Executive Summary

In December 2003, the United States Department of Agriculture (USDA) announced the discovery of a cow with bovine spongiform encephalopathy (BSE or "mad cow disease") in Washington State. Shortly thereafter, the Secretary of Agriculture announced several new steps designed to further reduce the risk that meat from affected animals would reach humans. Following that time, the Food and Drug Administration (FDA) considered new rules to help prevent the spread of BSE among cattle through contaminated animal feed. USDA Secretary Veneman convened a panel of international experts (formally known as the International Review Subcommittee of the Secretary's Advisory Committee on Foreign Animal and Poultry Diseases) to evaluate USDA's investigation of the BSE cow and BSE risk management measures and to advise USDA regarding possible further steps to address BSE in the United States.

We have used the simulation model developed by the Harvard Center for Risk Analysis (HCRA)(Cohen 2003a; Cohen 2003b) to evaluate the risk of BSE spreading among cattle in the U.S. and the potential for humans to be exposed to contaminated tissues. We model the response of the U.S. agricultural system for 20 years following the import of BSE-infected cattle. Key predictions made by the HCRA simulation model include the number of additional new cases of BSE that develop subsequent to the hypothetical introduction of infected animals into the U.S., the amount of BSE infective agent, measured as cattle oral $ID_{50}s$ potentially available in human food, and the epidemic's basic reproduction rate, R_0. We present results as distributions reflecting the probabilistic nature of the model and the processes simulated. In addition, we conduct sensitivity analyses to evaluate the extent to which alternative assumptions shift these distributions.

Our updated "base case" represents the circumstances in the U.S. prior to the December 2003 discovery of the animal with BSE in Washington State. We then analyze the impact of risk management measures adopted by USDA, considered by FDA, or proposed by the International Review Subcommittee since that discovery[1].

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[1] Just before the completion of this report, FDA published proposed rules governing the disposition of animals that die before being sent to slaughter. This analysis does not consider those proposals (see *Federal Register*, 70(193): 58569-58601, October 6, 2005).

Because of updated scientific data about infectious tissues, new information about compliance with the FDA feed controls, new assumptions regarding beef consumption, and structural changes in the model related to the disposition of non-ambulatory cattle, the base case projections differ slightly from those reported in our October, 2003 BSE Final Report (Cohen 2003a).

In addition, because of interest by the USDA Food Safety Inspection Service (FSIS) in how rule changes might affect the contribution of specific tissues to potential human exposure, we took steps to ensure greater numerical stability and more reliable representation of very low probability events. First, we conducted 750,000 trials of our standard base case scenario. That scenario models the U.S. cattle population and contamination of the human food supply for 20 years following the introduction of 10 BSE-infected cattle. For computational convenience, we then decreased the number of trials conducted (from 750,000 to 50,000 per scenario) and increased the number of infected animals introduced (from 10 to 500). Effectively, the numerical precision of a set of trials (expressed as the standard error of the mean divided by the estimated mean) depends on the product of the number of trials run and the number of infected animals introduced. Hence, the 50,000 trials of the base case with 500 infected animals introduced (25 million infected animals introduced in total) yielded even more precise estimates than the 750,000 trials of the base case with 10 infected animals introduced (7.5 million infected animals introduced in total).

Results indicate that the arithmetic mean of the resulting projections scaled by the ratio of the number of infected animals introduced (i.e., by 500 divided by 10, or 50). For example, the average number of new BSE infections increased from 3.5 animals to 180 animals (rounded to two significant digits), while the average contamination of human food increased from 75 cattle oral ID_{50}s to 3,800 ID_{50}s. Although the introduction of 500 BSE-infected cattle into the U.S. is extremely unlikely, this scenario allowed us to achieve satisfactory numerical stability using far less computer time. For this reason, all alternative scenarios and sensitivity analyses assumed the introduction of 500 infected cattle. In evaluating the results of the analyses in this report it should be recognized that the hypothetical introduction of 500 infected animals is simply for computational convenience and has no basis in any estimate of potential U.S. risk.

Sensitivity analysis identified the assumed rate of misfeeding (*i.e.*, the deliberate or accidental administration to cattle of feed containing ruminant protein and designated for non-

ruminants only) as an important parameter. Assigning the misfeeding rate the pessimistic value assumed in our sensitivity analysis increased the expected number of new BSE cases over 20 years by a factor of almost 15 compared to the base case (*i.e.*, from 180 to 2,600), while the mean value of R_0 increased from 0.24 in the base case to 0.89. However, information available to quantify the misfeeding rate at the time this analysis was conducted was extremely limited, leading to a wide range of estimates for this influential parameter. Better information would substantially narrow the range of plausible projections generated by the model. Lengthening the assumed incubation period by a factor of two decreased the mean number of newly BSE-infected cattle from 180 to 43 and potential human exposure from 3,800 cattle oral ID_{50}s to 1,900 cattle oral ID_{50}s. Other parameters evaluated as part of the sensitivity analysis (mislabeling and contamination rates, render reduction factors, beef on bone consumption rates, and the success of *antemortem* inspection at detecting clinically ill BSE cattle) were far less influential.

We found that the food safety measures enacted by USDA all reduce potential human exposure to BSE infectivity but have little effect on spread of BSE in the cattle population. Removing non-ambulatory ("downer") cattle from the human food supply reduces predicted potential human exposure by about 3% (leaving a mean of 3,700 cattle oral ID50s). Removing high risk tissues, often called specified risk materials or SRMs, from animals over 30 months of age almost completely eliminates potential human exposure, reducing it to 11 cattle oral ID_{50}s. Prohibiting only the use of advanced meat recovery (AMR, derived from the skull and backbone) on animals over 30 months of age reduces potential human exposure by approximately two-fifths to 2,200 ID_{50}s. It is worth noting that these are relative reductions to what is already a small risk in absolute terms, especially in light of the fact that these simulations reflect the assumed introduction of 500 infected cattle into the U.S. None of the combined measures yielded substantial improvements over their components.

We evaluated two measures under consideration by FDA, including a prohibition on the use of ruminant blood in ruminant feed, and the requirement that plants producing both prohibited material (*i.e.*, ruminant-derived material) and non-prohibited material use dedicated production lines. Our analysis indicates that neither of these actions would have much impact on the spread of BSE. Our earlier report (Cohen 2003a) concluded that blood contributes relatively little to the spread of BSE. Similarly, our earlier work suggests that cross-contamination is a relatively minor factor.

The International Review Subcommittee convened by Secretary Veneman has suggested the possibility of a ban on specified risk material from animals 12 months and older for both human food and animal feed. We evaluate the impact of this ban assuming perfect compliance. Our analysis suggests that this measure is extremely effective at reducing potential human exposure, decreasing it by more than 99% relative to the base case. Because we assumed that the ban also removes SRMs from dead stock prior to their rendering, the measure achieves a substantial reduction in the spread of BSE among cattle, decreasing the number of new infected BSE cases in the U.S. to 35 from 180. We predict that another suggestion made by this group, the removal of all animal-derived protein from cattle feed, would decrease the number of new BSE cases from 180 to 170 over 20 eyears. The remaining cases result primarily from misfeeding of rations containing ruminant proteins (feed intended for other species), to cattle. This measure has a small predicted impact on potential human exposure.

Overall, it is clear that by eliminating the most BSE-infectious tissue from human food, specified risk material bans have a substantial impact on potential human exposure. Eliminating this material from cattle feed can have an important impact on the spread of BSE among cattle if steps are taken to ensure that such bans also cover dead stock. It is important to note that we have not systematically evaluated all possible SRM bans (*e.g.*, prohibitions that set cutoffs at different ages than those evaluated here). Nor have we evaluated the potential risks resulting from the disposal of SRMs and other costs associated with these bans.