potentially infected with vCJD during travel to the UK (see Table 1). The model also predicts the number of donors that potentially have agent present in their plasma that may possibly donate to plasma pools used to manuafacture pdFVIII in the US.

Additional technical information and details on the model calculations of potential vCJD risk and modeling approaches are provided in Appendix A and described in sections in A - IV.C.

IV. C. 1. b. Estimation of the number of US plasma donors with a history of extended travel to France potentially infected and vCJD agent is present in the blood

The FDA risk assessment model assumes that the likely source for vCJD risk in US plasma donors is associated with those donors who have a history of travel to the UK from 1980 – 1996, or travel to France or other countries in Europe since 1980. Presumably the greatest vCJD risk resides with travel to the UK since the BSE epidemic was several orders of magnitude larger and the number of vCJD cases greater than that of any other country or region. However, donors who traveled to France are potentially at risk but that risk is likely significantly lower than that of the UK. France likely imported BSE-contaminated feed materials in the 1980s and 1990s and approximately 5% of its beef was supplied by the UK at the time of its BSE epidemic. To date, France has reported 20 cases of vCJD supporting the notion that there may be vCJD infection risk for US donors that may have traveled to or resided in France since 1980.

The FDA risk assessment model incorporates information from current guidance for geographic donor deferrals for vCJD (FDA 2002) to estimate potential vCJD risk for donors with a history of travel to countries where BSE has occurred. FDA guidance (2002) indicates that for donors with a history of travel to France "we now recommend deferral of blood and plasma donors with a history of 5 or more years of cumulative residence or travel in France since 1980." This portion of the model calculates the potential residual US vCJD risk based on the estimated vCJD prevalence among US plasma donors who traveled to France since 1980 and donated to plasma pools used to manufacture pdFVIII. The residual vCJD risk includes risk associated with donors who do not meet criteria for donor deferral (e.g., donors with a history of less than 5 years of travel to France), or who meet those criteria, but fail to be deferred due to limitations of the donor screening process. The model considers factors such as duration of travel, calendar year of travel, age of donor, type of donation (Source or recovered plasma), possible incubation period of the disease, and whether vCJD agent is present in the blood of a vCJD infected donor. The outcome of this portion of the model predicts the number of US plasma donors potentially infected with vCJD and results are shown in Table 4.4. The model goes on to predict the number of donors with a history of travel to France infected with vCJD that may potentially have agent present in their blood at the time of donation.

Additional technical details on the model calculations of potential vCJD risk for donors with a history of travel to France can be found in Appendix A – in sections under A-IV. C.1.b.

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

The FDA risk assessment model incorporates information from current guidance for geographic donor deferrals for vCJD (FDA 2002) in estimating potential vCJD risk for donors with a history of travel to countries where BSE has occurred. The model quantifies potential residual vCJD risk for US plasma donors. The model assumes that the residual vCJD risk likely originates from two sources, one source of potential risk is associated with donors with deferrable risk that continue to donate due to limitations in the donor screening process. The second source of vCJD risk is associated with donors with a history of travel that was less than the deferrable period (blood donors with a history of less than 5 years of travel to Europe). FDA guidance (2002) indicates that for donors with a history of travel to countries in Europe (other than the UK) "the current recommendation is to exclude from transfusion use, blood and blood components from donors with a history of 5 or more years of residence or travel in Europe outside of the UK". Furthermore, for donors with a history of travel to countries in Europe (other than the UK and France) the FDA guidance (FDA 2002) states "...we do not recommend that you defer Source plasma donors who have lived or traveled in Europe for 5 or more years".

The FDA risk assessment model reflects FDA guidance for vCJD deferral of Source Plasma and recovered plasma donors. Because the guidance recommendations for each type of plasma were different the model estimated the potential vCJD risk as follows:

- Recovered plasma donors – the FDA risk assessment **calculated** the potential vCJD risk because deferral was **recommended** for donors with a history of 5 or more years of residence or travel to countries in Europe (other than the UK)
- Source Plasma donors - the FDA risk assessment did **not calculate** the potential vCJD risk because deferral was **not recommended** for donors with a history of 5 or more years of residence or travel to countries in Europe (other than the UK and France).

The term "countries in Europe" as used in this portion of the risk assessment is defined as all countries in Europe (other than the UK and France). The UK and France BSE risk is assumed to be higher than that of other countries in Europe, therefore the potential donor vCJD risk for donors with a history of residence or travel to the UK and France described in sections IV.C. 1. a. and IV.C. 1. b.(and sections in Appendix A – under sections A-IV.C. 1. a. and A-IV.C. 1. b.), respectively, of this document. Also, US donors with a history of residence on US military bases in Europe may have a higher potential vCJD risk so their risk was calculated separately and is described in section IV.C.1.d.

This portion of the model calculates the vCJD prevalence, or number of US blood donors who traveled to other countries in Europe (other than the UK and France) since 1980 and were potentially infected with vCJD and donated to recovered plasma pools used to manufacture pdFVIII. Recovered plasma is plasma that is separated or "recovered" from a unit of whole blood soon after the blood is collected. The model considers factors such as duration of travel, calendar year of travel, age of donor, type of donation, possible incubation period of the disease, and whether vCJD agent is present in the blood of a vCJD infected donor. The outcome of this portion of the model predicts the number of US blood (recovered plasma) donors who are potentially infected with vCJD and have agent present in their plasma.

The model assumes that one of the most likely sources for vCJD risk in US plasma donors is associated with those donors who have a history of travel to the UK from 1980 – 1996, and France and other countries in Europe since 1980. Text in subsequent sections of this document will specifically discuss the potential vCJD infection risk for US plasma donors with a history of travel to countries in Europe (other than the UK and France) since 1980. Presumably the greatest vCJD risk resides with travel to the UK since 1980 since the BSE epidemic was several orders of magnitude larger and the number of vCJD cases greater than that of any other country or region. France is likely at significantly lower risk than the UK but the risk is still likely higher than the vCJD risk of other countries in Europe. There have been 20 cases of vCJD reported in France as of August 2006.

Donors who traveled to other countries in Europe (other than the UK or France) are potentially at risk but that risk is likely significantly lower than that of the UK, and France. Many European countries (other than the UK and France) likely imported BSE-contaminated feed materials in the 1980s and 1990s and approximately 1.5% of their beef may have been imported from the UK at the time of its BSE epidemic. The potential for BSE exposure to donors who traveled to or resided in other countries in Europe is possible. Hence, there may be a vCJD infection risk for blood donors who may have traveled to or resided in a European country (other than the UK and France) for periods greater than 5 years since 1980. The current US vCJD geographic deferral policy defers blood donors with a history of travel or residence in a country in Europe (other than the UK and France) for 5 years or more since 1980. Source Plasma donors who resided in a country in Europe (other than the UK and France) are not deferred from donation. Because Source Plasma donors are not deferred from donation, their risk is not estimated by the model. Therefore, this portion of the model only estimates potential vCJD risk for US recovered plasma donors who traveled to countries in Europe (other than the UK) since 1980.

Additional technical details on the model calculations of potential vCJD risk for donors with a history of travel to countries in Europe (other than the UK and France) can be found in Appendix A – in sections under A-IV. C.1.c.

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

The FDA risk assessment model incorporates information from current guidance for geographic donor deferrals for vCJD (FDA 2002) in estimating potential vCJD risk for donors with a history of travel to countries where BSE has occurred. The FDA guidance (2002) indicates that for donors with a history of service on US military bases in Europe "we recommend that you should indefinitely defer current and former US military personnel, civilian military personnel, and their dependents who were stationed at European bases for 6 months or more during the time periods outlined (in the document)".

The model quantifies potential residual vCJD risk for deferrable donor populations. The residual vCJD risk likely includes two possible sources of risk. One source of risk is associated with donors with deferrable risk that continue to donate because of limitations in the donor screening process. A second possible source of risk is associated with donors who have a history of travel that is less than the deferrable period (blood donors with a history of less than 5 years of travel to Europe). For the purposes of this risk assessment we assumed that exposure to the BSE agent and potential vCJD infection of military personnel or dependents may have occurred during their deployment to US military bases in the UK, France and other European countries during the period from 1980 through 1996, through consumption of BSE contaminated beef procured for use on US military bases from the UK.

Exposure via UK beef likely varied but the model assumes that up to 35% of beef consumed on military bases in Europe came from the UK. The model assumes that approximately 2% of US blood and plasma donors may have been military, military family or their dependents posted to US military bases in the UK or elsewhere in Europe from 1980 through 1996 (TSEAC, 2002). It was further assumed that the average deployment period was 2 years. Because data on military service of plasma donors was not available, the risk assessment used data available on military deployment by whole blood donors.

Additional technical details on the model calculations of potential vCJD risk for donors with a history of military service in countries in Europe can be found in Appendix A – in sections under A-IV. C.1.d.

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

Euroblood is whole blood that was collected at several different collection centers in Europe and shipped to and used by transfusion centers in the United States. The practice was stopped in 2002 with the implementation of geographic vCJD deferrals. The blood was used largely on in the New York City metropolitan area and possibly in other areas on the east coast of the US

The model assumed that a total of 1.2% of US blood donors may have received Euroblood (TSEAC, 2002). To our knowledge there are no specific data available for plasma donors, therefore, data for blood donors was used in this risk assessment.

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

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

This portion of the model sums the total number of all potential US donors that may have been infected with vCJD from different sources. The model estimates the total number of all plasma donors who may be infected with vCJD during extended residence, travel or military service in the UK, France, or other countries of Europe. Potential vCJD risk is also estimated for donors that may have received Europblood. Furthermore, the model estimates the number of total US donors potentially infected with vCJD and have agent present in their plasma.

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

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

Additional technical information and details of analyses and modeling approaches for estimating potential vCJD in the model are provided in Appendix A under section **A - IV.C.1.**

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

No validated test is currently available to detect the presence of vCJD agent in blood or plasma. The donor questionnaire, administered to all blood donors, can be used to potentially screen donors for potential vCJD risk based on travel history, specifically involving extended travel to the UK, France or other countries in Europe where BSE was known to occur. In 1999 the FDA implemented a donor deferral policy aimed at reducing the potential risk of donations from those potentially exposed to the BSE agent during extended travel to the UK, France and other countries of Europe. Current policies (FDA 2002) defer blood and plasma donors:

- diagnosed with vCJD or other forms of CJD
- at increased risk for CJD, e.g. the donors have received a dura mater transplant, or human pituitary-derived growth hormone; the donors have blood relatives diagnosed with CJD
- with a history of a 3-month or longer travel/residency period in the UK between 1980-96
- with a history of a 5-year or longer travel/residency period in France since 1980
- current or former US military personnel, civilian military personnel, and their dependents resided in Northern Europe for 6 months or more between 1980-90, or resided in military bases elsewhere in Europe for 6 months or more from 1980 to 1996
- received a transfusion of blood or blood components in the UK since 1980
- injected bovine insulin since 1980 unless it is confirmed that injected bovine insulin was not made after 1980 from UK cattle, and
- whole blood donors with a 5-year or longer travel/residency period in Europe (other than the UK) since 1980

Deferral of donors with a history of travel to BSE countries is an effective tool for eliminating a significant portion of potential vCJD risk in US donors. The model incorporates information on the effectiveness of US deferral policies in reducing potential vCJD risk and potential vCJD prevalence in the US donor population.

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.

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.

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.

Specific technical information and details of analyses and modeling approaches in estimating the effectiveness of donor deferral policies in reducing potential vCJD risk in US donors are provided in Appendix A under section **A - IV.C.2.**

Model Results:
The largest source of potential vCJD risk in US plasma donors is presumably associated with donors who traveled to or resided for extended periods of time in the UK, France and other countries of Europe since 1980. These donors might be exposed to the BSE agent in contaminated beef products and infected with vCJD during travel and residence abroad. Other populations in the US at potential risk for vCJD include US military deployed for extended periods of time in the UK or other countries of Europe and individuals in the US who received blood collected in Europe ("Euroblood"). The prevalence of BSE in the US cattle population is very low and therefore there is a very low probability that domestic dietary exposure to the BSE agent would give rise to human vCJD cases. Because of this very low prevalence, risk via US domestic dietary exposure was assumed to be negligible in the model.

The FDA FVIII risk assessment model uses the concept of relative risk to semi-quantitatively estimate the vCJD risk for US plasma donors with a history of travel to the UK, France and other countries of Europe since 1980. Relative risk is the vCJD risk in a population relative to the UK vCJD relative risk of 1 (or 100%), which is equal to the prevalence of vCJD in the UK. Elements used in the model to calculate vCJD risk for travelers include travel destination (UK, France or other countries of Europe), duration of travel, specific year of travel, and age of donor. The estimated vCJD risk for all potential routes was summed to generate the total mean predicted number of potential vCJD-infected plasma donors in the US. Because of current policies, a blood or plasma donor potentially infected with vCJD has a high probability (85% - 99% chance) of being deferred from donation. Since 2002 FDA has recommended that individuals who resided in the UK for a period of 3 months or more from 1980 to 1996, or resided in France or other countries of Europe for a period of 5 years or more since 1980 be deferred from donating blood or plasma. The model assumes the deferral policy in the US is approximately 85% to 99% effective in reducing the vCJD risk for blood and plasma-derived products. **Table 4.4** (below) shows results from the model predicting the mean number per year of potential vCJD-infected donors and the number of potential vCJD donors who are likely not deferred from donation and donate to plasma pools used to manufacture pdFVIII.

Although it is likely that most would be deferred by the current policy, some plasma donors potentially infected with vCJD may not be deferred and may donate to plasma pools used in the manufacture of pdFVIII. Totaling the estimated number of US donors potentially infected with vCJD yields a mean of approximately 0.01 donors per year based on calculations using a vCJD case-based epidemiological model estimated prevalence of ~1.8 in 1,000,000 (Clarke and Ghani 2005), or a mean of approximately 1.160 donors per year using calculations based on a tissue sample surveillance study yielding a prevalence estimate of 1 in 4,225 (Hilton *et al* 2004) (**Table 4.4**).

Table 4.4 Model Results: Annual Number of US plasma donors predicted by model to be potentially infected with vCJD and donate to plasma pools used to manufacture pdFVIII. Results from model provided for two different UK vCJD prevalence estimates. In the table the mean value is shown above with the 5th and 95th percentiles in parentheses below: The total number of vCJD donors for each prevalence estimate has been rounded to nearest decimal place.

	Model Output for LOWER vCJD Case Prevalence estimate of ~1.8 in 1,000,000 based on Clark and Ghani (2005)		***Model Output for HIGHER vCJD Infection Prevalence based on estimate of 1 in 4,225 by Hilton, et al (2004)***	
	Mean number (5th - 95th perc)[a] US plasma donors with history of travel to:		**Mean number (5th - 95th perc)[a] US plasma donors with history of travel to:**	
	United Kingdom	***France, Europe, or* Military Service**	**United Kingdom**	***France, Europe, or* Military Service**
Total number vCJD donors for all US pdFVIII pools Prior to screening	*0.0493* (0–0)[b]	*0.0108* (0–0)[b]	*5.32* (0–13)	*0.77* (0–3)
Number vCJD donors NOT DEFERRED (ineffective screening)	*0.0035* (0–0)[b]	*0.0007* (0–0)[b]	*0.39* (0-2)	*0.056* (0–0)[b]
Number vCJD donors NOT DEFERRED (short-term travel <3 mos. UK; <5 yrs. FR and EU)	*0.0049* (0–0)[b]	0.0017 (0–0)[b]	*0.483* (0–2)	0.0343 (0–0)[b]
Total number vCJD infected donors NOT DEFERRED Donate to pdFVIII Plasma Pools	***0.013*** (0–0)[b]		***1.160*** (0–4)	

[a] The 5th- 95th perc (percentiles) are the minimum and maximum numbers that define the range of values constituting the 90% confidence interval. Accordingly, the mean risk estimates generated by the model should fall within this defined interval at least 90% of the time.

[b] For a 5th and 95th percentile interval of 0 and 0, respectively, the model estimates that for at least 90% of pdFVIII recipients the risk is zero. At low vCJD prevalence, donation by a vCJD infected donor to a pdFVIII plasma pool would be rare and more than 90% of pdFVIII product lots (of vials) would not be predicted to contain vCJD agent.

IV. D. Annual total percentage of all plasma pools potentially containing a vCJD donation that are used to make pdFVIII in the US

Model Results:
The percentages of source or recovered plasma pools, potentially containing vCJD agent, used to manufacture pdFVIII in the US were estimated by the model. The majority of pdFVIII is manufactured from Source Plasma and the minority from recovered plasma. Manufacturers provided information to FDA on the approximate range and average number of donations per plasma pool which was combined with information on market share to develop two aggregate statistical distributions, one each representing donations for source and for recovered plasma pools. The distributions were used to predict the number of donations per source or recovered plasma pool in the model. The model used information on the number of donations per pool by type (either source or recovered), combined with estimated yield of pdFVIII per pool, and estimated the total number of plasma pools used to manufacture pdFVIII products distributed in the US in 2002.

As a general comment, the number of donations per plasma pool influences the potential exposure risk for infrequent recipients of plasma derivatives. The use of fewer donations and smaller plasma pools during manufacturing would result in a lower percentage of plasma pools potentially containing vCJD agent and potentially expose a lower percentage of infrequent recipients to vCJD (if present). Frequent recipients of plasma-derived products would likely face a similar level of risk of potential vCJD exposure whether large or small numbers of donations per plasma pool are used in manufacturing.

Lower UK vCJD prevalence estimate of ~1.8 in 1,000,000 (based on Clarke and Ghani, 2005). The lower prevalence estimate used in the FDA model suggested that an average of 0.027% of all US plasma pools used to manufacture pdFVIII in the year 2002 potentially contained the vCJD agent (bottom, **Table 4.5**). The lower disease prevalence is associated with model results predicting a much lower percentage of plasma pools potentially containing vCJD agent. In fact, on average >99.9% of the time plasma pools would be predicted not to contain a donation from a vCJD infected donor. Only an average 0.10% recovered plasma pools would be predicted by the model to contain a vCJD donation from a US donor in any given year. Of interest at the lower prevalence, the model predicts that the occurrence of a recovered plasma pool with a vCJD donation would be infrequent (as indicated by 5th and 95th percentile values of 0); occurring (as estimated by the model), at a rate of 1 in 100 years. Also at the lower prevalence, a vCJD donation in a Source Plasma pool would be predicted to be even more infrequent and predicted by the model to occur at a rate of 1 in 200 years.

Higher UK vCJD prevalence estimate of 1 in 4,225 (Hilton et al 2004). The higher prevalence estimate used in the FDA model suggested that an average of 2.41% of all US plasma pools used to manufacture pdFVIII in 2002 were predicted by the model to contain vCJD agent (**Table 4.5**). It should be noted that fewer recovered plasma pools than Source Plasma pools are used in the US annually to produce pdFVIII. Also, recovered plasma pools contain the largest number of plasma donations. Since recovered plasma pools

contain many more donations than Source Plasma pools the likelihood that a recovered plasma pool may contain a donation from an individual potentially infected with vCJD is considerably higher than for a Source Plasma pool. Using the higher UK vCJD prevalence estimate, the model predicts that on average, 9.12% of recovered pools and 0.96% of Source Plasma pools potentially contain vCJD agent.

Table 4.5 Annual Percentage of US Plasma Pools Potentially containing a vCJD Donation. Results from model include only those US plasma pools used annually to manufacture pdFVIII.

- Results provided for two different UK vCJD prevalence estimates.

	Model Output for LOWER vCJD Case Prevalence estimate of ~1.8 in 1,000,000 based on Clark and Ghani (2005)		Model Output for HIGHER vCJD Infection Prevalence based on estimate of 1 in 4,225 by Hilton, et al (2004)	
	Source Mean (5^{th} - 95^{th} perc)[a]	Recovered Mean (5^{th} - 95^{th} perc)[a]	Source Mean (5^{th} - 95^{th}) perc)[a]	Recovered Mean (5^{th} - 95^{th} perc)[a]
Percent pools potentially containing vCJD agent	0.01% (0 – 0%)[b]	0.10% (0 – 0%)[b]	0.96% (0 – 5.88%)	9.12% (0 – 40.17%)
Average percent pools potentially containing vCJD agent	**0.027 %** (0 – 0 %)[b]		**2.41 %** (0 – 10 %)	

[a] The 5^{th}- 95^{th} perc (percentiles) are the minimum and maximum numbers that define the range of values constituting the 90% confidence interval. Accordingly, the mean risk estimates generated by the model should fall within this defined interval at least 90% of the time.

[b] For a 5^{th} and 95^{th} percentile interval of 0 and 0, respectively, the model estimates that for at least 90% of pdFVIII recipients the risk is zero. At low vCJD prevalence, donation by a vCJD infected donor to a pdFVIII plasma pool would be rare and more than 90% of pdFVIII product lots (of vials) would not be predicted to contain vCJD agent.

Additional technical details on the calculation of the annual total percentage of all plasma pools potentially containing a vCJD donation that are used to make pdFVIII in the US are provided in Appendix A in sections under A-IV. D.

IV. E. Module 2: Estimation of Quantity of vCJD agent in a plasma pool that contains a donation from a donor potentially infected with vCJD

Based on limited available data (see below), FDA believes that the quantity of infectivity present in blood from a vCJD infected individual in i.v. ID_{50} is likely represented by a distribution with the following characteristics: Minimum value = 0.1, 5^{th} percentile = 2,

Most likely value = 10, 95th percentile = 30, and Maximum value= 1,000 i.v. ID_{50}. Given the possible parameters, statistical distributions were fitted to the selected parameters using Best Fit part of the @Risk Professional software package (Palisade Corporation, New York). Using the software we determined that a log normal statistical distribution of (2, 12, 30) i.c. ID_{50}/ml (5th percentile, most likely, and 95th percentile) with minimum and maximum of 0.1 and 1,000, respectively, provided the best fit.

Conclusions from several research groups arrive at somewhat similar estimates for the quantity of infectivity that might be present in the whole blood of mice and hamsters. Using a mouse model and human CJD Brown *et al* (1999) found a range from 0.5 to 15 mouse i.c. IU per ml which we assumed to be roughly equivalent to 1 to 30 i.c. ID_{50} (assuming a linear dose-response for infectivity). An infectious unit is the quantity of infectivity associated with a 100% probability of infection in recipients and roughly equates to two ID_{50} units (1 IU = 2 ID_{50}). Brown *et al* (1998, 1999) conducted experiments to determine the infectivity of buffy coat material and plasma but not red blood cells. Assuming that red blood cells retain approximately 25% of the infectivity of whole blood, then the infectivity present in whole blood could be estimated to be in the range of approximately 10 i.c. ID_{50} and 20 i.c. ID_{50} per ml. Cervenakova *et al* (2003) found levels as high as 20 – 30 infectious doses per ml (40-60 i.c. ID_{50} per ml) associated with buffy coat and plasma during incubating and symptomatic stages of the disease. Red blood cells were not found to be infectious. Transfusion of blood products using the hamster scrapie model by Rohwer suggests that addition of infectivity levels derived for individual blood components would generate a titer for whole blood of approximately 2 to 20 i.c. ID_{50}/ml. Summarizing the above literature it seems that the range of reported values for infectivity ranged from 0.5 to as high as 30 i.c. ID_{50} with the possibility that at times the infectivity present in blood may exceed this range.

Assumption used in the model: Whole blood collected from a vCJD-infected individual can vary from person to person in the quantity of infectivity it contains. The model used a log normal statistical distribution to represent the variability and uncertainty of the quantity of infectivity in blood. It was assumed that whole blood from an infected person potentially carries a minimum of 0.1 i.c. ID_{50} per ml, a 5th percentile of 2 i.c. ID_{50} per ml, a medium of 12 i.c. ID_{50} per ml, a 95th percentile of 30 i.c. ID_{50} per ml and a maximum of 1,000 i.c. ID_{50} per ml. Attempts to identify vCJD infectivity titers in human blood have not been successful, but the assay sensitivity for vCJD *in vitro* and in animal models is limited (Bruce *et al* 2001 and Wadsworth *et al* 2001). Wadsworth *et al* estimated a limit of sensitivity of about 1,000 ID_{50}/ml by their assay meaning that infected blood containing less than 1,000 ID_{50} would not have elicited infection or disease in their animal model, hence infectivity would not have been detected(Wadsworth, 2001).

IV.E.1. Quantity of vCJD agent present in a donation of a specific donor potentially infected with vCJD

This section of risk assessment estimated quantity of vCJD agent in each vCJD plasma pool that may be used to make pdFVIII. Quantity of infectious agent present in plasma