

Tentative translation

Food safety risk assessment relate to the use of pig-derived proteins in feed

October, 2007

Food Safety Commission

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History of deliberation

November 12, 2003	Requesting the food safety risk assessment by the Minister of Agriculture, Forestry and Fisheries to the Chairperson of the Food Safety Commission (Shou-An No.3367 as of November 11, 2003)
November 20, 2003	20th Meeting of the Food Safety Commission (Explanation of requests)
March 26, 2004	7th Meeting of the Prion Expert Committee
April 22, 2004	8th Meeting of the Prion Expert Committee
June 18, 2004	11th Meeting of the Prion Expert Committee
March 14, 2007	43rd Meeting of the Prion Expert Committee
June 28, 2007	45th Meeting of the Prion Expert Committee
August 7, 2007	46th Meeting of the Prion Expert Committee
August 23, 2007	203rd Meeting of the Food Safety Commission (report)
August 23 –	
September 21, 2007	Hearing of public opinion and information sessions
September 28, 2007	Report from the Chairperson of the Prion Expert Committee to the Chairperson of the Food Safety Commission
October 4, 2007	209th Meeting of the Food Safety Commission (report) Notification from the Chairperson of the Food Safety Commission to the Minister of Agriculture, Forestry and Fisheries

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1. Introduction

The Food Safety Commission was asked for their opinions on the food safety risk assessment (hereinafter, “risk assessment”) ¹⁾ related to the amendment of feed standards specified by the Law Concerning Safety Assurance and Quality Improvement of Feeds Related to the Use of Pig-Derived Proteins in Feed (Law No. 35, 1953) (hereinafter, “Feed Safety Law”), by the Ministry of Agriculture, Forestry and Fisheries according to the Food Safety Basic Law (Law No. 48, 2003) (relevant documents were received on November 12, 2003).

The Prion Expert Committee, referred to by the Food Safety Commission for risk assessment, conducted a review and reached the following conclusion: “We found no scientific evidence that the use of meat-and-bone meal, steamed bone meal and hydrolyzed protein derived from pigs and poultry (hereinafter, “pig-derived meat-and-bone meal”) as feed for pigs and poultry causes BSE infection and BSE transmission. Therefore, the direct food health effect on humans from using pig-derived meat-and-bone meal as feed for pigs and poultry can be negligible.” The Chairperson of the Food Safety Commission notified the Minister for Agriculture, Forestry and Fisheries of the following risk assessment results on June 24, 2004: “The use of pig-derived meat-and-bone meal in feed for pigs and poultry should be approved only in facilities where appropriate management for the prevention of cross contamination can be implemented. In addition, to aid scientific assessment of cross contamination, further efforts should be made in developing techniques with high sensitivity and accuracy, and a safety assessment system should be established in the future” ²⁾.

The Ministry of Agriculture, Forestry and Fisheries provided an explanation of the risk management measures, based on the risk evaluation results, at the 19th Meeting of the Prion Expert Committee (held on January 21, 2005), then decided to approve the use of pig-derived meat-and-bone meal in feed for pigs and poultry after April 1, 2005 as far as its manufacturing process was confirmed to separate from those of other animal-derived proteins by the Minister of Agriculture, Forestry and Fisheries ³⁾.

The use of pig-derived meat-and-bone meal as feed for fish culture was not reviewed because of insufficient data ²⁾.

Subsequently, since the data on the use of pig-derived meat-and-bone meal as feed for fish culture was submitted by the Ministry of Agriculture, Forestry and Fisheries ^{4), 5)}, and reviewed by the Prion Expert Committee at the 43rd Meeting of the Prion Expert Committee (held on March 14, 2007), the 45th Meeting of the Prion Expert Committee (held on June 28, 2007) and the 46th Meeting of the Prion Expert Committee (held on August 7, 2007).

2. Measures by the Ministry of Agriculture, Forestry and Fisheries

The Ministry of Agriculture, Forestry and Fisheries will amend the ministry ordinance according to the Feed Safety Law to approve the use of pig-derived meat-and-bone meal as feed for fish culture.

For usage, the following measurements as those required for the use of pig-derived meat-and-bone meal as feed for pigs and poultry are required;

- Materials should be separated from other animal-derived proteins at material collection sites (i.e. slaughterhouses, distributors, etc.) to prevent contamination.
- Dedicated containers should be used for material transport and management using

material-supply management sheets should be conducted.

- Manufacturing of pig-derived meat-and-bone meal should be completely separated from the manufacture of other animal-derived proteins.
- Manufacturing records should be kept for 8 years.
- Dedicated containers should be used for the transport of manufactured pig-derived meat-and-bone meal, and management using supply management sheets for pig-derived meat-and-bone meal should be conducted.

3. Pig-derived meat-and-bone meal

Pig-derived meat-and-bone meal is defined as follows according to the document submitted by the Ministry of Agriculture, Forestry and Fisheries:

“Pig-derived meat-and-bone meal” refers to meat-and-bone meal, steamed bone meal and hydrolyzed protein, derived from pigs and poultry.

“Meat-and-bone meal” refers to powdered meal produced by heat-treatment to separate fat from materials such as bone, viscera and scrap meat, followed by drying and crushing.

“Steamed bone meal” refers to finely-crushed powdered meal produced by heating and pressurizing bone to remove fat and water content.

“Hydrolyzed protein” refers to material produced by degrading viscera, scrap meat, and milk protein, into liquid form by protease and chemical treatment, then powdered or pasted for use in feed.

4. Process separation status in feed plants

According to the Ministry of Agriculture, Forestry and Fisheries, as of April 2005, among the 94 feed plants that manufacturing and shipping feeds using pig-derived meat-and-bone meal, 59 plants manufactured only feeds for livestock other than ruminants. Furthermore, at 35 plants manufacturing feeds for ruminants and feeds for livestock other than ruminants, all manufacturing processes were separated ⁴⁾.

5. Regulations and usage status overseas

In the EU, the use of processed animal proteins for feeding farmed animals is banned, and so is the use of pig-derived meat-and-bone meal in feed for fish culture ^{6), 7)}.

In the US and Canada, using proteins derived from mammals, excluding pigs and horses, and all products containing them, as feed for ruminants is banned. However, proteins derived from pigs and poultry can be used in feed for fish culture ⁸⁾.

6. Food safety risk assessment

The food safety risk assessment related to use of pig-derived meat-and-bone meal in feed for fish culture was reviewed in the 43rd, 45th and 46th Meetings of the Prion Expert Committee. Outcomes of the meetings are summarized as follows:

(1) Susceptibility to and transmissibility of BSE prion in pigs and poultry

The food safety risk assessment related to the use of pig-derived proteins in feed ²⁾ concluded that there was no scientific evidence confirming that pigs and poultry are infected

with BSE prion and transmit BSE in a normal situation ^{9), 10), 11), 12), 13)}. In addition, a report from the Scientific Steering Committee of the European Commission concluded that pigs are not infected with BSE orally in view of the above study results, epidemiological status of BSE infection in pigs in Britain, study on BSE infection in pigs, and that there is no scientific evidence to suggest that handling pig organs and tissues as specified risk materials ¹⁴⁾.

(2) Cross contamination during manufacturing and distribution

The risk of BSE infection in humans from using pig-derived meat-and-bone meal in feed for fish culture was evaluated. Cross contamination occurs during manufacturing and distribution, and then humans may be infected a) by ingesting fish fed with prion-contaminated feed, or by eating beef from cattle fed with the contaminated fishes as feed (fish meal); b) by ingesting beef from cattle fed with feed cross-contaminated by prion-contaminated feed for fish culture; and c) Humans are infected by drinking water contaminated by prion-contaminated feed for fish culture. Therefore, infection risks to humans are reduced by preventing prion cross contamination of feeds for fish culture.

Cross-contamination risks of using pig-derived meat-and-bone meal as feed for fish culture are evaluated as follows:

(a) Material supply ⁴⁾

Since materials are separated to prevent contamination with other materials at the collection sites, including slaughterhouses and distributors, and managed by using dedicated containers for transport and supply management sheets for pig-derived materials, the risks of cross contamination are considered low.

(b) Rendering plants ⁴⁾

The manufacturing of pig-derived meat-and-bone meal is conducted separately from the manufacture of other animal-derived proteins during the rendering processes in rendering plants. In addition, management using supply management sheets for pig-derived meat-and-bone meal is implemented and the manufacturing records are kept for 8 years. The manufactured pig-derived meat-and-bone meal is transported in dedicated containers to mixed-feed plants. So far, 22 facilities manufacturing pig-derived meat-and-bone meal for feed have been examined by the Minister of Agriculture, Forestry and Fisheries. No violation has been found during annual inspection by the Food and Agricultural Materials Inspection Center (formerly the Fertilizer and Feed Inspection Station). Therefore, cross-contamination risks in rendering plants are considered extremely low.

(c) Mixed-feed plants ⁴⁾

Feeds for fish culture are manufactured using pig-derived meat-and-bone meal and vegetable products in feed manufacturing processes for pig, poultry, and fish, and separated from the manufacturing processes of ruminant feed (as ruled on April 1, 2005). In addition, the products are labeled with “Feed for fish culture”, and manufacturing and distribution records are kept for 8 years. These records are inspected by the Food and Agricultural Materials Inspection Center twice a year. Therefore, cross-contamination risks in mixed-feed plants are considered extremely low.

(d) Distributors and fish farmers⁴⁾

By feed distributors, Details such as the purchaser and sales destination of manufactured feeds is recorded and products are labeled with “Feed for fish”. In addition, prefectural governments conduct on-site inspection of distributors to check that feed manufacturing is appropriate. Furthermore, prefectural fishing-industry extension workers^a provide instructions for the use of feed for fish culture as part of technical training for the fish industry. Staff of the prefectural fisheries Experimental stations and the agricultural administration offices of the Ministry of Agriculture, Forestry and Fisheries conduct inspections and provide instruction on the proper use of feed.

Therefore, feeds are properly used and the cross-contamination risks as a result of mistakes in use or distribution are considered very low.

(3) Susceptibility to and transmissibility of TSE prion in fish

A brain homogenate from mice (C57/BL) infected with scrapie prion (139A) was injected orally into turbot and trouts (0.05 ml, equivalent to $10^{6.6}$ LD₅₀) and via other routes; intracerebral (0.03 ml, equivalent to $10^{6.4}$ LD₅₀), intraperitoneal (0.1 ml, equivalent to $10^{6.9}$ LD₅₀), and intramuscular (0.1 ml, equivalent to $10^{6.9}$ LD₅₀)¹⁵⁾. Day 1–90 after administration, parts of organs (brain, intestine, spleen, and muscle) were injected intracerebrally into mice to demonstrate infectivity.

In one of eight trout that received oral injection, infectivity was observed in the intestine, but not in other organs, at day 1 after injection. At day 15 or later after injection, no infectivity was demonstrated in all the organs of the turbot and trouts. However, infectivity was demonstrated in some parts of the organs of the turbot and the trouts, which received injection via routes other than oral injection, at days 15 and 90 after injection. Furthermore, when trout intestine was immersed in a solution containing scrapie prion, prion was detected in the layer of the intestinal mucosa, but did not migrate to the serosa. Based on these results, it is considered that scrapie prion is adsorbed into the mucosal layer of the fish intestine without remaining in the fish intestine at day 15 or later, but is not taken into the body cavity through the intestinal wall.

Next, BSE prion-infected bovine materials were injected orally and intracerebrally to trouts and sea breams¹⁶⁾. Day 1–120 after injection, no clinical symptoms (i.e. abnormal swimming) were seen. And no infection was demonstrated by histological, immunohistological and Western blotting investigation of organs.

In addition, one report suggested that there is a high homology among prion protein genes of edible fishes such as salmon, trout and sea bass, while the homology of prion protein genes between mammalian and fish was less than 40%¹⁷⁾, and thus a high “species barrier” is presumed to exist. However, another recent finding demonstrated a high homology between mammalian prion protein genes and those of puffer fish¹⁸⁾.

Of the research recently evaluated, none indicate natural infection with TSE prion in

^a “Fishing-industry extension workers” refers to persons staffed in prefectural governments, who keep up with trends and technical advances in the fishing industry to provide appropriate technical instruction according to the Guidelines for Fishing Industry Improvement and Promotion (Permanent Secretary of Agriculture, Forestry and Fisheries Notice 16 Suishin No. 1023, as of March 16, 2005).

cultured fish and wild fish nor indicate that mammalian prion causes structural changes and propagation of fish prion ¹⁷⁾.

Based on these findings, invasion and propagation of TSE prion via the fish intestine seems unlikely.

The use of fish product-derived proteins, such as fish meal, in cattle feed was banned according to the regulation of the ordinance concerning the ingredients and specifications of feed and feed additives (The Ordinance from the Ministry of Agriculture, Forestry and Fisheries, No. 35, 1976) as a preventive measure against BSE spread by the Ministry of Agriculture, Forestry and Fisheries. Therefore, if prion contaminates fish, the risks to humans via cattle is negligible.

(4) Prion in the environment (water systems)

The susceptibility to and transmissibility of BSE prion in pigs and poultry are considered low. Furthermore, since measures against cross contamination are taken during each stage of process of using pig-derived meat-and-bone meal for feed for fish culture, the susceptibility to and transmissibility of TSE prion in fish are considered low even if prion contaminates feed materials for fish culture. However, since the use of feed for fish culture is not at all small, prion risks to humans through the environment (water systems) were investigated using the findings such as characteristics and consumption of feed for fish culture and culture statuses ⁵⁾.

Using the infectivity titer of BSE prion in terminally-infected BSE cattle, estimated by a BSE prion infection test in Britain ¹⁹⁾, it is assumed that almost the same number of cattle, carrying BSE prion at the BSE test detection limit or lower, as that of the BSE-infected cattle born before 2001 (about 10 cattle annually) existed and entered slaughterhouses ²⁰⁾. Subsequently, the probability of events occurring, and the infectivity titer when these events do occur, were investigated using “worst case scenario” in slaughterhouses, retail sites and during rendering.

As a result, the probability of a Japanese person drinking BSE prion-contaminated water in a year is 4.2×10^{-3} – 4.2×10^{-5} (maximum risk: 4.2 times in 1,000 years) based on the “worst case scenario.” The total infectivity titer in this situation is estimated at 0.001–0.15CoID₅₀ (CoID₅₀: Cattle Oral Infectious Dose 50%), therefore, accumulation of about 60–10,000 BSE infected cattle is required annually to reach 1 CoID₅₀.

The risk to humans is considered to be far lower than the value calculated above in light of the “species barrier” and the above situation is difficult to imagine realistically. Therefore, the risk to humans via the environment (water systems) is considered negligible.

Besides, according to the findings of the BSE risk assessment in the water environment ²¹⁾, prion molecules are not uniformly distributed in water, but are likely to adhere to solid substances. Therefore, the actual risk is considered to be far lower than that calculated above.

7. Conclusion

(1) Susceptibility to and transmissibility of BSE prion in pigs and poultry that are used for materials is low. The material collection sites are separated to prevent contamination with other materials. The manufacturing processes for ruminants are separated from those for

other animals in rendering plants and mixed feed plants. In addition, cross contamination is prevented during storage and transport of feed for fish culture and ruminants.

The risk to humans as a result of cross contamination are considered low enough, if the management measures by the Ministry of Agriculture, Forestry and Fisheries are observed in each stage of processing from material supply to feed use for fish culture on fish farms.

- (2) Even if BSE prion is contaminated in feed materials for fish culture, according to the findings obtained so far, it is highly unlikely that prion infects fish to propagate in a normal situation, and that humans eat prion-infected fish or prion invades other animals for propagation directly via feed. In addition, risks to humans are considered negligible in light of the risks to humans via the environment (water systems).
- (3) Since no scientific information on BSE susceptibility of horses is available at present, it is impossible to evaluate the food health effects on humans through the use of horse-derived meat-and-bone meal, steamed bone meal and hydrolyzed protein in feed for pigs, horses and poultry, or fish culture.

8. In closing

- (1) The Ministry of Agriculture, Forestry and Fisheries shall inform the Food Safety Commission of the management measures conducted based on this assessment. Furthermore, the manufacture and use of pig-derived meat-and-bone meal in feed for fish culture should be only allowed for facilities where appropriate management for preventing cross contamination can be implemented. Efforts should be made to observe relevant management procedures.
- (2) Many characteristics of prion remain unknown scientifically and only limited information is available. Therefore, further studies are required for risk assessment. Should any new findings and technical innovation be obtained in the future, regarding the scientific knowledge on which this assessment is based, this assessment will need to be revised.

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