



## Fish and Prions: Meat and Bone Meal Is Safe For Aquaculture Feeds

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### Issue:

Meat and bone meal (MBM) is a by-product of the animal rendering industry and less expensive than fish meal. MBM is high in protein, generally digestible to most fish, and a good source of minerals. Ash content may limit the use of MBM in fish feeds. Research has demonstrated that MBM can partially or totally replace fish meal when used at levels of 5% to 15% in fish feeds provided that the feed is formulated to contain adequate amounts of essential amino acids.

Recently, there has been speculation about the safety of eating farmed fish that have been fed MBM rendered from cattle because farmed fish could be infected by prions, the causative agents of Transmissible Spongiform Encephalopathies (TSEs). The speculation is that the fish could subsequently transmit variant Creutzfeldt-Jakob disease (V-CJD) to humans.

### Background:

Proteinaceous infectious agents (prions) are hypothesized to be the principle cause of TSEs in animals. Usually, prions refers to the aggregates of prion protein (PrP), a normal membrane binding glycoprotein with unknown physiological function found in fish, reptiles, amphibians, birds and mammals (Liao et al. 2005). The function of the prion protein remains unknown, but is known to be bound to the external surface of cells and found in many body tissues, the highest levels being found in the brain. While it has been reported that the passage of TSE agents between animals of different species is usually impaired by the species barrier, the scientific community has conducted experiments using different animal species, including fish, as recipients of a TSE (sheep scrapie) agent to answer public concern about safety of food possibly contaminated with TSE agents.

### Research:

Sequence data documenting the existence of PrP's in fish has revealed the presence of this transcript in various tissues of fish species such as gilthead sea bream (*Sparus aurata*), Japanese seabass (*Lateolabrax japonicus*), Japanese flounder (*Paralichthys olivaceus*), and Fugu (*Takifugu rubripes*). PrP's can be found in the brain, spleen, and heart (Christen et al. 2008; Favre-Krey et al. 2007; Liao et al. 2005). Indeed, PrP's in fish are quite different from mammalian prions according to the detailed genetic analyses conducted by the authors.

Multiple *in vitro* and *in vivo* experiments have showed that fish tissues taken at different time points after oral or parenteral inoculation with PrP's cannot provoke scrapie disease after intracerebral inoculation in recipient mice (Loredana et al.

2006). In a more recent study, the group by Dala Valle et al. (2008) investigating prion infectivity in fish, found that PrP's can be absorbed by the intestinal mucosa and that it persisted in the fish gastrointestinal tract for up to 3 days in pyloric caeca and for up to 7 days in the distal intestine. However, they did not remain longer than 15 days in the fish intestine and furthermore they did not cross the intestinal barrier.

### **Practical Considerations:**

It is also important to note that a very large proportion of fish feeds are manufactured using extrusion. Extrusion is a type of high pressure and temperature cooking and effective in destroying misfolded prions. In the unlikely event that that prions could make their way into fish feeds, the number and infectivity potential would be almost completely destroyed by feed processing.

It's also important to remember:

- BSE has been extremely rare in the U.S. and extensive testing for the past several years indicates it may be eradicated. (Among the 735,213 cattle sampled in the 7 years prior to March 17, 2006, two infected indigenous animals were identified in addition to the 2003 imported cow from Canada. All three were animals born before the U.S. banned the practice of feeding recycled ruminant protein to other ruminants. The USDA BSE surveillance continues, and will detect BSE at 1 infected animal per 1,000,000 adult cattle. No cases have been detected in the U.S. for more than three years.) The probability of the presence of defective prions in MBM is extremely low.
- The rendering process reduces the infectivity of defective prions by 100 to 1000 fold, so even if they were present, the chance of an infective dose in MBM would be even more remote.
- New feed regulations from FDA remove what little risk remains by requiring the removal of brain and spinal cord (and thus, the main source of prions) from all cattle over 30 months before rendering for animal (or fish) feed.

### **Conclusions:**

The unique characteristics of prions will offer many new avenues for research. There is compelling evidence of the role of prions in TSE diseases, but the cause - effect relationship in animals remains a hypothesis.

Research shows that PrP's can persist in intestinal and caeca submucosa of fishes (Chiesa & Harris 2009) following oral administration. However, the hypothesis in mammals that misfolded prions are multiplied in the intestine and then exported is not the same in fish, as the fish intestine produces a very small amount of prions and the wrong kind.

The theory that fish fed MBM though either natural feeding or manufactured feeds play a role in the transmission of TSE's is far from a scientific validated statement. To suggest additional regulation is needed "just in case," because "we don't know for sure" would be irresponsible.

## References

Chiesa R. and D.A Harris (2009) Fishing for Prion Protein Function. PLOS Biology 7(3): e75

Christen B., K. W. Thrich and S. Hornemann (2008) Putative prion protein from Fugu (*Takifugu rubripes*). FEBS 275: 263-270

Favre-Krey L., M. Theodoridou, E. Boukouvala, C. H. Panagiotidis, A. I. Papadopoulos, T. Sklaviadis and G. Krey (2007) Molecular characterization of a cDNA from the gilthead sea bream (*Sparus aurata*) encoding a fish prion protein. Comparative Biochemistry and Physiology, Part B 147: 566–573

Liao M., Z. Zhang, G. Yang, X. Sun, G. Zou, Q. Wei, and D. Wang (2005) Cloning and characterization of prion protein coding genes of Japanese seabass (*Lateolabrax japonicus*) and Japanese flounder (*Paralichthys olivaceus*). Aquaculture 249: 47– 53

Loredana I., B. Novoa, A.Z. Dalla, F. Cardone, R. Aranguren, M. Sbriccoli, S. Bevivino, M. Iriti, Q. Liu, V. Vetrugno, M. Lu, F. Faoro, S. Ciappellano, A. Figueras and M. Pocchiari (2006) Scrapie infectivity is quickly cleared in tissues of orally-infected farmed fish. BMC Veterinary Research (2):21-27

Rivera-Milla E., B. Oidtmann, C. H. Panagiotidis, M. Baier, T. Sklaviadis, R.Hoffmann, Y. Zhou, G.P. Solis, C. A. O. Stuermer, and E. Malaga-Trillo (2005) Disparate evolution of prion protein domains and the distinct origin of Doppel- and prion-related loci revealed by fish-to-mammal comparisons. FASEB Article doi:10.1096/fj.05-4279fje

Dalla Valle A.Z., M. Iriti, F. Faoro, C. Berti and S. Ciappellano (2008) *In vivo* prion protein intestinal uptake in fish. APMIS (116): 173-180

USDA "BSE Ongoing Surveillance Plan" (Jul 20, 2006)  
[http://www.aphis.usda.gov/newsroom/hot\\_issues/bse/](http://www.aphis.usda.gov/newsroom/hot_issues/bse/)

USDA "An Estimate of the Prevalence of BSE in the United States" (July 20, 2006)  
[http://www.aphis.usda.gov/newsroom/hot\\_issues/bse/downloads/BSEprev-estFINAL\\_7-20-06.pdf](http://www.aphis.usda.gov/newsroom/hot_issues/bse/downloads/BSEprev-estFINAL_7-20-06.pdf)

## Contacts:

Sergio F. Nates, Ph.D., President, Fats and Proteins Research Foundation.  
Phone: 703-683-2914; e-mail: [snates@nationalrenderers.com](mailto:snates@nationalrenderers.com).

David L. Meeker, Ph.D., MBA, Senior Vice President, Scientific Services, National Renderers Association. Phone: 703-683-2633; [dmeeker@nationalrenderers.com](mailto:dmeeker@nationalrenderers.com).

National Renderers Association, 801 North Fairfax Street, Suite 205, Alexandria, VA 22314;  
phone, 703/683-0155; fax, 703/683-2626; e-mail : [renderers@nationalrenderers.com](mailto:renderers@nationalrenderers.com)  
Web site address: [www.nationalrenderers.org](http://www.nationalrenderers.org)