}) \quad \text{(IV.C.1.d-13)}$$

A-IV. C. 1. d. iv. c. Number of US recovered plasma donors with a history of deployment to a US military base in the UK or other countries in Europe during the period 1980-1996 and potentially infected with vCJD

Variable: $DR_{vCJD\text{-}R\text{-}DOD(age)y}$ - Potential number of recovered plasma donors infected during deployment and residency on or near US military bases in Europe from 1980-1996 by age, and year of deployment

$$DR_{vCJD\text{-}R\text{-}DOD(age)y} = Binomial(DR_{R\text{-}DOD(age)y}, \Pr_{vCJD\text{-}DR\text{-}DOD(age)y}) \quad \text{(IV.C.1.d-14)}$$

Variable: $DR_{vCJD\text{-}R\text{-}DOD}$ - Potential number of recovered plasma donors infected during residency on US military bases in Europe from 1980-1996 is represented by the equation:

$$DR_{vCJD\text{-}R\text{-}DOD} = \sum_{y=1980}^{1996} \sum_{age=18-19}^{70-74} DR_{vCJD\text{-}R\text{-}DOD(age)y} \quad \text{(IV.C.1.d-15)}$$

A-IV. C. 1. d. iv. d. Recovered plasma donors with a history of deployment to a US military base in the UK or other countries in Europe: Potential number of donors in the last half of vCJD incubation period and vCJD agent is present in the blood

This portion of the model calculates the potential number of vCJD infected recovered plasma donors who are in the last half incubation period of the disease and presumably may contain vCJD agent in their blood (or are prionemic).

Variable: $Pr_{LH\text{-}y}$ -The probability a vCJD-infected donor had vCJD agent present in their blood and plasma at the time of donation (was prionemic) in the year 2002 (calculated in A-IV.C.1.d.v.b).

Variable: $DR_{vCJD\text{-}R\text{-}DODy}$- Total number of recovered plasma donors potentially infected with vCJD in year y during military deployment on or near bases in Europe (calculated in A-IV. C. 1. d. v. c.)

Variable: $DR_{vCJD\text{-}R\text{-}DOD\text{-}LHy}$ - Total number of recovered plasma donors potentially infected with vCJD in year y during military deployment on or near bases in Europe and in the last half incubation period of the disease.

$$DR_{vCJD-R-DOD-LHy} = Binomial(DR_{vCJD-R-DODy}, \Pr_{LH-y}) \quad \text{(IV.C.1.d-16)}$$

A-IV. C. 1. d. iv. e. Number of all vCJD infected plasma donors during deployment to a US military base in a country in Europe from 1980-1996

Variable: $\mathbf{DR_{vCJD-DOD}}$ - Potential number of total plasma donors infected during residence on US military bases in Europe from 1980-1996

$$DR_{vCJD-DOD} = \sum_{y=1980}^{1996} DR_{vCJD-S-DOD} + \sum_{y=1980}^{1996} DR_{vCJD-R-DOD} \quad \text{(IV.C.1.d-17)}$$

Variable: $\mathbf{DR_{vCJD-DOD-Def}}$ - Potential number of total plasma donors infected during residence on US military bases in Europe from 1980-1996 and meet deferral criteria

Assumption used in the model: Current policy defers individuals who have been deployed or resided on a US military base in Europe from 1980 to 1996 for a cumulative stay of 6 months or more. We assumed all US Department of Defense (DOD) deployments are 6 months or longer, and therefore, all individuals have a history of deployment to a US military base in Europe are deferred.

$$DR_{vCJD-DOD-Def} = DR_{vCJD-DOD} \quad \text{(IV.C.1.d-18)}$$

A-IV. C. 1. d. iv. f. Potential number of all plasma donors in the last half of vCJD incubation period and have vCJD agent present in the blood

This portion of the model estimates the potential number of all vCJD infected plasma donors with a history of military service posted at a US military base in the UK or countries in Europe fron 1980-1996 who are in the last half incubation period of the disease and their blood and plasma presumably contain infectious vCJD agent (or are prionemic).

Variable: $\mathbf{DR_{vCJD-DOD-LH}}$ - Potential number of total plasma donors infected during residence on US military bases in Europe from 1980-1996 and are in the last half incubation period of the disease

$$DR_{vCJD-DOD-LH} = \sum_{y=1980}^{1996} DR_{vCJD-S-DOD-LH} + \sum_{y=1980}^{1996} DR_{vCJD-R-DOD-LH} \quad \text{(IV.C.1.d-19)}$$

Variable: $\mathbf{DR_{vCJD-DOD-Def}}$ - Potential number of total plasma donors infected during residence on US military bases in Europe from 1980-1996 and meet deferral criteria

$$DR_{vCJD-DOD-Def} = DR_{vCJD-DOD} \quad \text{(IV.C.1.d-20)}$$

Variable: DR_{Tot} - (calculated in section A-IV.B.3.) Annual number of plasma donors

Variable: DR_S - (calculated in section A-IV.B.1.) Annual number of Source Plasma donors

Variable: DR_R - (calculated in section A-IV.B.2.) Annual number of recovered plasma donors

Variable: $Perc_{DR\text{-}Eurob}$ - Percentage of blood donors who were Euroblood recipients

Assumption used in the model: 1.2% plasma donors were Euroblood recipients

Variable: DR_{Eurob} - Annual number of plasma donors who were Euroblood recipients

$$DR_{Eurob} = DR_{Tot} \times Perc_{DR-Eurob} \quad \text{(IV.C.1.e-1)}$$

Variable: $DR_{S\text{-}Eurob}$ - Annual number of Source Plasma donors who were Euroblood recipients

Assumption used in the model: We assumed 1.2% of US Source Plasma donors were Euroblood recipients

$$DR_{S-Eurob} = DR_S \times Perc_{DR-Eurob} \quad \text{(IV.C.1.e-2)}$$

Variable: $DR_{R\text{-}Eurob}$ - Annual number of recovered plasma donors who were Euroblood recipients – represented by the equation:

$$DR_{R-Eurob} = DR_R \times Perc_{DR-Eurob} \quad \text{(IV.C.1.e-3)}$$

A-IV. C. 1. e. Annual number of US plasma donors who have been Euroblood recipients

A-IV. C. 1. e. i. Annual number of US plasma donors who have been Euroblood recipients

A-IV. C. 1. e. ii. Annual number of potential vCJD-infected Euroblood donors and estimated annual units of Euroblood potentially containing vCJD agent

This section of the model estimates the quantity of Euroblood units predicted to have been transfused into US plasma donors in a one year period, the number of European donors involved, the number of possible vCJD infected European Euroblood donors, and the total quantity of vCJD infected units given by the Euroblood donors.

Variable: $DNBl_{UK(age)}$ - Blood donations in the UK by age of donors.

Data used in the model: Information about UK blood donors was provided by CDSC (2005).

Variable: $Perc_{DN\text{-}UK(age)}$ - Percentage distribution of the blood donations in the UK by donor age, and is represented by equation:

$$Perc_{DN-UK(age)} = DN_{BI-UK(age)} / \sum_{age=18}^{>65} DN_{BI-UK(age)} \quad \text{(IV.C.1.e-5)}$$

Variable: $EUBL_{(age)}$ - Units of Euroblood that were donated by a specific age group of European donors and transfused into US plasma donors

Total units of Euroblood received by US plasma donors of one year period is allocated by age of European donors based on the age distribution of UK blood donors

Assumption used in the model: We assumed the age distribution for Euroblood donors is the same as UK blood donors

$$EUBL_{(age)} = EUBL_{Tot} \times Perc_{DN-UK(age)} \quad \text{(IV.C.1.e-6)}$$

Variable: $DR_{EUBL(age)}$ – The number of European donors were grouped by age in five-year increments (e.g., 20-24 yrs, etc) and the 18-19 yr old group that have contributed Euroblood that may have been transfused into US plasma donors per one year period

Each European donor may give multiple donations in a single year; however the chance of more than one donation from same donor being shipped to the US and used by US plasma donors is expected to be small.

Assumption used in the model: Each unit of Euroblood received by US plasma donors of one year-period came from different European donors and is expressed by the equation:

$$DR_{EUBL(age)} = EUBL_{(age)} \quad \text{(IV.C.1.e-7)}$$

The probability of infection of individual European blood donors is calculated below based on the probability of infection per individual UK resident and the relative risk of a resident in a country elsewhere in Europe (other than France) compared to the risk of a UK resident.

Variable: R_{EU} – The cumulative risk of an individual European resident from 1980 till the present; assumes that the cumulative risk of a UK individual from 1980 through 1996 is 1 (same variable as used in (A-IV.C.1.c.iii)

Variable: $Pr_{vCJD\text{-}UK(age)}$ - Probability of infection for individual UK resident of a specific age group (same variable as used in (A-IV.C.1. c. iv.).

Variable: $Pr_{vCJD\text{-}EU(age)}$-Probability of infection for an individual European resident of a specific age group.

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

$$\Pr_{vCJD-EU(age)} = \Pr_{vCJD-UK(age)} \times R_{EU} \quad \text{(IV.C.1.e-7)}$$

Variable: $DR_{vCJD\text{-}EUBL(age)}$-Annual number of infected European donors who contributed Euroblood that was transfused into US plasma donors during a one-year period by age group.

Number of infected Euroblood donors among each age group was estimated using a binomial distribution function with the estimated total number of donors in the subgroup ($DR_{EUBL(age)}$ estimated in section A-IV.C. 1.e. ii) and the probability of infection for the individual of this age group of Euroblood donors ($Pr_{vCJD\text{-}DR\text{-}EUBL(age)}$ estimated in this section A-IV. C. 1. e. ii) as parameters of the distribution.

$$DR_{vCJD-EUBL(age)} = Bionomial(DR_{EULL(age)}, \Pr_{vCJD-EU(age)}) \quad \text{(IV.C.1.e-8)}$$

Variable: $EUBL_{vCJD}$ - Total units of infected Euroblood received by US plasma donors of one year period

Potential infected European donor may give multiple donations in a single year, however the chance of more than one donation being from a single infected European donor being shipped to the US, and used by US plasma donors is expected to be small.

Assumption about variable: One infected European donor produces one unit of infected Euroblood.

$$EUBL_{vCJD} = \sum_{age=18-19}^{>65} DR_{vCJD-EUBL(age)} \quad \text{(IV.C.1.e-9)}$$

A-IV. C. 1. e. iii. Annual number of plasma donors potentially infected with vCJD via transfusion with Euroblood

A-IV. C. 1. e. iii. a. Annual potential number of vCJD infected plasma donors

Variable: $Pr_{vCJD\text{-}EUBL}$ - Probability a single unit of Euroblood contains vCJD agent

$$\Pr_{vCJD-EUBL} = EUBL_{VCJD} / EUBL_{Tot} \quad \text{(IV.C.1.e-10)}$$

Variable: $Pr_{vCJD\text{-}EUBL\text{-}Recip}$ - Probability a Euroblood recipient is infected with vCJD

Assumption used in the model: We assumed that a Euroblood recipient is likely infected if he/she receives one unit or more of blood blood from a vCJD-infected donor.

$$\Pr_{vCJD-EUBL-recip} = 1 - Binomdist(0, EUBL_{avg}, \Pr_{vCJD-EUBL}, false) \quad \text{(IV.C.1.e-11)}$$

APPENDIX A

The Excel function Binomdist (n, N, p, false) calculates the probability of n "success" outcomes in a test, if the outcome of each trial of the test is either "success" or "failure", the probability of getting the outcome of "success" in an individual trial throughout the test is a constant p, and the number of trials in the test is N. In the problem we addressed here the outcomes are the probability of a donation being from a Euroblood recipient that receives a donation that is either infected or not infected. In equation IV.C.1.e-11, $Binomdist(0, EUBL_{avg}, Pr_{vCJD\text{-}EUBL}, false)$ calculated the probability of a recipient receiving no infected unit (n=0), under the condition that average number of units received by a recipient is $EUBL_{avg}$ (N=$EUBL_{avg}$) and probability a single unit of Euroblood being infected is $Pr_{vCJD\text{-}EUBL}$ (p=$Pr_{vCJD\text{-}EUBL}$).

The number of Source and recovered plasma donors infected through transfusion with Euroblood was estimated using a binomial distribution function with the estimated total number of source and recovered plasma donors who have received Euroblood ($DR_{S\text{-}EUBL}$ and $DR_{R\text{-}EUBL}$ estimated in section A-IV.C. 1.e. ii.) and the probability of infection for the individual Euroblood recipient ($Pr_{vCJD\text{-}EUBL\text{-}receip}$ estimated in section A-IV. C. 1. e. iii) as parameters of the distribution. The total estimated number of potential plasma donors infected due to transfusion using Euroblood is the sum of potential infected source and recovered plasma donors.

Variable: $DR_{vCJD\text{-}S\text{-}EUBL}$ - Annual Number of Source Plasma donors being infected due to transfusion with a Euroblood unit:

$$DR_{vCJD-S-EUBL} = Binomial(DR_{S-EUBL}, \Pr_{vCJD-EUBL-recip}) \quad \text{(IV.C.1.e-12)}$$

Variable: $DR_{vCJD\text{-}R\text{-}EUBL}$ - Annual number of recovered plasma donors possibly infected via transfusion with a unit of Euroblood

$$DR_{vCJD-R-EUBL} = Binomial(DR_{R-EUBL}, \Pr_{vCJD-EUBL-recip}) \quad \text{(IV.C.1.e-13)}$$

Variable: $DR_{vCJD\text{-}EUBL}$ - Annual number of all plasma donors possibly infected through transfusion with a unit of Euroblood

$$DR_{vCJD-EUBL} = DR_{vCJD-S-EUBL} + DR_{vCJD-R-EUBL} \quad \text{(IV.C.1.e-14)}$$

Variable: $DR_{vCJD\text{-}EUBL\text{-}Def}$ - Annual number of plasma donors possibly infected through transfusion with a unit of Euroblood and meet deferral criteria and presumably deferred from donation.

Variable: $DR_{vCJD\text{-}EUBL\text{-}Res}$ - Annual number of plasma donors potentially infected via transfusion with a unit of Euroblood and does not meet deferral criteria and likely not deferred from donation.

Under current blood donation policies recipients of Euroblood are not deferred and represented by the expressions:

$$DR_{vCJD-EUBL-Def} = 0 \quad \text{(IV.C.1.e-15)}$$

$$DR_{vCJD-EUBL-Res} = DR_{vCJD-EUBL} \quad \text{(IV.C.1.e-16)}$$

A-IV. C. 1. e. iii. b. Annual number of plasma donors that received Euroblood and are potentially infected and vCJD agent is present in the blood

Assumption used in the model: All infected Euroblood recipients have vCJD agent present in their blood (prionemic)

Variable: $DR_{vCJD\text{-}EUBL\text{-}Pn}$ - Annual number of plasma donors infected via transfusion using Euroblood and are prionemic in 2002

$$DR_{vCJD-EUBL-Pn} = DR_{vCJD-EUBL} \quad \text{(IV.C.1.e-17)}$$

Variable: $DR_{vCJD\text{-}EUBL\text{-}Def\text{-}Pn}$- Annual number of plasma donors infected via transfusion using Euroblood and may have vCJD agent present in their blood and plasma (prionemic) in 2002 and meet deferral criteria

$$DR_{vCJD-EUBL-Def-Pn} = DR_{vCJD-EUBL-Def} \quad \text{(IV.C.1.e-18)}$$

Variable: $DR_{vCJD\text{-}EUBL\text{-}Res\text{-}Pn}$- Annual number of plasma donors who are possibly infected with vCJD via transfusion with Euroblood, that had vCJD agent present in their blood and plasma (prionemic) in 2002 and did not meet deferral criteria (likely not deferred)

$$DR_{vCJD-EUBL-Res-Pn} = DR_{vCJD-EUBL-Res} \quad \text{(IV.C.1.e-19)}$$

A-IV. C. 1. f. Total number all plasma donors who may potentially be infected with vCJD through all sources of exposure and vCJD agent is present in the blood

Variable: $DR_{vCJD\text{-}S\text{-}Pn}$ - Estimated total annual number of Source Plasma donors infected with vCJD wh potentially had the agent present in blood and plasma (prionemic) in 2002:

$$DR_{vCJD-S-Pn} = DR_{vCJD-S-UK-LH} + DR_{vCJD-S-FR-HL} + DR_{vCJD-S-DOD-LH} + DR_{vCJD-S-EUBL-Pn} \quad \text{(IV.C.1.f-1)}$$

Variable: $DR_{vCJD\text{-}R\text{-}Pn}$ - Estimated total annual number of recovered plasma donors potentially infected with vCJD with the agent present in blood and plasma (prionemic) in 2002

$$DR_{vCJD-R-Pn} = DR_{vCJD-R-UK-LH} + DR_{vCJD-R-FR-HL} + DR_{vCJD-R-EU-LH} + DR_{vCJD-R-DOD-LH} + DR_{vCJD-R-EUBL-Pn}$$

(IV.C.1.f-2)

Variable: $DR_{vCJD\text{-}Pn}$ - Total annual number of all US plasma donors potentially infected with vCJD with the agent present in blood and plasma (prionemic) in 2002

$$DR_{vCJD-Pn} = DR_{vCJD-S-Pn} + DR_{vCJD-R-Pn} \quad \text{(IV.C.1.f-3)}$$

APPENDIX A

A-IV. C. 2. Annual number of all US plasma donors potentially infected with vCJD agent present in the blood and who may not be deferred by questionnaire screening

A-IV. C. 2. a Annual number of US Source Plasma donors potentially infected and vCJD agent is present in the blood that may not be deferred by questionnaire screening

Variable: Eff_{Def} - Effectiveness of US donor deferral policy

Assumption about variable: Based on advice from the TSEAC at the October 31, 2005 meeting, the FDA model assumed 85-99% of potential vCJD infected donors would have been deferred just prior to donation.

Variable: $DR_{vCJD\text{-}S\text{-}Def\text{-}Pn}$ - Estimated annual number of Source Plasma donors potentially infected with and having vCJD agent present in blood and plasma (prionemic) that are deferred by current policy

$$DR_{vCJD\text{-}S\text{-}Def\text{-}Pn} = DR_{vCJD\text{-}S\text{-}UK\text{-}Def\text{-}Pn} + DR_{vCJD\text{-}S\text{-}FR\text{-}Def\text{-}Pn} + DR_{vCJD\text{-}S\text{-}DOD\text{-}Pn} \quad \text{(IV.C.2-1)}$$

Assumption about variable: This population includes the potential Source Plasma donors with vCJD agent present in blood and plasma (prionemic) that have long-term travel history to the UK (≥3 mo), and France (≥ 5 yrs); and a history of military deployment (or military dependent, etc.) in Europe from 1980 – 1996.

Variable: $DR_{vCJD\text{-}S\text{-}Res}$ - Estimated annual number of Source Plasma donors potentially infected with vCJD with agent present in blood and plasma (prionemic) that have short term travel history (UK (<3 mo), and France and/or Europe (< 5 yrs); and not deferred by deferral policy.

$$DR_{vCJD\text{-}S\text{-}Res\text{-}Pn} = DR_{vCJD\text{-}S\text{-}UK\text{-}Res\text{-}Pn} + DR_{vCJD\text{-}S\text{-}FR\text{-}Def\text{-}Pn} + DR_{vCJD\text{-}S\text{-}DOD\text{-}Pn} \quad \text{(IV.C.2-2)}$$

Assumption about variable: This population includes the potential Source Plasma donors with vCJD with agent present in blood and plasma (prionemic) that have short-term travel history to the UK (< 3 mo), France (< 5 yrs), and a history of receiving Euroblood.

Variable: $DR_{vCJD\text{-}S\text{-}Pn\text{-}NR}$ - Annual total number of potential Source Plasma donors with vCJD agent present in blood and plasma (prionemic) and were not removed by deferral screening

Assumption used in model: This includes potential Source Plasma donors with vCJD agent present in blood and plasma (prionemic) who meet deferral criteria but for a variety of reasons are not deferred.

$$DR_{vCJD\text{-}S\text{-}Pn\text{-}NR} = DR_{vCJD\text{-}S\text{-}Res\text{-}Pn} + DR_{vCJD\text{-}S\text{-}Def\text{-}Pn} \times (1 - Eff_{Def}) \quad \text{(IV.C.2-3)}$$

A-IV. C. 2. b Annual number of US recovered plasma donors potentially infected and vCJD agent is present in the plasma that may not be deferred by questionnaire screening

Variable: Eff_{Def} - Effectiveness of donor deferral policy

Assumption about variable: Based on advice from the TSEAC at the October 31, 2005 meeting, the FDA model assumed 85-99% of potential vCJD infected donors would have been deferred just prior to donation.

Variable: $DR_{vCJD\text{-}R\text{-}Def\text{-}Pn}$ - Estimated annual number of potential recovered plasma donors with vCJD agent present in blood and plasma (prionemic) who are deferred by current policy

$$DR_{vCJD\text{-}R\text{-}Def\text{-}Pn} = DR_{vCJD\text{-}R\text{-}UK\text{-}Def\text{-}Pn} + DR_{vCJD\text{-}R\text{-}FR\text{-}Def\text{-}Pn} + DR_{vCJD\text{-}R\text{-}EU\text{-}Def\text{-}Pn} + DR_{vCJD\text{-}R\text{-}DOD\text{-}Pn} \quad \text{(IV.C.2-4)}$$

Assumption about variable: Model includes potential recovered plasma donors with vCJD agent present in blood and plasma (prionemic) that have long term travel history to the UK (≥3 mo), France (≥ 5 yrs), and Europe (≥5 yrs); and history of military deployment, military dependent or related travel or residence in Europe.

There is a possibility that some individuals that traveled to the UK, France, and other countries in Europe since 1980 stayed for periods of time that were shorter than the deferral period, were exposed to BSE agent, and were infected with vCJD. These individuals represent a source of residual risk – or the remaining risk after interventions (in this case donor deferral policies) are applied. The section below addresses the calculation of residual risk for non-deferred at risk donors that traveled for periods of time that were shorter than recommended guidelines.

Variable: $DR_{vCJD\text{-}R\text{-}Res}$ - Annual number of potential Source Plasma donors with vCJD agent present in blood and plasma (prionemic) that have short term travel history and are not covered by and deferred by deferral policy.

$$DR_{vCJD\text{-}S\text{-}Res\text{-}Pn} = DR_{vCJD\text{-}S\text{-}UK\text{-}Res\text{-}Pn} + DR_{vCJD\text{-}S\text{-}FR\text{-}Def\text{-}Pn} + DR_{vCJD\text{-}S\text{-}DOD\text{-}Pn} \quad \text{(IV.C.2-2)}$$

Assumption about variable: Estimation of the possible vCJD residual risk includes potential Source Plasma donors with vCJD agent present in blood and plasma (prionemic) that have short term travel history to the UK (< 3 mo), France (< 5 yrs), history of travel to Europe and history of receiving Euroblood.

Variable: $DR_{vCJD\text{-}S\text{-}Pn\text{-}NR}$ - Annual total of potential Source Plasma donors with vCJD agent present in blood and plasma (prionemic) and were not removed by deferral screening

Assumption used in model: This includes all potential donors with vCJD agent present in blood and plasma (prionemic) that do not meet deferral criteria and who meet deferral criteria but wrongly not deferred.

$$DR_{vCJD-S-Pn-NR} = DR_{vCJD-S-Res-Pn} + DR_{vCJD-S-Def-Pn} \times (1 - Eff_{Def}) \quad \text{(IV.C.2-3)}$$

Variable: $DR_{vCJD-R-Pn-NR}$ - Annual total of potential recovered plasma donors with vCJD agent present in blood and plasma (prionemic) not removed by deferral screening

$$DR_{vCJD-R-Pn-NR} = DR_{vCJD-R-Res-Pn} + DR_{vCJD-R-Def-Pn} \times (1 - Eff_{Def}) \quad \text{(IV.C.2-4)}$$

A-IV. C. 2. c Total number of all US plasma donors potentially infected and vCJD agent is present in the plasma but may not be deferred by questionnaire screening

The total number of all US plasma donors potentially infected with vCJD with agent present in blood and plasma (prionemic) that may not be deferred by questionnaire screening was determined by summing the estimates generated for both Source and recovered plasma donors that may not be deferred by current screening procedures, and is described by the equation:

$$DR_{vCJD-Pn-NR} = DR_{vCJD-S-Pn-NR} + DR_{vCJD-R-Pn-NR} \quad \text{(IV.C.2-5)}$$

A-IV. C. 3. Total number of all US plasma donations potentially containing vCJD agent

Variable: $Freq_{DN-S}$ –Average frequency of donations from a single Source Plasma donor who contributes Source Plasma for FVIII manufacture (times/year)

Variable: DN_{vCJD-S} - Annual number of potential vCJD donations of Source Plasma

$$DN_{vCJD-S} = DR_{vCJD-S-Pn-NR} \times Freq_{DN-S} \quad \text{(IV.C.2-6)}$$

Assumption used in the model: The average frequency of donations from a single Source Plasma donor who contributes Source Plasma for a FVIII plasma pool used in manufacturing ranges from [redacted] and most likely to be [redacted] based on data from pdFVIII manufacturers.

Variable: $Freq_{DN-R}$ –The average frequency of donations from a single recovered plasma donor who contribute plasma for pdFVIII manufacture (times/year) is 1.

Variable: DN_{vCJD-R} - Annual number of potential vCJD donations of recovered plasma

$$DN_{vCJD-R} = DR_{vCJD-R-Pn-NR} \times Freq_{DN-R} \quad \text{(IV.C.2-7)}$$

Assumption used in the model: The average frequency of donations from a single blood donor that contributes recovered plasma for pdFVIII manufacture is 1.

A-IV. C. 4. Probability that a US plasma donation potentially contained vCJD agent among all donations

Variable: $\mathbf{Pr(DN_{vCJD\text{-}S})}$ - Probability a donation of Source Plasma contained vCJD agent

Variable: $\mathbf{DN_S}$-Annual units of Source Plasma used to make pdFVIII (calculated in A-IV. B. 1)

$$\Pr(DN_{vCJD-S}) = DN_{vCJD-S} / DN_S \qquad \text{(IV.C.4-1)}$$

Variable: $\mathbf{Pr(DN_{vCJD\text{-}R})}$ - Probability a donation of recovered plasma contained vCJD agent.

Variable: $\mathbf{DN_R}$-Annual number of units of recovered plasma used to make pdFVIII from plasma collected in the US (calculated in A-IV. B. 2).

$$\Pr(DN_{vCJD-R}) = DN_{vCJD-R} / DN_R \qquad \text{(IV.C.4-2)}$$

A-IV. C. 5. Probability of a Source or recovered plasma pool potentially containing a vCJD donation(s)

A-IV. C. 5. a. Probability that a plasma pool may contain a specific number of vCJD donations

Assumption used in the model: Consistent with manufacturing practices in which commingling of Source and recovered plasma is uncommon, the risk assessment considered plasma pools to consist entirely of only Source Plasma donations or only recovered plasma donations.

Variable: $n_{vCJD\text{-}DN\text{-}pool}$ - Designated number of vCJD donors in a single plasma pool.

Assumption used in the model: The number of vCJD donations in a single vCJD pool could be 0, 1, 2, 3 or 4; but because of the low prevalence of vCJD most of the time there would be 0 vCJD donations in a pool

Variable: $DR_{pool\text{-}S}$ -Size of Source Plasma pool (donors/pool)

Data used in the model: Based on information provided to the FDA by pdFVIII manufacturers, an individual Source Plasma pool may contain 6,000 to 60,000 donors. A statistical distribution representing the variation in the size (number of donations per pool) of plasma pools used in the manufacture of pdFVIII was generated by combining information on pool size with information on the percentage of market share for several individual pdFVIII products.

Variable: $Pr(n_{vCJD\text{-}DR\text{-}pool\text{-}S})$- Probability a Source Plasma pool containing $n_{vCJD\text{-}DN\text{-}pool}$ infected donations ($n_{vCJD\text{-}DR\text{-}pool}$ =0, 1, 2, 4)-are determined by density frequency of $DR_{pool\text{-}S}$ at $X=n_{vCJD\text{-}DR\text{-}pool}$

Variable: $DN_{pool\text{-}R}$ -Size of recovered plasma pool (donors/pool)

Data used in the model: Based on information from manufacturers, individual Source Plasma pool may contain 6,000 to 60,000 donors.

Variable: $Pr_{(n_{vCJD\text{-}DR\text{-}pool\text{-}S})}$- Probability a Source Plasma pool containing $n_{vCJD\text{-}DN\text{-}pool}$ infected donations ($n_{vCJD\text{-}DR\text{-}pool}$=0, 1, 2, 4)-are determined by density frequency of $DR_{pool\text{-}S}$ at $X=n_{vCJD\text{-}DR\text{-}pool}$

Variable: $DN_{pool\text{-}R}$ -Size of recovered plasma pool (donors/pool)

Data used in the model: Based on information provided to the FDA by pdFVIII manufacturers, an individual recovered plasma pool may contain 150,000 to 360,000 donors. As with Source Plasma pools described above, a statistical distribution representing the variation in the size (number of donations per pool) of plasma pools used in the manufacture of pdFVIII was generated.

Assumptions used in the model: The size of recovered plasma pools was represented in the model by using a uniform distribution ranging from 150,000 to 360,000 donations per pool (Figure 4-3) – representing the range of pool sizes used by manufacturers of pdFVIII. The uniform distribution provided the best fit for the range of possible recovered plasma pool sizes that may be used in the US to manufacture pdFVIII.

Variable: $Pr_{(n_{vCJD\text{-}DN\text{-}pool\text{-}R})}$-Probability a recovered plasma pool containing $n_{vCJD\text{-}DN\text{-}pool}$ infected donations ($n_{vCJD\text{-}DN\text{-}pool}$=0, 1, 2, 4)-are determined by density frequency of $DR_{pool\text{-}R}$ at $X=n_{vCJD\text{-}DR\text{-}pool}$

A-IV. C. 5. b. Probability a plasma pool may potentially contain a vCJD donation(s)

Variable: $Pr(vCJD\text{-}pool_S)$-Probability of a Source Plasma pool containing one or more vCJD donations

$$\Pr(vCJD\_pool_S) = 1 - \Pr(n_{vCJD-DN-poolS} = 0) \quad \text{(IV.C.5-1)}$$

Variable: $Pr(vCJD\text{-}pool_R)$-Probability of a recovered plasma pool containing one or more vCJD donations

$$\Pr(vCJD\_pool_R) = 1 - \Pr(n_{vCJD-DN-pool_R} = 0) \quad \text{(IV.C.5-2)}$$

Variable: $Pr(vCJD\text{-}pool)$-The Probability that a plasma pool (including Source and recovered plasma pools) contained one or more vCJD donations. The distribution for pool size (or number of donations per pool) incorporated information on pool size.

Variable: $Perc_S$ – Percentage of Source Plasma pools used to manufacture pdFVIII in the US

Variable: $Perc_R$ – Percentage of recovered plasma pools used to manufacture pdFVIII in the US

Assumption used in the model: Estimates suggest that approximately [redacted] of pdFVIII products were made from Source Plasma, and [redacted] were made from recovered plasma.