Tentative translation

Risk assessment concerning "the comparability between risks of consuming beef and internal organs regulated by the beef export verification program of the United States/Canada and risks of consuming beef and internal organs of Japanese cattle"

December 2005

Food Safety Commission, Japan

Contents

History of deliberation

May 24, 2005	Food safety risk assessment concerning “the comparability of bovine spongiform encephalopathy (BSE) risks of consuming beef and internal organs imported from the United States under the control of the current U.S. domestic regulations and the Beef Export Verification Program for Japan and risks of consuming beef and internal organs of cattle slaughtered and distributed in Japan”, and “the comparability of bovine spongiform encephalopathy (BSE) risks of consuming beef and internal organs imported from the Canada under the control of the current Canadian domestic regulations and the Beef Export Verification Program for Japan and risks of consuming beef and internal organs of cattle slaughtered and distributed in Japan”, was requested from the Minister of Health, Labour and Welfare and the Minister of Agriculture, Forestry and Fisheries, and relevant documents were received.
May 26, 2005	The 96th Food Safety Commission (explanation of requests)
May 31, 2005	The 25th Prion Expert Committee
June 21, 2005	The 26th Prion Expert Committee
July 14, 2005	The 27th Prion Expert Committee
August 1, 2005	The 28th Prion Expert Committee
August 24, 2005	The 29th Prion Expert Committee
September 12, 2005	The 30th Prion Expert Committee
September 26, 2005	The 31st Prion Expert Committee
October 4, 2005	The 32nd Prion Expert Committee
October 24, 2005	The 33rd Prion Expert Committee
October 31, 2005	The 34th Prion Expert Committee
November 2, 2005	The 118th Food Safety Commission (report on the results of deliberation (draft))
November 2 - November 29, 2005	Public comments (Collect opinions and information) （The public meetings were held for an exchange of views in 7 major cities in Japan.）
December 1, 2005	The 122nd Food Safety Commission (Report on the summary of the public meetings)
December 8, 2005	The 123rd Food Safety Commission (Report on the summary of collected opinions and information) (Final deliberation)

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1 Introduction

1.1 History

In accordance with the regulations of Article 24, Paragraph 3, the Food Safety Basic Law (Law No. 48, 2003), the Food Safety Commission was requested for opinions concerning the comparability of bovine spongiform encephalopathy (BSE) risks of consuming beef and internal organs (hereinafter referred to as “beef and others”) imported from the United States/Canada under the control of the current U.S./Canadian domestic regulations and the Beef Export Verification Program for Japan and risks of consuming beef and others of cattle slaughtered and distributed in Japan by the Ministry of Health, Labour and Welfare (MHLW) and the Ministry of Agriculture, Forestry and Fisheries (MAFF) of Japan (Relevant documents were received on May 24, 2005) [1), 2)].

Review on the consultation by the Food Safety Commission to initiate deliberation

Review by the Food Safety Commission to initiate deliberation on the consultation has reached the following conclusions [3)]: The MHLW and the MAFF of Japan shall (1) fully explain the background and contents of the consultation and concepts of items for consultation in the Prion Expert Committee in the future, (2) make efforts to present additional data that are requested by the Prion Expert Committee, and (3) assume responsibility for inspecting compliance with management measures of the United States and Canada, associated with beef and others exported to Japan. On this basis, the Prion Expert Committee takes a neutral, independent position for deliberation based on scientific knowledge.

Questions in initiating a review on the consultation in the Prion Expert Committee

Relationship between the Food Safety Commission (risk assessment organization) and the risk management organization

The risk assessment organization scientifically assesses human health effects, while the risk management organization makes a comprehensive judgment based on the assessment results from the risk assessment organization and determines management measures, and it must not shift the blame to the assessment organization. Thus, the risk management organization holds its own accountability for the management measures to the people in Japan. Assessment works have been continued in the interim report [4)] and in the revision of domestic BSE measures [5)] without reconfirming the relationship between the risk assessment organization and the risk management organization. This was considered to be a cause of problems.

1.2 Background and history of the present consultation

Before the submission of the present consultation, there were some criticisms: If there is a Japan-U.S. agreement, there is no reason for the risk management organization to consult with risk assessment organization. In addition, there was a suspect that domestic BSE measures were revised based on the premise that the import ban would be lifted. The deliberation took place after the risk management organization expressed their views on these points.

Explanation and views presented by the risk management organization on the history and themes that led to the present consultation

History

1) Import ban on beef and others produced in the United States and Canada

BSE-positive cattle were discovered on May 21, 2003 in Canada [6] and December 24, 2003 in the United States [7]. In accordance with the Food Hygiene Law [8] and the Domestic Animal Infectious Diseases Control Law [9], the MHLW and the MAFF of Japan immediately took measures to place a tentative ban on import of beef, beef products, and others. The Agreement on the Application of Sanitary and Phytosanitary (SPS) Measures [10] sets down the following provision for taking tentative measures: Efforts must be made to collect additionally required data for more objective risk assessment, and the said sanitary and phytosanitary measures should be reexamined within a reasonable period.

2) Talks to lift the import ban on beef and others produced in the United States and Canada

After BSE-positive cattle were discovered in the United States, the MHLW, the MAFF of Japan, and the head office of the Food Safety Commission (observer) immediately dispatched experts to the scene to investigate the origin of BSE-positive cattle, facts associated with breeding of cattle that shared the farm, surveillance systems, and measures such as prohibition of feeding, and published the results in January 2004 [11]. Then, Japan-U.S. working-level meetings and professional/scientific meetings of scientists and scholars of Japan and the United States were held. Based on the agreement reached in the 3rd Japan-U.S. director-general level talks concerning BSE, held on April 24, 2004, a Japan-U.S. BSE working group, including experts and professionals, was established. Seven items including BSE inspection methods and removal methods of specified risk material (SRM) were discussed three times from both technical and professional viewpoints to lift the import ban on U.S. beef, and the results were summarized in a report of expert and professional meetings concerning BSE [12].

3) History surrounding the Japan-U.S. and Japan-Canada talks

In September 2004, the Food Safety Commission published the "interim report" of Japanese measures against bovine spongiform encephalopathy (BSE) and delivered a notice to the MHLW, and the MAFF of Japan [4]. On October 15, 2004, both Ministries consulted the Food Safety Commission for revision of measures against BSE in Japan [13]. Subsequently, in the 4th Japan-U.S. director-general level talks on October 23, 2004, both Japan and U.S. governments reached conclusions that they will lift the ban on bilateral beef trade based on scientific reasons under the condition of setting approval processes in each country, and that the United States sets the Beef Export Verification Program for Japan that lays down (1) SRM removal in cattle of all ages and (2) issuing of certificates of beef and others derived from cattle aged 20 months or younger (individual or herd age certificates or age certificates by grading carcasses) to lift the ban on U.S. beef export to Japan. Further, they agreed that approval processes of each country should be set, including deliberation by the Food Safety Commission [14]. The import conditions confined to beef and others derived from cattle aged 20 months or younger was set based on the contents of the aforementioned revision of domestic measures [13], submitted to the Food Safety Commission, taking into account the Japanese assertion about the necessity to conduct BSE inspection from food-safety viewpoints, besides SRM removal in cattle of all ages. After the talks, Japan and the United States continued to hold working-level talks about the Beef Export Verification Program for Japan. Meanwhile, the deliberation by the Food Safety Commission regarding the revision of domestic measures, commenced on October 26, 2004, and responses from the Food Safety Commission were delivered to both Ministries in May 2005 [5)]. Following this occasion, the present consultation began on May 24 [1)].

In Canada, BSE-positive cattle were discovered on May 21, 2003. Data of the field survey, generation status, and countermeasures were collected, and the results were published in July 2003 [15)]. Talks with the Canadian government continued, and in November 2004, Japan and Canada held working-level talks on the Beef Export Verification Program for Japan [16)] that lays down (1) SRM removal in cattle of all ages, (2) issuing of certificates of beef and others derived from cattle aged 20 months or younger (individual or herd age certificates). The premise of this Program was a domestic approval process that includes deliberation in the Food Safety Commission concerning lifting the ban on Canadian beef import. The talks led to the present consultation on May 24 [2)].

Purpose of the consultation

The MHLW and the MAFF of Japan explain the purpose of the consultation as follows [17)]:

1) Attitudes toward the revision of the domestic measures

Food safety regulations, both domestic and import measures, have been implemented based on securing scientific rationality. According to the Food Safety Basic Law, except in emergency cases, a food safety risk assessment must be conducted based on the latest scientific knowledge to lay down measures [18)]. Domestic BSE measures were urgently laid down in October 2001, considering the situation, where age of cattle, as well as international standards, standards of the European Commission (EC), and expert opinions of that time, could not necessarily be confirmed and the public felt strong anxiety. Thus, assessment of the measures had been the issue. In September 2004, after the Food Safety Commission summarized the results of the assessment and inspection of the domestic measures, revision of the domestic measures was submitted in October 2004 [13)], and the MHLW and the MAFF of Japan made an arrangement for a risk management organization based on the verdict in May 2005 [5)].

2) Attitudes toward the consultation

The risk assessment associated with lifting the ban on import of the U.S./Canadian beef and others should be based on the latest scientific knowledge concerning the comparability between risks of consuming beef and others that were imported under certain conditions laid down in Japan-U.S. talks and risks of consuming beef and others produced in Japan, since the ban on the import at that time was a tentative one associated with BSE occurrence in both countries. It was difficult to confirm the comparability of the safety of U.S. beef and others with the safety of Japanese beef and others merely with the U.S. domestic measures, thus, after discussion from technical and professional viewpoints in the Japan-U.S. talks, the Beef Export Verification Program for Japan [19)] was set as an additional measure, which lays down (1) SRM removal in cattle of all ages, and (2) issuing of age certificates of individual animals or herd based on the product records or by grading carcasses for beef and others derived from animals aged 20 months or younger. Canadian beef and others were also considered in the same manner [20].

3) Attitudes toward the risk management measures

If the import ban is lifted, the MHLW and the MAFF of Japan will conduct on-site inspections to confirm the effectiveness of the Beef Export Verification Program for Japan. After receiving the verdict of the consultation from the Food Safety Commission, the MHLW and the MAFF of Japan will determine whether or not to lift the import ban on the U.S./Canadian beef, and fulfill the accountability for the contents through risk communication and others.

1.3 Fundamental policy on the deliberation

To assess the comparability between health risks derived from beef and others imported under the Beef Export Verification Program of the United States/Canada for Japan and risks of consuming foods derived from beef and others of cattle slaughtered in Japan, differences between the assessment items of U.S./Canada and Japan (risks of live cattle and beef), used in the consultation for the revision of Japanese BSE measures, were fundamentally examined and comprehensively assessed (Fig. 1). The main items included (1) risks of live cattle: comparison of the external challenge, internal challenges (degree of exposure and propagation), and inspection and surveillance, and (2) risks of beef and others: comparison of slaughtered cattle, each slaughtering process, and risks of meat and others. Specific figures were used for the assessment, wherever possible, for comparative analysis between the data of Japan and U.S./Canada; however, quantitative assessment was considered difficult due to many unclear points that may arise and insufficient available data, and thus investigation was conducted based on qualitative assessment with a pessimistic scenario.

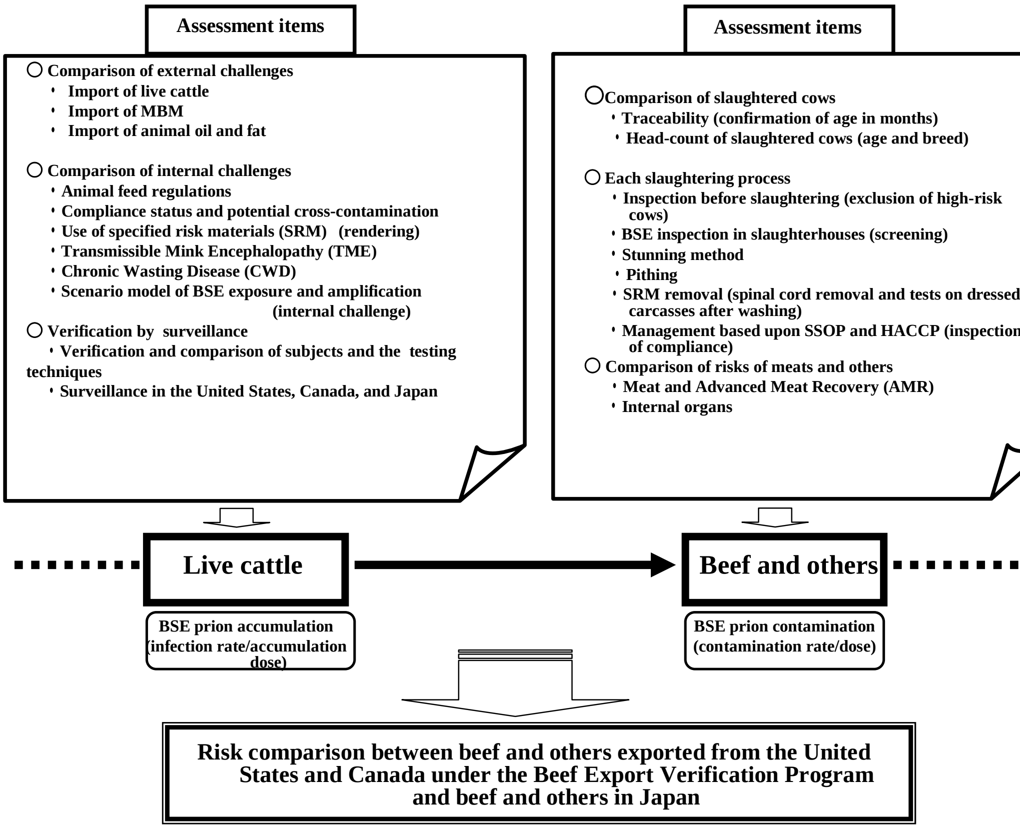

Fig. 1 Summary of Risk assessment model used in this report

2. Risk assessment - Live cattle (infection rate and cumulative level of BSE prion)

BSE contamination status of live cattle in the United States is assessed in absolute numbers, but to consider the BSE contamination rate, the differences in the herd sizes [farmed cattle: approximately 4.5 million in Japan, 95 million in the United States (approximately 20 times); cattle slaughtered annually: approximately 1.3 million in Japan, 35 million in the United States (approximately 30 times)] must also be considered [21].

In Canada, BSE contamination status is also assessed in absolute numbers, but to consider the BSE contamination rate, the differences in the herd sizes (farmed cattle: approximately 15 million (approximately 3 times larger than that of Japan), including approximately 8 million beef cattle, 1.6 million dairy caws, and 5 million calves; cattle slaughtered annually: approximately 4.5 million (approximately 3 times larger than that of Japan)) must also be considered [21].

2.1 Comparison of external challenges

Import of live cattle

In 1989, the United States banned the import of ruminants from Britain and other countries where BSE occurred [22]. In 1997, the import of live cattle from Europe was also banned [22]. In terms of the import of live cattle from high-risk countries for BSE during a period of the 1980s to the 1990s, the United States imported 323 to 327 live cattle (the difference between the two statistics was represented in range) from Britain [23]. Among them, all 117 live cattle tested negative for BSE and were disposed of [23], and they are not regarded as a risk factor. Thus, the risk factor of the live cattle imported from Britain is considered to range from 206 to 210 [(323-117) to (327-117) animals: 1980 to 2003]. In addition, the United States imported 563 to 1,762 heads of cattle from European countries other than Britain [23]. Among them, 66 or 51 (Each value depends on different statistics: animals that did not enter the rendering system as a result of a retrospective investigation, and cattle imported during the period that is not included as a risk factor) were not considered as a risk factor [23]. Therefore, the risk factor of the live cattle imported from European countries other than Britain is considered to range from 497 to 1,711 [(563-66) to (1,762-51) animals: 1980 to 2003].

Also, approximately 0.16 to 0.6 million heads of cattle and 1 million were imported annually from Canada in the 1980s (1986 to 1989) and 1990s, respectively [23]. Between 1990 and 2003, 0 to 242 heads of cattle (the difference between the two statistics was represented in range) were imported from Japan [23].

Assuming that the contamination rate of European countries other than Britain is 100-fold lower than that of Britain at that time [24], the United States imported 206 to 210 live cattle from Britain and approximately 5 to 17 live cattle (497/100 to 1,711/100), a reduced value to the cattle of Britain, from European countries other than Britain.

Meanwhile, Japan imported 33 and 16 dairy cows from Britain and Germany, respectively [25] [The dairy cows imported from Germany are 0.16, a reduced value to the cows of Britain (16/100)].

Since it is unlikely that the external challenge in Canada and Japan influenced the contamination in the United States they are not considered at present, and thus the risk in the United States is approximately 211 to 227 heads of cattle [(206+5) to (210+17)]. According to the pessimistic scenario, the contamination rate is estimated to be approximately 6 to 7 times [(211/33) to (227/33)] higher than that of Japan. The optimistic scenario is that, considering that 96% of imported cattle of the United Sates are beef cattle unlike those of Japan [23], and that dairy cows are BSE-positive at approximately 4-fold higher rate than beef cattle due to differences in feeding such as starter in Britain at that time [26), 27)], the actual risk is estimated to be approximately 1.5 to 1.8 times [approximately (6 to 7)/4] higher than that of Japan (Thirty-three animals (all dairy cows) were imported from Britain at that time.). Based on the above assumptions, the risk of imported live cattle is estimated to be approximately 1.5 to 7 times higher than that of Japan.

In 1990, Canada banned the import of live cattle from Britain and Ireland [22]. In addition, the import of live cattle from countries where BSE occurred was banned in 1994, and the import of live cattle from countries other than BSE-free countries was banned in 1996 [22]. Between 1980 and 2003, Canada imported 231 to 698 live cattle (the difference between the two statistics was represented in range) from Britain [28]. Among them, the import of 500 heads of cattle (cattle used in either statistics) that were considered to be imported in 1993 was highly suspected as a result of a detailed investigation [28], thus they are not regarded as a risk factor. A retrospective investigation on the 231 animals imported between 1980 and 1990, indicated that possibly 117 animals have entered the rendering system, but the remaining 114 were not regarded as a risk factor [28]. Thus, the risk of the live cattle imported from Britain is considered to range from 117 to 198 heads [(231-114) to (698-500) heads: 1980 to 2003].

Canada imported 308 to 324 heads of cattle from European countries other than Britain [28]. Among them, 58 and 33 (each value depends on different statistics: animals excluded from the rendering system, and those imported during the period that was considered risk-free) were not regarded as a risk factor [28]. Thus, the risk of the live cattle imported from European countries other than Britain is considered to range from 250 to 291 heads [(308-58) to (324-33) heads: 1980 to 2003]. Canada also imported approximately 16,000 to 340,000 heads of cattle annually from the United States.

Assuming that the contamination rate of European countries other than Britain is 100-fold lower than that of Britain at that time [24], Canada imported 117 to 198 live cattle from Britain and approximately 3 live animals (250/100 to 291/100), a reduced value to cattle of Britain, from European countries other than Britain. The external challenge of live cattle in Canada is approximately 120 to 201 heads (117＋3 to 198 ＋ 3). Since the external challenge in the United States was unlikely to influence the contamination in Canada it is not considered at present. Based on the above assumptions, the external challenge in Canada is estimated to be approximately 4 to 6 times ((120/33) to (201/33)) higher than that of Japan.

Import of meat-and-bone meal

In 1989, the United States banned the import of meat-and-bone meal (MBM) from Britain and other countries where BSE occurred [22]. In 1997, the import of MBM of ruminants from European countries was banned, and in 2000, the import of processed protein of all kinds of animals from European countries was also banned [22]. The United States imported 5 to 140t of MBM from Britain (1980 to 2003) [23]. Among them, 39t imported in 1989 (unconfirmed by the British export statistics) and 77t imported between 1997 and 1999 (derived from non-mammals) were not considered as the object of risk [23]. Thus, the risk of the MBM imported from Britain is estimated to be 5 to 24t [140-(39+77)].

The United States imported 684 to 2,129t from European countries other than Britain (1980 to 2003) [23]. In addition, 227,572 to 405,863t was imported from Canada [23].

Meanwhile, although Japan did not import MBM from Britain (except import between 1995 and 2000 of approximately 9,000t of bone meal and others that underwent high-temperature and high-pressure processing), approximately 56,000t was imported from Italy between 1987 and 2001, and approximately 31,000t (heat-treated) was imported from Denmark between 1999 and 2001 [25].

Assuming that the contamination rate of European countries is 100-fold lower than that of Britain at that time, the United States imported approximately 12 to 45t from Britain [(684 to 2,129)/100+(5 to 24)], and Japan imported approximately 560t (approximately 56,000/100); thus, the risk of the United States is estimated to be approximately 12 to 47-fold lower than that of Japan.

In 1988, Canada banned the import of MBM from countries other than the United States [22]. In 1990, the import ban of MBM was lifted for BSE-free countries, and in 2000, the import of processed proteins of all kinds of animals from countries other than BSE-free countries was banned [22].

Between 1980 and 2003, Canada imported 0 to 149t of MBM (the difference between the two statistics was represented in range) from Britain [28]. However, all the 149t is MBM of non-mammals [28] and is not regarded as a risk factor. Since the import of MBM from Britain is 0t, its external challenge is negligible.

In addition, 5,710 to 11,046t of MBM (the difference between the two statistics was represented in range) was imported from European countries other than Britain, of which 5,699 to 11,046t (except 0 to 11t imported from Ireland) was derived from non-ruminants [28] and thereby was not considered. Thus, the external challenge of MBM imported from European countries other than Britain is estimated to be 0 to 11t [(5,710-5,699) to (11,046-11,046)]. Besides, 0 to 26t and approximately 250,000 to 310,000t of MBM were imported annually from Japan and the United Sates, respectively [28]. Since the contamination in Japan and the United States was unlikely to have profound effects on the contamination in Canada, they are not considered at this time.

Assuming that the contamination rate of European countries was 100-fold lower than that of Britain at that time, Canada imported approximately 0 to 0.11t (0/100 to 11/100), a reduced value to MBM in Britain. Thus, the external challenge of MBM in Canada is approximately 5,100-fold lower than that of Japan (560t, a reduced value to MBM in Britain).

Import of animal oil and fat

Japan imported 1,245t of animal oil and fat from the Netherlands in the 1990s [25].

There is no actual import of animal oil and fat from the Netherlands by the United States [29]. The import from other European countries before 1994 is unknown [29]. Since 1995, most animal oil and fat were imported from Canada, and import from other European countries amounted to approximately 643t [29]. In addition, approximately 3,000t and 2,000t were imported in 1999 and 2001 from Argentine (GBR assessment: level 1), respectively, and a small proportion was imported from Mexico, New Zealand, Pakistan, and China [29]. Since the animal fat and oil from Canada was unlikely to influence the external challenge of the United States they are not considered at present.

There is no actual import of animal oil and fat from the Netherlands by Canada [29]. The import from other European countries before 1994 is unknown [29]. Since 1995, most animal oil and fat were imported from the United States, and import from other European countries amounted to less than 100t [29]. Since the animal fat and oil from the United States was unlikely to have profound effects on the external challenge of Canada they are not considered at present.

Thus, the risks derived from the animal fat and oil in the United States and Canada are approximately 2-fold and 12-fold lower than that of Japan, respectively.

Comparison of external challenges in the United States/Canada and Japan

The major European countries imported several thousand live cattle from Britain (Ireland: approximately 33,000, Germany: approximately 6,500, Portugal: approximately 10,000, and France/Netherlands: 3,000 to 5,000) and several thousands tons of MBM from Britain (France/Netherlands: 25,000t, Belgium: 12,000t, Ireland: 7,200t, Italy: 4,200t, and Germany: 1,200t) [25]. BSE external challenge in the United States, Canada, and Japan are <10 to 100-fold lower than those of the above-mentioned European major countries. When the risks of imported live cattle are selectively assessed, the United States and Canada are approximately 1.5 to 7-fold and 4 to 6-fold more intensely contaminated than Japan, respectively, and in terms of the contamination of MBM, the United States and Canada are approximately <12 to 47-fold and <5,100-fold less intensely contaminated than Japan, respectively, and in terms of the risks of animal fat and oil, the United States and Canada are approximately 2-fold and <12-fold less intensely contaminated than Japan, respectively. Thus, the overall external challenge in the United States and Canada are considered comparable with those in Japan. When the risks of imported live cattle are selectively assessed considering the improper feed regulations, the contamination caused by the external challenge in the United States and Canada are estimated to be approximately <1.5 to 7-fold and <4 to 6-fold higher than that of Japan.

2.2 Comparison of internal challenges

Animal feed regulations

The risks associated with domestic BSE propagation differ between dairy cows, for which milk substitute and starter are used, and pastured beef cattle. Approximately 80% and 90% of domestic cattle are destined for beef in the United States and Canada, respectively, while approximately 60% of domestic cattle in Japan are reared as such [21]. The potential effects of these structural differences in farming on domestic exposure and amplification must be taken into consideration. However, the critical risk factors in internal challenge are associated with use of SRM, feed regulations, and the compliance of the regulations.

In August 1997, the United States banned feeding of proteins derived from mammals to ruminants by law [30]. The feed regulations included (1) a ban on use of proteins derived from mammals, except for certain kinds of proteins (e.g., blood), in feed materials for ruminants, (2) mandatory labeling such as "No feeding to ruminants" when banned materials are used as feed materials, (3) mandatory record retention of feeding and feed production, and (4) mandatory separation of equipment and facilities, and mandatory cleaning of manufacturing processing equipment for prevention of cross-contamination. However, neither feeding of proteins derived from ruminants to pigs and chickens was banned or feeding of poultry residual dross, poultry manure, and garbage to cattle was banned.

In the United States, BSE-positive cows were discovered in December 2003 and public comment was called for in January and July 2004, concerning the regulations of use of bovine blood/blood products and garbage [31], and concerning exclusion of SRM from animal feed materials and downer and dead animals and reinforcement of preventive measures against cross-contamination such as specified feed production facilities for ruminants [32], respectively, but these regulations have not been implemented as of 2005. Thus, cross-contamination is not considered to be completely prevented in the United States even today. On October 4, 2005, the Food and Drug Administration (FDA) published a draft revision of feed regulations as safety measures against BSE [33]. This draft revision banned use of high-risk regions that may mediate BSE in foods and feedstuff for all animals. The banned high-risk regions included (1) brains and spinal cords of cattle aged 30 months or older, (2) brains and spinal cords of cattle of all ages that are unexamined or unfit for human consumption, (3) entire carcass of a bovine animal that is unexamined or unfit for human consumption in case where its brain and spinal cord is not removed, (4) animal fat and oil containing ≥0.15% insoluble impurities derived from regions banned by the present regulations, and (5) mechanically recovered meat derived from regions banned by the present regulations.

In August 1997, Canada banned feeding ruminant-derived proteins to ruminants by law [34]. As in the United States, the feed regulations included (1) a ban on use of proteins derived from mammals, except certain kinds of proteins, in feed materials for ruminants, (2) mandatory labeling such as "No feeding to ruminants" when banned materials are used as feed materials, and (3) mandatory record retention of feeding and feed production. To protect Canadian cattle from cross-contamination, public comment concerning SRM exclusion in manure and feedstuff, including pet food, was called for in December 2004 [35] [36], but these regulations have not been implemented yet as of October 2005.

In Japan, the MAFF issued a notice in April 1996 that ruminant-derived MBM should not be used as feedstuff for ruminants [37], but no preventive measures against cross-contamination were taken. After BSE-positive animal was confirmed in September 2001, use of all mammal-derived proteins in feedstuff was banned by law in October (prevention of cross-contamination) [38]. In April 2005, after preventive measures against cross-contamination were completely established in both hardware and software, the regulations that banned the use of pig-derived proteins in feedstuff for pigs and chickens were lifted [39].

While Japan issued a notice on feed regulations in April 1996, the United States and Canada enforced the law on feed regulations in August 1997. In Japan, complete feed regulations to prevent cross-contamination have been enacted into law since October 2001, but not in the United States and Canada. According to the European model used in the revision of domestic regulations, the risk-reduction effect of the feed regulations, excluding prevention of cross-contamination, is expected to reduce the BSE contamination rate to 0.26 to 0.6 in 3 years [40-42]. Thus, domestic exposure in the United States, Canada, and Japan is considered to have increased since the 1990s, reaching the maximum level to cattle born before the regulations were implemented, and gradually decreased to cattle born after the implementation (Based on the European data, the domestic exposure to cattle born in 2004 is expected to be reduced to approximately 1/4 [0.1 to 0.36 = (0.29 to 0.6)×(0.29 to 0.6)] of the maximum level). It is expected that in Japan, where the complete feed regulations were enacted into law, the contamination rate in cattle born after 2002 will decline rapidly; however, the reduction rate has not changed in the United States and Canada even today. At present, the contamination rate of cattle aged 20 months or younger and which are born after 2004 is estimated to be a little bit higher (1.5-fold) in the United States and Canada than in Japan.

Compliance status and potential cross-contamination

In terms of feed mills in the United States, separation of equipment and facilities and cleaning of manufacturing processing equipment were made compulsory in 1997 (mandatory documentation and proposal of cleaning process at the time of examination) [30]. However, it is difficult to completely eliminate contaminants by routine cleaning. As of May 2005, 80% of rendering facilities (205/255) and 99% of feed mills (6,121/6,199) became specialized facilities (facilities that deal with either banned materials or non-banned materials) [43]. The compliance with the feed regulations in feed mills in the United States is inspected by examining officers of the FDA and others according to the guideline, and the results are published [44]. In addition, the General Accounting Office (GAO) regularly inspects the compliance with feed regulations, and makes recommendations on points that need improvement [45]. According to these reports, the compliance rate before 1998 was 30 to 70% [46]. The compliance rate was as low as 50 to 58% when the law was enforced in 1997, but most noncompliances were minor, simply associated with documentation, and not critical such as the use of banned materials [47]. According to the investigation conducted in June 2005, the compliance rate was approximately 97% [48]. As for cross-contamination risks, distribution after manufacturing in feed mills and feed mixing in farmhouses are also critical factors. According to the FDA report in June 2005, among 12,575 factories and others (the number of operating factories according to the FDA survey), there are 3,288 factories that deal with regulated products, including 8 factories that need regulatory intervention, and 90 factories that do not need regulatory intervention but need instructions for improvement; thus, the compliance rates of feed regulations associated with feed mixing in farmhouses, wholesaling, retailing, transportation, and others was 97.1%[48]. Since feeding of poultry residual dross, poultry manure, and garbage to cattle is not prohibited, there remain potential cross-contamination risks. The GAO report on February 25, 2005 states, "the FDA feed regulations have been improved. But its effectiveness is limited, thus cattle in the United States are continuously exposed to BSE epidemic risks." [45].

In Canada, the compliance with the feed regulations is inspected by examining officers of the Canadian Food Inspection Agency (CFIA) in accordance with the program. After two BSE-positive cows were discovered in Canada in January 2005, the Canadian Government inspected the effectiveness of the feed regulations that had been implemented since 1997 based on the inspection results of the CFIA. Consequently, the Government announced that the regulations were virtually observed in more than

90% of feed mills and rendering factories [49]. Specialization of feed and rendering industrial facilities by species is under progress, and 79% of rendering facilities (23/29) and 83% of feed mills (456/550) are specialized as of May 2005 [43]. As for mixed feed, a tendency is observed for mixing farmhouses to produce the feed by species [50].

The compliance rate of feed regulations in Japan at the time of the notification (April 1996) [37] was almost comparable with that of the United States. According to the results of the on-site inspection on all farmhouses in September 2001, 165 farmhouses (5,129 heads of cattle) were reported to have fed MBM prepared by in-house mixing and others [51]. However, a ban on use [38] and import [52] of MBM and incineration of SRMs at slaughterhouses (except for the vertebral column) [53] have been enacted into law since October 2001. In the inspection of 1,274 cases in 665 manufacturers, concerning the compliance with prevention of cross-contamination and separation of production process lines, there were 3 cases of violation [54]. Separation of feed production lines between pigs/chickens and cattle, and separation of their facilities were completed at the end of March 2005 [54]. The potential cross-contamination in Japanese cattle (born before 2002), born before the compliance with the complete feed regulations, cannot be denied, but the risk of feedstuff is considered extremely low as of January 2004.

Under the present feed regulations, the possibility remains that the cross-contamination in the United States and Canada occurs at a certain rate in the future.

Use of specified risk materials (SRMs) (rendering)

Specified risk materials (SRMs) are considered to account for 99.4% of the infectivity of BSE-positive cattle [55]. Thus, whether SRMs are disposed of after incineration or used as feedstuff after rendering is the most critical point in assessing the exposure and propagation risk of domestic cattle. In Japan, SRMs are removed from slaughtered cattle of all ages, and are incinerated [53]. Also, bovine MBMs derived from regions other than SRMs are incinerated [56]. On the other hand, in the United States and Canada, SRMs of cattle aged 30 months or older are not used for food [57], but the removed SRMs are used as feedstuff for pigs and chickens after rendering [58]. Same is the case for SRMs derived from animals died in farms, animals that are not used for food in slaughterhouses (downers and abnormal animals), and all healthy animals aged 30 months or younger. In this sense, SRMs derived from all the cattle are used for feedstuff. A ban on use of SRMs for feedstuff was strongly warned by the International Inspection Team in January 2004 [59].

As described above, the FDA published a draft revision of the feed regulations that banned use of high-risk materials in food and feedstuff for all animals on October 4, 2005 [33].

Transmissible Mink Encephalopathy (TME)

In the United States and Canada, occurrence of transmissible mink encephalopathy (TME) has been confirmed as TSE (Transmissible Spongiform Encephalopathy) other than BSE. Scrapie infection via sheep given as feed has been considered to be the cause. Some argue that downer cattle that were given as feed cause TME in the United States. However, considering that TME occurrence is rare in the United States, and that in the farms where TME occurred in 1985 no TME had occurred in spite of feeding of beef internal organs of diseased and slaughtered cattle in the past decades, even if there were animals that might be the cause of TME at that time, the number is considered extremely small [60]. Furthermore, since feeding of mink-derived proteins to cattle was prohibited in 1997 [30], TME is considered to pose little risk to cattle and other ruminants [61].

Based on the above findings, the risk of TME in cattle born after February 2004 in the United States and Canada is considered extremely low at present.

Chronic Wasting Disease (CWD)

In 1967, spongiform encephalopathy in mules was discovered in Fort Collins, Colorado, U.S. where mule deers and red deers were in the pasture or in captivity. Besides mules, it is infectious to red deers, elks, and Rocky Mountain elks. Up to present, the occurrence has been reported in Colorado, Kansas, Minnesota, Montana, Nebraska, Oklahoma, South Dakota, Wyoming, New Mexico, Wisconsin, and Illinois in the United States, and Saskatchewan (1996) and Alberta in Canada [60]. The CWD incidence rate in captured elks is reported to be <1% to 71% (other reports suggest approximately <1% to 17% in mule deers and white-tailed deers and <1% in elks) [62].

At present, there is no evidence of involvement of CWD in BSE infection in the United States and Canada [63]. However, considering the fact that CWD is actively studied mainly in the United States at present, we have not reached the stage of drawing a conclusion on whether or not CWD may be a cause of BSE. Nevertheless, rendering facilities of ruminant feedstuff have prohibited the acceptance of corpses of deers and elks since 1997 in the United States and Canada [30] [34].

Scenario model of BSE exposure and amplification (internal challenge)

According to the risk assessment conducted by the EU Scientific Steering Committee, the infectivity titer of one BSE-infected adult bovine animal is estimated to be 8,000 ID_{50} (ID_{50}: median infection dose) [55], and specified risk materials are considered to account for 99.4% of it [55]. Based on this assumption, when SRMs are not disposed of, almost all the infectivity titer would enter rendering, no matter how one BSE-positive animal might be slaughtered (P=1, Assuming that the infectivity titer is approximately 10,000 ID_{50}, the following is considered.). Assuming that the infectivity titer is reduced to approximately 1/100 by 20 minutes of rendering treatment at 133℃ and 3 atm, according to the OIE standard [64], the infectivity titer of MBM and others (including animal fat and oil) per animal is estimated to be approximately 100 ID_{50}. It is difficult to estimate each probability of cross-contamination in rendering facilities as well as during the feed production process, transportation/distribution, and mixing in farmhouses, but assuming that these amount to 10%, the probability after cross-contamination is P=0.1 (1/10).

Assuming that 10% of MBM that enters rendering is consumed by pigs and chickens and returns to cattle via cross-contamination or poultry residual dross, poultry manure, and garbage, the infection dose is approximately 10 ID_{50}.

If 100 heads of BSE-positive cattle are slaughtered annually, they enter rendering 100 times at P=1; assuming that the frequency of cross-contamination is 1/10 in a year, infection might occur 10 times a year (100/10) with the total infection dose of approximately 100 ID_{50} (10 ID_{50}×10 times). According to this scenario, the infection scale is in a static state. When the regulations reduce the probability of cross-contamination or a cross-contamination dose below this level, infection is also reduced. When this level is not achieved, infection spreads. When the probability of infection is reduced, the epidemic pattern is predicted to change into a discontinuous one in the long term such as 10 times/year, 5 times/year, and furthermore, to 1 time/year, 1 time/2 years, and 1 time/5 years (Figure 2).

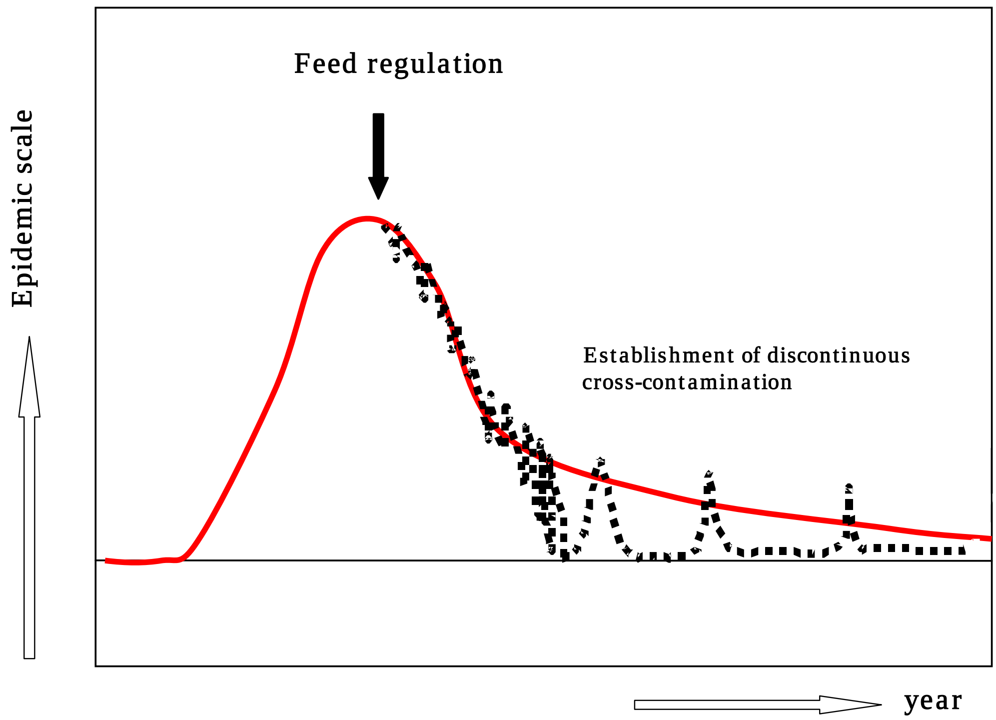

Fig.2 Schematic representation of epidemic Pattern of Cross-Contamination (Image)
When discontinuous, nonuniform, and sporadic epidemic occurs, and the product of contamination frequency (%) and contamination dose (%) is 100, the epidemic is repeated after an average incubation period without change of the epidemic scale. Reduction of contamination dose and contamination frequency diminishes the epidemic scale.

2.3 Verfication by surveillance

Verification and comparison of subjects and the testing techniques

Surveillance in the United States

BSE inspection in the United States has been aimed at surveillance, and histopathological tests have been conducted since May 1990 on cattle aged 24 months or older and with central nervous system manifestation or abasia [46)]. The Animal and Plant Health Inspection Service (APHIS) and the National Veterinary Services Laboratories (NVSL) have introduced an immunohistochemical (IHC) method since 1993 [65) 66)]. The number of tested cattle between 1990 and 2001 was 16,829 [67)]. The number of subject cattle have increased since 2002 to approximately 20,000 high-risk cattle annually, and 57,654 heads of cattle were inspected using histopathological tests and the IHC method between 2002 and May 31, 2004 [67)]. As a result, the first BSE case in the United States was discovered in December 2003. The subsequent epidemiological study reported that this cow was not born in the United States but was imported from Canada [68)]. After this incidence, according to the advice of the international inspection team, an expanded surveillance began since June 2004 [69)]. In this expanded surveillance, ELISA (enzyme-linked immunosorbent assay) was used in primary test, and the IHC method was used in confirmatory test as before. The number of inspected cattle amount to 383,477 as of July 3, 2005 [70)]. Among them, the second BSE case in the United States was detected in June 2005 [71)].

Table 1. Surveillance in the United States

Year	Cattle strongly suspected of BSE and/or cattle with central nervous system manifestation	Downer cattle	Dead cattle	Total
1990				40
1991				175
1992				251
1993				736
1994	493	199		692
1995	521	223		744
1996	877	266		1,143
1997	2,494	219		2,713
1998	736	344		1,080
1999	651	651		1,302
2000	786	1,895		2,681
2001	808	4,464		5,272
2002	2,280	14,951	2,759	19,990
2003	893	16,560	3,090	20,543
2004 (Until May 31)	1,398	9,392	6,331	17,121
June 2004-July 3, 2005	1,704	32,989	348,784	383,477

Note: Breakdown between 1990 and 1993 is unknown (reference data for the consultation in the United States (29))

In the expanded surveillance, a commercial Plateria kit is introduced for the ELISA method (primary test) [72], and is used in a total of 13 institutes including the NVSL and 12 voluntarily participating State Veterinary Diagnostic Laboratories (SVDL) [73]. The ELISA method was conducted on 369,467 heads of cattle by May 29, 2005, of which three were tested inconclusive [74], but were tested negative by the IHC method, which was conducted as the confirmatory test.

In June 2005, the Office of Inspector General (OIG) demanded confirmatory tests of these three by the Western Blot (WB method). The above diagnosis institutes lacked both a facility and experience of the WB method, thus the National Animal Disease Center (NADC) performed the test, and one was revealed positive. This sample was also tested positive by both the WB and IHC methods at the Veterinary Laboratories Agency (VLA) in Britain. In the United States, the IHC method was performed again using a different antibody, and a positive result was obtained at this time [71] [75]. The ELISA had not been conducted before the expanded surveillance in June 2004, neither had the WB method before May 2005. Thus, unlike the young cattle and atypical cases detected by the ELISA and WB method in Japan (tested negative by the IHC method), undetectable BSE cases might have been overlooked by the IHC method in the United States. As a result, the WB method described in the OIE Manual of Standards has been added to the confirmatory test since June 2005 [76], however, no official document on details about the WB method that will be introduced in the United States has been presented to the Prion Expert Committee to date.

Thus, the surveillance in the United States might have detected more BSE cattle than reported.

Surveillance in Canada

Canada initiated a surveillance program in 1992. The aim was to identify the presence of BSE in Canada. Several thousands of cattle with central nervous system manifestation or abasia were examined between 1992 and 2003 [77) 78)]. In 1993, BSE infection was confirmed in one cow imported from Britain, and the cow was disposed of without being used in food or feed. At that time, all the cattle imported from Britain was disposed of, and a BSE testing by IHC method took place, but all the cattle were tested negative [79)]. After the discovery of a BSE cow in May 2003 (the first case in Canada), the aim of the surveillance shifted to the assessment of BSE prevalence in adult cattle, and the expanded surveillance began after the ELISA was introduced in January 2004. In 2004, 23,550 heads of cattle were inspected, and 30,000 are scheduled for inspection annually after 2005 (20,949 were inspected between January 2005 and April 18, 2005). As a result of the initiative, the second case in Canada was discovered on January 2, 2005, and the third case on January 11, 2005 [77)].

Histopathological tests and the IHC method have been introduced to the BSE surveillance in Canada since 1992 and 1994, respectively [79)]. After the discovery of the first case in Canada, the WB method was introduced in September 2003, and the ELISA in 2004 [79)]. Currently, a simple WB method and the ELISA are performed at state veterinary pathology laboratory, which belong to the TSE inspection organization network, and 6 CFIA network facilities. Positive samples are then sent to the BSE Reference Laboratory in the National Centre for Foreign Animal Diseases (NCFAD) for confirmatory test by the IHC method. However, the WB method is used when the brain stem (obex) cannot be identified anatomically due to sample conditions, or when conflicting results are obtained by a rapid test and the IHC test [78) 80)].

Table 2. BSE Surveillance in Canada

Year	Downer cattle[1)]	Dead cattle	Others[2)]	Total
1992				225
1993				645
1994				426
1995				269
1996				454
1997				759
1998				940
1999				895
2000				1,020
2001				1,581
2002	1,990	1,387	0	3,377
2003	2,129	1,335	2,263	5,727
2004	14,092	9,193	265	23,550
2005	12,287	8,578	84	20,949

1) Cattle that were slaughtered in an emergency or exhibited abnormalities in the antemortem inspection in slaughterhouses are included.

2) Cattle that were farmed with BSE cattle and thus were disposed of, healthy cattle, and others are included.

3) Breakdown between 1994 and 2001 is unknown (reference data for the consultation in Canada (28))

Reference: Reference data for the consultation in Canada(28); Supplementary document associated with food safety risk assessment (submitted on June 10, 2005)

Surveillance in Japan

In Japan, surveillance by histopathological tests of cattle with central nervous system manifestation and others in farms is under operation since 1996 [81)]. Between 1996 and 2001, 2,247 heads of cattle were tested, and the first BSE-positive case was discovered in September 2001 [81)].

Subsequently, test objects and number of cattle expanded sequentially, and as a general rule, dead cattle that are 24 months or older have been included in test objects since April 2003 [81)]. Accordingly, blanket testing of dead cattle aged 24 months or older began in April 2004 [81)].

The ELISA is performed as a primary test at livestock hygiene service centers, and positive samples are tested using the WB method and the IHC method at the National Institute of Animal Health [82)]. A final diagnosis is made by expert members at the technical research meeting of the risk management organization [82)].

By the end of September 2005, 202,398 high-risk cattle (those with central nervous system manifestation and dead cattle aged 24 months or older) were tested by the ELISA, and 4 positive cases were detected by the IHC and WB methods. In addition, 788 suspected cases were tested using the ELISA by 2005 (by the time when the 20th case of BSE-positive in Japan was discovered), but no positive cases were detected.

In October 2001, BSE screening tests of all slaughtered cattle in slaughterhouses began in order to prevent use of BSE-positive animals in food [12]. Primary test is performed by the ELISA, then confirmatory test by the WB method, pathological tests, the IHC method. In BSE testing of slaughtered cattle of all ages, the ELISA is performed as primary test at 114 meat inspection stations throughout Japan (this year's plan), and positive cases are subjected to secondary test at 3 confirmatory testing laboratories in Japan by the WB method (National Institute of Infectious Diseases and Hokkaido University) and by pathological tests and the IHC method (National Institute of Infectious Diseases and Obihiro University of Agriculture and Veterinary Medicine) [12]. By October 31, 2005, 4,974,937 heads of cattle were tested, of which 15 were diagnosed BSE-positive in "the Expert Committee of BSE Diagnosis" of the MHLW [83]. The results of this screening test at slaughterhouses are also useful as surveillance data to comprehend the status of BSE contamination correctly.

Apparently, improvement of surveillance by adding subject animals, number of subject animals, and test methods, will enable detection of more BSE-positive cattlein many countries, besides in the United States and Canada.

Consideration of the testing techniques

1) Sampling

Most BSE incidents are sporadic, and unlike other infectious diseases, it is difficult to estimate the extent of contamination by random testing. Among the 20 BSE-positive animals detected in Japan, only four (except for the first case) were detected by the testing of dead animal that fell into high-risk cattle. Indeed, these four were detected around the same time when blanket testing of dead cattle aged 24months or older was initiated, or later. The extent of BSE contamination in Japan has finally become estimable based on the results of the 4-year blanket testing in slaughterhouses and the 1.5-year blanket testing of dead cattle that are 24 months or older. This indicates the limitation of sampling of only high-risk cattle in the BSE testing that the OIE proposes. The indication must be noted when the results of the surveillance in the United States and Canada, conducted only by random testing of high-risk cattle, are examined to comprehend the current status of BSE contamination.

2) Collecting materials

In Japan, the medulla oblongata is divided into two by a sagittal section, and one is used for biochemical tests by the ELISA and the WB method, and the other is used for pathological tests and the IHC method [84]. The standard operation procedure Appendix 1 of the NVSL only indicates the obex of the medullae oblongata, an examination site, does not specify a sampling method that considers confirmatory test [72].

3) Primary test

The BIO-RAD's ELISA kit is used for the primary test in the United States [72]. In Canada, the BIO-RAD's and Prionics' kits are used in the primary test [77] [78]. All these kits are assessed and approved by the EU. In Japan, BIO-RAD's, Enfer's, and Fujirebio's kits are used [12], which have the similar sensitivities as those used in the United States and Canada.

4) Confirmatory test

a) The WB method

In the United States and Canada, the WB method described in the OIE Manual of Standards (SAF Immunoblot) is used [76]. A separation and refinement method based on Diringer's papers in 1995 and 1997 is described in the manual as an example. This method is designed to separate and refine SAF by combining detergent treatment, ultracentrifugation, and PK treatment, and the efficiency of separation and refinement in every test, i.e., SAF detection sensitivity measured at each confirmatory testing laboratory, must be specified.

In Japan, the WB method is performed using the remaining sample of the primary test (350 μg) and samples that are newly obtained from the obex. A lot-controlled mouse scrapie sample is used as a positive control. Detection sensitivities of each blot are ensured by comparison with the detection limit of this positive control.

b) Immunohistochemical test (IHC method)

The IHC method was the only one test method in the United States from 1993 to the end of May 2005. The testing protocol of the IHC method is specified in the NVSL SOP GPPISOP 0032.03 [72]; unlike the OIE protocol, formic acid treatment is not performed and thus it influences the biosafety of laboratory workers. Verification of antibodies used in the United States is required, as their potential effects on detection sensitivity cannot be ruled out. The IHC method used in the confirmatory test, reported by Canada, follows the method in the OIE manual, and thus there is no need to consider the reduction in detection sensitivity, including that of image data [85].

5) Expert committee for diagnosis

In Japan, cases that underwent the confirmatory test, whether positive or negative, are judged by the Expert Committee based on the results of the ELISA, WB, and IHC methods [12]. Judgment is based on comprehensive assessment of test results. It is said that the U.S. Expert Committee members consist of pathologists probably because the IHC method was the only confirmatory test, but the members are not disclosed. The WB method is scheduled for introduction to the confirmatory test in June 2005, and thus, participation of other experts who are not involved in the testing as members should be requested to assess the results of the ELISA, WB, and IHC methods comprehensively.

The positive cases in the primary inspection in Canada are examined by several BSE diagnosis kits assessed by the EU Committee (including kits that are not approved in Japan), in addition to the confirmatory test by the IHC method, for comprehensive assessment and judgment. The authority and responsibility associated with the BSE diagnosis are imposed on the professional views of the National BSE Laboratory, and ultimately on the representative of this laboratory [86].

Extrapolation from the surveillance data in the United States/Canada and Japan

According to the BSE testing data in Japan and the data of the expanded surveillance in the United States and Canada, the detection rates are 0.0028% in Japan (2004), 0.00026% in the United States (June 2004 to June 21, 2005), and 0.0038% in Canada (June 1, 2004 to June 21, 2005) [87].

The total number of cattle farmed is approximately 95 million and 4.5 million in the United States and Japan, respectively [21]. Among them, the numbers of adult animals (as for cows, in general, "adults" indicate delivered cows, while young cows do heifers) are reported to be approximately 42 million in the United States (beef cattle: approximately 33 million, dairy cows: approximately 9 million), and approximately 1.92 million in Japan (beef cattle: approximately 0.77 million, dairy cows: approximately 1.15 million) [88]. The annual numbers of cattle that die in farms and those disposed of at slaughterhouses are approximately 0.94 million and 0.19 million in the United States, and approximately 98,100 and 8,300 in Japan (downers aged 24 months or older), respectively [88]. In addition, the annual number of cattle slaughtered is approximately 33.5 million and 1.26 million in the United States and Japan, respectively [88].

According to the BSE testing data in 2003, the number of healthy slaughtered cattle tested in Japan is approximately 1.26 million (adult animals: 0.9 million), of which 2 BSE-positive cases were discovered, while no BSE-positive case was discovered among healthy slaughtered cattle in the United States, since only few tests are conducted on healthy slaughtered cattle in the surveillance. With regard to cattle that died in farms or were disposed of at slaughterhouses, approximately 0.11 million were tested in Japan, of which 3 BSE-positive cases were discovered, while the number of the tested animals in the United States was 0.39 million, which accounted for 35% of the total, and one BSE-positive case was discovered [88]. Thus, 3 BSE-positive cases (1×100/35) are estimated to be discovered in all the cattle that die in farms or are disposed of at slaughterhouses (1.13 million). The positive ratio between healthy slaughtered adult cattle and those that die in farms or are disposed of at slaughterhouses is 1 (2/0.9 million):12.3 (3/0.11million) in Japan. When this ratio is extrapolated to the data of the United States, the number of BSE-positive cattle is estimated to be one discovered in 2.7 million healthy slaughtered adult cattle (3/1.13 million×2.70 million×1/12.3). Assuming the same contamination rate in young animals, 1 or 2 BSE-positive cases will be discovered annually in Japan, and 32 BSE-positive cases in the United States.

In Canada, according to the results of the expanded surveillance that has been implemented until present (June 1, 2004 to June 21, 2005), 2 BSE-positive cows were discovered, and the detection rate was 0.0038%. The tested cattle (52,817) accounted for approximately 66% of the total high risk object cattle in the surveillance (approximately 80,000) [97]. Three BSE-positive cows (all of them were downer) have been discovered to date. If the same extrapolation is conducted in Canada, as conducted in the United States, the number of BSE-positive cattle is estimated to be 2 in 53,000 high-risk cattle, and 3 if all the 80,000 animals are tested. Assuming that healthy slaughtered adult cattle account for 20% of all the slaughtered cattle (0.9 million) and the positive rate of 12.3 between healthy cattle and high-risk cattle is extrapolated, 3 BSE-positive cases will be discovered in 0.9 million heads of cattle (3/80,000×0.9 million×1/12.3). If the same contamination rate is applied to young cattle, 22 BSE-positive cases will be discovered annually in 3.6 million cattle (6×3.6 million/0.98 million).

The presented figures are based on the limited data; therefore, there is a risk of overestimating the influence. In Japan, 6 to 7 BSE-positive animals are discovered annually, while approximately 5 to 6-fold and 4 to 5-fold BSE-positive cattle are estimated in the United States and Canada, respectively. Considering the BSE contamination rate adjusted by population, annual BSE-positive animals per one million are estimated to be 5 to 6 in Japan, approximately 1 in the United States, and 5 to 6 in Canada. However, as described in the section "Assessment and Comparison of Inspection Techniques", the size and system of BSE inspection differ markedly between Japan and the United States/Canada. Thus, this difference must be considered when using this extrapolated data.

Table 3. Verification by BSE Inspection Data (2003)

	U.S.	Canada	Japan	Supplements
Number of farmed cattle	95 million	15 million	4.5 million	Adult cattle account for half of the total farmed cattle
Adult cattle	42 million {Beef cattle: 33 million; Dairy cow : 9 million	9 million {Beef cattle: 5 million; Dairy cow : 1 million	2 million {Beef cattle: 0.77 million; Dairy cow: 1.15 million	Japan; Beef cattle: Dairy cow=4 : 6 U.S.;Beef cattle: Dairy cow =8 : 2
Number of cattle slaughtered annually	33.5 million	4.3 million	1.3 million	Percentages of sick cattle disposed of in slaughterhouses are comparable between Japan and the United States
･Cattle disposed of in slaughterhouses (sick or abnormal cattle)	0.19 million (0.57%)		8,300 (0.66%)	In Japan, the death rate in farms is higher in dairy cows.
･Cattle died in farms	Beef cattle : 0.5 million (1.5% in 33 million) Dairy cow : 0.44 million (4.8% in 9 million) High-risk cattle : 1.13 million	High-risk cattle: 53,000	Beef cattle: 11,300 (1.7% in 0.77 million) Dairy cow: 86,800 (8.7% in 1.15 million) High-risk cattle: 0.106 million	
Inspection data				
･Healthy slaughtered cattle	No inspection (2.7 million of cattle that are 30-month-old or older)	No inspection	2 cattle in 1.26 million (9 cattle in 4.4 million) (0.9 million of cattle that are 30-month-old or older)	2 cattle in 0.9 million healthy adult cattle in Japan
･Healthy adult cattle: high-risk cattle	2.7 million: 1.13 million = approx. 1 : 3	0.9 million : 80,000 = approx. 3 : 3	0.9 million : 0.11 million = approx.2 : 3 The positive rate of high-risk cattle is 12.3-fold higher than that of healthy adult cattle	About 1 cattle according to the percentage in Japan (when healthy adult cattle that are 30-month-old or older in the United States are inspected)
･High-risk cattle	Approx. 1 in 0.39 million cattle (35%) inspected Approx. 3 cattle / year (when all high-risk cattle in the United States are inspected)	2 positive cattle in 53,000 About 3 cattle / year (when all high-risk cattle in Canada are inspected)	3 in 0.11 million cattle (11 cattle in 0.2 million)	
The possibility of detection in adult cattle (cattle that are 30-month-old or older in total)	4 cattle / 3.8 million (excluding young cattle)	6 cattle / 0.98 million (excluding young cattle)	5 cattle / 1 million (excluding young cattle)	
Risks in young cattle infected below the detection limit	About 32 cattle / 30 million 36 cattle / year: about 1 cattle is detected in 0.95 million.	22 cattle / 3.6 million 28 cattle / year: about 1 cattle is detected in 0.16 million.	Approx. 1-2 cattle / 0.3 million 6-7 cattle / year: about 5 cattle are detected in 1 million.	

2.4 Summary of risks of live cattle

(1)When the absolute values of BSE external challenge in Japan, the United States, and Canada are compared, the risks arising from imported live cattle are estimated to be 1.5 to 7-fold in the United States and 4 to 6-fold in Canada, and the risks arising from imported MBM and animal oil and fat are estimated to be ≤1/12 to 1/47 in the United States and ≤1/5,100 in Canada, compared with those in Japan. (2) In terms of internal challenge of BSE, the feed regulations seem to have inhibitory effects on BSE amplification; however, considering the use of SRMs in the United States and Canada and their incomplete prevention of cross-contamination from feed, exposure risks in the United States and Canada are considered higher than those in Japan. Taking these facts into account, an optimistic view is that the contamination risks in the United States and Canada are comparable with those in Japan, and a pessimistic view is that the risks could be approximately 10 (7×1.5)-fold higher than those in Japan. (3) BSE testing in the United States and Canada utilizes the data from limited bovine population, and BSE test-positive cases might have been overlooked due to problems in the test techniques and others. Proper assessment is difficult due to limited data collected from the surveillance, but when the absolute numbers extrapolated from this data are compared, the risks are estimated to be 5 to 6-fold and 4 to 5-fold higher in the United States and Canada than those in Japan, respectively. Considering the approximately 20-times larger breeding scale and approximately 30-times larger slaughtering scale in the United States and approximately 3-times larger breeding and slaughtering scale in Canada than those in Japan, comparison of BSE contamination rates suggest the possibility that the number of BSE-contaminated animals per million head in Japan is comparable to that in Canada, and is slightly less than that in the United Sates. (4) In the future risk assessment, continuous improvements of the surveillance in the United States and Canada in subjects, headcounts, and test methods are considered important. In addition, surveillance data of the United States and Canada should be comprehended constantly by the Japanese risk management organization, and it is possible that the risks are reassessed based on the data.

3 Risk assessment --beef and internal organs (contamination rates and levels)

To assess the risks of cattle aged 20 months or younger in the risk assessment of live cattle in the United States and Canada, cattle of all ages were analyzed as a background. In terms of the risks of beef and others, risks of beef derived from animals aged 20 months or younger in the United States and Canada are compared with those derived from cattle of all ages in Japan for assessment.

3.1 Comparison of slaughtered cattle

Traceability (confirmation of age)

The subject cattle to be assessed are those of all ages in Japan, and those aged 20 months or younger that are to be confirmed by the Beef Export Verification Program for Japan, in the United States and Canada.

In the United States, cattle are divided into those aged 30 months or older and those under 30 months based on the tooth alignment check after slaughtering [89]. In addition, cattle aged 20 months or younger are classified by their birth certificates or A40 grading of their carcasses [19) 90]. Birth certificates enable individual recognition from slaughterhouses to feedlots, but trace back of all animals from feedlots to breeding facilities, via rearing facilities, is difficult since ear-tagging is not compulsory. However, use of ear-tagging is rapidly growing in breeding facilities, and it has been reported that birth certificates are being issued by recording the birth date when the first calf of the year is confirmed in a herd of a breeding facility [58].

The A40 analysis data report [90] of approximately 4,500 head of cattle (3,338 were used as samples of which ages were traceable) in November 2004 was as follows: (1) Carcasses of all the 21-months-old animals (237) were A50 grade or higher; thus, no carcass with A40 grade or lower was included. (2) Carcasses of 18 to 21-months-old animals (1,748) were A50 grade or higher; thus, no carcass with A40 grade or lower was included. (3) Based on these data, the probability that carcasses of animals aged 21 months or older are A40 grade or lower is 1.92% or below with 99% reliability (additional data (439 samples) reduced the probability to 0.95% or below with 99% reliability [91]).

In the United States, 25.1 million young animals account for approximately 90% of cattle slaughtered annually; thus, when 10% of them are A40 in the carcass grading, the total number is approximately 2.51 million. In case cattle aged 21 months or older are included, the total number is approximately 48,000 to 24,000 head/year or below. Assuming that 1 out of 1 million young cattle is contaminated, the probability that one BSE-positive animal is included in this group is estimated to be less than once in 20 times at most (once or less in approximately 20 years; once in 40 years according to a tracing report).

In Canada, a bovine individual recognition program, designed for the investigation of livestock disease and food safety issues, has been implemented since January 2001, and participation in this program has been made compulsory since July 1, 2002. At this point, registration of birth dates is not made compulsory, but farm producers will be able to enter them voluntarily after March 2005 [92)-95]. Thus, individual recognition is feasible in Canada, but the age confirmation system can only be applied partly to cattle aged 20 months or younger.

In Japan, a system that ensures traceability of production stages has been implemented since December 2003, and ages of all slaughtered animals can be confirmed [96].

Head-count of slaughtered cattle (age and breed)

In the United States, approximately 90% of beef cattle that are slaughtered annually (approx. 25.1 million) [approx. 24.3 million head of beef cattle out of approx. 27 million slaughtered annually (approx. 16.5 million steers＋approx. 10.5 million non-delivered cattle including approx. 4 million dairy breeds) ＋0.8 million calves]] are reported to be 20 months or younger [97, 98]. As of 2005, animals that are judged by birth certificates account for approximately 10% or 25% of those slaughtered annually at present; however, according to some reports, the number is growing rapidly with export to Japan in mind [58, 99]. In addition, animals with A40 grade are reported to account for approximately 10% of cattle slaughtered annually at present [99]. In Canada, most of the 4.3 million head of cattle slaughtered annually are aged 20 months or younger [21, 100].

In Japan, approximately 1.3 million heads (all ages) are slaughtered annually: beef breeds include approximately 0.24 million young animals (Japanese steers) and approximately 0.22 million delivered cows (female Japanese cows); dairy breeds include approximately 0.42 million young cattle (dairy fattened bulls) and approximately 0.35 million delivered cows (dairy cows) [101].

Considering the epidemiological data in Britain, BSE testing data in Japan (all of the 20 BSE-positive cases were Holstein-Friesian dairy cows, including 18 delivered dairy cows and 2 fattened steers [102]), and differences in risks due to different farming manner after birth such as artificial breast-feeding, risks of beef breeds and young cattle are considered relatively lower than those of dairy breeds and delivered cows, respectively.

3.2 Comparison of each slaughtering process

Inspection before slaughtering (exclusion of high-risk cattle)

In the United States and Canada, visual inspection on the gait of all the cattle delivered to a slaughterhouse is conducted by veterinary officers or by meat inspectors under supervision of veterinary officers. Animals with central nervous system manifestation, dead and downer animals, that are detected in the inspection before slaughtering, are banned from use in food. High-risk cattle are excluded from meat production lines, and BSE inspection is implemented mainly on them in the expanded surveillance [103) -105)]. The high-risk cattle excluded from use in food enter rendering.

In large-scale slaughterhouses in the United States and Canada, approximately 5,000 head of cattle are inspected daily in a series of process [58) 106) 107)]. Two inspectors work on shift, thus one inspector examines approximately 2,500 animals. Assuming that 300 animals are inspected per hour, one inspector works for approximately 8 hours. In other words, approximately 12 seconds are spent to inspect each animal before slaughtering.

In Japanese berthing facilities in slaughterhouses, a veterinarian conducts a visual inspection. In the largest slaughterhouse in Japan, a maximum of approximately 400 heads of cattle are inspected daily in 3 lines [104)]. Two lines have a capacity of inspecting a maximum of 175 per line and 150 are inspected in the other line. At present, the two lines with the capacity of inspecting 175 per line are constantly running at full capacity, and 50 to 150 are inspected in the other line with the capacity of inspecting 150 animals. One veterinarian is assigned to each line. Since the inspection is conducted for 4 hours in the morning, it takes approximately 80 seconds to inspect each animal before slaughtering. Due to the difference in duration of time for visual inspection, the possibility of overlooking abnormal animals in large-scale slaughterhouses in the United States and Canada cannot be denied. Considering the higher BSE positive rate among high-risk cattle compared with that in healthy slaughtered cattle, proper inspection before slaughtering is required.

On the other hand, in the United States and Canada, downer animals are excluded from use in food by the present inspection before slaughtering, thus the possibility of the scenario that BSE-positive cases with neurological abnormalities aged 20 months or younger that are subjects of the Beef Export Verification Program for Japan, are overlooked in the inspection before slaughtering is considered extremely low (See BSE epidemiological data in Britain: at the time of high-level contamination, one 20-months-old BSE animal was discovered among 0.18 million BSE cattle [108].).

BSE inspection in slaughterhouses (screening)

In Japan, the first BSE cow was discovered in September 2001, and BSE testing on slaughtered cattle of all ages began in October 2001 to exclude BSE-positive animals from use in meat [54]. Subsequently, since August 2005, the subject of mandatory BSE screening tests has changed from cattle of all ages to those aged 21 months or older [109]. Optional BSE screening tests of cattle of all ages are performed on a voluntary basis as of October 2005. In the United States, screening tests are not conducted at slaughterhouses, and only few slaughtered healthy cattle aged 30 months or older are tested for surveillance (34 animals as of July 25, 2005) [110].

In the United States and Canada, BSE screening tests are not virtually conducted on healthy slaughtered cattle, and thus risk avoidance by screening test is impossible.

Stunning method

Stunning is used in the United States, Canada, and Japan.

In most slaughterhouses in the United States and Canada, penetrating captive bolt stun guns are used, of which compressed-air stun guns that use air injection have been prohibited in the United States since January 2004 [57], and in Canada since 2000 [79], because they might cause contamination of visible brain pieces, called giant emboli, into the circulatory system of a stunned animal.

According to the surveillance of 160 facilities conducted in Japan at the end of October 2004, the stunning methods were as follows: Stun guns (slaughter guns) were used in 149 slaughterhouses, and the tip of the bolt enters the cranial cavity. In one of these facilities, air guns that give air shocks but do not penetrate into the cranial cavity were used. In addition, slaughter hammers were used in 30 slaughterhouses, and stun guns were jointly used in 19 facilities among them. Methods that use compressed-air or gas injection into the cranial cavity were not used in any slaughterhouses [111].

Pithing

In Japan, as of December 2004, approximately 80% of slaughtered cattle undergo pithing [112], while pithing is prohibited by the Humane Slaughter Act in the United States, and by the Meat Inspection Law in Canada [54]. In Japan, to prohibit pithing, slaughterhouses where pithing was prohibited were publicized (April 2005) [113], and in addition, improvement of facilities toward the ban on pithing in slaughterhouses is promoted today.

Risks posed by pithing can be ignored in the United States and Canada. In Japan, 80% of slaughtered animals undergo pithing, thus the contamination risks of central nervous tissue, posed by pithing, are considered higher than those in the United States and Canada.

SRM removal (spinal cord removal and tests on dressed carcasses after washing)
SRMs are removed from all slaughtered cattle in Japan.

According to the domestic regulations in the United States and Canada, SRMs that should be removed from all ages of cattle include the tonsils (cattle aged 30 months or older in Canada) and the small intestine (only the distal ileum after October 2005), while the spinal cord, brain, eyeballs, and vertebral column are removed only from cattle aged 30 months or older [57) 114)].

Based on the Beef Export Verification Program for Japan, SRMs are removed from all cattle exported to Japan [19) 20)]. SRM removal is visually examined by meat inspectors (veterinarians) in Japan and meat inspectors (including veterinarians) in the United States and Canada [114)-116)].

In Japan, immediately after the BSE occurrence in September 2001, a technique of removing the spinal cord after split liner and washing was used due to the unavailability of equipment that absorb the spinal cord. Absence of residual spinal cord tissue in the vertebral column is visually inspected in all animals by meat inspectors. To introduce this technique, its effectiveness in removing the spinal cord is demonstrated by the test using glial fibrillary acidic protein (GFAP) as a marker by the research group of the MHLW [117)]. Subsequently, a suction method to remove the spinal cord before split liner has become widely used, and is used by 91.9% of slaughterhouses today (as of January 2005) [111)]. Removal of spinal cords in these cattle is confirmed by the above meat inspectors.

In the United States, removal of the spinal cord in cattle aged 30 months or older has been made compulsory by regulations, and according to the Beef Export Verification Program for Japan, after removing the spinal cord from all cattle and washing carcasses, removal is confirmed by meat inspectors. In major packers, the spinal cord is removed after split liner by 2 or 3 workers using a suction machine, and carcasses are washed 5 or 6 times with warm or cold water. Absence of residual spinal cord in the vertebral column is visually inspected by inspectors and the workers [58) 116)]. The effectiveness of this technique to remove the spinal cord has not been scientifically demonstrated by the test using GFAP as a marker.

Management based on SSOP and HACCP (Inspection of compliance)
In Japan, procedures are documented as SSOP (Sanitation Standard Operating Procedures), and operation records are preserved [118)], thus the management by HACCP (Hazard Analysis and Critical Control Point) has not been made compulsory. As of March 2005, SSOP was prepared in all the slaughterhouses that had been inspected until then. In the United States and Canada, procedures are documented in SSOP and HACCP, and operation records are preserved [89) 119)].

In Japan, as a result of the domestic revision, inspection of the compliance with SSOP for hygienic management, including SRM removal, has been increased to twice a year [120)]. However, inspections of SRM removal and others as well as the results have not been publicized to date.

The United States Department of Agriculture, Food Safety and Inspection Service (FSIS) published that 1,036 violations of the SRM removal regulation, which has been made compulsory for meat process manufacturers, were confirmed between January 2004 and May 2005 [121]. In the case of violation, the authority examines safe conditions and orders the violators to take remedial action. The confirmation of the 1,036 violations indicates "the inspectors determined that regulations were not strictly put into practice, and thus immediately took remedial action."

The 1,036 cases of violations included (1) 405 cases associated with the HACCP plan, such as unstored certificates of age in months and SRM removal, and defects in the plan, (2) 467 cases associated with handling of SRMs, such as improper washing of knives and saws, improper removal of spinal cords and tonsils, and improper hand-washing, and (3) 164 cases associated with record storage, such as defects in SSOP and HACCP implementation records, SRM removal and SRM removal training records, and confirmation record of age in months. After remedial actions were taken for these nonconforming cases, the actions were confirmed and the operation of 6 facilities was halted.

3.3 Comparison of risks of meats and others

Distribution of BSE prion in the live body

To assess BSE risks of meat, distribution of BSE prion in BSE-positive cattle must be considered. At the Veterinary Laboratories Agency in Britain, distribution of BSE prion in the living body was examined by bioassay using tissues of experimentally-infected bovine animals [122) 123)]. The bovine animals that were inoculated intracerebrally with the muscle emulsion of the other bovine animals that were killed at 6, 18, 26, and 32 months after oral administration did not develop BSE-like symptoms by 71, 99, 71, and 98 months after inoculation, respectively. Meanwhile, the animals that were inoculated intracerebrally with the distal ileum emulsion of the other bovine animals that were killed at 6, 10, and 18 months after oral administration developed the symptoms after an average 27, 22, and 24 months of incubation periods, respectively. Moreover, 1 of 5 animals that were inoculated intracerebrally with the palatine tonsil emulsion of the other animals killed at 10 months after oral administration developed symptoms after 45 months of incubation period [122) 123)].

In terminally-ill animals with BSE symptoms and the BSE-positive animals (94 months old) detected in high-risk cattle, BSE prion were also detected in areas other than specified risk materials [124) 125)], thus the presence of BSE prion in the muscle (branch of a nerve) cannot be denied. Although the data obtained from the ongoing experiment is limited, BSE prion has not been detected from the muscle of experimentally-infected animals during the incubation period in a bioassay using bovine animals, up until the present. To obtain correct data, the results, including those from infection experiments conducted in Japan, must be observed closely and scrutinized in the future. In Britain and Germany, a large-scale sampling experiment is also underway.

In 1992, at the peak of BSE occurrence, BSE animal, as young as 20-months-old, was discovered in Britain. The incubation period has been prolonged along with a decreased contamination level; thus, the youngest BSE animals were 49-months-old in 2004, and 38-months-old in 2005. Thus, to study the age and prion distribution in the living bodies of BSE-positive cattle, BSE contamination levels in the area must also be considered.

Meat and Advanced Meat Recovery (AMR)

The percentages of cattle aged 30 months or older in major packers in the United States and Canada vary with facilities, but it ranges from <1% to about 10% [58]. Cattle aged 30 months or older are stored in other lines in a refrigerator, and strict measures to prevent mix-up with other cattle aged 30 months or younger are taken, such as attaching a blue tape on the shoulder and thigh, and applying blue edible ink to the vertebral column, for quick distinction. Furthermore, they are scrapped and processed in other lines, or, on the final day of the week to prevent mix-up of meat and bone pieces [58].

The present Beef Export Verification Program for Japan states that measures to prevent mix-up of beef and others, derived from cattle aged 21 months or older and 20 months or younger will be implemented. Accordingly, products must be identified by packages such as by indicating separate lines, washing; as with beef and others, measures must be taken for easy distinction from other carcasses and beef products, when carrying out carcasses from the facility.

In Japan, there are no special measures by age of months at present.

AMR is a method to collect the remaining pieces of meat from the carcasses bones after meat is removed, without crushing bones, by blowing high-pressured water or air to the bones of carcasses. Because of the risks of SRM contamination, regulations concerning AMR have been tightened in the United States and Canada, as exemplified by a ban on use of AMR for the skulls and vertebral columns of cattle aged 30 months or older [57]. Meat obtained by AMR is not a subject of the Beef Export Verification Program for Japan.

Internal organs

In terms of bovine internal organs, there is a record of export to Japan of tongues, from which the tonsils were removed, and intestinal tracts, stomachs, livers, bladders, and others, from which the distal ileums were removed [126].

The risks of the small intestine other than the distal ileum are considered to be risks posed by BSE prion accumulation and SRM contamination. In terms of findings associated with the infectivity of the small intestine other than the distal ileum, experimental results in Britain and Japan are available: (1) In the infection experiment conducted in Britain, no infectivity in the small intestine other than the distal ileum was demonstrated at 6 months after oral administration of the brain of a BSE infected bovine cattle[127], and (2) as a result of investigation on the accumulation of BSE prion protein in each tissue of 3 BSE-positive animals discovered in Japan, BSE prion protein accumulation was found in the distal ileum of two animals by using the WB method, and one by the IHC method, but none in the small intestine other than the distal ileum [128].

In association with the above results, FSIS announced a draft revision of the interim final regulations concerning “bovine internal organs used in food and cosmetics” (implemented on October 7, 2005; opinions are called for until November 7, 2005), which approved the use of the small intestine, from which the distal ileum has been removed, in food and cosmetics [129]. The risks of SRM contamination are the same as those of meat; risk avoidance is considered possible by properly removing SRMs such as the spinal cord and distal ileum to prevent contamination of SRMs to other tissues.

In addition, risks of the tongues are posed by attachment and contamination of tonsil tissue, thus in the United States and Canada, risk avoidance is thoroughly pursued by publishing a manual (SSOP) with photographs of points to remember in cutting out the tongue [119] [130].

Meanwhile, since age determination by A40 grading is conducted using carcasses after refrigeration, during which mix-up with internal organs without A40 grade might occur, unless they are identified corresponding to the carcasses, internal organs cannot be exported to Japan only with age determination by A40 grading, but internal organs that can be managed with identification corresponding to their carcasses can be exported to Japan.

3.4 Summary of contamination risks of beef and internal organs

In terms of risks of beef and others, comparison between the risks of beef derived from cattle aged 20 months or younger in the United States/Canada and risks of beef derived from cattle of all ages in Japan shows that (1) the certification of age in months is not streamlined in the United States and Canada, unlike in Japan. In particular, A40 judgment might not completely exclude 21 months or older cattle. However, considering the background risks of live cattle, the probability that BSE-contaminated cattle are included in this group is thought to be very low. (2) In terms of exclusion of abnormal animals by the tests before slaughter, we cannot deny that a risk of overlooking abnormal animals in large-scale slaughterhouses in the United Sates and Canada may be higher than that in Japan. However, the probability of the following scenario is considered very low: the subjects of the present Beef Export Verification Program for Japan, i.e., BSE-positive cattle with nerve abnormalities aged 20 months or younger, are overlooked in the tests before slaughter. (3) Since BSE screening tests for healthy slaughtered cattle are virtually not conducted in the United States and Canada, risk avoidance by tests is impossible. However, the probability of finding BSE-positive cases among the subjects of the present Beef Export Verification Program for Japan, i.e., cattle aged 20 months or younger, by the BSE inspection is considered very low. (4) In terms of the slaughtering process, the risk management measures by stunning, SRM removal, and procedures (SSOP and HACCP) differ slightly between Japan and the United States/Canada; however, when each measure is not properly practiced, risk avoidance by these measures becomes incomparable between Japan and the United States/Canada. (5) Pithing is banned by the law in the United States and Canada whereas in Japan, approximately 80% cattle undergo pithing and thus are high at risks. (6) As for the compliance with regulations, in the United States, cases of violations are inspected, corrected by remedial actions, and published. On the other hand, neither an inspection nor a report of a similar kind is present in Japan. (7) In terms of beef and others, as long as the conditions of the Beef Export Verification Program for Japan ((i) SRM removal in cattle of all ages, (ii) certificate for beef and others of cattle aged 20 months or younger, and (iii) separate management of products for Japan from that of other products, such as a separate treatment line, washing, identification, packaging, and labeling of products) are observed, the probability of BSE prion contamination is considered very low. Internal organs cannot be exported only with an identification of A40 age in months, and can only be exported when managed and identified with corresponding dressed carcasses.

4 For conclusion

The objects of the risk assessment in the present consultation included beef and internal organs for food (tongues and major internal organs excluding SRMs and beef), but processed products were not included. The assessment was conducted on the assumption that the risk management organization takes the responsibility of the compliance with the Beef Export Verification Program.

(1) When the risks of beef and internal organs, subjects compared in the present consultation, are considered, Japanese cattle are those of all ages that are slaughtered at slaughterhouses, including those born before 2001 (aged 4-year-old or older) when feed regulations were not implemented thoroughly (complete feed regulation). As of 2005, 5 or 6 BSE-positive cases are detected annually. Other risks are infected animals below the detection limit. Thus, the contamination level is the sum of level of each year, and the subjects are cattle delivered to slaughterhouses. On the other hand, the subject populations in the United States and Canada are cattle aged 20 months or younger: those that are born after February 2004. Thus, the risk assessment indicates the contamination level as of February 2004.

(2) When background risks are considered, the rates of BSE contamination in Japan and Canada are comparable (5 to 6 animals/million). According to the surveillance data in the United States, approximately 1 animal/million of BSE contamination and approximately 2 to 3 animals/million of external challenge are estimated [5 to 6 animals in Japan × approx. 10-fold ÷ 20 (feeding scale)].

Table 4 Risk Levels in Live Cattle

	U.S.	Canada	Japan
Subjects of risk assessment	20-months-old or younger	20-months-old or younger	All ages
Number of subject slaughtered cattle (p.a.)	Approx. 25.1 million	Approx. 3.6 million	Approx. 1.3 million
Rate of BSE-positive cattle (per million)	2 to 3	5 to 6	5 to 6
Infection dose	Detection limit-below detection limit	Detection limit-below detection limit	Positive cattle were excluded

(3) In the risk assessment of beef and others in the United States and Canada, there was no method but a method to compare the principles of risk reduction measures. When data was available, efforts were made to compare effectiveness as much as possible; however, data was limited in its availability. The Beef Export Verification Program was assessed with an assumption that it was observed, since it is not implemented at present.

Table 5 Risk Levels of Beef and Internal Organs and Possible Import

	U.S.	Canada	Japan
Inspection before slaughter (exclusion of abnormal cattle)	Approx. 12 seconds per animal There is a greater risk of overlooking abnormal cattle than in Japan, but the risk of overlooking cattle aged 20 months or younger with BSE symptoms is extremely small since downer cattle are excluded from food.		Approx. 80 seconds per animal
Stunning	In use Comparable level with Japan		In use
Pithing	No risk		Higher risk in Japan (Pithing is used in 80% of cattle. Risks are avoided by excluding positive cattle in BSE inspection)
SRM removal	Meat inspectors conduct a visual inspection to confirm no residual spinal cord in the spinal column. However, the effectiveness of spinal cord removal has not been demonstrated scientifically. According to the Beef Export Verification Program, SRMs are due to be removed from cattle of all ages.		Slaughter inspectors conduct a visual inspection to confirm spinal cord removal. To introduce this technique, its effectiveness in removing the spinal cord was confirmed by a test using glial fibrillary acidic protein (GFAP) as a marker by the research group of the Ministry of Health, Labour and Welfare.
AMR (Advanced meat recovery)	Import was banned by the Beef Export Verification Program (excluded by the Program)		None
HACCP, SSOP	HACCP and SSOP are implemented. Inspection of the compliance, information disclosure, and improvement of cases of violations.		SSOP is implemented. Effectiveness is measured by a questionnaire survey.
Limitation in age identification Meat Birth certificate of 20-months-old	〔Birth certificate〕 10%: approx. 2.5 million cattle	〔Birth certificate〕 20%: approx. 0.7 million cattle	Approx. 1.3 million cattle
A40 grading	〔A40〕 10%: approx. 2.5 million cattle		
Internal organs Birth certificate of 20-months-old	〔Birth certificate〕 10%: approx. 2.5 million cattle	〔Birth certificate〕 20%: approx. 0.7 million cattle	Approx. 1.3 million cattle

(4) At present, based on the age identification method, subject cattle of import, which have birth certificates, are estimated to be approximately 5 million and 0.7 million from the United States and Canada, respectively, for meat, and approximately 2.5 million and 0.7 million from the United States and Canada, respectively, for internal organs.

5 Conclusions

The past domestic risk assessment could virtually demonstrate the effectiveness and other aspects of the BSE measures, thus assessments have been conducted based on them. However, since the present consultation was conducted outside Japan, assessment of risks of beef and others in the United States and Canada must be based on the assessment of the principles stated in documents, the some data from risk management organizations, and the supplemental remarks of expert members. Thus, it must be taken into account that there were also unclear aspects. In addition, assessment had to be conducted under the assumption that the Beef Export Verification Program was observed.

Many points remained unclear in the data from the United States and Canada both in quality and in quantity, and assessment had to be conducted with the assumption that the management measures are observed. Thus, we must say that it is difficult to assess scientifically the comparability of the BSE risks in the United Sates/Canada. On the other hand, assuming that the Beef Export Verification Program presented by the risk management organization (mandatory SRM removal in all cattle, export limitation of age to 20 months or younger, etc.) is observed, the difference in the risk levels of beef and others derived from cattle in the United Sates/Canada and those in Japan is considered very small.

The risk management organization holds the responsibility to confirm these assumptions, and if the assumptions are not observed, the results of assessment will be different from the ones presented.

If the risk management organization decides to take measures to lift the import ban after consideration of the above-mentioned, the Prion Expert Committee is obliged to receive reports on the effectiveness of the Beef Export Verification Program and the results of assessment of compliance with the Program from the management organization, provided that the assessment was conducted based on the assumptions. Subsequently, the management organization is obliged to report to the public.

6 Supplementary items for conclusion

To respond to the present consultation, two points should be emphasized. Firstly, as described in the history of the consultation, the responsibilities of the risk assessment organization and the risk management organization must be defined. When the risk management organization judges and implements measures according to the present verdict, the organization must be accountable of the results to the public, and must hold the responsibility of ensuring compliance with the Beef Export Verification

Program by the exporting countries in lifting the import ban.

Secondly, to respond to the present consultation, the Prion Expert Committee of the Food Safety Commission compared the differences in the domestic measures in Japan, the United Sates, and Canada. The consultation demands risk assessment, assuming additional conditions for the Beef Export Verification Program for Japan, and the risk assessment was also assessed, assuming the compliance with the Beef Export Verification Program. Thus, establishment of hardware and software for observance of the Beef Export Verification Program and its inspection are most critical. In case the Beef Export Verification Program is not observed, the assessment results are invalid.

We would like to add the following points that were controversial in the course of the risk assessment:

In terms of SRM removal, the current status of surveillance in slaughterhouses in the United States and Canada is unknown, and the effectiveness of the warranty of good safety by the risk management organization remains uncertain. In particular, contamination of pieces of spinal cord into beef and others can be a risk factor, even in a small amount. In such a case, as for SRM removal, it is unclear whether the risks of beef and others derived from cattle in the United States and Canada are comparable with those in Japan. Thus, the inspection system for spinal cord removal must be reinforced.

To accurately comprehend the BSE contamination status in the United States and Canada, and to implement proper management measures, sufficient surveillance of cattle, including healthy animals, must be expanded and maintained. Even if the management measures become effective to some extent, and the epidemic becomes discontinued and localized, or sporadic, at least continuous surveillance of all high-risk cattle must be maintained.

To prevent BSE exposure and propagation in the United States and Canada, ban on the use of SRMs, which account for 99.4% infectivity of BSE prion, is essential. The use of SRM must be banned not only in feed for cattle but also in feed of other animals, which might cause cross-contamination.

The present risk assessment was conducted under the assumption that the Beef Export Verification Program for Japan was observed. Thus, the management organizations must assure the compliance. The risk management organization must establish a system that assures proper implementation of risk-mitigation measures for beef and internal organs that are exported from the United States/Canada to Japan. An accreditation system of slaughterhouses of beef and others exported to Japan as well as a management system, including periodical official on-the-spot inspection of these facilities, are considered effective.

Even if the risk management organization decides to lift the export ban, import should be suspended when management measures are not properly observed, such as when certificate of the birth age in months is absent, SRMs are improperly removed, and there is a possible mix-up with beef derived from cattle aged 21 months or older during slaughtering and distribution, all of which lead to a serious situation of undeniable risks to humans.

(References)

1. Consultation document issued on May 24, 2005 by the Ministers of Ministry of Health, Labour and Welfare (MHLW) and Ministry of Agriculture, Forestry and Fisheries (MAFF) (Document No. Shoku-an 0524001 of MHLW and Sho-an 1380 of MAFF)
2. Consultation document issued on May 24, 2005 by the MHLW and MAFF (Document No. Shoku-an 0524002 of MHLW and Sho-an 1382 of MAFF)
3. Minutes of the 96th meeting of the Food Safety Commission of the Cabinet Office
4. Measures against bovine spongiform encephalopathy (BSE) in Japan; Interim report, the Food Safety Commission of the Cabinet Office (September 2004)
5. Food safety risk assessment associated with measures against bovine spongiform encephalopathy (BSE) in Japan; the Food Safety Commission of the Cabinet Office (May 2005)
6. Summary of the report of the investigation of Bovine Spongiform Encephalopathy (BSE) in Alberta, Canada (summary of the first domestic case in Canada); Reference data for consultation in Canada (11), CFIA (Canadian Food Inspection Agency), July 2, 2003
7. BSE occurrence in the United States; Press release of the Ministry of Agriculture, Forestry and Fisheries of Japan, December 26, 2003(http://www.maff.go.jp/www/press/cont/20031226press_7.htm)
8. Food Hygiene Law (Law No. 233, 1947), Article 9, Paragraph 2
9. Domestic Animal Infectious Diseases Control Law (Law No. 166, 1951), Articles 37, 40, and 44
10. Agreement on the application of sanitary and phytosanitary measures (SPS agreement); Reference data for consultation in the United States (1), WTO, Article 5, No. 7
11. Overseas research associated with BSE occurrence in the United States; Reference data for consultation in the United States (8), Press release of the MAFF of Japan, January 19, 2004 （http://www.maff.go.jp/www/press/cont/20040119press_4.htm）
12. Expert and working-level meeting concerning BSE (WG) report; Reference data for consultation in the United States (11), July 22, 2004
13. Consultation document issued on October 15, 2004 by the MHLW and MAFF (Document No. Shoku-an 1015001 of MHLW and Sho-an 5410 of MAFF)
14. Joint press statement by the Japan and U.S. governments concerning lifting the ban on beef and beef product trade; Press release of the MAFF of Japan, October 23, 2004 (http://www.maff.go.jp/www/press/cont2/20041023/kossi.htm)
15. Overseas research associated with BSE occurrence in Canada; Reference data for consultation in Canada (8), Press release of the MAFF of Japan, July 9, 2003 (http://www.maff.go.jp/www/press/cont/20030709press_6.htm)
16. Summary of Japan-Canada working-level meeting concerning BSE; Reference data for consultation in Canada (9), November 8, 2004 (http://www.maff.go.jp/www/press/cont2/20041108press_11.htm)
17. Minutes of the 25th meeting of the Prion Expert Committee, Food Safety Commission, the Cabinet Office
18. Food Safety Basic Law (Law No. 233, 1951), Article 11, Paragraph 3

19. USDA Export Verification (EV) Program (draft); Supporting data for consultation in the United States, United States Department of Agriculture (USDA), May 26, 2005
20. CFIA standards of slaughter of cows exportable to Japan and processing of beef products; Supporting data for consultation in Canada, CFIA, May 16, 2005
21. Feeding conditions of cattle in the United States and Canada (including feedstuff) and detailed information of object cattle in risk assessment (breed, age distribution, feeding conditions, and others); supplementary documentation associated with food safety risk assessment (6) (submitted on June 10, 2005)
22. Summary of BSE measures in the United States and Canada in chronological order; supplementary documentation associated with food safety risk assessment (2) (submitted on June 10, 2005)
23. Working group report on the assessment of the Geographical BSE-Risk (GBR) of United States of America 2004; Reference data for consultation in the United States (31), European Food Safety Authority (EFSA)
24. Update of the opinion of the scientific steering committee on the Geographical Risk of Bovine Spongiform Encephalopathy (GBR); Scientific Steering Committee (SSC), January 11, 2002
25. Investigation on the source and route of bovine spongiform encephalopathy (BSE) infection - a debrief report of epidemiological analysis conducted by the BSE epidemiological investigation team; investigative commission concerning bovine spongiform encephalopathy (BSE), BSE epidemiological investigation team, September 2003
26. The BSE Inquiry Vol.16 Reference Material
27. Horn Committee’s report, October 2000
28. Working group report on the assessment of the Geographical BSE-Risk (GBR) of Canada 2004; Reference data for consultation in Canada (31), EFSA
29. The amount of animal fat and oil production in the United States and Canada and import from foreign countries; supplementary documentation associated with food safety risk assessment (5) (submitted on October 21 2005)
30. Title 21 Code of Federal Regulations, Sec.689.2000; Reference data for consultation in the United States (21), August 4, 1997
31. Expanded “Mad Cow” Safeguards Announced to Strengthen Existing Firewalls Against BSE Transmission; Press release of the Food and Drug Administration (FDA), November 26, 2004 (http://www.fda.gov/bbs/topics/news/2004/hhs_012604.html)
32. FDA AND USDA REQUEST COMMENTS AND SCIENTIFIC INFORMATION ON POSSIBLE NEW BSE SAFEGUARDS; Reference data for consultation in the United States (24), website of the FDA Center for Veterinary Medicine (CVM), CVM Update, July 9, 2004
33. FDA Proposes Additional “Mad Cow” Safeguards; FDA press release, FDA News, October 4, 2005 (http://www.fda.gov/bbs/topics/news/2005/new01240.html)
34. CFIA Canada’s Feed Ban Regulations (Canada Gazette, Part, Vol.131, No.16, p2317); Reference data for consultation in Canada (23), CFIA, July 25, 1997
35. New Regulation Proposed For BSE-Related Feed Controls; Reference data for consultation in Canada (25), CFIA News Release, December 10, 2004

36. Backgrounder on New Regulations Proposed for BSE-Related Feed Controls; Reference data for consultation in Canada (26), CFIA News Release, December 10, 2004
37. Management of feed materials of ruminant tissue; Notification No. 8-5 of the MAFF of Japan, April 16, 1996
38. Ministerial ordinance to revise part of the ministerial ordinance associated with, but not limited to, the ingredient specification of feed and feed additives and others; the ministerial ordinance No. 133 of the MAFF of Japan, October 15, 2001
39. Ministerial ordinance to revise part of the ministerial ordinance associated with, but not limited to, the ingredient specification of feed and feed additives and others; the ministerial ordinance No. 15 of the MAFF of Japan, February 28, 2005
40. BSE: Statistics-Confirmed cases of BSE in GB by year of birth where known; website of DEFRA（Department for Environment Food and Rural Affairs）
(http://www.defra.gov.uk/animalh/bse/statistics/bse/yrbirth.html)
41. Geographical Distribution of Countries that reported BSE Confirmed Cases since 1989; website of OIE（Office International des Epizooties）(http://www.oie.int/eng/info/en_esb.htm)
42. Avis du Comite d'Experts Speciallise sur les ESST sur le suivi de l'epizootie d'ESB en France
43. A field investigation on BSE measures in the United States and Canada (report); Reference data for consultation in the United States (26), website of the MAFF of Japan, May 19, 2005
44. CVM Update-Update on Feed Enforcement Activities to Limit the Spread of BSE; Reference data for consultation in the United States (23), CVM, March 17, 2005
45. MAD COW DISEASE, GAO-05-101. FDA's Management of the Feed Ban Has Improved, but Oversight Weaknesses Continue to Limit Program Effectiveness; Reference data for consultation in the United States (25), General Accounting Office (GAO), February 25, 2005
46. Report on the Assessment of the Geographical BSE-Risk（GBR）of the UNITED STATES of AMERICA; Scientific Steering Committee (SSC), July 2000
47. Questions and answers concerning bovine spongiform encephalopathy (BSE); Reference data for consultation in the United States (12), website of the U.S. Embassy in Japan, March 3, 2005（http://japan.usembassy.gov/j/p/tpj-j20050304-50.html）
48. CVM Update-Update on Feed Enforcement Activities to Limit the Spread of BSE; website of CVM, June 10, 2005
(http://www.fda.gov/cvm/bse0605.htm)
49. Feed Ban Review; Reference data for consultation in Canada (24), CFIA, March 2, 2005
50. North American Feed Complex Multi-Client Study; SPARKS COMPANIES INC., May 2004
51. Feedstuff containing meat-and-bone meal to cows (the 15th edition); Press release of the MAFF of Japan, October 25, 2001
52. Emergency measures of temporary ban on import of animal processed protein (possible feedstuff such as meat-and-bone meal); Notification of the MAFF of Japan, Document No. 13 Sei-Chiku 3326, October 1, 2001
53. The ministerial ordinance to revise part of the enforcement regulations of the Slaughterhouse Law; the ministry ordinance, Document No. 209 of the MHLW, October 17, 2001

54. 1. A list of different points of BSE measures between the United States/Canada and Japan; Supplementary data associated with food safety risk assessment (1) (submitted on June 10, 2005)
55. Opinion on the Scientific Steering Committee on the human exposure risk（HER）via food with respect to BSE, Scientific Steering Committee (SSC), December 10, 1999
56. Present management of meat-and-bone meal and others; Notification of the MAFF of Japan, Document No. 13 Sei-Chiku 3388, October 1, 2001
57. Federal Register/Vol.69, No.7; Reference data for consultation in the United States (30), January 12, 2004
58. Verification of security of beef production and distribution stages in the United States; International comparative study associated with the safety of livestock food system (Grant-in-Aid for Scientific Research 2002-2004, Basic Research (B) (1)), Study result report, Chapter 1 , Satoshi Kai, March 2005
59. Report on Measure Relating to BSE in the United States (Investigative report of the international investigation team relating to the BSE measures in the United States); Reference data for consultation in the United States (9), The Secretary’s Foreign Animal and Poultry Disease Advisory Committee’s Subcommittee, February 2, 2004
60. Yamanouchi, K., Onodera, T.; Mystery of BSE (bovine spongiform encephalopathy); Prion disease <the 2nd edition>, August 20, 2002
61. Williams, E. S., Miller, M. W. Transmissible spongiform encephalopathies in non domestic animals; origin transmission and risk factors; Rev. sci. tech. Off. Int. Epiz., (2003) 22:145-156
62. Miller, M.W., Williams, E.S., McTarty, C.W., Spraker, T.R., Kreeger, T.J., Larsen, C.T., Thorne, E.T. Epizootiology of chronic wasting disease in free-ranging cervids in Colorado and Wyoming. J Wildl Dis. (2000)36:676-690.
63. Williams, E.S. Chronic Wasting Disease Vet Pathol (2005) 42:530-49
64. Schreuder, B. E. C., Geertsma, R. E., van Keulen, L. J. M., van Asten, J. A. A. M., Enthoven, P., Oberthur, R.C., de Koeijer, A. A., Osterhaus, A. D. M. E. 1998. Studies on the efficacy of hyperbaric rendering procedures in inactivating bovine spongiform encephalopathy (BSE) and scrapie agents; Vet Rec, Vol.142: 474-480.
65. BSE Surveillance; website of APHIS (Animal and Plant Health Inspection Service), May 20, 2004 (http://www.aphis.usda.gov/lpa/issues/bse/bse-surveillance.html)
66. Evaluation of the Potential for BSE in the United States; Reference data for consultation in the United States (32), Harvard Center for Risk Analysis, November 26, 2001
67. Additional Question and Requests to USDA; Reference data for consultation in the United States (29), April 2005
68. Summary of the Epidemiological Findings of North American Bovine Spongiform Encephalopathy Positive Cattle; Reference data for consultation in the United States (35), USDA, April 2005
69. BSE Surveillance Plan; Reference data for consultation in the United States (27), APHIS, March 15, 2004
70. Details of surveillance in the United States (data according to areas, ages, and others); Supplementary data associated with food safety risk assessment (5) (submitted on July 8, 2005)

71. Data of the inconclusive positive cattle published by the U.S. government on June 10; Supplementary data associated with food safety risk assessment (6) (submitted on July 8, 2005)
72. Detailed inspection protocols or manuals of ELISA, WB, and IHC methods used in laboratories in the United States; Supplementary data associated with food safety risk assessment (4) (submitted on September 9, 2005)
73. BSE Network Labs; website of NVSL, May 17, 2004 (http://www.aphis.usda.gov/vs/nvsl/labcertification/BSElabs.htm)
74. BSE Test Results; website of APHIS (http://www.aphis.usda.gov/lpa/issues/bse_testing/test_results.html)
75. The second BSE-positive cow in the United States; Supplementary data associated with food safety risk assessment (1) (submitted on July 29, 2005)
76. Inspection methods in the United States; Supplementary data associated with food safety risk assessment (2) (submitted on August 22, 2005)
77. National Bovine Spongiform Encephalopathy (BSE) Surveillance program; Reference data for consultation in Canada (28), CFIA, March 24, 2005
78. Surveillance; Reference data for consultation in Canada (29), CFIA, May 2005
79. Technical Overview of BSE in Canada; Government of Canada, June 2005
80. Confirmatory inspection methods for BSE in Canada (introduction of western blot); Supplementary data associated with food safety risk assessment (7) (submitted on July 8, 2005)
81. Document 2; supporting data submitted in the 21st Prion Expert Committee of the Food Safety Commission, March 11, 2005
82. Guideline for specific domestic animal infectious diseases control associated with bovine spongiform encephalopathy; MAFF of Japan, November 29, 2004
83. Screening test results of bovine spongiform encephalopathy (BSE); website of the MHLW. （http://www.mhlw.go.jp/houdou/0110/h1018-6.html）
84. Summary of inspection methods of transmissible spongiform encephalopathy; MHLW. September 20, 2005
85. Reference data: Diagnosis of BSE-positive cattle and age distribution and others in the surveillance in Canada; Supplementary data associated with food safety risk assessment (submitted on July 29, 2005)
86. Judgment systems of BSE confirmatory inspection results in the United States and Canada (the number of members in the Expert Committee, specialized fields of experts, procedures of the judgment, and others); Supplementary data associated with food safety risk assessment (1) (submitted on October 21, 2005)
87. The number of BSE-positive cattle in Japan when the BSE surveillance conducted in the United States and Canada is applied in Japan; Supplementary data associated with food safety risk assessment (3) (submitted on July 8, 2005)
88. Reference data: Comparison of surveillance between Japan and the United States; Supplementary data associated with food safety risk assessment (submitted on July 29, 2005)
89. Examples of representative SSOP and HACCP in the United States and Canada; Supplementary data associated with food safety risk assessment (2) (submitted on July 8, 2005)

90. Study report on age determination of cattle and relevant documents; Reference data for consultation in the United States (36)
91. Reference data: Addition to the final report "The investigation on physiological maturity of beef carcasses"; Supplementary data associated with food safety risk assessment (submitted on July 8, 2005)
92. Attachment 3.0 Age Verification; Reference data for consultation in Canada (34), CFIA, March 25, 2005
93. Attachment 3.1 Canadian Cattle Identification Agency; Reference data for consultation in Canada (35), CFIA, March 25, 2005
94. Attachment 3.2 Agri-Traçabilité Québec (ATQ); Reference data for consultation in Canada (36), CFIA, March 25, 2005
95. Attachment 3.3 Audit protocol to verify the accuracy of birth date information in the CCIA and ATQ; Reference data for consultation in Canada (37), CFIA, March 25, 2005
96. Document 3-2; About Tracability of Compliance Status; Document distributed on the day of the 16th Prion Expert Committee of the Food Safety Commission
97. OVERVIEW OF THE U.S. BEEF INDUSTRY; Reference data for consultation in the United States (13), USDA, October 2004
98. Livestock Slaughter 2004 Summary; Reference data for consultation in the United States (15), National Agriculture Statistics Service, USDA
99. Reference data 1. The percentage of object cattle in the Beef Export Verification Program using production records or physiological maturity of beef carcasses; Supplementary data associated with food safety risk assessment (submitted on September 22, 2005)
100. Overview of Canada's Safeguards; Reference data for consultation in Canada (14), CFIA, February 21, 2005
101. Monthly report of livestock-marketing statistics; Reference data for consultation in the United States (17), the Statistics Division in the MAFF of Japan, March 2005.
102. Q&A concerning bovine spongiform encephalopathy (BSE), status of BSE confirmation; website of the MHLW.
（http://www.mhlw.go.jp/topics/0103/tp0308-1.html）
103. Implementation status of antemortem inspection by veterinarians in the United States and roles of veterinarians in slaughter lines; Supplementary data associated with food safety risk assessment (5) (submitted on August 22, 2005)
104. Comparison of inspection systems in slaughterhouses between Japan and the United States; Supplementary data associated with food safety risk assessment (2) (submitted on September 9, 2005)
105. Roles and authorities of veterinary officers and inspectors in slaughterhouses; Supplementary data associated with food safety risk assessment (1) (submitted on September 22, 2005)
106. Structure of packers and the numbers of workers and slaughtered cattle; Supplementary data associated with food safety risk assessment (7) (submitted on June 10, 2005)
107. Structure of packers and the number of slaughtered cows (Canada); Supplementary data associated with food safety risk assessment (1) (submitted on June 20, 2005)

108. BSE: Statistics-Youngest and oldest cases by year of onset-GB (Passive surveillance only); Website of the Department for Environment, Food and Rural Affairs (DEFRA) (http://www.defra.gov.uk/animalh/bse/statistics/bse/yng-old.html)
109. Ministerial ordinance to revise part of the enforcement regulation of the Special BSE Measures Law related to the MHLW; Document No. 110, July 1, 2005
110. Surveillance (1): Ages distribution of cattle that underwent surveillance (according to the categories, beef cattle and dairy cows, areas, and others); Supplementary data associated with food safety risk assessment (3) (submitted on July 29, 2005)
111. Document 3-2:Investigation results of BSE measures; Document distributed on the day of the 17th Prion Expert Committee of the Food Safety Commission
112. Document 3-1: About Review on Domestic Measures; Document distributed on the day of the 16th Prion Expert Committee of the Food Safety Commission
113. Guideline for complete ban on pithing; Notification No. 0419001 of the director of the Security Monitoring Section, Food Safety Division, Pharmaceutical and Food Safety Bureau, MHLW. April 19, 2005
114. Removal of Specified Risk Materials (SRMs) from Cattle Slaughtered in Establishments Inspected under the Meat Inspection Regulations in 1990; Reference documentation for consultation in Canada, CFIA, July 24, 2003
115. Document No. 13: (1) Operation flowchart in slaughterhouses (assignment of inspectors at each stage) in the United States and Canada compared with that of Japan; Supplementary data associated with food safety risk assessment (submitted on July 8, 2005)
116. Confirmation of removal of spinal cord by meat inspectors in packers in the United States and Canada; Supplementary data associated with food safety risk assessment (submitted on October 21, 2005)
117. M. Shinagawa (chief investigator) "Study on bovine spongiform encephalopathy (BSE)" General/assigned study report; Grant-in-Aid for Scientific Research of the MHLW, Special Research Project for Health Science, 2001.
118. Research results relating to BSE measures; Document distributed on the day of the 21st Prion Expert Committee of the Food Safety Commission.
119. Reference data 1: SSOP associated with the removal of tonsils in slaughterhouses in Canada; Supplementary data associated with food safety risk assessment (submitted on August 22, 2005)
120. Investigation on BSE measures; Notification No. 1007001 of the director of the Security Monitoring Section, Food Safety Division, Pharmaceutical and Food Safety Bureau, MHLW, October 7, 2005
121. Data relating to the status of the compliance with regulations of hygienics in slaughterhouses and others in the United States; Supplementary data associated with food safety risk assessment (8) (submitted on September 9, 2005)
122. Wells, G. A., Hawkins, S. A., Green, R. B., Austin, A. R., Dexter, I., Spencer, Y.I., Chaplin, M.J., Stack, M. J., Dawson, M. Preliminary observations on the pathogenesis of experimental bovine spongiform encephalopathy (BSE): an update. Vet Rec. (1998)142: 103-106.

123. Wells, G. A., Spiropoulos, J., Hawkins, S. A., Ryder, S. J. Pathogenesis of experimental bovine spongiform encephalopathy: preclinical infectivity in tonsils and observations on the distribution of lingual tonsil in slaughtered cattle. Vet Rec. (2005)156: 401-407.
124. Buschmann, A., Groschup, M.H. Highly bovine spongiform encephalopathy-sensitive transgenic mice confirm the essential restriction of infectivity to the nervous system in clinically diseased cattle. J Infect Dis. (2005) 192: 934-942.
125. Iwamaru, Y., Okubo, Y., Ikeda, T., Hayashi, H., Imamura, M., Yokoyama, T., Shinagawa, M. : PrPSc distribution of a natural case of bovine spongiform encephalopathy; International Symposium Prion Disease Food and Drug Safety, Sendai, Japan, 2004.
126. Beef, internal organs, tongues, and other regions imported from the United States and Canada before the import ban; Supplementary data associated with food safety risk assessment (6) (submitted on September 9, 2005)
127. Opinion on TSE infectivity distribution in ruminant tissues (state of knowledge, December 2001); Scientific Steering Committee (SSC)
128. Prion distribution in the body of the three BSE-positive cows in Japan; Excerpt of the Prion Symposium 2005, August 26, 27, 2005
129. To Allow Use of Small Intestine from U.S. And Eligible Countries; FSIS (http://www.fsis.usda.gov/News_&_Events/NR_090705_01/index.asp)
130. Management of tonsils and the status of implementation in the United States; Supplementary data associated with food safety risk assessment (6) (submitted on August 22, 2005)

Invasion risk of live cattle in the United States between 1980 and 2003

Regulations		
Regulations		･1989 Import ban on ruminants and ruminant-derived meat-and-bone meal from Britain and countries where BSE occurred ･1991 Import ban on ruminant meats such as beef from countries where BSE occurred ･1997 Import ban on ruminants and ruminant-derived meat-and-bone meal from all European countries ･2000 Import ban on meat-and-bone meal of all animals from Europe

Exporter	**CD (A report from the United States to EU) Export data of the Eurostat and others is indicated in parenthesis (cattle)** **1980-2003**	**Remarks**
Britain	323 (327) 206 (210) when 117 cattle out of risk account are subtracted	･Ten cattle were imported between 1990 and 1992 through Canada. ･Breeding cattle for meat and dairy cows accounted for 96% and 4% of the imported cows, respectively. ･The cattle imported from Britain in 1995 were traced back (retrospective surveillance), and 117 cattle alive in 1995 were disposed of (samples were collected for diagnosis, and slaughtered bodies were incinerated). (All the cattle were negative for BSE in histopathological and IHC tests). Fifty-two of these 117 cows were from the BSE-occurred group. ･According to the Harvard risk evaluation, the United States imported 334 cattle from UK between January 1981 and July 1989, of which 161 cattle were killed and disposed of in a manner with no potential contamination into food and feedstuff. The remaining 173 cattle did not belong to the BSE-occurred group, but might have entered rendering. Breeding cattle for meat and dairy cows accounted for 94.8% (164) and 5.2% (9) of these 173 cows, respectively.
European countries (except Britain)	563 (1,762) 497 (1,711) when cattle out of risk account are subtracted	･According to the Harvard risk evaluation, 397 breeding cattle were imported from Swiss, France, Italy, and Belgium between 1983 and 1987.
Ireland	162 (233) 136 (233) when 26 cattle out of risk account are subtracted	･According to the CD, 26 of these 162 cattle were not considered as a risk factor (22 cattle were traced back and excluded from rendering, and 4 cows were demonstrated to be born in a quarantine).
Belgium	6 (6) 0 (6) when cattle out of risk account are subtracted	･According to the CD, 40 breeding cows were imported from these 4 countries between 1996 and 1997. (40 cattle including 6 cattle from Belgium, 28 cattle from Germany, 3 cattle from Austria, and 3 cattle from Italy) As a result of tracing back these 40 cattle, none entered rendering in the United States; thus, they are not considered as a risk. ･Two cattle exported from Italy in 1981 (Eurostat) were imported in the period that does not fall into a risk factor, thus were not considered as a risk.
Germany	46 (430) 18 (430) when cattle out of risk account are subtracted	
Austria	3 (0) 0 (0) when cattle out of risk account are subtracted	
Italy	8 (23) 5 (21) when cattle out of risk account are subtracted	
Denmark	0 (12)	･There is a wide difference in the figures between the CD and Eurostat (no cow according to the CD).
Netherlands	0 (607) 0 (558) when cattle out of risk account are subtracted	･There is a wide difference in the figures between the CD and Eurostat (no cow according to the CD) ･Forty-nine cattle exported in 1982 (Eurostat) were imported in the period that does not fall into a risk factor, and thus were not considered as a risk.
France	235 (403)	
Swiss	103 (48)	
Canada	16,655,685 (15,494,687) 13,019,248 (11,689,972) when cattle out of risk account are subtracted	･After 1986, 0.235-1.7 million cattle were imported annually. ･3,636,437 cattle exported before 1992 (3,804,715 cattle according to other data) were imported in the period that does not fall into a risk factor, thus were not considered as a risk. ･More than 80% of the imported cattle were fattening or slaughter cattle; thus, 20% were considered as a BSE invasion risk.
Japan	242 (0)	･As a result of traceback, up to 39 cattle might have entered rendering.

References: European Food Safety Authority Working group report on the assessment of the Geographical BSE-Risk (GBR) of United States of America 2004; Reference document for the consultation in the United States 31
Evaluation of the Potential for BSE in the United States (Harvard Center for Risk Analysis); Reference document for the consultation in the United States 32, November 26, 2001

Invasion risks of live cattle in Canada between 1980 and 2003

Regulations	・1988 Import ban on meat-and-bone meal from countries other than the United States ・1990 Import ban on live cattle from Britain and Ireland Lifting the ban on meat-and-bone meal import from BSE free countries Mandatory notification of BSE ・1991 Import ban on beef products from countries where BSE occurred ・1994 Import ban on live cattle from countries where BSE occurred ・1996 Import ban on live cattle and beef products from countries other than BSE free countries ・2000 Import ban on animal processed protein of all kinds of animals from countries other than BSE free countries	
Exporter	**CD (Country Dossier)** Export data of the Eurostat and others is indicated in parenthesis (cattle)	**Remarks**
	1980-2003	
Britain	231 (698) 117 (198) when cattle out of the risk account are subtracted	・According to the CD, there is no record of live cattle import from the UK after 1991 ・According to the Eurostat, 500 cattle were imported in 1993. This import is described as "male calves" in the Eurostat and updated UK export statistics, but is not mentioned in the original UK export statistics. As a result of detailed investigation, this import of 500 cattle was determined as highly suspicious. Thus, these 500 cattle were not considered as a risk. Furthermore, the BSE risk evaluation in Canada, conducted by the CFIA, says "There is no import record from the UK after 1990". ・According to the CD, 231 cattle between 1980 and 1990 included 108 slaughtered cattle, 9 dead cattle (they might have entered the rendering system), 37 cattle sent back to the Britain, 76 cattle incinerated, and 1 cow buried (this did not enter the rendering system, and thus was not considered as a risk) (・After 1978, meat-and-bone meal for livestock food had not been imported from BSE contaminated countries; thus, BSE invasion in Canada is likely to have been caused by live cattle imported from the UK in 1980s. The number of cattle imported from the Britain, which may be dead or slaughtered and underwent the rendering process to enter the animal feedstuff system in the late 1980s, has amounted to a maximum of 68 until 1990. Among them, 10 cattle were shipped from farms where BSE was discovered, of which 2 cattle belonged to the birth cohort of BSE-positive cows imported in 1993 (Reference document for the consultation in Canada 14).)
European countries (except Britain)	308 (324) 250 (291) when cattle out of risk account are subtracted	
Ireland	16 (20) 0 (20) when cattle out of the risk account are subtracted	・Sixteen cattle between 1980 and 1990 (20 cattle according to the Eurostat) included 9 slaughtered cattle, 3 dead cattle, and 4 incinerated cattle These did not enter the rendering system, and thus were not considered as a risk.
Hungary	0(12)	
Germany	7(4)	
Austria	9 (0) 0 (0) when cattle out of the risk account are subtracted	・Nine cattle exported before 1987 (none according to other data) were imported in the period that does not fall into a risk factor, and thus were not considered as a risk.
Italy	11(15) 0 (4) when cattle out of the risk account are subtracted	・Eleven cattle exported before 1982 (also 11 cattle according to other data) were imported in the period that does not fall into a risk factor, and thus were not considered as a risk.
Denmark	28(28) 7 (7) when cattle out of the risk account are subtracted	・Nineteen of 28 cattle were buffaloes imported in 2000 (including 1 incinerated and 18 disposed buffaloes). Nine cattle other than buffaloes included 1 exported cattle, 1 disposed cattle, and others unknown.
Netherlands	1 (1) 0 (0) when cattle out of the risk account are subtracted	・One cattle exported before 1984 (also one cattle according to other data) was imported in the period that does not fall into a risk factor, and thus was not considered as a risk.
France	201(203)	
Swiss	35(41)	
U.S.	2,377,697 (1,500,001) 1,558,032 (1,295,520) when cattle out of the risk account are subtracted	・16,000-340,000 cattle were imported from the United States annually. Most of them were steers and undelivered cows. ・90% of the cattle imported from the United States were fattening cattle or slaughter cattle. ・819,665 cattle exported before 1992 (204,481cattle according to other data) were imported in the period that does not fall into a risk factor, and thus were not considered as a risk.
Japan	18 (0) 0 (0) when cattle out of the risk account are subtracted	・Twenty-two or more cattle were imported from Japan (through the United States), including 4 exported (sent back) cattle, 14 disposed cattle, and 4 slaughtered cattle (the 4 cattle sent back are excluded from the left figures) These did not enter the rendering system and thus were not considered as a risk.

References: European Food Safety Authority Working group report on the assessment of the Geographical BSE-Risk (GBR) of Canada 2004; Reference document for the consultation in Canada 31
①Overview of Canada's Safeguards, February 21, 2005
②Confirmation that Canada has an epidemiologically effective feed ban under which BSE is destined for eradication; Reference document for the consultation in Canada 14

Invasion risk of meat-and-bone meal in the United States between 1980 and 2003		
Regulations		・1989 Import ban on ruminants and ruminant-derived meat-and-bone meal from Britain and countries where BSE occurred ・1991 Import ban on ruminant meats such as beef from countries where BSE occurred ・1997 Import ban on ruminants and ruminant-derived meat-and-bone meal from all European countries ・2000 Import ban on meat-and-bone meal of all animals from Europe
Exporter	**CD (A report from the United States to EU)** **Export data of the Eurostat and others is indicated in parenthesis (ton)**	**Remarks**
	1980-2003	
Britain	5 (140) 5 (24) when meat-and-bone meal out of the risk account are subtracted	・Thirty-nine tons in 1989 were not considered as a risk since they could not be confirmed in the revised export statistics of Britain. ・Seventy-seven tons between 1997 and 1999 were considered to include only nonmammalian MBM (Export of mammalian MBM from Britain has been illegalized since March 27, 1996), and thus were not considered as a risk in the GBR. ・The Harvard risk evaluation said "There is no solid data that suggest the kind and composition of the feedstuff imported from the United States between 1980 and 1990".
European countries (except Britain)	684 (2,129)	
Denmark	464 (382)	・There is a proposition that these import products were not derived from ruminants and thus did not contribute to the BSE risk, although this has not been demonstrated.
France	165 (0)	
Italy	36 (1,376)	
Netherlands	19 (118)	
Belgium	0 (10)	・In these countries, there was no import according to the CD, while there was according to the Eurostat.
Greece	0 (55)	
Ireland	0 (180)	
Spain	0 (8)	
Canada	405,863 (227,572) 329,942 (227,572) when meat-and-bone meal out of the risk account are subtracted	・Since 1989, 18,000-44,000 tons of meat-and-bone meal have been imported annually. ・75,921 tons exported before 1992 (0 ton according to other data) were imported in the period that does not fall into a risk factor, and thus were not considered as a risk.

References: European Food Safety Authority Working group report on the assessment of the Geographical BSE-Risk (GBR) of United States of America 2004; Reference document for the consultation in the United States 31
Evaluation of the Potential for BSE in the United States (Harvard Center for Risk Analysis); Reference document for the consultation in the United States 32, November 26, 2001

Invasion risk of meat-and-bone meal in Canada between 1980 and 2003

Regulations	
Regulations	・1988 Import ban on meat-and-bone meal from countries other than the United States ・1990 Import ban on live cattle from Britain and Ireland Lifting the ban on meat-and-bone meal import from BSE free countries Mandatory notification of BSE ・1991 Import ban on beef products from countries where BSE occurred ・1994 Import ban on live cattle from countries where BSE occurred ・1996 Import ban on live cattle and beef products from countries other than BSE free countries ・2000 Import ban on animal processed protein of all kinds of animals from countries other than BSE free countries

Exporter	CD (Country Dossier) Export data of the Eurostat and others is indicated in parenthesis (ton)	Remarks
Britain	0 (149) 0 (0) when meat-and-bone meal out of risk account are subtracted	・According to the Eurostat, the MBM between 1993 and 1996 is nonmammalian MBM. Thus, that was not considered as a risk. ・Since March 27, 1996, export of mammalian MBM from Britain has been illegalized; thus, the MBM imported after this date was considered to include only nonmammalian MBM. Thus, that was not considered as a risk, either.
European countries (except Britain)	11,046 (5,710) 0 (11) when meat-and-bone meal out of risk account are subtracted	
Denmark	10,946 (5,661) 0 (0) when meat-and-bone meal out of risk account are subtracted	・The MBM from Denmark was derived from pork and chicken, imported for fish culture. Thus, that was not considered as a risk.
France	1 (13) 0 (0) when meat-and-bone meal out of risk account are subtracted	・The MBM from France was derived from birds, imported for fish culture. Thus, that was not considered as a risk.
Germany	99 (0) 0 (0) when meat-and-bone meal out of risk account are subtracted	・The MBM from Germany was derived from chicken, imported for fish culture. Thus, that was not considered as a risk.
Belgium	0(25) 0(0) when meat-and-bone meal out of risk account are subtracted	・The MBM from Belgium was hemoglobin. Thus, that was not considered as a risk.
Ireland	0(11)	
Japan	26(0)	
U.S.	287,103 (351,673) 252,334 (312,329) when meat-and-bone meal out of risk account are subtracted	・The major export country of MBM is the United States according to the CD; 0.25 million tons (0.31 million according to other data) of MBM is imported annually . ・34,769 tons of MBM (39,344 tons according to other data) was imported before 1992, a period that does not fall into a risk factor, and thus was not considered as a risk.

Import of Animal oil and fat (ton)

U.S. 1995 -2004		
Exporter	Canada	355,643
	Germany	574
	France	65
	Sweden	4
	Argentine	5,123
	New Zealand	586
	Mexico	56
	Pakistan	26
	China	0.3

Canada 1995-2004		
Exporter	U.S.	129,088
	New Zealand	65
	India	18
	Senegal	0.2

Japan 1989-2000		
Exporter	Netherlands	1,245
	Swiss	0.02

Reference: A debrief report of the epidemiological analysis by the BSE Epidemiological Investigation Team, September 2003
Animal oil and fat production and imports from each country in the United States and Canada; Supplementary data associated with food safety risk assessment (5) (submitted on October 21)