

医薬品 研究報告 調査報告書

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<p>一般的名称</p>	<p>解凍人赤血球濃厚液</p>		<p>研究報告の公表状況</p>	<p>ABC Newsletter. 2006 Sep 1; 16.</p>	<p>公表国</p>	
<p>販売名(企業名)</p>	<p>解凍赤血球濃厚液「日赤」(日本赤十字社) 照射解凍赤血球濃厚液「日赤」(日本赤十字社)</p>				<p>英国</p>	
<p>研究報告の概要</p>	<p>使用上の注意記載状況・その他参考事項等</p> <p>解凍赤血球濃厚液「日赤」 照射解凍赤血球濃厚液「日赤」</p> <p>血液を介するウイルス、細菌、原虫等の感染 vCJD等の伝播のリスク</p>					
<p>報告企業の意見</p>			<p>今後の対応</p>			
<p>エジンバラ大学の研究者らは、検査を実施した全ての手術器具に、CJD感染をもたらす危険性がある量の残留タンパク質の汚染があることを認めたとの報告である。</p>			<p>今後も引き続き、プリオン病に関する新たな知見及び情報の収集に努める。</p>			

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GLOBAL NEWS: (continued from page 15)

Scientists hope to be able to use stem cells, the earliest form of cells, to regenerate the organs and tissues of patients with disabling injuries. One Premier League footballer, playing in the northwest of England, said: "We decided to store our new baby's stem cells for possible future therapeutic reasons, both for our children and possibly for myself." The player, who declined to be named, added: "As a footballer, if you're prone to injury, it can mean the end of your career, so having your stem cells – a repair kit, if you like – on hand makes sense." He is one of five professional footballers who have frozen their children's stem cells with Liverpool-based CryoGenesis International (CGI), one of about seven commercial stem cell "banks" in Britain. In the past five years, more than 11,000 British parents have paid up to £1500 (\$3,700) to store their babies' stem cells in the banks in order to grow tissue, should their children become ill. One professional footballer known to have stored stem cells for his children's future use is the Frenchman Thierry Henry, the Arsenal and France striker. There is no indication that he intended them for his own use. (Source: *London Sunday Times*, 8/27/06) ♦

INFECTIOUS DISEASE UPDATES:**BSE/CJD/vCJD**

A new study has found that surgical instruments still have the potential to harbor Creutzfeldt-Jakob disease (CJD) even after sterilization. Edinburgh University researchers found every instrument they tested was contaminated with enough protein residue to pose a potential infection risk. The researchers tested instruments taken at random from five National Health Service hospital trust sterile service departments. Results of the study, financed by the Department of Health, appeared last month in the *Journal of Hospital Infection*. CJD, a degenerative and fatal brain disease, is thought to be caused by mutated proteins called prions. These twisted proteins are known to be able to cling to the surface of surgical instruments, and are remarkably difficult to remove by standard decontamination processes, which involve the use of detergents and super-heating. A number of patients have contracted CJD from contaminated instruments during surgery. The Edinburgh team found an average level of protein contamination of 0.2 micrograms per square millimeter of instrument, much higher than the dose needed to cause infection in humans. The highest doses were found on instruments used to remove tonsils – one of the tissues known to harbor prions. Lead researcher Bob Baxter, PhD, from the University's chemistry department, said, "You can never get something 100 percent clean, but we were surprised at how much protein there was." Dr. Baxter said hospitals take measures to quarantine surgical instruments if a patient is known to be at high risk of carrying CJD. The Edinburgh team has developed a more effective way to sterilize instruments with a technique called gas plasma sterilization using radio waves to excite the molecules of harmless gases, creating charged atoms called ions and radicals which effectively scour the surface of the instruments. Dr. Baxter has recommended the widespread introduction of gas plasma cleaning to the Department of Health. (Source: BBC News, 8/24/06) Citation: Baxter RL, *et al.* Quantitative analysis of residual protein contamination on reprocessed surgical instruments. *J Hosp Infect.* 2006;63(4):439-44.

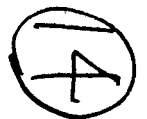
Researchers exploring the likelihood that variant Creutzfeldt-Jakob (vCJD) disease might be spread via the reuse of surgical instruments have called for more data in order to allay fears over the possible transmission of the deadly infection. Their study was published in the online edition of the *Journal of the Royal Society Interface*. Scientists based at both the London School of Hygiene & Tropical Medicine and the National Creutzfeldt-Jakob Disease Surveillance Unit at Western General Hospital in Edinburgh report that key factors determining the scale of any epidemic are the number of

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医薬品
医薬部外品 研究報告 調査報告書
化粧品

識別番号・報告回数		報告日		第一報入手日 2006年11月29日	新医薬品等の区分 該当なし	厚生労働省処理欄
一般的名称	人ハプトグロビン		研究報告の 公表状況	FDA/Transmissible Spongiform Encephalopathies Advisory Committee December 15, 2006	公表国 アメリカ	
販売名 (企業名)	ハプトグロビン注-ヨシトミ(ベネシス)					
研究報告の概要	トピック I: 米国で認可されたヒト血漿由来第 VIII 凝固因子製剤 (pdFVIII) の使用が関与する可能性がある vCJD についての FDA のリスク評価、及び公衆衛生局の考えられる対応 FDA は、血友病 A およびフォンウィルブランド病患者(vWD)によって使用される米国で認可された pdFVIII に係る vCJD リスク評価文書 (Draft Quantitative Risk Assessment of vCJD Risk Potentially Associated with the Use of Human Plasma-Derived Factor VIII Manufactured Under United States License From Plasma Collected in the US) を作成した。 リスク評価を行った背景には、2003 年以来、英国で輸血により vCJD に感染したと見られる 3 例が発見されたことがある。米国では BSE は 3 例発見されたのみで、米国で vCJD に感染したケースはまったくないため、血漿供与者が米国で生産された牛肉を食べて vCJD に感染するリスクは極度に低いと考えられる。しかし、米国の少数の供血者が英国、フランス、その他のヨーロッパ諸国への旅行や滞在で BSE に曝露された可能性はあり、従って一定のリスクを否定できない。これら供血者の一部は知らずに食事を通して vCJD に感染した可能性があり、米国で製造される pdFVIII に使われる血漿のプールにこれら感染者の血漿が入った恐れはある。供血停止政策で大部分の vCJD リスクは排除されている可能性が高いが、供血停止基準に合致しない供血者や、基準に合致していてもスクリーニングで排除されなかった供血者からのリスクは残存する。FDA はコンピュータシミュレーション・モデルを用い、pdFVIII 製品を利用した重症血友病 A 患者及び重症 vWD 患者について vCJD 病原体曝露の確度とそのレベルおよび vCJD 感染リスクを推定した。FDA は、TSEAC にこのリスク評価文書を提示し、リスク評価の結果と解釈及びこの情報を医師、患者並びに一般大衆に知らせることに関する伝達の要点についての助言を求めようとしている。					使用上の注意記載状況・ その他参考事項等
	トピック II: pdFVIII での伝達性海綿状脳症 (TSE) 感染性実験のクリアランス pdFVIII のリスクを、2・3、4・6及び7・9の log クリアランス値を使って評価した。血友病 A の重症患者のリスクは、英国組織サーベイに基づく vCJD の高感染率を仮定した場合は年間平均 1/159 ~ 1/100,000,000、低感染率を仮定した場合は 1/21,500 ~ 1/3,200,000,000 と予想される。 FDA は委員会に対して以下の質問を行った。①製造工程をスケールダウンシスパイキングモデルを使った実験で示された TSE 病原体のミニマムのリダクション値によって、製品の vCJD 安全性が強化されるか? ②もし委員会が vCJD 安全性を強化するミニマムの TSE リダクションを定めた場合、承認を受けた pdFVIII のリダクション値がそれより低い場合に FDA は如何なる対応をしなければならないか?					
報告企業の意見					今後の対応	
2006年12月15日開催の米国海綿状脳症委員会の議題であり、資料の中に血液凝固第VIII因子製剤のvCJDについてのFDAのリスク評価案及び公衆衛生局の考えられる対応案が示されている。これまで血漿分画製剤によってvCJDを含むプリオン病が伝播したとの報告はない。しかしながら、万一vCJD感染者の血漿が本剤の原料に混入した場合には、製造工程においてプリオンを低減し得るとの報告があるものの、製剤から伝播する可能性を完全には否定し得ない。そのため、弊社の血漿分画製剤の製造工程におけるTSE感染性低減に関する検証実験を加速し、自社データを早期に取得し、工程評価を行い、必要に応じて工程改善を実施する予定である。					vCJD に関連する情報については、今後も注視することとする。	

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**TRANSMISSIBLE SPONGIFORM ENCEPHALOPATHIES ADVISORY
COMMITTEE MEETING**

December 15, 2006

ISSUE SUMMARY

Topic I: FDA's Risk Assessment for Variant Creutzfeldt- Jakob Disease (vCJD) Potentially Associated with the Use of US Licensed Human Plasma-Derived Factor VIII (pdFVIII, Antihemophilic Factor) Products, and Potential Public Health Service Responses

Issue: FDA has prepared a risk assessment of the potential, but unproven, risk related to pdFVIII products, which are used by some patients with the blood clotting disorders hemophilia A and von Willebrand disease. The risk of the potential of pdFVIII products to transmit vCJD, the agent which causes the human form of "Mad Cow Disease," is highly uncertain, but appears likely to be very low. FDA is presenting the risk assessment to the TSEAC to seek advice on key message points concerning both the risk assessment and appropriate ways to communicate this information to physicians, patients, and the general public. Prior to the TSEAC meeting, FDA has obtained input on the risk communication from individual special government employees (SGE's) who represent various hemophilia advocacy organizations.

BACKGROUND:

vCJD is a fatal neurodegenerative disease acquired through infection with the agent that causes bovine spongiform encephalopathy (BSE) by consumption of beef products from infected cattle. The first human cases of vCJD were reported in the United Kingdom (UK) in 1996, and as of August 2006, 195 cases have been reported worldwide, 162 of them in the UK.

In 1999, based on the potential, but unknown risk of vCJD from blood products, and consistent with advice from TSEAC, FDA recommended deferral of blood and plasma donors who had traveled or lived for 6 months or longer in the UK from the presumed start of the BSE outbreak in the UK in 1980 until the end of 1996 when the UK had fully implemented a full range of measures to protect animal feed and human food from contamination with the infectious agent causing BSE. In January 2002, FDA recommended enhancing the vCJD geographical donor deferral policy by reducing the time that an otherwise suitable blood donor might have spent in the UK from six to three months. FDA also recommended deferring donors who had spent five or more years in France or cumulatively in any European country listed by the USDA as either having had BSE or having a significant risk of BSE, and adding certain other measures to reduce potential risk, such as deferring any donor with a history of blood transfusion in the UK after 1979. Taken together, these steps were estimated to have excluded donors representing slightly more than 90% of the potential BSE/vCJD risk while deferring about 7% of otherwise suitable donors. Since 2002, TSEAC has several times reviewed FDA vCJD/CJD blood donor deferral policies, most recently advising FDA to recommend deferral of blood donors transfused in France. FDA has issued draft guidance containing such recommendations..

Since 2003, three presumptive transfusion transmitted cases of vCJD have been reported in the UK. Two of the transfusion recipients died of vCJD, whereas the third had vCJD infection detected after death from an unrelated cause. Each had received transfusions of red blood cells from individuals who were asymptomatic at the time of donation, but who later died from vCJD. The strong likelihood that transmission of vCJD occurred via transfusion of red blood cells in the UK increased the concern that products manufactured from the plasma portion of human blood might also pose a risk of vCJD transmission. Note, however, there have been no reported cases of vCJD in any recipients of plasma derived products in the UK, where risk is considered greatest, or anywhere else in the world. In the fall of 2004 UK authorities notified recipients of a number of plasma derivatives that they might be at increased risk of vCJD. These products included coagulation factors VIII, IX, and XI, as well as antithrombin III, and intravenous immune globulins.

Because BSE occurs at an extremely low level in US cattle (only three reported cases: two in US born cattle and one in a cow imported from Canada), and there have been no human cases of vCJD acquired in the US, any risk of plasma donors acquiring vCJD by consuming domestically produced beef is thought to be extremely low. However, it is possible that a small population of US donors may have been exposed to the BSE agent during travel or residence in the UK, France, or other countries of Europe and may therefore be at some risk for vCJD. Some of these donors may have been unknowingly infected with vCJD through dietary exposure and then contributed donations to plasma pools used to manufacture pdFVIII in the U.S. The donor deferral policy likely removes most of the vCJD risk; however, there may be residual risk in the US donor population for persons who do not meet criteria for donor deferral, or who meet those criteria, but fail to be deferred due to limitations of the donor screening process.

FDA has developed a computer-based simulation model to try to estimate the potential risk and understand factors involved in determining and potentially reducing the degree of risk. The model and various risk estimate results and uncertainties are presented in the document "A Draft Quantitative Risk Assessment of vCJD Risk Potentially Associated with the Use of Human Plasma-Derived Factor VIII Manufactured Under United States (US) License From Plasma Collected in the US" provided as a separate attachment. The results are estimates of the probability and level of exposure to the vCJD agent and the possible risk of vCJD infection in patients with severe hemophilia A (HA) and the severe form of von Willebrand disease (vWD) (Type 3) who have used human pdFVIII product manufactured in the US.

The parameters used in this risk assessment were derived after receiving recommendations from the TSEAC about another risk assessment, the "Draft Risk Assessment: Potential Exposure to the vCJD agent in United States Recipients of Factor XI Coagulation Product Manufactured in the United Kingdom" at the February 8, 2005 meeting; from discussion at a meeting of the TSEAC on October 31, 2005 on several risk assessment model inputs for plasma derivatives and potential vCJD risks specifically related to pdFVIII; and from peer review by non-FDA experts in risk assessment.

The ranges of uncertainty and variability in the input parameters of the risk assessment are great, resulting in very large uncertainty in the model's outputs that estimate potential risk. Additionally, because scientific data on the level of exposure to the vCJD agent and the

likelihood of certain human health outcomes, such as infection and illness, are lacking, estimates for the infectious risk generated in the risk assessment may not be accurate. For these reasons, it is not possible to provide an actual estimate of the vCJD risk to individual patients potentially exposed to the vCJD agent through plasma-derived products.

Additionally, the absence of any reported cases of vCJD in repeatedly exposed recipients of plasma derivatives in the UK, where risk is thought to have been greatest, or anywhere else in the world, further suggests that the actual risk of vCJD from pdFVIII is likely to be very low.

Nevertheless, FDA believes it is appropriate to share both the findings of and the uncertainties in our risk assessment for pdFVIII with physicians, patients, and the general public since it is possible that the risk is not zero. Advice will be sought from the TSEAC in December concerning communication of the findings of the risk assessment and its interpretation, given the very wide range of uncertainty in the estimate of vCJD risk. Advice will also be sought on potential steps that may help to better understand as well as to further reduce any risks.

DISCUSSION:

A. Risk Assessment and Interpretation

The FDA risk assessment estimates the risk of vCJD infection as a function of product exposure for different assumed levels of vCJD infectious agent clearance in manufacturing of pdFVIII and under two assumed levels of vCJD prevalence in the UK. The risk assessment utilizes a probability-based statistical sampling model that evaluates successively the impact on vCJD risk of individual processes used in the production of human pdFVIII beginning with plasma donation, extending through manufacturing steps, and finally, addressing utilization by various representative patient subpopulations. Input data for parameters used in the model such as clearance, vCJD prevalence, and pdFVIII usage are represented as statistical distributions that express the underlying uncertainty and variability. Each run of the model randomly samples one number from the distribution for each parameter; this is done thousands of times to generate a single distribution representing the final risk estimate that expresses, where possible, the accompanying uncertainty of these risk estimates. A sensitivity analysis, conducted by varying values of key parameters within the input range of the model and observing the effect on the predicted outcomes, determined that three major factors in the model greatly influenced potential vCJD risk: reduction of the infectious agent by the manufacturing process, intensity of pdFVIII utilization by the patient, and differing estimates of disease prevalence in the UK.

One of the most influential risk assessment parameters for vCJD risk is the manufacturing process, which may reduce or eliminate the amount of the vCJD agent in the final product. Because of the uncertainty and variability in the levels of vCJD clearance afforded during the manufacturing process for any pdFVIII product, the model evaluated three separate categories of reduction in infectivity that the product may have undergone during manufacturing including 2-3 log₁₀, 4-6 log₁₀, and 7-9 log₁₀ reduction. These three categories are meant to span the possible range of uncertainty and variability in reduction of vCJD agent for marketed pdFVIII products. Based on currently available experimental studies, FDA believes that all US licensed pdFVIII products probably achieve at least a 4 log₁₀ of vCJD level of clearance during manufacture.

Another major variable affecting potential risk is the quantity of product used by patients in different treatment groups. For purposes of this model only patients with severe HA were considered because their higher use of product would put them at higher risk than patients with mild or moderate forms of the disease. Severe HA patients account for approximately 50% of the total HA population. Approximately 25% of all HA patients use pdFVIII products, while most others use recombinant FVIII. Data from a CDC sponsored epidemiological study on HA patients were used to generate the statistical distribution of pdFVIII usage by patients. Using these estimates, the risk assessment evaluated different treatment regimens including patients on prophylaxis, prophylaxis plus inhibitor, prophylaxis plus inhibitor plus immune tolerance, episodic treatment, and episodic treatment plus inhibitor. It also evaluated the potential of patients with severe von Willebrand disease (vWD) to be exposed to the risk of infection with vCJD through the use of pdFVIII. These patients must use plasma-derived sources of FVIII/von Willebrand factor because there is presently no recombinant von Willebrand factor.

The prevalence of vCJD in the United Kingdom population was used to estimate vCJD exposure and therefore prevalence in US donors who traveled to the UK, France and other European countries. For purposes of the risk assessment, we used two different estimates of vCJD prevalence in the UK. One estimate is based on epidemiological modeling of actual reported cases and an estimate of future vCJD cases in the UK. The other estimate is based on testing for prion protein in a relatively small tissue (tonsil and appendix) surveillance study. At present it is not possible to know which of the two estimates of vCJD prevalence in the UK provides a better estimate of the true prevalence.

The vCJD case prevalence based on epidemiological modeling of actual reported cases and an estimate of future vCJD cases in the UK yielded an estimate of approximately 1.8 vCJD cases per million. There are a number of limitations to this estimate based on simplifying assumptions that contribute to considerable uncertainty in the final case estimates. These assumptions include the intensity of human exposure to the BSE agent, the length of the incubation period, and how a person's age and genetic background could influence exposure, disease susceptibility, and incubation period. However, it is possible that the prevalence of vCJD in the UK is higher than this estimate if there are people infected who never develop the disease (but can still spread the infection) or if some individuals take an extremely long time to become ill. Therefore, we also used a second approach to estimate vCJD infection prevalence based on testing for prion protein in a relatively small tissue (tonsil and appendix) surveillance study. This approach yielded an estimate of 1 in 4,225 (237 infections per million). Limitations to this study that contribute to uncertainty include the fact that this study was not controlled using tissues from a non-BSE exposed population and false positive findings cannot be ruled out. It is also not known whether this finding of prion protein in tissues is a reliable marker for vCJD pre-clinical infection or for an individual's capability to transmit the infection through blood donation.

After accounting for the age distribution, incubation period, country, year and duration of travel, these two different prevalence estimates have been used to predict the number of vCJD donations that could be present in variably sized pools of US donated plasma.

Results

See Risk Assessment, including the Executive Summary, and especially Tables I.A and II.A in the Executive Summary and attached here in an Appendix.

Interpretation

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. Donor deferral criteria in place since 1999 have reduced the risk of donation by exposed persons.

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 log₁₀ (or 10,000 fold) or greater manufacturing process reduction of the vCJD agent. Assuming a 4-6 log₁₀ manufacturing process reduction, the modeling predicts that the potential risk per person per year for patients with severe HA using pdFVIII ranges from 1 in 15,000 for the higher vCJD prevalence estimate and high product usage, to 1 in 9.4 million for the lower vCJD prevalence estimate and low product usage. While higher levels of clearance are likely to reduce risk, it is not possible at this time to determine with certainty if a specific product may be less or more safe than another due to the wide range of methods used for clearance studies currently available, the results themselves, and gaps in information. Although results of the model suggest that exposure to vCJD agent could occur, and that there is a potential risk of infection that is likely to be generally 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. Despite the uncertainties in the model, we believe this is information that patients and physicians might consider when making treatment decisions.

B. Risk Management Strategy, Key Message Points, and Communication Strategy

Risk Management Strategy

FDA's current risk management strategy for vCJD has evolved in response to emerging epidemiologic findings and basic scientific developments pertinent to the epidemic. The overall risk management strategy for vCJD includes:

- Deferral of donors at increased risk of vCJD based on epidemiological data, and withdrawal of products at increased vCJD risk
 - Donor deferrals: Guidance since August 1999 (most recently updated in January 2002) to defer donors with "geographic risk," e.g. that visited or resided in countries where BSE prevalence is higher; deferral of donors that used UK-sourced bovine insulin; deferral of donors transfused in the UK since 1980 (note also draft guidance published in August 2006 for deferral of donors transfused in France since 1980).
 - Withdrawal of implicated blood components and plasma derivatives is recommended if a donor is diagnosed with vCJD

- Facilitating development, validation, and information sharing (including product labeling) regarding the performance of manufacturing processes in clearance of TSE agents from blood products.
 - FDA reviews requests for TSE clearance labeling claims which may be approved if detailed, validated TSE clearance study data are provided
 - On September 18, 2006, FDA discussed with TSEAC the feasibility and scientific value of standardized assessments of TSE clearance in the manufacturing processes for pdFVIII. The topic will be addressed again at this meeting
- Facilitating development of candidate donor screening and diagnostic tests for vCJD and other TSEs
 - FDA has held meetings with candidate test kit manufacturers to discuss developmental pathways
 - A public discussion of validation for donor screening tests for vCJD and other TSEs was discussed with the TSEAC on September 19, 2006
- Risk assessment and communication to inform patients and physicians about the current scientific understanding regarding vCJD risk from blood products and to help in informing treatment decisions
 - FDA has engaged in periodic reassessment of TSE epidemiology and pathogenesis to determine whether guidance/policies need to be revisited in light of new information
 - FDA performed risk assessments for potential exposure to vCJD in investigational pdFXI made from plasma donated in the UK, and for pdFVIII made from plasma donated in the US

The risk assessments that FDA has performed for potential exposure to vCJD from licensed pdFVIII made from US plasma has led us to consider further actions. Based on the finding that, despite very large uncertainties in the risk assessment models and generally low risk estimates, the risk of vCJD exposure from these products may not be zero, and we are taking the following steps:

- The risk assessment model has indicated that the level of TSE agent clearance during product manufacturing is one of the most important parameters for vCJD risk. For this reason, FDA seeks to improve our understanding of the actual prion clearance in manufacturing by encouraging standardized clearance studies of the different pdFVIII products, and, potentially, by setting minimum standards for TSE agent clearance.
- Although the risk of vCJD exposure from US pdFVIII products is likely to be very low, and it may not be zero, and FDA is encouraging physicians and patients to consider this risk in making treatment decisions.

DRAFT Risk Communication Messages

Based on the findings of the risk assessment FDA has developed key message points and additional, background information about the risk of vCJD in pdFVIII made from US donor plasma. They include the following:

Key Messages

vCJD (variant Creutzfeldt Jakob Disease, the agent which causes the human form of “Mad Cow Disease”) is rare, even in the UK. Infection is not known to have been acquired in the US and there is no evidence that any US plasma donor has had vCJD. FDA has put steps in place to reduce the risk of transmission by deferring plasma donation from individuals with the most potential risk of exposure, those who lived in affected areas for significant time periods. Exposure to vCJD through pdFVIII could still potentially occur if someone traveled or resided briefly in the UK or another area where TSE is present, and became infected without knowing it from eating infected meat, and then donated plasma. While blood transfusion has transmitted vCJD in the UK, pdFVIII products go through additional manufacturing steps likely to help remove the agent and reduce or eliminate the risk of transmitting the disease.

FDA used a computer risk assessment model to help estimate any remaining potential risk to US pdFVIII recipients. While there are still many uncertainties, and it is not possible to estimate risk for specific individuals, the model suggests that any potential risk to the health of most US pdFVIII recipients is likely to be very low. Also, no cases of vCJD have yet been reported in patients receiving such products either in the UK, where the risk is highest, or anywhere else in the world.

Because so much is unknown about vCJD and its incidence, the risk assessment performed by FDA has a lot of uncertainty, making it impossible to precisely estimate any risk. However, we wanted to provide information about the risk assessment so that patients and health care providers can consider the matter, where appropriate, in their treatment decisions.

Additional Information

vCJD is a very rare, fatal disease that can infect a person for many years before making people sick by destroying cells in the brain.

Most cases of vCJD have occurred in the UK and individuals there are thought to be at higher risk for the disease than individuals elsewhere.

Beef products contaminated with the infectious agent of BSE are the main cause of vCJD. As of August 2006, world-wide, 195 cases have been reported, 162 of them in the UK. Food risk in the US blood donor population is expected to be very low as there have been only three cases of BSE found in US cattle (two US born, and one imported from Canada) and safeguards are in place to prevent infected beef products, if present, from entering human food.

While most vCJD is due to eating infected beef products, there is convincing evidence that the disease has also been transmitted by red blood cell transfusion. In