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MINISTRY OF LIVESTOCK, AGRICULTURE AND FISHERIES

General Department of Livestock Services

Epidemiology Unit

Animal Health Emergency Plan

(Plan de Emergencias Sanitarias Animales: PLAEMSA)

I. Bovine Spongiform Encephalopathy

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CONTENTS

INTRODUCTION

The elaboration of contingency plans for the diseases declared as exotic in the country is one of the tasks assigned to the Epidemiology Unit of the General Department of Livestock Services.
Here follows the first plan elaborated on Bovine Spongiform Encephalopathy (BSE).
It is intended for the use of official and private veterinarians, and producers and it is complemented with the corresponding Surveillance Plan.
Plans are dynamic and therefore suggestions on changes or modifications are welcomed.

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1. Nature of the disease

Bovine Spongiform Encephalopathy (BSE) is a progressive neurological disease of adult cattle, characterized by a long incubation period, followed by a degenerative process of the Central Nervous System (CNS), which leads to the death of the affected animal. The disease was first recognised in 1986. Its appearance was probably the consequence of changes in the methods of meat-and-bone meal manufacture, which allowed for the recycling of its agent and its spread among cattle.

1.1 Aetiology

BSE is caused by an unconventional agent or prion, an altered form of a normal membrane protein, which in turn induces the same alterations in normal host proteins –auto-replication property– thus increasing the amount of pathogenic protein in host cells. Spongiform Encephalopathies or prion diseases are characterised by the accumulation of a protease resistant form of a protein – amyloid.

The agent is extremely resistant to high temperatures, irradiation and chemical disinfectants.

According to the similarities with scrapie, infectivity would be present in the Central Nervous System (CNS) and in lympho-reticular tissues of the affected animals.

Experimental results have proved that infectivity distribution in BSE cases is more limited.

1.2 Species susceptible to infection

BSE was first recognised in cattle in Great Britain in1986. It was then diagnosed in zoo antelope, domestic cat and wild captive felidae.

By means of intracerebral inoculation of brain tissue from affected cattle, the disease was reproduced in cattle, sheep, goats, pigs, mice and mink but not in chicken.

Transmission via oral exposure was achieved in sheep, goats and mink but neither pigs nor chicken showed BSE signs after more than 4 years of being fed with brains of infected cattle.

In human beings, the most frequent Spongiform Encephalopathy is Creutzfeldt-Jakob Disease (CJD), which occurs in its sporadic form throughout the world, with an average rate of one case every million people. CJD also occurs in its hereditary form, and also in iatrogenic form.

In 1996 it was proved that BSE agent affected human beings originating a variant sporadic form of CJD, described as (v-CJD).

This led the WHO to recognise BSE as a zoonosis in 1996.

1.3 Occurrence in the world and in Uruguay

The table 1 shows BSE occurrence in the world. A case of Spongiform Encephalopathy was never detected in any animal species in our country. As for CJD, sporadic cases and four hereditary cases were detected in Uruguay.

1.4 Diagnostic criteria

The examination of tissues collected in the post-mortem is essential to confirm diagnosis. However, affected animals show distinctive clinical signs. Due to the long incubation period, clinical signs appear in animals around 5 years of age.

Persons handling suspected animals or tissues must take precautions to minimise exposure risk to BSE.

Table 1- Number of Bovine Spongiform Encephalopathy cases

	Year															
Country	87[1]	88	89	90	91	92	93	94	95	96	97	98	99	00	01	02
Austria	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	-
Belgium	-	-	-	-	-	-	-	-	-	-	1	6	3	9	46	21
Czech Republic	-	-	-	-	-	-	-	-	-	-	-	-	-	-	2	-
Denmark	-	-	-	-	-	1	-	-	-	-	-	-	-	1	6	1
Finland	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	-
France	-	-	-	-	5	-	1	4	3	12	6	18	31	161	274	91
Germany	-	-	-	-	-	1	-	3	-	-	2	-	-	7	125	54
Great Britain	446	2514	7228	14407	25359	37280	35090	24438	14562	8149	4393	3235	2301	1443	1202	534
Greece	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	-
Ireland	-	-	15	14	17	18	16	19	16	73	80	83	91	149	246	209
Israel	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1
Italia	-	-	-	-	-	-	-	2	-	-	-	-	-	-	48	4
Japan	-	-	-	-	-	-	-	-	-	-	-	-	-	-	3	2
Liechtenstein	-	-	-	-	-	-	-	-	-	-	-	2	-	-	-	-
Luxemburg	-	-	-	-	-	-	-	-	-	-	1	-	-	-	-	1
Poland	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1
Portugal	-	-	-	1	1	1	3	12	15	31	30	127	159	149	110	18
Slovakia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	5	-
Slovenia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	1
Spain	-	-	-	-	-	-	-	-	-	-	-	-	-	2	82	80
Switzerland	-	-	-	2	8	15	29	64	68	45	38	14	50	33	42	8
The Netherlands	-	-	-	-	-	-	-	-	-	-	2	2	2	2	20	13

(1) Includes year 1986
Source: OIE. Updated August 29, 2002.

1.4.1 Clinical signs

Most frequent signs are apprehension, pelvic limb incoordination and excessive reaction to sensorial stimuli.

First clinical signs observed, ordered by its frequency are nervousness, kicking, difficulties in movement, loss of bodily condition, loss of weight, a reduction in milk yield. Neurological signs can be classified in alterations of:

a) Behaviour
b) Sensation
c) Posture and movements

Most frequent signs (80% of cases) are apprehension, hyperaesthesia and ataxia.

1.4.2 Pathology

No macroscopical changes are evident. Through histopathological examination spongiform changes in certain brain areas, in particular in the obex (99,99% of cases) are detected.

1.4.3 Laboratory tests

To date, there is no valid test for BSE diagnosis in the live animal. DILAVE laboratory carries out histopathological and immunohistochemical tests.

1.4.4 Differential diagnosis

In BSE differential diagnosis the following diseases have to be taken into account:

- acetonemia
- metabolic disorders as hypocalcaemia and hypomagnesaemia
- hepatoencephalopathy
- polioencephalomalacia
- ryegrass staggers
- intoxication caused by plants
- rabies
- intoxication caused lead
- bacterial encephalitis (for example encephalic listeriosis)
- malignant catarrhal fever associated with sheep
- babesiosis (*Babesia bovis*)
- botulism
- cerebro-cortical necrosis
- traumatisms
- tumours

If BSE cases should be detected it is highly probable that they will be associated with imported animals.

Contaminated veterinary therapeutic products, as well as chirurgical material, must be considered as a potential infection source. Should the source of a BSE outbreak be a therapeutic product, the disease would be more spread than it would be if its source were imported cattle, and therefore its control and eradication would be more difficult. The same would happen if the source of the infection should be in feedstuff.

1.5 Resistance and immunity

1.5.1 Natural and passive immunity

There is no evidence that immunity system play any part in resistance to BSE.

1.5.2 Active immunity

There is no acquired immunity to BSE agent.

1.5.3 Vaccination

It is not applicable to this disease.

1.6 Epidemiology

BSE epidemiology is mainly determined by a long incubation period. Exposed animals can be infected by the agent in an unknown period (during the first year of life, according to estimations) before showing first clinical signs.

1.6.1 Incubation period

Main incidence is in animals 4 to 5 years of age, considering that infection took place during the first year of life.

OIE, in its BSE Code establishes that "BSE has a long incubation period, measurable in years"

1.6.2 Agent persistence

- **Environment**

For the Scrapie agent, a period of persistence in the environment of up to 30 months has been described. Although the BSE agent persistence was supposed to be similar, this was not proved yet.

In some cases total inactivation may not be achieved, even with treatments with dry heat at 160ºC during 24 hours (see 3.2.4)

- **Live animals**

In animals infected with BSE agent, infective material accumulates mainly in the CNS and the lympho-reticular tissues. Since there is no immune response to eliminate the agent, and due to the long incubation period, live animals in their incubation period, showing no clinical signs, have been the main source of BSE introduction to other countries.

- **Products and sub products of animal origin**

Prion survives the decomposition of the carcass and the procedures for the manufacture of sub products.

The thermal process required implies temperatures from 134 to 138ºC at 3 bar, during 20 minutes.

1.6.3 Transmission

Live animals

There is no evidence of the horizontal or vertical transmission among cattle. However, cases of direct transmission between cows and their calves have been described, but not in a number that could perpetuate the epizootics in Great Britain.

Cases of BSE in antelopes in British zoos, caused by contaminated feed, have been reported. The possibility of transmission between females of these animals and their offspring is not to be discarded.

Similar cases occurred in domestic cats. The recognition of the disease in these species (1989) coincided with BSE appearance in cattle.

Genetic material

There is no evidence on the transmission of BSE through semen. Recent studies have proved the absence of infectivity in embryos, if their processing is carried out according to International Embryo Transference Society (IETS) rules.

Products of animal origin

The primary origin of BSE is still discussed, however epidemiological research suggest it was a consequence of the incorporation to feedstuffs of meat-and-bone meal (MBM) with high concentrations of scrapie agent. Most of the cases were the result of exposure to the agent during the first year of life. The increase in the incidence of infections was due to the increase in the concentration of the agent in MBM, through the rendering of infected cattle. According to certain hypothesis, the infectivity of the agent may have been increased in cattle after several passages through the species.

The ban on the feeding of MBM to ruminants (in 1988) and to all farm species (in 1996) in Great Britain has lead to a progressive decline in BSE cases (see table 1).

Suspicion on milk substitutes as a transmission factor has been reported, since -even though it is forbidden to incorporate ruminants proteins to milk substitutes- these do contain tallow that may have protein residue

Biological products

Spongiform Encephalopathies agents may be transmitted by inoculation of biological products derived from therapeutic products (iatrogenic transmission) such as:

- biological products derived from CNS extracts, in the same way CJD was transmitted among human beings due to the use of extracts of human hypophysis. It is unlikely that such products could be imported and used.
- a therapeutic agent to the production of bacterial vaccines to which an infected agent (brain cultures) was incorporated during manufacturing process.

Although from a theoretical point of view this represents a risk, no published epidemiological evidence suggests that this was a means for the introduction of BSE in any case.

Fomites

Transmission by means of fomites is not of great concern. However, measures must be taken to avoid the eventuality of the transmission by means of instruments used in veterinary surgery.

Vectors

There is no evidence on the transmission of BSE through vectors, insects or arthropods.

1.6.4 Factors leading to transmission

The main factor causing the transmission of BSE is the feeding with MBM. The use of MBM in ruminants feed is forbidden in Uruguay since 1996.

1.7 Introduction form and introduction risk

The main risk for the introduction of BSE to Uruguay is the importation of live cattle; therefore any BSE occurrence in the country should be an isolated fact. After the disease was first recognised in 1986, Uruguay imported only two bovines from countries were -at that moment or after- indigenous cases of BSE occurred.

The possibility of iatrogenic transmission or transmission through feedstuffs is considered to be adequately controlled.

2. Eradication and control principles

Eradication and control principles are:

- The slaughter of all clinically affected animals
- The conduction of a rigorous risk assessment process, including the monitoring of all risk animals

The first step would be to associate the disease with an imported animal, iatrogenic transmission or illegal feedstuffs. Together with the outbreak control plan, an enhancement of the national surveillance plan will be needed. This surveillance plan shall be designed to take into account the possibility that the infection affects other premises.

The impossibility to achieve the total inactivation of the agent has certain consequences. The risk of horizontal transmission through carcasses is low, except when the agent is incorporated through feeding with MBM. Potentially contaminated areas (necropsies room and laboratory) must be cleaned and disinfected.

2.1 Risk assessment

Risk assessment process will lead to:

- determine the source of the outbreak
- identify risk animals corresponding to the case(s) identified
- classify infection risk for other animal groups

The following definitions are established considering that imported animals, contaminated feedstuffs or iatrogenic transmission are involved in the outbreak.

- **Affected animals:** those showing clinical signs of BSE
- **Animals with similar risk:** any imported animal coming from the same premises affected animals came, as well as brothers and sisters of the affected animals on their mother side.
- **Exposed animals:** affected animals progeny, raised in close contact (calves in contact with placentas of animals that afterwards showed signs of BSE).
- **Low risk animals:** mothers of the affected animals AI and TE products from affected animals and animals of the same premises that were not in direct or indirect contact with affected animals.

Risk assessment process will be dynamic and adjusted in accordance to the results of the monitoring of the animals with similar risk, exposed animals and low risk ones. Each group of animals shall be identified separately.
Based on risk assessment, the eradication strategy shall include

- the establishment of adequate security measures in identified premises (see 2.2.1)
- the monitoring of all deaths of suspected animals (see 2.2.3)
- the selective slaughter of animals (see 2.2.5)

2.2 Methods to prevent the spread of the disease and pathogen elimination methods

2.2.1 Quarantine and movements control

Infected premises containing animals with similar risk, exposed animals or low risk animals shall be put in quarantine.

Zoning

It is not considered to be appropriate in case of BSE.
It may be expected that if the disease were detected it would be limited to a single premise or to a few number of outbreaks, easy to isolate.

2.2.2 Monitoring

The monitoring aims to determine the source of the infection and if there are other potentially infected herds. Priorities in monitoring must be in accordance with previously stated risk categories.
Should the source of the infection happen to be a therapeutic agent or an infected feedstuff, the problem will be more difficult. The long incubation period will not allow the confirmation of the contamination of such therapeutic agent or infected feedstuff.

2.2.3 Surveillance

Suspected animals must be carefully examined at fixed intervals to detect the presence of any suspicious clinical sign. The CNS of any animal developing BSE compatible clinical signs and not showing any response to treatments must be examined in laboratory.
BSE is a compulsory notifiable disease. BSE surveillance plan its available at the General Department of Livestock Services.

2.2.4 Treatment of infected animals

It is not possible.

2.2.5 Destruction of the animals

Affected animals shall be slaughtered, material collected for laboratory examination (Surveillance manual) and the bodies incinerated. Should incineration not be possible, the animals shall be buried in a land not used for farming.
Exposed animals shall be slaughtered, material collected for laboratory examination and the bodies incinerated or buried.
Low risk animals may be slaughtered and used for human consumption after histopathological examination of brains has been carried out with negative results.

2.2.6 Treatment of products

Due to the difficulties in achieving the total inactivation of the BSE agent, it is not practical to treat products to decontaminate them.
High risk products must be eliminated by incineration.

2.2.7 Elimination

OIE Animal Health Code states that affected animals must be completely destroyed. When it is possible, the bodies must be incinerated. Since this may be difficult for operational reasons, burial may be carried out provided that the place is not used for farming for several years. It has been proved that sheep

brains with scrapie were still infectious after being buried for more that three years.

If the carcasses do not contain specific risk materials, infectivity is eliminated by treating the material at 133ºC, during 20 minutes under a pressure of 3 atm., provided that the pieces of organic matter do not exceed 50mm in length.

Until now it is impossible to apply this technology in MBM manufacturing plants in Uruguay.

2.2.8 Decontamination

Decontamination procedures must be applied to any material in close contact with infected carcasses.

The following procedures could be applied:

a) steam sterilization at 134-138ºC, during more than 20 minutes. For materials that have a value that justifies it, (and whenever possible).
b) steam sterilization at 121ºC with sodium hydroxide 1M (40gr/lt).
c) immersion in sodium hypochlorite at 1.4% during 30 minutes for surfaces.
d) immersion in sodium hydroxide 1M during more than 1 hour.
e) in a recent publication a sterilization by means of ozone is mentioned (it has not been confirmed)
f) tissu fixation by means of formalin stabilises scrapie agent and therefore prevents described steam sterilization. A solution of formic acid is used as inactivation agent in histopathological studies.
g) if a case should occur, the corresponding health authority will establish decontamination measures to be applied.

2.2.9 Vaccination

It is not applicable.

2.2.10 Grazing management

There is no evidence on the excretion of the BSE agent. Unlike in scrapie grazing management would be of no use.

2.2.11 Predators control

Measures shall be taken to prevent the carnivores and omnivores, as well as cattle and sheep with osteophagic habits (in areas with lack of calcium and phosphors), from getting to the carcasses of cattle and sheep

2.2.12 Vectors control

It is not applicable.

2.2.13 Information to the public

Dissemination in the media must be carefully considered. It is necessary to inform the public, and specially the one related to livestock industry, on the characteristics of any outbreak and its commercial consequences.

Discussions with public health authorities should be carried on to avoid a collective hysteria and specially to provide information on real health risks for public health.

Another aspect to be considered is the information to international markets, due to the implications it would have on trade, specially on the cattle meat sector.

2.3 Security precautions

As it has been stated BSE agent has been transmitted to human beings giving origin to v-CJD. Personnel handling potentially infected materials shall take measures to avoid exposure to the agent.

When handling materials that may contain high agent concentration they shall wear gloves and eye protection.

Environment contamination must be minimized during necropsies procedures.

Measures must be taken so that meat and meat products of affected animals or animals with similar risk do not enter the human or animal food chain

2.4 Feasibility of the control in Uruguay

If the occurrence of a case were due to imported animals, it is estimated that the control and eradication would be feasible and fast.

If it would derive from medicaments or feedstuffs, a specific policy would have to be defined, and a prolonged surveillance plan would have to be carried out to achieve control and eradication.

3. Policies and their basis

3.1 General policy on BSE

BSE is an OIE List B disease, which has had significant effects on international trade of cattle and its products.

A policy to eradicate the disease as soon as possible will be achieved by employing a combination of strategies including:

- an adequate management and control of risk animals in order to maximise the efficiency of the eradication plan.
- the slaughter of clinical affected animals, exposed animals and animals with similar risk (see 2.1)
- total or partial depopulation. It shall be carried out if there were doubts on the status of the animals of the herd
- immobilization of all cattle from infected or suspected premises.
- monitoring and surveillance to determine the exacts limits of the outbreak and to gather additional evidence to re-establish the BSE free country status.
- a risk assessment to identify the cattle that could have been infected or could be related with confirmed cases.
- an awareness campaign to obtain maximum cooperation from the industry and the society

Should BSE occur in Uruguay, it is impossible that the disease spreads outside the premises initially affected. It is not necessary to establish control or restricted areas.

A BSE case would probably have effects on cattle and products exports, at least in the short term, and could arise anxiety in the domestic meat and milk market.

Should a BSE outbreak occur in Uruguay, the General Department of Livestock Services will be responsible for the carrying out of control and eradication measures according to the rules of this manual.

3.2 Control and eradication strategy

The strategy will be to immediately destroy and to eliminate infected animals, to isolate affected premises and to carry out the monitoring and the risk assessment in order to gather information to take a series of eradication measures. The strategy is independent from the origin of the outbreak.

BSE is considered a non-contagious disease. Therefore, vertical or horizontal transmission is improbable, although some mechanisms of transmission of the agent are not clear enough yet.

As infected and related risk animals are being destroyed and affected premises isolated, the global situation shall be determined by means of laboratory studies, monitoring and risk assessment. Premises identified as suspect in the monitoring will have to be isolated and the movements of animals and products in them controlled.

Since the presence of the disease will have consequences on domestic and international trade, a close relationship shall have to be established with the

industry, the media, the Public Health Ministry and the public in general, as an integral part of the eradication campaign.

3.2.1 Sanitary slaughter

Sanitary slaughter shall be adopted only in certain groups of animals to avoid expensive and long surveillance processes or due to internal or foreign pressures.

Should the disease occur in a few herds, the sanitary slaughter of affected animals shall be carried out. Risk assessment will define actions and strategies to be put into practice. This may comprise sanitary slaughter and laboratory study of animal groups with high risk (animals with similar risks and exposed animals, see 2.1).

The future actions to be taken shall be determined by the results of the study of these groups of animals.

In the case of a BSE outbreak not related with imported animals, its source will have to be determined with a number of animals high enough to establish the prevalence and distribution of the infection.

3.2.2 Isolation and movements control

Isolation will be imposed on infected and suspected premises and a control of movements and products shall be carried out until the situation is clearly established.

Future decisions will be based in the results of the epidemiological research. It is not expected that restrictions for the majority of animals and products will be necessary.

The establishment of restricted or control areas for BSE is not deemed necessary.

3.2.3 Treatment of the affected animals

There is no available treatment for BSE and affected animals shall be destroyed as it has previously been stated

3.2.4 Treatment of products and sub products of animal origin.

There is no effective treatment for products derived from affected animals.

Should an outbreak of BSE occur, the following measures must be taken immediately: a) the prohibition on the trade of specific risk materials b) the prohibition on the rendering of ruminants

It is not necessary to establish any restriction over crops and grains.

3.2.5 Vaccination

It is not applicable.

3.2.6 Monitoring and surveillance

The monitoring will be capital in determining the source for the introduction of the disease.

The research on suspected premises shall be based on previous contacts with affected animals from suspected premises. Future actions will depend on risk classification of concerned animals.

Retrospective monitoring will attempt to find the possible sources, that is to say: introduction of animals from affected countries, use of biological products or other iatrogenic source or illegal feed.

If the introduction were due to a single administration of a biological therapeutic agent, it is very probable that there would be affected animals in a similar state of neurological degenerative lesions in several localizations. We must take into account however, that the incubation period is very variable.

The information on infection rate will help in the risk assessment for the herd of reference and for other herds exposed to the same product.

The failure to identify the source will not allow for the definition of the herd of reference and the research and surveillance will have to be broadened before defining the control and eradication strategy.

3.2.7 Media and public relations

Media and public relations should be taken specially into account. A case of BSE in the country is very likely to be widely disseminated by the media as a potential risk for human health, leading to unnecessary concern and a significant reduction in cattle meat consumption.
This must be prevented by means of precise information coming from a single official source and a clear and close coordination between the different organisations involved.

3.3 Social and economic consequences

The main consequence of BSE occurrence in Uruguay would be the costs associated with international restrictions in cattle and cattle products trade: if drastic measures regarding isolation and slaughter were not taken, economic consequences would be very serious.
Domestic market would be affected due to the concern regarding food safety in meat and milk. There are uncountable examples of how the reduction of consumption and prices affects the whole meat industry, although other industries, such as white meat production, would benefit from this panic.
An isolated case of the disease, if the reaction is immediate an clear, would have a minimal impact. An example of this is the Canadian case in 1993.

3.4 Criteria to prove the BSE free status

To date, Uruguay has been declared by the European Commission in risk level 1. It was declared BSE free by Canada and USA, and it is following the procedures to be declared BSE free country by the OIE, as approved by the last General Assembly (on May 2002). Also, a program for the training and control of veterinarians and producers is being carried out.
Should a case appear, quick actions will be required to destroy affected animals and possibly high risk animals also.
If the number of animals were not too high, the slaughter and diagnostic research will be preferable than a long and expensive isolation and surveillance plan.

3.5 Indemnification

As provided in article 14 of Law 16082 of 18 October, 1989 (Permanent Indemnification Fund).

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