Questions and Answers on vCJD and pdFVIII

Q. What is vCJD and how is it spread?

A. Variant CJD, or vCJD, is a very rare, fatal disease that can infect a person for many years before making them sick by destroying brain cells. Eating beef products contaminated with the infectious agent of bovine spongiform encephalopathy, or BSE (popularly known as "Mad Cow Disease"), is the main cause of vCJD.

Most cases of vCJD have occurred in the United Kingdom (UK). Individuals in the UK are at a greater risk for this rare disease than individuals elsewhere because of their higher potential exposure to infected beef in their diet. As of October 2006, there have been 196 cases of vCJD reported worldwide, 162 of them in the UK. In the US, there have been two cases of vCJD. The two human cases from the United States had lived in the UK during a key exposure period of the UK population to the BSE agent.

The incidence of vCJD in the UK (new case reports) peaked in 1999 and has declined thereafter. In the UK, where most cases of vCJD have occurred, the current risk of acquiring vCJD from eating beef and beef products appears to be negligible, perhaps about 1 case per 10 billion servings.

Only three cases of BSE have been found in US cattle, and safeguards are in place to help prevent infected beef products from entering our food supply. These safeguards include restricting importation of cattle and beef products from countries with BSE, a surveillance program to detect BSE in the USA, prohibiting the use of high-risk animal-derived proteins in cattle feed, prohibiting meat from sick cattle for human consumption, and requiring the removal of high-risk materials from carcasses of cattle over a certain age.

While vCJD is primarily due to eating infected beef products, three people in the UK who became infected with the vCJD agent had received blood cells from donors who later developed vCJD. Two of the blood cell recipients developed vCJD and died from the disease. The third died of an unrelated illness. To date, there have been no reports of vCJD transmission by close personal contact (such as hugging, kissing, or being in the same room with someone that has vCJD) or sexual contact.

Q. Is it known that pdFVIII can transmit vCJD?

A. No. However, pdFVIII is made from plasma. Plasma is the liquid part of blood remaining after the cells are removed. Animal studies show that if blood carries the vCJD agent, so can the unprocessed plasma.

Manufacturing steps used in making pdFVIII products have been shown to help remove infectious agents, including agents related to vCJD. They may reduce or eliminate most risk even if a vCJD infected donor contributed plasma.

Q. What is the likelihood that a patient who received pdFVIII could become infected with vCJD?

A. The US Public Health Service (PHS) including the FDA, CDC, and NIH, believes that the risk of developing vCJD infection from pdFVIII made from US plasma is most likely to be extremely small. This is based on the results of the risk assessment. It is also based on the lack of any reported cases of vCJD following decades of use by patients who received plasma-derived blood products, including in the UK, where the risk is considered greatest. While the risk is most likely to be extremely small, there are many major uncertainties in the computer model, and a precise estimate of the risk is not currently possible. Right now, there is no test available to detect vCJD in blood donors or recipients. There is no way of knowing whether a person is infected if they do not show symptoms of the disease.

At this time FDA, CDC, and NIH are not aware of any cases of vCJD having been reported worldwide in patients receiving plasma-derived clotting factors, including pdFVIII. This includes patients who have received, over a long period of time, large amounts of clotting factor products manufactured from plasma donations from the UK, where the risk of vCJD is highest.

Q. Why did FDA do a vCJD risk assessment for pdFVIII?

A. We conducted a risk assessment for pdFVIII because it is made from the fraction of plasma that is likely to contain more of the vCJD infectious agent, if present, than the rest of the plasma, from which other products, such as albumin and immunoglobulins, are made. The FVIII containing fraction is further processed using a variety of methods that are likely to reduce or potentially eliminate vCJD from the final pdFVIII product.

Q. **What is the risk of vCJD to patients who receive transfusion products like red blood cells and plasma?**

A. The PHS, including the FDA, CDC, and NIH, believes that the risk of vCJD to patients who receive transfusion products like red blood cells and plasma is extremely small in the US. In addition, in the US, FDA has taken a number of steps to further reduce the potential vCJD risk from blood products. These steps include donor deferral recommendations, and quarantine and withdrawal of products at increased vCJD risk. Donor deferral guidance, first issued in August 1999 and subsequently updated, includes, among other things, deferral of donors who visited or resided in countries where BSE prevalence is relatively high. Also, blood components and plasma derivatives are to be withdrawn if a donor is later diagnosed with vCJD.

The potential spread of vCJD through cell or plasma transfusion is limited by these deferral and quarantine measures that are in place. However, if there were to be a unit of blood cells collected from a donor at risk and it is infused, very few recipients would be affected. In contrast, hundreds of patients might potentially be affected with the use of a contaminated plasma derivative if there were not significant reduction of vCJD infectivity during the manufacturing process.

Q. Why is FDA informing patients, healthcare providers, and the public about vCJD and pdFVIII now?

A. The FDA has recently completed its risk assessment. While the risk is most likely to be extremely small, we do not know the risk with certainty. We therefore think it is important that a person who receives pdFVIII be aware of the results of the risk assessment and have the opportunity to discuss any questions he or she may have with a suitable health care provider, such as a hemophilia specialist. The first case of probable vCJD infection transmission by transfusion in the UK was reported in December 2003, and the second case in July 2004. These events prompted UK authorities to communicate the potential risk of vCJD to recipients of clotting factors and some other plasma derived products in 2004. FDA initiated its risk assessment analysis for FVIII in 2004, presented a discussion of the model input parameters to the Transmissible Spongiform Encephalopathies Advisory Committee (TSEAC) in October 2005, and published a summary of this meeting on its website (http://www.fda.gov/ohrms/dockets/ac/cber05.html#TransmissibleSpongiform). Since then, FDA with scientific advice from the TSEAC and other experts has made further refinements to the risk assessment model. Results of this extensive analysis are now available.

FDA, CDC, NIH, and Office of Public Health and Science (OPHS), with advice from patient advocates and communication experts, have now developed these key message points and communication materials to accurately convey the possible risk to patients, health care providers, and others who may have an interest.

Q. Should patients inform their primary health care providers about a possible vCJD exposure from US licensed pdFVIII?

A. Advising your primary health care provider (e.g. a family physician, internist, hemophilia specialist, etc.) about your history of having received pdFVIII can be beneficial in that your provider can tell you about any new information that may become available, interpret its significance, and advise you about further action that might be appropriate in the future. However, sharing your personal health information is your choice.

Q. Do patients who receive pdFVIII need to do anything special when seeking dental or surgical care?

A. At this time, the US Public Health Service (PHS) does not believe there is a need for pdFVIII recipients to inform their surgeons or dentists about the recipient's potential exposure to vCJD. Also, there is no recommendation for surgeons and dentists to take any special precautions based on such potential exposures. This belief is based on the results of the FDA risk assessment, as well as on the lack of known cases of vCJD transmission from plasma-derived clotting factor products in the UK or anywhere else in the world.

In the UK, public health authorities notified recipients of plasma-derived products such as pdFVIII, that they may have an increased risk of vCJD in addition to the risk from eating potentially contaminated UK beef products. The UK health authorities notified patients to inform their surgeons and dentists about their potential exposure, as a public health

precaution intended to prevent possible secondary spread of the disease from dental and surgical instruments. The PHS, including the FDA, CDC, and NIH, does not believe that such notifications are necessary in the US. This is based on the extremely small risk in the US suggested by the FDA risk assessment, and on the lack of known cases of vCJD transmission from plasma-derived clotting factor products in the UK or anywhere else in the world. Given this information, the PHS believes that the potential risks of altering the standard current precautions with respect to reusable surgical and dental instruments, and instruments used for invasive procedures outweigh any potential benefits.

PHS agencies will continue to monitor and reevaluate the situation as new information becomes available.

Q. What can recipients of pdFVIII do with this information?

A. While no new actions are recommended now, you can stay informed by keeping in contact with a hemophilia specialist such as one at a Hemophilia Treatment Center if you are enrolled, to find out about new scientific advances in this field such as testing and diagnosis, and also to monitor your general health. In addition, FDA is encouraging physicians and patients to consider this information about pdFVIII and vCJD, in the larger context of known and potential risks for pdFVIII and alternative therapies when making treatment decisions.

Q. What are Hemophilia Treatment Centers, and where can I find out about them?

A. Hemophilia Treatment Centers (HTC) are a network of federally funded, comprehensive care clinics that promote the management, treatment, and prevention of complications experienced by persons with hemophilia and other hereditary bleeding disorders.

You can find information about HTC's on the following CDC websites:

1. CDC informational posting, containing information about the kinds of services provided by federally funded HTC's, at: http://www.cdc.gov/ncbddd/hbd/care_model.htm

2. A directory of federally-funded HTC's is available at http://www.cdc.gov/hbd/htc_list.htm.

3. Regional HTC websites are also a good place for information

Q. Where can I find more information about vCJD and pdFVIII?

A. You can find additional information on these websites

FDA

1. FDA informational posting, containing current pdFVIII risk assessment, fact sheet, and briefing materials: http://www.fda.gov/ohrms/dockets/ac/cber06.html

2. Blood Products Advisory Committee meeting – summary of recent TSEAC meeting and statement about FXI from the UK, on October 21, 2006: (http://www.fda.gov/ohrms/dockets/ac/04/transcripts/2004-4074t1.htm)
3. TSEAC meeting with discussion of first FXI draft risk assessment, on February 8, 2005, and discussion of UK risk communication for plasma derivatives: http://www.fda.gov/ohrms/dockets/ac/cber05.html#TransmissibleSpongiform
4. TSEAC Meeting with further discussion of the FDA risk assessment model, October 31, 2005: http://www.fda.gov/ohrms/dockets/ac/cber05.html#TransmissibleSpongiform
5. TSEAC Meeting with update on FXI risk assessment, September 18, 2006: http://www.fda.gov/ohrms/dockets/ac/cber06.html#TransmissibleSpongiform

CDC

Information on vCJD: Center for Disease Control and Prevention, at http://www.cdc.gov/ncidod/dvrd/vcjd/index.htm

Regional HTC websites

USDA

Information on bovine spongiform encephalopathy ("Mad Cow Disease"): US Department of Agriculture, at http://www.aphis.usda.gov/newsroom/hot_issues/bse.shtml

Patient Organizations:

1-800-HANDI
National Hemophilia Foundation
Hemophilia Federation of America
Committee of Ten Thousand
World Federation of Hemophilia

Questions to FDA may be addressed through the Office of Communication, Training, and Manufacturers Assistance (OCTMA), at 1-800-835-4709, or octma@cber.fda.gov.