**Tentative translation**

※This report hereafter might be revised, or tables and figures might be added to this report.

# Food Safety Risk Assessment

# Related to Measures Against

# Bovine Spongiform Encephalopathy (BSE) in Japan

**May 6, 2005**

**The Food Safety Commission**

**The Prion Expert Committee**

**Contents** **Page**

## 1. Introduction

### 1.1 Background

The Food Safety Commission's Prion Expert Committee reviewed Japan's overall strategies and measures concerning Bovine Spongiform Encephalopathy (BSE) in order to evaluate the risk in this country of cattle infecting humans with BSE prions, and to examine the effectiveness of measures to reduce such risks. The Committee's findings, compiled and made public in its Interim Report[1)] in September 2004, were submitted to the Ministry of Health, Labour and Welfare, and the Ministry of Agriculture, Forestry and Fisheries of Japan.

Upon receiving the Committee's Interim Report, the Ministry of Health, Labour and Welfare (MHLW) and the Ministry of Agriculture, Forestry and Fisheries (MAFF) of Japan began deliberations on the revision of BSE measures. Revisions have been proposed in four areas of BSE measures: (1) BSE testing at slaughterhouses; (2) ensuring complete removal of SRMs; (3) reinforcement of securing feed ban effectiveness; and (4) promoting further BSE research studies.

The Food Safety Commission was subsequently requested by MHLW and MAFF, in accordance with Paragraph 1 (13) and Paragraph 3 of Article 24 of the Food Safety Basic Law (Law No. 48; 2003), to submit a health risk assessment on food related to BSE measures in Japan (Paragraph 11 (1) of this Law)[2)] (relevant documents received October 15, 2004).

In response to the request from MHLW and MAFF, the Food Safety Commission has been hosting, with the support of various prefectural governments, MHLW, and MAFF, a series of meetings to exchange opinions. These meetings have been held at 50 locations throughout all of the country's 47 prefectures[3)] to provide reference sources for discussions by the Prion Expert Committee and other bodies, as well as to ensure that the opinions of a wide range of concerned parties are reflected in the discussions.

In the meetings for exchanging opinions held throughout the country, calls were heard for ensuring complete removal of SRMs and thorough implementation of feed bans, as well as for promotion of research and development in such areas as BSE testing technology and the mechanism of BSE occurrence. Opinions regarding whether or not to revise the BSE testing age of cattle were divided. Some supported the current policy of blanket testing of cattle regardless of the age due to such concerns as the many scientific uncertainties, and fears surrounding BSE and the impact on beef consumption; and others gave support to the proposed revision so as to test cattle aged

21 months or older. Through these meetings, there were those who acknowledged gaining a better understanding of BSE risks in Japan, and others who suggested the need to conduct a fair and unbiased risk assessment by the Food Safety Commission regarding the issue of importing U.S. beef. In the course of deliberations held during the drafting of the Prion Expert Committee's Interim Report, discussions arose focusing on the detection limit of BSE testing. The discussions revolved around BSE test results in which extremely young steer, aged 21 and 23 months, tested positive for BSE infection as a result of blanket testing conducted at slaughterhouses on cattle, yet cattle aged 20 months or younger have never been diagnosed as positive. Because it was difficult to set a scientifically appropriate age range to be excluded from BSE testing, the description concerning this issue in the Conclusions of the Interim Report was confined to facts and data. However, a request was included among the issues submitted to the committee from MHLW and MAFF, to consider from the viewpoint of risk management, the revision of the current policy of the blanket testing so as to exclude cattle aged 20 months and younger from mandatory testing.

With regard to the four areas of BSE measures which were submitted for deliberation: (1) BSE testing at slaughterhouses; (2) ensuring complete removal of SRMs; (3) reinforcement of securing feed ban effectiveness; (4) further promotion of BSE research the committee examined overall effectiveness of BSE-related measures established by MHLW and MAFF, such as BSE surveillance, feed bans, traceability, screening test and removal of SRMs at slaughterhouses. This evaluation report is based on the results of risk assessments performed by the committee. In order to draw up this Report, the Prion Expert Committee held a total of eight meetings; on October 26, November 16, December 6, December 22, January 21, February 24, March 11, and March 28.

This Report consists of 1. Introduction, 2. Basic Concept for Risk Assessment, 3. Evaluation and Opinions on the Inquired Issues, 4. Conclusions, and 5. Closing Remarks.

## 1.2 Main Points of Discussion Leading Up to Start of Sessions

### 1.2.1 Background to deliberations after the Chairman and Vice Chairman were entrusted with drawing up the Interim Report

A question was raised by Committee Member Dr. Yamanouchi regarding the process subsequent to the discussion by the Prion Expert Committee, on how the Interim Report was drafted and was approved by the Food Safety Commission. In response to this inquiry, Dr. Yoshikawa as the Chairman of the Prion Expert Committee, Dr.

Kaneko as the Vice Chairman of the Committee, and Mr. Murakami as the Director for Risk Assessment Division of the Food Safety Commission provided explanations from their respective standpoints regarding the issue. In summarizing the explanation, Dr. Yoshikawa commented on the need to make efforts to ensure transparency.

### 1.2.2 Main points of discussions regarding the details of the inquiry

(1) Revision of the age criterion for BSE testing

The Interim Report pointed out the many scientific uncertainties and lack of data about BSE, as well as the limits of testing sensitivity. The Report also included recommendations regarding the removal of SRMs, feed bans, and further surveys and research. Dr. Yamanouchi questioned the intent of proposing revision of blanket testing to age-based testing, when the Interim Report did not recommend setting any age range to be excluded from BSE testing due to the lack of scientific proof supporting it. The MHLW responded by stating that the revision was proposed to ensure scientific rationality based on statements in the Conclusions of the Interim Report.

The relevant statements in the Conclusions were modified after the Chairman was entrusted with drawing up the Report. Dr. Kaneko offered a rather broad explanation, pointing out that the statements have been interpreted in different ways by the scientists and the government, which is attributable to differences in their perspectives , and also that the Interim Report may have been drawn up a little too hastily. Dr. Yoshikawa expressed agreement with this commentary. Committee Member Dr. Shinagawa expressed concern that the reason behind the haste to submit this report is unclear, particularly as transition measures will be implemented for three years following the revision of blanket testing to age-based BSE testing. The MHLW responded by stating that the transition measures are to be implemented to help avoid any confusion.

Committee Members Dr. Yamanouchi and Dr. Yokoyama respectively expressed their views that proposals regarding the revision of the blanket testing program seemed to be connected to the issue of importing beef from the United States. The MHLW responded by stating that the purpose of the proposal was to ensure scientific rationality. With regard to the importing of US beef, Dr. Terada as the Chairman of the Food Safety Commission added that there were plans to discuss this topic as a separate issue.

(2) Traceability

Committee Member Dr. Kitamoto brought up the point that the traceability information should include not only where and how the cattle were raised, but also information on the use of pithing in the slaughtering process, in order to facilitate communication with consumers. Dr. Kitamoto also expressed the hope that discussions of this issue would

lead to a ban on pithing. In response to this, MAFF stated that, in collaboration with MHLW, this issue will be put on the agenda for future discussion.

(3) Feed bans

Dr. Yoshikawa and Dr. Yamanouchi pointed out the need for investigating the actual distribution of feed after the ban on the use of meat and bone meal (MBM) in feed.

(4) SRM removal and pithing

Dr. Yamanouchi requested that the specific details for improving SRM control be disclosed. Dr. Yamanouchi and Dr. Kitamoto requested the disclosure of the specific objectives for the banning of pithing.

### 1.3 Basic policies for deliberation

Japan's BSE measures are comprised of (1) grasping the actual situation regarding BSE contamination (active surveillance); (2) prevention of the spread of BSE among cattle at farms (feed bans); (3) management systems implemented at farms to trace the production history of each cattle (traceability system); (4) measures to reduce risk at each slaughterhouse (screening out infected cattle through BSE testing, removal of SRMs, and ensuring safety when slaughtering cattle). Meetings are to be held to examine the effectiveness of these measures and make comprehensive judgements.

The following points have been confirmed as concrete policies for the deliberation:

(1) The issue of revising the blanket testing policy should be regarded as risk assessment of cattle born in or after July 2003, which is one and a half years after the implementation of feed bans in October 2001.

(2) In evaluating the changes in risk resulting from revision of the blanket testing policy, both qualitative risk assessment and quantitative risk assessment should be conducted.

(3) In order to conduct quantitative risk assessment, an assessment model should be created by organizing scientific data obtained to date. In creating an assessment model, problems surrounding the assessment and the limitations of the assessment should be clarified, so as to prevent the obtained figures from causing misunderstanding.

(4) The risk assessment results should be consolidated into an opinion, or a compilation of multiple opinions.

(5) To secure the confidence of consumers, it is necessary to discuss the problems raised through risk communication, and make every effort to ensure that the results of these discussions are also reflected in the risk assessment-based opinions. It is important to be aware that these procedures differ from the reporting procedures followed by conventional advisory councils of risk management organizations, and that this is the first crucial issue undertaken by the Food Safety Commission.

## 2. Basic Concept for Risk Assessment

Changes in the risk of human infection as a result of excluding cattle younger than a certain age from mandatory BSE testing shall be estimated by an overall evaluation of the effectiveness of various measures for risk reduction, such as feed bans, BSE testing, removal of SRMs, improvements in slaughtering methods, in accordance with the model shown in Fig. 1.

Risk assessment can essentially be divided into two categories: qualitative risk assessment and quantitative risk assessment. However, as very little is known scientifically about BSE and its pathogenesis, risk assessment must depend almost entirely on qualitative methods. Furthermore, even with quantitative methods, only relatively simple models are used for risk assessment. For example, risk assessments performed in the EU employ qualitative methods, except on products for which sufficient data from experiments already exist, such as gelatin or animal oil and fat. In performing the Assessment of geographical BSE Risk (GBR), introduction risk from outside sources, such as the importation of live cattle, MBM, and other products, is quantitatively evaluated, while amplification risk of BSE prions in the country is qualitatively evaluated.

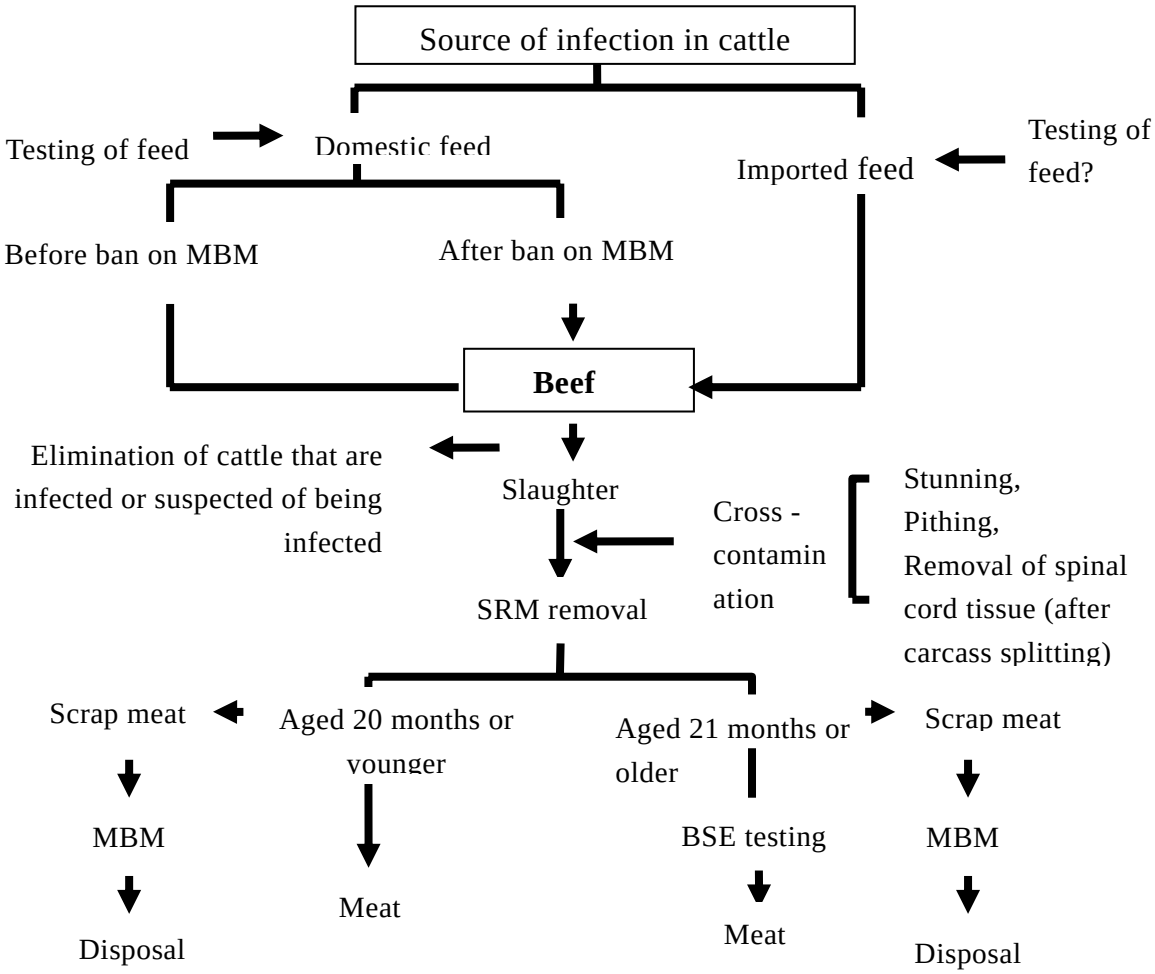
Quantitative risk assessment is preferable because it is an objective method. However, in the case of BSE, because of the extremely limited amount of scientific data available, no internationally accepted model has been created. Consequently, it is important to understand that quantitative risk assessment is a provisional calculation carried out based on certain preconditions. In this case, it is essential that the stochastic methodology based on preconditions, as well as any problems or other related issues, be clearly stated.

When the Prion Expert Committee performs quantitative risk assessments, it conducts its evaluation from the aspect of exposure risk estimated from of the quantity of BSE prions, which is the cause of infection in humans, as well as from the aspect of

probability theory regarding the risk reduction effects from BSE testing and SRM removal.

## 2.1 Model of the Concept

Fig. 1 Basic Concept for Risk Assessment (Model) (Flow chart illustrating how BSE prions are transmitted to meat)




## 2.2 Main points at issue

(1) Effectiveness of feed bans

Whenever an outbreak of BSE has been confirmed in a country, the Japanese government's policy has been to halt imports of live cattle from that country. There has been a complete ban on importing MBM since October 2001.[4)] Japan relies on imports for approximately 90% of its concentrate feeds , such as feed grains, which are used as raw material in the domestic production of compound and mixed feed.[5)] Although imported feed consists mostly of single-ingredient feed such as grain, compound feed and mixed feed manufactured overseas are also imported (approximately 0.5% or less

of the total amount used in Japan).[6] Because the true situation with regard to BSE contamination in exporting countries is unclear, there is no way of predicting whether it is possible to prevent compound or mixed feed adulterated with MBM from being imported into the country. Consequently, the ingredients that go into compound or mixed feed will be added to the items for which feed importers must submit notification.[7] Therefore the effectiveness of the feed ban remains unclear, although it can be assumed that compound and mixed feed produced overseas and imported into Japan do not present a high risk.

In contrast, due to the implementation of such measures as the separation of MBM production lines in rendering plants,[8] and the ongoing efforts of the compound feed manufacturing plants to produce feed exclusively for a particular type of livestock or to separate the production process lines in each plant, the regulations for feed produced in Japan can be considered, to a certain extent, to be effective in avoiding risk. Moreover, according to the administrative guidance governing such issues as standards for ingredients in feed and feed additives, it is forbidden to mix animal protein into compound feed.[9] Furthermore, to monitor the actual compliance with these regulations, on-the-spot inspections are carried out at manufacturing facilities.[10), 11)]

In order to estimate how long it will take to drain the contaminated feed produced prior to the feed regulations implemented in 2001,various turnover periods must be taken into account. A rendering plant would have a two or three-day turnover period, the turnover period at a manufacturing facility would be one month, and a farm would have the feed in stock for about three months.[12] Altogether, it could take more than six months for the feed to be completely depleted. However, the age of cattle that is relevant to the focus of this agenda is 20 months or younger. As these cattle were born in or after July 2003, it can be assumed that there is very little possibility they have been given feed produced before the implementation of the feed regulations.

Meanwhile, tests, although few, have been conducted on feed produced in Japan to check whether MBM has been mixed into the feed[10] (724 tests were conducted between October 2001 and the end of March 2004). From these on-the-spot testings, MBM has been detected in only one case[13] (in February 2005, protein derived from poultry was detected in cattle feed at a compound feed plant where cattle feed and poultry/pig feed containing chicken meal were produced on the same production line). Therefore, it is considered that feed monitoring has been effective to some extent. Due to technical limitations of the testing method, however, more emphasis is placed on providing instructions to ensure compliance with laws and regulations with efforts being made to check the submitted notifications from feed manufacturers.[7]

A system that enables traceability in the production stage was made mandatory in December 2003, and traceability in the distribution stage became mandatory in December 2004.[7),14)] Traceability in the production stage has proved effective in identifying and eliminating BSE case cohort *. The effectiveness of traceability in the distribution stage has yet to be verified.

(2) BSE testing

In order to grasp the true state of the prevalence of BSE in Japan, testing of risk cattle (dead cattle and cattle with central nervous system symptoms) was initiated in April 1996. Tests at that time targeted animals that had been brought in to have their health condition evaluated. From October 2001, however, BSE testing became mandatory for not only cattle that exhibited clinical symptoms, but also all dead cattle aged 24 months or older. From April 2004, upon completion of testing facilities in all of the prefectures in Japan, testing of all cattle aged 24 months or older became mandatory. [7),15)] From April 1996 to the end of January 2005, testing was performed on a total of 140,196 animals, out of which four tested positive for BSE[15)] (three were dead cows, and the other cow detected through BSE active surveillance, was the first case in Japan to be diagnosed as BSE-positive). The delay in establishing a system for testing dead cattle created difficulties in determining the true state of the prevalence of BSE in Japan, and had a major impact on the results of the present risk assessment.

Because the total number of cattle that have tested positive for BSE is small, it is difficult at the present time to discern any trends with regard to BSE infection among young cattle. However, two out of the twelve animals that tested positive in BSE testing at slaughterhouses were young (as of March 27, 2005). This is a ratio that is impossible to ignore. As the distribution of BSE prions is not uniform throughout the body, if tissues containing high concentrations of BSE prions are mixed into feed, it could cause young cattle to become infected.

---

*Definition of a BSE case cohort *:

- All Cattle that has been raised together with and fed the same feed as the BSE cases, aged 12 months or younger, during its first year of life.
- All Cattle that was born of female cases either within two years before the mother developed BSE symptoms (in other words, diagnosed as infected with BSE) or after the mother developed BSE symptoms.

Research and development is currently underway in Japan to increase the sensitivity of the BSE testing method to make it possible to detect infection in young cattle. Testing methods developed overseas include a method that does not use proteinase K as well as a method that focuses on a monoclonal antibody, which enables specific immunohistological detection of BSE prion protein. Therefore, there is a probability that young cattle testing positive for BSE infection will continuously be found in the future.

(3) SRM removal

SRMs have been defined as the head, including the brain, eyes, and tonsils, but excluding the tongue and cheek meat .SRMs also includes the spinal cord and distal ileum (2 meters from connection to caecum). Removal of these SRMs in the course of slaughtering has been compulsory since October 2001. Furthermore, from February 16, 2004, the vertebral column, which contains dorsal root ganglia, has been banned from use in human food supply. The MHLW conducted a nationwide questionnaire survey to verify compliance with the regulation requiring removal of SRMs. [16] The results of the survey showed that SSOP (Sanitation Standard Operating Procedures) had been established and were being followed in approximately 90% of the slaughterhouses in Japan.[17] It can therefore be considered that the regulation has been effective in risk avoidance to a certain extent.

According to future policies announced by MHLW,[18] the current irregular inspections will be revised, and regular inspections will be carried out twice a year to check whether SSOP and its methods of verification have been documented and whether records have been kept on the implementation of SSOP. Additionally, whether removal of the spinal cord by suction has been carried out prior to carcass splitting, what method is used to incinerate SRMs, what method is used to remove spinal cord tissue after carcass splitting, and the method used to wash dressed carcasses will also be subjects of investigation. The results shall be made public.[18] However, more time will probably be needed before assurance can be given that all SRMs have been removed with certainty.

(4) Pithing

Pithing is a procedure used in the slaughtering process at approximately 70% of slaughterhouses in Japan (used on an estimated 80% of all slaughtered cattle).[17] The pithing procedure involves inserting a wire-like instrument into the head of a stunned cattle to destroy the spinal nerve tissue, thereby preventing reflexive kicking by the animal. Because MHLW does not yet have sufficient grounds to set specific steps towards the banning of this procedure, the Ministry has not yet announced any goals or

objectives to ban pithing. Reports from overseas,[19] however, point out the risks caused by pithing.

## 3. Evaluation and Opinions on the Inquired Issues

### 3.1 Qualitative risk assessment

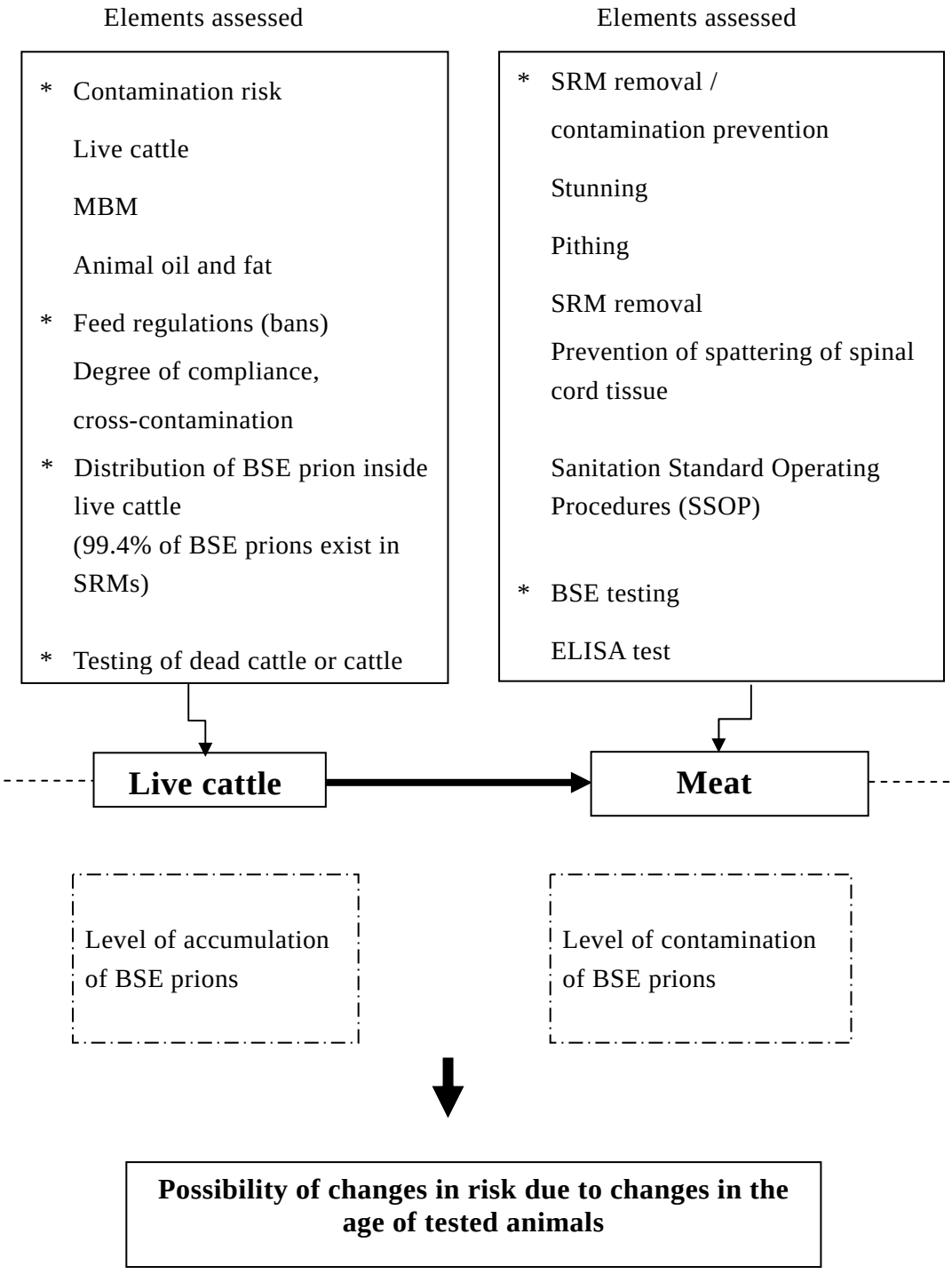
#### 3.1.1 Basic concept of qualitative risk assessment

The level of accumulation of BSE prions as of March 2005 in cattle born in July 2003 or later shall be estimated based on the rate of infection and amount of accumulation. Although the rate of infection and amount of accumulation shall be based as much as possible on quantitative data, the results shall be assessed qualitatively. Furthermore, should cattle from this period be slaughtered, the possible level of BSE prion contamination in the meat shall be estimated based on the contamination rate and amount of contamination. This contamination rate and amount of contamination shall be based as much as possible on quantitative data, but the results shall be assessed qualitatively as is the case with live cattle. The elements to be evaluated are shown in Fig. 2 below.

Changes in the level of risk, that may be caused by exempting cattle younger than 21 months of age from BSE testing, shall be qualitatively assessed.

In doing so, the elements for which quantitative data exists should be utilized as a reference to determine the level of risk, and where such data does not exist, opinions from experts should be taken into consideration.

**Fig. 2 Basic concept of qualitative risk assessment**



### 3.1.2 Concrete methods of qualitative risk assessment

#### 3.1.2.1 Elements related to the level of accumulation of BSE prions in beef cattle

##### 3.1.2.1.1 Risk of contamination from other countries

The "BSE Epidemiology Investigation Team Report of the Results of Epidemiological Analysis,"[20] released in September 2003, pointed out the possibility that the outbreak of BSE in Japan was caused by live cattle imported from Germany and the U.K. in the 1980s, MBM imported from Italy, animal oil and fat imported from the Netherlands. It was also pointed out that live cattle had been imported from Canada.

Importing live cattle from the U.K. has been banned since July 1990. Since then, each time the first BSE incident has been identified in a country, bans have been imposed on importing live cattle from the relevant country. In October 2001, Japan implemented a complete ban on MBM imports. In addition, if animal oil and fat for use in animal feed was stated as having no more than 0.15% insoluble impurities, it became mandatory for the products to be accompanied by a certificate issued by the exporting country attesting to this claim. Upon the outbreak of BSE in Canada in May 2003, an import ban was imposed on all live cattle and meat from the country. An identical ban was imposed on the United States when the first case of BSE in U.S. was confirmed in December 2003. In October and November 2003, a total of ninety-two live animals were imported from the United States,[21] but these cattle have been kept under observation.

Therefore, the BSE contamination risk in Japan from imported live cattle, MBM, or animal oil and fat can be viewed as "negligible" since July 2003, which is when cattle that would be 20 months old as of March 2005 were born.

##### 3.1.2.1.2 Feed bans

In April 1996, the Government issued an administrative guidance banning the use of products containing ruminant animal tissues, such as MBM in feed for ruminant animals. To ascertain compliance with this administrative guidance, on-the-spot inspections of all cattle-raising farms were carried out in September 2001. The inspections revealed that 165 farms were giving MBM and other such feed to their cattle.[22] However, in follow-up inspections, none of the cattle from these farms tested positive for BSE infection. Although the use of MBM has been completely banned since October 2001, a steer born in October 2001 (23 months old) and a steer born in

January 2002 (21months old) tested positive for BSE infection. MBM that had been left over in the market, or feed made from MBM of other types of livestock that had been contaminated with MBM from cattle may have been used. Since October 2001, on-the-spot inspections have been carried out on feed importers, manufacturers, feed dealers, and cattle-raising farms, to check for contamination of compound feed by MBM. Incidents of contamination have not been found through the inspections. .

With regard to imported feed, even before October 2001, every feed importer has been obligated by the Feed Safety Law to submit information including its name, the kinds of feed it imports and other details[7),]. However, because compound feed production relies heavily on imported ingredients and an accurate grasp of the extent of worldwide BSE contamination is lacking, raw materials used to manufacture compound and mixed feed will be added among the items to be submitted.

Prior to October 2001, compound feed for cattle and feed for chickens/pigs containing MBM derived from cattle were manufactured on the same production lines in some factories. Therefore the possibility of cross-contamination of feed can not be denied.[23)] Since July 2003, manufacturing facilities have been requested to establish production lines used exclusively for cattle feed .[24)] By the end of October 2004, a total of 96 out of 136 factories had complied with this requirement and had completed the separation of production lines. All manufacturing facilities are expected to have exclusive production lines by March 31, 2005.[9)] As of July 2003, one year and nine months had passed since a complete ban was imposed on the use of MBM, leaving very little chance that any MBM produced before the ban still remained. Therefore, concerning cattle born in or after July 2003, the possibility of being given feed containing domestic MBM is “negligible.”

Consequently, it can be surmised that the infection rate caused by cross-contamination from domestic feed for cattle born in or after July 2003 is “very low,” and the amount of accumulation is “negligible.” However, the risk of cross-contamination from feed manufactured overseas and imported into Japan has not been verified.

#### 3.1.2.1.3 Distribution of BSE prions inside the bodies of live cattle

According to the Scientific Steering Committee of the European Commission, 99.4% of the BSE prions are concentrated in SRMs.[25)] In 2004, BSE prion proteins were detected by Western blot test in the adrenal gland and peripheral nerve tissue, including the tibial and sciatic nerves, of a dead cow aged 94 months (Japan’s 11$^{th}$ confirmed case of BSE).[26)] The quantity of BSE prion proteins detected in the dead cow was considerably less than the amount found in the trigeminal ganglia, which is currently designated as

SRM. Moreover, in infectivity experiments conducted by the United Kingdom's Veterinary Laboratories Agency, in which bioassays were done on peripheral nerves of cattle 32 months after they had received inoculations, no case of infection was observed.[27)] The results of the infectivity experiment conducted by the United Kingdom's Veterinary Laboratories Agency[28)] show that infection was confirmed in the distal ileum of cattle 6 to 18 months after they were administered BSE prions, and in the brain, spinal cord, dorsal root ganglia, and trigeminal ganglia 32 months after administration. However, as SRMs are removed from all cattle during the slaughtering process, the risk of contamination of the meat from BSE prions, either before or after the revision of the procedure, is perceived to be extremely low. A factor that must be considered with the abovementioned experiment is the extremely small number of subject animals. Three animals aged 22 months, one animal aged 26 months, and two animals aged 32 months were used in the experiment. Large-scale experiments are currently underway in the U.K., and results obtained from these experiments may provide additional information.

#### 3.1.2.1.4 Testing of BSE case cohort

With regard to the elimination of BSE case cohort, regulations setting forth the definition of BSE case cohort, as well as details related to the culling of such animals, were established in October 2001. By the time the 15th BSE-infected cattle was confirmed, a total of 720 animals had been designated as BSE case cohort. However, none of this BSE case cohort tested positive for BSE infection.

#### 3.1.2.1.5 Testing of dead cattle

Active surveillance was initiated in April 2001 to carry out testing on dead cattle. In September 2001, surveillance was enhanced (notification was issued mandating testing and incineration of cattle displaying central nervous system symptoms), and from April 2004, testing has become mandatory for all dead cattle aged 24 months or older. In accordance with these measures, BSE testing had been conducted on a total of 138,912 dead animals as of the end of January 2005: 1,169 animals in 2001; 4,313 animals in 2002; 48,416 animals in 2003; 85,087 animals in 2004. As a result, in addition to the first case of BSE confirmed in Japan, BSE testing uncovered three other cases as of March 2005 (a 94-month-old cow, the 11th case confirmed in Japan; a 48-month-old cow, the 14th case; and a 102-month-old cow, the 15th case).[15)] All of these cows were incinerated. Although the use of MBM in feed has been banned in Japan since October 2001, the delay in the start of testing on dead cattle has made it difficult to grasp the true state of BSE contamination in Japan.

Based on the abovementioned information, the risk regarding the level of BSE prion accumulation in live cattle born since July 2003 falls in the range of “very low” to “low.”

#### 3.1.2.2 Elements examined in regard to the level of BSE prion contamination in meat

##### 3.1.2.2.1 SRM removal / contamination prevention

###### 3.1.2.2.1.1 Stunning

Stun guns (guns used for slaughtering animals) are used for stunning cattle at 93.1% of the slaughterhouses in Japan, as of December 2004.[17] Although there have been reports that stunning causes tissue from the central nervous system to migrate into the cow’s blood,[29] no quantitative data has been reported indicating the contamination rate or the amount of contamination in meat from SRMs. Nevertheless, the level of BSE prion contamination in meat as a result of stunning is considered to range from “very low” to “low.”

###### 3.1.2.2.1.2 Pithing

There is insufficient data to perform quantitative risk assessment of pithing. Pithing is carried out at 71.9% of the slaughterhouses in Japan (used on approximately 80% of all slaughtered cattle), as of December 2004. While it is generally accepted that the contamination rate of meat from SRMs as a result of pithing cannot be completely ignored, the amount of contamination can be presumed to be small. Furthermore, the risk regarding the level of accumulation of BSE prions in live cattle born since July 2003 falls in the range from “very low” to “low.” Therefore, the risk presented by pithing to this cohort of cattle is evaluated to be in the range of “very low” to “low.”

###### 3.1.2.2.1.3 SRM removal

Removal of SRMs has been mandatory since October 2001, and is being carried out at all slaughterhouses in Japan, as of March 2005. SRM removal is believed to cut the infectious does by 99.4%. Therefore, if SRMs can be removed with complete certainty, the risk of meat becoming contaminated by BSE prions can be considered to be “very low.”

###### 3.1.2.2.1.4 Prevention of spattering of spinal cord tissue

As of January 2005, there are six facilities out of a total of 160 slaughterhouses that do not carry out carcass splitting.[30] Of the 154 facilities where carcass splitting is carried out, nearly 100% of them (from 99.4% to 100%) implement some means to prevent the spattering of tissue.[30] Furthermore, there are 125 facilities (91.9%)[17] that carry out suction removal of spinal cord tissue prior to carcass splitting. Suction removal of spinal cord tissue is between 52.5% and 99.1% effective,[31] but washing the dressed carcass and removing the spinal cord dura matter after splitting results in the carcass appearing to be 100% free of any visual evidence of contamination by spinal cord fragments.[17] This is confirmed by inspectors at the slaughterhouses. However, testing that uses a protein contained in the spinal cord called GFAP as a marker protein has resulted in some cases in which minute traces of GFAP are detected on the surface of the lower portion of the dressed carcass.[32] All cattle that test positive for BSE are disposed of Saws, knives, and other utensils, are washed and disinfected after slaughtering each cattle. Furthermore, by removal of the spinal cord and washing the dressed carcass, the risk of BSE prions contaminating meat is greatly reduced. In light of all of the measures described above, the risk of BSE prion contamination in meat from spinal cord tissue can be considered to be “very low.”

#### 3.1.2.2.1.5 Sanitation Standard Operating Procedures (SSOP)

As of January 2005, SSOP have been established at 155 facilities (93.4%).[30]

Although it is difficult to ascertain the impact that the absence of SSOP may have on the level of BSE prion contamination of meat, it can be considered to be “low.”

### 3.1.2.2.2 Testing of slaughtered cattle

#### 3.1.2.2.2.1 ELISA test

In May 2001, testing was initiated at slaughterhouses in Japan on at-risk cattle. Since October 2001, all slaughtered cattle in Japan undergo an ELISA screening test, followed by a confirmation test using the Western blot method and a microscopic pathological/immunohistochemical examination. As of March 26, 2005, approximately 4.27 million animals had undergone testing in Japan, resulting in twelve cows testing positive for BSE infection. Of the twelve BSE-infected cows in Japan, test results from Western blot method showed that the amounts of BSE prions accumulated in the two cases of 21-months and 23-months of age were much lower, estimated at between 1/500 to 1/1000 of the amount, than in the other BSE-infected cattle.[33] The detection sensitivity of the current ELISA test is regarded to be 1 m.i.c. $LD_{50}$.[44] The amount of BSE prions accumulated in the other cattle that tested positive for BSE infection is

deemed to range from 500 to 1000m.i.c. $LD_{50}$. Should the current blanket testing program be revised, and cattle aged 20 months or younger be excluded from BSE testing, it is believed that even if BSE infection is detected in cattle born in or after July 2003, the amount of accumulation would be close to the detection limit of approximately 1 m.i.c. $LD_{50}$.

#### 3.1.2.2.3 Miscellaneous

##### 3.1.2.2.3.1 Traceability

The traceability system was initiated in January 2002. In December 2003, traceability was made mandatory in the production stage, and subsequently in the distribution stage in December 2004.[7)] This system enabled identification of each cattle born in or after July 2003. Consequently, the level of meat BSE prion contamination in meat caused by defect in identification, is viewed as “negligible.”

##### 3.1.2.2.3.2 Elimination of cattle testing positive

Since October 2001, BSE testing has been properly carried out in accordance with Testing Guidelines,[34)] to eliminate every cattle that tests positive. Therefore, for cattle born since July 2003, the level of BSE prion contamination in meat can be considered to be “negligible.”

Based on the abovementioned information, the risk regarding the level of BSE prion contamination of meat from cattle born in or after July 2003 falls in the range of “negligible” to “very low.”

### 3.1.3 Qualitative risk assessment of revisions to age criterion for BSE testing

Details regarding evaluations of “3.1.2.1 Elements related to the level of accumulation of BSE prions in beef cattle” and “3.1.2.2 Elements examined in regard to the level of BSE prion contamination in meat” have been summarized in Table 1.

Table 1:Effectiveness of BSE countermeasures reflected in assessment of the levels of BSE prion accumulation in live cattle and of meat contamination.

| Age (in months) (as of March 2005)<br>Month and year of birth | | Aged 0 to 20 months<br>Born on or after July 1, 2003 | |
|---|---|---|---|
| | | Blanket testing | Testing cattle aged 21 months or older |
| Level of BSE prion accumulation in live cattle (infectivity, amount of accumulation) | ・Risk of contamination from other countries<br>Live cattle<br>MBM (meat bonemeal)<br>Animal oil and fat | Negligible | Negligible |
| | ・Domestic feed bans degree of compliance, cross-contamination | Negligible – Very low | Negligible – Very low |
| | ・Imported compound and mixed feed | Unknown | Unknown |
| | ・Level of BSE prion accumulation<br>Infection rate<br>Amount of accumulation* | Very low<br>Small | Very low<br>Small |
| | ・Testing of BSE case cohort | No cattle tested positive | No cattle tested positive |
| | ・Testing of dead cattle aged 24 months or older | Negligible<br>(Dead cattle are incinerated and not sent on for rendering) | Negligible<br>(Dead cattle are incinerated and not sent on for rendering) |
| Level of BSE prion contamination in meat (contamination rate, amount of contamination) | ・SRM removal / contamination prevention<br>Stunning<br>Pithing<br>SRM removal<br>Prevention of spattering of spinal cord tissue<br>Sanitation Standard Operating Procedures (SSOP) | Very low – Low<br>Very low – Low<br>Very low<br>Very low<br>Low | Very low – Low<br>Very low – Low<br>Very low<br>Very low<br>Low |
| | ・Test at slaughtered cattle<br>ELISA test<br>Rate of positive detection<br>Amount of contamination | Very low<br>Negligible – Very small | Testing is not conducted on cattle aged 20 months or younger<br>Negligible – Very small |
| | ・Others<br>Traceability<br>Elimination of cattle testing positive | Negligible<br>Negligible | Negligible<br>Negligible |

*in cases of cattle that tested positive

**Categories defining the assessment levels:**

| | |
|---|---|
| Infectivition rate: | Negligible, Very low, Low, Medium, High, Unknown |
| Contamination rate: | Negligible, Very low, Low, Medium, High, Unknown |

| | |
|---|---|
| Amount of accumulation: | Negligible, Very small, Small, Medium, Large, Unknown |
| Amount of contamination: | Negligible, Very small, Small, Medium, Large, Unknown |

Categories for final assessment:

| | | |
|---|---|---|
| **Risk:** | Level of accumulation (Infection rate, amount of accumulation) | Negligible, Very low, Low, Medium, High, Unknown |
| **Risk:** | Level of contamination (Contamination rate, amount of contamination) | Negligible, Very low, Low, Medium, High, Unknown |

Concerning cattle aged 20 months or younger as of March 2005, which would be cattle born in or after July 2003, it is believed that the prevalence of infection is “very low,” and the amount of BSE prion accumulation in infected cattle is “small.” Furthermore, at present, the BSE contamination rate in meat as a result of the slaughtering process is believed to be “very low,” and the amount of contamination to be between “negligible” and “very small.”

If BSE testing is changed from blanket testing to testing cattle aged 21 months or older, the risk remains unchanged, provided there are no BSE-infected cattle aged 20 months or younger with amount of BSE prion accumulation that exceeds the detection limit. Should such infected cattle exist, an increase in the risk would be undeniable. Nevertheless, the BSE prion contamination rate of meat can still be considered to be “very low” and the amount of contamination to be between “negligible” and “very small.”

The risk can be further reduced by means of establishing feed regulations requiring the submission of notifications reporting the ingredients contained in imported compound and mixed feed, as well as the thorough implementation of SRM removal, including the banning of pithing, and prevention of SRM cross-contamination.

### 3.1.4 Problems related to the present risk assessment

There are a number of problems, such as those described below, involving gaps and limitations in the data.

1. Gaps in the data
   Lack of data regarding SRMs from cattle aged 19 months to 31 months

2. Lack of data for quantitative risk assessment
   Infection rate and infectious dose of BSE prions
   Contamination rate and amount of BSE prion contamination s in meat

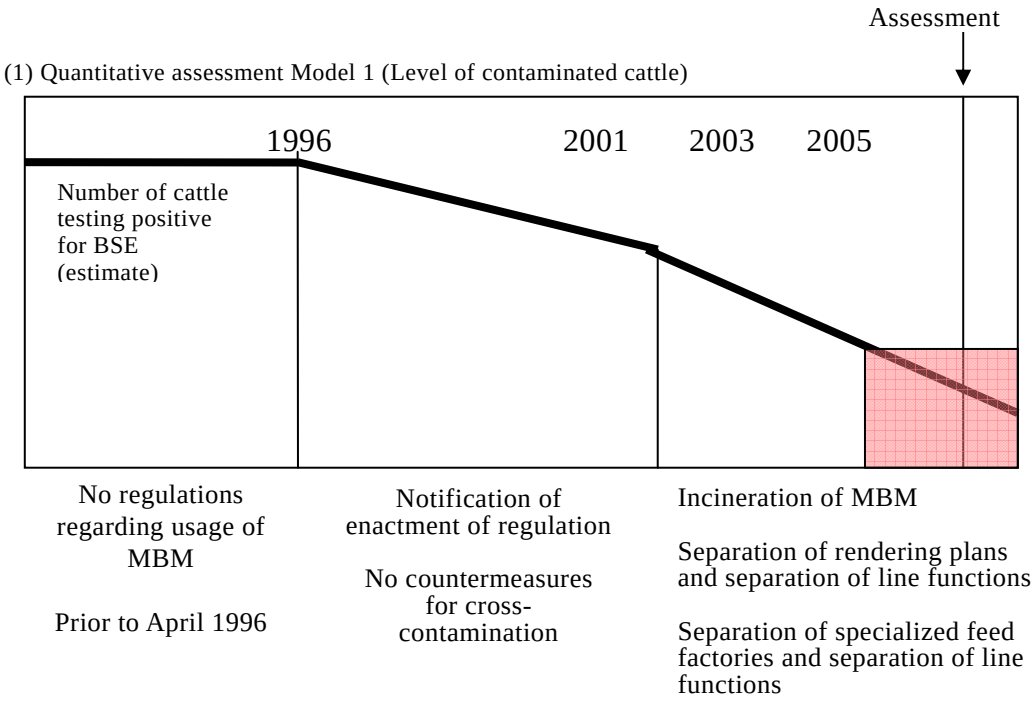
3. Lack of objective standards for determining level of output data after processing input data

4. Lack of consideration on unreliability of and fluctuations in data
   Quantitative (either deterministic or stochastic) risk assessment will be necessary in the future.

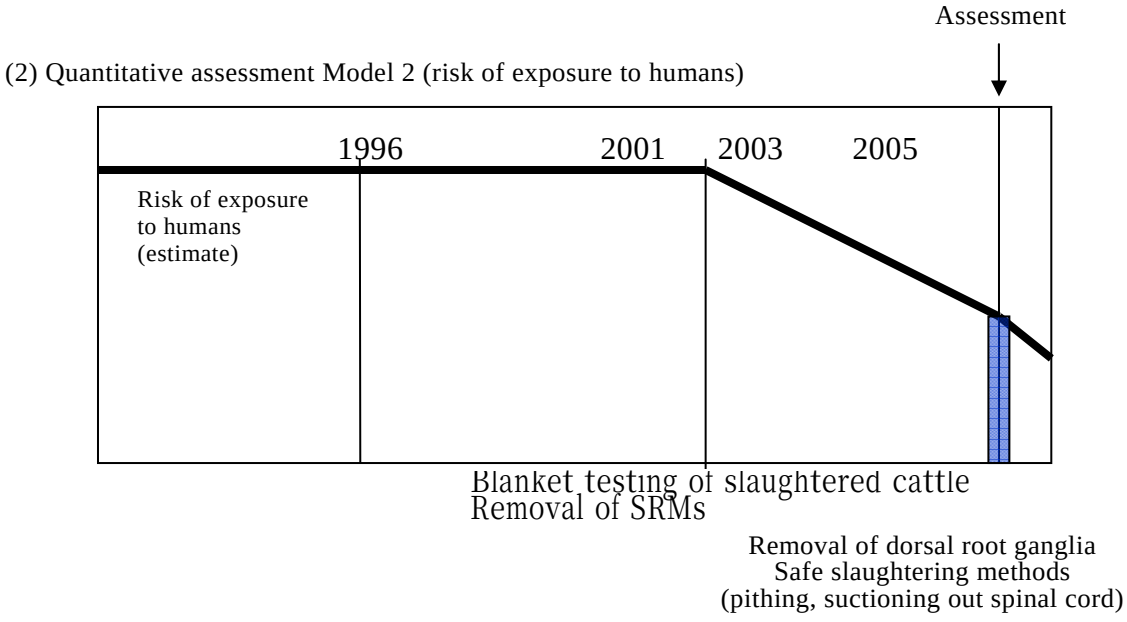
## 3.2 Provisional calculation of quantitative risk assessment of revision to age criterion for BSE testing

### 3.2.1 Assessment from the aspect of exposure risk

#### 3.2.1.1 Assessment model




Cattle that are the subjects of this quantitative risk assessment are those cattle meeting the age criterion of being born in or after July 2003 and aged 20 months or younger (Represented by the coloured square in the chart)



Overall quantitative risk assessment is carried out on risk originating from cattle born in or after July 2003 and aged 20 months or under, taking into consideration the exposure risk to humans as of 2005.

Furthermore, as described earlier, quantitative risk assessments are carried out from both the aspect of examining the exposure risk based on the amount of BSE prions, which are the source of BSE infection, and from the aspect of examining by means of stochastic approach, the effectiveness of BSE testing and SRM removal in reducing risk.

Basic concept of Model 1 for quantitative risk assessment

(1) Estimated extent of BSE contamination in Japan

* Obtained data is data from blanket testing conducted at slaughterhouses since October 2001

* Testing of dead cattle, which began in 2002. However, mandatory testing of all dead cattle aged 24 months or older was not initiated until April 2004.[15)]

* BSE testing results[35), 36)] from the EU for 2001 and 2002 were used to create a model to estimate the extent of BSE contamination in Japan. Data[35), 36)] from the EU for 2001 and 2002 was also used to estimate the rate of BSE infection in the cohorts of the dead cattle.

(2) The effectiveness of the notification announcing the ban on the use of MBM in feed was examined for the period from April 1996, when this notification was released, until the complete ban was imposed in October 2001. On-the-spot inspections carried out in September 2001 at all cattle-raising farms in Japan showed that there were 165 farms giving MBM and other such feed to their cattle.[23)] However, in follow-up inspections, no cattle tested positive for BSE infection. As of March 27, 2005, a total of sixteen animals have tested positive for BSE infection. Twelve of the sixteen animals had been born before the feed ban notification was issued in 1996. Of the other four animals born before the feed ban notification, one was born in 1999, another in 2000, and the remaining two animals were born after the complete ban was imposed in 2001.

As is the case in Japan, measures for banning the use of MBM in Europe are categorized into two types.

The first measure prohibits the use of MBM originating from ruminant animals in feed for ruminant animals. This measure, however, is incapable of preventing cross-contamination of cattle feed by MBM originating from cattle. Epidemiologically, the effectiveness of this measure is viewed as being the difference between the number of

BSE-infected cattle born before and the number of BSE-infected cattle born after implementation of the ban (born after ban: BAB).

However, in situations where traceability systems have not yet been firmly established, there is no way of knowing the birth date of BSE-infected cattle with any accuracy. To cope with this, the assessment should be made based on an additional five years, which is the average BSE incubation period.

Many European countries introduced rapid diagnostic testing systems to screen for BSE in 1999 and 2000, switching from passive surveillance to active surveillance. However, the data before and after switching systems is not compatible with each other. Therefore, the data is separated into before and after the switchover of the systems, and assessments are conducted separately on the respective sets of data.

The second measure mandates the incineration of MBM originating from ruminant animals, and bans its use as feed or any other purpose for all animals. This measure will, in theory, prevent cross-contamination, making it more effective than measure (1) described above.

However, in spite of this measure, BSE-infected cattle have been found that were born after the implementation of this measure (born after real ban, or BARB), and it is also acknowledged that total prevention of contamination is very difficult.

BSE testing data[35), 36)] disclosed in Europe is used to project the changes in the extent of BSE contamination in Japan.

<u>Basic concept of Model 2 for quantitative risk assessment</u>

(1) Risk avoidance by conducting blanket testing at slaughterhouses

* At present, as of 2005, blanket testing is conducted at every slaughterhouse in Japan, ensuring that cattle that test positive in either the preliminary or secondary BSE screening are removed from human food supply. One of the purposes of risk assessment is to project how many cattle are actually BSE-infected, but have escaped detection because their prion accumulation levels are below the detection sensitivity of current BSE testing. Another purpose is to estimate, in the event the current blanket testing is revised so only cattle aged 21 months or older are screened, how many cattle younger than 21 months would be BSE-infected with prion accumulation level above the detection sensitivity, but would escape detection because of the age criterion. .

(2) Safe slaughtering methods at slaughterhouses

* According to a survey conducted by MHLW in October 2004,[17] of the 160 slaughterhouses currently operating in Japan, stun guns are used in the slaughtering process at 149 facilities, and pithing is employed at 115 facilities.
* It has been reported that there is a possibility pithing may cause fragments of tissue from the destroyed brain to migrate into the blood stream.[19] At present, as of March 2005, pithing is conducted at 70% of the slaughterhouses in Japan[17] on 80% of all slaughtered cattle.[18] Therefore, it can be assumed that of all the cattle slaughtered in this country, one in five is not subject to pithing.

(3) SRM removal
* The removal and incineration of SRMs is mandated by the Special Measures Law on Bovine Spongiform Encephalopathy. At all of the 154 slaughterhouses where carcass splitting is carried out, inspectors check to ensure that no spinal cord tissue fragments are adhering to the dressed carcass.[17] However, 11 of the 166 slaughterhouses (includes slaughterhouses for the slaughter of sheep or goats) had not established SSOP for removing SRMs and preventing cross contamination when slaughtering and dismembering animals[30] (as of the end of January 2005).
* At present, as of 2005, the head, spinal cord, vertebral column (dorsal root ganglia), and distal ileum, etc., are removed as SRMs. Recently, there has been a report of a case where BSE prions were found to have also accumulated in the peripheral nerves of a BSE-infected cow. On the other hand, an EU risk assessment report estimates that 99.4% of the infectious dose can be removed through currently conducted SRM removal procedures.[25] However, as young cattle may not always exhibit the BSE prion protein accumulation pattern that corresponds to the estimates in the EU risk assessment report, corrections will be necessary upon further research and study.

(4) Risk reduction by removal of spinal cord prior to carcass splitting
Carcass splitting is a process that has a high potential for contaminating a dressed carcass. Removing the spinal cord before carcass splitting, as well as washing the carcass and removing the spinal cord dura matter after splitting the carcass, are effective methods of preventing fragments of spinal cord tissues from contaminating the dressed carcass.

#### 3.2.1.2 BSE contamination in Japan

The data that can be utilized to estimate the state of BSE contamination in Japan comes from the results of blanket testing of cattle at slaughterhouses, which was initiated in October 2001. However, this data does not include BSE testing data of dead cattle, which are highly likely to be infected with BSE. Although testing of all dead cattle

aged 24 months or older has been mandatory since April 2004,[15] sufficient data for analysis has not yet been obtained. There is a large number of cattle from the cohorts of the four infected young cattle, one born in each of the years 1999, 2000, 2001, and 2002, that are still alive, as none of them are more than five years old. Therefore, there is a lack of data, and the only data presently available for analysis, comes from cattle born between the last half of 1995 and the first half of 1996. It is therefore important that these circumstances and the uncertainty of extrapolating from limited available data be considered when viewing the figures shown below.

When the age distribution of cattle born in 1995 and 1996 and confirmed as BSE-positive in Japan is extrapolated to the age distribution pattern of BSE-positive cases in the EU detected through active surveillance in 2001 and 2002[35), 36)], the following estimate can be made. The estimate takes into consideration the circumstances and conditions described below. Figures showing the number of cattle that tested positive for BSE at slaughterhouses in Japan include cattle that are healthy as well as those that exhibit clinical symptoms not associated with BSE. In the EU statistics, however, cattle that test positive for BSE at slaughterhouses, but exhibit clinical symptoms not associated with BSE infection are classified as risk cattle. Therefore, if the total number of cattle that tested BSE-positive at slaughterhouses in Japan is extrapolated to the EU active surveillance data, in order to estimate the number of BSE-positive cattle that could potentially be discovered among dead or other high-risk cattle at farms in Japan, it is anticipated that the resulting estimated total will be greater than the actual number of BSE-infected cattle. However, because the data resulting from the testing of dead cattle in Japan is regarded as insufficient for analysis, the present estimate of the state of BSE contamination in this country has been made based on the number of cattle that tested BSE-positive at slaughterhouses.

Of the cattle born in Japan in 1995 and 1996, the cattle that have so far been confirmed at the slaughterhouses as BSE-positive are two 5-year-old animals, four 6-year-old animals, one 7-year-old animal, and one 8-year-old animal. As the start of blanket testing was in October 2001, full year data had likely been collected for the 6- and 7-year-old cattle. Therefore, the data of four 6-year-old BSE- positive animals formed the basis for the values that were extrapolated to the previously mentioned EU age distribution of BSE-infected cattle.[35), 36)] As the result, the numbers of BSE-positive cattle that would be found through testing at the time of slaughter were estimated to be one 4-year-old animal, three 5-year old animals (the calculations projected two 5-year-old animals would test positive for BSE, but three animals have actually tested positive so far), four 6-year-old animals, four 7-year-old animals, and five animals aged 8 years old or older, for a total of seventeen BSE-positive animals. According to the estimates, four 7-year-old animals would test positive, but only one animal actually

found to be BSE-infected. These estimates require further study and verification based on test results obtained in the future.

Results obtained through EU surveillance programs show that the number of cattle testing positive for BSE infection is four times greater for high-risk cattle, such as cattle exhibiting neurological symptoms suspicious of BSE infection or dead cattle, than it is for cattle testing positive from among healthy cattle.[36)] If this factor is applied directly to Japan, the number of high-risk cattle that would test positive for BSE is estimated at sixty-eight; four times the seventeen animals estimated to test positive at slaughterhouses. Since April 2004, BSE testing has been mandatory in Japan on dead cattle aged 24 months or older. Of all the dead cattle born in 1995 or 1996 and underwent testing during the one year period from April 2004 to March 1, 2005, two animals tested positive for BSE. The estimate requires further study and verification based on test results obtained in the future.

Based on the estimates described above, the seventeen animals were test positive at slaughterhouses and the sixty-eight animals estimated to test positive from among high-risk cattle, which are removed from the food supply, would together make a total of eighty-five. This is the maximum total number estimated to test positive in the cohort of cattle born during the two-year period of 1995 and 1996. Therefore, the maximum number of BSE-infected cattle for one year is estimated to be forty-three.

**< References >**

Age distribution of cattle that tested positive for BSE based on EU active surveillance program (2001, 2002)[35), 36)]

(This data does not include dead cattle aged less than 24 months.)

| Age (in years) | 2 | 3 | 4 | 5 | 6 | 7 | 8 or more |
|---|---|---|---|---|---|---|---|
| No. of cows | 4 | 13 | 161 | 579 | 1125 | 1022 | 1346 |

#### 3.2.1.2.1 Prior to feed bans (from 1996 to 2001)

With regard to the effectiveness of the notification announcing the ban on the use of MBM in feed for the period from April 1996, when this notification was released, until the complete ban was imposed in October 2001, the government, as described earlier, carried out on-the-spot-inspections in September 2001 at all cattle-raising farms in

Japan. The inspection results showed that there were 165 farms giving MBM and other such feed to their cattle. [22] However, follow-up BSE testing resulted in no cattle testing positive. At that time, there were no measures in place to prevent cross contamination.

Evaluation on the impact of the bans on feeding MBM to ruminant animals in European countries is described below. In the U.K., the effectiveness of the feed bans can be seen in the reduction in the number of BSE-occurrence. Looking at the year of birth (three-year average) of cattle in which BSE occurred, the average number of BSE-occurrence in cattle born during the three years following the MBM ban in 1988 fell to 0.29 of the average for the three-years prior to the implementation of the bans.[37] In Switzerland, the base-point of comparison was set at five years after the implementation of the feed bans, taking into account the incubation period for BSE. Thus, three-year average of the number of cattle that tested positive for BSE five years after the implementation of feed bans, was used as a reference. As a result of the MBM ban and other feed regulations implemented in 1990, the average number of BSE occurrence in three years after the feed bans dropped to 0.6 of the average number of BSE occurrence prior to the feed bans. [38] In the case of France, as with Switzerland, the number of cattle that tested positive for BSE five years after the implementation of feed bans was used as a reference, taking into account the incubation period for BSE. In France, the 1996 ban on the use of SRMs in feed resulted in the average number of BSE occurrence in three years dropping to 0.37 of the average number prior to the ban.[39] In Ireland, the ban on SRMs in feed in 1997 resulted in a drop to 0.55 of the number prior to the ban.[38] And in Germany, the ban on the use of MBM in feed resulted in a drop to 0.44.[38]

Results of the ban on the use of MBM and SRMs in feed for ruminant animals (the proportion of the number of cows testing positive for BSE before and after the ban)

| U.K. (1988) | Switz. (1990) | France (1996) | Ireland (1997) | Germany (1996) |
|---|---|---|---|---|
| 0.29 | 0.6 | 0.37 | 0.55 | 0.44 |

In Japan, a measure banning the use of MBM originating from ruminant animals in feed for ruminant animals was implemented by means of the issuance of administrative guidance by the government in April 1996. As this measure resulted in the same degree of effectiveness as the bans implemented by the various European countries mentioned above, it is believed that the scale of infection for the period leading up to October

2001, when the complete ban of MBM and the incineration of MBM originating from ruminant animals was initiated, progressed as described below.

(i) It is surmised that the effectiveness of administrative guidance issued by the Japanese government in 1996 banning the use of MBM falls somewhere between the effectiveness of the bans implemented by the U.K. and Switzerland, which respectively showed the greatest and smallest degree of effectiveness (0.29 to 0.6). However, the measures implemented by European countries show the effectiveness over a three-year period. Therefore, assuming the risk reduction resulting from the ban over the six-year period from 1995 to 2001 to be the square of the risk reduction resulting from the three-year period of the ban, the scale of contamination is estimated to be 0.1 to 0.36 of that of 1996 [calculated as (0.29 to 0.36) × (0.29 to 0.36)].

However, taking into account the five-year incubation period allowed for the onset of BSE, it is thought that any actual impact in Japan from the administrative guidance, issued by the government in 1996 banning the use of MBM, will become apparent from around 2002. Furthermore, cattle from the cohort that have already reached the average age of BSE onset, in other words, cattle born from the latter half of 1996 through 1998, have not tested positive for BSE, pointing to the possibility that this ban has been effective. Another conclusion drawn from these results is the possibility that contamination by BSE prions has occurred sporadically in Japan.

(ii) Up to this point, estimates regarding the scale of contamination have been based on cattle that have tested positive for BSE. However, as the BSE tests have limits, the figures indicating the number of cattle testing positive for BSE do not represent the total number of cattle infected with BSE. This report works under the assumption that the number of cattle infected with BSE is 1.5 times the number of cattle testing positive for BSE. The reasoning behind this assumption can be shown by the formula below. (A) [the estimated number of cattle infected with BSE in the U.K.: approximately 1,000,000 animals[40)]]÷[the number of cattle officially recognized as having actually contracted BSE in the U.K.: approximately 180,000 animals[37)]] =6.; (B) [the number of cattle in 2002 in the EU testing positive for BSE through active surveillance[36)]] ÷ [the number of cattle in groups targeted for conventional passive surveillance that tested positive for BSE in the EU in 2002] =4. (A) ÷ (B) = 1.5.

(iii) In the cohort of cattle born in 2001, it is estimated that between six and twenty-four animals were infected with BSE [forty-three animals × (0.29 to 0.6) × (0.29 to 0.6)] × 1.5).

#### 3.2.1.2.2 After feed bans (from October 2001 to July 2003)

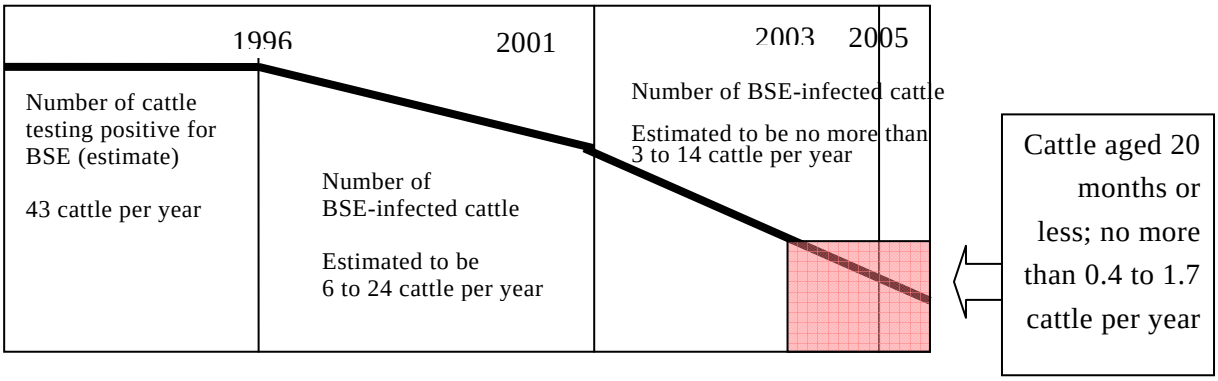
Cattle born in or after July 2003 are the cattle to be exempted from BSE testing under the proposed revision of the testing program.

In October 2001, a complete ban, referred to as the "real ban," on the use of MBM originating from ruminant animals was implemented, and regulations for rendering plants and factories producing compound feed have subsequently been strengthened.[9)]

(i) As a result of the complete ban (the real ban) in the U.K. in 1996, the average number of BSE occurrence over the two years following the implementation of the complete ban dropped to 0.1 of the average number prior to the complete ban.[41)] In Switzerland, the number of cattle testing positive for BSE five years after the implementation of the ban was used as a reference, taking into account the incubation period for BSE. The complete ban in 1996 resulted in the average number of BSE occurrence in two years after the complete ban dropping to 0.55 of the average number in three years prior to the complete ban.[41)] The effectiveness of the 2000 complete ban in Germany and France cannot be verified until 2007.

(ii) If the degree of effectiveness of the measures completely banning MBM in Japan from October 2001 is to fall between the results obtained in the U.K. and Switzerland, the scale of contamination of cattle in the cohort born in or after July 2003 should be between 0.1 and 0.55 of the scale of contamination in October 2001.

(iii) Supposing that the number of cattle born in 2001 infected with BSE is between six and twenty-four (Refer to 3.2.1.2.1 Prior to feed bans (from 1996 to 2001)), it is estimated that the number of cattle becoming infected with BSE from among the cohort of cattle born in or after July 2003 is no greater than three to fourteen animals per year ($6 \times 0.55$ to $24 \times 0.55$). According to statistics compiled by MAFF, cattle slaughtered at younger than 21 months of age account for approximately 12% of all slaughtered cattle.[42)] Therefore, the scale of BSE infection among cattle born in or after July 2003 and aged 20 months or under is projected to be no greater than 0.4 to 1.7 animals per year ($3 \times 0.12$ to $14 \times 0.12$).




### 3.2.1.3 Risk in Japan of human exposure to BSE (2005)

#### 3.2.1.3.1 Basic concept of infectious dose

Known facts collected to date(Data on studies conducted in the U.K. pertaining to infection)

In pathogenicity experiment conducted in the U.K., 4-month old calves were each orally given 100g of brain tissue from BSE-infected cattle, and the progress of infection of the calves was followed. Between 6 and 18 months after the administration of the BSE-infected cattle brain tissues, infectivity was confirmed in the distal ileum of the calves. BSE infectivity was confirmed in the central nervous system 32 to 40 months after administration. Clinical symptoms appeared 35 months after administration. Based on the results of this study, if the infectious dose for each 1g of brain tissue is assumed to be $10ID_{50,}$ the overall infectious dose of an adult cattle showing symptoms of BSE infection is estimated to be approximately $8000ID_{50}$ ( 50% infectious dose by oral administration to cattle).

Moreover, two experiments were conducted to study dose-response for infectivity. In the experiments, quantities ranging from 300g to 1g and 1g to 1mg of brain tissue from cattle exhibiting BSE symptoms were given orally to calves.[27)] From the group of calves that were orally given 300g to 1g of brain tissue from BSE-infected cattle, the $1ID_{50}$(the dose that causes disease in one animal with probability of 50% ) was estimated to be 0.38g[48)]. In the experiment in which calves ingested 1g to 1mg of brain tissue, the smallest quantity of brain tissue resulting in infection was 1mg.

(Data related to BSE testing)

Approximately 4.27 million animals have been tested for BSE in Japan (as of March 26, 2005), out of which twelve animals tested positive. Of these twelve animals, the 8th and 9th confirmed BSE cases were young steer with OD values (optical density value obtained by an ELISA test) near the detection limit. Results of Western Blot analysis showed that the amount of BSE prion proteins accumulated in the obex of the medulla oblongata of these young steer was speculated to be barely 1/500 to 1/1000 of the amount found in other cattle testing positive for BSE.[33)] Western Blot analysis of the 5th and 11th BSE cases estimated the accumulation of BSE prion proteins in the spinal cord and cerebellum to be 1/10, the cerebrum and distal ileum to be not more than 1/100, and peripheral nerves to be not more than 1/1000, of the amount of BSE prion proteins accumulated in the obex. [43)]

However, this data is based on the data from a limited number of subjects. Should more sensitive testing methods for use at slaughterhouses be developed in the future, the estimates presented here may need to be reviewed.

#### 3.2.1.3.2 Reduction of the exposure risk by means of BSE testing and removal of SRMs

Reduction of risk and detection limit with regard to BSE testing at slaughterhouses

Current testing has successfully eliminated twelve BSE-positive animals from food supply.

However, it is widely accepted that the current testing system has limitations in the detection sensitivity. In the preliminary tests, OD values detected by ELISA method is used for determination. The detection threshold of this method, expressed as the infectious dose by means of intercerebral inoculation of mice, is $1ID_{50}$. Therefore, it can be surmised that the infectious dose in the obex of a BSE-infected cattle escaping detection by current testing methods is lower than this.[44)] Furthermore, in the U.K., experiments on infection confirmed BSE infectivity in the ileum of young cattle, even when infectivity could not be detected in the central nervous system. Therefore, the removal of SRMs is essential for reducing the risk of contamination.

At slaughterhouses, current as of January 2005, as a part of the slaughtering of cattle, testing is carried out on the obex after the removal of the head. After evisceration, the carcass is split and dressed. Therefore, SRMs that may potentially contaminate dressed carcasses for human consumption include minute brain tissue fragments spattered when pithing is carried out and spinal cord matter which could contaminate the carcass while butchering, and dorsal root ganglia adhering after the butchering.

Hardly any researches have been conducted to date and data needed to analyze these risks are unavailable.
The average number of cases of spinal cord tissue fragments adhering to the carcass is assumed five cattle or 20%.

There is a 20% chance that spinal cord tissue fragments have not been completely removed, although washing the carcass is believed to reduce the possibility of any fragments remaining to 2% or less

#### 3.2.1.3.3 Risk of human exposure to BSE in the case testing conducted on cattle aged 21 months or older BSE

The scale of BSE-infected cattle included in the cohort of cattle aged 20 months or younger, born in or after July 2003, is thought to be no greater than 0.4 to 2 animals per year (Refer to 3.2.1.2.2 Feed bans (from October 2001 to July 2003) (iii)). Two possible scenarios were envisioned for risk assessments; one is of the case when BSE infection cannot be detected and the other is when it can be detected.

Risk assessment - Scenario 1

The possibility has always been high that there have been BSE-infected cattle in the cohorts of cattle aged 20 months or younger. However, no cattle aged 20 months or younger has ever tested positive for BSE infection. Even if one BSE-infected cattle is present in this cohort of cattle, the cattle tests negative for infection because the BSE prion accumulation is below the test's detection limit. As a result, risk reduction is dependent on the removal of SRMs. Under these circumstances, should the age of cattle targeted for BSE testing be set at 21 months or older, the risk of human exposure to BSE remains unchanged.

Risk assessment – Scenario 2

The possibility of cattle in the cohort of cattle aged 20 months or younger testing positive for BSE infection cannot be ignored. There is no data for BSE testing in the EU for cattle aged 20 months or younger. According to data obtained from BSE testing in the EU,[35) 36)] the peak in cattle testing positive for BSE infection is seen in 6-year old cattle. The age distribution of cattle sent to slaughterhouses in the EU and in Japan is considered to be similar. From this data, it can be extrapolated that the number of 3-year old cattle is 1/100 of the number of 6-year old cattle.

Moreover, based on EU data, the number of 3-year old cattle testing positive for BSE infection, represents 1/250 of the total number of cattle that tested positive. Data from Japan showed that of the twelve animals that tested positive for BSE infection, none were aged 20 months or younger; however, there were steer aged 21 and 23 months that tested positive for BSE infection.

If the number of cattle becoming infected with BSE from among the cattle born in or after July 2003 is no greater than three to fourteen animals per year (Refer to 3.2.1.2.2 After feed bans (from October 2001 to July 2003) (iii)), then the number of cattle to test positive for BSE infection would be 2/3 this number, or two to nine animals (3 × 2/3 to 14 ×2/3) (1/1.5 Refer to 3.2.1.2.1 Prior to feed bans (from 1996 to 2001) (ii)).

If the EU data (1/250) is applied to estimate potential BSE infection, the possibility of cattle younger than 3 years of age to test positive is estimated to be 0.008 to 0.036 animals per year (2 × 1/250 to 9 × 1/250). On the other hand, if the Japanese data is used, the possibility of cattle younger than 3 years of age to test positive for BSE infection would be 0.3 to 1.5 animals per year (2 × 2/12 to 9 × 2/12). In either case, if these formulas are applied to cattle aged 20 months or younger, it is surmised that the numbers will be even lower.

If testing is conducted only on cattle aged 21 months or older, the risks represented by these figures are to pass undetected.

However, the possibility that 20% the spinal cord tissue fragments from undetected BSE-infected cattle may remains , and after washing the carcass the possibility of any fragments remaining will be reduced to 2% or less.

Moreover, the level of accumulated BSE prions of the BSE-infected cattle is estimated to be close to that of 21-month and 23-month cattle that tested positive. Therefore, it can be surmised that if the level of accumulation is near the detection limit of current BSE testing, this level is $1ID_{50}$ as measured by the intracerebral inoculation of mice.

### 3.2.2 Views on quantitative risk assessment regarding revision of testing age

Changes in risk regarding cattle aged 20 months or under should the BSE testing policy be changed from blanket testing to testing cattle aged 21 months or older.

| Age<br>(as of March 2005)<br>Month of birth | Aged 0 to 20 months<br>Born in or after July 2003 | |
|---|---|---|
| | blanket testing | Test cattle aged 21 months or older |
| ELISA test | Yes | Cattle aged 0 to 20 months are not tested |
| BSE-infected cattle<br>・infection rate<br>・amount of BSE prion accumulation | ・no greater than 0.4 to 2 cattle per year<br>・level of detection limit ($1ID_{50}$ intracerebral inoculation of mice) | ・no greater than 0.4 to 2 cattle per year<br>・level of detection limit ($1ID_{50}$ intracerebral inoculation of mice) |
| BSE-positive cattle<br>・detection rate<br>・amount of BSE prion accumulation | ・no greater than 0.008 to 0.036 cattle aged less than 3 years old per year (no greater than 0.3 to 1.5 cattle per year, if based on Japanese data)even lower in ages younger than 20months<br>・level of detection limit ($1ID_{50}$ intracerebral inoculation of mice) | ・Cattle aged 0 to 20 months are not tested |
| BSE prion contaminationin meat<br>・level of contamination<br>・amount of contamination | ・20% chance of spinal cord tissue fragments remaining; reduction to 2% through washing the dressed carcass<br>・level of detection limit ($1ID_{50}$ intracerebral inoculation of mice) | ・20% chance of spinal cord tissue fragments remaining; reduction to 2% through washing the dressed carcass<br>・level of detection limit ($1ID_{50}$ intracerebral inoculation of mice) |

Based on the data shown above, it is speculated that the increased risk brought about by changing the current policy of conducting BSE testing on all cattle at slaughterhouses to testing cattle aged 21 months or older, will correspond to the risk from cattle aged 20 months or under, that have developed sufficient BSE prion accumulation to be detected through testing. The increased risk is estimated as below.

If the EU data is applied to estimate potential BSE infection, the possibility of cattle younger than 3 years of age to test positive is estimated to be 0.008 to 0.036 animals per year. On the other hand, if the Japanese data is used, the possibility of cattle younger than 3 years of age to test positive for BSE infection is 0.3 to 1.5 animals per year. In either case, if these formulas are applied to cattle aged 20 months or under, it is surmised that the numbers will be even lower. If testing is conducted only on cattle aged 21 months or older, the risks represented by these figures are to pass undetected.

The risk of BSE prion contamination in meat resulting from the aforementioned young cattle is estimated as follows. Assuming that there is a 20% chance of spinal cord tissue

fragments escaping removal, and the figure shall be reduced to 1/10 through washing the carcass, the frequency of contamination would be 0.02.Also assuming that the amount of BSE prions accumulated in the spinal cord tissue fragments is approximately equal to the amount in the brain, the amount of contamination in meat is estimated to be close to the detection limit ($ID_{50}$ with intracerebral inoculation of mice). This is the risk to pass undetected when the current policy of BSE testing at slaughterhouses is revised so as to test cattle aged 21 months and older

With regard to estimating quantitative risk, every effort has been made to use valid quantitative data in order to minimize uncertainty. When using data that is highly uncertain, estimations were based on the worst case scenario.

This is the basic stance of risk assessment; it is necessary to understand the uncertainty involved in the estimations, as the results have been reached based on extrapolation from a limited amount of data. Verification of the assessments in this report will be necessary based on knowledge and data that will be obtained in the future through investigation and research in such areas as testing at slaughterhouses, the results of the testing of dead cattle, and the development of practical testing methods of higher sensitivity, .

### 3.3 Views regarding the risk reduction effect of the removal of SRMs

The actual state of the Abattoir Law

According to a survey conducted by the MHLW in October 2004,[17] of the 160 slaughterhouses currently involved in the slaughter of cattle, 149 of these facilities use stun guns in the slaugthering process, and 115 slaughterhouses conduct pithing. Moreover, in accordance with the Special Measures Law on Bovine Spongiform Encephalopathy, the removal and incineration of SRMs which are considered to be the cause of over 99% of overall amount of contamination in cattle, has been made compulsory. At all of the 154 slaughterhouses where carcass splitting is carried out, test inspectors have verified that no spinal cord tissue fragments are adhering to the dressed carcass as a result of carcass splitting.[17] However, 11 of the 166 slaughterhouses (including slaughterhouses of sheep or goats) had not established SSOP for removing SRMs and preventing cross contamination when slaughtering animals[30] (as of January 2004).

Verifying the implementation of measures for removal of SRMs and prevention of cross contamination

Currently, inspections regarding the removal of SRMs, i.e.the head (with the exception of the tongue and meat from the cheeks), spinal cord, distal ileum (2 meters from connection to caecum), and the vertebral column, are conducted at irregular intervals (approximately once a year).[18)] Moreover, inspections of methods such as stunning, pithing, and carcass splitting, that may cause the spattering of spinal cord tissue are conducted when the need arises.[17)]

As reported in the "Interim Report," if removal of SRMs can be ensured, the risk of humans becoming infected with vCJD will be greatly reduced. This is a key measure in dealing with BSE in countries all over the world as well as in Japan. Therefore, it is essential for all slaughterhouses to implement schemes to ensure that SRMs are removed, and constantly check whether or not methods for preventing contamination by SRMs are effective. At present, however, there are still some slaughterhouses that have not documented any sanitary standards of operating procedures for the removal and incineration of SRMs and the verification method, nor have kept records of their implementation.

The MHLW plans to conduct;

(1) on-the-spot inspections on a regular basis to get a true picture of SRM control at slaughterhouses, in order to ascertain the degree of compliance with laws and regulations or other related notifications regarding SRM control. These inspections will check stunning methods and ascertain whether or not pithing is being carried out, and also mandate, should it be necessary, the establishment of sanitation standards of operating procedures for the removal and incineration of SRMs and their verification methods as well as written records of their implementation;

(2) inspections on a regular basis to check whether or not spinal cord tissue has been removed prior to carcass splitting, as well as to check methods of SRM incineration, methods of spinal cord tissue removal after carcass splitting is carried out, and washing methods of dressed carcasses. The results of these inspections will be made public;

(3) scientific research to develop an evaluation method regarding prevention of SRM contamination during the processing of slaughtered animals, and promote the practical application of such evaluation methods at slaughterhouses.

In view of the critical significance of the removal of SRMs as described above, it is essential to pursue these measures. And it is necessary to evaluate the effectiveness of such measures in avoiding risks, establish specific objectives, and carry out these measures. Furthermore, if any inadequacy is recognised in SRM control, the

government must not only provide guidance to draw up and implement a systematic plan to appropriately improve the current situation, but also closely monitor the progress of the improvement.

It has been pointed out[19] that when pithing is carried out, there is a possibility that brain or spinal cord tissue will leak out from the hole created by the stunning process, resulting in contamination of meat, the slaughterhouse facilities, and other elements, and that pithing can cause migration of brain and spinal cord tissue to other organs via the blood stream, making it necessary to promote the prohibition of pithing in order to ensure the safety of meat. At present, approximately 30% of the slaughterhouses in Japan no longer employs pithing[17] but it is necessary to further promote the prohibition of pithing. While the course of action taken by the MHLW to "continue discussions with the intent to promote a policy prohibiting pithing" is very important, it is essential that implementation programs with concrete objectives are established, and every effort must be made for swift and reliable implementation of such programs.

### 3.4 View on feed bans

(1) Prevention of cross-contamination from imported feed
In accordance with the Feed Safety Law, it is mandatory for every feed importer to submit information such as its name, the address of its head office, the location of its sales facilities, the location of its storage facilities, the kinds of feed it imports, and other details. However, it is not possible to know the kinds of raw materials contained in compound or mixed feed from the submitted information.[7] For the future, to ensure that proteins derived from animals do not mix into feed, it is essential to tighten and enhance enforcement of regulations on feed imports[20), 45] that might cause BSE.

For this purpose, adding the raw materials of imported compound and mixed feed to the categories of information that must be reported, and carrying out on-the-spot inspections by the Fertilizer and Feed Inspection Services (an Incorporated Administrative Agency) upon the understanding of what raw material consists the imported feed, are essential to the thorough implementation of measures to prevent proteins derived from ruminant animals from mixing in feed.

(2) Thorough implementation of regulations for feed dealers
At present, feed dealers, with the exception of retailers, i.e. those who sell feed exclusively to farmers, must comply with regulations for feed dealers requiring them to submit such information as described above.[7] However, including retailers among the feed dealers targeted for observation with regard to compliance with feed bans is seen as an effective risk avoidance measure to strengthen inspection and guidance systems

related to feed dealers, leading to more thorough compliance with regulations for the keeping and storing of feed by feed dealers.

(3) Thorough implementation of regulations for cattle-raising farms
Currently, efforts are being made to ensure that all farmers are informed of, and provided guidance on the relevant laws and regulations, through field inspections carried out on three types of livestock (cattle, pigs, and poultry) by regional agricultural administration offices, and on-the-spot inspections conducted by prefectural authorities. Regional agricultural administration offices carry out the field inspections on the three types of livestock on a rotating basis.[7)] The number of farms, the contents of the inspection, and other details of the on-the-spot inspections are left up to the discretion of the prefectural authorities.[7)]

Therefore, in order to enhance the system for carrying out inspections and providing guidance, thereby preventing improper use and misappropriation of feed at cattle-raising farms, it is important to ensure complete compliance with BSE measures through such measures as annual field inspections of cattle-raising farms by regional agricultural administration offices or other government authorities, presentation of the matters that need to receive intensive inspection and guidance by the prefectural authorities, and disclosure of the inspection results. It is also necessary to develop a quantitative assessment method, verify the effectiveness of the enhanced measures, and establish clear objectives.

To ensure the total eradication of BSE from Japan, it is critically important to make sure that BSE infection shall not occur, by thoroughly implementing feed bans, and preventing the transmission of BSE prions among cattle.

### 3.5 Further promotion of research and study of BSE

To this day, MHLW and MAFF have been carrying out research and study activities on BSE, including studies on testing methods and surveillance. Since the outbreak of BSE in Japan, the two Ministries have been engaged in a wide range of efforts, such as developing a rapid, highly sensitive testing method to be carried out at slaughterhouses, conducting experiments involving the inoculation of animals to understand the pathogenesis of BSE infection, developing detection technology capable of detecting BSE prion proteins contained in feed or meat, and studies on contamination prevention methods.[46)]

It is essential that a wide range of research and study be promoted to combat BSE, including finding BSE-infected cattle through testing methods with a high degree of

sensitivity and specificity, ensuring the safety of meat by preventing SRM contamination, and investigation into the mechanism that leads to the onset of BSE.Therefore, it is essential for both Ministries to promote the development of BSE testing methods, the development of assessment systems to evaluate measures to prevent SRM contamination, and promote research and study through experiments involving animal inoculation and oral ingestion of BSE by cattle to uncover the mechanism of the accumulation of BSE prion proteins.

Special attention should be given to acquisition, transportation, storage, etc., of samples that are necessary to facilitate implementation of research and study.[47)] If test samples cannot be acquired promptly, progress cannot be made in BSE research. Moreover, it is also necessary to continue research on identifying the causes of BSE, which will contribute to BSE measures.

Furthermore, basic research on prions and research to provide data needed to perform risk assessments is also very important. Scientific and quantitative risk assessment is impossible unless such research and study is promoted.

## 4. Conclusions

The conclusions described below are in response to the inquiries (1) through (4) issued by the Ministry of Health, Labour and Welfare (MHLW) and the Ministry of Agriculture, Forestry and Fisheries (MAFF) of Japan.

(1) Revision of current policy as to exempt cattle under a certain age from BSE testing conducted at slaughterhouses, and promotion of research and development of testing technology

In order to estimate the impact in the case when the current policy of conducting BSE testing on all cattle at slaughterhouses is revised from April 2005, so that only cattle aged 21 months and older will be subject to compulsory testing, a qualitative comparison was conducted between the two cases of testing all cattle and of testing cattle aged 21months and older, concerning the levels of BSE accumulation in live cattle and contamination in meat. The results show that in both cases, the levels of BSE accumulation and contamination in meat all fall into the range of “negligible” to “very low.” Provisional estimates based on the quantitative evaluation also lead to a similar conclusion. From these results, it can be concluded that the level of impact upon human health via food (in other words, health risk in food) caused by the revision of testing age would rise no higher than “very low.”

A summary of the recommendations regarding the promotion of research and development of testing technology are described in "(4) Further promotion of BSE research studies."

(2) Ensuring removal of SRM

The removal of SRM is an essential measure that will lead to the reduction of the risk of contracting vCJD for the people of Japan. Therefore, conducting regular surveys at slaughterhouses to verify compliance with measures for SRM management and implementation of appropriate methods to prevent contamination from SRMs, is an effective way to prevent such risks.

To further reduce the risk of BSE contamination of meat, it is essential to set concrete steps towards a total ban on pithing, and to implement these steps as soon as possible. In order to prevent the spattering of spinal cord tissue, it is essential to continually ensure compliance with Sanitation Standard Operating Procedures (SSOP) on slaughtering methods. Furthermore, it is important to verify the effectiveness of SRM management procedures. Although there is no currently available effective alternative technology to stunning, it is also important that implementation of effective alternatives be explored in the future.

(3) Enhancing the enforcement of feed bans

Requiring notification of the ingredients in imported compound and mixed feeds is an effective way of reducing the risk of cattle exposure to BSE prions. In order to verify the effectiveness of the feed bans, it is also important to strengthen the inspection and guidance systems with regard to feed importers, feed manufacturers, feed distributors and dealers, and cattle ranchers. Concrete objectives need to be established and achieved as soon as possible.

(4) Promoting further BSE research studies

There is a definite need for the development of testing methods with greater sensitivity. The MHLW and MAFF must make substantial efforts to provide specimens, including younger cattle, for testing, as well as arranging for their transport and storage, in order to facilitate the implementation of BSE research. Any new data that is obtained will serve as an important resource for future risk assessments. The development of methods to assess the effectiveness of SRM contamination prevention measures and other measures for avoiding risks should be promoted, as well as propelling research involving animal inoculation tests to clarify, among other things, the mechanism that allows the accumulation of BSE prion proteins. Furthermore, in addition to basic research, research for the preparation of data essential to performing risk assessments should be promoted.

## 5. Additional Remarks

When promoting the complete removal of SRMs (particularly the banning of pithing) and securing the effectiveness of feed bans based on the evaluations made in this report, MHLW and MAFF should establish concrete goals and build a system that enables objective evaluation.

It is essential to continuously verify the effectiveness of relevant measures, including measures that will be implemented based on this evaluation. Annual reports on the results of surveys and discussions related to all BSE measures should be submitted to the Prion Expert Committee to receive evaluations, and efforts should be made to obtain public consensus through risk communication and other means.

Concerning inquiry regarding revisions to the age criteria for BSE testing, the following two criticisms should be taken into consideration.

(1) The influence on BSE prion accumulation in live cattle exerted by imported compound and mixed feed is still unknown, and countermeasures that should be implemented remain an unresolved issue. With regard to the removal of SRMs, there are plans to reinforce such measures as the establishment of a system to monitor the removal of SRMs and the banning of pithing. As there is very little scientific knowledge currently available, that can be used to evaluate the impact of very low levels of BSE contamination on health risk in food, it is more reasonable to carry out the revision of blanket testing to age-based testing after confirming the effectiveness of the measures mentioned above.

(2) It goes without saying that promoting the development of technology to refine testing sensitivity is essential not only for BSE, but also for any infectious disease. However, should testing be conducted only on cattle aged 21 months or older, voluntary blanket testing which is regarded as a means of avoiding confusion, will be necessary, otherwise it will become impossible to evaluate test results of young cattle under this age limit.

Due to lack of available data and the scientific uncertainties surrounding BSE and prion diseases, further promotion of research and study is essential to provide necessary data for risk assessments. Scientific knowledge forms the basis of risk assessment. Should any new data or innovative technologies be obtained in the future, regarding the scientific knowledge on which this assessment is based、this assessment will need to be revised.

Based on data accumulated from the past in Japan and other relevant data that can be applied to making assessments, this is a report on comprehensive evaluation of the risk related to young cattle and other issues as of March 2005, essentially by evaluating the various risks that are considered to be in the background, such as the level of BSE contamination, and the effectiveness of various measures, and the elimination of cattle that have tested positive for BSE infection through testing at slaughterhouses, safe slaughtering methods, and the removal of SRMs. In other words, this report does not represent a risk assessment compiled solely on the factor of age, independent of other underlying risks such as those mentioned above. Therefore, when a risk assessment of BSE infection in other countries is performed in the future, it can be surmised that a diverse range of data will be needed to perform a comprehensive evaluation.

(Reference documents)


1. Interim Report; Cabinet Office, Food Safety Commission, Prion Expert Committee.
2. Inquiry (Ministry of Health, Labour and Welfare, Food Safety Committee Notification No. 1015001; Consumer Safety Committee Notification No. 16 - 5410; October 15, 2004.)
3. Handout distributed at 20th Meeting of the Food Safety Commission's Prion Expert Committee. 4.
4. Handout distributed at 17th Meeting of the Food Safety Commission's Prion Expert Committee. Doc. 3-3: 15.
5. Handout distributed at 17th Meeting of the Food Safety Commission's Prion Expert Committee. Doc. 3-3: 13.
6. Handout distributed at 17th Meeting of the Food Safety Commission's Prion Expert Committee. Doc. 3-3: 27.
7. Handout distributed at 16th Meeting of the Food Safety Commission's Prion Expert Committee. Doc. 3-2: 2.
8. Handout distributed at 17th Meeting of the Food Safety Commission's Prion Expert Committee. Doc. 3-3: 5.
9. Handout distributed at 16th Meeting of the Food Safety Commission's Prion Expert Committee. Doc. 3-2: 4-7.
10. Handout distributed at 16th Meeting of the Food Safety Commission's Prion Expert Committee. Doc. 3-2: 9.
11. Handout distributed at 16th Meeting of the Food Safety Commission's Prion Expert Committee. Doc. 3-2: 28.
12. Handout distributed at 16th Meeting of the Food Safety Commission's Prion Expert Committee. Doc. 3-2: 21.
13. Ministry of Agriculture, Forestry and Fisheries press release: Cases of violation of the criteria and standards for the Feed Safety Law. March 2, 2005.
14. Handout distributed at 16th Meeting of the Food Safety Commission's Prion Expert Committee. Doc. 3-2: 67.
15. Handout distributed at 21st Meeting of the Food Safety Commission's Prion Expert Committee. 2.
16. Handout distributed at 16th Meeting of the Food Safety Commission's Prion Expert Committee. Doc. 3-1: 76.
17. Handout distributed at 17th Meeting of the Food Safety Commission's Prion Expert Committee. Doc. 3-2: 4,5.
18. Handout distributed at 16th Meeting of the Food Safety Commission's Prion Expert Committee. Doc. 3-1: 1.

19. Anil MH, Love S, Williams S, Shand A, McKinstry JL, Helps CR, Waterman-Pearson A, Seghatchian J, Harbour DA. Potential contamination of beef carcasses with brain tissue at slaughter. *Vet. Rec.* 1999; 145(16):460-462.
20. BSE Epidemiological Surveillance Team. Report on Results of Epidemiological Analysis. Ministry of Agriculture, Forestry and Fisheries. September 2003.
21. Trade statistics. Ministry of Finance.
22. Handout distributed at 16th Meeting of the Food Safety Commission's Prion Expert Committee. Doc. 3-2: 11.
23. Handout distributed at 16th Meeting of the Food Safety Commission's Prion Expert Committee. Doc. 3-2: 8.
24. Handout distributed at 18th Meeting of the Food Safety Commission's Prion Expert Committee. Doc. 3.
25. Scientific Steering Committee. Opinion on the Scientific Steering Committee on the human exposure risk (HER) via food with respect to BSE, Adopted on 10 December 1999.
26. Handout distributed at 16th Meeting of the Food Safety Commission's Prion Expert Committee. Doc. 2.
27. Matthews, D: Proc. International Conference: TSE in Animal Populations – Fact and Fiction. Colorado, September 10-11, 2003
28. Scientific Steering Committee. Opinion on TSE Infectivity Distribution in ruminant Tissues (State of Knowledge, December 2001), Adopted by the Scientific Steering Committee at its meeting of 10-11 January 2001.
29. Love, S., Helps, C.R., Williams, S., Mckinstry, J.L., Brown, S.N., Harbour, D.A., Anil, M.H. Methods for detection of haematogenous dissemination of brain tissue after stunning of cattle with captive bolt guns. *J. Neuroscience Methods.* 2000, 99; 53-58
30. Handout distributed on the day of the 21st Meeting of the Food Safety Commission's Prion Expert Committee.
31. Ministry of Health, Labour and Welfare's Grant-in-Aid for Scientific Research, 2001. A Health Science Special Research Project. Comprehensive and independent reports: *Research on bovine spongiform encephalopathy.* Principal researcher: Morikazu Shinagawa; Department of Veterinary Public Health, Obihiro University of Agriculture and Veterinary Medicine.
32. Ministry of Health, Labour and Welfare's Grant-in-Aid for Scientific Research, 2003. A Food Safety Assurance Research Project. Comprehensive and individual reports: *Improving prion detection technology, and Research on the mechanism of infection and onset of bovine spongiform encephalopathy*. Principal researcher: Tetsutaro Sata; National Institute of Infectious Diseases.
33. Yamakawa Y, Hagiwara K, Nohtomi K, Nakamura Y, Nishijima M, Higuchi Y, Sato Y, Sata T and the Expert Committee for BSE Diagnosis, Ministry of Health,

Labour and Welfare of Japan. Atypical Proteinase K-Resistant Prion Protein(PrPres) Observed in an Apparently Healthy 23-Month –Old Holstein Steer. *Jpn. J. Infect. Di*s. 2003; 56.

34. Bovine spongiform encephalopathy (BSE) Testing Manual. Ministry of Agriculture, Forestry and Fisheries. October 2003.
35. European Commission: Report on the monitoring and testing of bovine animals for the presence of bovine spongiform encephalopathy (BSE) in 2001. 2001.
36. European Commission: Report on the monitoring and testing of ruminants for the presence of transmissible spongiform encephalopathy (TSE) in 2002. 2002.
37. DEFRA (Department for Environment Food and Rural Affairs). Website: (http://www.defra.gov.U.K./animalh/bse/statistics/bse/yrbirth.html)
38. OIE (Office International des Epizooties) Website: (http://www.oie.int/eng/info/en_esb.htm)
39. Avis du Comite d'Experts Speciallise sur les ESST sur le suivi de l'epizootie d'ESB en France
40. World Health Organization: Understanding the BSE threat. WHO/CDS/CSR/EPH/DIS/2002.6 Geneva, Switzerland, October 2002.
41. European Commission: Report on the monitoring and testing of ruminants for the presence of transmissible spongiform encephalopathy (TSE) in the EU in 2003, including the results of the survey of prion protein genotype in sheep breeds. 2003.
42. On the National Livestock Breeding Center (Independent Administrative Agency). Website: Based on Tabulated Results of the National Cattle Identification Database; Cattle slaughtered in 2003 categorized by age and breed. URL: http://www.id.nlbc.go.jp/html/kouhyouDL.htm
43. Ministry of Health, Labour and Welfare's Grant-in-Aid for Scientific Research, 2002. An Research Project on Emergency Measures for Overcoming Hepatitis and Other Diseases. (Field of research: bovine spongiform encephalopathy) Independent research report: *Biochemical detection of variant-type prion proteins.* Yoshio Yamakawa, Department of Cytochemistry, National Institute of Infectious Diseases.
44. Dealys, J. P., Comoy, E., Hawkins, S., Simons, S., Schimmel, H., Wells, G., Grassl, J., and Moynagh, J. Screening slaughtered cattle for BSE. *Nature*, 2001;409:476-77.
45. Sugiura, K. Risk of introduction of BSE into Japan by the historical importation of cattle from the United Kingdom and Germany. *Preventive Vet. Med.* 2004; 64:191-200.
46. Handout distributed at 16th Meeting of the Food Safety Commission's Prion Expert Committee. Doc. 3-2: 56-66.

47. Handout distributed at 17th Meeting of the Food Safety Commission's Prion Expert Committee. Doc. 3-3: 38.
48 Lary, G. Paisley., Julie, Hostrup-Pedersen. *Preventive Veterinary Medicine,*2005;68:263-275.

## 6. (Reference) For the Future

### 6.1 Quasi-quantitative risk assessment model for effectiveness of SRM removal in risk reduction (Personal draft of model by Chairman of Prion Expert Committee)

There has never been a model for performing a quantitative assessment of the effectiveness of procedures for avoiding risks at slaughterhouses. This has not been done because of the difficulty in modeling the processes carried out at slaughterhouses into risk weighting factors.However, I have drawn up a risk prevention model on my own. The figures have no scientific basis. Nevertheless, I have created this model based on my personal belief that a model is indispensable not only for risk assessment with a view towards development of preventive medicine measures, but also to establish objectives for risk management and to evaluate the effectiveness of the objectives.

Concept of quantitative assessment of exposure risk (Model)

| BSE testing at slaughterhouses is initiated in October 2001<br><br>If testing is not carried out at slaughterhouse, add 20 points | Pithing | Suction removal of spinal cord tissue | Washing done after carcass splitting | Dura matter removal | Risk point | Removal of SRMs initiated in October 2001<br><br>If SRM removal is not carried out, add 20 points |
|---|---|---|---|---|---|---|
| | Yes | No | No | No | 20 | |
| | | | Yes | No<br>Yes | 18<br>8 | |
| | | Yes | No | No | 15 | |
| | | | Yes | No<br>Yes | 10<br>6 | |
| | No | No | No | No | 10 | |
| | | | Yes | No<br>Yes | 6<br>4 | |
| | | Yes | No | No | 4 | |
| | | | Yes | No<br>Yes | 2<br>1 | |

Shown below is a model calculation that was done based on the quantitative model shown above, and represents the effectiveness of risk avoidance from 2001 to December 2004. Also shown below is the estimated effectiveness of banning pithing hereinafter, based on the assumption that pithing will be reduced by 50% from current figures, and the estimated effectiveness of removal of spinal dura matter when carried out 90% of the time.

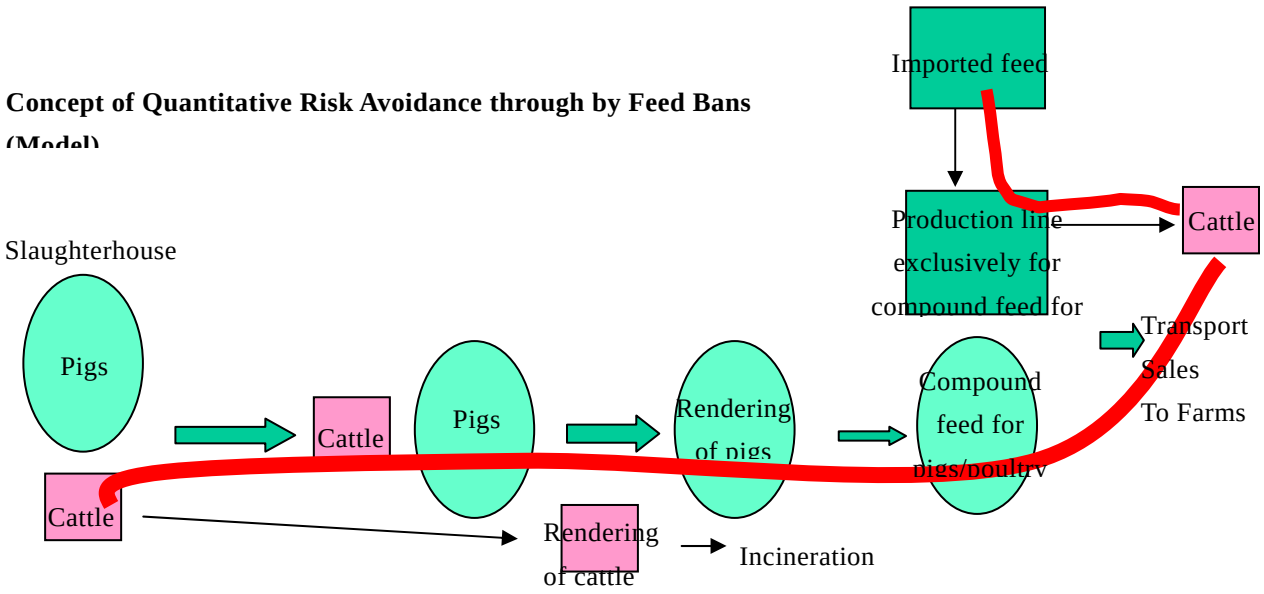
It is essential that research and study needed to perform risk assessment be carried out in the future, and provide scientific basis to this model.

| BSE testing | Pithing | Spinal cord suction | Washing after carcass splitting | Dura matter removal | Risk point | SRM | |
|---|---|---|---|---|---|---|---|
| No testing prior to October 2001<br>20 | Yes | No | No | No | 20 | No removal prior to October 2001<br><br>20 | 60 |
| Blanket testing December 2002<br><br>1 | Yes | No | Yes | No | 18×0.1 | No removal of spinal cord<br><br>4 | 14.6 |
| | | Yes | No | No | 15×0.4 | | |
| | | | Yes | No | 10×0.3 | | |
| | No | No | Yes | No | 6×0.1 | | |
| | | | Yes | No | 2×0.1 | | |
| Blanket testing December 2003<br><br>1 | Yes | No | Yes | No | 18×0.1 | Removal of vertebral column<br><br>1 | 8.1 |
| | | Yes | Yes | Yes | 10×0.7 | | |
| | No | Yes | Yes | No | 2×0.1<br><br>1×0.1 | | |
| Blanket testing December 2004<br><br>1 | Yes | No | Yes | No | 18×0.1 | Removal of vertebral column<br><br>1 | 6.3 |
| | | Yes | Yes | Yes | 6×0.7 | | |
| | No | Yes | Yes | No | 2×0.1<br><br>1×0.1 | | |
| Objective of revision<br><br>Testing of cattle 21 months or older<br><br>1 | Yes | No | Yes | No | 18×0.1 | Removal of vertebral column<br><br>1 | 3.2 |
| | | Yes | Yes | Yes | 6×0.1 | | |
| | No | Yes | Yes | Yes | 1×0.8 | | |

## 6.2 Quasi-quantitative risk assessment model for effectiveness of feed bans in risk reduction (Personal draft of model)

There has never been a model for performing a quantitative assessment of the effectiveness of procedures for avoiding risks during the feed production process. This has not been done because of the difficulty in modelling all of the feed producing processes, including cross-contamination factors, into risk weighting factors. However, I have drafted a risk prevention model on my own. The figures have no scientific basis. Nevertheless, I have created this model based on my personal belief that a model is indispensable not only for risk assessment with a view towards development of preventive medicine measures, but also to establish objectives for risk management and to evaluate the effectiveness of the objectives.

**Concept of Quantitative Risk Avoidance through by Feed Bans (Model)**



Concept of quantitative assessment on avoiding risk regarding feed (Model 1)

| **Slaughter-house** | **Rendering plant** | **Feed plant: domestic feed** | **Risk point** | **Feed plant: imported feed** | **Risk point** |
|---|---|---|---|---|---|
| Exclusively for cattle; Exclusively for pigs/ poultry | Exclusively for cattle; Exclusively for pigs/ poultry | Exclusively for cattle; Exclusively for pigs/ poultry | 1 | Exclusively for cattle; Exclusively for pigs/ poultry | 1 |
| | | Separated lines | 2 | Separated lines | 2 |
| | | Mixed lines | 5 | Mixed lines | 5 |
| | Separated lines | Exclusively for cattle; Exclusively for pigs/ poultry | 5 | Exclusively for cattle; Exclusively for pigs/ poultry | 1 |
| | | Separated lines | 7 | Separated lines | 2 |
| | | Mixed lines | 10 | Mixed lines | 5 |
| | Mixed lines | Exclusively for cattle; Exclusively for pigs/ poultry | 20 | Exclusively for cattle; Exclusively for pigs/ poultry | 1 |
| | | Separated lines | | Separated lines | 2 |
| | | Mixed lines | | Mixed lines | 5 |
| Separated lines | Exclusively for cattle; Exclusively for pigs/ poultry | Exclusively for cattle; Exclusively for pigs/ poultry | 7 | Exclusively for cattle; Exclusively for pigs/ poultry | 1 |
| | | Separated lines | 9 | Separated lines | 2 |
| | | Mixed lines | 12 | Mixed lines | 5 |
| | Separated lines | Exclusively for cattle; Exclusively for pigs/ poultry | 9 | Exclusively for cattle; Exclusively for pigs/ poultry | 1 |
| | | Separated lines | 12 | Separated lines | 2 |
| | | Mixed lines | 15 | Mixed lines | 5 |
| | Mixed feed | Exclusively for cattle; Exclusively for pigs/ poultry | 20 | Exclusively for cattle; Exclusively for pigs/ poultry | 1 |
| | | Separated lines | | Separated lines | 2 |
| | | Mixed lines | | Mixed lines | 5 |

| | | | | | |
|---|---|---|---|---|---|
| Mixed feed | Exclusively for cattle; Exclusively for pigs/ poultry | Exclusively for cattle; Exclusively for pigs/ poultry | | Exclusively for cattle; Exclusively for pigs/ poultry | 1 |
| | | Separated lines | 20 | Separated lines | 2 |
| | | Mixed lines | | Mixed lines | 5 |
| | Separated lines | Exclusively for cattle; Exclusively for pigs/ poultry | | Exclusively for cattle; Exclusively for pigs/ poultry | 1 |
| | | Separated lines | 20 | Separated lines | 2 |
| | | Mixed lines | | Mixed lines | 5 |
| | Mixed lines | Exclusively for cattle; Exclusively for pigs/ poultry | | Exclusively for cattle; Exclusively for pigs/ poultry | 1 |
| | | Separated lines | 20 | Separated lines | 2 |
| | | Mixed lines | | Mixed lines | 5 |

Concept of quantitative assessment on avoiding risk regarding feed (Model 2)

| **Slaughter-house** | **Rendering plant** | **Feed plant: domestic feed** | **Risk point** | **Feed plant: imported feed** | **Risk point** |
|---|---|---|---|---|---|
| Prior to October 2001<br><br>Exclusively for cattle; Exclusively for pigs/ poultry<br><br>Mixed lines | Exclusively for cattle; Exclusively for pigs/ poultry<br><br>Mixed lines | Exclusively for cattle; Exclusively for pigs/ poultry<br><br>Mixed lines | 1 × 0.1<br><br>20 × 0.1 | Exclusively for cattle; Exclusively for pigs/ poultry<br><br>Mixed lines | 1 × 0.1<br><br>5 × 0.9<br><br>**22.7** |
| | | Exclusively for cattle; Exclusively for pigs/ poultry<br><br>Mixed lines | 20 × 0.8 | | |
| December 2002<br><br>Incineration of SRM from cattle<br><br>Exclusively for cattle; Exclusively for pigs/ poultry<br><br>Line separation | Exclusively for cattle; Exclusively for pigs/ poultry | Exclusively for cattle; Exclusively for pigs/ poultry<br><br>Mixed lines | 1 × 0.1<br><br>5 × 0.1 | Exclusively for cattle; Exclusively for pigs/ poultry<br><br>Mixed lines | 1 × 0.1<br><br>5 × 0.9<br><br>**16.2** |
| | | Exclusively for cattle; Exclusively for pigs/ poultry | 10 × 0.2 | | |
| December 2003<br><br>Incineration of SRM from cattle<br><br>Exclusively for cattle; Exclusively for pigs/ poultry | Exclusively for cattle; Exclusively for pigs/ poultry | Exclusively for cattle; Exclusively for pigs/ poultry<br><br>Line separation | 1 × 0.1<br><br>2 × 0.1 | Exclusively for cattle; Exclusively for pigs/ poultry<br><br>Mixed lines | 1 × 0.1<br><br>5 × 0.9<br><br>**14.0** |
| | | Exclusively for cattle; Exclusively for pigs/ poultry<br><br>Line separation | 10 × 0.2<br><br>12 × 0.6 | | |
| December 2004<br><br>Incineration of SRM from cattle<br><br>Exclusively for cattle; Exclusively for pigs/ poultry | Exclusively for cattle; Exclusively for pigs/ poultry | Exclusively for cattle; Exclusively for pigs/ poultry | 1 × 0.2 | Exclusively for cattle; Exclusively for pigs/ poultry<br><br>Mixed lines | 1 × 0.1<br><br>5 × 0.9<br><br>**13.6** |
| | | Exclusively for cattle; Exclusively for pigs/ poultry | 10 × 0.4<br><br>12 × 0.4 | | |

| | | | | | |
|---|---|---|---|---|---|
| Revision of feed regulations<br><br>Incineration of SRM from cattle<br><br>Exclusively for cattle; Exclusively for pigs/ poultry | Exclusively for cattle; Exclusively for pigs/ poultry | Exclusively for cattle; Exclusively for pigs/ poultry | 1 × 0.2 | Exclusively for cattle; Exclusively for pigs/ poultry<br><br>Notification of imported feed | 1 × 1<br><br>**9.2** |
| | | Exclusively for cattle; Exclusively for pigs/ poultry | 10 × 0.8 | | |