Quick Summary for the Transmissible Spongiform Encephalopathies Advisory Committee (TSEAC)

February 20, 2003

(revised 2/24/03)

This quick summary is provided as an unofficial overview of February 20, 2003 TSEAC meeting until the transcripts are available.

The Committee received an update on the blood supply since the implementation of the variant Creutzfeldt-Jakob Disease (vCJD) final guidance by FDA on October 31, 2002. They were informed of Health and Human Services (HHS) goals to monitor blood shortages, long-term collection and utilization trends, and inventories at major collection facilities and reserve depots. They received an overview of FDA's new TRANS-Net Blood and Reagent Shortage Monitoring System and a brief summary of the existing DHHS program to monitor blood inventories at 26 "sentinel" hospitals and 3 community blood collection centers. The Committee then listened to presentations from blood centers and related organizations on their efforts to monitor current blood supplies and their concerns in meeting future demands on this supply. Consensus from blood industry speakers was that the new vCJD deferral guidance had a substantial but not yet quantified impact on blood supply.

The Committee also received an update on variant CJD and bovine spongiform encephalopathy **(**BSE) epidemiology and measures being taken in different countries to protect humans from food-borne exposures to the BSE agent.

The Committee's charge was to determine if FDA should consider adding a labeling claim for transmissible spongiform encephalopathy (TSE) agent clearance in plasma derivatives, in cases where manufacturers have submitted detailed clearance studies demonstrating robust and reproducible TSE removal. Dr. Mahmood Farshid (OBRR/FDA) presented information on validation of viral clearance from plasma derivatives, as a paradigm for studies of TSE clearance in the manufacture of plasma derivatives. Dr. Dorothy Scott (OBRR/FDA) then reviewed the challenges inherent in TSE agent clearance studies and the degree to which variations in specific manufacturing procedures can affect TSE partitioning. Dr. Stephen Anderson (OBE/FDA) then presented a model risk analysis for the likelihood of TSE (CJD and vCJD) agents in three plasma-derived products based upon specific published TSE clearance data. The model accounted for prevalence of donors incubating CJD and vCJD, the maximum probable titers of TSE agents in human blood, plasma pool size, specific TSE clearance during steps for manufacturing each product, and dose of final product that a patient may receive annually. The committee then heard a presentation from Dr. Sol Ruiz, outlining the current European Agency for the Evaluation of Medicinal Products (EMEA) thinking on risk reduction for TSE in plasma derived products. Dr. Henry Baron presented industry-generated data from TSE clearance studies, including summed clearance steps for different products, comparison of clearance of animal-adapted TSE agents to human

TSEs, bridging of bioassays to Prp^{Sc} immunoassays, and comparison of different types of infectious TSE preparations used as spiking materials in clearance studies.

After discussion of the current label for plasma products and the possible effects that could result from changing that label, the Committee was asked the following questions:

- Assuming adequacy of decontamination procedures in product manufacturing, should FDA consider labeling claims for TSE clearance in plasma derivatives, based upon specific demonstration of TSE removal during manufacturing?

  The Committee voted: 12 yes, 1 no, 0 abstained.

- If so, please comment on whether such data would support the following draft wording for labeling:

  > "Because this product is made from human plasma, it carries the risk of transmitting infectious agents, e.g. viruses, and, theoretically, the CJD agent. It has been demonstrated that [the manufacturer]'s manufacturing process provides substantial clearance of agents similar to those causing CJD and vCJD. Thus the theoretical risk of transmission of CJD or vCJD is considered extremely remote."

Some committee members expressed concern over having products with two different labels and the impact that this would have on product cost, use, and medical insurance reimbursement. The Committee also made several suggestions for consideration by FDA regarding wording changes in the label such as separating statements regarding viruses and TSE's, and a suggestion to be more quantitative. The Committee discussed the need to standardize the type of studies and the magnitude of reduction that should be demonstrated in order for a product to be considered eligible to receive the new label. They suggested that FDA proactively consider how to evaluate TSE clearance studies and that FDA prospectively define evaluation parameters. The Committee was in agreement that validation of TSE agent clearance in the manufacturing of plasma products was important and that sponsors should be encouraged to perform these studies, and provide that information in the form of official submissions, to FDA.

Please refer to the committee transcripts for a detailed account of the meeting.