

confirmed from the experimentally infected cattle as early as 6 months post-exposure. In this proposed rule, we take these findings into account when establishing measures to mitigate the risk of infectious levels of the BSE agent being present in animals and animal products imported from a BSE minimal-risk region. For example, with regard to bovines, because BSE infectivity has not been found in most bovine tissues until at least 32 months post-exposure, we believe that by requiring that bovines imported into the United States from BSE minimal-risk regions be less than 30 months of age, the risk of the BSE agent being present at infectious levels in most tissues in the animal is minimized. The 30-month age limit is accepted internationally in BSE standards set by various countries and is consistent with OIE recommendations. Similarly, the proposed regulations would require that imported meat from bovines be derived from animals less than 30 months of age when slaughtered. However, because of evidence that the BSE agent may be present at infectious levels in the distal ileum of infected bovines as early as 6 months post-exposure, we would require that the intestines of bovines imported into the United States be removed at slaughter, and that meat imported from bovines from BSE minimal-risk regions be derived from animals from which the intestines were removed at slaughter.

Although the risks associated with age can be mitigated by accepting for import only animals or commodities derived from animals of an age where even high risk tissues (discussed below) are unlikely to have infectious levels of the BSE agent, restrictions applicable to age alone may not always be possible or sufficient. For instance, in the case of wild cervids, because it is not always possible to determine the age of the cervids, we believe that alternative risk measures, discussed below, are necessary.

Research demonstrates that the incubation period for BSE is apparently linked to the infectious dose received—*i.e.*, the larger the infectious dose received, the shorter the incubation period (EU SSC 2002). While some cases of BSE have been found in animals less than 30 months of age, these are relatively few and have occurred primarily in countries with significant levels of circulating infectivity (*i.e.*, where infected ruminants are used for feed for other ruminants, which in turn become infected). The conditions, discussed above, for qualifying for a BSE minimal-risk region guard against such circulating infectivity.

Similar observations regarding the importance of the size of the infectious dose were made in sheep and goats (EU SSC 2002). In these animals, infectivity could not be demonstrated in most tissues until at least 16 months post-exposure to the agent.

In summary, infected cattle over 30 months of age or sheep and goats over 16 months of age may have levels of the abnormal prion in affected tissues that are sufficient to infect other animals fed protein derived from these tissues. Infected animals less than 30 months of age or sheep and goats less than 16 months of age are unlikely to have infectious levels of the prion protein (EU SSC 2002; Wells, *et al.*; 1994; Wells, *et al.*; 1998).

Animals that were born before the feed ban but were not fed risk material, such as wild ruminants or domestic livestock in the minimal-risk region that were fed solely materials that are extremely unlikely to contain the infectious agent, are unlikely to contain infectious levels of BSE.

#### *Tissue Localization*

Some bovine tissues have demonstrated infectivity, whereas others have not. Tissues that have demonstrated infectivity, and thus are likely to contain the infectious agent in infected cattle, are brain, tonsil, spinal cord, eyes, trigeminal ganglia, dorsal root ganglia, and distal ileum. (Please note that, as discussed above, the age of an animal is a key factor in whether the animal is likely or unlikely to be infected. Cattle less than 30 months of age unlikely to be infected with BSE, and, therefore, even the tissues listed above, except for the distal ileum, from such animals are unlikely to contain the infectious agent.) Affiliated tissues or structures such as skull or vertebral column are considered risk materials because of the difficulty in separating out small tissues such as dorsal root ganglia from the vertebral column. Possibilities for cross contamination from risk materials must be considered also. However, even cattle carrying the infectious agent are unlikely to carry that agent in tissues that have not demonstrated infectivity (*e.g.*, muscle, liver, skin, hide, milk, embryos) or products derived from these tissues<sup>5</sup> (also, Wells, *et al.*; 1994; Wells, *et al.*; 1998).

The risks associated with tissue localization can be mitigated by accepting only tissues that are unlikely

to have infectious levels of the agent, due to the nature of the tissue or the age of the animal (in cattle under 30 months of age, only the distal ileum is such a risk material), or commodities derived from those tissues.

#### *Source Species*

Tissue distribution of the agent varies with species. Results from experimental infections of sheep have shown that the BSE prion is distributed more widely in sheep tissues than in cattle.<sup>6</sup> This distribution is similar to the distribution of scrapie (a transmissible spongiform encephalopathy present in the United States) infections in sheep. In these infections, the agent may be found in the lymphoreticular system and in peripheral nerves (Foster *et al.*; 1996; Foster *et al.*; 2001).

However, no natural infections with BSE have yet been confirmed in sheep, although testing is ongoing in Europe. Similarly, no natural infections have been confirmed in goats, although actual experiments have not been conducted in the species. In the absence of actual data, distribution of the agent in goat tissues has been assumed to be similar to distribution of the agent in sheep tissues, based on the fact that scrapie acts very similarly in sheep and goats.

Similarly, natural infection of cervids (deer and elk species) with BSE has not been documented, and no challenge studies on cervid susceptibility to BSE have been conducted. In the absence of actual data, it is assumed that distribution of any BSE agent in cervid tissues would be similar to the distribution of the chronic wasting disease agent in cervid tissues, which is a naturally occurring transmissible spongiform encephalopathy.

#### *Prevalence of BSE*

The possible prevalence of disease in the region of origin will influence the risk. Prevalence of the disease will be lower in a country with adequate prevention and control measures; thus, animals from such a region will be at lower risk of being exposed to infection. The risks associated with prevalence can be mitigated by accepting commodities only from a country with low prevalence that can be classified as minimal or low risk.

<sup>5</sup> Wrathall, A.E., *et al.*; 2002; Studies of embryo transfer from cattle clinically affected by bovine spongiform encephalopathy (BSE); Veterinary Record; 150; pg 365–378.

<sup>6</sup> Foster, J.D., *et al.*; 1996; Detection of BSE infectivity in brain and spleen of experimentally infected sheep; Veterinary Record; 139; pg 912–915.  
Foster, J.D., *et al.*; 2001; Distribution of the prion protein in sheep terminally affected with BSE following experimental oral transmission; J. Gen. Virol.; 82; pg 2319–2326.