QUICK SUMMARY

TRANSMISSIBLE SPONGIFORM ENCEPHALOPATHIES ADVISORY COMMITTEE

February 12 & 13, 2004

This quick summary is provided as an unofficial overview of the February 12 & 13, 2004 TSEAC meeting until the official transcripts become available.

Topic # 1 – Informational presentations on risk of transfusion transmission of variant Creutzfeldt-Jakob Disease (vCJD)

Dr. Robert Will, National CJD Surveillance Unit discussed the presumptive transfusion-transmitted case of vCJD in the U.K. The recipient was one of 48 people who are known to have received blood from donors incubating vCJD. (Twelve have survived more than four years after the transfusion.) Dr. Will estimated that the likelihood of the recipient, age 62, contracting vCJD from non-transfusion BSE exposure in the U.K. was between 1/15,000 and 1/30,000. Dr. James Sejvar, Centers for Disease Control, reviewed CJD Surveillance in the United States. Both the speaker and the Committee were concerned that the general rate of autopsies in the U.S. is very low, compromising efforts to identify cases of CJD; efforts are being made by the CDC, in cooperation with state public health authorities, to increase the likelihood of obtaining tissue from possible CJD cases in the U.S. Dr. Steven Anderson, FDA, then presented a comparison of the transfusion risk of CJD vs. vCJD, based upon transfusion lookback studies. He found that current data are insufficient to demonstrate a statistically significant difference due to small numbers. Dr. Robert Rohwer presented rodent TSE transfusion transmission studies, including a leukodepletion experiment. In the hamster experimental model this experiment demonstrated that only about half the infectivity was removed by leukofiltration. Dr. Paul Brown reviewed current studies of transfusion-transmission of TSEs in primates. Squirrel monkeys received transfusions of blood components from squirrel monkeys infected with vCJD, sCJD, or GSS (Fukuoka-1 strain). Five years after transfusion, one transmission has been reported in a recipient of blood from a GSS-infected donor monkey. The experiment is ongoing. Committee members expressed concern regarding the risk of transfusion transmission of vCJD. They encouraged more studies and support to continue ongoing studies in order to obtain more information on the transfusion transmission of vCJD and CJD. At the open public hearing, concern was expressed that families have great difficulty in obtaining diagnoses of CJD and reporting these to the CDC. Members were also concerned about safety of surgical instruments reused after exposure to patients with CJD.

Topic # 2 – Update on Bovine Spongiform Encephalopathy (BSE) in the United States

The Committee listened to presentations from the USDA (APHIS and FSIS) regarding the reported case of BSE in Washington State and heard an overview of steps now in place or currently being implemented to reduce the risk for further occurrence of BSE in

this country. These measures include enhanced USDA Food Safety Regulations for BSE and several others planned by FDA, as well as the implementation and enforcement and planned augmentation of FDA's rule prohibiting the feeding of most mammalian proteins to ruminants (the ruminant "Feed Ban").

Topic #3 - Models for Risk-Based Sourcing of Bovine Materials in FDA-regulated medical products

The Committee listened to two BSE-related risk assessment studies, one from the Harvard Center for Risk Analysis mainly directed at the risk of BSE for U.S. cattle, and one from FDA estimating the possible risk of human exposure to the BSE agent in the U.S. They then discussed factors to consider in risk-based sourcing models for bovine materials. While the Committee did not vote, several members requested more inspection and better compliance of the U.S. Feed Ban along with more testing of cattle, including apparently healthy animals. Members were encouraged that the USDA had detected BSE in the U.S.; and suggested that representatives of all U.S. government agencies involved in protecting the country against BSE meet and take all steps needed to assure public safety. They endorsed implementing the national tracking system for cattle proposed by the USDA (especially for imported animals), better risk assessment studies, and testing of more cattle. (Some members suggested routine testing of all cattle over 30 months of age.) Members felt that additional BSE surveillance would enable a better assessment of the risk to food and medicinal products in the U.S. Committee members requested a review of how various European countries had responded to the recognition of BSE and suggested that the U.S. might implement those procedures that had been most effective.

Topic #4 - Minimizing risks of TSE agents in FDA-regulated medicinal products

The Committee listened to a series of overviews by FDA staff of the current safeguards in place for assuring the safety of blood products, human tissues, vaccines and other biologics, drugs, medical devices, and foods, including dietary supplements. The Committee also heard a summary of European (EMEA) guidelines for safeguards regarding ruminant materials used to manufacture medicinal products. In Open Public Hearing, a representative of Pall Corporation mentioned early efforts to remove prions from plasma by the use of a novel filter. Members then discussed the need for additional safeguards in the U.S. in light of the recent case of presumptive transfusion-transmission of vCJD in the U.K. and the report of a BSE-positive cow here. The Committee had not been asked to vote on any specific recommendations, however, members did agree that that FDA had done an excellent job by anticipating the transfusion-transmitted case; they then discussed a number of additional major steps that might be taken to increase safety of and public confidence in FDA-regulated products containing or manufactured from bovine-derived materials.

Committee members saw a need to increase testing of cattle entering the U.S. food chain, full traceability of livestock and better compliance with the U.S. Feed Ban (including

assurances that it is scrupulously implemented at the farm level). Some committee members requested more realistic risk assessment studies of the current BSE situation and increased efforts to define the real magnitude of the BSE problem in the U.S. These members proposed that the government collect more data and re-examine the current assumptions used for USDA and FDA risk assessment models. Some committee members cautioned that, due to the increasing number of countries recognizing BSE, current FDA policies for sourcing of animals for medicinal products based solely on geography (from "BSE-free" countries) might no longer be feasible. The few remaining countries of impeccable BSE-free status may not be able to meet the demand for bovine-derived materials. The Committee agreed that, for bovine-derived materials used in the manufacture of injectable and implantable medical products, some system for careful sourcing of animals, perhaps using selected herds ("negligible-risk" herds), might now be considered.

Committee members encouraged conducting more studies to determine the clearance (removal or inactivation) of TSE agents from high-risk products. Several committee members requested the complete prohibition of high-risk bovine materials in medicinals, foods and dietary supplements. Committee members also requested that labeling disclose the country of origin for bovine materials used in these products. Members repeated their request for meetings of senior federal officials (USDA, CDC, NIH & FDA) to coordinate U.S. government efforts in reducing the potential health risks from BSE in this country.

Regarding the nation's blood supply, committee members expressed satisfaction that the current donor deferrals now in place were effective and concluded that that placing more restrictions on donors at this time would decrease supply and not be beneficial. The Committee discussed the implications of experimental studies on effects of leukoreduction on blood-borne scrapie infectivity with special concern that a substantial portion of infectivity remained in plasma after this procedure. Members agreed that leukoreduction of donated blood cannot be relied upon to decrease CJD agent infectivity in blood components significantly and should not replace the donor deferral policy. For vaccines, the Committee recommended that more studies be done on the susceptibility of cell cultures to prion infectivity in order to determine the risk of products made from master seed and cell banks manufactured using bovine materials from BSE countries or of unknown source.