

**POTENTIAL vCJD RISK FROM US LICENSED PLASMA-DERIVED
FACTOR VIII (PDFVIII, ANTIHEMOPHILIC FACTOR) PRODUCTS:
Summary Information**

Key Points:

- In recent years, questions have been raised concerning the risk from variant Creutzfeldt-Jakob disease (vCJD) to hemophilia A and von Willebrand disease patients who receive US licensed plasma-derived Factor Eight (pdFVIII, Antihemophilic Factor) products. Since 2003, three people, all in the UK, have probably acquired the vCJD agent through blood cell transfusions. This has increased concern for the potential of vCJD transmission by blood products.
- The principal concern is to what extent if any, there could have been contamination of U.S. clotting factors with vCJD. This is particularly true of donors who may have traveled to countries with a higher prevalence of vCJD and BSE than in the U.S.
- Variant Creutzfeldt-Jakob Disease originally came from a disease in cattle called bovine spongiform encephalopathy (BSE, or "mad cow disease"). Transmission of the BSE agent to humans, leading to vCJD, is believed to occur primarily via ingestion of cattle products contaminated with the BSE agent. Both BSE and vCJD are invariably fatal brain diseases with incubation periods typically measured in years.
- From 1995 through October 2006, 196 human cases of vCJD were reported worldwide, with 162 cases in the United Kingdom (UK), and with two cases in the United States. The two human cases in 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 (new case reports) in the UK peaked in 1999 and has been declining 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.

- Based on a recently completed risk assessment, the US Public Health Service, including FDA, CDC, and NIH, believes that the risk from vCJD to hemophilia A and von Willebrand disease patients who receive US licensed pdFVIII products is most likely to be extremely small, although we do not know the risk with certainty.
- FDA, CDC, and NIH are not aware of any cases of vCJD having been reported worldwide in patients with hemophilia or other blood clotting disorders. This includes those who have received, over a long period of time, large amounts of blood clotting products manufactured from plasma donations from the UK where the risk of vCJD is highest.
- In the United States, pdFVIII products have not been made from the plasma of anyone known to have developed vCJD, and no one who received any of these products is known to have developed vCJD. There is no test yet available to detect vCJD infection in healthy donors or recipients.
- FDA used a computer model to assess the risk of vCJD from the current use of these products. However, there are many major uncertainties in the computer model, and a precise estimate of the risk is not currently possible. Again, there is no test yet available to detect vCJD infection in healthy donors or recipients.
- Contacting a hemophilia specialist such as one at a Hemophilia Treatment Center is a good way to learn about new information as it becomes available. More information about Mad Cow Disease and vCJD is available on these websites:

- Centers for Disease Control and Prevention:
<http://www.cdc.gov/ncidod/dvrd/vcjd/index.htm>
- US Department of Agriculture: <http://www.usda.gov>
- Information also may be obtained from:
1-800-HANDI; the National Hemophilia Foundation;
Hemophilia Federation of America; Committee of Ten
Thousand; World Federation of Hemophilia

Additional information:

Approximately 2,500 people with hemophilia A and 250 people with severe von Willebrand disease use pdFVIII products in the US. pdFVIII is manufactured from the plasma of thousands of blood donors and is used to prevent or treat bleeding episodes. Although pdFVIII products are **not** made from plasma donated by anyone known to have developed vCJD, it is still hypothetically possible that a person using pdFVIII could have been exposed to the agent that causes vCJD if someone who felt well was carrying the infection at the time of blood or plasma donation.

The FDA, CDC, and NIH have no knowledge of any connection between plasma-derived clotting factor use, including pdFVIII, and the development of vCJD. The steps used to manufacture plasma-derived products have the potential to remove the vCJD agent if it were present. Also, the US has taken steps to reduce the potential vCJD risk from blood and plasma by deferring donors who visited or resided in countries where BSE and vCJD prevalence is relatively high.

Because of the finding that blood cell transfusions probably can transmit vCJD, FDA used a computer model to conduct a risk assessment to estimate the possible risk of vCJD that might occur from the use of US-licensed pdFVIII products that are on the market today. A person could be at risk if a blood donor unknowingly carried the vCJD agent at the time of donation.

The risk assessment results suggest that the risk from vCJD to hemophilia A and von Willebrand disease patients who receive US licensed pdFVIII products is most likely to be extremely small in the United States.

Because of many unknowns, it is not possible to precisely estimate a person's individual risk. There is no test to determine if a person has been exposed to vCJD.

There have been no reports of vCJD in patients using any plasma-derived clotting factor in the UK, where the risk is highest, or anywhere else in the world.

While the FDA, CDC, and NIH believe that the risk of vCJD is most likely to be extremely small, we think it is important that a person who receives pdFVIII be aware of this issue. We also believe it is important that the patient has the opportunity to discuss any questions he or she may have with a suitable health care provider, such as a hemophilia specialist.