considered. A total of 3 positive appendix tissues were identified among 12,676 tissue samples tested, yielding a mean UK vCJD prevalence estimate of 1 case per 4,225. This prevalence estimate was further adjusted to account for the age of the patients surveyed (mostly 20 – 29 year olds) to arrive at a total population-based estimate of UK vCJD prevalence.
This study was not controlled using tissues from a non-BSE exposed population, and false positive interpretations of the findings cannot be ruled out. It is also not known whether this staining of appendiceal tissues is a reliable marker for vCJD pre-clinical infection or for an individual's capability to transmit the infection through blood donation. However, while unconfirmed, the findings from this study provide a higher prevalence estimate and therefore should also be considered. A more detailed description of the derivation of the tissue surveillance-based estimate and further discussion of the limitations of the tissue surveillance study can be found in section IV. A. 2. below.

Two spreadsheet models were developed for the FDA risk assessment – one for each of the two prevalence estimates – but otherwise the models were identical in all other ways. We describe the surveillance variables and assumptions in the sections immediately below.

IV. A. 1. UK vCJD prevalence estimated using epidemiological modeling results (Clarke and Ghani 2005) and diagnosed vCJD cases for 2002 and 2003

The first approach used to estimate UK vCJD prevalence in the FDA model relied largely on epidemiological modeling results (Clarke and Ghani 2005) that estimated future 70 vCJD cases in the UK for the years 2004 – 2080. Since the FDA model estimates the baseline vCJD infection risk for pdFVIII product used in the year 2002, we assumed the potential risk for US donors should be calculated based on a UK vCJD prevalence that included all vCJD cases and potentially incubating vCJD infections in the year 2002. Therefore to estimate the number of cases and future vCJD infections in the UK for the years 2002 – 2080 we added the 32 known diagnosed cases in years 2002 and 2003 and the estimated future 70 vCJD cases (Clarke and Ghani 2005). We assumed that the 70 future cases predicted by Clarke and Ghani (2005) would be incubating vCJD infection in 2002. Therefore, the FDA model estimated an average of 102 cases and incubating vCJD infections for the year 2002 and assumed a 95% confidence interval of 42 – 222 cases. The results of the input information and calculations for the number of vCJD cases in the UK in 2002 are summarized in **Table 4.1.** Assuming the population of the UK in 1997 is approximately 58 million, the prevalence of vCJD (United Kingdom Office for National Statistics, 1997) would be a mean of approximately 1.8 vCJD infections per million population (102 potential vCJD cases / 58 million).

Table 4.1. FDA model estimation of UK vCJD cases for years 2002 – 2080.

	Diagnosed vCJD cases in the UK (Health Protection Agency, 2006)			**Estimation of future UK vCJD cases** (Clark and Ghani 2005)	**FDA model: Estimation of UK vCJD cases for years 2002 - 2080**
Year(s)	**2002**	**2003**	**Total**	**2004 - 2080**	**2002 - 2080**
Number of vCJD	16	16	32	70 (10 – 190)	102 (42 – 222)

cases					

There are some limitations associated with estimates of future vCJD cases and vCJD incidence in the UK generated by epidemiological modeling based on the current reported vCJD cases. Many of the published models of future vCJD cases or vCJD incidence in the UK, including Clarke and Ghani (2005) and Cooper and Bird (2003), use simplifying assumptions in generating their predictions. Although these simplifying assumptions are a necessary part of vCJD case estimation efforts, they contribute considerable uncertainty to the final case estimates. Generally, the types of assumptions used to estimate vCJD cases fall into four general areas. First, the models must estimate the number of clinical and pre-clinical BSE-infected cattle slaughtered in the UK to estimate the intensity of human exposure to the BSE agent. Second, they assume a level of effectiveness of the 1989 Specified Ban on Offals which was assumed to reduce the quantity of infectious BSE agent in the food supply, thereby reducing human exposure in the UK. Third, the models generate an appropriate mathematical representation (or statistical distribution) for the incubation period, which is represented by many usi a unimodal statistical distribution. There may be constraints on the incubation period used in the model (e.g., the vCJD incubation period of all individuals in the population would not exceed 40 years, etc.). Fourth, many of the modeling approaches incorporate age-specific dependencies that influence exposure, susceptibility to the disease, and incubation period. Depending on the assumptions used, estimates of future cases of vCJD have varied considerably. Past estimates of vCJD cases from epidemiological models predicted from 250 to 440 future cases under certain assumptions (d'Aignaux et al 2001). As actual reported vCJD cases peaked in 2000 and have since been declining, predicted estimates of future cases have decreased (Boelle et al 2003, Clarke and Ghani 2005, Cooper and Bird, 2003).

There are additional uncertainties in predicting future vCJD cases that might arise from individuals with different genetic backgrounds and susceptibilities in the UK population. To date, all known cases of vCJD have occurred in individuals that were methionine homozygous (MM genotype) at codon 129 of the prion protein gene (PNRP). Recent research has identified two individuals who were valine homozygous (VV genotype, also called non-MM genotype) at PRNP codon 129 (Ironside *et al* 2006) among the three prion protein positive samples identified by Hilton *et al* (2004). Clarke and Ghani (2005) did incorporate the possibility of wider genetic susceptibilities in some of their estimates of future vCJD cases. However, because no cases of clinical vCJD have been identified in individuals with non-MM genotype, it is uncertain whether these individuals will in fact develop or transmit clinical disease. Therefore, any estimation of the incubation period for potential cases with the non-MM genotype would rely heavily on assumptions, which adds considerable uncertainty to any estimate of the size or number of cases in a possible secondary wave of vCJD cases that might occur in non-MM individuals.

IV. A. 2. UK vCJD Prevalence derived from a Tissue Surveillance study

We used a second approach for estimating UK vCJD prevalence drawing on results from a tissue surveillance study that tested lymphoreticular tissue samples (tonsils and appendices) for prion protein accumulation. The study was a retrospective survey of stored tonsil and appendix tissues surgically removed from UK patients in 1995 and subsequent years. The authors identified appendix samples from 3 patients as positive for lymphoreticular accumulation of prion protein out of a total of 12,674 patient samples tested (Hilton *et al* 2004). No tonsil biopsies showed such findings. The significance of the detection of prion protein in the appendix is not certain, and it is not known whether this test is a

reliable marker for either vCJD pre-clinical infection or the ultimate development of disease. Nor is it known whether or not such detection is a marker for an individual's potential capability to transmit infection through blood donation. Results from the tissue surveillance study are summarized in **Table 4.2.** Assuming the sensitivity and specificity of the testing method is 100%, this translates roughly to a vCJD prevalence of of 237 cases per million (95% CI: 49 – 692 cases per million) for all age groups. The authors (Hilton et al 2005) indicated that approximately 60% of the samples tested (from 7,600 patients) came from patients 20-29 years of age. Among the 20-29 year old group we calculated a vCJD prevalence of approximately 400 cases per million for which we assumed a 95% CI of 100-1200 cases per million.

Table 4.2. Summary of surveillance testing of tonsil and appendix tissues in the UK.

Reference	Ages of population examined	Years tissue taken	Number of positives	Total samples examined	Rate per million (95% CI)
Hilton DA, et al. 2004	10 – 60+ yrs (60% of patients were 20-29 yrs)	1995 - 1999	3 Appendices	14,964 Appendices 1,739 Tonsils 4,029 excluded	237/million (49–692 per million)

There are some possible limitations of using the Hilton *et al* tissue surveillance study in estimating vCJD prevalence. In their tissue survey, Hilton *et al* stressed that there were uncertainties and suggested caution in attempting a prevalence estimate for infection or a prediction of future vCJD cases in the UK based on detection by immunohistochemical staining of lymphoreticular accumulation of prion protein in three of 12,674 adequate tissue samples studied. First, because the stage of vCJD infection during which the appendix first accumulates detectable amounts of abnormal prion protein is not known and because the accumulations might not be uniformly distributed throughout the tissue, the prevalence of infection might have been underestimated. Second, because the study design (lacking examination of a large number of similarly obtained appendices from a non-BSE-epidemic country) did not permit an estimate of specificity of the method or an independent confirmation of results, it is possible that the results might have been false positives leading to an overestimation of prevalence. In their paper the authors stated: "Although immunohistochemical accumulation of PrP in lymphoreticular tissues has not been demonstrated in any disease other than vCJD, the significance of the positive samples in this study is not certain. In one case, the immunohistochemical pattern of immunoreactivity resembled that seen in appendix tissue from pre-clinical and autopsied cases of vCJD, but in the other two cases, a more finely granular pattern of staining was present in relation to follicular dendritic cells, raising the possibility that these may be false positives. However, we have been unable to demonstrate PrP immunoreactivity in a range of other disorders including other human prion diseases, neoplastic disease, or a range of inflammatory conditions."

Assumption used in the model: All vCJD cases that occur after 2002 are incubating in year 2002.

Prevalence of vCJD among the UK population and the vCJD risk from using plasma-derived factor products are expected to be different from year to year since 1980. In this risk assessment, the potential vCJD risk for pdFVIII products was estimated for the baseline year of 2002, but the results and conclusions also are likely to reflect the current vCJD risk for recipients of pdFVIII. Prevalence of vCJD in 2002 for a specific age population in the UK was extrapolated from two estimates of prevalence discussed above based on age information of reported vCJD cases. The prevalence derived from above two different approaches varied by approximately 130 fold. The discrepancy reflects the limitation on the current knowledge of the disease. In order to evaluate the impact of uncertainty in estimation of vCJD prevalence, the FDA risk assessment provides estimated risk outcomes stratified by two estimates of prevalence.

Assumption used in the model: Our model assumed that distribution of asymptomatic cases across age groups would be the same as the distribution of observed symptomatic cases.

Additional technical information and details of analyses and modeling approaches are provided in Appendix A under section A - IV.A.

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

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.

This module estimates the annual number of plasma pools that are used to manufacture pdFVIII from plasma collected in the United States, the number of pools that potentially contain a donation from an infected plasma donor, and the potential quantity of vCJD agent that may be present in a positive pool. The potential vCJD risk for US plasma donors is likely associated with dietary exposure to BSE agent during periods of travel or residence in the at-risk geographic areas where BSE occurred. The percentages of blood donors with a history of travel or residency in BSE countries, who are military members who resided in bases in UK and elsewhere in Europe during 1980-1996, and who are recipients of "Euroblood" were obtained from 1980-1996 Blood Donor Travel Survey conducted by American Red Cross (TSEAC 2000). The percentage was calculated by destination (e.g., the UK, France or other European countries) and duration of travel.

Two different types of plasma are used in manufacture of pdFVIII. Source Plasma is collected through plasmapheresis, a process that separates red blood cells from plasma and returns red blood cells to the donor. Recovered plasma is prepared from whole blood units collected from blood donors. Source

Plasma accounts for approximately 80% of the total plasma collected annually in the United States, and recovered plasma accounts for the remaining 20%. Source Plasma donors are usually younger than blood (recovered plasma) donors, and are thought to travel less so presumably their vCJD risk may be somewhat lower than that of blood donors. However, because of their younger age demographic, Source Plasma donors are likely to be more susceptible to vCJD infection. Additionally, Source Plasma pools are usually smaller and contain larger volume donations (an average of 700 milliliters) from fewer donors than recovered plasma pools (average volume of a donation is ~200 milliliters). Plasma from fewer donors reduces the chance that a plasma pool may contain a donation from an infected donor. However, because Source Plasma donors are allowed to donate more frequently, and give more plasma per donation, there is a greater chance that if a vCJD infected donor were in the Source Plasma donor pool that they may contribute multiple donations to a single plasma pool or donate to multiple pools. However, blood deferral policies instituted beginning in 1999 are believed to have reduced the risk of vCJD donations by more than 90%. The effectiveness of the deferral policy in removing potential vCJD risk from the donor and donation pool is included in the FDA model. Because of the unique characteristics and potential differences in risk for Source and recovered plasma donations and plasma pools, the FDA risk assessment modeled Source and recovered plasma pools separately, and considered factors that may result in different risk for pdFVIII product made from each of the two types of plasma.

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

Age is an important factor in estimating potential vCJD risk for US plasma donors. The FDA model is organized by age groups 18 and 19 yr olds, 10-14, 15-29, etc. (by five yr age groups to age 69) and calculates all risk information and makes all adjustments based on age groups. Each of these age groups forms a "bin" and in each of these bins donors are categorized by country of travel, vCJD prevalence (or relative risk) for country of travel, duration of travel, year of travel, type of donation (Source or recovered), donation rate, etc. The output at the end of this portion of the model is an estimation of the number of US donors in each age group that are potentially infected with vCJD. The model further incorporates the effect of FDA donor deferral policies, implemented beginning in 1999, that are believed likely to reduce the possible risk from blood donors potentially infected with vCJD by ~ 90%.

This specific portion of the model estimates potential age specific vCJD risk for both Source and recovered plasma donors. As mentioned above, donor age is an important factor associated with frequency of travel and susceptibility to the disease and influences the vCJD risk for a particular type of donor. For instance, Source Plasma donors as a group are generally younger than recovered plasma donors (see percentages of donors for Source and recovered plasma donors by age group in **Table 4.3**). Also, the younger Source Plasma donor population likely travels less, and thus, likely has a lower potential vCJD risk. However, this lower risk may be offset by the possibility that younger persons may be more susceptible to infection by the vCJD agent. The purpose of this portion of the model is to characterize plasma donors and their donations according to donor age to more accurately estimate the number of potential vCJD infected donors and donations containing vCJD agent. In turn this information will be used to estimate the probability that a plasma pool used in the manufacture of pdFVIII may contain a donation with vCJD agent.

Additional technical information and details of analyses and modeling approaches are provided in Appendix A under section **A - IV.B.**

Table 4.3. Reported vCJD cases in the UK and percent of US Source Plasma and blood (recovered plasma) donors by age groups

Age group	<10	10-14	15-19	18-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	>70
Reported vCJD cases in UK (through 2003)[a] (%)	0	5 (3.4%)	27 (18.4%)		32 (21.8%)	30 (20.4%)	22 (14.9%)	13 (8.8%)	5 (3.4%)	3 (2%)	5 (3.4%)	0 (0%)	5 (3.4%)		
Age distribution of US Source Plasma donors (%)[b]	0	0	0	12%	29.3%	14.1%	14.1%	9.6%	9.6%	5.8%	5.8%	0%	0%	0%	0%
Age distribution of US Blood (Recovered plasma) donors[c]	0	0	0	5%	13%	8%	10%	12%	13%	12%	11%	7%	4%	5%	0%

[a] Hilton *et al.* 2004

[b] Plasma Protein Therapeutics Association (Jan 07, 2005). Where data were organized in broader age group we allocated donor equally among smaller 5 year age groups

[c] Data provided to FDA by Westat in 2002

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

The purpose of this section of the model is to estimate the prevalence of vCJD in US donors who may have been exposed to the BSE agent and potentially infected with vCJD during travel, residence, military service in the UK, France or other countries in Europe since 1980. The vCJD prevalence in U donors is then used to estimate the probability that a plasma pool may contain a donation from a vCJDinfected donor with infectious agent in their blood at the time of donation.

The starting material for manufacturing pdFVIII is a plasma pool containing donations from thousands of donors. The probability that a plasma pool contains a donation with vCJD agent is a function of the prevalence of vCJD in the US donor population and the total number of donors and donations present in a pool used to manufacture pdFVIII. For US donors with a history of travel, a key factor in estimating the vCJD risk is the region or country of travel, i.e., the UK, France or other countries in Europe, since 1980. From there we make several adjustments to the vCJD prevalence for US donors. The model incorporates the age of donors into the estimate of vCJD prevalence – donation rate for various age groups is important since the majority of donors are less than 40 years of age. Furthermore, vCJD prevalence for each age group is determined. Since vCJD primarily affects younger persons (median age 28 yrs) and donors are younger – they are at particular risk for vCJD and may unknowingly transmit the agent via donations. The model further adjusts vCJD prevalence based on the year of travel – for instance, a traveler in 1992 that visited the UK at the height of the BSE epidemic faces a higher BSE exposure risk and risk of vCJD infection than someone who traveled to the UK in 1997 after more

stringent food controls were implemented in the UK. Also, the model incorporates information on the duration of the travel based on survey information of travel history for whole blood users. Also considered in the model is the type of donation – whether Source Plasma or for recovered plasma, since the number of donations by an individual per year varies dramatically for these two types of plasma. Finally, the model assumes that *a plasma donation from a vCJD infected individual contains the infectious vCJD agent*, and thus poses a potential risk, if the individual is in the last half of the incubation period for the disease (and likely prionemic). However, current deferral policies prevent potentially infected donors with a history of extended travel or residence to BSE countries since 1980 from donating blood. *This geographic deferral policy effectively lowers the prevalence of vCJD in the US donor population by removing donors with a history of extended travel or residence in the UK and other countries in Europe since 1980.* The FDA risk assessment incorporates the effectiveness of current geographic deferral policy in reducing the risk of vCJD transmission through plasma derivatives. The final outputs or results from the model offer estimates of the potential number of Recovered and Source Plasma donors who may be infected with vCJD, and the model further derives an estimate of the number of infected donors who may actually have agent in their blood at the time of donation.

FDA evaluated a number of possible sources of exposure to the BSE agent that could potentially result in infection with vCJD in US plasma donors. The model and risk assessment assumes that the greatest potential vCJD risk for US plasma donors was likely associated with exposure to the BSE agent during extended travel or residence in the United Kingdom (for 3 months or more from 1980 – 1996), or France and other countries in Europe (5 or more years since 1980).

The following sections in the document describe in detail our mathematical approach for modeling and estimating the risk for US plasma donors who lived or resided in:

- United Kingdom from 1980 – 1996 for ≥ 3 months (Described in Appendix A - section A-IV.C.1.a.)
- France - since 1980 for ≥ 5 years (Described in section IV.C.1.b. and in Appendix A – sections in A-IV.C.1.b.)
- Other countries in Europe – since 1980 for ≥ 5 years (does not include plasma donors) (Described in section IV.C.1.c. and in Appendix A – sections in A-IV.C.1.c.)
- US Military personnel or their dependents – deployed in UK or other countries in Europe since 1980 (Described in section IV.C.1.d. and in Appendix A – sections in A-IV.C.1.d.)
- Euroblood recipients in US – that received blood collected from donors in Europe (Described in section IV.C.1.e. and in Appendix A – sections in A-IV.C.1.e.)

Dietary exposure in the US through consumption of domestic beef potentially contaminated with BSE agent was considered negligible based on our calculations, and was not included in the final model of this risk assessment.

Assumption used in the model: The BSE exposure risk for an individual on extended travel or during residence to the UK, France, or other countries in Europe since 1980 is proportional to the duration of the stay or time spent. For instance a person who lived in the UK for one year has one-fifth the risk of a donor who spent five years.

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

The model considered all major potential sources of vCJD infection for US plasma donors. The most likely cause of vCJD is dietary exposure of donors to the BSE agent through the consumption of BSE-contaminated beef during travel to a country where BSE was present in the cattle population. Accordingly, the greatest risk of BSE exposure in the UK likely occurred during the period from 1980 to 1996. The BSE exposure risk for France was likely lower than that of the UK and likely present since 1980. Also, other countries in Europe likely posed an even lower risk than France of human exposure to the BSE agent since 1980. Generally, because of the higher prevalence of BSE in the UK in the late 1980s and early-to-mid-1990s and the higher occurrence of vCJD in the UK human population (currently 162 cases as of August 2006), US donors who traveled to the UK from 1980 through 1996 are likely at higher risk for vCJD infection than donors who traveled to other European countries in the same time period. This model uses the concept of relative risk to estimate the vCJD risk (and prevalence) for a donor population – a value of 1 is used for the UK and this is equal to the vCJD prevalence. Relative risk is used to compare the risk of other regions to that of the UK and is estimated based on factors such as amount of contaminated feed, percentage of meat from the UK, number of cases of BSE, vCJD, etc. In subsequent sections on estimating risk for donors that traveled to France, France is assumed to have a relative risk of 0.05, since they received about 5% of their beef and feed supply from the UK and also have reported domestically-acquired vCJD cases.

The potential vCJD risk faced by US plasma donors exposed to vCJD during travel or residence in the UK (since 1980) is assumed in the model to be proportional to the time a donor spent in the UK (or France or other countries in Europe), and also a function of the age of the donor, and year of travel. Duration of travel is an indicator of possible exposure and we assumed that the probability of exposure was proportional to the time spent in the UK from 1980 - 1996. The longer the duration of travel, the higher the risk of human exposure to the BSE agent. The magnitude of possible exposure to the BSE agent is also influenced by the specific year of travel. The risk is the highest when travel took place during the peak of BSE epidemic in 1992. The FDA risk assessment grouped plasma donors based on age, destination, duration and year of travel, estimated the number of donors, probability of an individual being infected, and potential number of infected donors for each group. Then, numbers of infected donors from all groups were summed to arrive at an estimate of the total number of potential vCJD infected donors in the US that may contribute to FVIII plasma pools. The vCJD agent may only be present in the blood of an infected person during the last half of the disease. Accordingly, the FDA risk assessment considered only those vCJD infected donors who were in the last half incubation period of the disease as being capable of possibly transmitting the disease to others through their plasma donations.

The FDA risk assessment evaluates the effectiveness of current geographic deferral policy in reducing the risk of vCJD transmission through plasma derivatives. Current policy defers individuals with history of long term travel in BSE epidemic areas since 1980, providing a barrier for donors potentially infected, thus effectively lowering the vCJD prevalence in the US donor population by an estimated 90% or more. However, there may be residual risk associated with donors who do not meet criteria for donor deferral, or who meet those criteria, but fail to be deferred due to limitations of the donor screening process. Although current policy defers US donors that received transfusions while in the UK

or France since 1980, the FDA risk assessment did not estimate the potential vCJD risk for these donors.

Assumption used in the model: vCJD risk for the US plasma donor population is a sum of the risk from all exposure sources.

Assumption used in the model: The FDA risk assessment assumed vCJD agent is present in the plasma of infected person only in the last half of the incubation period of the disease, based on animal studies on vCJD infectivity of blood.

Assumption used in the model: The mean incubation period for vCJD is 14 years, and the median incubation period is 13 years.

The United Kingdom has the highest number of reported BSE and vCJD cases in the world. US plasma donors that traveled to the UK during 1980-1996 are considered at risk of exposure to the BSE agent and possibly infected with vCJD. Donors that traveled to France and other countries in Europe are assumed to be at significantly lower risk since the BSE epidemic in those regions was many times smaller than in the UK. This part of the model further characterizes the plasma donors of each age group who have history of travel or residence to the UK (for $\geq$ 3 months from 1980 – 1996), and France or other countries in Europe (for $\geq$ 5 yrs since 1980), by duration and calendar year of travel, estimated the number of potential donors who may be infected, and number of donor who may be in the last half incubation period (prionemic) at year 2002.

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

This portion of the model calculates the potential vCJD risk for US plasma donors who traveled to the UK since 1980 and estimates the potential number of donors with vCJD agent present in their blood and donated to plasma pools used to manufacture pdFVIII. For blood and plasma donors with a history of travel to the UK FDA guidance (2002) currently recommends that blood and plasma collection centers "....defer blood and plasma donors who have traveled or resided in the U.K. for a cumulative period of 3 or more months between 1980 and the end of 1996." The deferral policy likely eliminates much approximately 90% of the potential vCJD risk associated with donor travel to BSE countries when the disease was present. The model incorporates the effectiveness of the deferral policy in reducing risk. However, residual vCJD risk remains from two sources. One source includes potential risk associated with deferrable donors that continue to donate because of limitations in the donor screening process. The second potential source is associated with donors with a history of travel that is less than the deferrable period (blood or plasma donors with a history of less than 3 months of travel to the UK).

In addition to the effectiveness or deferral policies, the residual risk of vCJD infection in US donors is calculated based on the proportion of time spent in the UK by US donors compared to a UK resident whose risk is equivalent to the UK vCJD prevalence. Additionally, the model considers factors such as 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 who were