Table 5.1A. Model Results for All HA Patients who use a Hypothetical Factor VIII Product with 4-6 log_{10} Manufacture Process Reduction of vCJD Agent: *Predicted Annual per Person Exposure to vCJD i.v. ID_{50} and Mean Potential per Person Annual vCJD Risk:*

- For patients with SEVERE disease, and
- Two different UK vCJD prevalence estimates.

				4 - 6 Log_{10} Reduction Factor (LRF)			
				Model Output for LOWER vCJD Case Prevalence of ~4.5 in 1,000,000 based on Clark and Ghani (2005)		Model Output for HIGHER vCJD Infection Prevalence of 1 in 4,225 by Hilton *et al* (2004)	
Treatment Regimen	Inhibitor Status	Est. Total Number patients in US	Mean quantity FVIII used per person per year [a] [b] (5th - 95th perc)	Mean exposure to vCJD iv ID_{50} [a] per person per year [b] (5th - 95th perc) [c]	Mean potential vCJD risk per person per year [b] (5th - 95th perc) [c]	Mean exposure to vCJD iv ID_{50} [a] per person per year [b] (5th - 95th perc) [c]	Mean potential vCJD risk per person per year [b] (5th - 95th perc) [c]
Prophylaxis	No Inhibitor	578	157,949 IU [d] (21,000 - 382,000)	5.10×10^{-7} (0-0) [c]	1 in 4.0 million (0-0) [c]	3.2×10^{-6} ($0 - 1.50\times10^{-5}$)	1 in 63,000 (0 - 1 in 13,000)
	With Inhibitor – No Immune Tolerance	63	190,523 IU [d] (27,000 - 448,000)	5.90×10^{-7} (0-0) [c]	1 in 3.4 million (0-0) [c]	3.90×10^{-6} ($0 - 1.90\times10^{-5}$)	1 in 53,000 (0 - 1 in 11,000)
	With Inhibitor – With Immune Tolerance	62	558,700 IU [d] (33,000 - 1,593,000)	1.80×10^{-6} (0-0) [c]	1 in 1.1 million (0-0) [c]	1.10×10^{-4} ($0 - 5.40\times10^{-4}$)	1 in 18,000 (0 - 1 in 3,700)
Episodic	No Inhibitor	946	85,270 IU [d] (46,000 - 245,000)	2.80×10^{-7} (0-0) [c]	1 in 7.1 million (0-0) [c]	1.70×10^{-6} ($0 - 8.20\times10^{-6}$)	1 in 115,000 (0 - 1 in 24,000)
	With Inhibitor	151	160,458 IU [d] (5,000 - 489,000)	5.00×10^{-7} (0-0) [c]	1 in 4.0 million (0-0) [c]	3.30×10^{-6} ($0 - 1.50\times10^{-5}$)	1 in 61,000 (0 - 1 in 13,000)

[a] Some numbers on quantity of product used that also appear in the 2006 FDA Risk Assessment have been rounded for simplification in the 2010 Updated FDA Risk Assessment.

[b] iv ID_{50} represents the probability that 50% of those exposed to 1 ID_{50} intravenously may become infected with vCJD.

[c] Mean potential annual vCJD risk – the risk of potential vCJD infection based on animal model dose-response information. Mean potential annual vCJD risk = Total mean quantity iv ID_{50} per year x 0.5 (50 % chance infection from ID_{50}).

[c] Risk estimates generated by the model should fall within the interval defined by the 5th - 95th perc (percentiles) 90% of the time.

[d] IU - represents International units of Factor VIII and may be expressed using the term "unit" or "units" in this document.

[c] For a 5th and 95th percentile interval of 0 and 0, respectively, the model estimates that for at least 95% 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.

Table 5.1B. Model Results for Total Population-based Exposure and Potential vCJD Risk for All Hemophilia A patients who use a Hypothetical pdFVIII Product with 4-6 log_{10} Manufacture Process Reduction of vCJD Agent: Predicted annual per person exposure to vCJD i.v. ID_{50} and mean potential per person annual vCJD risk:

- For patients with SEVERE disease, and
- Two different UK vCJD prevalence estimates.

			4 - 6 Log_{10} Reduction Factor (LRF)			
			Model Output for LOWER vCJD Case Prevalence of ~4.5 in 1,000,000 based on Clark and Ghani (2005)		Model Output for HIGHER vCJD Infection Prevalence of 1 in 4,225 by Hilton *et al* (2004)	
	Est. Total Number severe HA patients in US	Mean quantity product used per person per year	Mean exposure to vCJD iv ID_{50} [a] per person per year [b] (5th - 95th perc) [c]	Mean potential vCJD risk per person per year [b] (5th - 95th perc) [c]	Mean exposure to vCJD iv ID_{50} [a] per person per year [b] (5th - 95th perc) [c]	Mean potential vCJD risk per person per year [b] (5th - 95th perc) [c]
Mean total annual exposure and population risk	1,800	243 million IU [d]	7.79×10^{-4} (0-0) [c]	1 in 2,600 years (0-0) [c]	4.90×10^{-3} ($0 - 2.39\times10^{-1}$)	1 in 41 years (0 - 1 in 8)

[a] iv ID_{50} represents the probability that 50% of those exposed to 1 ID_{50} intravenously may become infected with vCJD.

[b] Mean potential annual vCJD risk – the risk of potential vCJD infection based on animal model dose-response information. Mean potential annual vCJD risk = Total mean quantity iv ID_{50} per year x 0.5 (50 % chance infection from ID_{50}).

[c] Risk estimates generated by the model should fall within the interval defined by the 5th - 95th perc (percentiles) 90% of the time.

[d] IU - represents International units of Factor VIII and may be expressed using the term "unit" or "units" in this document.

[c] For a 5th and 95th percentile interval of 0 and 0, respectively, the model estimates that for at least 95% 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 95% of pdFVIII product lots (of vials) would not be predicted to contain vCJD agent.

V. C. Model results: Estimated Annual Potential Exposure to i.v. ID_{50} vCJD Agent and Potential vCJD Risk through Human pdFVIII used to Treat Severe von Willebrand Disease (vWD)

Individuals with von Willebrand disease (vWD) vary in severity of disease, those with Type 3 disease have severe disease; this assessment specifically addresses potential vCJD exposure and risk for persons with severe vWD. FDA estimates that approximately 250 vWD patients have severe vWD disease in the United States and use human plasma-derived FVIII products to control their disease (Tables 5.2A. and 5.2 B.) The FDA model suggests that it is possible that some of these vWD patients using human pdFVIII may potentially be exposed to vCJD agent if present in US manufactured product. Results from the risk assessment model for patients with vWD and treated with pdFVIII product with a 4-6 log_{10} manufacturing process reduction of vCJD agent are shown in Tables 5.2A. and 5.2 B. Generally results are expressed for patients with von Willebrand disease (vWD) clinical treatment groups of either Prophylaxis or Episodic treatment.

Table 5.2A. Results von Willebrand Disease (vWD) Patients[1] with Severe Disease: Predicted Potential Annual Exposure to vCJD i.v. ID_{50} and vCJD Risk:

- Assuming a processing reduction of 4-6 $\log_{10}$, and
- Two different UK vCJD prevalence estimates.

				4 - 6 $\log_{10}$ Reduction Factor (LRF)			
				Model Output for LOWER vCJD Case Prevalence of ~4.5 in 1,000,000 based on Clark and Ghani (2005)		Model Output for HIGHER vCJD Infection Prevalence of 1 in 4,225 by Hilton, et al (2004)	
		Est. Total Number patients in US	Mean quantity product used per person per year (5^{th} - 95^{th} perc)[c]	Mean exposure to vCJD iv ID_{50}[a] per person per year (5^{th} - 95^{th} perc)[c]	Mean potential vCJD risk per person per year[b] (5^{th} - 95^{th} perc)[c]	Mean exposure to vCJD iv ID_{50}[a] per person per year (5^{th} - 95^{th} perc)[c]	Mean potential vCJD risk per person per year[b] (5^{th} - 95^{th} perc)[c]
YOUNG vWD (< 15 yrs of age)	*Prophylaxis*	39	165,713 IU[d] (9900, 454300)	5.10×10^{-7} (0 - 0)[c]	1 in 3.8 million (0 - 0)[c]	3.40×10^{-6} (0 – 1.60×10^{-5})	1 in 59,000 (0 - 1 in 12,000)
	Episodic	60	11,045 IU[d] (1020, 34350)	3.60×10^{-8} (0 - 0)[c]	1 in 56 million (0 - 0)[c]	2.30×10^{-7} (0 – 9.50×10^{-7})	1 in 830,000 (0 - 1 in 210,000)
ADULT vWD (> 15 yrs of age)	*Prophylaxis*	73	186,880 IU[d] (17000, 540000)	5.80×10^{-7} (0 - 0)[c]	1 in 3.4 million (0 - 0)[c]	3.80×10^{-6} (0 – 1.80×10^{-5})	1 in 53,000 (0 - 1 in 11,000)
	Episodic	78	86,923 IU[d] (2200, 240000)	2.70×10^{-7} (0 - 0)[c]	1 in 7.1 million (0 - 0)[c]	1.80×10^{-6} (0 – 8.50×10^{-6})	1 in 114,000 (0 - 1 in 23,000)

[1] Number (percent) patients in a CDC sponsored study with 6 states to survey treatment of Hemophilia A and B conducted 1993 - 1998. Our analysis included 14 patients (<15yrs) and 28 patients (>15yrs) (total = 42) on prophylaxis or episodic treatment with Humate-P only and no record of inhibitor.

[a] Some numbers on quantity of product used that also appear in the 2006 FDA Risk Assessment have been rounded for simplification in the 2010 Updated FDA Risk Assessment

[b] iv ID_{50} represents the probability that 50% of those exposed to 1 ID_{50} intravenously may become infected with vCJD.

[c] Mean potential annual vCJD risk – the risk of potential vCJD infection based on animal model dose-response information. Mean potential annual vCJD risk = Total mean quantity i.v. ID_{50} per year x 0.5 (50 % chance infection from ID_{50})

[d] Risk estimates generated by the model should fall within the interval defined by the 5^{th} - 95^{th} perc (percentiles) for 90% of the time.

[e] IU - represents International units of Factor VIII and may be expressed using the term "unit" or "units" in this document.

[f] For a 5^{th} and 95^{th} percentile interval of 0 and 0, respectively, the model estimates that for at least 95% 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 95% of pdFVIII product lots (of vials) would not be predicted to contain vCJD agent.

Estimation of Factor VIII product utilization by patients with severe von Willebrand disease. FDA obtained data on pdFVIII utilization, presumably used in the treatment of severe von Willebrand disease, from the CDC. Details of the CDC – Six state collaborative study are described in the section above (section IV.G.2) on FVIII utilization. Annual usage of product by vWD patients was estimated based on an assumption that this patient class largely uses Humate P. Therefore, only records for patients utilizing Humate P were extracted from the CDC - Six state study conducted from 1993 – 1998 and used to develop statistical distributions of product usage for young vWD (<15 yrs old) patients and adult vWD (> 15 yrs old) patients. The mean quantity of product utilized per year per patient group is shown in Table 5.2A. and Table 5.2B.

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Table 5.2B. Von Willebrand Disease (vWD) Patients[1] with Severe Disease: Predicted Total Population-based Exposure to vCJD i.v. ID_{50} and Potential vCJD Risk:

- Assuming a processing reduction of 4-6 $\log_{10}$, and
- Two different UK vCJD prevalence estimates.

			4 - 6 $\log_{10}$ Reduction Factor (LRF)			
			Model Output for LOWER vCJD Case Prevalence of ~4.5 in 1,000,000 based on Clark and Ghani (2005)		Model Output for HIGHER vCJD Infection Prevalence of 1 in 4,225 by Hilton et al (2004)	
	Est. Total Number severe vWD patients in US	Mean Total quantity FVIII used by all patients per year	Mean exposure to vCJD iv ID_{50}[a] of all patients per year (5^{th} - 95^{th} perc)[c]	Mean population – based potential vCJD risk[b] (5^{th} - 95^{th} perc)[c]	Mean exposure to vCJD iv ID_{50}[a] of all patients per year (5^{th} - 95^{th} perc)[c]	Mean population – based potential vCJD risk[b] (5^{th} - 95^{th} perc)[c]
Mean total annual exposure and population risk	250	27.5 million IU[d,e]	8.60×10^{-6} (0 - 0)[c]	1 in 23,000 years (0 - 0)[c]	5.59×10^{-3} (0 – 2.72×10^{-2})[c]	1 in 358 years (0 - 1 in 74)

[1] Mean Total quantity FVIII used by all patients was incorrectly reported as 29.9 million IU in the FDA 2006 risk assessment, the value of 27.5 million IU is the correct value

Number (percent) patients in a CDC-sponsored study with 6 states to survey treatment of Hemophilia A and B conducted 1993 - 1998. Our analysis included 14 patients (<15yrs) and 28 patients (>15yrs) (total = 42) on prophylaxis or episodic treatment with Humate P only and no record of inhibitor.

[a] iv ID_{50} represents the probability that 50% of those exposed to 1 ID_{50} intravenously may become infected with vCJD.

[b] Mean potential annual vCJD risk – the risk of potential vCJD infection based on animal model dose-response information. Mean potential annual vCJD risk = Total mean quantity i.v. ID_{50} per year x 0.5 (50 % chance infection from ID_{50})

[c] Risk estimates generated by the model should fall within the interval defined by the 5^{th} - 95^{th} perc (percentiles) 90% of the time.

[d] IU - represents International units of Factor VIII and may be expressed using the term "unit" or "units" in this document.

[e] For a 5^{th} and 95^{th} percentile interval of 0 and 0, respectively, the model estimates that for at least 95% 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 95% of pdFVIII product lots (of vials) would not be predicted to contain vCJD agent.

Potential exposure of severe von Willebrand disease patients to vCJD agent: Results based on lower epidemiological model estimated prevalence of ~4.5 in 1,000,000 (Clarke and Ghani, 2005). Adult vWD (>15yrs of age) patients with severe disease on prophylaxis consumed the largest quantities of pdFVIII product annually and may potentially be at greater vCJD risk. Using the lower epidemiological model prevalence estimate, analysis of pdFVIII utilization data indicated that 73 Adult vWD patients on prophylaxis treatment regimen used an average of 186,880 IU and are potentially exposed to an average of 5.80×10^{-7} i.v. ID_{50} per person per year, and representing an average potential vCJD risk of 1 in 3.4 million per person per year (Table 5.2A.). At this level of risk, only 1 vCJD infection would be predicted to occur in an average of approximately 46,600 years. As mentioned earlier the 5^{th} and 95^{th} percentile intervals for all of the model outputs using the lower prevalence estimate (~4.5 per million) in Table 5.2A. are from 0 to 0 meaning that the chance of an infected donor donating to a plasma pool would be an infrequent event. Greater than 95% of the time the model estimates the risk to be zero because vCJD agent was not present in pdFVIII product used during treatment. However, the model predicts that 0.03% of the time the exposure to vCJD agent may be greater than zero, and there is a possible but low risk of vCJD infection.

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Totaling the model results reveals that the approximately 250 severe vWD patients in the US used a total of 27.5 million IU, and are potentially exposed to an average total of 8.60×10^{-5} i.v. ID_{50} per year. This represents an average potential vCJD risk of 1 in 23,000 **(Table 5.2B.)** or (as predicted by the model) roughly equal to one vCJD infection observed over a time span of approximately 23,000 years in the population of 250 severe vWD patients.

Potential exposure of severe von Willebrand disease patients to vCJD agent: Results based on higher prevalence estimate of 1 in 4,225 (Hilton et al 2004). At the higher surveillance prevalence estimate, among the vWD patient populations examined by the model, results **(Table 5.2A.)** indicated that adult vWD (>15yrs of age) patients with severe disease on prophylaxis used the largest quantities of pdFVIII product annually and may potentially be at greater vCJD risk. Analysis of pdFVIII utilization data indicated that 73 Adult vWD patients on prophylaxis treatment regimen used an average of 186,880 IU per person per year and are potentially exposed to an average of 3.80×10^{-5} i.v. ID_{50} per person per year, representing an average potential vCJD risk of 1 in 53,000 per person per year **(Table 5.2A.)**. At this level of risk, only 1 vCJD infection would be predicted to occur in an average of approximately 721 years for the population of 73 Adult vWD patients on prophylaxis treatment regimen.

The potential risk of vCJD infection for the entire population was calculated using the higher surveillance prevalence estimate. The model results shows that the approximately 250 severe vWD patients in the US used a total of 27.5 million IU **(Table 5.2B.)**, and are potentially exposed to an average total of 5.59×10^{-3} i.v. ID_{50} per year. This represents an average potential vCJD risk of one vCJD infection observed over a time span of 358 years for the population of 250 severe vWD patients in the U.S.

Range of Predicted Annual Mean Potential vCJD risk per HA patient for pdFVIII (Table 6)

The FDA risk assessment for potential vCJD infection risk for US manufactured pdFVIII generates results for several scenarios that reflect two key factors that greatly influence the final risk estimates including: (1) Reduction in vCJD agent in pdFVIII product during manufacture, and (2) UK vCJD prevalence estimate. As indicated earlier, the model used two widely different prevalence estimates, one lower prevalence estimate based on epidemiological modeling of predicted vCJD cases in the UK (Clarke and Ghani, 2005) of approximately 4.5 in 1 million and one higher prevalence estimate based on surveillance data of UK patient tissue samples (Hilton et al 2004) of 1 in 4,225. The use of these two estimates gives rise to a difference in results generated by the model that vary by an average of approximately 60 fold.

The model evaluated two separate categories of reduction in infectivity including 4-6 log_{10}, and 7-9 log_{10}. These two hypothetical categories were chosen to span the possible range of reduction of vCJD agent for pdFVIII products. **Table 5.3A. and 5.3B.** displays model results for a lower prevalence estimate and a higher prevalence estimate at all two levels of reduction. These two largest contributors to the final risk estimate also contribute to the greatest uncertainty in the model. Results from the model shown in **Tables 5.3A. and 5.3B.** indicate that there is a difference of approximately 60,000 fold between the lowest and highest risk estimates of each patient group.

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Table 5.3A. Range of *Predicted Annual Mean Potential per HA Patient vCJD risk for pdFVIII – at two levels of clearance: 7-9 log_{10} and 4-6 log_{10} at Higher Prevalence and Lower Prevalence estimates*

				7 - 9 Log10 Reduction Factor (LRF)		4 - 6 Log10 Reduction Factor (LRF)	
				Model Output for LOWER vCJD Case Prevalence of ~4.5 in 1,000,000 based on Clark and Ghani (2005)	Model Output for HIGHER vCJD Infection Prevalence of 1 in 4,225 by Hilton et al (2004)	Model Output for LOWER vCJD Case Prevalence ~4.5 in 1,000,000 based on Clark and Ghani (2005)	Model Output for HIGHER vCJD Infection Prevalence of 1 in 4,225 by Hilton et al (2004)
Treatment Regimen	Inhibitor Status	Est. Total Number patients in US	Mean quantity product used per person per year (5th - 95th perc)[a]	Mean potential vCJD risk per person per year (5th - 95th perc)[b]		Mean potential vCJD risk per person per year (5th - 95th perc)[b]	
Prophylaxis	No Inhibitor	579	187,849 IU[c] (21,000, 982,000)	1 in 4.0 million (p-p)[e]	1 in 69 million (p - 1 in 13 million)	1 in 4.0 million (p-p) e	1 in 63,000 (p - 1 in 13,000)
	With Inhibitor - No Immune Tolerance	63	190,523 IU[c] (27,000, 448,000)	1 in 3.3 billion (p-p)[e]	1 in 58 million (p - 1 in 11 million)	1 in 3.4 million (p-p) e	1 in 53,000 (p - 1 in 11,000)
	With Inhibitor - With Immune Tolerance	62	559,700 IU[c] (53,000, 1,593,000)	1 in 1.1 billion (p-p)[e]	1 in 18 million (p - 1 in 3.7 million)	1 in 1.1 million (p-p) e	1 in 18,000 (p - 1 in 3,700)
Episodic	No Inhibitor	946	89,270 IU[c] (46,000, 245,000)	1 in 7.1 billion (p-p)[e]	1 in 115 million (p - 1 in 24 million)	1 in 7.1 million (p-p) e	1 in 115,000 (p - 1 in 24,000)
	With Inhibitor	161	160,488 IU[c] (5,000, 489,000)	1 in 3.6 billion (p-p)[e]	1 in 69 million (p - 1 in 13 million)	1 in 4.0 million (p-p) e	1 in 61,000 (p - 1 in 13,000)

[a] Some numbers on quantity of product used that also appear in the 2006 FDA Risk Assessment have been rounded for simplification in the 2010 Updated FDA Risk Assessment

[b] ID_{50} represents the probability that 50% of those exposed to 1 ID_{50} intravenously may become infected with vCJD.

[c] Mean potential annual vCJD risk – the risk of potential vCJD infection based on animal model dose-response information. Mean potential annual vCJD risk = Total mean quantity in ID_{50} per year x 0.5 (50 % chance infection from ID_{50})

[d] Risk estimates generated by the model should fall within the interval defined by the 5th - 95th perc (percentiles) 90% of the time.

[e] IU - represents International units of Factor VIII and may be expressed using the term "unit" or "units" in this document.

[f] For a 5th and 95th percentile interval of 0 and 0, respectively, the model estimates that for at least 95% 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 95% of pdFVIII product lots (of vials) would not be predicted to contain vCJD agent.

This range or difference in the estimates of about 10 -20 million fold is reflected in the higher and lower prevalence results generated by the model shown in **Table 5.3A.** for each HA patient treatment group with severe disease. On closer inspection of the results in **Table 5.3A:** for patients with the most intensive pdFVIII product use, that is, the 62 patients on prophylaxis-with inhibitor and with immune tolerance, the effect of clearance on mean potential vCJD risk across the three ranges of clearance can be seen. At the low end of risk, the mean potential vCJD risk per patient per year risk (at 7-9 log_{10} and the lower prevalence estimate) is 1 in 1.1 billion. For patients on episodic treatment with no inhibitor who have a less intensive annual use of product, the model predicts the lowest risk (at 7-9 log_{10} and the lower prevalence estimate) to be 1 in 7.1 billion.

Table 5.3B. Range of Total Population-based Exposure and Potential vCJD Risk from Model Predicted HA population with severe disease annual vCJD Exposure and Risk associated with use of plasma-derived Factor VIII:

- Lower Prevalence assumptions of Prevalence of 4.5 in 1,000,000 and 7-9 log_{10} reduction, and
- Higher Prevalence assumptions of Prevalence of 1 in 4,225 and 4-6 log_{10} reduction.

			7 - 9 Log_{10} Reduction Factor (LRF)		4 - 6 Log_{10} Reduction Factor (LRF)	
			Model Output for LOWER vCJD Case Prevalence of ~4.5 in 1,000,000 based on Clark and Ghani (2005)	Model Output for HIGHER vCJD Infection Prevalence of 1 in 4,225 by Hilton et al (2004)	Model Output for LOWER vCJD Case Prevalence of ~4.5 in 1,000,000 based on Clark and Ghani (2005)	Model Output for HIGHER vCJD Infection Prevalence of 1 in 4,225 by Hilton *et al* (2004)
	Est. Total Number severe vWD patients in US	Mean Total quantity FVIII used by all patients per year	Mean population – based potential vCJD risk[a] [b] [c] (5th - 95th perc)	Mean population – based potential vCJD risk[a] [b] [c] (5th - 95th perc)	Mean population – based potential vCJD risk[a] [b] [c] (5th - 95th perc)	Mean population – based potential vCJD risk[a] [b] [c] (5th - 95th perc)
Mean total annual exposure and population risk	1,800	243 million IU	1 vCJD infection in 2.6 million years[c] (0-0)	1 vCJD infection in 40,000 years (0 -1 in 8,000)	1 vCJD infection in 2,800 years (0 -0)	1 vCJD infection in 41 years (0 -1 in 8)

[a] Mean potential annual vCJD risk – the risk of potential vCJD infection based on animal model dose-response information.

[b] Risk estimates generated by the model should fall within the interval defined by the 5th - 95th perc (percentiles) 90% of the time.

[c] For a 5th and 95th percentile interval of 0 and 0, respectively, the model estimates that for at least 95% 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 95% of pdFVIII product lots (of vials) would not be predicted to contain vCJD agent.

The results from the risk assessment model shown in **Table 5.3A.** show a wide range of difference in the predicted risk and displays the range in our uncertainty and knowledge in predicting the potential vCJD infection risk for HA patients who use US manufactured human pdFVIII. However, as further scientific information and data become available in the future, the uncertainty in the model may decrease and the estimates of vCJD risk for recipients of pdFVIII may become more precise.

Evaluating the total vCJD infection risk for the severe HA population of 1,800 by summing the total annual exposure (at the higher vCJD Infection prevalence estimated), the model predicts that the population would use a total average of approximately 243 million IU FVIII. If the patient population used product that attained a clearance of 7-9 $\log_{10}$ and assuming the lower prevalence the model predicts that for the total patient population the mean total annual risk would be 1 infection in 2.6 million years representing a negligible vCJD risk that would likely not give rise to new cases of the disease.

V. D. Sensitivity Analysis

A sensitivity analysis was conducted to determine which inputs in the model would have the largest impact on estimates of exposure to ID50s of the agent responsible for causing vCJD. The sensitivity analysis used the exposure of an adult hemophilia patient who uses FVIII for prophylactic treatment and has developed immunity and inhibitors as the baseline. The baseline also assumed an average log reduction during processing of 4-7 logs. From this baseline, eight inputs—Efficiency of Deferral, Yield, IC to IV conversion, Prevalence in UK, IBL, Donors per Pool, Usage, and Log Reduction—were sequentially set to a constant low or high value while the rest of the model was unchanged. The low and high values were either the minimum and maximum or the 5th and 95th percentile (See Table 5.4). The sensitivity test was run using both the clinical and tissue prevalence estimates. For both the clinical and tissue models, the sensitivity test for the prevalence in the UK ranged from the 5th percentile of the clinical prevalence estimate to the 95th percentile of the tissue prevalence estimate.

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Table 5.4. Input Variables included in Importance Analysis

Description of variables	Name of input variable	Importance analysis values
Entire range of estimated vCJD prevalence in UK (cases/million)	$Prev_{vCJD\text{-}UK}$	Minimum: 0.62 Maximum: 1,123
Efficiency of donor deferral policy	Eff_{Def}	Minimum: 85% Maximum: 99%
Efficiency of i.c. versus i.v. route	$A_{ic\text{-}iv}$	Minimum: 0.1 Maximum: 1
Number of donors per plasma pool	DR_{Pool}	Minimum: 6500 Maximum: 360000
Quantity of i.c. infectivity in infected human blood	I_{bl}	5th perc: 2 95th perc: 30
Manufacturing yield of FVIII (IU/L plasma)	Y_{VIII}	Minimum: 130 Maximum: 270
Log Manufacture Reduction of vCJD agent	R_{Log}	Minimum: 2 Maximum: 9
FVIII used per year (IU/year).	IU_{yr}	5th perc: 10000 95th perc: 4000000

The results of the sensitivity analysis are shown in tornado graphs (**Figure 2. A. and 2. B.**). The tornado graphs are centered on the mean exposure estimates for the clinical and tissue prevalence scenarios. The inputs are ordered from top to bottom based on the size of the absolute difference between the estimated mean exposure when the input was set to a high value compared to a low value. Bars extend from the overall mean exposure estimate to the estimates when the input was held constant at a low or high value.

For both the higher tissue (Figure 2.A.) and lower clinical (Figure 2.B.) prevalence scenarios, the log reduction during manufacturing had the largest impact on the estimate of exposure. In the clinical scenario using the Lower vCJD Case Prevalence estimate, the mean estimated exposure with log reduction during manufacturing set to 2 and is 1.2×10^{-3} compared to the baseline estimate of 1.7×10^{-6}. In the tissue prevalence scenario using the Higher vCJD Infection Prevalence estimate, the mean estimated exposure with log reduction during manufacturing set to 2 is 6.9×10^{-2} compared to the baseline estimate of 1.0×10^{-4}. Prevalence in the UK has the second highest impact on estimated exposure in the clinical prevalence scenario. The rest of the inputs in the clinical (Lower vCJD Prevalence) prevalence scenario have a relatively small impact on the estimated prevalence. In the tissue (Higher vCJD Prevalence) prevalence scenario, usage of FVIII had the second largest impact on the estimate of overall exposure followed by the number of donors per pool. The remaining inputs had relatively small impacts on the exposure estimate.

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Figure 2.A.

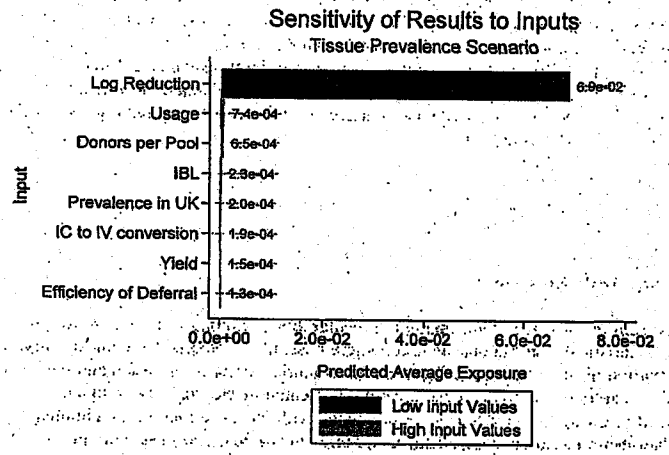
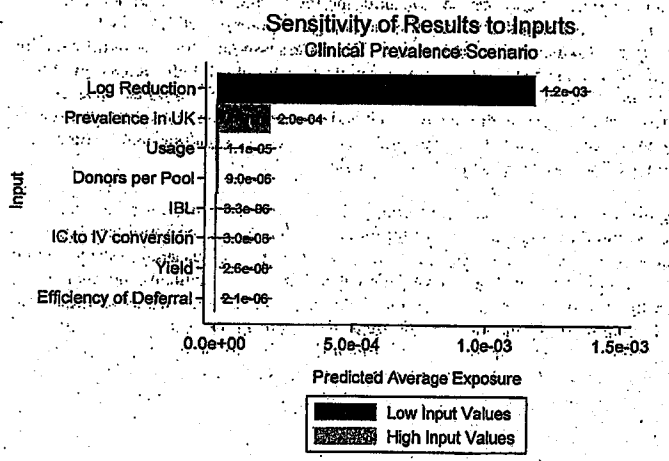


Figure 2.B.



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General Comments on Model Outputs

The risk estimations in this section of the risk assessment are predicated on the assumption that there is homogeneous mixing and dispersion of vials from all pools among all donors. In reality, vials may not be dispensed homogeneously and it is likely that patients draw from only one or a few manufactured lots of pdFVIII product in a given year. FDA did not have data to model this non-homogeneous dispensing of pdFVIII but the model can be used to estimate the average maximal level of i.v. ID_{50} exposure if on a very rare chance all vials used by a patient in a given year happened to contain vCJD agent.

V. E. Uncertainty and Data Gaps

Uncertainty arises from the absence of information or availability of limited information. In our probabilistic model statistical distributions are used, where possible, to represent the uncertainty of much of the information used in the model. There are uncertainties in the information and the model that we were unable to quantify and that are not represented in the final risk estimates. Some of the difficult to quantify uncertainties are associated with the extrapolation of a human dose-response relationship based on animal data, an assumed linear dose response with no uncertainty or variability bounds, and assumption of infectivity in the last 50% of the incubation period. We express the uncertainty of the final risk estimates generated from the model using a mathematical mean (average) of exposure in ID_{50} units and the 5^{th} and 95^{th} percentiles of a statistical distribution representing the probabilities and range of potential vCJD risk. The uncertainty for the risk estimates generated by this FVIII risk assessment model is significant and decision makers should use the results with caution. Similarly, patients and physicians should understand that the uncertainties are too great at this time to determine the presence, absence or degree of actual risk. In the future, additional research and information may be substituted for assumptions or used to improve estimates for the individual parameters and ultimately improve the precision of the final risk estimates generated by the model.

Even considering the associated uncertainty of estimated risks, risk assessment provides an estimate of risk based on the current and known information. It is still a useful tool that can inform the science-based decision making process. It can identify data gaps and research priorities where additional research and information would have the greatest impact on enhancing the final risk estimates. The sensitivity analysis results in Section IV.D. indicated that the risk assessment results are highly dependent upon log reduction of vCJD agent (R_{Log}) during the manufacturing process. The modeled estimates were based upon levels of reduction seen for manufacturing steps of several different types of plasma-derived products that were similar in some but not all respects to those used in the manufacture of FVIII products. More high quality data on the levels of vCJD agent clearance achieved during the pdFVIII manufacturing would likely improve the final risk estimate generated by the FDA model. Given the lack of data on vCJD agent clearance for pdFVIII uncertainty is considerable.

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Better information on when infectivity is present in human blood during the incubation period is a critical factor in the model, especially if the higher vCJD infection prevalence estimate (of 1 in 4,225) is in the range of the actual vCJD prevalence, and would improve predictions generated by the model. There are no data available on the level of infectious units or ID_{50} units present in the bloodstream of vCJD infected individuals at the time of blood donation. The model extrapolates an estimate of the level of vCJD agent that might be present in human blood based on data from several animal models. However, the presence and level of agent present in an infected individual at the time of blood donation could differ from our assumption and this adds to the uncertainty of the risk assessment outcomes.

The model estimates exposure to the vCJD agent in the form of intravenous ID_{50} units. Data are not available to estimate the probability of various clinical outcomes, such as infection or illness that might be predicted to arise from exposure to a particular level of agent. Although we did estimate a probability of infection in our model, the uncertainty associated with the estimate is considerable. However, a meaningful dose-response model would need to be generated for vCJD exposure in humans to improve estimates of the probability of adverse clinical outcomes for humans. The type of data needed to generate a dose-response model that would improve the quality of TSE risk assessment predictions would necessitate injection of groups of animals at several different concentrations of ID_{50}, including low doses below 1 ID_{50} using a protocol that mimics transfusion transmission of vCJD in humans. Both infection and duration of the incubation periods at several different i.v. ID_{50} concentrations would be useful endpoints for developing informative dose-response relationships. Given the state of the current TSE science, estimates of the probability of vCJD infection or illness arising from exposure to the vCJD agent are still extremely uncertain. Nevertheless risk assessment is a tool that provides insight into important factors where additional research is needed into production processes, tools, or strategies that may further reduce vCJD risks and advance product safety for patients.

The manufacturing processes for pdFVIII are highly varied – therefore, any potential clearance of the vCJD agent during production is likely variable and dependent upon the specific steps used to produce the final product. For example, the techniques applied in fractionation process vary from manufacture to manufacture including the sizes of plasma pools used for producing pdFVIII, the yield of products, and the reduction of infectivity during processing varies within a limited range from batch to batch. In addition the utilization of pdFVIII varies from individual to individual. This risk assessment considers the typical production and utilization. Uncertainty from the model should be appreciated. Human plasma-derived FVIII is typically prepared through successive steps of large scale fractionation during the manufacturing process. Cryoprecipitation is the first and a common step in preparation of pdFVIII. Afterward, cryoprecipitate undergoes further fractionation procedures such as precipitation, absorption/desorption, ion exchange and filtration to yield intermediate purity FVIII. In certain cases some hospitals may prepare small amount of cryoprecipitate FVIII from small plasma pools (1-8 donations/pool) for special treatment purposes. Preliminary risk assessment results indicated that the risk that vCJD would be transmitted through cryoprecipitated AHF is relatively low due to the small size of plasma pool and small numbers of donors involved. This risk assessment uses two ranges of possible clearance of vCJD agent from pdFVIII of 4-6 $\log_{10}$, and 7-9 $\log_{10}$ to cover the possible ranges for all pdFVIII products presently in the marketplace.

V. F. Conclusions

Results from the FDA pdFVIII risk assessment model suggest that the risk of vCJD infection from US manufactured pdFVIII generally appears likely to be very low, but may not be zero. For US plasma donors, the major source of vCJD risk is dietary exposure during travel and/or residency in the UK, France, or other countries in Europe since 1980. Although donor deferral criteria in place since 1999 have reduced the risk of donation by exposed persons some are not deferred and potentially may donate plasma that contains the vCJD agent. However, the model suggests that the likelihood of a vCJD contaminated plasma pool is low.

Manufacturing processes for human pdFVIII products likely reduce the quantity of vCJD agent, if present, but the level of reduction through manufacturing steps is not precisely known. Clearance of TSE agents in manufacturing appears to vary among products, but has not been measured in standardized studies which might allow more meaningful direct comparisons. Based on currently available experimental studies, it is estimated that pdFVIII products potentially have 4 $\log_{10}$ (or 10,000 fold) or greater manufacturing process reduction of the vCJD agent. Assuming a 4-6 $\log_{10}$ manufacturing process reduction, the modeling predicts that the potential risk per person per year for patients with severe HA using pdFVIII ranges from1 in 10,000 for the higher vCJD prevalence estimate and high product usage to 1 in 4.0 million for the lower vCJD prevalence estimate and low product usage. Due to the wide range of methods used for clearance studies currently available, gaps in information, and the results of the model, it is not possible at this time to determine with any certainty if a specific product may be less or more safe than another.

Although results of the model suggest exposure to vCJD agent is possible, and there is a potential risk of infection that is likely to be very low, it is not possible for the model to provide a *precise* estimate of the vCJD risk in general, or of the actual risk to individual patients. Although the actual risk is highly uncertain, the risk assessment model indicates that the most important factors affecting risk are the clearance of the vCJD agent though manufacturing steps, the amount of product that individuals used, and the vCJD prevalence in the UK donor population.

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APPENDIX A

Supplemental technical information for the FDA Risk Assessment

Appendix A provides additional technical information of modeling approaches and details of data used in specific sections (but not all sections) of Section IV. The heading and numbering of each section in this appendix mirrors the sections in "Section IV. Exposure Assessment" portion of the risk assessment document and the model spread sheet. The model was developed using @Risk computer software version 5.5 (Palisade Co.).

Most of the data and information used in the model were converted to statistical distributions, whenever possible, representing the variability and uncertainty associated with the input variables. In general, we used a single value, or point estimate, if no information was available that could be used to quantify the variability and uncertainty. We used a uniform distribution, represented by a minimum and maximum value, when there was only enough information to define a range; a triangular distribution, represented by a minimum, most likely, and maximum value, when there was enough information to define a range and most likely value. Other more sophisticated parametric distributions were used when there sufficient data available so that we could evaluate, or 'fit', several possible distributions and choose the distribution that best reflected the pattern of the data. In other cases, we used point estimate for sets of correlated input variables such as donation rates by individual age group and percentage travel by destination. Applying statistical distributions to these variables would greatly complicate the model and expand the computational time required to generate model results by several days. We believe point estimates give a reasonable representation of the input variables. However, we do acknowledge that the use of point estimates may underestimate the uncertainty associated with the input variables.

Module 1. Prevalence of vCJD in the United Kingdom (including section A-IV. A.)

A- IV.A. Prevalence of vCJD in the United Kingdom (Module 1)

A-IV. A.1. UK asymptomatic vCJD infections estimated using epidemiological modeling results (Clarke and Ghani 2005) and adjusted for all three genotypes

A-IV.A.1.a. Estimation of the number asymptomatic vCJD infections in UK in 2002

Variable: $Asym\text{-}vCJD_{ux}$ - Number of asymptomatic vCJD infected individuals in the UK in year 2002.

See worksheet "Model-IV. Exposure Assessment" for full calculations.

Predicted vCJD clinical cases from 2002 onward include 32 vCJD cases diagnosed from 2002 to 2003 and 70 (95% CI of 10-190) cases predicted by Clarke and Ghani (2005) for years from 2004 to 2080. This gives a total of 102 predicted clinical cases (95% CI: 42-222 cases) from 2002 onward. Predicted total

vCJD clinical cases from 2002 onward represent the number of asymptomatic vCJD individuals in 2002 among *PRNP*-129-MM (MM) genotype, because, to date, all reported clinical vCJD cases have been come from MM genotype.

The number of asymptomatic vCJD individuals in 2002 among MM genotype was used in 2006 risk assessment for calculation of UK vCJD case prevalence. However, recent evidence suggested that all genotypes including persons who are Methionine-Valine (MV) heterozygous or Valine (VV) homozygous at codon 129 of PRNP are susceptible to the disease. Reports of *PRNP*-129-non-MM (non-MM) genotype individuals with immuno-histochemical evidence of vCJD infection detected post-mortem have been published in the literatures (Peden 2004, Ironside 2006). In 2009, FDA began updating the risk assessment. As part of that work and the 2010 update we multiplied the case prevalence estimate used in 2006 version of the risk assessment by a factor of 2.5, which expands the previous Lower vCJD Case Prevalence estimate based on only the MM population to include the MVand VV genotyped populations as well. The factor of 2.5 was derived from dividing 100% (representing whole population) by 40% (representing percentage of MM population). Therefore, the estimated total number of asymptomatic vCJD infections in overall UK population of all genotypes in 2002 has an average of 255 cases ((32 +.70) x 2.5 = 255) with a 5th percentile of 105 cases ((32+10) x 2.5 = 105) and 95th percentile of 555 cases ((32+190) x 2.5 = 555). This new estimate was used in 2010 update of the FDA risk assessment for calculation of vCJD case prevalence estimate for UK population.

A-IV. A.1. b. Age distribution of asymptomatic vCJD for different genotypes

Cases of vCJD occur in relatively young individuals (median age of 26 years (Wadsworth and Collinge, 2007)) compared to classic CJD. Blood and plasma donors are usually range from 18 – 40 years of age, among whom the vCJD prevalence would be expected to be higher than that of the general population (Table A.1-1). Because age specific rates of donation and vCJD infection would likely have a large effect on the final risk estimate, the FDA model carefully characterizes the age specific prevalence of vCJD and donation rate. Age specific vCJD prevalence rates are calculated for each five year age group beginning at age group of 10 – 14 yrs, 15-19 yrs and so on – and applied throughout the FDA model in estimating vCJD risk and prevalence for the residents of different geographic regions (UK, France and other countries in Europe) and the US blood and plasma donors who traveled to those regions.

The 2006 version of FDA model used age information on reported vCJD clinical cases to calculate the age-specific percentage and prevalence of vCJD infections. The age specific percentage of reported vCJD cases is shown in **Table IV.A.1-1**. For a more accurate calculation the 2010 updated version of FDA model used age at the infection (shifting toward younger age to include incubation period) to calculate the age-specific percentage and prevalence of vCJD infections.

Table IV.A.1-1. 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	0	0	0	5%	13%	8%	10%	12%	13%	12%	11%	7%	4%	6%	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

A-IV. A. 1. b. i. Percentages of PRNP genotypes in the population

Variable: $Perc_{MM}$, $Perc_{MV}$ and $Perc_{VV}$: Percentages of MM, MV and VV genotypes among the population.

Assumption used in the model: The model assumes 40%, 50% and 10% population are MM, MV and VV genotypes, respectively (Alpeovitch et al 1999), these values were used as point estimates in the model..

A-IV.A.1.b.ii. Percentage asymptomatic vCJD attributed to age groups and genotypes

Calculations for this section are in the model worksheet "age-asy-vCJD", and are described in detailed below:

Variable: $vCJD_{UKage}$ - Reported vCJD cases in the UK by 5-year age groups (through 2003) beginning at 10 – 14 yrs, 15-19 yrs and so on.

Data used in the model: Data on the vCJD cases in the UK was derived from Hilton et al. (2004). The data includes cases through the end of 2003.

Variable: $Perc_{vCJDage}$ Percentage vCJD cases attributed by each age group from 10 – 14 yrs, 15-19 yrs and so on.

Assumption used in the model: We assume each of four age groups, 55-59 yrs, 60-64 yrs, 65-69 yrs and 70-74 yrs, contributes same percentage in vCJD cases. Five reported cases (**Table IV.A.1-1.**) have been identified in the 55-74 yr age range (specifically, three reported cases in the age-specific prevalence grouping shown in Hilton et al. (2004) for persons aged 55-74 yrs and two cases of blood transfusion vCJD (each > 64 yrs of age) (Llewelyn 2004, Peden 2005)). We used an average of 1.25 cases for each of the four age groups, 55-59 yrs, 60-64 yrs, 65-69 yrs and 70-74 yrs to estimate the percentages for each group.

Variable: $Pr(infected)_{MM\text{-}age}$, $Pr(infected)_{MV\text{-}age}$, $Pr(infected)_{VV\text{-}age}$: Probability of infection at a specific age for a specific genotype.

The probability of infection was calculated as cumulative form of distribution of age at time of initial infection. The distribution of age at time of initial infection was calculated by left shifting the distribution of age at diagnosis for MM genotype, which was generated using age information on reported clinical cases, by a unit representing incubation period for MM genotype.

Assumption used in the model: Probability *PRNP*-129-MV and -VV genotypes having been infected at specific age are same as -MM genotype; and some of -MV and -VV will eventually develop overt disease, and their blood may contain the infectious vCJD agent for a portion of the incubation period.

Assumption used in the model: Three genotypes were equally susceptible to the disease, thus, the derived distribution of age at time of initial infection for MM genotype was also applied to other two genotypes.

Assumption used in the model: Based on information of BSE and vCJD epidemics, estimated incubation period for MM genotype ranges from 10 to 15 years.

The estimation of incubation periods for MV and VV genotypes remains complicated and more uncertain, because so far there have been no clinical cases reported from MV and VV genotypes. Given this considerable uncertainty, we made simplifying assumptions that the incubation period for MV and VV is 20 year longer than that for MM genotype. The 95th percentile values of incubation period for MV and VV are 55 years, which was estimated based on the maximum incubation period for kuru (Collinge 2006).

Assumption used in the model: The incubation period is presented by gamma distribution with median of 12 year (90%CI; 5-35 years) for *PRNP*-129-MM genotype and a median of 32 years (90%CI; 25-55 years) for non-MM genotypes.

Variable: $Pr(diagnosed)_{MM\text{-}age}$, $Pr(diagnosed)_{MV\text{-}age}$, $Pr(diagnosed)_{VV\text{-}age}$: Probability of being diagnosed at a specific age for a specific genotype given infection.

Probability of being diagnosed is calculated as cumulative form of distribution of age at time of diagnosis. The distribution of age at diagnosis for MM genotype is generated using age information on reported clinical cases. The distribution of age at time of diagnosis for MV and VV genotype is generated by right shifting distribution of age at time of diagnosis for MM by a unit representing extra incubation period needed for MV and VV compared to MM genotype.

Assumption used in the model: The extra incubation period needed for MV and VV compared to MM genotype is approximately 20 years.

Variable: $Pr(asym\text{-}vCJD)_{MM\text{-}age}$, $Pr(asym\text{-}vCJD)_{MV\text{-}age}$, $Pr(asym\text{-}vCJD)_{VV\text{-}age}$: Probability of asymptomatic vCJD infections for a specific age group and genotype.

The probability of asymptomatic vCJD infections is calculated by a joint probability of being infected and not being diagnosed. An example equation for MM genotype is shown below:

$$\Pr(asym-vCJD)_{MM-age} = \Pr(\text{inf}\,eced)_{MM-age} \times (1-(\Pr(diagnosed)_{MM-age}) \qquad \text{(IV.A.1-1)}$$

Variable: $Perc_{asy\text{-}vCJD(age)\text{-}MM}$, $Perc_{asy\text{-}vCJD(age)\text{-}MV}$, and $Perc_{asy\text{-}vCJD(age)\text{-}VV}$: Percentage asymptomatic vCJD cases attributed to different age groups and genotypes.

The probability of asymptomatic vCJD infections were normalized so that all age groups of all genotypes added up to 1, then, multiplied by percentage of three genotype in the population to arrive percentages of asymptomatic vCJD cases attributed to different age groups and genotypes.

A-IV. A. 1. b. iii. Number of asymptomatic vCJD in a specific age group with a specific genotype

See worksheet "Model-IV. Exposure Assessment" for display of full calculations.

Variable: $Asy\text{-}vCJD\text{-}MM_{age}$, $Asy\text{-}vCJD\text{-}MV_{age}$, $Asy\text{-}vCJD\text{-}VV_{age}$ - Number of asymptomatic vCJD infected individuals from a specific age group in year 2002.

Variable: $Asym\text{-}vCJD_{ux}$ - Number of asymptomatic vCJD infected individuals in the UK in year 2002 (estimated in section IV-A.1.a)

$$Asym\text{-}vCJD\text{-}MM_{age} = Asym\text{-}vCJD_{ux} \times Perc_{asy\text{-}vCJD(age)\text{-}MM} \qquad \text{(IV.A.1-2)}$$

A-IV. A. 1. c. Prevalence of asymptomatic vCJD in the UK by age and genotype

Variable: $Pop_{UK(age)}$- Population in the UK by age groups (Thousands).

Data used in the model: The data for UK population were sourced from UK government statistics (UK National Statistics, 2005). Where UK data were organized in broader categories of 10 to 15 years we allocated population equally among smaller 5 year age groups.

The prevalence of asymptomatic vCJD cases in the UK by age group and genotype is estimated using the equation:

$$Prev_{Asym\text{-}vCJD(age)\text{-}MM} = Asym\text{-}vCJD\text{-}MM_{(age)}/(Pop_{UK(age)} \times Perc_{MM} \qquad \text{(IV.A.1-3)}$$

A-IV.A.2. UK asymptomatic vCJD infections derived from a tissue surveillance study (Hilton *et al* 2004)

This estimate was used in FDA 2006 risk assessment as UK vCJD infection prevalence, and remained same in the updated 2010 version of the FDA risk assessment.

A-IV.A.2.a. UK asymptomatic vCJD prevalence of 20-30 years age group

A retrospective tissue surveillance study (Hilton et al 2004) examined 12,674 tonsil and appendix tissue samples surgically removed from UK patients for the accumulation of vCJD infectious agent. The research found 3 samples positive. This data was converted to an average rate of vCJD in the UK population of 1 in 4,225 or prevalence of 237 cases per million (Hilton et al 2004). 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, and the 3 positive samples were also from this age group. Demographic information of reported vCJD cases (Table IV.A.1-1) indicated that the younger population (20 -29 yrs of age) that was deliberately oversampled in this study may have been more susceptible to the disease. The vCJD prevalence among UK population derived from the surveillance study might, therefore, be over-represented by the 20-29 years age group. Therefore, we used tissue surveillance data to calculate the vCJD prevalence for 20-30 years age group (one of age categories used in the model) using 60% sample size as denominator. We used 3 positives out of 7604 tested samples from age groups of 20-30 years (60% x 12674=7604) to determine the most likely value (3/7604) and 95% confidence intervals (determined using statistic procedure BinomialXac in software STATXAC). Assuming the sensitivity and specificity of the testing method is 100%, we calculated a vCJD prevalence of approximately 400 cases per million for which we assumed a 95% CI of 100-1200 cases per million for 20-30 year old group.

Variable: $Prev_{Asym\text{-}vCJD20\text{-}30}$ Prevalence of asymptomatic vCJD infected individuals in the UK 20-30 year old age group (cases/million)

Assumption used in the model: The vCJD infectious agent is present in the blood of the individual when the accumulation of prion protein can be detected in lymphoreticular tissue.

Assumption used in the model: Prevalence of vCJD asymptomatic individuals in the UK 20-30 year old age group is likely to be 400 cases/million, 95% CI=100-1200 cases/million.

A-IV.A.2.b. UK vCJD prevalence in specific age group with specific genotype

We determined the proportional difference between the percentage asymptomatic vCJD cases from the 20-30 years age group and that from each of the other age groups (estimated in A-IV.A.1.b.ii) and multiplied the estimated asymptomatic vCJD cases among 20-30 year age group to arrive the number of asymptomatic vCJD cases for remaining age groups.

Variable: $Pop_{UK(age)}$- Population in the UK by age groups (Thousands).

Variable: $Asym\text{-}vCJD_{UK\text{-}30}$ - The number of asymptomatic vCJD infected individuals in the 20-30 yr-old UK age group. This variable is represented by the equation:

$$Asym\text{-}vCJD_{UK\text{-}30} = Prev_{vCJD\text{-}UK\text{-}30} \times Pop_{UK\text{-}30} \qquad \text{(IV.A.2-1)}$$

Variable: $Asym\text{-}vCJD\text{-}MM_{(UK)}$, $Asym\text{-}vCJD\text{-}MV_{(UK)}$ $Asym\text{-}vCJD\text{-}VV_{(UK)}$- Number of asymptomatic vCJD infected individuals in the UK by age groups of specific genotype.

Assumptions used in the model: Three genotypes are equally susceptible to the disease; therefore, total infection cases for a specific age group are attributed to three genotypes in proportion to the population sizes of three genotypes.

As an example, the number of asymptomatic vCJD individuals in the UK of specific age group with a MM genotype was estimated using the following equation:

$$Asym\text{-}vCJD\text{-}MM_{(UK)} = Asym\text{-}vCJD_{UK\text{-}30} \times (Perc_{vCJD(UK)} / Perc_{vCJD\text{-}UK\text{-}30}) \times Perc_{MM} \qquad \text{(IV.A.2-2)}$$

Variable: $Prev_{Asym\text{-}vCJD\text{-}MM(UK)}$ $Prev_{Asym\text{-}vCJD\text{-}MM(UK)}$- Prevalence of asymptomatic vCJD infected individuals in the UK for specific age group with a specific genotype (cases/million).

Calculation for the prevalence of asymptomatic vCJD cases in the UK specific age group with specific genotype is same as shown in section IV.A. 1. c.

Module 2. Potential vCJD risk for US plasma donors and plasma pools (including sections A-IV.B., A-IV.C. and A-IV.D.)

A-IV.B. Estimation of vCJD prevalence in US plasma donors and plasma pools

Based on data FDA received from several manufacturers we assumed that a plasma pool used to manufacture pdFVIII product in the US in the year 2002 consisted of 6,000 to 360,000 donations, and several donations in the pool likely came from the same donor. In this section of the model the estimated vCJD prevalence in UK population was used to generate variables and parameters for calculation of vCJD prevalence in US plasma donors and the potential number of vCJD donors or donations that might be present in a plasma pool.

A-IV. B. 1. Annual number of plasma donors (See worksheet "Model-IV. Exposure Assessment")

A-IV. B. 1. a. Source Plasma collection in the United States: characterized by donor age

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Variable: DN_s– Annual number of Source Plasma units used to make pdFVIII.

Assumption used in the model: Based on data FDA received from manufacturers it was assumed that, on average, 3.3 million units of Source Plasma were used in each year to make pdVIII. It was further assumed that there is a 10% standard deviation in the number of Source Plasma units used to make pdFVIII for any given year.

Data used in the model: The information on annual units of pdFVIII made from Source Plasma collected in the US and unit volume of Source Plasma was collected from pdFVIII manufacturers.

Variable: DR_s–Annual number of donors who contribute Source Plasma for manufacture of pdFVIII.

Assumption used in the model: It was assumed that there are approximately 1 million Source Plasma donors in the US each year. It was further assumed that Source Plasma from any individual donor may be used to make pdFVIII. Therefore, we calculated that there were approximately 1 million donors who contributed Source Plasma for the manufacture of pdFVIII. It was further assumed that there could be a 10% standard deviation in the number of donors in any given year.

Variable: Age – Age information for US plasma donors was grouped in a two year increment for 18-19 years old because the model assumed that 18 was assumed to be the minimum age of donation. The remaining population was grouped by 5-year increments – including 20- 24yrs old, 25-29yrs old, and so on

Variable: $DR_{S_{percAge}}$- The percentage of Source Plasma donors from a given age group.

Data used in the model: Distribution of US Source Plasma donors by age was obtained from the Plasma Protein Therapeutics Association (2005). Where data (PPTA, 2005) were organized in broader age groups of 10 years or 15 years, we generated 5-year age subgroups by allocating the percentage equally among each subgroup.

Variable: $DR_{S(age)}$– The annual Source Plasma donors by age groups who contribute plasma for pdFVIII manufacturing is represented by the equation:

$$DR_{S(age)} = DR_S \times DR_{S\text{-}perc(age)} \qquad \text{(IV.B.1-1)}$$

A-IV.B.1.b. Recovered plasma collection in the United States: Characterized by donor age

Variable: DN_R - Annual units of recovered plasma used to make pdFVIII.

Assumption used in the model: It was assumed that approximately 1,800,000 units of recovered plasma are used to make pdFVIII annually. This estimation was generated by back calculation beginning with the

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total quantity of pdFVIII manufactured in the US. It was further assumed that there was a 10% standard deviation in the number of units for any given year.

Data used in the model: The annual number of total units of pdFVIII manufactured from Recovered Plasma collected in the US was estimated by back calculation. The calculation was based on the total quantity of annual units of pdVIII product made from Recovered Plasma collected in the US. We can further estimate the number of donations used to make the pdFVIII from Recovered Plasma using estimates in the literature for the average yield of pdFVIII 187 units per liter of plasma (WFH, 2004) and average volume of single unit of recovered plasma (200 ml per unit). The information on annual units of pdFVIII made from Recovered Plasma collected in the US was collected from pdVIII manufacturers.

Variable: $DN_{B\_perc(age)}$ – The percentage of blood units donated by a given age group.

Data used in the model: Distribution of blood units by donor age group was obtained from Westat data provided to FDA in 2002 (Data shown in Table IV. A.1.-1).

Variable: $DN_{R(age)}$ – Annual units of recovered plasma used to make pdFVIII by donor age group

$$DN_{R(age)} = DN_R \times DN_{Bl-perc(age)} \qquad \text{(IV.B.1-2)}$$

Variable: $DR_{R(age)}$ – Annual number of donors by age group who contribute recovered plasma that is used for manufacture of pdFVIII

Assumption used in the model: Each unit of recovered plasma used to make pdFVIII comes from different donors. Therefore, number of donors from an age group equals the number of donations from that age group.

The annual number of recovered plasma donors by age group was calculated using the equation:

$$DR_{R(age)} = DN_{R(age)} \qquad \text{(IV.B.1-3)}$$

Variable: DR_R - The annual total of potential recovered plasma donors who contribute the plasma that is used for manufacture of pdFVIII, which was estimated in the model using the summation function:

$$DR_R = \sum_{age=18-19}^{70-74} DR_{R(age)} \qquad \text{(IV.B.1-4)}$$

Assumption used in the model: Minimum age for a qualified donor is 18 years.

A-IV.B.1.c. Total plasma donors and donations- for manufacture of pdFVIII in the US

Variable: DR_{Tot} - The annual total of potential plasma donors who contribute plasma for pdFVIII manufacturing is estimated by summing the number of Source Plasma donors and recovered plasma donors.

Variable: DN_{Tot} - The annual total of potential plasma units used to make pdFVIII is estimated by summing the number of Source Plasma donations and recovered plasma donations.

A-IV.B.2. Annual number of plasma donors potentially infected and whose blood may contain vCJD infectivity

This section of the model estimated the annual number of US plasma donors potentially exposed to vCJD, and infected during travel or residence in BSE epidemic regions, and potential number of infected donors whose blood contains vCJD agent at the time of donation in year 2002. We modeled five potential sources of risk for plasma donors separately, travelers to the UK, travelers to France, travelers to the other countries in Europe, military personal who have been deployed to military bases in Europe and Euroblood recipients.

A-IV.B.2.a. US plasma donors with history of travel to the UK: Annual number potentially infected and whose blood may contain vCJD agent

This section estimated numbers of donors who have history of travel to the UK and numbers of donors who might have been infected during travel in UK and whose blood may contain vCJD agent in 2002. Detailed calculations are on the model worksheet "IV. B. 2. a Travel-UK". The results of calculations were drawn back to the model main worksheet "Model-IV. Exposure Assessment" for subsequent calculations of the model.

A-IV.B.2.a.i. US plasma donors with history of travel to the UK: Percentage of donors and duration of travel (see worksheet "IV. B. 2. a Travel-UK")

The risk of vCJD infection in US plasma donors is a function of the intensity of exposure to the BSE agent. FDA model assumed the intensity of exposure to be proportional to the amount of time spent or duration of travel in the UK and the prevalence of BSE in UK cattle during the period from 1980 – 1996. In the early 1980s human exposure may have begun at a low level as BSE spread among the UK cattle population. The BSE epidemic expanded throughout the 1980s and peaked in 1992, then, risk started to decrease as animal feed measures were implemented and more stringent human food chain controls were implemented in 1996. We assume that the likelihood that infected animals or products from BSE-infected animals in the UK entered the human food supply after 1996 was small. The FDA model used data from the National Blood Donor Travel Survey 1980-1996 (TSEAC 2000) to derive estimates of the percentages of US donors with a history of extended travel or residence (>=3 months) in the UK during 1980-1996, and to derive the frequencies for various durations of travel less than 5 years. The accumulated durations of travel of 3 months or more corresponds to the length of time in the current policy that defers donors from blood donation.

The travel survey data on blood donors has limitations because it may not exactly reflect the travel histories of Source Plasma donors. Some may argue that source plasma donors travel less frequently than their blood donor counterparts so use of data on blood donors may overestimate the risk. Unfortunately, to our knowledge there is no travel data available on Source Plasma donors. Therefore, we assumed that Source Plasma donor travel characteristics to the UK and other countries in Europe since 1980 are similar

to those of whole blood donors and used this information in the risk assessment. Recovered Plasma is plasma that is separated or "recovered" from a unit of whole blood soon after the blood is collected. As expected, the characteristics of Recovered Plasma donors mirror those of whole blood donors.

Data used in the model: National Blood Donor Travel Survey 1980-1996 was conducted by the American Red Cross and presented at the Transmissible Spongiform Encephalopathies Advisory Committee (TSEAC 2000).

Variable: i - The duration interval used to group donors who traveled to the UK from 1980-1996 based on the quantity of time spent in the UK during the period from 1980 – 1996.

Variable: D_i - The average duration of time (in months) for interval i representing the duration of travel or residence by US donors in the UK during the period from 1980 – 1996.

Variable: $CumPerc_{BDR\text{-}UKi}$ – The cumulative percentage of blood donors who traveled to the UK within duration interval i or longer.

Variable: $Perc_{BDR\text{-}UKi}$ - Percentage of blood donors who traveled to the UK within duration interval i. This variable was converted from $CumPerc_{BDR\text{-}UKi}$

Variable: $Perc_{BDR\text{-}UKi/UK}$ - The percentage of blood donors who traveled for a specific duration interval i among all donors who have ever traveled to the UK is represented by the equation:

$$Perc_{BDR-UKi/UK} = (Perc_{BDR-UKi} / CumPerc_{BDR-UK,i>1day-1month}) \times 100\% \qquad \text{(IV.B.2.a-1)}$$

A-IV.B.2.a.ii. US plasma donors with a history of travel to the UK: Percentage and number of donors in each age group by year and duration of travel

For the purposes of our analyses we grouped all donors who traveled to the UK between 1980 and 1996 into age groups of five year increments (20 – 24yrs, 25 – 29 yrs, and so on). Because the minimum age of donation is 18 years of age, the model also included the donor group 18 & 19 years of age. The percentage of donors in each age group who traveled to the UK between 1980 and 1996 was calculated based on the total number of donors, total number donors who traveled to the UK between 1980 and 1996, and the age specific odds ratio for travel.

Characteristics of blood donors on travel including the percentage of donors from each age group who traveled to the UK during period between 1980 and 1996, and distribution of donor travel by duration. This information was applied to plasma donors for estimation of the number of plasma donors from each age group who have traveled or resided in the UK from 1980 to 1996 for specific periods of time. Furthermore, the model used data that detailed the number of annual visits of US travelers to the UK to allocate donor travel specifically to an individual calendar year.

Assumption used in the model: There was zero exposure to the BSE agent for donors who traveled to the UK prior to 1980 and after 1996.

A-IV.B.2.a.ii.(1). US Source Plasma donors with history of travel to the UK: Estimation of the annual number of source plasma donors who traveled to the UK in a specific year by age group

The model generates categories (or bins) for Source Plasma donors by year of travel, so estimates of the risk can be more accurate by incorporating the information about dynamic change of BSE epidemic in the UK.

Variable: y - Calendar year of travel.

Variable: V_y - Number of visits by year to the UK by US travelers (in thousands)

Data used in the model: Number of visits by year to the UK by US travelers (UK Government Statistics, 2005).

Assumption used in the model: US Source Plasma donors have similar travel patterns as the larger US population.

Assumption used in the model: It was assumed that no US traveler visited the UK more than once per year. This may potentially overestimate the vCJD risk for US plasma donors (because repeat travel by the same donor is not addressed) and underestimate it in certain other cases (travelers who visit multiple times per year). FDA found no data that quantified the numbers of multiple visits or repeat visits by the same traveler that likely occurred for US donors with a history of UK travel.

Variable: $V_{y/1996}$ - The number of visits to the UK by US travelers in year y compared to the number of visits in 1996 is represented by the equation:

$$V_{y/1996} = V_y / V_{1996} \qquad \text{(IV.B.2.a-2)}$$

Variable: DR_y (calculated in section A-IV.B.1.) - The annual number of source Plasma donors.

Variable: $DR_{y,a}$ (calculated in section A-IV.B.1.) - The annual number of source Plasma donors by age group.

Variable: $Perc_{DR\text{-}UK}$ Percentage of donors who have history of travel to the UK. This percentage was derived based on American Red Cross's Donor Travel Survey.

Variable: Odd_{Travel} - Age specific odd ratios for travel compared to the age group 18-19 years.

Data used in the model: The odds ratios for likelihood of travel for each age group were derived from the travel data obtained from 1980-1996 blood donor travel survey. An odds ratio of 1 was assigned to the donor group aged 18-19 years. The odds ratios for other age groups is a function of the travel frequency of those age groups compared to the travel frequency of the age group of 18-19 years

Variable: $DR_{S\text{-}UK(age)(1980\text{-}1996)}$ - Number of Source Plasma donors who traveled to the UK from 1980 through 1996 by age group in five-year increments and 18-19 yr old age cohort.

Assumptions used in the model: The same percentage of Source Plasma donors traveled to UK as blood donors.

The number of Source Plasma donors who traveled to the UK from 1980 to 1996 by age group is represented by:

$$DR_{S-UK(age)(1980-196)} = DR_{a} \times Perc_{DR-UK} \times (DR_{S(Age)} \times Odd_{T(age)}) / \sum_{Age=18-19}^{70-74} (DR_{S(Age)} \times Odd_{T(age)}) \qquad \text{(IV.B.2.a-3)}$$

Source Plasma donors with a history of travel to the UK among each age group ($DR_{S\text{-}UK(age)(1980\text{-}1996)}$) was allocated to individual travel years based on the yearly distribution of visits to the UK by US travelers (UK National Statistics, 2005). The yearly distribution of travel visits by each age group was adjusted to exclude the probability of travel of young donors (18-22 year old in 2002) in early years of BSE epidemic when they were not born. For example, donors of 18 years of age in 2002 were born in 1985, therefore, had no chance of travel and exposure to the BSE agent prior to 1985; those 19 years of age in 2002 had no chance of travel prior to 1984, those 20 years of age in 2002 had no chance of travel prior to 1983, those 21 years of age in 2002 had no chance of travel prior to 1982, and those 22 years of age in 2002 had no chance of travel in 1980.

Variable: $DR_{S\text{-}UK(age)y}$ - the number of Source Plasma donors who traveled to the UK in year *y* by age group

Assumptions used in the model: The yearly travel trend for blood and plasma donors are the same as trend for the general US population

The number of US Source Plasma donors who have traveled to the UK in year y between 1980 - 1996 is represented by the equation:

$$DR_{S-UK(age)y} = DR_{S-UK(age)} \times V_{y/1996} / \sum_{y=1980}^{1996} V_{y/1996} \qquad \text{(IV.B.2.a-4)}$$

A-IV. B. 2. a. ii.(2). US Source Plasma donors with history of travel to the UK: Duration of travel by age group

This section of the model used the data on the number of Source Plasma donors who have traveled to the UK in a specific year and divided those individuals into sub-categories by durations of stay. The model used categories of duration of stay used in the ARC's report for Blood Donor Travel Survey (TSEAC, 2000).

Variable: *i* - The duration interval used to group blood donors who had traveled to UK from 1980 - 1996 based on the time they spent in the UK (same variable used in section A-IV. B. 2. a. i.).

Variable: D_i - The average duration of time for interval *i* (months) (same variable used above in section A-IV. B. 2. a. i).

Variable: $DR_{S\text{-}UK(age)y}$ - the number of Source Plasma donors who traveled to the UK in year *y* by age group (calculated in A-IV. B. 2. a. ii (1))

Variable: $Perc_{Dn\text{-}UK/UK}$ - The percentage of blood donors who traveled for a specific duration interval *i* among all donors who have ever traveled to the UK (calculated in A-IV.B.2.a.i)

Variable: $DR_{S\text{-}UK(age)y,i}$ - Number of Source Plasma donors within a specific age group that traveled to the UK in year *y* for a duration of *i* and is represented by the equation:

$$DR_{S-UK(age)y,i} = DR_{S-UK(age)y} \times Perc_{DR-UK/UK} \qquad \text{(IV.B.2.a-5)}$$

A-IV. B. 2. a. ii.(3). Number of US recovered plasma donors with a history of travel to the UK in a specific year from 1980 – 1996 by age group

Calculations in this section are similar to the calculation for Source Plasma donors shown in section A-IV.B.2.a.ii.(1).

A-IV. B. 2. a. ii. (4). US recovered plasma donors with history of travel to the UK: Duration of travel by age group

Calculations in this section are similar to the calculation for Source Plasma donors shown in section A-IV.B.2.a.ii.(2).

A-IV. B. 2. a. iii. US plasma donors with a history of travel to the UK: Adjustment of relative risk to account for variations in BSE risk by specific year and travel duration

The FDA model assigned residents of the UK for any five-year period or longer from 1980 through 1996 a relative risk value of 1 (the highest value) for vCJD risk, because the BSE epidemic in UK cattle and exposure of the human population to the BSE agent in the UK was greater than any other country. This was determined based on FDA guidance (2002), considering the factors such as domestic UK beef consumption, the rate and number of vCJD cases, and indigenous BSE cases that may have occurred (TSEAC 2004).

A-IV.B.2.a.iii.(1). Accumulated risk for individual UK residents from 1980 through 1996

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

Assumption used in the model: The UK population has the highest risk of exposure to BSE or vCJD, we assumed the average accumulated risk for each UK individual is 1. The vCJD risk value of 1 corresponds to the vCJD prevalence among the UK population estimated in section IV-A.

A-IV.B.2.a.iii.(2). US plasma donors with a history of travel to the UK: Adjustment for the proportional individual BSE exposure risk for the UK population per year between 1980 and 1996.

Presumably there were dramatic variations in the BSE exposure risk, and hence, the human vCJD infection risk that occurred from year to year between 1980 and 1996. BSE was first diagnosed in the United Kingdom in 1986 and the epidemic peaked in 1992, a year when the risk of exposure to the BSE agent would have likely been highest for residents and visitors to the UK. Therefore, the model calculated the proportional BSE risk per year (e.g., the BSE exposure risk in a given year compared to the total accumulated BSE risk in the period from 1980 to 1996) in order to incorporate the changing dynamics of the BSE epidemic since 1980 and to account for the difference exposure risk for the donors who traveled to the UK at the different years.

Variable: y – year of travel (same as variable used above in section A-IV.B 2.a.ii.) by US plasma donor to the UK between 1980 and 1996.

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

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

Assumptions used in the model:

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

The proportional BSE risk in the UK per specific year between 1980 and 1996 is represented by the equation:

$$R_{UKy} = R_{UK} \times BSE_{UKy} / \sum_{y=1980}^{1996} BSE_{UKy} \qquad \text{(IV.B.2.a-9)}$$

A-IV.B.2.a.iii.(3). US plasma donors with a history of travel to the UK: BSE exposure risk and vCJD risk in year y for a period of i, during the period from 1980 to 1996.

The FDA model update for 2010 assumed the potential vCJD risk for the US plasma donors who traveled to the UK was also a function of duration. The potential vCJD risk for the US plasma donors who traveled to the UK in a specific year for a specific duration was calculated using a pro-rated monthly rate, which was calculated based on the proportional BSE exposure risk in the UK in the specific year.

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

Assumptions used in the model:

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

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

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

$$R_{DR\text{-}UKy,i} = (R_{UKy}/12) \times D_i \qquad \text{(IV.B.2.a-10)}$$

for i<=1 years;

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

$$R_{DR\text{-}UKy,i} = (Average(R_{UKy} : R_{UK(y+Roundup((i_{years})}))/12) \times D_i \qquad \text{(IV.B.2.a-11)}$$

for 5 years >$i \geq$ 1 year;

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

$$R_{DR\text{-}UKy,i} = 1 \qquad \text{(IV.B.2.a-12)}$$

for $i \geq$ 5 years

A-IV.B.2.a.iv. US plasma donors with a history of travel to the UK: Probability of infection with vCJD based on duration of travel, age and genotype

This section describes the portion of the model that estimates the probability that a US plasma donor in a specific age group of a specific genotype, who traveled to the UK for a specific duration in a specific year during the time-span of 1980 through 1996, was infected with vCJD. In this revised risk assessment we incorporate the effect of all three donor genotypes for codon 129 of PNRP on the probability of infection, which was not considered in 2006 risk assessment. The vCJD prevalence for the UK population of specific age and genotype are calculated in risk assessment section A-IV.A. It represents the probability of infection for an average UK resident, who have value of 1 for vCJD risk. The probability of infection for an US plasma donor was adjusted for the year of travel and duration of the stay using vCJD risk associated with year of travel and duration of the stay calculated in section A-IV.B.2.a.iii. So far, there has been no sufficient information differentiating the susceptibility of MV and VV genotypes. In the updated 2010 version of the FDA model, MV and VV genotypes are modeled separately, but use same input values. Calculations for three genotypes are similar. Calculations for MM genotype are described below as an example.

Variable: $Pr_{Asym\text{-}vCJD\text{-}UK\text{-}MM(age)}$ – the probability of vCJD infection per individual UK resident of a specific age group for persons with the MM genotype

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

$$Pr_{asym\text{-}vCJD\text{-}UK\text{-}MM(age)} = Prev_{Asym\text{-}vCJD\text{-}MM(age)} \quad \text{(IV.B.2.a-13)}$$

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

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

$$Pr_{vCJD\text{-}MM\text{-}DR\text{-}UK(age)y,i} = Pr_{Asym\text{-}vCJD\text{-}UK(age)} \times R_{DR\text{-}UKy,i} \quad \text{(IV.B.2.a-14)}$$

Calculations for MV and VV genotypes are similar to those for MM genotype and are not repeated here.

A-IV. B. 2. a. v. Number of all US pdFVIII plasma donors with history of travel to the UK and potentially infected with vCJD

This section of the model estimates the total number of all US plasma donors potentially infected with vCJD during travel to the UK from 1980 through 1996. The model estimates the number of potentially infected Source and recovered plasma donors for each of three genotypes separately (described in the subsequent sections below) and sums them up to derive the total number of infected donors in the US.

A-IV.B.2.a.v.(1) Number US Source Plasma donors with history of travel to the UK and potentially infected with vCJD during travel to the UK

Plasma is collected from Source Plasma donors in a process called plasmapheresis in which an average of approximately 700 milliliters of plasma are collected from a donor. Source Plasma donors donate an average of 14 times per year, but can donate up to 48 times per year. This section of the model estimates the number of US Source Plasma donors potentially infected with vCJD during travel to the UK from 1980 through 1996. The three genotypes are calculated separately. The following equations summarized the calculation for MM genotype. Calculations for MV and VV genotypes are similar.

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

Variable: $DR_{S\text{-}UK(age)y,i}$ - Number of Source Plasma donors within a specific age group that traveled to the UK in year y for a duration of i (calculated in section A-IV. B. 2. a. ii.)

Variable: $Perc_{MM}$, $Perc_{MV}$, $Perc_{VV}$-the percentage of population who are either of the MM, MV or VV genotype (same as described in section A-IV.A.)

$$DR_{vCJD\text{-}S\text{-}UK\text{-}MM(age)y,i} = Bionomial(DR_{S\text{-}UK(age)y,i} \times Perc_{MM}, Pr_{vCJD\text{-}MM\text{-}DR\text{-}UK(age)y,i}) \quad \text{(IV.B.2.a-15)}$$

Variable: $DR_{vCJD\text{-}S\text{-}UK\text{-}MMy}$, $DR_{vCJD\text{-}S\text{-}UK\text{-}MVy}$, $DR_{vCJD\text{-}S\text{-}UK\text{-}VVy}$ - Number of Source Plasma donors who are either MM, MV or VV genotype and potentially infected with vCJD during travel/residency in the UK in year y.

$$DR_{vCJD\text{-}S\text{-}UK\text{-}MMy} = \sum_{Age=18\text{-}19yrs,i=1\text{-}30days}^{50\text{-}54yrs,\ >=5years} DR_{vCJD\text{-}S\text{-}UK\text{-}MM(age)y,i} \quad \text{(IV.B.2.a-16)}$$

Current deferral policy (FDA, 2002) defers individuals who have history of travel to the UK from 1980 through 1996 for an accumulated residence of 3 months or more from donating blood and plasma.

Variable: $DR_{vCJD\text{-}S\text{-}UK\text{-}MM\text{-}Defy}$, $DR_{vCJD\text{-}S\text{-}UK\text{-}MV\text{-}Defy}$ $DR_{vCJD\text{-}S\text{-}UK\text{-}VV\text{-}Defy}$- Number of Source Plasma donors who are either of the MM, MV or VV genotype and potentially infected with vCJD in year y who met deferral criteria and calculated using the equation below:

$$DR_{vCJD\text{-}S\text{-}UK\text{-}MM\text{-}defy} = \sum_{Age=18\text{-}19yrs,i=3\text{-}5months}^{50\text{-}45yrs\ >=5years} DR_{vCJD\text{-}S\text{-}UK\text{-}MM(age)y,i} \quad \text{(IV.B.2.a-17)}$$

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

$$DR_{vCJD\text{-}S\text{-}UK\text{-}MM\text{-}Resy} = \sum_{Age=18\text{-}19\ i=1\text{-}30days}^{50\text{-}54yrs\ >=3months} DR_{vCJD\text{-}S\text{-}UK\text{-}MM(age)y,i} \quad \text{(IV.B.2.a-18)}$$

Calculations for persons of the MV or VV genotypes are similar to those for MM genotype and are not repeated here.

A-IV.B.2.a.v.(2) Number of US Recovered Plasma donors with history of travel to the UK and potentially infected with vCJD during travel to the UK

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

This section of the model estimates the number of US recovered plasma donors potentially infected with vCJD during travel to the UK from 1980 through 1996. The calculations for recovered plasma donors in this section are similar to the calculations for source plasma donors shown on section A-IV.B.2.a.v.(1).

A-IV.B.2.a.vi. Number of US Plasma donors with a history of travel to the UK and potentially infected and with vCJD agent present in their blood

Perhaps the most critical component of the model is the estimation of whether a plasma donation was collected from a vCJD-infected donor that contained infectious vCJD agent in their blood at the time of donation. The 2006 version of risk assessment model assumed that vCJD infected individuals have infectious vCJD agent present in the blood during the last half of the incubation period. The updated 2010 FDA risk assessment assumed the vCJD infectious agent is likely present in the blood of an infected individual on average after 75% of the incubation period has elapsed and used a range of 50% - 90% to represent the uncertainty associated with the duration of the incubation period where infectious is present in the blood.

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

Assumption used in the model: This risk assessment assesses the risk for pdFVIII product made in 2002.

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

$$T_{Inf-2002y} = 2002 - y \qquad \text{(IV.B.2.a-19)}$$

Variable: $I_{bl\text{-}MMy}$, $I_{bl\text{-}MVy}$, $I_{bl\text{-}VVy}$ –Index variable representing whether blood is infectious (and infectious agent is present in the blood of a donor who traveled in year y (yes=1, no=0).

Variable: IP_{MM}, IP_{MV}, IP_{VV}- Incubation periods for donors who are either MM, MV or VV genotypes (in years, same as described in section A-IV.A)

Variable: $IP_{inflbl\text{-}MM}$, $IP_{inflbl\text{-}MV}$, $IP_{inflbl\text{-}VV}$- Portions (percentages) of donors allocated by either MM, MV or VV genotypes and who are in the late stages of incubation period and infectious agent is present in blood.

If $T_{Inf\text{-}2002y} >= IP_{inflbl\text{-}MM} \times IP_{MM}$

Then, $I_{bl\text{-}MMy}=1$ (agent present in blood)

Otherwise, $I_{bl\text{-}MMy}=0$ (agent not present in blood) (IV.B.2.a-20)

A-IV.B.2.a.vi.(1). Number of US Source Plasma donors with a history of travel to the UK and potentially infected with vCJD and whose blood contains vCJD agent

This section of the model calculates the number of Source Plasma donors who may potentially contain infectious vCJD agent in their blood at the time of donation

Variable: $DR_{vCJD\text{-}S\text{-}MM\text{-}UK\text{-}inflbly}$, $DR_{vCJD\text{-}S\text{-}MV\text{-}UK\text{-}inflbly}$, $DR_{vCJD\text{-}S\text{-}VV\text{-}UK\text{-}inflbly}$-Annual number of source plasma donors of MM, MV ad VV genotypes with infectious agent in the blood

Variable: $DR_{vCJD\text{-}S\text{-}MM\text{-}UK\text{-}def\text{-}inflbly}$, $DR_{vCJD\text{-}S\text{-}MV\text{-}UK\text{-}def\text{-}inflbly}$ $DR_{vCJD\text{-}S\text{-}VV\text{-}UK\text{-}def\text{-}inflbly}$-Annual number of source plasma donors of MM, MV ad VV genotypes with infectious agent in the blood and are deferred based on current policy

Variable: $DR_{vCJD\text{-}S\text{-}MM\text{-}UK\text{-}res\text{-}inflbly}$, $DR_{vCJD\text{-}S\text{-}MV\text{-}UK\text{-}res\text{-}inflbly}$ $DR_{vCJD\text{-}S\text{-}VV\text{-}UK\text{-}res\text{-}inflbly}$-Annual number of source plasma donors of MM, MV ad VV genotypes with infectious agent in the blood and not deferred based on current policy

Equations for calculations of above variables for MM genotype were summarized below:

If $I_{bl\text{-}MMy}=1$,

Then,

$$DR_{vCJD\text{-}S\text{-}MM\text{-}UK\text{-}inflbly} = DR_{vCJD\text{-}S\text{-}UK\text{-}MMy} \qquad \text{(IV.B.2.a-21)}$$

$$DR_{vCJD\text{-}S\text{-}MM\text{-}UK\text{-}def\text{-}inflbly} = DR_{vCJD\text{-}S\text{-}UK\text{-}MM\text{-}defy} \qquad \text{(IV.B.2.a-22)}$$

$$DR_{vCJD\text{-}S\text{-}MM\text{-}UK\text{-}res\text{-}inflbly} = DR_{vCJD\text{-}S\text{-}UK\text{-}MM\text{-}resy} \qquad \text{(IV.B.2.a-23)}$$

Otherwise,

$$DR_{vCJD\text{-}S\text{-}MM\text{-}UK\text{-}inflbly} = 0 \qquad \text{(IV.B.2.a-24)}$$

$$DR_{vCJD\text{-}S\text{-}MM\text{-}UK\text{-}def\text{-}inflbly} = 0 \qquad \text{(IV.B.2.a-25)}$$

$$DR_{vCJD\text{-}S\text{-}MM\text{-}UK\text{-}res\text{-}inflbly} = 0 \qquad \text{(IV.B.2.a-26)}$$

The three variables below sum the above estimates over the year and genotypes, and were presented on the work sheet "Mode-IV. Exposure Assessment" for the subsequent calculation of the model.

Variable: $DR_{vCJD\text{-}S\text{-}UK\text{-}inflbl}$- Total number of source plasma donors whose blood contains vCJD agent

Variable: $DR_{vCJD\text{-}S\text{-}UK\text{-}def\text{-}inflbl}$- Total number of source plasma donors whose blood contains infectious agent and are deferred based on current policy

Variable: $DR_{vCJD\text{-}S\text{-}UK\text{-}res\text{-}Inf\text{-}bl}$ Total number of source plasma donors whose blood contains infectious agent and are not deferred based on current policy

A-IV. B.2.a.vi.(2). Number of US recovered plasma donors with history of travel to the UK and potentially infected and whose blood contains vCJD agent

This section of the model calculates the number of recovered plasma donors who may potentially contain infectious vCJD agent in their blood at the time of donation. The calculations are similar to the calculation for source plasma donors described in section A-IV.B.2.a.vi.(1).

A-IV.B.2.b. US plasma donors with history of travel to France: Annual number potentially infected and whose blood may contain vCJD agent

This section estimated the numbers of donors who have a history of travel to France and estimates the numbers of donors who might have been infected during travel to France and whose blood contains vCJD agent in 2002. Detailed calculations are on the model worksheet "IV.B.2.b Travel-FR". The results of calculations are intermediate calculations contained in the model worksheet "Model-IV. Exposure Assessment" and are used subsequent calculations in the model.

Assumption used in the model: There was exposure risk for donors who traveled to France since 1980.

As mentioned in previous sections the FDA model assumes there is essentially no exposure risk for the donors who travel to the UK after 1996, since stringent human food chain controls were implemented in the UK in 1996. However, the FDA model assumed that there is exposure risk for the donors who travel to France after 1996, since there has no similar measures implemented in France.

A-IV.B. 2. b. i. US plasma donors with a history of travel to France: Percentage of donors and travel duration

In this section, blood donors are characterized by frequency and duration of travel to France since 1980. The FDA model used data from the National Blood Donor Travel Survey 1980-1996 (TSEAC 2000) to derive estimates of the percentages of US donors with a history of extended travel or residence ($\geq$ 5 years) in France since 1980, and to derive the frequencies for various durations of travel for less than 5 years. Since the baseline year to estimate potential vCJD risk for US donors in our model was 2002, trends in the National Blood Donor Travel Survey 1980-1996 (TSEAC 2000) were extrapolated for the years of 1997-2002 when necessary to estimate potential travel characteristics and risk beyond 1996. The calculations in this section are similar to the calculations for donors with history of travel to UK shown in section A-IV.B.2.a.i.

A-IV.B.2.b.ii. US plasma donors with a history of travel to France: Percentage and number of donors by age group, year of travel and duration of travel

This part of risk assessment calculates the annual number of US Source Plasma and recovered plasma donors that traveled to France by specific year(s) and for a specific duration of time since 1980 by age. The calculations in this section are similar to the calculations for donors with history of travel to UK shown in section A-IV.B.2.a.ii.

A-IV.B. 2.b.iii. US plasma donors with history of travel to France: Adjustment of the vCJD risk for France to account for variations in French BSE risk by specific year and travel duration

As indicated in previous sections the FDA model assumed that the relative vCJD risk for UK residents residing for any five-year period or longer from 1980 through 1996 have a value of 1. The vCJD relative risk value of 1 represents a prevalence equivalent to 100% of the UK asymptomatic and symptomatic vCJD prevalence. Based on information in FDA guidance (2002), the relative vCJD risk value for France is 0.05 (French vCJD prevalence is 5% of the UK vCJD prevalence) because risk of exposure to BSE in France was smaller than the risk in the UK. The vCJD risk value is assigned based on factors such as domestic UK beef consumption, and the approximate rate and number of vCJD cases, and indigenous BSE cases that may have occurred (TSEAC 2004). France received meat and bone meal from the UK during the BSE epidemic, and additionally approximately 5% of its beef was imported from the UK. As of August 2006, France reported 20 cases of vCJD in its human population. Current US vCJD geographic deferral policy defers donors with a history of residence in France for a period of 5 years or more since 1980.

A-IV.B.2.b. iii. (1). US plasma donors with a history of travel to France: Average cumulative risk of individual resident of France since 1980

Variable: R_{FR} – The cumulative risk of individual residents of France from 1980 till present

Assumption used in the model: The average cumulative risk of a resident of France since 1980 is 0.05 relative to 1, the average accumulated risk of UK individual since 1980, based on UK beef imports, vCJD cases and indigenous BSE in France

A-IV.B.2.b.iii.(2). US plasma donors with history of travel to France: Proportional risk of individual resident per year since 1980

Variable: y – year (same variable used in A-IV.B.2.a iii.)

Variable: BSE_{UKy} (same variable used in A-IV.B.2.a.iii.)

Variable: BSE_{FRy} - Annual numbers of reported BSE cases in France including indigenous and imported cases

Data used in the model: Data on the annual number of reported BSE cases in France was obtained from the World organization for animal health (OIE) (2005).

Variable: R_{FR_y} - Proportional risk in France in a specific year

Assumptions used in the model:

- Variant CJD Risk in France occurred starting in 1980 to the present. Evidence indicates that vCJD and BSE cases are still emerging.
- Risk is additive, and can be pro-rated in a yearly and further monthly basis.
- Yearly rate of the risk in France is proportional to the reported BSE annual cases (including indigenous and imported cases) in France.

A-IV.B.2.b.iii.(3). US plasma donors with a history of travel to France: Potential vCJD risk for donors who traveled in year y for a period of *i*

Calculations for this section are similar to the calculations for the donors who traveled to the UK shown in section A-IV.B.2.a.iii.(3).

A-IV.C. 1. b. iv. US plasma donors with history of travel to France: Probability of vCJD infection for donor based on year, duration of travel, age and genotype

This section describes the portion of the model that estimates the potential probability that a US plasma donor in a specific age group of a specific genotype who traveled to France in a specific year for a specific duration since 1980 was infected with vCJD. Calculations for this section are similar to the calculations for the donors who traveled to the UK shown in section A-IV.B.2.a.iv.

A-IV.B. 2.b.v. Total number of all US plasma donors with a history of travel to France: Number potentially infected with vCJD

Calculations for this section are similar to the calculations for the donors who traveled to the UK shown in section A-IV.B.2.a.v.

A-IV.B.2.b.vi. Number of US Plasma donors with history of travel to France and potentially infected and vCJD agent is present in the blood

Calculations for this section are similar to the calculations for the donors who traveled to the UK shown in section A-IV.B.2.a.vi.

A-IV.B.2.c. US plasma donors with history of travel to other countries in Europe: Annual number potentially infected and whose blood may contain vCJD agent

This section estimated numbers of donors who have a history of travel to other countries in Europe, other than the UK and France, and numbers of donors who might have been infected during travel in these regions and whose blood may contain vCJD agent in 2002. Detailed calculations are shown on the model worksheet "IV.B.2.c Travel-EU". The results of calculations are drawn from the model worksheet "Model-IV. Exposure Assessment" and used to perform subsequent calculations for the model.

Assumption used in the model: There was exposure risk for donors who traveled to the other countries in Europe since 1980.

With similar reason, FDA model considered there is exposure risk for donors who traveled to other countries in Europe after 1996 as those traveled to France.

A-IV.B. 2.c. i. US plasma donors with a history of travel to other countries in Europe: Percentage of US donors and travel duration

In this section, blood donors are characterized by frequency and duration of travel to other countries in Europe since 1980. The FDA model used data from the National Blood Donor Travel Survey 1980-1996 (TSEAC 2000) to derive estimates of the percentages of US donors with a history of extended travel or residence (≥ 5 years) in Europe since 1980, and to derive the frequencies for various durations of travel for less than 5 years. Since the baseline year to estimate potential vCJD risk for US donors in our model was 2002, trends in the National Blood Donor Travel Survey 1980 - 1996 (TSEAC 2000) were extrapolated for the years of 1997-2002 when necessary to estimate potential travel characteristics and risk beyond 1996. The calculations in this section are similar to the calculations for donors with history of travel to the UK are shown in section A-IV.B.2.a.i.

A-IV.B.2.c.ii. US plasma donors who traveled to other countries in Europe: Total number by year of travel, duration of travel and by age group

This section of the risk assessment calculates the annual number of US plasma donors who traveled to other countries in Europe (other than the UK and France) since 1980. The calculations in this section are similar to the calculations for donors with history of travel to UK shown in section A-IV.B.2. a.ii.

A-IV.B.2.c.iii. US plasma donors who traveled to other countries in Europe: Adjustment of vCJD risk to account for variations in EU BSE risk by duration of travel and duration

As indicated in previous sections the FDA model assumed that the relative vCJD risk for UK residents residing for any five-year period or longer from 1980 through 1996 have a value of 1, the vCJD risk value for France was assumed to be 0.05. Based on information in FDA guidance (2002) FDA model also assumed vCJD risk value for other countries in Europe was 0.015. The vCJD risk value is assigned based on factors such as domestic UK beef consumption, and the rate and number of vCJD cases, and indigenous BSE cases that may have occurred (FDA 2002). Other countries in Europe (other than the UK and France) received meat and bone meal from the UK during the BSE epidemic and approximately 1.5% of their beef was imported from the UK. Current US vCJD geographic deferral policy defers blood

donors with a history of residence in other countries in Europe (other than the UK and France) for a period of 5 years or more since 1980; this policy does not include Source Plasma donors.

The calculations in this section are similar to the calculations for donors with history of travel to France shown in section A-IV.B.2. B. iii.

A-IV. B. 2. c. iv. US plasma donors with a history of travel to other countries in Europe: Probability of vCJD infection based on year, duration, age and genotype

This section describes the portion of the model that estimates the potential probability that a US plasma donor in a specific age group, who traveled to other countries in Europe for a specific duration since 1980 was infected with vCJD. The calculations in this section are similar to the calculations for donors with history of travel to the UK shown in section A-IV.B. 2. a. iv. and are not shown.

A-IV.B.2.c.v. Number of US plasma donors with a history of travel to other countries in Europe: Number potentially infected with vCJD.

The calculations in this section are similar to the calculations for donors with history of travel to the UK shown in section A-IV.B.2.a.v.

A-IV. B.2.c.vi. Number of US plasma donors who traveled to other countries in Europe: Number potentially infected and whose blood contains vCJD agent

The calculations in this section are similar to the calculations for donors with history of travel to the UK shown in section A-IV.B. 2. a. vi.

A-IV.B.2.d. US plasma donors deployed by the military in the UK or other countries in Europe: Annual number potentially infected and whose blood contains vCJD agent

This section of the model estimated the number of donors who might have been infected with vCJD when they were military personnel or dependents deployed to US military bases in the UK, France and other countries in Europe during the period from 1980 through 1996. Detailed calculations are on the model worksheet "IV.B.2.d. Military". The results of the calculations refer to the model main worksheet "Model-IV. Exposure Assessment" and are used for subsequent calculations in the model.

All donors who have been deployed in the UK or other countries in Europe are deferred by current policy. Current donor deferral policy indefinitely defers donors who have been deployed to the military bases in the UK or other countries in Europe for more than six months.

A-IV.B.2.d.i. US plasma donors deployed by Military: Percentage of US plasma donors deployed at US military bases during the years 1980 through 1996

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

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

Assumption used in the model: Approximately 3% of US blood donors have been military residents in European countries between 1980 and 1996 (TSEAC 2002). There were no data for plasma donors, therefore, data for US blood donors was used to estimate the number of US donors stationed in US military facilities during the period 1980-1996

- The FDA model assumed that the same percentage of plasma donors have been in the military and deployed in European countries as blood donors.
- Source plasma donors would have similar donation demographics and characteristics as whole blood donors.

A-IV. B. 2. d. ii. US plasma donors deployed by Military: Number of donors by year of deployment since 1980

A-IV.B.2.d.ii.(1). US plasma donors deployed by Military: Number of Source Plasma by year of deployment

Variable: y - Calendar year of deployment

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

Variable: $Perc_{DR\text{-}DOD_y}$ – Percentage of Source Plasma donors who have a history of military deployment in Europe in a specific year y.

$$Perc_{DR\text{-}DOD_y} = (DOD_y / \sum_{y=1980}^{1996} DOD_y) \times 100\% \qquad \text{(IV.B.2.d-1)}$$

Variable: age - age of donors were grouped by five-year increments (e.g., 20-24, etc.) and the 18-29 year old group (same variable used above in section A-IV.B.2.a.ii.)

Variable: $DR_{S(age)}$ – Age of donors of Source Plasma (calculated in section A-IV.B. 1.)

Variable: $Perc_{DR\text{-}DOD}$ – Percentage of Source Plasma donors who have a history of military deployment in Europe since 1980 (calculated in section A-IV. B. 2. d. i)

Variable: $DR_{S\text{-}DOD(age)}$ - Estimated annual number of Source Plasma donors who have history of military deployment in the UK or Europe by age

The estimated annual number of Source Plasma donors who have a history of military deployment in Europe by age is represented by the equation:

$$DR_{S\text{-}DOD(age)} = DR_{S(age)} \times Perc_{DR\text{-}DOD} \quad \text{(IV.B.2.d-2)}$$

Variable: $DR_{S\text{-}DOD(age)y}$ – Number estimated annual number of Source Plasma donors who resided on military bases in Europe by age and deployment year

$$DR_{S\text{-}DOD(age)y} = DR_{S\text{-}DOD(age)} \times Perc_{DR\text{-}DOD_y} \quad \text{(IV.B.2.d-3)}$$

A-IV. B. 2. d. ii. (2). US plasma donors deployed by Military: Number of recovered plasma donors deployed by year

The calculations in this section are similar to the calculations for source plasma donors shown in section A-IV.B. 2. d. ii. (1).

A-IV.B.2.d.iii. US plasma donors deployed by Military: Adjustment of the Relative Risk for the proportional variation in the BSE exposure risk in the UK and the military deployment duration per specific year during the period from 1980 - 1996

Assumption used in the model: The relative risk value of US military residents in other countries in Europe from 1980 through 1996 is 0.35. This estimate is based on the assumption that approximately 35% of the beef consumed by military personnel in Europe between 1980-1996 was imported from the UK (FDA 2002).

Assumption used in the model: It was assumed that there was a two consecutive years of residence on a base for each deployment.

Variable: y – Year of deployment (same variable used above in A-IV.B.2.a.iii)

Variable: y_{epi} – The specific year of BSE epidemic in the UK (same variable used above in A-IV.B.2.a. iii).

Variable: BSE_{UKy} - Number of diagnosed BSE cases in the UK by year from 1980 through 1996 (same variable used above in A-IV.B.2.a.iii)

Data used in the model: Data are from the World organization for animal health (OIE 2005). Data were not collected for individual years prior to 1997. A total of 446 cases of BSE were reported by other countries in Europe during the time period from 1980 through 1996 and were allocated to individual years by assuming the cases were increasing in a linear fashion by year.

Variable: R_{Base} - vCJD risk for donors that resided on US military bases in Europe throughout the period between 1980 and 1996

Assumptions used in the model: The vCJD risk for US military facilities in Europe was present from 1980 through 1996. There was negligible vCJD risk after 1996 – the model assumed the major source of vCJD risk for US military bases in Europe was associated with imported UK beef. When food chain controls were implemented in the UK in 1996 – the model assumed the risk to be negligible.

Variable: R_{Basey} - Proportional vCJD risk for donors that resided on US military bases in Europe in a specific year

Assumptions used in the model:

- It was assumed that the vCJD risk was additive and can be prorated on a yearly basis.
- The vCJD risk in a specific year was assumed to be proportional to the reported number of BSE cases in the UK in that specific year.

Proportional vCJD risk in the US military bases in a specific year was calculated by the equation:

$$R_{Basey} = R_{Base} \times BSE_{UKy} / \sum_{y=1980}^{1996} BSE_{UKy} \quad \text{(IV.B.2.d-4)}$$

Variable: $R_{DR\text{-}DOD_y}$ - Risk of individual military personnel who lived in Europe for a period of two years starting from deployment year y.

Assumption used in the model: The model assumed an average of two consecutive years of deployment:

$$R_{DR\text{-}DOD_y} = R_{Basey} + R_{Base(y+1)} \quad \text{(IV.B.2.d-5)}$$

A-IV.B.2.d.iv. US plasma donors deployed by the Military: Estimation of probability of vCJD infection for an individual plasma donor by year of deployment, age and genotype

The calculations in this section are similar to the calculations for donors who traveled to the UK shown in section A-IV.B.2.a.iv.

A-IV. B. 2. d. v. US plasma donors deployed by Military: Number of all US plasma donors potentially infected with vCJD during residence at a US military base in the UK or other countries in Europe from 1980 to 1996

This section estimates the number of Source plasma and recovered plasma donors with a history of deployment in the UK or other countries in Europe during the period from 1980 through 1996, and potentially infected with vCJD. The calculations in this section are similar to the calculations for donors who traveled to the UK shown in section A-IV.B.2.a.v.

A-IV.B.2.d.vi. US plasma donors deployed by the Military: Potential number of donors with whose blood contains vCJD agent

The calculations in this section are similar to the calculations for donors who traveled to the UK shown in section A-IV.B.2.a.vi. and are not shown.

A-IV.B.2.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 in the New York City metropolitan area and possibly in other areas on the east coast of the US. To our knowledge there are no specific data available for plasma donors, therefore, data for blood donors was used in this risk assessment. Detailed calculations are on the model worksheet "IV.B.2.e. Euroblood". The results of the calculations are derived from model main worksheet "Model-IV. Exposure Assessment" and are used for subsequent calculations in the model..

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

A-IV.C.1.e.i. (1) annual number of US plasma donors who had received Euroblood

Variable: DR_{Tot} - (calculated in section A-IV.B.1.) 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.1.) 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

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

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

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

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

$$DR_{R-Eurob} = DR_R \times Perc_{DR-Eurob} \quad \text{(IV.B.2.e-3)}$$

A-IV.C.1.e.i.(2) Annual number of Euroblood transfused into US plasma donors and number of European donors who donated blood

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:

$$Perc_{DN-UK(age)} = DN_{Bl-UK(age)} / \sum_{age=18}^{\geq 65} DN_{Bl-UK(age)} \quad \text{(IV.B.2.e-4)}$$

Variable: $EUBL_{(age)}$ – Number of 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

$$EUBL_{(age)} = EUBL_{Tot} \times Perc_{DN-UK(age)} \quad \text{(IV.B.2.e-5)}$$

Variable: $DR_{EUBL(age)}$ – The number of European donors were grouped by age in five-year increments (e.g., 20-24 yrs, and so on) and the 18-19 yr old group that 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:

$$DR_{EUBL(age)} = EUBL_{(age)} \quad \text{(IV.B.2.e-6)}$$

A-IV.B.2.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 model estimated 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. Since calculations were essentially similar for all three

genotypes, and for the sake of brevity, only calculations for MM genotype are shown below as an example:

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 and is same variable as used in A-IV.C.1.c.iii.

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

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

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

$$\Pr_{vCJD-EU-MM(age)} = \Pr_{asym-vCJD-UK-MM(age)} \times R_{EU} \quad \text{(IV.B.2.e-7)}$$

Variable: $DR_{vCJD\text{-}EUBL\text{-}MM(age)}$, $DR_{vCJD\text{-}EUBL\text{-}MV(age)}$, $DR_{vCJD\text{-}EUBL\text{-}VV(age)}$-Annual number of infected European donors of MM, MV or VV genotypes 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.B. 2. e. i) 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. B. 2. e. ii) as parameters of the distribution.

$$DR_{vCJD-EUBL-MM(age)} = Binomial(DR_{EUBL(age)} \times Perc_{MM}, \Pr_{vCJD-EU-MM(age)}) \quad \text{(IV.B.2.e-8)}$$

Variable: $EUBL_{vCJD}$ - Total units of Euroblood, collected from a vCJD infected donor, 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 Euroblood containing vCJD agent.

$$EUBL_{vCJD} = \sum_{age=18-19}^{\geq 65} DR_{vCJD-EUBL-MM(age)} + \sum_{age=18-19}^{\geq 65} DR_{vCJD-EUBL-MV(age)} + \sum_{age=18-19}^{\geq 65} DR_{vCJD-EUBL-VV(age)} \quad \text{(IV.B.2.e-9)}$$

A-IV. B. 2. e. iii. Annual number of plasma donors potentially infected with vCJD via transfusion with Euroblood

A-IV.B.2.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

$$\Pr_{vCJD-EUBL} = EUBL_{vCJD} / EUBL_{Tot} \quad \text{(IV.B.2.e-10)}$$

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 from a vCJD-infected donor.

$$\Pr_{vCJD-EUBL-recip} = 1 - Binomdist(0, EUBL_{avg}, \Pr_{vCJD-EUBL}, false) \quad \text{(IV.B.2.e-12)}$$

The Excel function Binomdist (n, N, p, false) calculates the probability of n "successful" outcomes in a test, if the outcome of each trial of the test is either a "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.B.2.e-12, $Binomdist(0, EUBL_{avg}, Pr_{vCJD\text{-}EUBL}, false)$ 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 Plasma and recovered plasma donors who have received Euroblood ($DR_{S\text{-}EUBL}$ and $DR_{R\text{-}EUBL}$ estimated in section A-IV.B.2.e.i.) and the probability of infection for the individual Euroblood recipient ($Pr_{vCJD\text{-}EUBL\text{-}receip}$ estimated in section A-IV.B.2.e.ii) 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 infected due to transfusion with a Euroblood unit:

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

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

$$DR_{vCJD-R-EUBL} = Binomial(DR_{R-EUBL}, \Pr_{vCJD-EUBL-recip}) \quad \text{(IV.C.1.e-14)}$$

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

$$DR_{vCJD\text{-}EUBL} = DR_{vCJD\text{-}S\text{-}EUBL} + DR_{vCJD\text{-}R\text{-}EUBL} \quad \text{(IV.B.2.e-15)}$$

Assumption used in the model: No Euroblood Recipient is deferred under current policy

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:

$$DR_{vCJD\text{-}EUBL\text{-}Def} = 0 \quad \text{(IV.B.2.e-16)}$$

$$DR_{vCJD\text{-}EUBL\text{-}Res} = DR_{vCJD\text{-}EUBL} \quad \text{(IV.B.2.e-17)}$$

A-IV.B.2.e.iii.b. Annual number of plasma donors that received Euroblood and are potentially infected and whose blood contains the vCJD agent

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

Variable: $DR_{EUBL\text{-}Inf\$bl}$ - Annual number of plasma donors infected via transfusion using Euroblood and whose blood contained vCJD agent in 2002

$$DR_{EUBL\text{-}Inf\$bl} = DR_{vCJD\text{-}EUBL} \quad \text{(IV.B.2.e-18)}$$

A-IV.B.2.f. Total number all plasma donors who may potentially be infected with vCJD and the vCJD agent may be present through all sources of exposure

This section sums the number of plasma donors who might have been exposed to vCJD through different sources. The calculations from this point forward are on the model worksheet "Model-IV. Exposure Assessment".

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

Variable: $DR_{UK\text{-}Def\text{-}Inf\$bl}$ - Estimated annual number of Plasma donors potentially exposed to vCJD in the UK and whose blood contains vCJD agent that are deferred by current policy.

Variable: $DR_{FR\text{-}Def\text{-}Inf\$bl}$ - Estimated annual number of Plasma donors potentially exposed to vCJD in France and whose blood contains vCJD agent that are deferred by current policy

Variable: $DR_{DOD\text{-}Inf\$bl}$ - Estimated annual number of Plasma donors potentially exposed to vCJD in the military base and whose blood contains vCJD agent that are deferred by current policy.

$$DR_{Def\text{-}Inf\$bl} = DR_{UK\text{-}Def\text{-}Inf\$bl} + DR_{FR\text{-}Def\text{-}Inf\$bl} + DR_{DOD\text{-}Inf\$bl} \quad \text{(IV.B.2.f-1)}$$

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

Variable: $DR_{Res\text{-}Inf\$bl}$ - Estimated annual number of Plasma donors potentially infected with vCJD with agent present in blood and plasma and are not deferred by deferral policy.

Variable: $DR_{UK\text{-}Res\text{-}Inf\$bl}$ - Estimated annual number of Plasma donors potentially exposed to vCJD in the UK and having vCJD agent and whose blood contains vCJD agent and are deferred by current policy

Variable: $DR_{FR\text{-}Res\text{-}Inf\$bl}$ - Estimated annual number of Plasma donors potentially exposed to vCJD and having vCJD agent and whose blood contains vCJD agent and are deferred by current policy

Variable: $DR_{Eurobl\text{-}Inf\$bl}$ - Estimated annual number of Plasma donors potentially exposed to vCJD and having vCJD agent and whose blood contains vCJD agent and are deferred by current policy

$$DR_{Res\text{-}Inf\$bl} = DR_{UK\text{-}Res\text{-}Inf\$bl} + DR_{FR\text{-}Def\text{-}Inf\$bl} + DR_{DOD\text{-}Inf\$bl} \quad \text{(IV.B.2.f-2)}$$

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

A-IV.B.3. Annual number of all US plasma donors potentially infected with vCJD and whose blood may contain vCJD agent and who may not be deferred by questionnaire screening

This section calculated the number of plasma donors with vCJD agent in the blood and who 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. Uniform distribution (0.85, 0.99) was used to represent the range of uncertainty associated with Effectiveness of US donor deferral policy.

A-IV.B.3.a. US plasma donors with a history of travel to the UK

Variable: $DR_{vCJD\text{-}S\text{-}UK\text{-}Inf\text{-}NR}$ - Annual number of potential Source Plasma donors with history of travel to the UK, with vCJD agent present in blood and plasma, and were not removed by deferral screening.

Variable: $DR_{vCJD\text{-}R\text{-}UK\text{-}Inf\text{-}NR}$ - Annual number of potential recovered plasma donors with history of travel to the UK, with vCJD agent present in blood and plasma, and were not removed by deferral screening.

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

$$DR_{vCJD-S-UK-Inf\,bl-NR} = DR_{vCJD-S-UK-Res-Inf\,bl} + DR_{vCJD-S-UK-Def-Inf\,bl} \times (1 - Eff_{Def}) \qquad \text{(A-IV.B-1)}$$

$$DR_{vCJD-R-UK-Inf\,bl-NR} = DR_{vCJD-R-UK-Res-Inf\,bl} + DR_{vCJD-S-UK-Def-Inf\,bl} \times (1 - Eff_{Def}) \qquad \text{(A-IV.B-2)}$$

A-IV.B.3.b. US plasma donors with a history of travel to France.

Calculations for this section are similar to the calculations for donors with a history of travel to the UK shown in section A-IV.B.3.a.

A-IV.B.3.c. US plasma donors with a history of travel to other countries in Europe.

Calculations for this section are similar to the calculations for donors with a history of travel to the UK shown in section A-IV.B.3.a.

A-IV. B. 3. d. US plasma donors with a history of deployment to military bases in Europe.

Calculations for this section are similar to the calculations for donors with a history of travel to the UK shown in section A-IV.B.3.a.

A-IV.B.3.e. U.S. plasma donors who have been Euroblood recipients.

Calculations for this section are similar to the calculations for donors with a history of travel to the UK shown in section A-IV.B.3.a.

A-IV.B.3.f. All U.S. plasma donors potentially with vCJD agent in the blood and who may not be deferred by questionnaire screening

This section sum up the vCJD donors of Source Plasma and recovered plasma exposed through different sources.

A-IV.B.4. Probability that a US plasma donor's blood potentially contained vCJD agent

Variable: $Pr(DR_{S\text{-}Inf\,bl})$, $Pr(DR_{R\text{-}Inf\,bl})$ - Probability a Source Plasma or recovered plasma donor contain vCJD agent in the blood

Variable: $DR_{vCJD\text{-}S\text{-}Inf\,bl\text{-}NR}$, $DR_{vCJD\text{-}R\text{-}Inf\,bl\text{-}NR}$ - Source Plasma or recovered plasma donors who potentially contained vCJD agent in the blood, but not deferred by donor screening.

Variable: DR_S, DR_R - Annual number of Source plasma or recovered plasma donors (calculated in A-IV.B.1)

$$Pr(DR_{S-Inf\,bl}) = DR_{vCJD-S-Inf\,bl-NR} / DR_S \qquad \text{(A-IV.B.4.-1)}$$

Calculations for the probability a recovered plasma donor containing vCJD agent in the blood are similar to the calculation for source plasma donors shown above.

A-IV.C. Estimation of annual number and percentage of plasma pools potentially containing vCJD agent

A-IV.C.1. Probability that a plasma pool may contain vCJD donations

A-IV.C.1.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 Plasma 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: $DR_{pool\text{-}S}$, $DR_{pool\text{-}R}$ -Size of Source Plasma or recovered Plasma pool (donors/pool)

Data used in the model: Information for Source Plasma pool size was collected by the FDA from pdFVIII manufacturers. FDA is unable to show the complete data provided by manufacturers since the information is confidential, so only necessary, relevant summary information on various pools and their sizes is provided. The size of Source Plasma pools ranged from 6,000 donors per pool to 60,000 donors per pool with mean of -(b)(4)- donations per pool. The distribution was generated based on the pool size data provided by pdFVIII manufacturers and the market share of the products based on information supplied annually to the FDA by manufacturers. Manufacturers supplied FDA with information on the average number of donations from individuals in the pool.

Data used in the model: Information for recovered plasma pool sizes was collected by the FDA from pdFVIII manufacturers. Again, FDA is unable to show the complete data provided by manufacturers since the information is confidential. The size of recovered plasma pool ranged from 150,000 to 360,000 donations per pool. The distribution was generated based on the pool size data provided by pdFVIII manufacturers and the market share of the products. Manufacturers supplied FDA with information on the average number of donations from individuals in the pool.

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

Assumption used in the model: The number of vCJD donors 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 donors in a pool.

Variable: $Pr(n_{vCJD\text{-}DR\text{-}pool\text{-}S})$, $Pr(n_{vCJD\text{-}DR\text{-}pool\text{-}R})$- Probability a Source or Recovered Plasma pool containing $n_{vCJD\text{-}DN\text{-}pool}$ ($n_{vCJD\text{-}DR\text{-}pool}$ =0, 1, 2, 3, 4) number of infected donors

$Pr(n_{vCJD\text{-}DR\text{-}pool\text{-}S})$ was determined by binomial density function, Binomdist($n_{vCJD\text{-}DR\text{-}pool}$, $DR_{pool\text{-}S}$, $Pr(DR_{S\text{-}infbl})$. Calculations of $Pr(n_{vCJD\text{-}DR\text{-}pool\text{-}S})$ are similar to the calculation of $Pr(n_{vCJD\text{-}DR\text{-}pool\text{-}S})$.

A-IV.C.1.b. Probability a plasma pool may potentially contain a vCJD donor(s)

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

$$\Pr(vCJD\_pool_S) = 1 - \Pr(n_{vCJD\text{-}DR\text{-}pools} = 0) \qquad \text{(IV.C.1-1)}$$

Calculation of probability for the recovered plasma pool is similar to the calculation for Source Plasma pool shown above.

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

Variable: $Perc_S$, $Perc_R$ – Percentage of Source Plasma or recovered plasma pools used to manufacture pdFVIII in the US

Assumption used in the model: Estimates suggest that approximately -(b)(4)- of pdFVIII products were made from Source Plasma, and -(b)(4)- were made from recovered plasma..

Based on the assumptions above that Source Plasma pools are used more frequently in the manufacture of pdFVIII and, on average contain fewer donors, the probability of a Source Plasma pool containing vCJD agent is different from the probability a recovered plasma pool containing vCJD agent. Overall probability of a single plasma pool (including Source Plasma and recovered plasma pool) containing vCJD agent is a probability weight based on the percentages of the two types of plasma pools (-(b)(4)- for Source Plasma and -(b)(4)- for recovered plasma pools) used to make pdFVIII. A discrete distribution (X1, X2; p1, p2) represents two discrete values for the probabilities that a pool may contain a vCJD donor, X1(or $Pr(vCJD\text{-}pool_S)$) and X2 (or $Pr(vCJD\text{-}pool_R)$) and the associated probabilities of each value occurring with the probabilities, p1 and p2, respectively. $Pr(vCJD\text{-}pool)$ is sampled from $Pr(vCJD\text{-}pools$ and $Pr(vCJD\text{-}pool_R$ using the discrete distribution:

$$Pr(vCJD - pools) = Discrete(Pr(vCJD\text{-}pool\text{-}s), Pr(vCJD\text{-}pool\text{-}R); Perc_S, Perc_R)) \qquad \text{(IV.C.1-2)}$$

Or

$$Pr(vCJD - pools) = Discrete(Pr(vCJD\text{-}pool\text{-}s), Pr(vCJD\text{-}pool\text{-}R); \text{---(b)(4)---})) \qquad \text{(IV.C.1-3)}$$

A-IV.C.2. Annual amount of pdFVIII distributed in the US

Variable: IU_{FVIII} -Annual number of all units of human pdFVIII manufactured and distributed in the US .

Data used in the model: Based on data provided to FDA from manufacturers, a total of -(b)(4)- million units of pdFVIII was made and distributed in the US.

Variable: $Perc_S$, $Perc_R$ – Represents the percentage of pdFVIII assumed in the model to be made from Source Plasma or recovered plasma (same as variable used in A-IV.C.1.b.)

Variable: $IU_{FVIII\text{-}S}$, $IU_{FVIII\text{-}R}$ –The total annual number of units of pdFVIII made from Source Plasma or recovered plasma. The total annual number of units of pdFVIII made from Source Plasma is represented by the equation:

$$IU_{FVIII\text{-}S} = IU_{FVIII} \times Perc_S \qquad \text{(IV.C.2-1)}$$

The calculation for the total annual number of units of pdFVIII made from recovered plasma is similar.

A-IV.C.3. Annual total number of all plasma pools used to make pdFVIII

The total number of plasma pools used to make pdFVIII in the US each year can be back-calculated from the total number of units of human plasma-derived pdFVIII distributed in the US each year. Based on information described in earlier sections, it was assumed that approximately -(b)(4)- of the total pdFVIII supply distributed annually in the US is manufactured from Source Plasma and -(b)(4)- from recovered plasma pools. Information on pool size (number of donors), average number of donations per donor, size of individual recovered plasma donations (200 mls) and Source Plasma donations (700 mls) were used to first determine the amount of plasma present in a pool. Then, data on the average yield of pdFVIII per liter of plasma (187 IU), was used to calculate the total number of Source Plasma and recovered plasma pools and the results were summed to determine the total number of plasma pools used to manufacture pdFVIII in the US each year. The total number (or percentage) of plasma pools potentially containing vCJD agent was determined in the model based on pool size and the probability that a pool contained a vCJD agent.

A-IV.C.3.a. Amount plasma per pool

Variable: DN_{V-S}, DN_{V-R} – Volume of single unit Source Plasma or recovered plasma (ml).

Variable: DR_{pool-S}, DR_{pool-R} – Number donors per Source Plasma or recovered plasma pool (same variable as used in A-IV.C.5).

Variable: $Freq_{DN-S}$, $Freq_{DN-R}$ –Average frequency of donations from a single plasma donor who contributed Source Plasma or recovered plasma for pdFVIII manufacture.

Data used in the model: The data for average number of units in a Source Plasma pool donated by a single donor was provided by blood centers. The Pert distribution (----(b)(4)---) was used to represent the average number of units in a Source Plasma pool from single donors, which is most likely -(b)(4)- and ranges from --(b)(4)--.

Assumption used in the model: All the plasma units in a recovered plasma pool comes from different donors. This is conservative assumption.

Variable: V_{pool-S}, V_{pool-R} — Volume of a Source Plasma or recovered plasma pool (ml).

$$V_{pool-S} = DR_{pool-S} \times Freq_{DN-S} \times DN_{V-S} \quad \text{(IV. C. 3-1)}$$

Calculations of V_{pool-R} are similar to the calculation of V_{pool-S} shown above.

A-IV.C.3.b. Annual number of plasma pools used to manufacture pdFVIII in the United States

Variable: $IU_{FVIII-S}$, $IU_{FVIII-S}$ -Annual units of pdFVIII made from Source Plasma or recovered plasma (calculated in A-IV.C.2)

Variable: Y_{avg} –Average yield of pdFVIII (IU/L plasma)

Assumption used in the model: Based on the data provided by WFH (1998) and FDA-CBER (2003) we assumed average yield of pdFVIII (including high purity and intermediated purity pdFVIII) being 187 IU per liter plasma.

The total number of Source Plasma pools and recovered plasma pools used each year in manufacturing US pdFVIII are calculated separately in the model. Estimates from each type of pool are then summed to get a total value for all pools.

Variable: $Pool_S$, $Pool_R$ –Annual number Source or Recovered Plasma pool used to make pdFVIII

$$Pool_s = Round((IU_s / Y_{avg}) / (V_{pool-s} / 1000)) \quad \text{(IV. C. 3-2)}$$

Calculations of $Pool_R$ are similar as calculations of $Pool_S$ shown above.

A-IV. C. 4: Annual number vCJD plasma pools used to manufacture pdFVIII in the United States and percentage of contaminated pools

This section of the model estimated the annual number of vCJD plasma pool that may appear in an individual year. The annual number of vCJD Source and Recovered Plasma donors are estimated in section A-IV.B.3. In this section each individual vCJD donor is allocated to individual plasma pools by plasma types. Total number of vCJD plasma pools, percentage plasma pool containing vCJD agent and percentage contribution of vCJD vials from a specific pool are determined.

Assumption used in the model: The annual number of vCJD pools is expected to be low because the US vCJD prevalence, Even among donors that traveled to the UK, France or other countries in Europe since 1980, is likely very low. The chance of a plasma pool containing plasma from more than one infected donors is negligible. The model assumed if more than one infected donors presented, they would present in different plasma pool.

Variable: $Pool_{vCJD-S}$, $Pool_{vCJD-R}$ – Annual number of Source Plasma or recovered plasma pools that contain vCJD agent used to make pdFVIII

Variable: $Pool_{vCJD}$ – Annual total plasma pools that contain vCJD agent used to make pdFVIII

Variable: $Pool_S$, $Pool_R$ –Annual number of Source Plasma or recovered plasma pools

Variable: $Perc_{vCJD-S-pool}$, $Perc_{vCJD-R-pool}$ -Percentage of Source Plasma or recovered plasma pools used to make pdFVIII that contains vCJD donations

$$Perc_{vCJD-S-pool} = (Pool_{vCJD-S} / Pool_S) \times 100\% \qquad \text{(IV.C.4-1)}$$

A-IV.D. Estimation of the Quantity of vCJD agent in a plasma pool that contains a donation from a donor infected with vCJD

A-IV.D.1. Quantity of vCJD agent present in a donation of a donor infected with vCJD

Variable: I_{bl} – Represents the i.c. ID_{50} present in the blood of individual infected donor (ID_{50}/ml) in the last half of the incubation period of vCJD.

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 median 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).

Variable: $I_{pl\text{-}perc}$ – Percent (%) i.v. ID_{50}s associated with plasma

Studies in animal models have shown that greater than 50% of transmissible spongiform encephalopathy agent present in whole blood is associated with plasma. Experiments by Gregori *et al.* (2004) using a hamster – sheep scrapie model showed that approximately 58% of infectivity in whole blood is associated with plasma.

Assumption used in the model: The model assumes that 58% of infectivity is associated with plasma.

Variable: $A_{ic\text{-}iv}$-Conversion factor for iv ID_{50} from i.c. ID_{50}.

Assumption used in the model: Exposure to infectivity by the i.v. route is between 1 and 10 times less efficient at causing infection than introduction via the intracerebral route. Using a value of 1 for the ratio of the lower bound of the efficiency is a conservative estimate and assumes that theoretically there would be no difference between the efficiency in initiating infection between the i.c. and i.v. routes.

Variable: DN_V-Volume of one unit of plasma, depending on plasma type (same as $DN_{V\text{-}S}$ used in A-IV. C. 3 for Source Plasma and same as $DN_{V\text{-}R}$ used in A-IV. C. 3 for Recovered Plasma)

Variable: I_{DN}-Quantity of vCJD agent in one donation of infected plasma (i.v. ID_{50}/ml)

$$I_{DN} = I_{bl} \times DN_V \times I_{Pl-perc} \times A_{iv-ic} \qquad \text{(IV.D.1-1)}$$

A-IV.D.2. Quantity of vCJD agent in a plasma pool containing a donation from donor infected with vCJD

Variable: $DN_{vCJD\text{-}DR\text{-}pool}$ – Number of donations from an infected plasma donor, which varies based on type of plasma donated. (same as $Freq_{DN\text{-}S}$ used in A-IV.C.3 for Source Plasma and same as $Freq_{DN\text{-}R}$ used in A-IV. C. 3 for recovered plasma)

Assumption used in the model: Data on the average number of donations per donor per pool were provided by manufacturers. We assumed the average number donations from individual donors varied from pool to pool. For Source Plasma, it was assumed that average number of donations from single donor ranges from (b)(4) donations per donor, with a most likely of (b)(4) average donations per donor. For recovered plasma, it was assumed that the most likely number of donations per donor was only 1.

Variable: I_{Pool} – Initial infectivity in an infected plasma pool is represented by the equation:

$$I_{Pool} = I_{DN} \times DN_{vCJD-DR-pool} \qquad \text{(IV.D.2-1)}$$

MODULE 3 (IV.E)– CLEARANCE OF vCJD INFECTIVITY DURING MANUFACTURE OF pdFVIII

A-IV. E. Clearance of vCJD infectivity during manufacture of pdFVIII

A-IV.E.1. Estimated quantity of vCJD agent per IU FVIII product made from a specific vCJD plasma pool

The FDA model employed two stratifications of clearance:

- 4 – 6 $\log_{10}$
- 7 – 9 $\log_{10}$

Each of these levels of clearance was modeled separately. Most of the results are presented for the 4-6 log_{10} reduction during manufacture processing in the risk characterization section (Section V.) of this risk assessment.

Assumptions used in the model: The model assumed there are potentially two levels of reduction that may be achieved: a lower level of reduction (a range of 4-6 logs, most likely, 5 log_{10})-represented by triangular distribution (4, 5, 6) and higher level of reduction (a range of 7-9 log_{10}, most likely, log_{10})-represented by triangular distribution (7, 8, 9).

Variable: DR_{Pool}- Size of plasma pool (number of donors/pool). Same as DR_{pool-S} used in A-IV.C.3 for Source Plasma and same as DR_{pool-R} used in A-IV.C.3 for Recovered Plasma)

Assumption used in the model: The size of the plasma pools used in manufacturing was assumed to vary from pool to pool. In this risk assessment model, two different general distributions were used to represent frequency distribution of sizes of Source Plasma and recovered plasma pool based on the data provided by pdFVIII manufacturers.

Variable: I_{Pool}- Initial infectivity in a specific infected plasma pool (calculated in A-IV.D.2)

Variable: R_{Log}- Potential log reduction in infectivity during processing

Variable: $I_{Pool-Ap}$- Remaining infectivity in a specific infected plasma pool after processing

$$I_{Pool-Ap} = I_{Pool} / 10^{R_{Log}} \qquad \text{(IV.E-1)}$$

Variable: DN_V-Volume of one unit of plasma, depending on plasma type (for Source Plasma, same as DN_{V-S} used in A-IV.D.2, recovered plasma, same as DN_{V-R} used in A-IV.D.1.)

Variable: Y_{FVIII}-Yield of pdFVIII (IU/L plasma)

Assumption used in the model: Based on the data provided by the World Federation of Hemophilia (2004) we assumed pdFVIII yield varies from pool to pool with minimum of 120, most likely of 187 and maximum of 250 IU per liter plasma.

Variable: I_{IU}- Quantity of infectivity in the pdFVIII product made from a specific infected pool (i.v. ID_{50} per IU)

$$I_{IU} = (I_{Pool-Ap} / (DR_{Pool} \times DN_{DR-Avg} \times DN_V)) \times 1000 / Y_{FVIII} \qquad \text{(IV.E-2)}$$

A-IV.E.2. Estimated percentage of FVIII vials that contain vCJD agent

Variable: $Perc_{vCJD-S-vial}$, $Perc_{vCJD-R-vial}$- Percentage vials made from Source Plasma and recovered plasma containing vCJD infectious agent.

Variable: $Perc_{vCJD-vial}$ – Overall percentage of vials containing vCJD infectious agent.

Assumption used in the model: Percentage of vials of pdFVIII containing vCJD infectious agent is same as the percentage pools containing vCJD infectious agent calculated in IV-C.4 for corresponding types of plasma.

Module 4 (IV.F): FVIII utilization and annual exposure

A-IV.F. pdFVIII utilization by HA and vWD patients and potential exposure to the vCJD agent

A-IV.F.1. Estimate of annual number of vCJD vials used by individual patient

A-IV.F.1.a. Patients with severe Hemophilia A disease

This risk assessment provides outputs that estimate the annual exposure for several patient subpopulations with Severe HA disease for patients in the following clinical treatment groups:

- Prophylaxis – No inhibitor
- Prophylaxis - With inhibitor
- Prophylaxis - With inhibitor and immune tolerance
- Episodic – No inhibitor
- Episodic - With inhibitor

The CDC and the six state Hemophilia Surveillance System project conducted from 1993-1998 collected a total of 17,848 records, each record representing a single year of medical data for a single HA patient. Patient medical records were obtained from treatment sites including: hemophilia treatment centers (HTCs), hospitals, clinics, physician's offices, home-care agencies, nursing homes, prison infirmaries, and dispensers of factor concentrates. The comprehensive study collected standardized information on patient demographics, clinical treatment and outcome data. The data, abstracted from medical records, tabulated all recorded factor concentrate utilization prescribed by quantity, type, purpose (e.g., prophylaxis, treatment of acute bleeds, or immune tolerance therapy) and total quantity used per calendar year. Among all the records collected in the study from 1993-1998, 1,993 were from HA patients with severe disease that had been treated with human pdFVIII and the records were further grouped into five clinical treatment subcategories based on treatment regimen, including: prophylaxis, no inhibitor; prophylaxis, with inhibitor; prophylaxis, with inhibitor and immune tolerance; episodic, no inhibitor; and episodic, with inhibitor. Data from each of the five subpopulations were analyzed individually using the statistical package "JMP" (SAS Institute, Cary, NC) to generate initial descriptive statistics and distributions of pdFVIII usage by the HA patients. The data containing annual pdFVIII utilization information for patients in each of the five treatment groups were further analyzed using Best Fit software (Palisade Corp, New York) to generate a statistical distribution(s) for each patient treatment group that best reflected the variation in pdFVIII utilization. Overall, the Generalized Beta distribution provided the

most reasonable and consistent fit for the pdFVIII utilization data among all of the patient treatment groups. The Generalized Beta distributions were then used in the model to approximate the distribution of utilization of pdFVIII in each of the five HA patient subpopulations. The distributions were truncated by minimum and maximum FVIII usage of each subpopulation. FDA used the original patient data to not only generate statistical distributions for each patient treatment subpopulation. FDA also used the original data to identify the minimum and maximum dosages used by patients in each specific treatment subcategory and truncated each distribution using these values. Graphical representations of the original data and the fitted Generalized Beta distributions are shown in Appendix C. We also provide a summary of the pdFVIII usage data from the CDC sponsored six state study, and also summarize the input Generalized Beta distributions generated with each subset of data in Table A-4.5.

Table A-4.5. Annual usage of pdFVIII by individual HA patients with severe disease-data and input distribution

		Original Data			Input distribution (Generalized Beta distribution)				
Treatment Regimen	Inhibitor Status	n	Mean	95% CI	α	β	(min, max)	Mean	90% CI
Prophylaxis	No Inhibitor	578	164394 IU	(13574, 518781)	1.5159	10.02	(300, 1200000)	157949	(21000, 382,000)
	With Inhibitor – No Immune Tolerance	63	198781	(7859, 937480	1.4640	6.2861	(2000, 1000000	190823	(27000, 448000)
	With Inhibitor – With Immune Tolerance	62	569707	(14315, 3222471)	0.8782	5.5081	(10000, 4000000)	558709	(33000, 1583000)
Episodic	No Inhibitor	946	90489	(3001, 345416)	0.9882	10.60	(0, 1000000)	85270	(4800, 245000)
	With Inhibitor	151	169710	(4099, 835729)	0.6950	3.6822	(2000, 1000000)	160458	(5000, 489000)

Variable: IU_{Tr} - Annual usage of pdFVIII by individual HA patient of a specific clinical group (IU/yr, person)

Variable: IU_{vial} - Vial size (IU/vial)

Assumption used in the model: We assumed there were equal numbers of vials for each of the four different package sizes (250, 500, 1000 and 1500 IU/vial) that are distributed in the US.

Variable: $Vial_{Tot}$ - Annual number of pdFVIII vials used by individual patient (vials/yr, person)

Assumption used in the model: We assumed individual patient uses pdFVIII products of the same package size throughout the whole year period of 2002 for which the model was run.

$$Vial_{Tot} = IU_{Tr} / IU_{Vial} \qquad \text{(IV.F.1-1)}$$

Variable: $Perc_{vCJD\text{-}vial}$ – Percentage pdFVIII vials containing vCJD agent

Variable: $Vial_{vCJD}$ - Annual number of pdFVIII vials used by individual patient (vials/yr, person)

$$Vial_{vCJD} = Binomial(Vial_{Tot}, Perc_{vCJD\text{-}vial}) \qquad \text{(IV.F. 1-2)}$$

A-IV.F.1.b. FVIII Utilization in patients with severe von Willebrand disease

The CDC and six state Hemophilia Surveillance System project conducted from 1993-1998 did not include patients with vWD. We assumed that vWD patients with severe disease would largely use Humate P product only for factor replacement treatment. A search of records in the Hemophilia Surveillance System project data revealed a total of 58 records that indicated Humate P had been used, among which, 8 records indicates patients had developed inhibitor, which are considered uncommon among vWD patients and were excluded from analysis. Among the 58 records, 35 were from Adults (≥15 yrs of age) and 23 records were from young persons (<15 yrs of age). Records for each age group were further grouped by clinical treatment using either a prophylaxis or episodic treatment regimen. Data were initially analyzed individually using the statistical package "JMP" (SAS Institute, Cary, NC) to generate descriptive statistics and statistical distribution(s) for each patient treatment group that best reflected the variation in pdFVIII utilization. The Generalized Beta distribution was identified as the best fit to the pdFVIII utilization data (as determined by using the software Best Fit (Palisade Corp, NY) and was used as the input distribution for pdFVIII usage by individual vWD patients in the model. Graphical representations of the original data and the fitted Generalized Beta distributions are shown in Appendix C. Table A-4.6. summarizes pdFVIII usage data from CDC sponsored study and the input distribution generated based on the data. FDA used data in the CDC and six state Hemophilia Surveillance System project conducted from 1993-1998 to estimate FVIII utilization by all vWD patients. The data represent only a sample of all possible vWD patients with severe disease in the US. FDA estimated that there were approximately 250 patients in the US with Type 3 vWD. To calculate the total number of patients in each age group and treatment regimen group we adjusted the 58 patient population to equal a total of 250 patients by multiplying the patient population in each group by a factor of 4.3 (250/58 = ~4.3). The utilization data for patients in each treatment regimen in the sample population were used in the risk assessment model to generate outputs for the annual exposure to vCJD for all vWD for Adult (>15 yrs of age) and Young (≤15 yrs of age) persons in the US among clinical treatment groups of prophylaxis and episodic.

Table A-4.6. Annual usage of pdFVIII by individual severe vWD patient -data and input distribution We need to update the information in this table – based on new calculations for a total of 58 cases (previously it was 50 cases)

	Original Input Data				Input Distribution (Generalized Beta distribution)				
Treatment Regimen	n	Percent of total population	Mean	95% CI	α	β	(min, max)	Mean	90% CI
Young (≤15 yrs of age)									
Prophylaxis	9	16%	164193	(9200, 504625)	0.4523	0.9784	(9200, 504625)	165713	(9900, 454000)
Episodic	14	24%	11122	(1010, 41850)	0.3900	1.1973	(1010, 41850)	11045	(1020, 34350)
Adult (>15 yrs of age)									
Prophylaxis	17	29%	187538	(15000, 772800)	0.5741	1.9589	(15000, 7728000)	18888 0.	(17000, 540000)
Episodic	18	31%	845558	(1000, 293800)	0.5656	1.4097	(1000, 293800)	66923	(2200, 240000)

Calculations of annual number of vCJD vials taken by individual vWD patient are similar to the calculations for HA patients shown in section A-IV. F.1.a.

A-IV.F.2. Quantityof vCJD agent in pdFVIII vials

This section of the model randomly picked vCJD vials from different vCJD pools simulated in section IV.D.2. and determine the amount of vCJD infectious agent contained in each random vCJD vial,

Variable: I_{Iu} - Quantity of infectivity in the pdFVIII product made from a specific infected pool (i.v. ID_{50} per IU) (calculated in section IV.F.)

A-IV.F.3. Estimation of annual exposure

This section of the model sums up the infectivity in all vCJD vials taken by individual patent during a one-year period.

A-IV.F.3.a. Patient with severe HA disease

Assumption used in the model: Infectivity varies for each individual vial taken by one patient during a one-year period. We did not considered the probability that patient buy a bulk package at a time, which may results in multiple vials from same vCJD pool, therefore with same infectivity

Variable: I_{yr} - Annual exposure to vCJD through use of pdFVIII (i.v. ID_{50}/yr, person)

$$I_{yr} = \sum_{i=1}^{Vial_{CJD}} I_{Iu} \times IU_{Vial} \qquad \text{(IV.F. 3-1)}$$

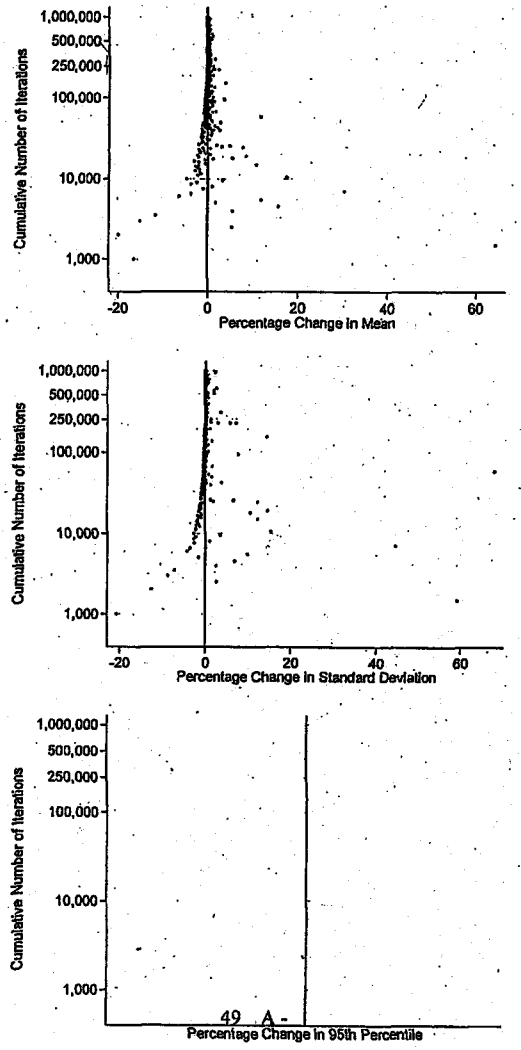
A-IV. F. 3. b. Patient with severe vWD

Calculations of annual exposure of individual vWD patient (i.v. ID50/yr, person) are similar to the calculations for HA patients shown in section A-IV. F.3.a.

Testing Convergence of the Model

We ran a million iterations of the model. Convergence was analyzed by examining the percent change in the estimate of mean exposure for each 500 iteration block of the model, cumulatively. That is, the mean exposure was calculated for the first 500 iterations, 1,000 iterations, 1,500 iterations, etc., to 1,000,000 iterations. For the last 10,000 iterations, the average percentage change for the mean exposure of hemophilia patients with no inhibitor using the log 4-7 reduction assumption and the clinical prevalence assumption was 0.012 percent. The results are shown in Figure 1.

Figure 1. Convergence for risk estimates for hemophilia patient group with no inhibitor under assumption of 4-7 log reduction using low prevalence estimate for UK vCJD prevalence. The 95th percentile was always 0 under the low prevalence assumption.



B 個別症例報告概要

○ 総括一覧表
○ 報告リスト

個別症例報告のまとめ方について

個別症例報告が添付されているもののうち、個別症例報告の重複を除いたものを一覧表の後に添付した（国内症例については、資料3において集積報告を行っているため、添付していない）。

別紙様式第４

感染症発生症例一覧

	番号	感染症の種類		発現国	性別	年齢	発現時期（年/月/日）	転帰	出典	区分	備考
		器官別大分類	基本語								
第15回	15-1	感染症および寄生虫症	B型肝炎	米国	男性	58歳	2010/07/20	未回復	症例報告	外国製品	識別番号：10000017（完了報告、追加報告） 報告日：2010年9月6日、2010年9月22日 MedDRA：Version（13.0）
	15-2	肝胆道系障害	肝炎	米国	男性	14歳	不明	不明	症例報告	外国製品	識別番号：10000016（完了報告） 報告日：2010年8月13日 MedDRA：Version（13.0）
	15-2	臨床検査	抗ＨＢｃＩｇＧ抗体陽性	米国	男性	14歳	2010/05/29	不明	症例報告	外国製品	識別番号：10000016（完了報告） 報告日：2010年8月13日 MedDRA：Version（13.0）
	15-3	臨床検査	抗ＨＢｃＩｇＧ抗体陽性	スウェーデン	男性	不明	2009/11/16	回復	症例報告	外国製品	識別番号：10000011（完了報告） 報告日：2010年7月9日 MedDRA：Version（13.0）
	15-3	臨床検査	抗ＨＢｓ抗体陽性	スウェーデン	男性	不明	2009/11/16	回復	症例報告	外国製品	識別番号：10000011（完了報告） 報告日：2010年7月9日 MedDRA：Version（13.0）
	15-4	肝胆道系障害	肝炎	米国	女性	不明	不明	不明	症例報告	外国製品	識別番号：10000007（完了報告） 報告日：2010年6月8日 MedDRA：Version（13.0）
	15-4	臨床検査	A型肝炎抗体陽性	米国	女性	不明	2006	不明	症例報告	外国製品	識別番号：10000007（完了報告） 報告日：2010年6月8日 MedDRA：Version（13.0）
	15-4	臨床検査	B型肝炎抗体陽性	米国	女性	不明	2006	不明	症例報告	外国製品	識別番号：10000007（完了報告） 報告日：2010年6月8日 MedDRA：Version（13.0）
	14-3	感染症および寄生虫症	B型肝炎	米国	女性	不明	不明	不明	症例報告	外国製品	識別番号：10000002（追加報告） 報告日：2010年6月7日 第14回症例番号14-3において報告したものの追加報告 MedDRA：Version（13.0）

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感染症定期報告の報告状況(2010/12/1～2011/2/28)

血対ID	ID	受理日	番号	報告者名	一般名	生物由来成分名	原材料名	原産国	含有区分	文献	症例	担当者審査者
100269	2	2010/12/13	100749	バクスター	乾燥イオン交換樹脂処理人免疫グロブリン	人免疫グロブリンG	人血漿	米国	有効成分	無	有	無
100270	3	2010/12/13	100750	バクスター	乾燥イオン交換樹脂処理人免疫グロブリン	人血清アルブミン	人血漿	米国	添加剤	無	有	無
100277	10	2010/12/15	100775	化学及血清療法研究所	乾燥スルホ化人免疫グロブリン	スルホ化人免疫グロブリンG、	ヒト血漿	米国、日本	有効成分	無	有	無
100296	29	2011/2/22	100917	CSLベーリング	人血清アルブミン 乾燥濃縮抗凝固因子フィブリノゲン加第XIII因子	ヘパリン	ブタ腸粘膜	中国	製造工程	無	有	無

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別紙様式第４

	番号	感染症の種類		発現国	性別	年齢	発現時期（年/月/日）	転帰	出典	区分	備考
		器官別大分類	基本語								
第12回	12-1	感染症および寄生虫症	肝炎ウイルスキャリアー	米国	不明	不明	1993	不明	症例報告	当該製品	識別番号：08000002（完了報告） 報告日：2008年12月22日 MedDRA: Version(11.1)
	12-2	感染症および寄生虫症	C型肝炎	米国	女性	48	2008/12/09	未回復	症例報告	外国製品	識別番号：08000034（完了報告） 報告日：2009年1月19日 MedDRA: Version(11.1)
	12-3	感染症および寄生虫症	C型肝炎	米国	女性	不明	不明	不明	症例報告	外国製品	識別番号：09000004（完了報告） 報告日：2009年5月18日 MedDRA: Version(12.0)
第11回	11-1	臨床検査	B型肝炎抗体陽性	米国	男性	17	2008/05	不明	症例報告	当該製品	識別番号：08000007（完了報告） 報告日：2008年6月5日 MedDRA: Version(11.0)
	11-2	感染症および寄生虫症	C型肝炎	米国	女性	不明	2008	不明	症例報告	当該製品	識別番号：08000018（追加報告） 報告日：2008年11月12日 第11回症例番号11-2において10月17日に報告したものの追加報告 MedDRA: Version(11.1)
	11-2	感染症および寄生虫症	C型肝炎	米国	女性	不明	2008	不明	症例報告	当該製品	識別番号：08000018（完了報告） 報告日：2008年10月17日 MedDRA: Version(11.0)
	11-3	感染症および寄生虫症	B型肝炎	スペイン	女性	不明	2008/6/3	未回復	症例報告	外国製品	識別番号：08000026（完了報告） 報告日：2008年10月31日 MedDRA: Version(11.1)

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別紙様式第４

	番号	感染症の種類		発現国	性別	年齢	発現時期（年/月/日）	転帰	出典	区分	備考
		器官別大分類	基本語								
第14回	14-1	臨床検査	抗HBcIgG抗体陽性	米国	男性	3歳	2010/01/28	不明	症例報告	外国製品	識別番号：09000025（完了報告） 報告日：2010年2月26日 MedDRA: Version(12.1)
	14-2	肝胆道系障害	急性肝炎	米国	女性	75歳	2010/03/01	軽快	症例報告	外国製品	識別番号：09000029（完了報告） 報告日：2010年3月24日 MedDRA: Version(13.0)
	14-3	感染症および寄生虫症	B型肝炎	米国	女性	不明	不明	不明	症例報告	外国製品	識別番号：10000002（完了報告） 報告日：2010年4月27日 MedDRA: Version(13.0)
	14-4	臨床検査	A型肝炎陽性	カナダ	男性	19歳	不明	不明	症例報告	外国製品	識別番号：10000008（完了報告） 報告日：2010年6月14日 MedDRA: Version(13.0)
第13回	13-1	臨床検査	C型肝炎陽性	米国	男性	65歳	2009/09	未回復	症例報告	外国製品	識別番号：09000017（完了報告） 報告日：2009年11月5日 MedDRA: Version(12.1)
	13-2	臨床検査	B型肝炎抗体陽性	米国	女性	32歳	2009/07/12	未回復	症例報告	外国製品	識別番号：09000013（完了報告） 報告日：2009年9月24日 MedDRA: Version(12.1)
	13-3	感染症および寄生虫症	B型肝炎	米国	女性	40歳	2009/05	回復	症例報告	外国製品	識別番号：09000012（完了報告） 報告日：2009年8月19日 MedDRA: Version(12.1)
	13-4	臨床検査	B型肝炎抗体陽性	米国	女性	37歳	2009/04/23	未回復	症例報告	外国製品	識別番号：09000014（完了報告） 報告日：2009年10月8日 MedDRA: Version(12.1)
	13-5	臨床検査	B型肝炎抗体陽性	米国	不明	新生児	2009/04/23	未回復	症例報告	外国製品	識別番号：09000015（完了報告） 報告日：2009年10月8日 MedDRA: Version(12.1)

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別紙様式第４

	番号	感染症の種類		発現国	性別	年齢	発現時期（年/月/日）	転帰	出典	区分	備考
		器官別大分類	基本語								
第5回	5-1	感染症および寄生虫症	C型肝炎	米国	男性	51歳	2005年9月	未回復	症例報告	当該製品	識別番号：05000456(追加報告) 報告日：2005年11月11日 MedDRA: Version(8.1)
	5-1	感染症および寄生虫症	C型肝炎	米国	男性	51歳	2005年9月	未回復	症例報告	当該製品	識別番号：05000456(完了報告) 報告日：2005年10月27日 MedDRA: Version(8.1)
	1-3	感染症および寄生虫症	C型肝炎	米国	男性	26歳	2002/11/19	不明	症例報告	当該製品	識別番号：03000006(追加報告) 報告日：2005年7月4日 第2回症例番号1-3において報告したものの追加報告 MedDRA: Version(8.0)
	1-3	感染症および寄生虫症	B型肝炎	米国	男性	26歳	2002/10/4	不明	症例報告	当該製品	識別番号：03000006(追加報告) 報告日：2005年7月4日 第2回症例番号1-3において報告したものの追加報告 MedDRA: Version(8.0)
	4-1	臨床検査	HTLV-1血清学的検査陽性	フランス	男性	6歳	2005年	不明	症例報告	当該製品	識別番号：05000001(追加報告) 報告日：2005年6月27日 第4回症例番号4-1において報告したものの追加報告 MedDRA: Version(8.0)
	4-1	臨床検査	HTLV-2血清学的検査陽性	フランス	男性	6歳	2005年	不明	症例報告	当該製品	識別番号：05000001(追加報告) 報告日：2005年6月27日 第4回症例番号4-1において報告したものの追加報告 MedDRA: Version(8.0)

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別紙様式第４

	番号	感染症の種類		発現国	性別	年齢	発現時期（年/月/日）	転帰	出典	区分	備考
		器官別大分類	基本語								
第10回		0*	0	0	0	0	0	0	0	0	* 当該調査期間に対象となる感染症報告はなかった
第9回		0	0	0	0	0	0	0	0	0	
第8回		0	0	0	0	0	0	0	0	0	
第7回	7-1	臨床検査	ＨＩＶ抗体陽性	米国	不明	小児	不明	不明	症例報告	外国製品	識別番号：06000022（完了報告） 報告日：2006年8月24日 MedDRA: Version(9.0)
第6回	5-1	感染症および寄生虫症	C型肝炎	米国	男性	51歳	2005年9月	未回復	症例報告	当該製品	識別番号：05000456(追加報告) 報告日：2006年2月15日 第6回症例番号5-1は前回報告における第5回症例番号5-1において報告したものの追加報告 MedDRA: Version(8.1)

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別紙様式第４

	番号	感染症の種類		発現国	性別	年齢	発現時期（年/月/日）	転帰	出典	区分	備考
		器官別大分類	基本語								
第３回	3-1	感染症および寄生虫症	Ｃ型肝炎	米国	女性	37歳	2004/5/21	不明	症例報告	当該製品	識別番号：04000023 報告日：2004年6月30日 MedDRA: Version(7.0)
	3-2	臨床検査	Ｂ型肝炎抗体陽性	米国	女性	63歳	2004/7/27	不明	症例報告	当該製品	識別番号：04000059 報告日：2004年9月7日 MedDRA: Version(7.0)
	3-2	臨床検査	Ａ型肝炎抗体陽性	米国	女性	63歳	2004/8/16	不明	症例報告	当該製品	識別番号：04000059 報告日：2004年9月7日 MedDRA: Version(7.0)
	3-3	臨床検査	Ｂ型肝炎抗体陽性	米国	女性	50歳代	2004/9月	不明	症例報告	当該製品	識別番号：04000082 報告日：2004年10月20日 MedDRA: Version(7.1)
	3-3	臨床検査	Ａ型肝炎抗体陽性	米国	女性	50歳代	2004/9月	不明	症例報告	当該製品	識別番号：04000082 報告日：2004年10月20日 MedDRA: Version(7.1)

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別紙様式第４

	番号	感染症の種類		発現国	性別	年齢	発現時期（年/月/日）	転帰	出典	区分	備考
		器官別大分類	基本語								
第４回	4-1	臨床検査	HTLV-1 血清学的検査陽性	フランス	男性	6歳	2005年	不明	症例報告	当該製品	識別番号：05000001(追加報告) 報告日：2005年4月25日 MedDRA: Version(8.0)
	4-1	臨床検査	HTLV-1 血清学的検査陽性	フランス	男性	6歳	2005年	不明	症例報告	当該製品	識別番号：05000001(完了報告) 報告日：2005年4月7日 MedDRA: Version(8.0)
	4-1	臨床検査	HTLV-2 血清学的検査陽性	フランス	男性	6歳	2005年	不明	症例報告	当該製品	識別番号：05000001(追加報告) 報告日：2005年4月25日) MedDRA: Version(8.0)
	4-1	臨床検査	HTLV-2 血清学的検査陽性	フランス	男性	6歳	2005年	不明	症例報告	当該製品	識別番号：05000001(完了報告) 報告日：2005年4月7日 MedDRA: Version(8.0)
	4-2	感染症および寄生虫症	Ｃ型肝炎	フランス	男性	不明	不明	不明	症例報告	外国製品	識別番号：04000129 報告日：2005年3月31日) MedDRA: Version(8.0)

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別紙様式第４

感染症発生症例一覧

	番号	感染症の種類		発現国	性別	年齢	発現時期	転帰	出典	区分	備考
		器官別大分類	基本語								
第15回	15-2	感染症および寄生虫症	サイトメガロウイルス感染	日本	女	3ヶ月	2010/07	未回復	自発報告	当該製品	10000039、2回(取下) 平成22年9月13日 MedDRA ver.13.0
	15-1	感染症および寄生虫症	A型肝炎	ドイツ	女	66	2009/06	不明	自発報告	外国製品	10000012、1回(完了;同一症例をアンチトロンビンIII 番号15-1で報告) 平成22年7月29日 MedDRA ver.13.0
	15-1	感染症および寄生虫症	医薬品を介する感染因子の伝播	ドイツ	女	66	2009/06	不明	自発報告	外国製品	10000012、1回(完了;同一症例をアンチトロンビンIII 番号15-1で報告) 平成22年7月29日 MedDRA ver.13.0
	15-1	臨床検査	肝酵素上昇	ドイツ	女	66	2009/06	不明	自発報告	外国製品	10000012、1回(完了) 平成22年7月29日 MedDRA ver.13.0
	15-1	臨床検査	A型肝炎抗体陽性	ドイツ	女	66	2009/06	不明	自発報告	外国製品	10000012、1回(完了) 平成22年7月29日 MedDRA ver.13.0
第11回	11-1	感染症および寄生虫症	C型肝炎	日本	女	33	2008/7/20	未回復	自発報告	当該製品	08000486、3回(完了;因果関係が否定されたため、報告対象外として完了報告) 平成20年11月5日 MedDRA ver.11.1
第5回	7	感染症および寄生虫症	C型肝炎	日本	女	70	2005/6/10	回復	自発報告	当該製品	05000058、2回(取下) 平成17年7月19日 MedDRA ver.8.0
	6	感染症および寄生虫症	サイトメガロウイルス性腸炎	日本	男	71	2005/5/21	軽快	自発報告	当該製品	05000049、2回(取下) 平成17年10月3日 MedDRA ver.8.
第4回	5	感染症および寄生虫症	C型肝炎	日本	女	28	2004/12	不明	自発報告	当該製品	04000290、3回(取下) 平成18年3月14日 MedDRA ver.7.1

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別紙様式第４

	番号	感染症の種類		発現国	性別	年齢	発現時期(年/月/日)	転帰	出典	区分	備考
		器官別大分類	基本語								
第2回	1-3	感染症および寄生虫症	C型肝炎	米国	男性	26歳	2003/8/30	軽快	症例報告	当該製品	識別番号：03000006 報告日；2004年1月7日 第1回症例番号1-3において報告したもの(FAX報告)の完了報告 MedDRA: Version(6.1)
	2-2	感染症および寄生虫症	C型肝炎	ドイツ	女性	6歳	1994/6/21	未回復	症例報告	外国製品	識別番号：04000013 報告日：2004年5月27日 MedDRA: Version(7.0)
第1回	1-1	臨床検査	C型肝炎ウイルス	米国	男性	不明	不明	未回復	症例報告	外国製品	識別番号：D03-31 報告日：2003年8月6日 MedDRA: Version(6.1)
	1-2	臨床検査	C型肝炎ウイルス	米国	男性	不明	不明	未回復	症例報告	外国製品	識別番号：A03-32 報告日：2003年8月6日 MedDRA: Version(6.1)
	1-3	感染症および寄生虫症	C型肝炎	米国	男	26歳	2003/8/30	軽快	症例報告	当該製品	識別番号：03000006 報告日：2003年11月28日 FAX報告：2003年11月19日) MedDRA: Version(6.1)

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100269	2	2010/12/13	100749	バクスター	乾燥イオン交換樹脂処理人免疫グロブリン	人免疫グロブリンG	入血漿	米国	有効成分	無	有	無
100270	3	2010/12/13	100750	バクスター	乾燥イオン交換樹脂処理人免疫グロブリン	人血清アルブミン	人血漿	米国	添加物	無	有	無

別紙様式第4

感染症発生症例一覧

	番号	感染症の種類		発生国	性別	年齢	発現時期	転帰	出典	区分	備考
		器官別大分類	基本語								
第15回	1	感染症および寄生虫症	A型肝炎	ドイツ	女	66	不明	不明	症例報告	外国製品	識別番号3-10000013 報告日:2010年08月06日
	1	臨床検査	A型肝炎抗体陽性	ドイツ	女	66	2009/6	不明	症例報告	外国製品	識別番号3-10000013 報告日:2010年08月06日
	2	感染症および寄生虫症	HIV感染	ドイツ	男	31	2009/4	不明	症例報告	外国製品	識別番号3-10000026 報告日:2010年10月27日
第14回	1	感染症および寄生虫症	A型肝炎	ドイツ	女	71	2009/12/14	不明	症例報告	外国製品	識別番号3-09000024 報告日:2010年8月20日*
	1	感染症および寄生虫症	B型肝炎	ドイツ	女	71	2009/12/14	不明	症例報告	外国製品	識別番号3-09000024 報告日:2010年8月20日*
	1	感染症および寄生虫症	C型肝炎	ドイツ	女	71	2009/12/14	不明	症例報告	外国製品	識別番号3-09000024 報告日:2010年8月20日*
	2	感染症および寄生虫症	HIV感染	イタリア	男	28	2004/11	不明	症例報告	外国製品	識別番号3-09000026 報告日:2010年2月26日 報告対象外報告:2010年3月29日
第13回	報告なし										
第12回	1	感染症および寄生虫症	C型肝炎	ドイツ	男	66	2009/5/1	不明	症例報告	外国製品	識別番号3-09000009 報告日:2009年07月22日
	2	感染症および寄生虫症	C型肝炎	ドイツ	女	77	2009/1/5	不明	症例報告	外国製品	識別番号3-08000039 報告日:2009年02月17日
	3	感染症および寄生虫症	C型肝炎	ドイツ	女	77	2009/1/5	不明	症例報告	外国製品	識別番号3-08000040 報告日:2009年02月17日
第11回	1	感染症および寄生虫症	HIV感染	ドイツ	男	35	不明	不明	症例報告	外国製品	識別番号3-08000029 報告日:2009年02月17日
	1	感染症および寄生虫症	B型肝炎	ドイツ	男	35	不明	不明	症例報告	外国製品	識別番号3-08000029 報告日:2009年02月17日
第10回	1	感染症および寄生虫症	B型肝炎	ドイツ	男	24	2008/1/10	不明	症例報告	外国製品	識別番号3-07000026 報告日:2008年4月1日
	2	感染症および寄生虫症	B型肝炎	ドイツ	男	24	2008/1/10	不明	症例報告	外国製品	識別番号3-07000031 報告日:2008年4月25日
	3	臨床検査	C型肝炎抗体陽性	日本	女	37	2007/9/11	不明	症例報告	当該製品	識別番号1-07000251 報告日:2008年4月30日
	4	感染症および寄生虫症	C型肝炎	ドイツ	女	60	2007/4/13	不明	症例報告	外国製品	識別番号3-08000005 報告日:2008年5月29日
第9回	1	感染症および寄生虫症	B型肝炎	日本	女	33	2007/8/7	回復	症例報告	当該製品	識別番号1-07000093 報告日:2007年10月11日
第8回	1	感染症および寄生虫症	C型肝炎	ドイツ	女	61	2007/1	不明	症例報告	外国製品	識別番号3-06000032 報告日:2007年3月30日
	1	臨床検査	C型肝炎陽性	ドイツ	女	61	2007/1	不明	症例報告	外国製品	識別番号3-06000032 報告日:2007年3月30日
第7回	1	感染症および寄生虫症	C型肝炎	ドイツ	女	41	2006/11/21	不明	症例報告	外国製品	識別番号3-06000029 報告日:2008年12月20日
	1	臨床検査	C型肝炎抗体陽性	ドイツ	女	41	2006/11/21	不明	症例報告	外国製品	識別番号3-06000029 報告日:2008年12月20日
	1	臨床検査	C型肝炎RNA陽性	ドイツ	女	41	2006/11/21	不明	症例報告	外国製品	識別番号3-06000029 報告日:2008年12月20日

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	番号	感染症の種類		発現国	性別	年齢	発現時期	転帰	出典	区分	備考
		器官別大分類	基本語								
第4回	4	感染症および寄生虫症	ブドウ球菌感染	日本	女	1	2004/11/24	軽快	自発報告	当該製品	05000029、2回(完了) 平成17年7月19日 MedDRA ver.8.0
第3回	3	感染症および寄生虫症	C型肝炎	日本	男	79	2003/10	未回復	症例報告	当該製品	04000082、2回目(完了) 平成16年7月14日 MedDRA ver.7.0
第2回	2	感染症および寄生虫症	B型肝炎	日本	男	76	2003/8/4	未回復	症例報告	当該製品	03000113、1回目(完了) 平成16年2月4日 MedDRA ver.6.1
	1	感染症および寄生虫症	B型肝炎	日本	女	55	2004/1/9	未回復	症例報告	当該製品	03000111、2回目(完了) 平成16年4月9日 完了報告 MedDRA ver.6.1

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	100277	10	2010/12/15		100775	化学及血清療法研究所	乾燥スルホ化人免疫グロブリン	スルホ化人免疫グロブリンG	ヒト血液	米国、日本	有効成分	有	有	無

資料３－１

供血者からの遡及調査の進捗状況について
（目次）

○　供血者からの遡及調査の進捗状況について
（平成23年5月17日付け血液対策課事務連絡）

○　供血者からの遡及調査の進捗状況について（回答）
（平成23年6月1日付け日本赤十字社提出資料）

○　薬事法第77条の4の3に基づく回収報告状況
（平成23年2月　～　平成23年5月分）

○　「血漿分画製剤のウイルス安全対策について」の実施状況について

○　血漿分画製剤のウイルス安全対策について
（平成15年11月7日付け医薬食品局4課長通知）

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100296	29	2011/2/22	100917	CSLベーリング	人血清アルブミン 破傷風抗毒素 フィブリノゲン 加第XIII因子	ヘパリン	ブタ腸粘膜	中国	製造工程	無	有	無

	番号	感染症の種類 器官別大分類	感染症の種類 基本語	発生国	性別	年齢	発現時期	転帰	出典	区分	備考
第6回	1	感染症および寄生虫症	C型肝炎	ドイツ	女	63	2005/11	不明	症例報告	外国製品	識別番号3-06000004 報告日：2006年5月18日
第5回	1	感染症および寄生虫症	B型肝炎	ドイツ	男	74	2005/10/21	死亡	症例報告	外国製品	識別番号3-05000494 報告日：2005年12月27日
	1	感染症および寄生虫症	輸血後肝炎	ドイツ	男	74	2005/10/21	死亡	症例報告	外国製品	識別番号3-05000494 報告日：2005年12月27日
	1	臨床検査	抗HBs抗体陽性	ドイツ	男	74	2005/10/21	死亡	症例報告	外国製品	識別番号3-05000494 報告日：2005年12月27日
	2	感染症および寄生虫症	B型肝炎	ドイツ	女	77	2005/9/28	未回復	症例報告	外国製品	識別番号3-05000493 報告日：2005年12月27日
第4回	1	感染症および寄生虫症	C型肝炎	ドイツ	不明	不明	不明	不明	症例報告	外国製品	識別番号3-04000125 報告日：2005年5月27日
	2	感染症および寄生虫症	ウイルス性肝炎	ドイツ	女	55	1995年	不明	症例報告	外国製品	識別番号3-04000122 報告日：2005年6月8日
第3回	1	臨床検査	C型肝炎陽性	ドイツ	男	68	2004/08	不明	症例報告	外国製品	識別番号3-04000088 報告日：2004年11月22日
第2回	報告なし										
第1回	1	感染症および寄生虫症	C型肝炎	フランス	男	57	2003/6/16	不明	症例報告	外国製品	識別番号D03-38 報告日：2003年9月4日 取り下げ報告：2003年11月7日
	2	感染症および寄生虫症	C型肝炎	ドイツ	男	不明	不明	後遺症	症例報告	外国製品	識別番号D03-40 報告日：2003年9月11日
	3	臨床検査	C型肝炎RNA陽性	ドイツ	女	71	2003/6/27	後遺症	症例報告	外国製品	識別番号D03-41 報告日：2003年9月11日
	4	感染症および寄生虫症	HIV感染	ドイツ	男	67	2000/4頃	後遺症	症例報告	外国製品	識別番号D03-47 報告日：2003年10月3日
	5	感染症および寄生虫症	C型肝炎	ドイツ	男	64	2003/7/2	後遺症	症例報告	外国製品	識別番号D03-51 報告日：2003年10月10日
	5	臨床検査	C型肝炎抗体陽性	ドイツ	男	64	2003/7/2	後遺症	症例報告	外国製品	識別番号D03-51 報告日：2003年10月10日
	5	臨床検査	C型肝炎RNA陽性	ドイツ	男	64	2003/7/2	後遺症	症例報告	外国製品	識別番号D03-51 報告日：2003年10月10日
	6	感染症および寄生虫症	サイトメガロウイルス感染	ドイツ	男	0	2003/6末	死亡	症例報告	外国製品	識別番号3-03000005 報告日：2003年11月19日
	6	臨床検査	サイトメガロウイルス抗体陽性	ドイツ	男	0	2003/6末	死亡	症例報告	外国製品	識別番号3-03000005 報告日：2003年11月19日
	6	臨床検査	サイトメガロウイルス抗体陽性	ドイツ	男	0	2003/6末	死亡	症例報告	外国製品	識別番号3-03000005 報告日：2003年11月19日
	6	臨床検査	サイトメガロウイルス検査陽性	ドイツ	男	0	2003/6末	死亡	症例報告	外国製品	識別番号3-03000005 報告日：2003年11月19日

＊：今回調査期間に追加報告を行った。

MedDRA/J Ver.13.1

事　務　連　絡
平成２３年5月１７日

日本赤十字社血液事業本部　御中

薬事・食品衛生審議会血液事業部会事務局
厚生労働省医薬食品局血液対策課

供血者からの遡及調査の進捗状況について

標記につきましては、平成２３年２月２日付け血安第３９号にて貴社血液事業本部長より資料の提出があり、これを平成２２年度第４回血液事業部会運営委員会に提出したところです。今般、平成２３年６月２７日（月）に平成２３年度第１回血液事業部会運営委員会が開催されることとなりましたので、下記の事項について改めて資料を作成いただき、平成２３年６月１日（水）までに当事務局あて御提出いただきますようお願いいたします。

記

１．「供血者の供血歴の確認等の徹底について」（平成１５年６月１２日付け医薬血発第 0612001 号）に基づく遡及調査に係る以下の事項
（１）遡及調査実施内容
①　調査の対象とした献血件数
②　上記①のうち、調査の対象とした輸血用血液製剤の本数
③　上記②のうち、医療機関に情報提供を行った本数
（２）個別 NAT 関連情報
①　（１）①のうち、個別 NAT の結果が陽性となった献血件数
②　上記①のうち、医療機関へ供給された製剤に関する報告件数
③　上記②のうち、受血者情報が判明した件数
④　上記③のうち、医薬品副作用感染症報告を行った件数

２．資料の作成に当たっての留意事項
①　本数又は件数については、病原体別及びその合計を明らかにすること。また、上記（１）の③及び（２）の①～③については、対象期間ごとに本数又は件数を記載すること。
②　本数又は件数については、平成２３年２月２日付け血安第３９号の提出時において判明したものに、その後の遡及調査の進展状況を反映させて記載すること。

血安第１８９号
平成２３年６月１日

厚生労働省医薬食品局血液対策課長 様

日本赤十字社
血液事業本部長

供血者からの遡及調査の進捗状況について（回答）

平成 23 年 5 月 17 日付事務連絡によりご連絡のありました標記の件について、別紙により報告いたします。

別紙

供血者から始まる遡及調査実施状況

平成23年3月31日現在

対象期間	平成21年4月1日 ～ 平成22年3月31日			平成22年4月1日 ～ 平成23年3月31日		
	HBV	HCV	HIV	HBV	HCV	HIV
(1)遡及調査実施内容						
①. 調査の対象とした献血件数(個別NAT実施件数)						
1)総数	1,806			1,858		
2)個別件数	1,688	69	49	1,735	75	48
② 上記①のうち、調査の対象とした輸血用血液製剤の本数						
1)総数	2,014			2,313		
2)個別本数	1,877	84	53	2,163	90	60
③ 上記②のうち、医療機関に情報提供を行った本数						
1)総数	2,014			1,679		
2)個別本数	1,877	84	53	1,566	69	44
(2)個別NAT関連情報						
①. 遡及調査実施対象〔(1)①〕のうち、個別NATの結果が陽性となった献血件数						
1)総数	144			100		
2)個別件数	144	0	0	100	0	0
② 上記①のうち、医療機関へ供給された製剤に関する報告件数						
1)使用された本数	140	0	0	98	0	0
2)医療機関調査中	0	0	0	0	0	0
3)院内で廃棄	6	0	0	5	0	0
4)不明	6	0	0	3	0	0
計	152	0	0	106	0	0
③ 上記②のうち、受血者情報が判明した件数						
1)陽転事例	1	0	0	3	0	0
2)非陽転事例	55	0	0	25	0	0
3)死亡	55	0	0	43	0	0
4)退院・未検査	19	0	0	14	0	0
5)陽性だが輸血前不明	10	0	0	13	0	0
計	140	0	0	98	0	0
④ 上記③のうち、医薬品副作用感染症報告を行った件数						
報告件数	1	0	0	3	0	0

*血液製剤等に係る遡及調査ガイドライン(平成20年12月26日一部改正)に基づく遡及調査対応基準を適用。

HBV ：HBs抗原CLEIA法確認試験（中和試験）又は個別NAT陽性の場合は遡及調査を行う。
：HBc抗体CLEIA法陽転の場合は遡及調査を行う。
HCV ：HCV抗体CLEIA法陽転の血液及び前回の血液について個別NATを実施し、いずれかが陽性の場合は遡及調査を行う。
HIV ：HIV抗体CLEIA法で陽転し、確認試験（WB法）又は個別NAT陽性の場合は遡及調査を行う。
共通 ：スクリーニングNAT陽転の場合は遡及調査を行う。

〈参考〉

供血者から始まる遡及調査実施状況

対象期間	平成11年4月1日～平成18年3月31日			平成18年4月1日～平成19年3月31日			平成19年4月1日～平成20年3月31日			平成20年4月1日～平成21年3月31日		
	HBV	HCV	HIV	HBV	HCV	HIV	HBV	HCV	HIV	HBV	HCV	HIV
① 調査の対象とした献血件数												
1)遡及調査の対象件数	23,104			2,193			2,694			5,219		
② 上記①のうち、個別NAT検査を実施した本数(検体数)												
1)本数(検体数)	23,104			2,193			2,694			5,219		
2)実施率	100%			100%			100%			100%		
③ 上記②のうち陽性が判明した本数												
本数	311	3	1	60	1	0	25	0	0	118	0	0
④ 上記①のうち医療機関に情報提供を行った件数												
1)血液製剤数(総数)	33,114			2,408			2,867			4,034		
個別本数				2,062	288	58	2,444	345	78	3,552	417	65
2)情報提供数	33,114			2,408			2,708			3,469		
個別件数				2,062	288	58	2,319	317	72	3,150	254	65
＊平成11年4月1日～平成17年3月31日までの情報提供数には、医療機関の廃院等による追跡不能数930件を含む												
⑤ 上記③のうち医療機関へ供給された製剤に関する報告件数												
1)使用された本数	326	3	1	51	2	0	26	0	0	94	0	0
2)医療機関調査中	0	0	0	0	0	0	0	0	0	0	0	0
3)院内で廃棄	16	0	0	2	0	0	2	0	0	5	0	0
4)不明	7	1	0	0	0	0	0	0	0	0	0	0
計	349	4	1	53	2	0	28	0	0	99	0	0
⑥ 上記⑤のうち、受血者情報が判明した件数												
1)陽転事例	17	1	1	4	1	0	4	0	0	3	0	0
2)非陽転事例	69	0	0	11	0	0	9	0	0	30	0	0
3)死亡	118	2	0	31	1	0	10	0	0	42	0	0
4)退院・未検査	15	0	0	0	0	0	0	0	0	0	0	0
5)陽性だが輸血前不明	7	0	0	1	0	0	0	0	0	0	0	0
計	226	3	1	47	2	0	23	0	0	75	0	0
＊個別NAT陰性(NATウインドウピリオド)の遡及調査対象血液の輸血により、受血者が陽転した例を含む												
⑦ 上記⑥のうち、医薬品副作用感染症報告を行った件数												
報告件数	16*	1	1	5	1	0	4	0	0	3	0	0
ウイルス別合計	HBV:28		HCV:2		HIV:1							

*受血者情報の陽転事例のうち医薬品感染症報告が行われていない平成12年3月の事例は、献血血液が遡及調査の対象(個別HBV-NAT陽性)となり、受血者の陽転化情報が得られたが、患者は原疾患により死亡した事例である。
*平成20年度は、遡及調査対応基準を改定した。(同年10月29日開催「薬事・食品衛生審議会血液事業部会運営委員会」にて了承済)

薬事法第７７条の４の３に基づく回収報告状況

○平成２３年２月～平成２３年５月

報告日	回収開始年月日	回収対象製品	製造番号	数量
平成23年2月2日	平成23年2月1日	照射赤血球濃厚液-LR「日赤」400mL由来	72-0127-3848	1
平成23年2月8日	平成23年2月7日	濃厚血小板-LR「日赤」10単位	28-7030-4640	1
平成23年2月16日	平成23年2月16日	赤血球濃厚液-LR「日赤」400mL由来	63-0325-9321	1
平成23年2月25日	平成23年2月23日	照射赤血球濃厚液-LR「日赤」200mL由来	12-1617-1592	1
平成23年2月25日	平成23年2月24日	新鮮凍結血漿-LR「日赤」成分採血由来	28-8035-7276	1
平成23年4月6日	平成23年4月4日	新鮮凍結血漿-LR「日赤」400mL由来	72-3924-6159	1
平成23年4月21日	平成23年4月18日	新鮮凍結血漿-LR「日赤」400mL由来	21-0527-7842	1
平成23年5月9日	平成23年5月4日	照射赤血球濃厚液-LR「日赤」400mL由来	23-3120-6443	1
平成23年5月9日	平成23年5月6日	新鮮凍結血漿-LR「日赤」400mL由来	37-5120-8267	1
平成23年5月13日	平成23年5月12日	新鮮凍結血漿-LR「日赤」400mL由来	51-0121-7035	1

「血漿分画製剤のウイルス安全対策について」の実施状況について

○ 経 緯

「血漿分画製剤のウイルス安全対策について」（平成１５年１１月７日付け薬食審査発第 1107001 号、薬食安発第 1107001 号、薬食監発第 1107001 号、薬食血発第 1107001 号。以下「通知」という。）の実施状況について、（社）日本血液製剤協会に所属し、血漿分画製剤を製造又は輸入している会員企業に対し報告を求めたところ、以下の結果が得られた。

① 通知記の３（１）前段に規定するウイルス・プロセスバリデーションの実施の有無

国内製造業者４社及び輸入販売業者５社のいずれにおいても、ウイルス・プロセスバリデーションが行われていた。

② 上記①に関する必要な書類等の整理及び保存の有無

国内製造業者４社及び輸入販売業者５社のいずれにおいても、必要な書類等の整理及び保存が行われていた。

③ 通知記の３（１）後段に規定するウイルスクリアランス指数が９未満の製剤の有無及び該当する製剤がある場合は、ウイルスの除去・不活化の工程の改善の検討状況

ウイルスクリアランス指数が９未満の製剤は、海外血漿を原料とし、日本国内に輸入されている２製剤がある。国内血漿を原料としている製剤及び輸入血漿を原料とし、日本国内で製造されている製剤には、９未満の製剤はない。

該当する製剤がある製造業者又は輸入販売業者の製造元においては、バリデーション結果の見直し、新たな不活化工程の追加等の検討等が行われている。

なお、米国及び欧州で採血された場合は、それぞれの地域における遡及調査ガイドラインに基づいた対応がなされている。

④ 通知記の３（２）に規定する原料のプールにおけるＮＡＴの実施の有無

国内製造業者４社及び輸入販売業者５社の製造元のいずれにおいても、原料のプールにおけるＮＡＴ検査が実施されている。

⑤ 通知記の６に規定する添付文書の改訂の有無

添付文書へ記載する文章及び記載場所について、日本血液製剤協会・添付文書委員会で協議・検討が行われ、平成15年12月17日に厚生労働省医薬食品局安全対策課の了承を得たところであり、平成16年1月から2月にかけて、血漿分画製剤及び人血液を用いる血液製剤代替医薬品の添付文書が改訂された。

薬食審査発第1107001号
薬食安発第1107001号
薬食監発第1107001号
薬食血発第1107001号
平成１５年１１月７日

（社）日本血液製剤協会理事長　殿

厚生労働省医薬食品局審査管理課長

厚生労働省医薬食品局安全対策課長

厚生労働省医薬食品局監視指導・麻薬対策課長

厚生労働省医薬食品局血液対策課長

血漿分画製剤のウイルス安全対策について

標記については、平成１５年１０月２４日に開催された平成１５年度第３回血液事業部会における検討結果を踏まえ、下記のとおりとし、発出日から適用しますので、貴職におかれては、貴会会員に対し当該対策が徹底されるよう周知をお願いします。ただし、平成１５年９月１７日に開催された平成１５年度第３回血液事業部会安全技術調査会において対応を保留することとされた、遡及調査により個別に核酸増幅検査（以下「ＮＡＴ」という。）を実施した結果、陽性血液の混入が判明した原料血漿由来の血漿分画製剤については、本通知の規定を遡って適用することといたします。

また、「血液製剤の当面のウイルス安全対策について」（平成１０年１１月２日付け厚生省医薬安全局安全対策課、監視指導課、血液対策課事務連絡）については、本通知をもって廃止することとします。

記

１　血漿分画製剤（以下「製剤」という。）の製造前には、生物由来原料基準（平成１５年厚生労働省令第２１０号）第２の２の（６）の規定に則り、その原血漿について、ウイルス（ＨＢＶ、ＨＣＶ及びＨＩＶをいう。以下同じ。）のＮＡＴを実施することとし、陽性となった場合は使用しないこと。

２　副作用等の報告（薬事法（昭和３５年法律第１４５号）第７７条の４の２第１項及び第２項に規定する副作用等の報告をいう。以下同じ。）等からの遡及調査に伴い、製剤（ロット）の製造後に個別にＮＡＴを実施することにより、陽性となった血液の原血漿への混入が判明した場合は、混入したウイルスの種類及び量（理論的な上限値を含む。）が特定され、かつ、製造工程において当該ウイルスが十分に除去・不活化されることが確認されれば、個別の分離血漿の段階にある原血漿を除き、当該製剤（ロット）を回収する必要はないものとすること。また、これらの特定及び確認は、厚生労働省医薬食品局血液対策課が、血液事業部会安全技術調査会の意見を聴いて行うものとすること。

なお、この場合において、混入したウイルスの量が、日本赤十字社が現に実施している５０プールのＮＡＴにより陰性が確認されるレベルであって、当該ウイルスに係るウイルスクリアランス指数（ウイルス力価の減少度を対数（$\log_{10}$値）で表したものをいう。以下同じ。）が９以上である製剤（ロット）については、当該ウイルスが十分に除去・不活化されていると平成１５年度第３回血液事業部会において判断されたので、当面は、個別の分離血漿の段階にある原血漿を除き、当該製剤（ロット）を回収する必要はないものとすること。

３　２の前段に規定する確認に資するため、あらかじめ、以下に掲げる措置を講じておくこと。

（１）ウイルスの除去・不活化等に係る書類等の整備及び工程の改善

製剤の製造工程において、ウイルスが十分に除去・不活化されていることを確認できるよう、ウイルス・プロセスバリデーションを実施しておくこと。また、必要な書類等を整理し、保存しておくこと。

さらに、「安全な血液製剤の安定供給の確保等に関する法律」（昭和３１年法律第１６０号）の第７条において、製造業者等の責務として「血液製剤の安全性向上に寄与する技術の開発」に努めることが規定されていることを踏まえ、より安全性の高い製剤の開発に努めること。特に、製造工程におけるウイルスクリアランス指数が９未満である製剤については、早期

にウイルスの除去・不活化の工程について改善を図ること。

（2）原料のプールを製造した際の検査
原料のプールを製造した際、当該プールについてＮＡＴを実施することとし、陽性となった場合は使用しないこと。また、当該ＮＡＴの検出限界が１００ＩＵ／ｍｌの精度となるよう精度管理を行い、必要な書類等を保存しておくこと。

4　以下の場合は、速やかに厚生労働省医薬食品局血液対策課に報告すること。
（1）遡及調査等により原血漿にＮＡＴで陽性となった血液の混入が判明した場合。
（2）3の（2）に規定する原料のプールを製造した際の検査でＮＡＴの陽性が判明した場合。
なお、当該報告があった場合は、「ＮＡＴガイドライン（仮称）」が策定されるまでの間、第三者機関においてＮＡＴの結果を検証することとしているので、血液対策課の指示に基づき当該機関に保管検体を提供すること。

5　副作用等の報告等からの遡及調査に伴い、製剤（ロット）の製造後に個別にＮＡＴを実施することにより、陽性となった血液の原血漿への混入が判明した場合であって、3の（1）及び（2）に掲げる措置が講じられていない等、2の前段に規定する確認ができない場合は、原則として、「医薬品等の回収に関する監視指導要領」（平成１２年３月８日付け医薬発第２３７号別添１）の規定に則り、当該製剤（ロット）を回収すること。
なお、副作用等の報告等からの遡及調査により、製剤（ロット）と感染症の発生との因果関係が否定できない場合には、以上の規定にかかわらず、速やかに厚生労働省医薬食品局安全対策課に報告するとともに、同要領の規定に則り、当該製剤（ロット）を回収すること。

6　既に、「生物由来製品の添付文書に記載すべき事項について」（平成１５年５月１５日医薬発第0515005号）に基づき、製剤のリスクに係る事項が添付文書に記載されているところであるが、なお入念的な措置として、同通知の記の１．（１）⑤に関連して、添付文書の重要な基本的注意に、以下に掲げる趣旨の文言を記載すること。
・　製剤の原材料である血液については、ミニプールでＮＡＴを実施し、ウイルスのＤＮＡ又はＲＮＡが検出されないことが確認されたものを使用しているが、当該ミニプールＮＡＴの検出限界以下のウイルスが混入している可能性が常に存在すること。

資料３－２

血液製剤に関する医療機関からの感染症報告事例等について

報告日	輸血された血液製剤	供血者数	供血者検査結果等	同一血液由来の他製剤等について	新規報告
H17.1.12	赤血球製剤 血小板製剤	16人	保管検体個別NAT　陽性2人 16人中12名が来訪 HBV関連検査陰性：12人 （個別NAT陽性の2人は、複数回再献血を行っているが、HBc抗体を含む関連検査が全て陰性であり、感染歴があった可能性は低い。）	原料血漿：3本確保済み。12本使用済み。 新鮮凍結血漿：12本全て医療機関へ提供済み。	平成17年10月18日以降、残る4人の来訪なし。
H17.2.4	赤血球製剤	9人 追跡対象は4人。	保管検体個別NAT：9人全て陰性 （当該患者のHBV-NATが陽性になる前の輸血の供血者は9人中4人。） 4人中3人来訪。 HBV関連検査陰性：2人 HBc抗体陽性：1人	原料血漿：7本確保済み。 新鮮凍結血漿：2本確保済み、2本医療機関へ提供済み。	平成18年4月25日以降、追跡調査対象の残る1人の来訪なし。
H17.6.23	赤血球製剤 新鮮凍結血漿	20人	保管検体個別NAT全て陰性 20人中18人が来訪。 HBV関連検査陰性：18人	原料血漿：17本中10本確保。 新鮮凍結血漿：6本中3本確保。 赤血球製剤：15本全て医療機関へ供給済み。	平成22年7月27日以降、残る2人の来訪なし。
H18.4.7	血小板製剤 赤血球製剤	53人	保管検体個別NAT全て陰性 53人中46人が来訪。 HBV関連検査陰性：43人 HBc抗体、HBs抗体陽性：2人 HBs抗体陽性：1人	原料血漿：51本中7本確保。44本使用済み。 新鮮凍結血漿：14本全て供給済み。	平成22年7月27日以降、残る7人の来訪なし。

輸血用血液製剤で感染が疑われる事例について　（平成２３年５月１７日時点）

【ＨＩＶ感染が疑われた事例】

報告日	輸血された血液製剤	供血者数	供血者検査結果等	同一血液由来の他製剤等について	新規報告
H15.9.5	赤血球製剤	8人	保管検体個別NAT全て陰性 8人中6人が来訪 HIV関連検査陰性：6人	新鮮凍結血漿：3本。使用済み。 原料血漿は流通停止。 新鮮凍結血漿を投与された患者3名のうち、1名は原疾患で死亡残り2名は輸血後（約6ヵ月後）抗体検査で陰性。	平成17年10月18日以降、残る2人の来訪なし

【ＨＢＶ感染が疑われた事例】

報告日	輸血された血液製剤	供血者数	供血者検査結果等	同一血液由来の他製剤等について	新規報告
H16.3.22	血小板製剤 赤血球製剤	37人	保管検体個別NAT全て陰性 37人中32人が来訪 個別NAT陰性：32人	新鮮凍結血漿：5本（供血者4人分由来） 使用済み。 残りは原料血漿。 新鮮凍結血漿を投与された患者5名のうち、陰性2名、不明3名。	平成18年10月17日以降、残る5人の来訪なし
H16.11.26	新鮮凍結血漿 赤血球製剤	48人	保管検体個別NAT全て陰性 48名中41人が来訪 HBV関連検査陰性：41人	原料血漿：2本確保。31本使用済み。 新鮮凍結血漿：16本。医療機関へ提供済み。 赤血球製剤：45本。医療機関へ提供済み。	平成21年4月22日以降、残る7人の来訪なし

平成２３年度感染症報告事例のまとめ（前回報告分以降）について

１　平成２３年２月３日報告分から２３年５月２日までに報告（新規及び追加）があった感染症報告（疑い事例を含む。供血者からの情報により開始した遡及調査によるものを除く。）は、輸血用血液製剤２５件である。
輸血用血液製剤の内訳は、
（１）Ｂ型肝炎報告事例：　１２
（２）Ｃ型肝炎報告事例：　７
（３）ＨＩＶ感染報告例：　０
（４）その他の感染症報告例：　６

２　Ｂ型肝炎報告事例
（１）輸血前後に感染症検査でHBs抗原（又はHBV-DNA）等が陽転した事例は１０例（輸血後NATで陰性又は輸血前後で陽性は１例）。
（２）血液製剤を提供した献血者の保管検体の個別ＮＡＴ陽性の事例は１例。
（３）輸血後に死亡（原疾患又は他の原因による死亡を除く）したとの報告を受けた事例は０例（劇症化例含む。）である。

３　Ｃ型肝炎報告事例
（１）輸血前後に抗体検査（又はHCV-RNA）等が陽転した事例は７例（輸血後NATで陰性又は輸血前後で陽性は０例）。
（２）使用した血液製剤を提供した献血者の保管検体の個別ＮＡＴ陽性事例は０例。
（３）輸血後に死亡（原疾患又は他の原因による死亡を除く）したとの報告を受けた事例は０例。

４　ＨＩＶ報告事例
（１）輸血前後に抗体検査等が陽転した事例は０例。
（２）使用した血液製剤を提供した献血者の保管検体の個別ＮＡＴ陽性事例は０例。
（３）輸血後に死亡（原疾患又は他の原因による死亡を除く）したとの報告を受けた事例は０例。

５　その他感染症報告事例
（１）Ｂ型肝炎及びＣ型肝炎以外の肝障害報告事例は０件。
（２）細菌等感染報告事例において、血液製剤を提供した献血者の保管検体の無菌試験陽性事例は０例。輸血後に死亡（原疾患又は他の原因による死亡を除く）したとの報告を受けた事例は０例。

報告日	輸血された血液製剤	供血者数	供血者検査結果等	同一血液由来の他製剤等について	新規報告
H18.6.5	赤血球製剤 新鮮凍結血漿	29人	保管検体個別NAT全て陰性 29人中28人来訪 HBV関連検査陰性：25人 HBs抗体、HBc抗体陽性：2人 HBs抗体陽性：1人	原料血漿：27本中11本確保。16本使用済み。 新鮮凍結血漿：8本中6本確保。2本供給済み。 赤血球製剤：18本全て使用済み。	平成21年4月22日以降、残る1人の来訪なし。
H19.2.20	赤血球濃厚液	3人	保管検体個別NAT全て陰性 3人中2人来訪 HBV関連検査陰性：2人	原料血漿：3本全て確保。	平成19年10月19日以降、残る1人の来訪なし。
H21.11.20	新鮮凍結血漿 血小板製剤 赤血球製剤	45人	保管検体個別NAT全て陰性 感染が疑われる輸血時の製剤の供血者23人 23人中21人来訪 HBV関連検査陰性：21人	原料血漿：20本中2本確保。18本使用済み。 新鮮凍結血漿：3本全て供給済み。 赤血球製剤：22本全て供給済み。	平成22年2月13日以降、1人が新たに来訪したが、残る2人の来訪なし。

【HCV感染が疑われた事例】

報告日	輸血された血液製剤	供血者数	供血者検査結果等	同一血液由来の他製剤等について	新規報告
H18.2.15	赤血球製剤 血小板製剤 新鮮凍結血漿	81人	保管検体個別NAT全て陰性 81人中78人来訪 HCV関連検査陰性：78人	原料血漿：70本中67本確保。3本使用済み。 新鮮凍結血漿：14本中11本確保。3本供給済み。 赤血球製剤：6本全て供給済み。	平成19年10月19日以降、残る3人の来訪なし

日赤管理番号	識別番号	FAX受付日	報告受領日	販売名(一般名)	患者性別	年代	原疾患	感染症名	投与年月	投与前検査(年月)	投与後検査(年月)	日赤投与前検査	日赤投与後検査	受血者個別NAT	献血者個別NAT	併用血液製剤等	備考	使用単位数	供血者再献血※	同一供血者製剤確保※	同一供血者製剤使用※	感染症等転帰	転帰	供血者発覚及の場合の供血者保管検体(抗原、抗体、NAT)(投与時点)	供血者発覚及の場合の供血者の検査値
3-1100010	A-10000102	2011/2/21	2011/3/7	新鮮凍結血漿-LR(新鮮凍結人血漿)	男	50	消化器疾患	B型肝炎	10/09	HBsAg(-)(10/09)	HBsAg(+)HBeAg(+)HBcAb(+)IgM-HBcAb(-)(11/02)	-	HBV-DNA(+)HBsAg(+)HBcAb(+)(11/02)	陽性(輸血後)	保管検体2本全部についてHBV-DNA(-)			4単位	0/2	2本の赤血球濃厚液-LRを製造。	赤血球濃厚液-LRは全て医療機関へ供給済み。	重篤	未回復			
3-1100013	A-10000104	2011/2/24	2011/3/11	赤血球濃厚液-LR(人赤血球濃厚液) 照射赤血球濃厚液-LR(人赤血球濃厚液(放射線照射))	女	70	血液腫瘍	B型肝炎	10/08-11	HBsAg(-)HBcAb(-)HBeAb(-)(10/06)	HBV-DNA(+)HBsAg(+)HBcrAg(+)HBsAb(-)HBcAb(-)HBeAb(-)HBsAg(+)HBsAb(-)(11/02)	HBV-DNA(-)ZHBsAg(-)HBsAb(-)HBcAb(-)(10/08)	HBV-DNA(+)HBsAg(+)HBsAb(-)HBcAb(-)(11/02)	陰性(輸血前)陽性(輸血後)	保管検体3本全部についてHBV-DNA(-)			4単位14単位	6/9(HBV関連検査陰性)	原料血漿1本は使用済み。	原料血漿1本は使用済み。	重篤	未回復			
3-1100020	A-10000111	2011/3/15	2011/3/25	照射濃厚赤血小板-LR(人血小板濃厚液(放射線照射)) 赤血球濃厚液-LR(人赤血球濃厚液) 照射赤血球濃厚液-LR(人赤血球濃厚液(放射線照射))	男	80	血液腫瘍	B型肝炎	10/07-11	HBsAg(-)HBcAb(-)(10/06)	HBsAg(+)HBeAb(-)HBcAb(-)(11/02)HBV-DNA(+)HBsAg(+)HBsAb(-)HBcAb(-)(11/03)	HBV-DNA(-)HBsAb(-)(10/06)	HBV-DNA(+)HBsAg(+)HBsAb(-)HBcAb(-)(11/03)	陰性(輸血前)陽性(輸血後)	保管検体31本についてHBV-DNA(-)		【献血者陽転化情報】 当該献血 2010年1月23日 HBV関連検査 陰性 個別HBV-NAT 陰性 次回献血 2011年3月28日 HBs抗体検査陽性(陽転献血) 個別HBV-NAT 陰性 【製剤情報】 当該検査陽(原材濃厚赤小板-LR)の同一採血番号製剤として、1本の原料血漿を製造していた。当該原料血漿は確保済みである。	170単位28単位2単位	21/31(20人はHBV関連検査陰性。一人は次回献血でHBs抗体検査陽性であった。)	30本の原料血漿、1本の新鮮凍結血漿-LR、1本の濃厚赤小板-LRを製造。原料血漿は全てHBV確保済み。新鮮凍結血漿-LRは確保済み。	濃厚赤小板-LRは医療機関へ供給済み。	非重篤	未回復		献血者検体(2011年3月28日採血、HBV陽性検体)と患者検体とでPreS/S領域をさむP領域の前半部の1550bpの塩基配列を比較したところ、全て一致していた。献血者と患者のHBウイルスはGenotype Bで塩基配列からSubtypeはaywと推定した。
3-1100022	A-10000113	2011/3/18	2011/3/30	赤血球濃厚液-LR(人赤血球濃厚液) 新鮮凍結血漿-LR(新鮮凍結人血漿)	女	30	産科(出血)	B型肝炎	10/11	HBsAg(-)HBsAb(-)(10/09)HBV-DNA(-)HBsAg(-)HBsAb(-)(10/11)	HBV-DNA(+)(11/02)HBsAg(+)HBeAg(-)HBsAb(-)HBcAb(+)HBeAg(+)HBsAb(+)(11/03)	-	-	-	保管検体8本全部についてHBV-DNA(-)			6単位10単位	5/9(HBV関連検査陰性)	3本の原料血漿、5本の赤血球濃厚液-LRを製造。原料血漿は全てで確保済み。	赤血球濃厚液-LRは全て医療機関へ供給済み。	重篤	未回復			

日赤管理番号	識別番号	FAX受付日	報告受領日	販売名(一般名)	患者性別	年代	原疾患	感染症名	投与年月	投与前検査(年月)	投与後検査(年月)	日赤投与前検査	日赤投与後検査	受血者個別NAT	献血者個別NAT	併用血液製剤等	備考	使用単位数	供血者再献血※	同一供血者製剤確保※	同一供血者製剤使用※	感染症等転帰	転帰	供血者発覚及の場合の供血者保管検体(抗原、抗体、NAT)(投与時点)	供血者発覚及の場合の供血者の検査値
				輸血によるHBV感染報告例(疑い例を含む。)																					
供血者陽性事例																									
3-1100006	A-10000097	2011/1/26	2011/2/8	赤血球濃厚液-LR(人赤血球濃厚液) 新鮮凍結血漿-LR(新鮮凍結人血漿) 照射濃厚赤小板-LR(人血小板濃厚液(放射線照射))	女	60	膵臓腫瘍疾患	B型肝炎	10/07	HBV-DNA(-)HBsAg(-)HBsAb(-)HBcAb(-)(10/7)	HBV-DNA(+)HBcAb(+)(11/1)HBV-DNA(+)HBsAg(+)HBsAb(-)HBcAb(+)(11/1)	-	HBV-DNA(+)(11/1)	陽性(輸血後)	保管検体15本についてHBV-DNA(-)1本HBV-DNA(+)		※HBV-DNA陽性輸血用血液(献血者)についての情報 ・同一採血献血番号:赤血球濃厚液-LRを1本製造。医療機関へ供給済み。 ・再来献血:3回献血に再来。(保管検体4本についてHBV-NAT実施予定) 2本の原料血漿、1本の新鮮凍結血漿-LR、3本の赤血球濃厚液-LRを製造。原料血漿は全て送付済み。新鮮凍結血漿-LRは医療機関へ供給済み。赤血球濃厚液-LRは2本は医療機関へ供給済み、1本は回収済み。 ・当該以前の献血:可能な限り過去に遡り、保管検体の個別NATが陰性と判定されるまで全ての輸血用血液、原料血漿を調査する。	14単位12単位38単位	9/19(HBV関連検査陰性)	10本の原料血漿、6本の赤血球濃厚液-LRを製造。原料血漿はすべて確保済み。	赤血球濃厚液-LRはすべて医療機関へ供給済み。	重篤	未回復		当該献血者検体(HBV陽性保管検体)と患者検体中のウイルスの塩基配列を比較したところ、当該保管検体はPOR下増幅しなかったため、塩基配列を決定することができなかった。そのため当該献血者のその後の献血再検体(2010年8月12日採血、HBV陽性保管検体)と患者検体とでPreS/S領域をさむP領域の前半部の1550bpの塩基配列を比較したところ、両者は全て一致した。献血者と患者のHBウイルスはGenotype Bで塩基配列からSubtypeはadwと推定した。
陽転事例																									
3-1100009	A-10000101	2011/2/16	2011/3/1	新鮮凍結血漿-LR(新鮮凍結人血漿) 照射赤血球濃厚液-LR(人赤血球濃厚液(放射線照射)) 赤血球濃厚液-LR(人赤血球濃厚液) 照射濃厚血小板-LR(人血小板濃厚液(放射線照射))	男	20	外傷・整形外科的疾患	B型肝炎	10/09-10	HBsAg(-)HBsAb(-)HBcAb(-)(10/09)	HBV-DNA(+)(11/01)	HBV-DNA(-)(-)HBcAb(-)(10/09)	HBV-DNA(+):(11/1)HBV-DNA(-)HBsAg(-)HBsAb(+)HBcAb(+)(11/2)	陰性(輸血前)陽性(輸血後)	保管検体22本全部についてHBV-DNA(-)		【献血者陽転化情報】 当該献血 10年2月3日 HBV関連検査陰性 保管検体 個別HBV-DNA(-) 次回献血 10年10月12日 HBV関連検査陰性 保管検体 個別HBV-DNA(+) 次々回献血 11年2月3日-スクリーニングNAT(HBV)陽性(陽転献血) 【製剤情報】 当該被疑薬(新鮮凍結血漿-LR)の同一採血番号製剤として、1本の赤血球濃厚液-LRを製造。赤血球濃厚液-LRは医療機関へ供給済み。また次回献血血液から、1本の原料血漿及び1本の赤血球濃厚液-LRが製造され、原料血漿は確保済みであり、赤血球製剤を輸血した患者は輸血前検査なし、輸血後HBV-DNA陰性、HBs抗原陰性、HBs抗体陽性、HBc抗体陽性であり、本剤との因果関係はないとの医師のコメントを得ている。	16単位4単位20単位35単位	4/22(2人はHBV関連検査陰性、1人はHBs抗体のみ陰性であり、当該献血時も同様であった。1人は次々回の献血(2011年2月3日採血)でスクリーニングNAT(HBV陽性であった。)	13本の原料血漿、1本の新鮮凍結血漿-LR、5本の赤血球濃厚液-LRを製造。原料血漿は全て確保済み。新鮮凍結血漿-LRは確保済み。	赤血球濃厚液-LRは全て医療機関へ供給済み。	非重篤	軽快		スクリーニングNAT陽転時検体(HBV陽性保管検体)と患者検体中のウイルスとでPreS/S領域を含むP領域の前半部の1560bpの塩基配列を比較したところ、両者は全て一致した。献血者と患者のHBウイルスはGenotypeCで塩基配列はSubtypeはadrと推定した。

日赤管理番号	識別番号	FAX受付日	報告受領日	販売名（一般名）	感染性別	年代	原疾患	感染症名	投与年月	投与前検査(年月)	投与後検査(年月)	日赤投与前検査	日赤投与後検査	受血者個別NAT	献血者個別NAT	併用血製剤等	備考	使用単位数	供血者再献血※	同一供血者製剤確保※	同一供血者製剤使用※	感染症等転帰	転帰	供血者発掘及の場合の供血者保管検体(抗原、抗体、NAT)(投与時点)	供血者発掘及の場合の供血者の検査値
3-1100033	A-1100014	2011/5/2	2011/5/2	新鮮凍結血漿-LR(新鮮凍結人血漿)	女	50	その他の疾患	B型肝炎	10/09	HBsAg(-)(10/06) HBsAb(-)(10/09)	HBsAg(+) HBsAb(-) HBcAb(-) HBsAg(+) HBsAb(-) HBcAb(-) (11/01) HBV-DNA(+) HBsAg(+) HBsAb(-) HBcAb(+) HBsAg(+) HBsAb(-) (11/04)	-	HBV-DNA(+) HBsAg(+) HBsAb(-) HBcAb(+) (11/04)	陽性（輸血後）	保管検体3本全部についてHBV-DNA(-)			6単位	2/30HBV調査検査陽性）	3本の赤血球濃厚液-LRを製造。	すべて医療機関へ供給済み。	軽快	軽快		
輸血後NATで陰性又は輸血前後で陽性																									
3-1100030	A-1100010	2011/4/13	2011/4/26	照射濃厚血小板-LR(人血小板濃厚液(放射線照射))	男	40	血液腫瘍	B型肝炎	11/02-03	HBsAb(-) HBsAb(-) HBcAb(-) (08/10) HBsAg(-) (11/01) HBsAb(-) HBcAb(-) (11/02)	HBV-DNA(-) HBsAg(-) HBsAb(-) HBcAb(-) (11/02)	HBV-DNA(-) HBsAg(-) HBsAb(+) HBcAb(-) (11/03)	陰性（輸血前）陰性（輸血後）	保管検体3本全部についてHBV-DNA(-)				30単位	1/30HBV調査検査陽性）	3本の原料血漿を製造。すべて確保済み。		非重篤	不明		
陽転未確認事例																									
3-1100032	A-1100013	2011/4/15	2011/4/27	照射赤血球濃厚液-LR(人赤血球濃厚液(放射線照射))	女	40	血液腫瘍	B型肝炎	10/11	-	HBsAg(-) HBsAb(-) HBcAb(-) (10/12) HBV-DNA(+) HBsAg(-) HBsAb(-) HBcAb(-) (11/4)	調査中	調査中	HBV関連検査実施予定	保管検体1本についてHBV-DNA(+)		当該輸血用血液の同一採血番号製剤は1本の原料血漿、確保済み。 【献血者陽転情報】 当該10年11月1日 HBV関連検査陰性(濃及調査) 個別HBV-DNA(+) 次回 11年5月17日スクリーニングNAT(HBV)陽性(陽転献血)	2単位	-	1本の原料血漿を製造、確保済み。	-	非重篤	未回復		

日赤管理番号	識別番号	FAX受付日	報告受領日	販売名（一般名）	感染性別	年代	原疾患	感染症名	投与年月	投与前検査(年月)	投与後検査(年月)	日赤投与前検査	日赤投与後検査	受血者個別NAT	献血者個別NAT	併用血製剤等	備考	使用単位数	供血者再献血※	同一供血者製剤確保※	同一供血者製剤使用※	感染症等転帰	転帰	供血者発掘及の場合の供血者保管検体(抗原、抗体、NAT)(投与時点)	供血者発掘及の場合の供血者の検査値
3-1100025	A-1100004	2011/4/4	2011/4/15	照射赤血球濃厚液-LR(人赤血球濃厚液(放射線照射))	女	60	血液腫瘍	B型肝炎	10/10—11/1	-	HBsAg(-) (10/11) HBsAg(-) (10/12) HBsAg(-) (10/12) HBsAg(-) (11/01) HBsAg(+) (11/02) HBsAg(+) (11/3) HBV-DNA(+) HBcAb(-) (11/3)	HBV-DNA(-) (10/10)	HBV-DNA(+) HBsAg(+) HBsAb(-) HBcAb(-) (11/03)	陰性（輸血前）陽性（輸血後）	保管検体4本全部についてHBV-DNA(-)			5単位	0/4	4本の原料血漿を製造。すべて確保済み。	-	非重篤	軽快		
3-1100027	A-1100007	2011/4/8	2011/4/21	新鮮凍結血漿-LR成分採血(新鮮凍結人血漿)照射濃厚血小板-LR(人血小板濃厚液(放射線照射))照射赤血球濃厚液-LR(人赤血球濃厚液(放射線照射))	女	70代	免疫系疾患	B型肝炎	10/12—11/02	HBsAg(-) (10/11)	HBV-DNA(+) (11/03)	-	HBV-DNA(+) HBsAg(-) HBsAb(-) HBcAb(+) (11/4)	陽性（輸血後）	保管検体14本(全部)についてHBV-DNA(-)		当該輸血血液は新鮮凍結血漿-LR成分採血のために同一採血番号製剤はない。 【献血者陽転情報】 当該 10年4月17日HBV関連検査適合(濃及調査) 個別HBV-NAT陰性 14回後 10年12月25日 スクリーニングNAT陽性(陽転献血) 当該献血から14回後陽転献血までに2本の新鮮凍結血漿-LR成分採血、10本の原料血漿を製造。いずれも全て確保済み。	80単位 120単位 20単位	21/34(HBV関連検査陰性)	17本の原料血漿を製造。すべて確保済み。	-	非重篤	不明		献血者検体(陽転献血時)HBV-DNA陽性)と患者検体とでPre S/S領域を含むP領域の前半部の1550bpを比較したところ、Genotypeの違いがあった。献血者のHBウイルスはGenotype Cで塩基配列からSubtypeはadrと推定した。患者のHBウイルスはGenotype Bで塩基配列からSubtypeはadwと推定した。
3-1100028	A-1100008	2011/4/11	2011/4/21	照射赤血球濃厚液-LR(人赤血球濃厚液(放射線照射))赤血球濃厚液-LR(人赤血球濃厚液)	男	50	胃・泌尿器系疾患	B型肝炎	10/01 10/03	HBV-DNA(-) HBsAg(-) HBsAb(+) HBcAb(-) (10/01)	HBV-DNA(-) HBsAg(-) HBsAb(-) HBcAb(-) (10/06) HBV-DNA(+) HBsAg(+) (11/04)	-	HBV-DNA(-) HBsAg(-) HBsAb(-) HBcAb(-) (10/06) HBV-DNA(+) HBsAg(-) HBsAb(-) HBcAb(-) (10/12) HBV-DNA(+) HBsAg(+) HBsAb(-) HBcAb(-) (11/04)	陽性（輸血後）	保管検体2本(全部)についてHBV-DNA(-)		当該輸血用血液の同一採血番号製剤として1本の新鮮凍結血漿-LRを製造。確保済み。 【献血者陽転情報】 当該 09年12月25日 HBV関連検査陰性(濃及調査) 個別NAT HBV-DNA陽性 次回 10年4月28日 スクリーニングNAT(HBV)陽性(陽転献血)	2単位 4単位	2/2(1人はHBV関連検査陰性、1人はHBs抗体のみ陽性であり当該献血時においても同様であった)	2本の原料血漿を製造。	原料血漿は全て使用済み。	重篤	不明		当該献血者検体(HBV陽性保管検体)と患者検体とのウイルスの塩基配列を検索したところ、当該保管検体は検体量不足のため、塩基配列を決定することができなかった。そのため、当該献血者の次回献血時検体(2010年4月28日採血、スクリーニングNAT(HBV)陽性検体)と患者検体とでPre S/S領域を含むP領域の前半部の1550bpの塩基配列を比較したところ、1箇所に相違があり、献血者検体の1箇所で塩基配列の欠失が見られた。欠失箇所の塩基の片側は患者検体の塩基と一致していた。その他の箇所は全て一致した。献血者と患者のHBウイルスはGenotype Cで塩基配列からSubtypeはadwと推定した。

日赤番号	識別番号	FAX受付日	報告受領日	販売名（一般名）	患者性別	年代	原疾患	感染症名	投与年月	投与前検査(年月)	投与後検査(年月)	目赤投与前検査	目赤投与後検査	受血者個別NAT	献血者個別NAT	併用血液製剤等	備考	使用単位数	供血者再献血※	同一供血者製剤確保※	同一供血者製剤使用※	感染症等転帰	転帰	供血者発覚及の場合の供血者保管検体(抗原、抗体、NAT)(投与時点)	供血者発覚及の場合の供血者の検査値
3-1100029	A-1100009	2011/4/12	2011/4/26	照射赤血球濃厚液-LR(人赤血球濃厚液(放射線照射))	男	30	消化器疾患	C型肝炎	08/08	HCVコアAg(-) HCV-Ab(-) (08/08)	HCV-RNA(+) (08/11)	HCV-RNA(-) (08/08)	HCV-RNA(+) HCV-Ab(+) (11/4)	陰性(輸血前) 陽性(輸血後)	保管検体2本全部についてHCV-RNA(-)			4単位	1/2(HCV関連検査陰性)	2本の原料血漿を製造。	原料血漿は全て使用済み。	重篤	未回復		
3-1100031	A-1100012	2011/4/14	2011/4/27	照射赤血球濃厚液-LR(人赤血球濃厚液(放射線照射)) 赤血球濃厚液-LR(人赤血球濃厚液)	男	30	腎・泌尿器系疾患 血液疾患 代謝疾患	C型肝炎	10/05-06	HCV-RNA(-) (10/05)	HCV-Ab(-) (10/06) HCV-RNA(+) (10/06) HCV-RNA(+)- (11/03) HCV-RNA(+) (11/03) HCV-Ab(+) (11/03)		HCV-RNA (+) HCV-Ab(+) (11/03)	陽性(輸血後)	保管検体8本についてHCV-RNA(-)			6単位 6単位	3/6(HCV関連検査陰性)	4本の原料血漿と2本の新鮮凍結血漿-LRを製造。	原料血漿は全て使用済み。 新鮮凍結血漿-LRは全て医療機関へ供給済み。	重篤	未回復		
3-1100034	A-1100015	2011/4/21	2011/5/2	照射赤血球濃厚液-LR(人赤血球濃厚液(放射線照射))	女	60	血液疾患 代謝疾患	C型肝炎	08/12 -10/01	HCV-Ab(-) (08/12)	HCV-Ab(+) (11/02) HCV-RNA(+) (11/04)	HCV-RNA (-) HCV-Ab (-) (09/12)	HCV-RNA (+) HCV-Ab(+) (11/04)	陰性(輸血前) 陽性(輸血後)	保管検体8本全部についてHCV-RNA(-)		本症例は被疑薬4本で言一組を入手し未完了報告を行ったが、その後の医療機関からの申し出により被疑薬2本追加(未完了報告(追加報告))には記載済み)。	8単位	2/8(HCV関連検査陰性)	4本の原料血漿と2本の新鮮凍結血漿-LRを製造。	原料血漿は全て使用済み。新鮮凍結血漿-LRは全て医療機関へ供給済み。	重篤	未回復		
輸血後NATで陰性又は輸血前後で陽性																									
(該当例なし)																									
臨転来確認事例																									
(該当例なし)																									
				輸血によるHIV感染報告例(疑い例を含む。)																					
(該当例なし)																									

日赤番号	識別番号	FAX受付日	報告受領日	販売名（一般名）	患者性別	年代	原疾患	感染症名	投与年月	投与前検査(年月)	投与後検査(年月)	目赤投与前検査	目赤投与後検査	受血者個別NAT	献血者個別NAT	併用血液製剤等	備考	使用単位数	供血者再献血※	同一供血者製剤確保※	同一供血者製剤使用※	感染症等転帰	転帰	供血者発覚及の場合の供血者保管検体(抗原、抗体、NAT)(投与時点)	供血者発覚及の場合の供血者の検査値
				輸血によるHCV感染報告例(疑い例を含む。)																					
供血者陽性事例																									
(該当例なし)																									
臨転事例																									
3-1100011	A-1000103	2011/2/22	2011/3/7	照射赤血球濃厚液-LR(人赤血球濃厚液(放射線照射))	男	60	消化器疾患	C型肝炎	10/12	HCV-Ab(-) (10/12)	HCV-RNA(+) HCV-Ab(+) (11/2)	HCV-RNA (-) HCV-Ab (-) (10/12)	HCV-RNA (+) HCV-Ab(+) (11/02)	陰性(輸血前) 陽性(輸血後)	保管検体3本全部についてHCV-RNA(-)			8単位	0/3	1本の原料血漿、2本の新鮮凍結血漿-LRを製造。原料血漿は全て確保済み。新鮮凍結血漿-LRは確保済み。		重篤	未回復		
3-1100016	A-1000107	2011/3/3	2011/3/17	照射濃厚血小板(人血小板濃厚液(放射線照射)) 照射濃厚血小板-LR(人血小板濃厚液(放射線照射)) 照射赤血球濃厚液-LR(人赤血球濃厚液(放射線照射))	男	70	血液腫瘍	C型肝炎	09/09-09 10/07-11/02 09/11-11/02	HCV-Ab(-) (08/08)	HCV-RNA(-) (09/10) HCV-Ag(-) (11/02) HCV-RNA(+) (11/02)		HCV-RNA(-) (09/10) HCV-RNA(+) (11/03)	陽性(輸血後)	保管検体28本全部について'HCV-RNA(-)			20単位 180単位 12単位		24本の原料血漿、2本の新鮮凍結血漿-LRを製造。原料血漿は20本確保済み。新鮮凍結血漿-LRは確保済み。	原料血漿4本は使用済み。	重篤	未回復		
3-1100019	A-1000110	2011/3/14	2011/3/25	照射赤血球濃厚液-LR(人赤血球濃厚液(放射線照射))	男	80	循環器疾患 消化器腫瘍	C型肝炎	10/10-12	HCV-Ab(-) (10/10)	HCV-Ab(+) (11/02) HCV-RNA(+) (11/03)	HCV-RNA (-) (10/10)	HCV-RNA (+) (11/03)	陰性(輸血前) 陽性(輸血後)	保管検体3本全部についてHCV-RNA(-)			10単位	1/5(HCV関連検査陰性)	4本の原料血漿、1本の新鮮凍結血漿-LRを製造。原料血漿はすべて確保済み。新鮮凍結血漿-LRは確保済み。		重篤	未回復		
3-1100023	A-1100002	2011/4/4	2011/4/15	赤血球濃厚液-LR(人赤血球濃厚液) 新鮮凍結血漿-LR(新鮮凍結人血漿)	男	10	先天性疾患	C型肝炎	11/01-02	HCVコアAg(-) HCV-Ab(-) (11/01)	HCV-Ab(+) (11/02) HCV-RNA(+) HCVコアAg(+) HCV-Ab(+) (11/03)	HCV-RNA(-) HCV-Ab(-) (10/8)	HCV-RNA(+) HCV-Ab(+) (11/3)	陰性(輸血前) 陽性(輸血後)	保管検体7本(全部)について'HCV-RNA(-)	ノイアート人血清アルブミンハプトグロビン		8単位 5単位	1/7(HCV関連検査陰性)	4本の原料血漿、3本の赤血球濃厚液-LRを製造。原料血漿は全て確保済み。	赤血球濃厚液-LRは全て医療機関へ供給済み。	重篤	未回復		

日赤番号	識別番号	FAX受付日	報告受領日	販売名(一般名)	患者性別	年代	原疾患	感染症名	投与年月	投与前検査(年月)	投与後検査(年月)	日赤投与前検査	日赤投与後検査	受血者個別NAT	献血者個別NAT	併用血液製剤等	備考	使用単位数	供血者再献血※	同一供血者製剤確保※	同一供血者製剤使用※	感染症等転帰	転帰	供血者発掘及の場合の供血者保管検体(抗原、抗体、NAT)(投与時点)	供血者発掘及の場合の供血者の検査値
3-1100005	A-10000090	2011/1/25	2011/2/8	照射赤血球濃厚液-LR(人赤血球濃厚液(放射線照射))	女	70	消化器疾患	細菌感染	11/01	-	輸血翌日13:30 BT 38.4℃、BP 100/54 16:30 BT 38.5℃ 翌々日13:30 発熱持続(38℃台) 患者血液培養よりKlebsiella pneumoniae検出。 輸血3日後5:00 BT 39.4℃ 10:00 BT 40.3℃、ICUへ。 採血にてWBC 19000まで上昇。感染focus検索を行ったが、明らかなfocusを認めず。 WBC 23500、CRP 19、エンドトキシン23、マキシピーム 1g x4日投与開始。免疫グロブリン 5g/日投与開始。 輸血4日後0:00 エンドトキシン吸着施行。 11:00 BT 38℃、BP 70～80/一台へ低下、SpO2 80%台半、P 150～160/min 患者血液培養より	同一採血番号の血液(2本)で細菌試験を実施、適合	-	-	-		被疑薬:採血12日目の照射赤血球濃厚液-LR(2本)	4単位		2本の原料血漿を製造、全て確保済み。	-	重篤	回復		
3-1100007	A-10000099	2011/2/6	2011/2/16	照射濃厚血小板-LR(人血小板濃厚液(放射線照射))	男	60	血液腫瘍	敗血症	11/01	-	6739 ℃ 院内にて実施の患者血培にてMorganella morganiiを検出	当該製剤のセグメントチューブ(2本)で細菌培養試験を実施。 試験結果:陰性	-	-	-		被疑薬:採血3日目の照射濃厚血小板-LR(2本)	20単位	-	2本の原料血漿を製造、全て確保済み。	-	重篤	未回復		

日赤番号	識別番号	FAX受付日	報告受領日	販売名(一般名)	患者性別	年代	原疾患	感染症名	投与年月	投与前検査(年月)	投与後検査(年月)	日赤投与前検査	日赤投与後検査	受血者個別NAT	献血者個別NAT	併用血液製剤等	備考	使用単位数	供血者再献血※	同一供血者製剤確保※	同一供血者製剤使用※	感染症等転帰	転帰	供血者発掘及の場合の供血者保管検体(抗原、抗体、NAT)(投与時点)	供血者発掘及の場合の供血者の検査値
				輸血による細菌等感染報告例(疑い例を含む。)																					
陽性等事例																									
3-1100004	A-10000095	2011/1/21	2011/2/1	照射赤血球濃厚液-LR(人赤血球濃厚液(放射線照射))	男	80	消化器疾患	細菌感染	11/01	-	10:30 赤血球製剤1本目輸血開始。 17:00 固作用なく輸血終了。 17:30 赤血球製剤2本目輸血開始。 18:00 悪寒、シバリング出現。 18:45 38℃台の発熱。SpO2低下し、O2 3L開始。 一時輸血中止、血圧低下、医療感等みられず抗菌薬開始しつつ輸血再開。 21:00 ロキソニン内服するが40.5℃まで体温上昇。輸血中止。 23:00 38.2℃、抗生剤ユナシン投与開始。 院内にて実施の静脈血培養よりCoagulase-negative staphylococci検出。	当該製剤及びセグメントチューブ(2本)で細菌培養試験を実施。陰性。 当該製剤2本のうち1本にて抗HLAクラスI抗体陽性。非溶血性固作用輸注検査実施。 抗血漿タンパク質抗体検査:陰性 血漿タンパク質欠損検査:欠損なし	-	-	-		被疑薬:採血10日目の照射赤血球濃厚液-LR(2本)	4単位	-	2本の原料血漿を製造、全て確保済み。	-	重篤	回復		

日赤番号	識別番号	FAX受付日	報告受領日	販売名(一般名)	患者性別	年代	原疾患	感染症名	投与年月	投与前検査(年月)	投与後検査(年月)	日赤投与前検査	日赤投与後検査	受血者個別NAT	献血者個別NAT	併用血液製剤等	備考	使用単位数	供血者再献血※	同一供血者製剤確保※	同一供血者製剤使用※	感染症等転帰	転帰	供血者発還及の場合の供血者保管検体(抗原、抗体、NAT)(投与時点)	供血者発還及の場合の供血者の検査値
3-110000 8	A-1000 0100	2011/2/8	2011/2/22	照射赤血球濃厚液ーLR(人赤血球濃厚液(放射線照射))	男	70	血液腫瘍	細菌感染	11/02	BT 36.8℃、BP 130/72、HR 62、SpO2 97%	輸血開始20分後 BT 37.0℃、BP 128/76、HR 70、SpO2 98% 1時間後、悪寒・戦慄出現、BT 41.1℃、BP 140/80、HR 98、SpO2は83%、輸血中止 2時間半後 BT 40.1℃、BP 120/70、HR 102、SpO2は98%、O2リザーバーマスク 15L/min 10時間後 BT 36.8℃、BP 102/60、SpO2は100%、O2カヌラ 1L/min 翌日発熱なし。 院内にて輸血直後に実施の患者血液培養にてPseudomonas aeruginosaを同定した。	投与中止の当該製剤(1本)で細菌培養試験を実施、試験結果：陰性 非溶血性副作用関連検査実施 抗血漿タンパク質抗体検査：陰性 血漿タンパク質欠損検査：欠損なし 抗白血球抗体検査：陽性	-	-	-		被疑薬：採血11日目の照射赤血球濃厚液-LR(1本)	2単位	-	1本の原料血漿を製造、確保済み。	-	重篤	回復		
3-110001 8	A-1000 0109	2011/3/14	2011/3/24	照射赤血球濃厚液ーLR(人赤血球濃厚液(放射線照射))	男	80	血液腫瘍	細菌感染	11/03	BT 36.5℃	2本目輸血終了後、BT 37.6℃、悪寒あり 1時間15分後、BT 40℃ 患者血液培養は陰性。	同一採血番号の血漿(2本)で無菌試験を実施、適合	-	-	-		採血10日目の照射赤血球濃厚	4単位	-	2本の原料血漿を製造、全て確保済み。	-	非重篤	回復		
3-110002 6	A-1100 0006	2011/4/7	2011/4/21	濃厚血小板-LR(人血小板濃厚液)	女	70	血液疾患	細菌感染	11/4	-	輸血開始 BT38.5℃ BP120/61 1時間10分後 シバリング出現。輸血中止 BT37.7℃ BP79/68 2時間40分後 BT38.4℃ 3時間40分後 BT38.3℃ 院内にて患者血液培養実施。陰性	投与中止の当該製剤(1本)で細菌培養試験を実施、陰性。 非溶血性副作用関連検査実施。 抗血漿タンパク質抗体検査：陰性 血漿タンパク質欠損検査：欠損なし	-	-	-			10単位	-	1本の原料血漿を製造。原料血漿は確保済み。	-	非重篤	回復		

平成 23 年 6 月 27 日開催
薬事・食品衛生審議会
運営委員会提出資料

別紙

日本赤十字社

試行的 HEV20 プール NAT 実施状況について

(輸血後 HEV 感染の予防対策)

1. 試行的 HEV20 プール NAT 実施状況

北海道赤十字血液センター管内
調査期間：平成 17 年 1 月 1 日～平成 23 年 4 月 30 日

	献血者数	HEV-RNA 陽性	陽性率
H17. 1～H18. 2*1	341, 174	45	1／7, 582
H18. 3～H23. 4*2	1, 404, 197	166	1／8, 459
合計	1, 745, 371	211	1／8, 272

*1 北海道センターにて NAT 実施（ALT 高値、検査不合格検体も含む）
*2 血漿分画センターにて NAT 実施（ALT 高値、検査不合格検体は除く）

2. HEV-RNA 陽性献血者の内訳
別添

No.	採血日	年齢	性別	ALT (IU/L)	HEV抗体		HEV RNA	問診該当 ※1	喫食歴調査		遡及対象供給製剤	受血者情報
					IgM	IgG			肉の種類	食べ方		
31	2006/01/02	22	F	12	−	−	+	有	ウシレバー、ウシ精肉	十分加熱	無	
32	2006/01/06	68	M	23	−	−	+	無	ウシレバー、ブタホルモン、ヒツジ精肉	半生	無	
33	2006/01/13	36	M	42	−	−	+	無	ウマ精肉、不明レバー ウシ精肉、ヒツジ精肉	生 半生	無	
34	2006/01/16	53	M	238	+	+	+	有	ウシレバー、ウシホルモン	十分加熱	無	
35	2006/01/13	31	M	43	−	−	+	有	不明レバー ブタ精肉、ヒツジ精肉	半生 十分加熱	無	
36	2006/01/17	48	M	25	−	−	+	無	回答なし		無	
37	2006/01/25	52	M	25	−	−	+	無	不明レバー、ヒツジ精肉	十分加熱	有	輸血後69日現在、HEVマーカーの陽転は見られず追跡調査終了
38	2006/01/30	39	F	22	−	−	+	無	回答なし		無	
39	2006/01/30	25	M	32	−	−	+	有	ウシ精肉、ウシホルモン、ブタ精肉	十分加熱	無	
40	2006/02/02	39	F	35	−	+	+	有	ウシレバー ウシレバー	生 半生	無	
41	2006/02/07	57	M	13	−	−	+	無	不明	不明	無	
42	2006/02/07	40	F	172	+	+	+	無	ウシ精肉	十分加熱	無	
43	2006/02/17	39	M	28	−	−	+	無	ブタホルモン、ブタレバー、ブタガツ、ヒツジ精肉 イノシシ精肉、ブタ精肉	半生 十分加熱	無	
44	2006/02/20	58	M	22	−	−	+	無	ヒツジ精肉	十分加熱	無	
45	2006/02/21	45	M	30	−	−	+	無	ウシ精肉 ブタ精肉、ブタレバー、ヒツジ精肉	半生 十分加熱	無	
46	2006/03/01	48	F	15	−	−	+	無	回答なし		無	
47	2006/03/01	50	F	29	−	−	+	無	回答なし		無	
48	2006/03/02	54	M	47	+	+	+	無	ウシ・ブタ(精肉、レバー、ホルモン)、ヒツジ精肉	十分加熱	無	
49	2006/03/27	40	F	12	−	−	+	無	回答なし		無	
50	2006/04/01	31	F	16	−	−	+		ヒツジ精肉	半生	無	
51	2006/04/04	30	F	14	−	−	+		ブタ精肉、不明レバー	十分加熱	無	
52	2006/04/12	38	M	45	+	+	+		ブタレバー、ウシ精肉、ブタ精肉、ヒツジ精肉	十分加熱	無	
53	2006/04/18	21	M	26	−	−	+		ウシ精肉、ウシホルモン ウシ精肉、ウシホルモン	半生 十分加熱	無	
54	2006/04/22	28	M	14	+	+	+		回答なし		無	
55	2006/04/26	46	M	19	−	−	+		ブタレバー	半生	無	
56	2006/05/18	82	M	27	−	−	+		ヒツジレバー	十分加熱	無	
57	2006/07/07	17	M	33	−	−	+		回答なし		無	
58	2006/07/11	34	F	10	−	−	+		回答なし		無	
59	2006/07/12	21	F	27	−	−	+		回答なし		無	
60	2006/07/22	49	M	46	+	−	+		ウシ精肉、ブタ精肉、ブタホルモン、ブタレバー	十分加熱	無	

別添

2. HEV-RNA陽性者の内訳

調査期間：2005年1月1日～2011年4月30日

No.	採血日	年齢	性別	ALT (IU/L)	HEV抗体		HEV RNA	問診該当 ※1	喫食歴調査		遡及対象供給製剤	受血者情報
					IgM	IgG			肉の種類	食べ方		
1	2005/01/04	32	M	57	−	−	+	無	不明レバー	生	無	
2	2005/02/07	38	F	11	−	−	+	無	ブタレバー	生	無	
3	2005/02/13	41	M	103	−	−	+	無	回答なし		無	
4	2005/03/25	65	F	17	−	−	+	無	回答なし		無	
5	2005/03/27	26	M	38	−	−	+	有	不明レバー(問診時)	生	有	赤血球製剤破損のため院内廃棄
6	2005/04/10	54	F	20	−	−	+	無	ウシ精肉	半生	無	
7	2005/04/15	59	F	16	−	−	+	無	ブタホルモン、シカ精肉	十分加熱	無	
8	2005/04/15	35	F	16	−	−	+	無	シカ精肉、ウシ精肉 ウシレバー、ヒツジ精肉	半生 十分加熱	無	
9	2005/04/20	25	M	24	+	+	+	無	ウシレバー、ウシ精肉 ウシホルモン、ヒツジ精肉	半生 十分加熱	有	感染なし
10	2005/04/28	22	M	44	−	−	+	無	回答なし		無	
11	2005/06/07	42	M	24	+	+	+	無	ウシ精肉 ウシホルモン、ブタ精肉、ヒツジ精肉	半生 十分加熱	有	原疾患により死亡
12	2005/06/22	51	M	52	−	−	+	無	回答なし		無	
13	2005/07/03	58	M	219	+	+	+	無	不明レバー、ブタ精肉	十分加熱	無	
14	2005/07/05	22	M	23	+	−	+	無	回答なし		無	
15	2005/07/05	38	M	15	−	−	+	無	ブタホルモン、ウシ精肉、ブタ精肉	半生	無	
16	2005/07/13	24	M	19	−	−	+	無	ウシレバー	生	有	原疾患により死亡
17	2005/08/02	33	M	49	−	−	+	無	ウシ精肉 ヒツジ精肉	生 半生	無	
18	2005/09/01	29	F	100	+	+	+	無	ウシホルモン、ヒツジ精肉 ウシレバー、ウシ精肉、ブタ精肉	半生 十分加熱	無	
19	2005/09/20	42	M	31	−	−	+	無	ブタホルモン、不明レバー、ヒツジ精肉	十分加熱	有	HEV感染(H17.11.1 運営委員会報告済み)
20	2005/09/27	20	F	10	−	−	+	無	ウシ精肉、ブタホルモン、ヒツジ精肉	十分加熱	無	
21	2005/10/21	41	M	12	−	−	+	無	回答なし		無	
22	2005/10/25	44	F	38	+	+	+	無	ウシ精肉、ブタ精肉	十分加熱	無	
23	2005/11/07	30	F	21	−	−	+	無	ブタホルモン、ウシ精肉、ヒツジ精肉 ブタホルモン、ウシ精肉、ブタ精肉、ヒツジ精肉	半生 十分加熱	無	
24	2005/11/07	31	F	12	+	+	+	有	ブタレバー、ブタホルモン、ウシ精肉	十分加熱	無	
25	2005/11/20	28	M	47	+	+	+	有	ウシレバー、ウマ精肉 ブタホルモン、ウシ精肉、ブタ精肉	生 十分加熱	無	
26	2005/11/29	35	F	333	+	+	+	有	回答なし		無	
27	2005/12/13	42	M	30	−	−	+	有	ウシ精肉、ヒツジ精肉 不明レバー、ブタ精肉	半生 十分加熱	有	原疾患により死亡
28	2005/12/13	30	M	11	−	−	+	有	不明レバー	十分加熱	有	HEV感染(H18.01.20 運営委員会報告済み)
29	2005/12/22	62	F	14	−	−	+	無	回答なし		無	
30	2005/12/27	42	F	14	−	−	+	無	回答なし		無	

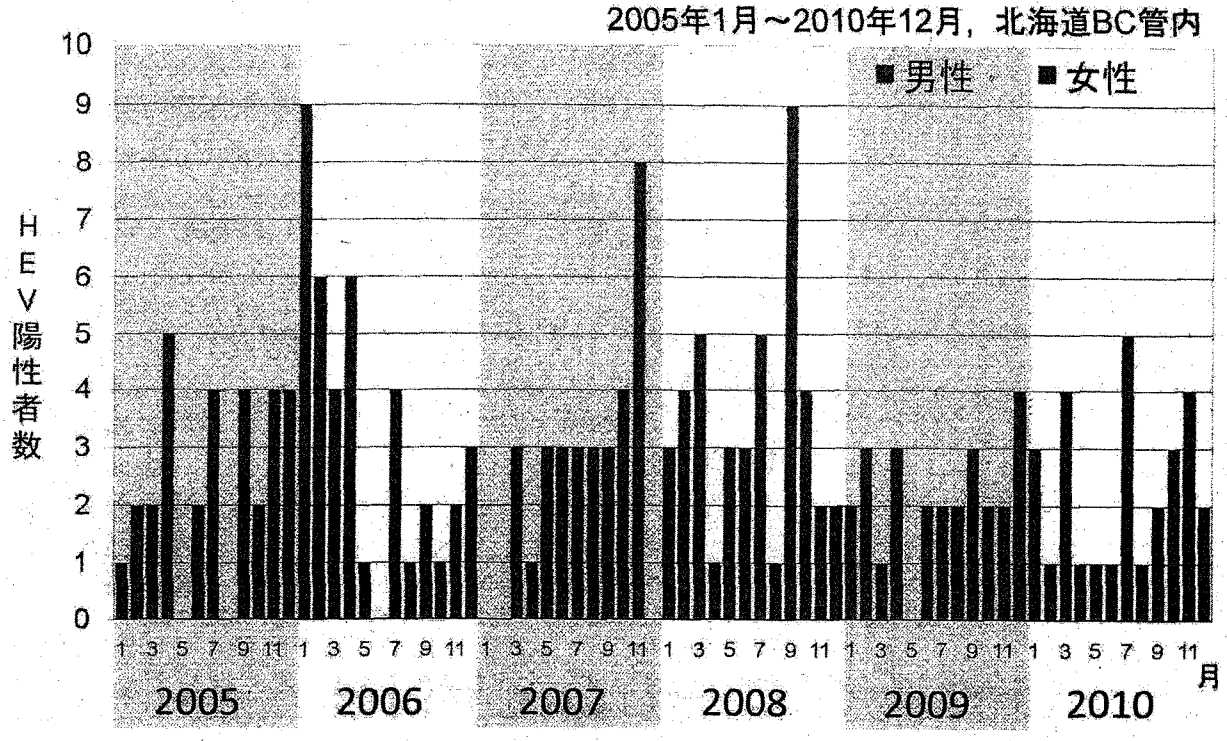
No.	採血日	年齢	性別	ALT (IU/L)	HEV抗体		HEV RNA	問診該当 ※1	喫食歴調査		遡及対象供給製剤	受血者情報
					IgM	IgG			肉の種類	食べ方		
91	2007/10/09	35	M	19	−	−	+		ブタ精肉	十分加熱	無	
92	2007/10/16	30	M	31	−	−	+		ウシ精肉、ブタ精肉、ヒツジ精肉	十分加熱	無	
93	2007/11/16	24	M	5	−	−	+		不明		無	
94	2007/11/16	54	M	22	−	+	+		ブタホルモン、ブタレバー	十分加熱	無	
95	2007/11/16	45	M	47	−	−	+		ブタ精肉 ブタレバー	十分加熱 半生	無	
96	2007/11/19	58	M	13	−	−	+		レバー、ホルモン	不明	無	
97	2007/11/19	24	M	46	−	−	+		不明		無	
98	2007/11/24	36	M	25	−	−	+		不明		無	
99	2007/11/29	42	M	21	−	+	+		不明		無	
100	2007/11/30	31	M	42	+	+	+		レバー	不明	無	
101	2008/01/08	35	M	36	−	−	+		ウシ精肉、ブタ精肉	十分加熱	無	
102	2008/01/17	48	F	13	+	+	+		ブタホルモン、シカ精肉 ウシ精肉	十分加熱 半生	無	
103	2008/01/29	57	M	22	−	−	+		ブタレバー、ブタホルモン	十分加熱	無	
104	2008/02/04	31	M	47	+	+	+		不明		無	
105	2008/02/08	57	M	20	−	−	+		ブタホルモン	十分加熱	無	
106	2008/02/13	42	M	35	−	−	+		不明レバー	十分加熱	無	
107	2008/02/13	60	M	37	+	+	+		不明		無	
108	2008/03/11	30	M	21	−	−	+		不明		無	
109	2008/03/25	34	F	26	−	−	+		喫食歴なし		無	
110	2008/03/26	32	M	41	+	+	+		ブタ精肉、ウシ精肉	十分加熱	無	
111	2008/03/29	54	M	28	−	−	+		ブタ精肉	十分加熱	無	
112	2008/03/30	19	F	9	−	−	+		不明レバー	十分加熱	無	
113	2008/04/16	48	M	13	−	−	+		不明		無	
114	2008/05/12	33	M	12	−	−	+		ブタ精肉、ブタホルモン	半生	無	
115	2008/05/26	39	F	29	−	−	+		不明		無	
116	2008/05/28	47	M	46	−	−	+		ブタホルモン	十分加熱	無	
117	2008/06/04	43	M	38	+	+	+		ウシレバー ウシホルモン、ウシ、ブタ、ヒツジ精肉	生 十分加熱	無	
118	2008/06/07	42	M	11	−	−	+		ウシレバー ブタ精肉	生 十分加熱	無	
119	2008/06/23	48	M	17	−	−	+		ウシ、ブタ、ヒツジ精肉	半生	無	
120	2008/07/10	39	M	32	−	−	+		ウシ、ブタ、ヒツジ精肉 ウシ、ブタ、ヒツジ精肉	半生 十分加熱	無	

No.	採血日	年齢	性別	ALT (IU/L)	HEV抗体		HEV RNA	問診該当 ※1	喫食歴調査		遡及対象供給製剤	受血者情報
					IgM	IgG			肉の種類	食べ方		
61	2006/08/01	82	M	18	−	−	+		ブタホルモン、ウシ精肉、ブタ精肉、ヒツジ精肉	十分加熱	無	
62	2006/09/06	44	F	14	−	−	+		喫食歴なし		無	
63	2006/09/29	66	M	15	−	−	+		ブタ精肉、ヒツジ精肉	十分加熱	無	
64	2006/10/21	29	M	22	−	−	+		不明		無	
65	2006/11/19	48	M	59	−	−	+		ウシ精肉、ブタ精肉	十分加熱	無	
66	2006/11/23	54	M	18	−	−	+		回答なし		無	
67	2006/12/01	43	M	55	−	+	+		ブタ精肉	十分加熱	無	
68	2006/12/04	60	M	46	+	+	+		ウシ精肉	十分加熱	無	
69	2006/12/04	47	M	40	+	+	+		ウシ精肉、ウシホルモン	十分加熱	無	
70	2007/03/01	33	M	41	−	−	+		ウシレバー	生	無	
71	2007/03/15	42	M	32	−	+	+		ブタレバー、ブタホルモン	半生	無	
72	2007/03/27	55	M	30	−	−	+		不明レバー	十分加熱	無	
73	2007/04/07	22	F	9	−	−	+		ユッケ ウシホルモン、ヒツジホルモン	生 十分加熱	無	
74	2007/05/16	47	F	15	−	−	+		ヒツジ精肉、ブタホルモン	十分加熱	無	
75	2007/05/18	40	F	27	+	+	+		ブタ生ハム(自家製)	半生	無	
76	2007/05/30	33	M	26	−	+	+		ヒツジ精肉、ブタホルモン	十分加熱	無	
77	2007/06/22	38	M	20	−	−	+		ウシ精肉、ヒツジ精肉	十分加熱	無	
78	2007/06/25	45	M	37	+	+	+		ブタ精肉 ヒツジ精肉	十分加熱 半生	無	
79	2007/06/27	37	M	18	−	−	+		ブタ精肉	十分加熱	無	
80	2007/07/24	57	M	24	−	−	+		喫食歴なし		無	
81	2007/07/29	37	M	48	−	−	+		不明レバー、ブタホルモン 不明レバー、ブタホルモン	十分加熱 半生	無	
82	2007/07/31	48	M	30	−	−	+		ブタ精肉、ブタホルモン、ブタレバー	十分加熱	無	
83	2007/08/01	48	M	33	−	−	+		ブタ精肉 ウシ精肉、ヒツジ精肉	十分加熱 半生	無	
84	2007/08/04	53	M	28	−	−	+		ヒツジ精肉 ヒツジ精肉	十分加熱 半生	無	
85	2007/08/26	50	M	60	−	−	+		ヒツジ精肉 ウシ精肉	十分加熱 生	無	
86	2007/09/05	41	M	29	−	−	+		喫食歴なし		無	
87	2007/09/18	41	M	23	−	−	+		ウシ精肉、ブタ精肉、ウシホルモン、ブタホルモン	半生	無	
88	2007/09/21	57	M	19	−	−	+		ブタホルモン	十分加熱	無	
89	2007/10/03	59	M	39	−	−	+		ブタレバー、ブタ精肉	十分加熱	無	
90	2007/10/03	19	M	40	−	−	+		喫食歴なし		無	

No.	採血日	年齢	性別	ALT (IU/L)	HEV抗体		HEV RNA	問診該当 ※1	喫食歴調査		遡及対象供給製剤	受血者情報
					IgM	IgG			肉の種類	食べ方		
151	2009/04/27	45	M	60	−	−	+		不明		無	
152	2009/06/04	65	F	24	−	−	+		不明ホルモン	不明	無	
153	2009/06/09	63	M	26	−	−	+		ブタ肉 シカ精肉	十分加熱 生	無	
154	2009/07/01	47	M	40	+	+	+		ウシ精肉、ブタホルモン	十分加熱	無	
155	2009/07/23	26	F	11	−	−	+		ブタホルモン ウシ精肉	十分加熱 生	無	
156	2009/08/01	40	M	26	−	−	+		ウシ精肉、ブタホルモン	十分加熱	無	
157	2009/08/14	41	M	14	−	−	+		不明		無	
158	2009/09/04	43	M	45	−	−	+		ウマ精肉	生	無	
159	2009/09/09	54	F	14	−	−	+		ウシレバー	半生	無	
160	2009/09/09	51	M	19	−	−	+		ブタ精肉	十分加熱	無	
161	2009/10/12	27	M	41	−	−	+		不明		無	
162	2009/10/27	52	M	29	−	−	+		ブタ精肉、ブタレバー	十分加熱	無	
163	2009/11/17	53	M	19	−	−	+		ウシ・ブタ精肉、ウシレバー	半生	無	
164	2009/11/26	26	M	29	−	−	+		不明		無	
165	2009/12/13	37	M	35	−	−	+		ウシレバー	生	無	
166	2009/12/17	37	M	15	−	−	+		ウシ精肉、ブタレバー、ウシ・ブタホルモン	十分加熱	無	
167	2009/12/24	64	M	40	−	−	+		ヒツジ精肉	不明	無	
168	2009/12/28	34	F	18	−	−	+		不明		無	
169	2010/01/17	41	M	25	−	−	+		ウシレバー	生	無	
170	2010/01/19	34	M	38	−	−	+		ブタホルモン	十分加熱	無	
171	2010/01/21	39	M	24	−	−	+		ブタレバー、ウシ精肉、ブタ精肉	十分加熱	無	
172	2010/02/26	26	F	15	−	−	+		ウシ精肉	十分加熱	無	
173	2010/03/04	50	M	21	−	−	+		シカ精肉	半生	無	
174	2010/03/17	47	M	18	−	−	+		ブタ精肉	十分加熱	無	
175	2010/03/17	28	M	11	−	−	+		不明		無	
176	2010/03/25	60	M	38	−	−	+		ブタ精肉	十分加熱	無	
177	2010/04/17	54	M	37	−	−	+		ウシレバー、ブタホルモン	十分加熱	無	
178	2010/05/19	36	F	14	−	−	+		不明ホルモン		無	
179	2010/06/19	35	M	31	−	−	+		不明ホルモン		無	
180	2010/07/13	25	M	17	−	−	+		回答なし		無	

No.	採血日	年齢	性別	ALT (IU/L)	HEV抗体		HEV RNA	問診該当 ※1	喫食歴調査		遡及対象供給製剤	受血者情報
					IgM	IgG			肉の種類	食べ方		
121	2008/07/11	39	M	28	−	−	+		不明		無	
122	2008/07/26	34	M	35	−	−	+		ウシ精肉、ブタ精肉	十分加熱	無	
123	2008/07/27	38	M	45	−	−	+		不明		無	
124	2008/07/30	24	M	10	−	−	+		不明		無	
125	2008/08/20	19	M	17	+	−	+		不明		無	
126	2008/09/03	30	M	28	−	−	+		不明		無	
127	2008/09/08	35	M	16	−	−	+		不明		無	
128	2008/09/09	23	F	24	−	−	+		ブタ、ヒツジ精肉	十分加熱	無	
129	2008/09/16	33	F	16	+	+	+		不明		無	
130	2008/09/16	58	M	21	−	−	+		不明		無	
131	2008/09/17	62	M	37	−	−	+		ウシレバー、ブタレバー	十分加熱	無	
132	2008/09/23	42	M	36	−	−	+		ブタ精肉、ブタレバー	十分加熱	無	
133	2008/09/25	35	M	16	−	−	+		不明		無	
134	2008/09/27	30	M	22	−	−	+		不明		無	
135	2008/10/10	50	M	31	−	−	+		ウシ、ブタ、ヒツジ精肉	不明	無	
136	2008/10/11	39	F	15	−	−	+		ウマ精肉	生	無	
137	2008/10/14	56	M	13	−	−	+		不明レバー	生	無	
138	2008/10/18	38	F	23	−	−	+		不明		無	
139	2008/11/03	37	M	22	−	−	+		ウシホルモン、ブタ精肉	半生	無	
140	2008/11/11	41	F	11	−	−	+		不明		無	
141	2008/12/05	52	M	18	−	−	+		ブタレバー	十分加熱	無	
142	2008/12/20	47	M	22	−	−	+		ウシ、ブタ、ヒツジ精肉	十分加熱	無	
143	2009/01/13	50	M	27	−	−	+		ウシ・ブタ(精肉、レバー、ホルモン)	十分加熱	無	
144	2009/01/27	55	M	17	−	−	+		不明		無	
145	2009/02/11	37	M	28	−	−	+		不明ホルモン	十分加熱	無	
146	2009/02/16	59	F	23	−	−	+		ブタレバー	不明	無	
147	2009/02/23	20	F	42	−	+	+		ウシ、ブタ精肉	半生	無	
148	2009/03/11	29	M	49	−	−	+		ブタレバー、ホルモン	十分加熱	無	
149	2009/04/16	35	F	29	−	−	+		ウシレバー ウシ・ブタホルモン	生 半生	無	
150	2009/04/24	38	F	42	−	−	+		不明ホルモン	不明	無	

HEV NAT陽性献血者の月別発生数（例）



北海道赤十字血液センター

No.	採血日	年齢	性別	ALT (IU/L)	HEV抗体 IgM	HEV抗体 IgG	HEV RNA	問診該当 ※1	喫食歴調査 肉の種類	喫食歴調査 食べ方	遡及対象供給製剤	受血者情報
181	2010/07/14	49	M	28	-	-	+		不明		無	
182	2010/07/19	49	M	21	-	-	+		なし		無	
183	2010/07/20	58	M	30	-	+	+		不明ホルモン、レバー	不明	無	
184	2010/07/29	44	M	17	-	-	+		ブタ精肉・レバー、ウシ・ヒツジ精肉	半生	無	
185	2010/08/01	50	M	14	-	-	+		ウシ精肉・ホルモン、ヒツジ精肉	十分加熱	無	
186	2010/09/19	60	M	23	-	-	+		不明レバー・ホルモン	半生	無	
187	2010/09/19	42	M	30	+	+	+		ウシ・ブタホルモン・レバー	十分加熱	無	
188	2010/10/02	26	M	45	-	-	+		ウシレバー	生	無	
189	2010/10/11	43	M	25	-	-	+		ブタレバー・ホルモン	不明	無	
190	2010/10/27	40	M	29	-	-	+		ブタレバー、ウシホルモン	半生	無	
191	2010/11/08	57	M	19	-	-	+		ブタホルモン	十分加熱	無	
192	2010/11/10	44	M	15	-	-	+		不明ホルモン	半生	無	
193	2010/11/19	38	M	33	-	-	+		ウシレバー	生	無	
194	2010/11/22	57	F	9	-	-	+		なし		無	
195	2010/12/03	40	M	41	-	-	+		なし		無	
196	2010/12/21	25	F	14	-	-	+		不明		無	
197	2011/01/21	44	M	12	-	-	+		ブタレバー、ホルモン、精肉	半生 十分加熱	無	
198	2011/01/27	58	F	17	-	-	+		不明		無	
199	2011/02/01	38	M	32	-	-	+		ブタレバー	半生	無	
200	2011/02/10	35	M	35	-	-	+		ウシ、ブタレバー、精肉	十分加熱	無	
201	2011/02/23	22	F	24	+	+	+		不明		無	
202	2011/03/13	47	M	23	-	-	+		不明ホルモン	不明	無	
203	2011/03/18	22	F	11	-	-	+		ウシ、ヒツジ精肉	半生 十分加熱	無	
204	2011/03/22	36	M	16	-	-	+		不明レバー	生	無	
205	2011/03/31	36	M	41	-	-	+		不明		無	
206	2011/04/05	20	F	15	-	-	+		不明ホルモン	不明	無	
207	2011/04/08	47	M	15	-	-	+		不明	不明	無	
208	2011/04/14	41	M	36	-	-	+		不明		無	
209	2011/04/16	25	M	22	-	-	+		不明レバー	不明	無	
210	2011/04/18	36	M	30	-	-	+		無	不明	無	
211	2011/04/28	43	M	27	+	+	+		ウシ精肉	半生	無	

※1：問診聴取項目内容
05年1月1日～05年10月31日：「過去3ヶ月以内にブタ、シカ、イノシシあるいは動物種不明の生肉、生レバーの喫食歴」
05年11月1日～06年03月31日：「過去3ヶ月以内に生肉（半生も含む）、レバー、ホルモン（動物種、焼き方を問わず）の喫食歴」、なお本調査は08年03月31日をもって終了

事　務　連　絡
平成２３年５月１７日

日本赤十字社血液事業本部　御中

薬事・食品衛生審議会血液事業部会事務局
厚生労働省医薬食品局血液対策課

血液製剤に関する報告事項について

血液事業の推進に御努力いただき、厚く御礼申し上げます。

さて、標記につきましては、平成２３年２月２日付け血安第４２号にて貴社から報告を頂いたところですが、平成２３年６月２７日（月）に平成２３年度第１回血液事業部会運営委員会が開催されますので、下記の事項について資料を作成いただき、平成２３年６月１日（水）までに当事務局あて御提出いただきますようお願いします。記の１２については、平成２３年２月１８日開催平成２２年度第４回血液事業部会運営委員会提出資料を更新のうえ、再度御提出ください。

なお、資料の作成に当たっては、供血者、患者及び医療機関の名称並びにこれらの所在地又はこれらの事項が特定できる情報を記載しないよう、個人情報及び法人情報の保護に特段の御配慮をお願いします。

記

１．平成１５年９月５日付けで報告された輸血用血液製剤でＨＩＶの感染が疑われる事例について、残る２人の供血者のその後の検査結果。来訪がなければ、その旨。

２．平成１６年３月２２日付けで報告された輸血用血液製剤でＨＢＶ（Ｂ型肝炎ウイルス）感染が疑われる事例について、残る５人の供血者のその後の検査結果。来訪がなければ、その旨。

３．平成１６年１１月２６日付けで報告された輸血用血液製剤でＨＢＶ（Ｂ型肝炎ウイルス）感染が疑われる事例について、残る７人の供血者のその後の検査結果。来訪がなければ、その旨。

４．平成１７年１月１２日付けで報告された輸血用血液製剤でＨＢＶ（Ｂ型肝炎ウイルス）感染が疑われる事例について、残る４人の供血者のその後の検

HEV RNAスクリーニング（例）

調査期間	2005.1－2010.12
検査総数	1,652,006
陽性者数	196
陽性率	0.012%（1/8,429）
年齢	17–68
男：女	147:49（75%:25%）
Genotype（G3:G4）	181:12（94%:6%）
Anti-HEV抗体	
IgM(−)/IgG(−)	158（81%）
IgM(+)/IgG(−)	3（ 2%）
IgM(+)/IgG(+)	26（13%）
IgM(−)/IgG(+)	9（ 5%）
動物内臓肉喫食歴*1	99/140（71%）
肝機能異常（ALT>45 IU/L）	35/60（58%）
G3：G4	31/55（56%）：4/5（80%）

*1：一般献血者の献血前動物内臓肉喫食歴　28%

北海道赤十字血液センター
（一部改変）

査結果。来訪がなければ、その旨。

5．平成１７年２月４日付けで報告された輸血用血液製剤でＨＢＶ（Ｂ型肝炎ウイルス）感染が疑われる事例について、残る１人の供血者のその後の検査結果。来訪がなければ、その旨。

6．平成１７年６月２３日付けで報告された輸血用血液製剤でＨＢＶ（Ｂ型肝炎ウイルス）感染が疑われる事例について、残る２人の供血者のその後の検査結果。来訪がなければ、その旨。

7．平成１８年４月７日付けで報告された輸血用血液製剤でＨＢＶ（Ｂ型肝炎ウイルス）感染が疑われる事例について、残る７人の供血者のその後の検査結果。来訪がなければ、その旨。

8．平成１８年６月５日付けで報告された輸血用血液製剤でＨＢＶ（Ｂ型肝炎ウイルス）感染が疑われる事例について、残る１人の供血者のその後の検査結果。来訪がなければ、その旨。

9．平成１９年２月２０日付けで報告された輸血用血液製剤でＨＢＶ（Ｂ型肝炎ウイルス）感染が疑われる事例について、残る１人の供血者のその後の検査結果。来訪がなければ、その旨。

１０．平成２１年１１月２０日付けで報告された輸血用血液製剤でＨＢＶ（Ｂ型肝炎ウイルス）感染が疑われる事例について、残る３人の供血者のその後の検査結果。来訪がなければ、その旨。

１１．平成１８年２月１５日報告、３月８日付けで追加報告された輸血用血液製剤でＨＣＶ（Ｃ型肝炎ウイルス）感染が疑われる事例について、残る３人の供血者のその後の検査結果。来訪がなければ、その旨。

１２．試行的ＨＥＶ２０プールＮＡＴについて、その後の調査実施状況。

血安第１９０号
平成２３年６月１日

厚生労働省医薬食品局血液対策課長 様

日本赤十字社
血液事業本部長

血液製剤に関する報告事項について（回答）

平成23年5月17日付事務連絡によりご依頼のありました標記の件については、下記のとおり資料を作成しましたので報告いたします。

記

1．平成15年9月5日付けで報告された輸血用血液製剤でＨＩＶの感染が疑われる事例について、残る2人のその後の来訪なし。(8名中6名が来所、検査は全て陰性)

2．平成16年3月22日付けで報告された輸血用血液製剤でＨＢＶ（Ｂ型肝炎ウイルス）感染が疑われる事例について、残る5人のその後の来訪なし。(37名中32名が来所、検査は全て陰性)

3．平成16年11月26日付けで報告された輸血用血液製剤でＨＢＶ（Ｂ型肝炎ウイルス）感染が疑われる事例について、残る7人のその後の来訪なし。(48名中41名が来所、検査は全て陰性)

4．平成17年1月12日付けで報告された輸血用血液製剤でＨＢＶ（Ｂ型肝炎ウイルス）感染が疑われる事例について、残る4人のその後の来訪なし。(16名中12名が来所、検査は全て陰性)

5．平成17年2月4日付けで報告された輸血用血液製剤でＨＢＶ（Ｂ型肝炎ウイルス）感染が疑われる事例について、残る1人のその後の来訪なし。(追跡調査対象の4名中3名が来所、HBV-DNAは全て陰性。1名はHBc抗体がEIA法のみ陽性HI法陰性、その他の者は全て陰性)

6．平成17年6月23日付けで報告された輸血用血液製剤でＨＢＶ（B型肝炎ウイルス）感染が疑われる事例について、残る2人のその後の来訪なし。（20名中18名が来所、検査は全て陰性）

7．平成18年4月7日付けで報告された輸血用血液製剤でＨＢＶ（B型肝炎ウイルス）感染が疑われる事例について、残る7人のその後の来訪なし。（53名中46名が来所、HBV-DNAは全て陰性。2名はHBc抗体及びHBs抗体陽性、1名はHBs抗体のみ陽性、その他の者は全て陰性）

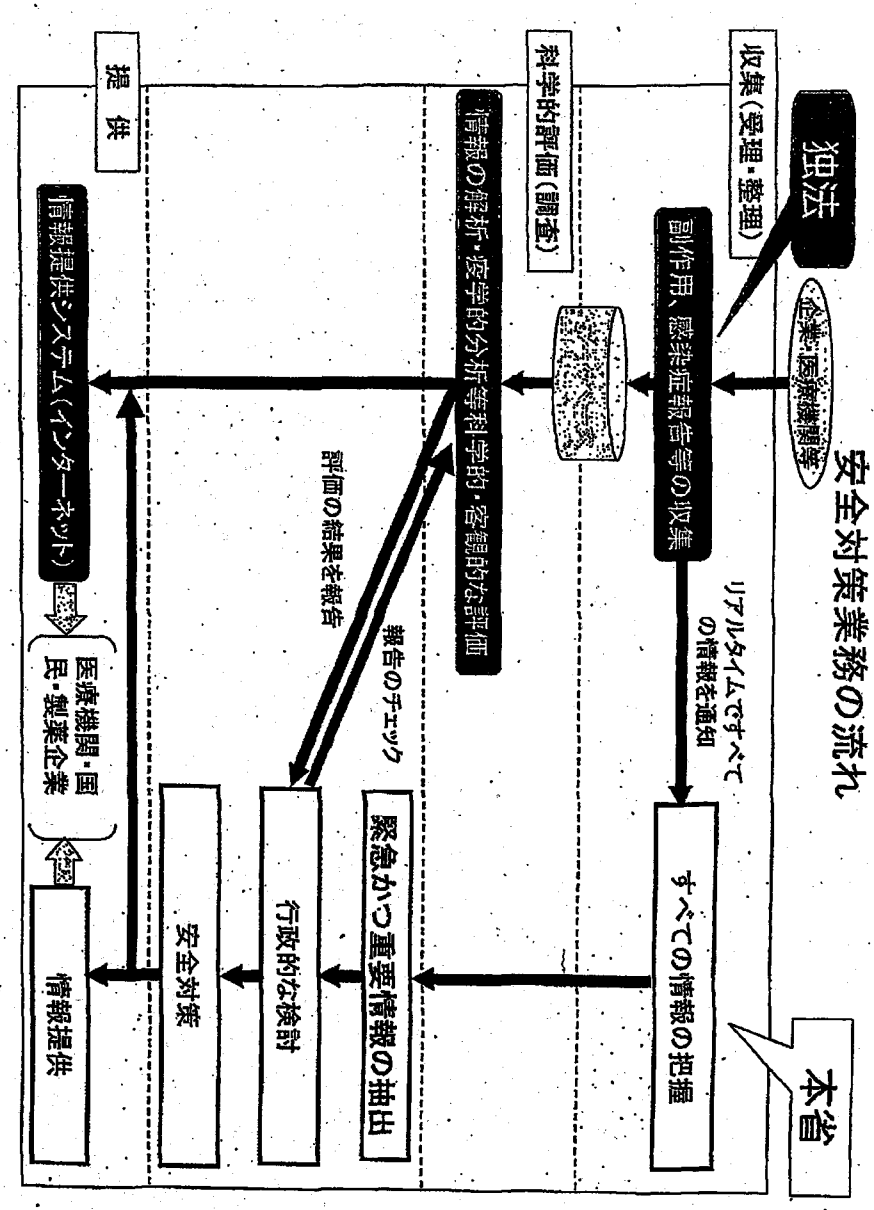
8．平成18年6月5日付けで報告された輸血用血液製剤でＨＢＶ（B型肝炎ウイルス）感染が疑われる事例について、残る1人のその後の来訪なし。（29名中28名が来所、HBV-DNAは全て陰性。2名はHBc抗体及びHBs抗体陽性、1名はHBs抗体のみ陽性、その他の者は全て陰性）

9．平成19年2月20日付けで報告された輸血用血液製剤でＨＢＶ（B型肝炎ウイルス）感染が疑われる事例について、残る1人のその後の来訪なし。（3名中2名が来所、検査は全て陰性）

10．平成21年11月20日付けで報告された輸血用血液製剤でＨＢＶ（B型肝炎ウイルス）感染が疑われる事例について、1人がその後献血に協力いただき、検査は陰性。残る2人のその後の来訪なし。（23名中21名が来所、検査は全て陰性）

11．平成18年2月15日報告、3月8日付けで追加報告された輸血用血液製剤でＨＣＶ（C型肝炎ウイルス）感染が疑われる事例について、残る3人のその後の来訪なし。（81名中78名が来所、検査は全て陰性）

12．試行的ＨＥＶ２０プールＮＡＴについて、その後の調査実施状況については別紙のとおり。



資料３－３

献血件数及びＨＩＶ抗体・核酸増幅検査陽性件数

年	献血件数（検査実施数）	陽性件数（）内女性 [ ]内核酸増幅検査のみ陽性	10万件当たり
	件	件	件
１９８７年　（昭和62年）	8,217,340	11（1）	0.134
１９８８年　（昭和63年）	7,974,147	9（1）	0.113
１９８９年　（平成 元年）	7,876,682	13（1）	0.165
１９９０年　（平成 2年）	7,743,475	26（6）	0.336
１９９１年　（平成 3年）	8,071,937	29（4）	0.359
１９９２年　（平成 4年）	7,710,693	34（7）	0.441
１９９３年　（平成 5年）	7,205,514	35（5）	0.486
１９９４年　（平成 6年）	6,610,484	36（5）	0.545
１９９５年　（平成 7年）	6,298,706	46（9）	0.730
１９９６年　（平成 8年）	6,039,394	46（5）	0.762
１９９７年　（平成 9年）	5,998,760	54（5）	0.900
１９９８年　（平成10年）	6,137,378	56（4）	0.912
１９９９年　（平成11年）	6,139,205	64（6）	1.042
２０００年　（平成12年）	5,877,971	67（4）[3]	1.140
２００１年　（平成13年）	5,774,269	79（1）[1]	1.368
２００２年　（平成14年）	5,784,101	82（5）[2]	1.418
２００３年　（平成15年）	5,621,096	87（8）[2]	1.548
２００４年　（平成16年）	5,473,140	92（4）[2]	1.681
２００５年　（平成17年）	5,320,602	78（3）[2]	1.466
２００６年　（平成18年）	4,987,857	87（5）[1]	1.744
２００７年　（平成19年）	4,939,550	102（3）[6]	2.065
２００８年　（平成20年）	5,077,238	107（3）[0]	2.107
２００９年　（平成21年）	5,287,101	102（6）[2]	1.929
２０１０年　（平成22年）	5,318,586	86（3）[1]	1.617
２０１１年（１～３月）　（平成23年）	1,327,109（速報値）	29（3）[0]	2.185

（注１）・ 昭和６１年は、年中途から実施したことなどから、3,146,940件、うち、陽性件数１１件（女性０）となっている。
（注２）・ 抗体検査及び核酸増幅検査陽性の血液は廃棄され、製剤には使用されない。
・ 核酸増幅検査については、平成１１年１０月より全国的に実施している。
（注３）・ 平成２３年は、１月～３月の速報値で集計している。

ＨＩＶ抗体・核酸増幅検査陽性献血者数内訳

1. 性別・年齢区分・国別

	男性			女性			合計		
	日本人	外国人	計	日本人	外国人	計	日本人	外国人	計
	人	人	人	人	人	人	人	人	人
16～19歳	34	1	35	11	0	11	45	1	46
20～29歳	521	29	550	46	4	50	567	33	600
30～39歳	503	13	516	25	2	27	528	15	543
40～49歳	179	1	180	11	1	12	190	2	192
50～69歳	80	0	80	7	0	7	87	0	87
合計	1317	44	1361	100	7	107	1417	51	1468

※ 昭和61年～平成23年3月（昭和61年については年途中から集計し、平成23年1月～3月については速報値で集計）

2．都道府県別（献血地別）

県別	61年	62年	63年	元年	2年	3年	4年	5年	6年	7年	8年	9年	10年	11年	12年	13年	14年	15年	16年	17年	18年	19年	20年	21年	22年	23年	合計	構成割合	ブロック別	
																													陽性献血件数	構成割合
	(件)	(件)	(件)	(件)	(件)	(件)	(件)	(件)	(件)	(件)	(件)	(件)	(件)	(件)	(件)	(件)	(件)	(件)	(件)	(件)	(件)	(件)	(件)	(件)	(件)	(件)	(件)	(%)	(件)	(%)
1.北海道			1			1	2	1	1	1		1	1	3	2	2	3	2	2	3	2	3	3	2	2	1	39	2.7		
2.青森			2									1					1	1	2	1	1	1		1	2		13	0.9		
3.岩手										1				1										3			5	0.3		
4.宮城							1	1				1	1	1		1	1	1	1	2				2			13	0.9	北海道	
5.秋田																1			1				1		1		4	0.3	・東北	
6.山形													1				1							1	1		4	0.3		
7.福島							1					2		1	1			1					1		1	1	9	0.6	87	5.9
8.茨城					1	1	4	2			1	2		1	2	1	1				1	1	1	5	1		25	1.7		
9.栃木					3	1				2	1	1		1		3		1		1	4	2	1	1	1	2	25	1.7		
10.群馬					1	1		1				1		1	3	1		2		3		2	1	3		1	21	1.4		
11.埼玉		1				1	1	2	1	2	3	3	3	3	3	3	3	3	5	2	1	3	2	8	3	1	57	3.9		
12.千葉							1	6	2	2	3	7	2	4	5	4	5	3	3	2	2	6	9	5	6	5	82	5.6	関東	
13.東京	10	6	4	10	10	11	12	11	14	21	18	18	19	27	26	29	23	25	24	22	24	17	21	19	25	5	451	30.7		
14.神奈川		1		1	1	4	1	3	4	2	5	3	4	3	5	3	5	5	8	4	5	5	5	1	2	1	81	5.5	742	50.5
15.新潟				1		1		1						1		2			1		2			2			11	0.7		
16.富山					2						1				1		1				1						6	0.4		
17.石川																2				1		3		1			7	0.5	北陸・	
18.福井			1							2							1	1									5	0.3	甲信越	
19.山梨					1	1					1					1											4	0.3		
20.長野							1	1			2						1				1	1					7	0.5	40	2.7
21.岐阜							1									1			1					1	2	1	8	0.5		
22.静岡						1	3		1						1	1		1	1			4		2	1		16	1.1	東海	
23.愛知		1			3	2		3	1	1			4	3	2	3	2	2	4	4	5	4	10	4	2		60	4.1		
24.三重											1	1	1		1			1		2				1			8	0.5	92	6.3
25.滋賀																1	3						1	2			7	0.5		
26.京都							2		2	1	1					2	5	2		4	5	1			2		27	1.8		
27.大阪	1	1	1	1	3		1	4	2	1	8	14	6	8	10	10	15	17	19	17	25	26	13	18	7	229	15.6		
28.兵庫						2		1	2				2	1	1	4	5	3		3	3	4	3	2		36	2.5	近畿	
29.奈良									1	2	3	1		1		1	1	1				1	1				13	0.9		
30.和歌山																		2				1	1				4	0.3	316	21.5
31.鳥取								1								1				1		1		1			5	0.3		
32.島根						1															1			3			5	0.3		
33.岡山								2										2	1	2	2	3	1				13	0.9	中国	
34.広島							2	1	1			1					1	2	6		2	2	1	4			23	1.6		
35.山口					1						2												1		1		5	0.3	51	3.5
36.徳島										1				1						1		1	1	1			6	0.4		
37.香川							1												1			1	2	2	1		8	0.5	四国	
38.愛媛												1	1	2	3	2	2			1	1	2		1			16	1.1		
39.高知																	1	1			1		1	1	1		6	0.4	36	2.5
40.福岡							1		2	2	2	1	1	1	1	2	4	2	2		3	1	3	2	4	1	35	2.4		
41.佐賀																											0	0.0		
42.長崎																	2					1	1	2		2	8	0.5		
43.熊本						1				2	1			1	2		1	2		1	1	2	2	2	1	1	20	1.4		
44.大分								1										2	1								4	0.3	九州	
45.宮崎														2						2		1	1	1			7	0.5	・沖縄	
46.鹿児島							1						2			1	1		1		1	1	2		2		12	0.8		
47.沖縄		1									1							2	3		1	5	1	3	1		18	1.2	104	7.1
合計	11	11	9	13	26	29	34	35	36	46	46	54	56	64	67	79	82	87	92	78	87	102	107	102	86	29	1468	100	1468	100

※　「構成割合」は統数処理しているため、合計が必ずしも１００％にはならない
※　平成23年については、1月～3月の速報値で集計

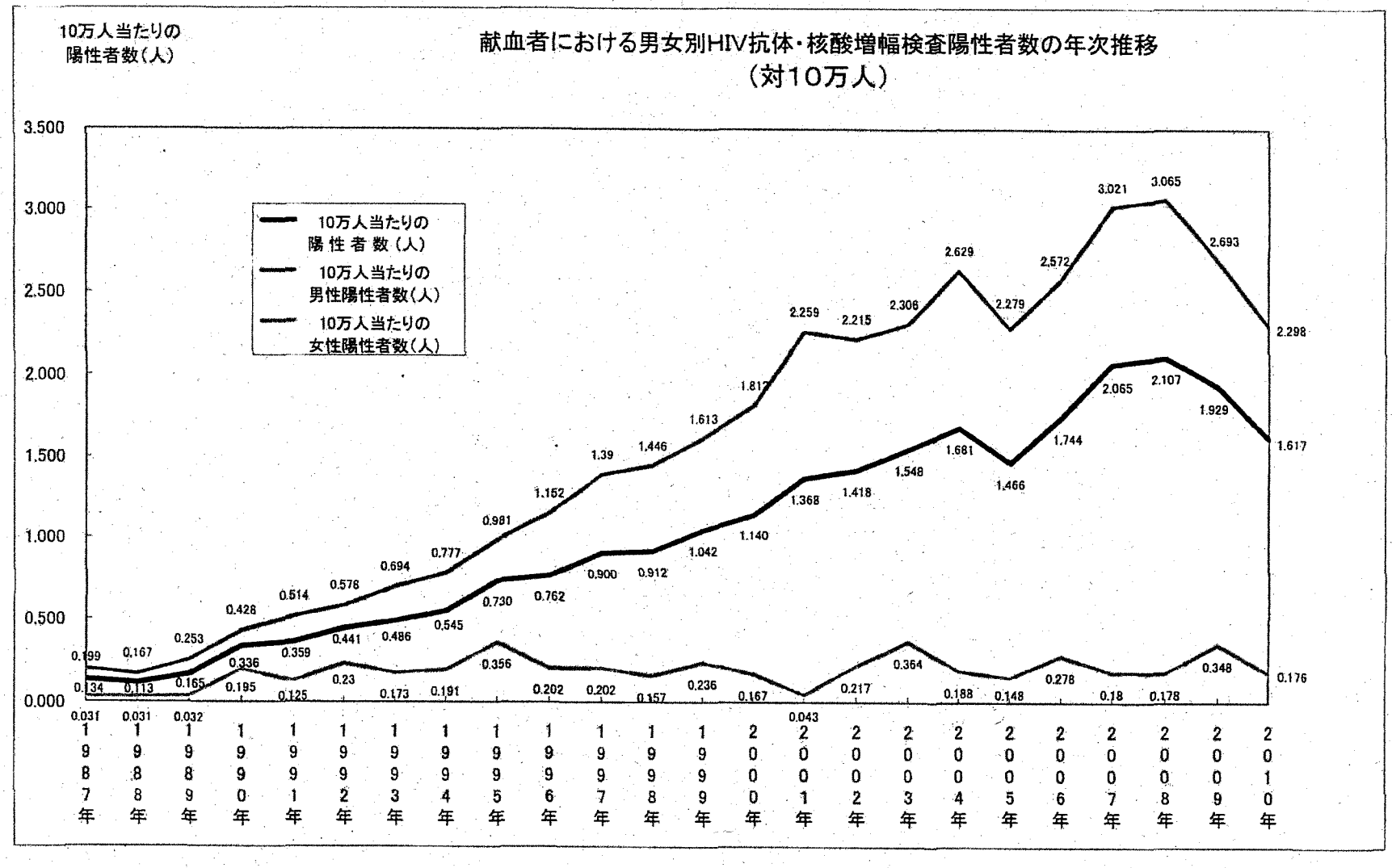
ブロック別ＨＩＶ抗体・核酸増幅検査陽性献血者

	平成18年			平成19年			平成20年			平成21年			平成22年			平成23年（1月～3月）（速報値）		
	献血者	陽性	10万人当たり	献血者	陽性	10万人当たり	献血者	陽性	10万人当たり	献血者	陽性	10万人当たり	献血者	陽性	10万人当たり	献血者	陽性	10万人当たり
	人	件	件	人	件	件	人	件	件	人	件	件	人	件	件	人	件	件
北海道・東北	674,411	3	0.445	647,438	4	0.618	651,215	5	0.768	677,073	9	1.329	690,050	7	1.014	157,472	2	1.270
関東	1,548,970	37	2.389	1,559,391	36	2.309	1,621,408	40	2.467	1,705,070	42	2.463	1,698,561	38	2.237	416,344	15	3.603
北陸・甲信越	337,810	4	1.184	330,485	4	1.210	335,848	0	0.000	340,901	3	0.880	340,203	0	0.000	88,539	0	0.000
東海	540,167	5	0.926	545,248	8	1.467	562,610	11	1.955	584,495	9	1.540	589,557	4	0.678	147,029	1	0.680
近畿	817,075	25	3.060	807,758	30	3.714	833,656	33	3.959	863,744	20	2.316	876,750	22	2.509	224,119	7	3.123
中国	335,666	5	1.490	316,087	5	1.582	316,509	4	1.264	329,443	4	1.214	330,284	5	1.514	82,892	0	0.000
四国	164,763	2	1.214	161,533	4	2.476	166,332	4	2.405	173,914	5	2.875	176,923	2	1.130	44,941	0	0.000
九州・沖縄	568,995	6	1.054	571,610	11	1.924	589,760	10	1.696	612,461	10	1.633	616,258	8	1.298	165,773	4	2.413
合計	4,987,857	87	1.744	4,939,550	102	2.065	5,077,238	107	2.107	5,287,101	102	1.929	5,318,586	86	1.617	1,327,109	29	2.185

年齢別HIV抗体・核酸増幅検査陽性献血者

	平成18年			平成19年			平成20年			平成21年			平成22年		
	献血者	陽性	10万人当たり	献血者	陽性	10万人当たり	献血者	陽性	10万人当たり	献血者	陽性	10万人当たり	献血者	陽性	10万人当たり
	人	件		人	件		人	件		人	件		人	件	
16才～19才	381,352	2 (1)	0.524	324,414	5	1.541	308,019	2	0.649	295,811	3	1.014	292,853	5	1.707
20才～29才	1,188,738	29 (2)	2.440	1,135,102	38 (2)	3.348	1,141,746	41	3.591	1,139,991	37 (1)	3.246	1,080,385	21 (1)	1.944
30才～39才	1,361,658	43 (2)	3.158	1,369,241	35 (1)	2.556	1,391,141	50 (1)	3.594	1,414,747	42 (3)	2.969	1,376,596	43 (1)	3.124
40才～49才	1,048,055	9	0.859	1,088,410	17	1.562	1,171,449	11 (1)	0.939	1,272,397	17 (2)	1.336	1,350,490	10	0.740
50才～59才	766,625	3	0.391	770,663	5	0.649	785,280	3 (1)	0.382	841,168	3	0.357	872,113	6 (1)	0.688
60才～	241,429	1	0.414	251,720	2	0.795	279,603	0	0.000	322,987	0	0.000	346,149	1	0.289
合 計	4,987,857	87 (5)	1.744	4,939,550	102 (3)	2.065	5,077,238	107 (3)	2.107	5,287,101	102 (6)	1.929	5,318,586	86 (3)	1.617

(注)陽性件数の()内女性


10万人当たりの
陽性者数(人)
献血者における男女別HIV抗体・核酸増幅検査陽性者数の年次推移
(対10万人)
10万人当たりの
陽性者数(人)
10万人当たりの
男性陽性者数(人)
10万人当たりの
女性陽性者数(人)
3.500
3.000
2.500
2.000
1.500
1.000
0.500
0.000
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0.167
0.253
0.428
0.514
0.578
0.694
0.777
0.981
1.152
1.39
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1.613
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