Risk for Human and Animal Health related to the revision of the BSE Monitoring regime in some Member States[1]

Scientific Opinion of the Panel on Biological Hazards

(Question No EFSA-Q-2008-007)

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PANEL MEMBERS

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SUMMARY

Following a request from the European Commission (EC), the Panel on Biological Hazards (BIOHAZ) was asked to deliver a scientific opinion on the Risk for Human and Animal Health related to the revision of the BSE Monitoring regime in some Member States.

The BIOHAZ Panel was invited to provide an assessment on the existence of a significant additional risk, if any, to human and animal health, compared with the situation at the time following the implementation of a revised BSE monitoring regime in the old 15 European Member States (EU15)[2]. The Panel was asked to consider age options between 30 and 60 months (with 6 months intervals) for BSE testing of healthy slaughtered cattle and between 24 months to 60 months (with 6 months intervals) for testing of at risk cattle in EU15 and compare the different scenarios.

It was then clarified with the EC that the mandate was focused on the assessment of possible differences between the BSE surveillance system at the time and the proposed review in terms of efficiency to monitor the epidemiological situation in the cattle population. Moreover, the term "significant" inserted in the terms of reference of the mandate was not to be considered in its statistical meaning.

Due to insufficient data quality it was not feasible to perform a complete assessment based on 6 month age intervals as asked by the EC. For certain age categories the assessment was limited to 12 month age periods.

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[2] Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, The Netherlands, Portugal, Spain, Sweden, United Kingdom.

The BIOHAZ Panel considered the regulatory framework at the time and analysed the data related on BSE surveillance in EU15 during the period 2001 - 2007. A statistical model of the future trend of the BSE epidemic was developed to address directly the terms of reference. It was noticed that for further extrapolation of the result of the model into the future, specific assumptions on the efficacy of the control measures since 2008 are required.

The BIOHAZ Panel highlighted that the purpose of the TSE surveillance in cattle in the EU is mainly to monitor the BSE epidemic and that BSE Passive Surveillance has been demonstrated to be a very insensitive detection system. Prevention of human exposure to the BSE agent and of animal exposure and propagation to TSE agents mainly relies respectively on the Specified Risk Material (SRM) removal and on the Feed Ban.

The Panel noted that in both the joint EU15 and in each of the individual EU15 countries in which sufficient data are available, the BSE epidemic has been constantly and significantly declining and is converging to the sensitivity limit of the current surveillance system.

The Panel further concluded that in case the age of BSE testing increases to 36, 48 or 60 months of age for healthy slaughtered animals less than one case for the first two age limits and less than two cases for the third age limit can be expected to be missed annually in EU15. Moreover, in case the age of BSE testing increases to 30, 36, 48 or 60 months of age for at risk animals less than one case for the first three age limits and less than three cases for the fourth age limit can be expected to be missed annually in EU15. Although the likelihood of detecting new cases in specific age groups is very low, there remains a small probability of detecting one or more cases in some of these groups.

Further considerations related to atypical BSE and to the ability of a TSE monitoring system in cattle to detect a re-emergence or an emergence respectively of BSE or a new hypothetical TSE were included in the Opinion.

The Panel noticed that an age limit of 24 month in at risk animals would result in: (i) an increased sensitivity of surveillance in case of BSE re-emergence, (ii) an optimised system for early and efficient detection of emerging new TSEs in cattle. Moreover it was highlighted that targeting at risk population and certain age groups would enable early changes in the trend of BSE epidemic to be detected.

The Panel recommended periodically revising the opinion based on the accumulation of new information on the 2002, 2003 and subsequent cattle birth cohorts. Furthermore, it was recommended that in any future TSE monitoring system in cattle the ability to follow the trend of the epidemic, to monitor for atypical BSE and to identify in an early and sensitive way a potential re-emergence of classical BSE or the emergence of a new TSE in cattle population should be considered. Moreover, it was noticed that an estimation of the number of undetected BSE infected bovines entering into the food chain would assist in quantifying the residual BSE exposure risk.

Key words: BSE, Revision monitoring regime, human health, animal health

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BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

The TSE Roadmap adopted by the Commission in July 2005 and endorsed by both the European Parliament and the Council states that amendments of certain TSE measures could now be envisaged without endangering the health of the consumer and the policy of eradicating BSE, provided that the positive trend observed in epidemiological situation continues and scientific conditions are in place. Among those possible amendments, a revision of BSE monitoring programmes for bovine animals is one of the topics of the Roadmap in a short and medium term period (2005-2009). Extensive epidemiological data on BSE has been collected via the EU BSE surveillance over the last 7 years and has demonstrated that the control measures in place have been efficient and that the prevalence of the disease is clearly declining or remained consistently at a low level. Since 2001 more than 52 million tests have been carried out in the European Community.

According to the TSE Regulation (Regulation (EC) N° 999/2001), a Member State which can demonstrate the improvement of its epidemiological situation may apply for a revision of its national BSE monitoring programme for both at risk (e.g. emergency slaughtered cattle, cattle with observations at ante mortem inspection and fallen stock) and healthy slaughtered cattle. The applying Member State shall demonstrate that there is a clearly declining or consistently low BSE prevalence on its territory, that it has implemented and enforced for at least 6 years a full BSE testing scheme and the Community legislation on total feed ban for farmed animals. The stringent eligibility criteria will limit a possible revision of their BSE monitoring programmes to the old 15 Member States[3].

TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

Based on the current favourable epidemiological BSE situation in eligible Member States and taking into account that the stringent preventive measures against BSE (SRM removal and total feed ban) will continue to apply in the future, the European Food Safety Authority is invited to provide an assessment on the existence of a significant additional risk, if any, to human and animal health, compared with the current situation following the implementation of the revised BSE monitoring regime in eligible Member States. The EFSA is invited to consider age options between 30 and 60 months (with 6 months intervals) for BSE testing of healthy slaughtered cattle and between 24 months to 60 months (with 6 months intervals) for testing of at risk cattle in eligible Member States and compare the different scenarios.

Clarifications on the Terms of Reference

After receiving the mandate it was clarified with the European Commission (EC) that the Terms of Reference were focused on the assessment of potential differences between the current BSE surveillance system and the proposed review in terms of efficiency to monitor the epidemiological situation in the cattle population. Moreover, the term "significant" inserted in the Terms of Reference of the mandate was not to be considered in its statistical meaning.

Due to insufficient data quality it was not feasible to perform a complete assessment based on 6 month age intervals as asked by the EC. For certain age categories the assessment was limited to 12 month age periods.

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[3] Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, The Netherlands, Portugal, Spain, Sweden, United Kingdom.

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ASSESSMENT

1. Introduction: regulatory background

After the start of the epidemic in the UK in 1986, BSE became a notifiable disease in EU in 1990 (EEC, 1990).

A number of BSE preventive measures to protect human and animal health were taken at EU level to prevent recycling and amplification of the BSE agent, as well as to minimize the human exposure risk.

The most important are:

- 27 July 1994: Mammalian proteins to ruminants ban in the whole EU (94/381/EC) (EC, 1994)
- 1 April 1997: Meat and Bone Meal production at 133°C/3bar/20min/100% relative humidity (96/449/EC) (EC, 1996)
- 1 October 2000: EU Specified Risk Material ban (97/534/EC, reinforced by 2000/418/EC) (EC, 1997; EC, 2000a)
- 1 January 2001: Compulsory rapid BSE tests on bovines above 30 months (2000/764/EC) (EC, 2000c), Total MBM ban including fishmeal (2000/766/EC) (EC, 2000d)
- 1 April 2001: Vertebral column above 12 months is defined as Specified Risk Material (2001/233/EC) (EC, 2001a)
- 1 July 2001: Regulation (EC) No 999/2001 of the European Parliament and of the Council lays down rules for the prevention, control and eradication of certain transmissible spongiform encephalopathies (EC, 2001b). This Regulation, defined as the TSE Regulation, brought all existing BSE measures as adopted over the years through more than sixty Commission Decisions into a single, comprehensive framework, consolidating and updating them in view of scientific advice and international standards. In addition it introduced a number of new instruments to manage the risk of BSE and other similar diseases such as scrapie in all animal species and relevant products.

Most of the measures taken from 2000 were based on the Scientific Steering Committee (SSC) 1998 Opinion on "Defining the BSE risk for specified geographical areas" (SSC, 1998) and its subsequent amendments, that gave rise to the Geographical BSE Risk (GBR) methodology. The GBR methodology is based on the assumption that BSE arose in the United Kingdom (UK) from a still unknown initial source and was propagated through the recycling of contaminated bovine tissues into animal feed. Later, the export of infected animals and infected feed provided the means for the spread of the BSE-agent to other countries where it was again recycled and propagated via the feed chain. A simplified model of the assumed BSE/cattle system is described in Figure 1.

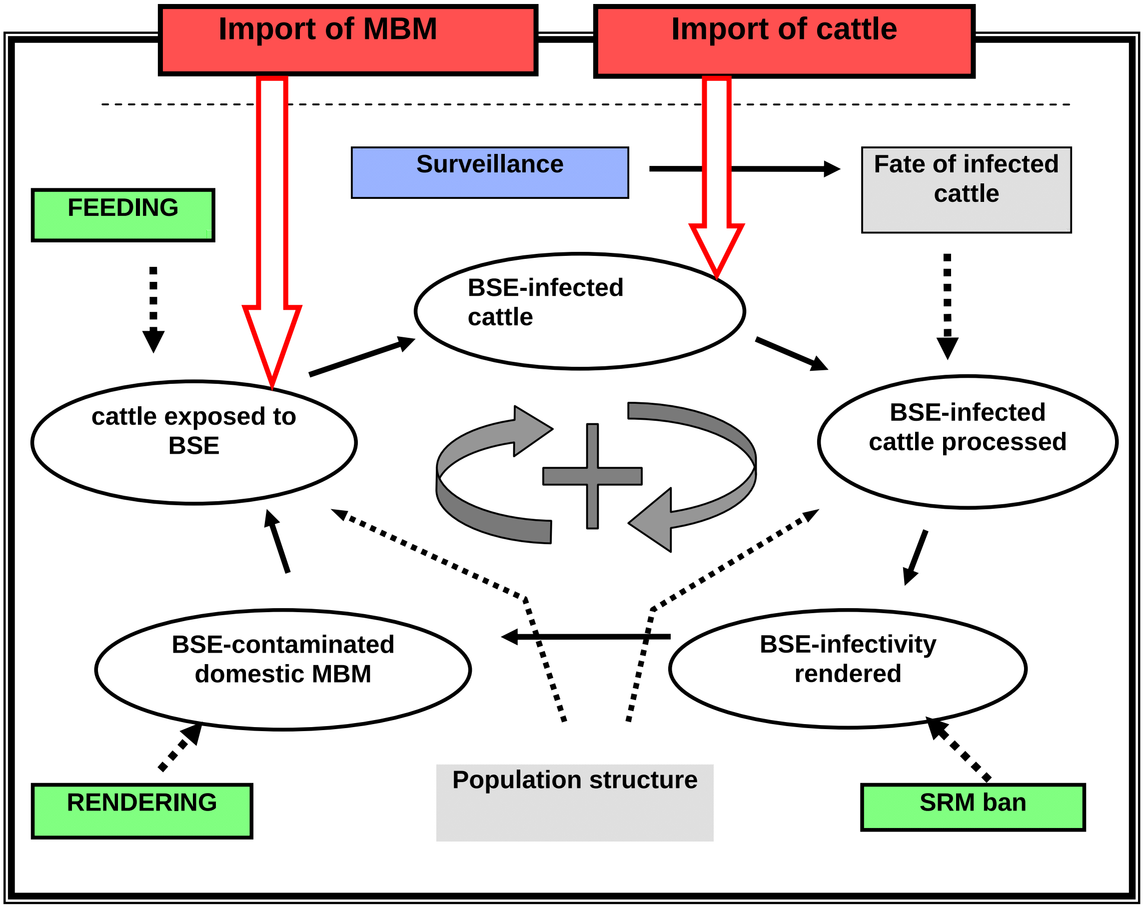

Figure 1. **The model of the BSE/cattle system.** From the EFSA 2007 Opinion on the "Revision of the Geographical BSE risk assessment (GBR) methodology" (EFSA, 2007)

Currently, Regulation (EC) No 999/2001 as amended, the TSE Regulation, (EC, 2001b), is the key piece of legislation to protect human and animal health from the risk of BSE and other TSEs.

1.1. Current BSE monitoring system in the EU

According to Art. 6 and Annex III, Chapter A, Section I., point 2. of Regulation (EC) No 999/2001 as amended, all healthy bovine animals slaughtered over 30 months of age and all bovine animals at risk (emergency slaughtered, fallen stock and presenting clinical signs at *ante mortem* inspection) over 24 months of age shall be tested for BSE utilising one of the approved rapid tests listed under Annex X to the TSE Regulation as amended (Tab. 1). It should be noted that stricter schemes can be applied in the EU Member States (MS).

Table 1. **Age at testing, in months, per target group.**

Target Group	Age at testing (months)
Healthy slaughtered	30
At risk animals	
Emergency slaughtered	24
Fallen stock	24
Presenting clinical signs at ante mortem inspection	24

This system is also known as BSE "Active Surveillance".

Besides this BSE monitoring system, according to Art. 11 and Art. 12, point 2. of the TSE Regulation as amended, any animal clinically suspected of being infected by a TSE shall be notified and examined in accordance with the testing methods laid down in Art. 20 of this same Regulation.

This system is also known as BSE "Passive Surveillance".

In this document the whole of BSE Active and Passive Surveillance is called "BSE Surveillance"

1.2. Current policy on Specified Risk Material removal in the European Union (EU)

Specified Risk Material (SRM) are tissues that are most likely to carry the infective BSE agent and that therefore shall be removed from the carcasses and disposed of.

According to Art. 8 and Annex V of Regulation (EC) No 999/2001 (EC, 2001b) as amended, the following bovine tissues shall be designated as SRM if they come from animals whose origin is in a Member State or third country or of one of their region with a controlled or undetermined BSE risk:

- "*the skull excluding the mandible and including the brain and eyes, and the spinal cord of animals aged over 12 months;*
- *the vertebral column excluding the vertebrae of the tail, the spinous and transverse processes of the cervical, thoracic and lumbar vertebrae and the median sacral crest and wings of the sacrum, but including the dorsal root ganglia of animals aged over 30 months; and*
- *the tonsils, the intestines from the duodenum to the rectum and the mesentery of animals of all ages.*"

Moreover, the TSE Regulation as amended in Annex V, point 2 states:

"*By way of derogation, the above listed tissues, whose origin is in Member States with a negligible BSE risk shall continue to be considered as specified risk material.*"

1.3. Current Feed ban in EU

Regarding the feeding provisions an EU wide ban on the feeding of mammalian proteins to ruminants was in place since July 1994 (EC, 1994). This ban was extended to a suspension on the use of all proteins derived from animals in feeds for any animal farmed for the production of food since 1 January 2001 (EC, 2000d), with some exceptions (i.e. fish meal for non-ruminants; tuber and root crops and feeding stuffs containing such products following the detection of bone spicules after a favourable risk assessment) (EC, 2005).

Currently, in the EU the use of proteins derived from animals in animal nutrition is regulated by two pieces of legislation, namely the Regulation (EC) No 999/2001 (TSE Regulation) (EC, 2001b) and the Regulation (EC) No 1774/2002 (Animal By-Products Regulation) (EC, 2002).

Regulation (EC) No 1774/2002 of the European Parliament and the Council lays down health rules concerning animal by-products not intended for human consumption. The key point concerning animal nutrition is represented by the exclusion of certain animal-derived materials from the feed chain. Under this Regulation, only materials derived from animals declared fit for human consumption following veterinary inspection may be used for the production of feeds, under some conditions and restrictions. The Regulation also bans intraspecies recycling. This Regulation shall not affect veterinary legislation having as its objective the eradication and control of certain diseases.

The use of proteins derived from animals in animal nutrition as foreseen by Regulation (EC) No 1774/2002 is overruled by the more stricter rules laid down in Art.7 of Regulation (EC) No 999/2001, introducing an EU wide ban on the use of proteins derived from animals as feed ingredient for all farmed animals.

The percentage of infringements to the feed ban in the old 15 Member States (EU15) during the period 2001 - 2005 is reported in Table 2.

Table 2. **Percentage of infringements to the feed ban in EU15** (source European Commission)*

Year	Ruminant feed		Non-ruminant feed		Raw material	
	N° Samples	% infr.	N° Samples	% infr.	N° Samples	% infr.
2001	24102	2.89 %	14751	4.03 %	2315	1.73 %
2002	26288	0.12 %	17521	0.55 %	8092	0.63 %
2003	20305	0.18 %	17661	0.41 %	11019	0.54 %
2004	20332	0.16 %	16141	0.69 %	12482	0.47 %
2005	11591	0.16 %	7844	0.56 %	4933	0.81 %

*__Explanatory note to the results as provided by the European Commission:__

- A significant number of the infringements were duplicates (from additional samples collected after 1 positive analysis) or rather infringements on labelling (fishmeal detected in non-ruminant feed which is not prohibited but was not marked on the label). The real percentage of infringements may therefore be lower. Member States were also requested to target the controls which may have increased the percentage of infringements.
- The results indicate that the number of infringements despite the very strict legal provisions at every stage (transport, storage, feed production, farms) does not become zero but remains at a very low level, in particular after 2001. This can be most likely explained by the adventitious presence of animal constituents in certain raw materials such as sugar beet pulp and fat and the presence of cadavers of rodents and birds in raw materials.
- It should be stressed that under the total feed ban provisions and applying a zero tolerance approach, the presence of animal constituents does not mean that ruminant proteins, potentially transmitting BSE, were present. Furthermore even if derived from ruminants, the removal and destruction of all specified risk materials from cattle, containing the BSE infectivity, and the low BSE prevalence in cattle further reduce the risk.

1.4. Considerations about current regulatory framework with respect to monitoring, SRM removal and feed ban

The main purpose of the TSE surveillance in cattle in the EU is to monitor the BSE epidemic.

The capacity of BSE tests to identify infected animals is limited to the late stage of the incubation period. Based on the first BSE pathogenesis studies realized in cattle after a 100g oral challenge, the likely detection of positive cases with rapid BSE tests was considered to be at about ¾ of the incubation time (EFSA, 2005). Recently, a more realistic level of field exposure (1 g) has been considered. In that situation, detection of cases by active surveillance is predicted by modelling to be only 1-2 months prior to the onset of clinical disease (Arnold *et al.*, 2007).

An estimation of the number of undetected BSE infected bovines entering the food chain was not performed in the framework of this mandate. Such estimation would assist in quantifying the residual BSE exposure risk.

The efficacy of BSE testing to exclude the entry of BSE infected animals into the food chain is limited and prevention of human exposure to BSE agent mainly relies on SRM removal policy. The EU SRM ban implemented on 1 October 2000 (EC, 2000b) was initially based on the Opinion of the Scientific Steering Committee on the Human Exposure Risk (HER) via food with respect to BSE (SSC, 1999) and actualised following evolution of scientific knowledge in the area.

The most effective measure for reducing BSE (and other TSE) agents propagation risk in domestic animal in the EU is the total EU wide ban on the use of animal protein in farmed animal feeds (with some exceptions like the use of fishmeal in non-ruminants).

Considering the current knowledge in the TSE field and the technical limitations (lack of efficient decontamination measures for animal proteins and limits for assessing traceability of products), the feed-ban is still considered as the key protection measure against emergence or re-emergence of TSE epidemics in farm animals.

In this context it is important to assess the sensitivity of the TSE monitoring system allowing an early identification of emergence or re-emergence of TSE agents in farm animals. The identification by the active surveillance system of previously undetected atypical BSE (L and H type) illustrates the usefulness and power of BSE monitoring in cattle population.

Consequently, the aspects which are relevant for a reviewed TSE monitoring system in cattle are:

- ability to follow the current trend of the epidemic;
- ability to monitor for atypical BSE, particularly with respect to the sensitivity and specificity of tests and the efficacy and efficiency of the collection, analysis and interpretation of this data from the field;
- early and sensitive identification of potential re-emergence of classical BSE or the emergence of a new TSE in cattle population.

2. Analysis of the Active BSE monitoring programme per category and age during the period 2001 - 2007.

The data on BSE surveillance used in this analysis were received from the European Commission on 29th April 2008.

Extensive epidemiological data on BSE has been collected via the BSE Active Surveillance over the last 7 years and has demonstrated that the control measures in place against BSE have been efficient and that the prevalence of the disease is clearly declining or remained consistently at a low level: the BSE prevalence (ratio per 10,000 animals tested) in EU15 detected by the BSE Active Surveillance was 1.22 in 2001, 1.38 in 2002, 1.05 in 2003, 0.66 in 2004, 0.49 in 2005, 0.31 in 2006 and 0.17 in 2007.

Since 2001 till the end of 2007 more than 65 million of tests have been carried out in the framework of BSE Active Surveillance in the EU15. Of these 5,022 animals were positive. These included 1,177 out of 56,723,311 healthy slaughtered cattle (21 per million), and 3,845 out of 8,519,376 at risk cattle (451 per million), while testing schemes differed between Member States. For example: Germany tested younger healthy stock than most Member States, and the UK older healthy stock during its Over Thirty Months Scheme. In the framework of BSE Passive Surveillance in EU15 during the period 2001 - 2007 19,331 bovine animals were tested and 2,404 were positive.

In 2007, no BSE cases were found in EU15 in the framework of BSE Surveillance in Belgium, Denmark, Finland, Greece, Luxemburg and Sweden.

Detailed epidemiological information on BSE monitoring can be found in TSE annual reports released by the Commission: www.ec.europa.eu/food/food/biosafety/bse/annual_reps_en.htm

With respect to the number of BSE cases detected through the BSE Active Surveillance in EU15 since 2001 the data per target group are reported in Tab. 3.

Table 3. **Number of BSE cases detected through the BSE Active Surveillance in EU15 during the period 2001 - 2007 per target group.**

Target Group	N° of detected BSE cases per year							Total
	2001	2002	2003	2004	2005	2006	2007	
Healthy slaughtered	279	286	265	151	94	69	33	1177
At risk animals								
Emergency slaughtered	321	509	329	179	125	31	5	1499
Fallen stock	396	605	425	305	206	162	101	2200
Presenting clinical signs at ante mortem inspection	36	27	29	24	18	10	2	146
Total	1032	1427	1048	659	443	272	141	5022

The total number of BSE cases detected through the BSE Surveillance (both Active and Passive) and the culling of animals in the framework of BSE eradication measures in EU15 during the period 2001 - 2007 per birth cohort and year of detection is reported in Tab. 4.

Table 4. **Number of BSE cases detected through the BSE Surveillance (Active and Passive) and the culling of animals in the framework of BSE eradication measures in EU15 during the period 2001 - 2007 per birth cohort and year of detection.**

Birth cohort	**N° of detected BSE cases per year**							**Total**
	2001	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**	
1980		1						1
1981	1							1
1982								
1983			1					1
1984	1	3				1		5
1985	1	2	2		1			6
1986	13	10	3	3	1			30
1987	21	30	9	6	6	1		73
1988	20	28	21	6		1		76
1989	25	37	21	17	5	5	1	111
1990	28	54	22	21	9	7	1	142
1991	66	78	47	27	22	8	1	249
1992	120	156	85	55	37	15	9	477
1993	330	245	179	94	56	27	17	948
1994	577	458	218	122	94	48	26	1543
1995	668	616	303	136	67	37	21	1848
1996	246	273	163	80	39	25	10	836
1997	43	91	153	86	35	23	6	437
1998	4	30	73	96	45	30	16	294
1999		6	24	51	60	36	16	193
2000			1	18	48	32	17	116
2001					8	8	1	17
2002					3	1	3	7
Total	2164	2118	1325	818	536	305	145	7411*

* Please note the total number of BSE cases is lower than in Tab. 5 since the year of birth of 21 BSE cases is unknown and they are then not considered under this table.

The number of BSE cases detected through the BSE Surveillance (Active and Passive) and the culling of animals in the framework of BSE eradication measures during the period 2001 - 2007 per Member State, birth cohort and year of detection is provided in Appendix A.

When interpreting the significance of these data the following points should also be considered:

- The likely point in the incubation period at which PrP^{res} is detectable with the rapid BSE tests depends on the infective dose (Arnold *et al.*, 2007). While the range of doses of exposure of field cases of BSE is not known, an oral attack rate study has shown that the mean incubation period arising from doses in the range 0.1-1g fits with that estimated for field cases (Wells *et al.*, 2007). For a 1g dose, it was found that PrP^{res} was detectable at 97% of the incubation period (Arnold *et al.*, 2007). This degree of under-detection has to be taken into account when estimating infection prevalence from surveillance data;

- A constant decline (about 35% per year) in the total number of cases (coming from both BSE Active and Passive Surveillance) has been recorded and is likely due to a reduction in exposure to the BSE agent in EU 15: from 2,164 cases in 2001 to 145 cases in 2007, and the number of cattle infected with BSE is likely to continue to decline.
- Out of this, 24 cases were related to animals born after the start of the total feed ban in 2001.
- The Geographical BSE Risk (SSC, 2002) as well as the stage of the BSE epidemic can vary considerably between Member States.

2.1. Overall situation in the old 15 Member States (EU15)

For the purpose of this assessment 3 main methods to analyse the trend of the BSE infection in the EU15 were considered.

A very simple method (Method 1) is to look at the age of detected cases in each calendar year (Saegerman *et al.*, 2005), where an increasing mean age of detection indicates a declining epidemic. The method has been used to demonstrate the reducing trend of infection in both the UK (Saegerman *et al.*, 2005) and Belgium (Saegerman *et al.*, 2006). Similarly, the method was applied to 10 most affected EU Member States (Ducrot *et al.*, 2008), where the majority of countries could be shown to have a clear increase over time, and the number of cases per capita of adult cattle could be shown to have a reducing trend in all of them. However, this method is not able to provide an assessment of the future trend of the BSE infection.

Age-Period-Cohort models (Method 2) were considered to perform the assessment but, although potentially helpful, were not used due to lack of data and the short time-frame.

An alternative method (Method 3) of exploring the trend of the rate of infection is to look at the number of cases in successive annual birth cohorts. This method is able to provide an assessment of the future trend of the BSE infection.

All these methods require a constant surveillance system over time. If the surveillance system changes, correcting calculations can be applied, but that requires more information. Therefore, for the majority of the EU15 the above methods are only appropriate to be applied to the case data since 2001, when active surveillance commenced.

Calculations based on Method 1 and 3 have been performed in this assessment to analyse the trend of BSE infection in EU15.

2.1.1. Calculations based on Method 1

The number of BSE cases, the BSE incidence per million cattle over 24 months of age and the average age of cases per year of detection in the EU15 MS, considering both Active and Passive Surveillance and the animals culled in the framework of BSE eradication measures, are shown in Tab. 5.

Table 5. **Number of BSE cases, incidence per million cattle over 24 months and average age in years of cases during the period 2001 - 2007 per year of detection in the EU15 MS (the data consider both Active and Passive Surveillance and the culling of animals in the framework of BSE eradication measures).**

Member State		**Year**							**Total**
		2001	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**	
Austria	N° cases	1	0	0	0	2	2	1	6
	Incidence	1.00	0.00	0.00	0.00	2.11	2.14	1.07†	
	Average age	5.0	NA	NA	NA	12.0	9.5	11.0	
Belgium	N° cases	46	38	15	11	3	1	0	114
	Incidence	30.32	26.07	10.55	7.80	2.17	0.72	0.00†	
	Average age	6.0	6.7	7.4	7.5	10.0	12.0	NA	
Denmark	N° cases	6	3	2	1	1	0	0	13
	Incidence	6.67	3.50	2.44	1.30	1.33	0.00	0.00†	
	Average age	5.0	5.3	6.5	14.0	9.0	NA	NA	
Finland	N° cases	1	0	0	0	0	0	0	1
	Incidence	2.42	0.00	0.00	0.00	0.00	0.00	0.00†	
	Average age	6.0	NA	NA	NA	NA	NA	NA	
France	N° cases	277	240	111	51	32	8	7	726
	Incidence	24.93	21.85	10.39	4.87	3.08	0.77	0.68†	
	Average age	6.4	7.2	8.1	8.8	9.4	9.3	10.7	
Germany	N° cases	125	106	54	65	32	16	4	402
	Incidence	19.39	16.97	8.79	10.84	5.46	2.78	0.69†	
	Average age	5.5	6.4	5.9	6.2	6.2	7.0	7.8	
Greece	N° cases	1	0	0	0	0	0	0	1
	Incidence	3.02	0.00	0.00	0.00	0.00	0.00	0.00†	
	Average age	5.0	NA	NA	NA	NA	NA	NA	
Ireland	N° cases	242	334	183	126	77	38	26	1026
	Incidence	79.45	111.06	61.15	41.37	25.08	12.38*	8.47*	
	Average age	6.6	7.8	8.7	9.8	10.1	11.1	11.6	
Italy	N° cases	50	36	31	8	8	7	2	142
	Incidence	15.47	11.92	10.35	2.80	2.74	2.54	0.72†	
	Average age	5.7	6.5	7.8	7.3	8.1	8.3	12.5	
Luxemburg	N° cases	0	1	0	0	1	0	0	2
	Incidence	0.00	10.33	0.00	0.00	10.78	0.00	0.00†	
	Average age	NA	6.0	NA	NA	4.0	NA	NA	
Netherlands	N° cases	20	24	18	6	3	2	2	75
	Incidence	11.19	13.49	10.05	3.47	1.78	1.23	1.23†	
	Average age	6.3	6.2	6.7	8.3	4.7	8.5	7.5	
Portugal	N° cases	110	86	133	92	53	32	11	517
	Incidence	142.17	110.55	170.12	113.23	64.45	39.19	13.47†	
	Average age	6.7	7.3	7.7	8.5	9.7	10.9	11.5	
Spain	N° cases	82	127	167	137	103	71	32	719
	Incidence	23.77	35.79	46.58	38.23	29.68	22.22	10.01†	
	Average age	6.4	6.5	6.8	6.8	6.7	7.6	9.1	
Sweden	N° cases	0	0	0	0	0	1	0	1
	Incidence	0.00	0.00	0.00	0.00	0.00	1.51	0.00†	
	Average age	NA	NA	NA	NA	NA	12.0	NA	
United Kingdom	N° cases	1203	1123	612	330	226	129	64	3687
	Incidence	243.66	228.28	125.11	66.95	45.98	26.45	13.12†	
	Average age	7.6	8.9	9.6	10.7	11.2	11.8	12.0	
EU15	N° cases	2164	2118	1326	827	541	307	149	7432§
	Incidence	54.43	54.20	34.39	21.72	14.36	8.15‡	3.95‡	
	Average age	7.0	8.1	8.6	9.1	9.5	10.2	11.0	

***** To estimate this incidence the 2005 adult cattle population of the country concerned was used.
† To estimate this incidence the 2006 adult cattle population of the country concerned was used.
‡ To estimate this incidence the 2005 adult cattle population of EU15 was used.
§ The number of cases is higher than in Tab. 4 since year of birth of 21 cases is unknown and they are not considered in that table.

The trend of the average age of BSE cases per year of detection in the EU15, considering both Active and Passive Surveillance and the culling of animals in the framework of BSE eradication measures, is shown in Fig. 1.

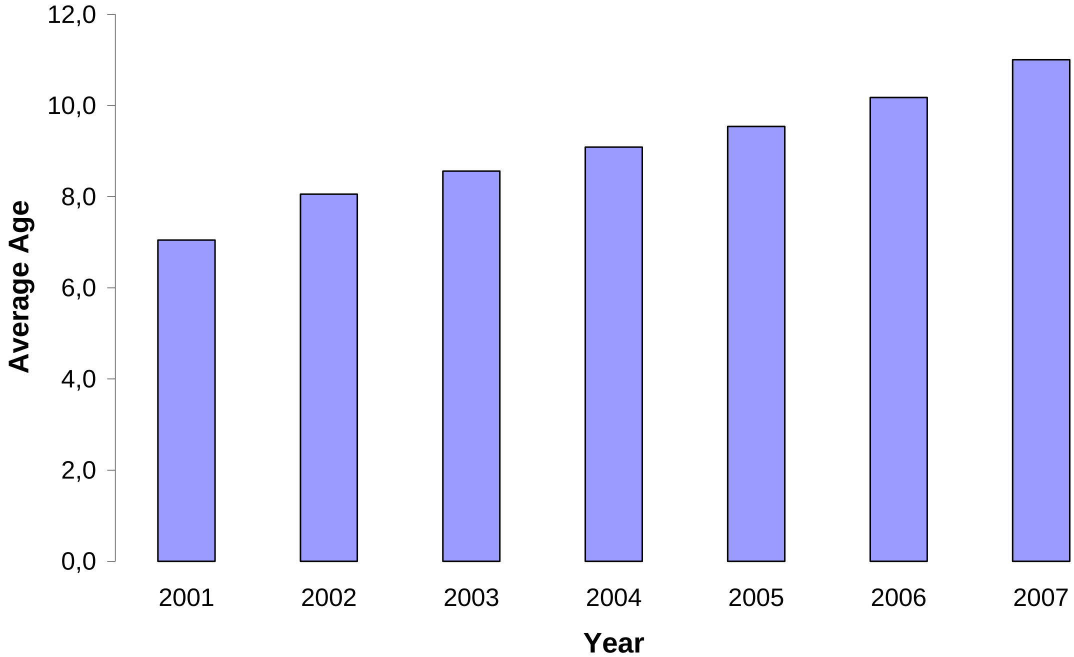

Figure 1. **Average age (in years) of BSE cases per year of detection in the EU15, considering both Active and Passive Surveillance and the culling of animals in the framework of BSE eradication measures.**

2.1.1.1. Conclusion from calculations based on Method 1

From the analysis of the average age per year we can conclude that in each country within the EU15 where a sufficient number[4] of cases have been found since 2001, the average age of the detected BSE cases per test year has increased during the last 7 years and at present it is higher than 7 in each country.

The shape of the age distribution of BSE cases depends on two aspects: the age distribution of the cattle population and the level of BSE transmission in the past (de Koeijer *et al.*, 2002).

Assuming that the age distribution of cattle in the countries has not changed substantially, this indicates that the transmission of BSE has decreased and the control measures have become more effective during the last 10 to 15 years.

Consequently in both the joint EU15 and in each of the individual EU15 countries in which sufficient data are available[5], the BSE epidemic has been constantly and significantly declining and is converging to the sensitivity limit of the current surveillance system.

[4] A minimum number of 50 cases was considered necessary to obtain reliable estimates.
[5] In countries with less than 50 cases statistical methods are not able to reliably estimate the trend but the number of cases remains very low.

2.1.2. Calculations based on Method 3

A spreadsheet with the calculations used when performing this method is provided as an Annex to this Opinion.

The reducing BSE infection pressure leads to an increase in the age of detection of the youngest case. This follows directly from the age at onset distribution and can be seen from the model calculations used for this method. It can also be observed directly from the surveillance data for the EU15, where the youngest age-group to have a positive case in the healthy slaughter stream was: 30-35 months in 2002, 36-47 months in 2003 and 2004, 48-59 months in 2005 and 2006, and 72-83 months in 2007. The likelihood of detecting cases in the younger age groups is decreasing very fast now.

A key determinant of the effectiveness of the 2001 reinforced feed ban across the EU will be the number of cases occurring in the cohorts of 1998 to 2004. Across the EU15, there has been a marked decrease in the number of cases occurring in post-2001 birth cohorts, both overall and in the individual countries (see Tab. 4 and Appendix A).

For the purpose of this calculation two different scenarios were used:

- **Scenario I**: assumes a constant incidence of BSE starting from the 2003 birth cohort (in practice the yearly estimate of the number of BSE cases per age group is the same from 2008 onwards);
- **Scenario II**: can be considered more realistic as it is derived from the observed data and assumes a continue decay rate of the BSE epidemic for cohorts since 2003 based on the cohort incidence decline in previous cohorts calculated by log-linear regression.

Due to the restricted data available for recent cohorts and to the methodologies applied the approach did not take into account the expected additional effect of the enhanced control measures taken in 2001 in the EU (see Appendix B). Moreover they are based on upper 95% confidence limit of the calculated expected number of cases. Consequently they can be considered as worst case scenarios.

For further extrapolation of these calculations into the future, specific assumptions on the efficacy of the control measures since 2008 are required.

The methodology used when performing these calculations is provided in Appendix B.

From the data analysis in Appendix A we find that countries with sufficient BSE cases for analysis (> 50 cases) all display a significant decrease in case numbers over at least the last three test years (2005-2007). More information on the BSE situation follows from observing the number of cases per birth cohort. As described in Appendix B, the number of cases in a birth cohort follows from modelling and not only includes the actual detected cases, but also an estimate of the cases which were expected before the active surveillance period and those which are still to come.

The analysis of the joint EU15 countries as a whole provided by the model, shows that the peak birth cohort was 1993. It may come as a surprise to find that the BSE epidemic within the EU15 was actually fading out since the 1993 birth cohort. This is easily explained when we evaluate a few countries separately by the same method. It follows from the large number of BSE cases in the UK, which represent about 50% of all the cases found since 2001. The peak cohort in the UK was 1987 (Ferguson *et al.*, 1998; Arnold and Wilesmith, 2004), whereas in most of the other countries the peak is found in the birth cohorts between 1995 and 1997. The decline of the epidemic in the UK during the 1990s is stronger than the slow increase in the rest of the EU15, so that overall, the BSE epidemic is declining already since the 1993 birth cohort.

The effect of the extra control measures since 2001 can be seen from a steeper decline in case numbers per birth cohort. This is clearly detectable in the joint EU15 data and even more pronounced in most of the individual countries (except the UK), proving that further reduction of BSE transmission was still feasible at the time.

2.1.2.1. Results from Scenario I

Since this scenario assumes constant incidence in birth cohort since 2003, these estimates will be the same for each year after 2008.

The expected total number of detected BSE cases (based on upper 95% confidence limit for birthcohorts since 2003) by calendar year and age category in this scenario is provided in Tab.6.

Table 6. **Expected total number of BSE cases (based on upper 95% confidence limit for birth cohorts since 2003) by calendar year and age category (in months) in Scenario I.**

Year	**Age category (months)**			**Total**
	30 - 35	**36 - 47**	**48 - 59**	
2008	0.23	0.54	4.17	4.94
2009	0.23	0.54	4.17	4.94
2010	0.23	0.54	4.17	4.94
Total	0.69	1.61	12.52	14.83

The expected number of BSE cases detected in the healthy slaughter stream (based on upper 95% confidence limit for birth cohorts since 2003) by calendar year and age category in this scenario is provided in Tab.7.

Table 7. **Expected number of BSE cases detected in the healthy slaughter stream (based on upper 95% confidence limit for birth cohorts since 2003) by calendar year and age category (in months) in Scenario I.**

Year	**Age category (months)**			**Total**
	30 - 35	**36 - 47**	**48 - 59**	
2008	0.08	0.10	1.44	1.62
2009	0.08	0.10	1.44	1.62
2010	0.08	0.10	1.44	1.62
Total	0.23	0.30	4.33	4.86

The expected number of BSE cases detected in the at risk stream (based on upper 95% confidence limit for birth cohorts since 2003) by calendar year and age category in this scenario is provided in Tab.8.

Table 8. **Expected number of BSE cases detected in the at risk stream (based on upper 95% confidence limit for birth cohorts since 2003) by calendar year and age category (in months) in Scenario I.**

Year	**Age category (months)**				
	24 - 29	**30 - 35**	**36 - 47**	**48 - 59**	**Total**
2008	0.00	0.15	0.32	1.98	2.46
2009	0.00	0.15	0.32	1.98	2.46
2010	0.00	0.15	0.32	1.98	2.46
Total	0.00	0.46	0.95	5.95	7.37

2.1.2.2. Results from Scenario II

The expected total number of detected BSE cases (based on upper 95% confidence limit for constant trend of reduction by birth cohorts since 2000) by calendar year and age category in this scenario is provided in Tab.9.

Table 9. **Expected total number of BSE cases (based on upper 95% confidence limit for birth cohorts since 2000) by calendar year and age category (in months) in Scenario II.**

Year	**Age category (months)**			
	30 - 35	**36 - 47**	**48 - 59**	**Total**
2008	0.10	0.31	3.42	3.83
2009	0.07	0.23	2.42	2.72
2010	0.06	0.17	1.75	1.98
Total	0.23	0.71	7.60	8.53

The expected number of BSE cases detected in the healthy slaughter stream (based on upper 95% confidence limit for constant trend of reduction by birth cohorts since 2000) by calendar year and age category in this scenario is provided in Tab.10.

Table 10. **Expected number of BSE cases detected in the healthy slaughter stream (based on upper 95% confidence limit for constant trend of reduction by birth cohorts since 2000) by calendar year and age category (in months) in Scenario II.**

Year	**Age category (months)**			
	30 - 35	**36 - 47**	**48 - 59**	**Total**
2008	0.03	0.06	1.18	1.27
2009	0.02	0.04	0.84	0.90
2010	0.02	0.03	0.61	0.66
Total	0.08	0.13	2.63	2.83

The expected number of BSE cases detected in the at risk stream (based on upper 95% confidence limit for constant trend of reduction by birth cohorts since 2000) by calendar year and age category in this scenario is provided in Tab.11.

Table 11. **Expected number of BSE cases detected in the at risk stream (based on upper 95% confidence limit for constant trend of reduction by birth cohorts since 2000) by calendar year and age category (in months) in Scenario II.**

Year	Age category (months)				Total
	24 - 29	30 - 35	36 - 47	48 - 59	
2008	0.00	0.06	0.18	1.63	1.88
2009	0.00	0.05	0.13	1.15	1.33
2010	0.00	0.04	0.10	0.83	0.97
Total	0.00	0.15	0.42	3.61	4.18

2.1.2.3. Conclusion from calculations based on Method 3

- According to these scenarios, in healthy slaughtered animals aged respectively up to 36, 48 or 60 months, less than one case for the first two age limits, and less than two cases for the third age limit, can be expected to be detected annually in EU15 by the current active surveillance system.
- According to these scenarios, in at risk animals aged respectively up to 30, 36, 48 or 60 months, less than one case for the first three age limits, and less than three cases for the fourth age limit, can be expected to be detected annually in EU15 by the current active surveillance system.
- Although the likelihood of detecting new cases in specific age groups is very low, there remains a small probability of detecting one or more cases in some of these groups.

2.1.3. Overall conclusions on future cases of classical BSE.

- In both the joint EU15 and in each of the individual EU15 countries in which sufficient data are available, the BSE epidemic has been constantly and significantly declining and is converging to the sensitivity limit of the current surveillance system.
- According to these scenarios, in healthy slaughtered animals aged respectively up to 36, 48 or 60 months, less than one case for the first two age limits, and less than two cases for the third age limit, can be expected to be detected annually in EU15 by the current active surveillance system.
- According to these scenarios, in at risk animals aged respectively up to 30, 36, 48 or 60 months, less than one case for the first three age limits, and less than three cases for the fourth age limit, can be expected to be detected annually in EU15 by the current active surveillance system.
- Although the likelihood of detecting new cases in specific age groups is very low, there remains a small probability of detecting one or more cases in some of these groups.

3. Atypical BSE

Systematic testing of cattle for abnormal prion protein has allowed the identification of two further, distinct types of cattle TSE, termed H- and L-(or BASE) type BSE, in a number of European countries (Casalone *et al.*, 2004; Jacobs *et al.*, 2007; Ducrot *et al.*, 2008; Polak *et al.*, 2008). Similar cases were also detected outside Europe (Japan and USA) (Hagiwara *et al.*, 2007; Clawson *et al.*, 2008). The total number of atypical BSE cases described in the world per country and type as of 1 September 2007 is reported in Tab. 12.

Table 12. **Number of atypical BSE cases described in the world per country and type as of 1 September 2007 (Ducrot *et al.*, 2008).**

Country	Total number of atypical BSE cases		Total
	H-type	L-type	
Belgium		1	1
Canada	1		1
Denmark		1	1
France	8	6	14
Germany	1	1	2
Italy		3	3
Japan		1	1
Netherlands	1	2	3
Poland	1	6	7
Sweden	1		1
UK	1		1
USA	2		2
Total	16	21	37

In France a retrospective study of all the TSE-positive cattle identified through the compulsory EU surveillance programme between 2001-2007 was recently published (Biacabe *et al.*, 2008).

This study indicates that all BSE H and L cases detected by rapid tests were observed in animals over 8 years old in either the at risk (9) or healthy slaughtered surveillance target group (4). Moreover, no BSE H and L were observed through BSE Passive Surveillance although, during retrospective interviews, the farmers and veterinarians for 6 of these animals reported clinical signs consistent with TSE in 3 fallen stocks. The reported frequency of H and L type TSE is respectively 1.9 and 1.7 cases per million of over 8 years old tested animals.

No comprehensive study of the prevalence of atypical BSE cases has been done in other EU Member States or in non EU countries and so caution needs to be applied before extrapolating to other countries.

The origin of these atypical TSE cases in cattle is currently unknown.

All EU atypical cases were born before the extended or real feed ban that came into law in January 2001 (Ducrot *et al.*, 2008). Hence, as with the type of BSE more frequently found (classical BSE), exposure of these animals to feed contaminated with low titres of TSE cannot be excluded. However, the distribution of H- and L-type cases in France by year of birth differs markedly from that for classical BSE and could be interpreted to indicate that both forms of atypical BSE are sporadic diseases which arise spontaneously.

H- and L-(or BASE) type BSE have been transmitted to inbred mice and Tg mice expressing bovine and ovine PrP by intra-cerebral challenge. L-type BSE has also been transmitted to transgenic mice expressing alleles of the human prion protein (Beringue *et al.*, 2006; Buschmann *et al.*, 2006; Beringue *et al.*, 2007; Capobianco *et al.*, 2007; Kong *et al.*, 2008).

Transmission and serial passage in inbred mice and Tg VRQ mice have been interpreted to indicate that, after interspecies passage, BASE could generate classical BSE (Beringue *et al.*, 2007; Capobianco *et al.*, 2007). However, it should be noted that L-BSE - classical BSE phenotypic convergence has not observed in other Tg mice, including mice expressing the ARQ allele of sheep PrP (Buschmann *et al.*, 2006; Beringue *et al.*, 2007). This phenomenon needs to be confirmed in an independent set of experiments but does raise the issue of a possible classical BSE re-emergence originating from atypical BSE cases.

The sensitivity and specificity of the TSE rapid screening tests are known for classical BSE but not for H- or L-type BSE. These tests use brainstem as the target tissue because this is where pathological lesions and PrP^{res} are first detected in the CNS of cattle (Hope *et al.*, 1988; Wells *et al.*, 1998). Unlike classical BSE, little is known about the pathogenesis of atypical BSE and the brainstem may not be the optimal target site for the detection of H- and L- type BSE (Casalone *et al.*, 2004). Consequently our current estimation of BSE H- and L- type prevalence could be biased (underestimation).

No data are available on distribution of the infectivity in peripheral tissues and body fluids of cattle with H- or L-type BSE. This lack of data prevents any assessment of the relative risk reduction efficacy of different SRM measures.

3.1. Conclusions on atypical BSE

1. Since no cases were detected in animals younger than 8 years old in EU15, it is highly unlikely that the increase in age for rapid testing up 60 months will reduce the likelihood of detection of atypical BSE by currently validated BSE rapid tests.
2. In view of uncertainties surrounding the sensitivity and specificity of current tests to detect atypical BSE and limited data on the incidence of atypical BSE cases, it is uncertain whether the current BSE surveillance system provides reliable data on the prevalence of atypical BSE.

4. Consideration about the ability of a monitoring system to detect new trends in the epidemiology of BSE

Currently EU BSE surveillance aims at detecting:

- any changes in the trend of the BSE epidemiology, like a decrease or an increase in the number of BSE cases per period in a given region, or in a specific cattle subpopulation (young animals, old animals);
- a hypothetical new emerging TSE in cattle, such as was done for atypical BSE.

4.1. Clinical surveillance

A surveillance system based on passive clinical surveillance only was in force before 2000 in most EU countries. However, severe limitations rendered it inappropriate as the only means for BSE surveillance (Ducrot *et al.*, 2008). Compared with the active surveillance, case ascertainment and case reporting efficacy of passive surveillance was very poor. Furthermore, passive surveillance abilities to detect BSE cases appeared to be strongly biased. For instance, cases on beef cattle were far less efficiently detected than those on dairy cows.

Because all these weaknesses, and given that (i) a change in the trend (country, animal type, symptoms) of BSE epidemics or (ii) the emergence of a new TSE form in cattle would both be unexpected, passive surveillance appears inadequate for TSE surveillance.

4.2. Targeted active surveillance

The implementation of BSE Active Surveillance in 2001 proved to be a very efficient tool for cattle BSE surveillance in the EU. It resulted in a significant increase in the incidence of BSE per million cattle alive in countries which had already detected BSE cases before the start of active surveillance, and showed that most EU countries did indeed have a low incidence of BSE (Ducrot *et al.*, 2008).

In EU15 for the period 2001 - 2007, 77% (3,845/5,022) of the BSE cases detected were found in at risk population while these animals represented only 13% (8,519,376/ 56,723,311+8,519,376) of the carried-out tests. According to these data the likelihood of finding BSE cases is more than 20 times higher in at risk population than in the healthy slaughtered cattle (Ducrot *et al.*, 2008). Consequently focusing BSE Active Surveillance on at risk animals could appear as an interesting option for BSE surveillance in cattle.

While incubation period and clinical manifestations of BSE in cattle are well known, these parameters in a hypothetical new TSE that could emerge in cattle are per definition unknown. The design of targeted active surveillance systems should integrate current knowledge on cattle TSEs and likely hypotheses to optimise a system for early and efficient detection of such new forms of TSEs.

Only 2 BSE cases younger than 24 months of age were reported in cattle in the EU[6]. Therefore an age limit of 24 months was suggested for an early detection of a possible re-emergence of BSE and emergence of a similar type of TSE in at risk cattle population (Ducrot *et al.*, 2008).

In the EU15, the BSE Active Surveillance on at risk animals between 24 to 48 months of age represents around 395,000[7] tests per year (which represent about 33% of the total number of

6 www.defra.gov.uk/vla/science/docs/sci_tse_stats_age.pdf

7 From 2002 up to 2007, an average 395,067 tests per year were carried on at risk cattle between 24 and 47 months of age; in more detail 103,177 per year in the 24-to-29 months category, 111,584 per year in the 30-to-35 months category, 180,306 per year in the 36-to-47 months category.

tests performed in at risk animals).

Although all BSE cases in the EU15 since 2005 have been in animals older than 48 months of age, the active TSE surveillance in younger at risk animals is important for the as-early-as-possible detection of the emergence of a hypothetical new TSE in cattle. This system will also lead to increased sensitivity of the surveillance for early detection of re-emerging BSE.

4.3. Sensitivity of the surveillance system

The previous conclusions can be made more specific, when an exact model is applied.

The efficiency of a surveillance system to detect (re-)emerging TSEs can be evaluated as follows. The actual age distribution of cases in real time can be estimated from a known age at onset distribution and the growth rate of the epidemic. For fast growing epidemics, the distribution shifts to younger ages, whereas for declining epidemics, it shifts to older ages (de Koeijer *et al.*, 2002). Assuming re-emergence of BSE, with an age at onset distribution as given in Appendix B, we find that 64% of all cases are expected to be found in the ages between 48 and 72 months, in a fast growing epidemic (exponential growth rate r =0.5 per year similar to UK in the 1980s) (de Koeijer *et al.*, 2004), and only 11% of the cases will be found in animals younger than 48 months.

For epidemics with slower growth (r = 0.2 per year), which is the more likely situation as long as some BSE control measures remain in place, only 5.5% of the cases can be found in the animals below 48 months of age and 55% of the cases between 48 to 72 months.

Thus the age at which a re-emerging BSE epidemic is most likely to be detected first is 48 to 72 months. Additional testing of other age categories will make the system more sensitive.

The above is valid for re-emerging BSE. Newly emerging TSEs may behave differently, for instance the epidemic may grow faster or the age at onset distribution may be higher for younger ages. In that case testing of younger animals becomes more efficient.

Atypical BSE has so far mainly been found in older animals. If that is an indication of what we can expect in potential future TSE epidemics, testing of older animals should certainly be part of a surveillance system that aims at early detection of new emerging TSEs.

Furthermore, testing of healthy slaughtered animals is less sensitive in comparison to testing at risk animals. Within the EU15, less than 20% of all cases are found in the healthy slaughtered stream.

4.4. Conclusion the ability of a monitoring system to detect new trends in the epidemiology of BSE

- BSE Passive Surveillance has been demonstrated to be a very insensitive detection system.
- In contrast active surveillance has been demonstrated to be a more appropriate method for BSE monitoring.
- Targeting at risk population and certain age groups would enable early changes in the trend of BSE epidemic to be detected.
- An age limit of 48 months of age in at risk animals would allow for the detection of the majority of the cases if classical BSE re-emerges.
- If a new TSE epidemic emerges in cattle, an optimised active surveillance system for its detection should integrate current knowledge on cattle TSEs and likely hypotheses for early and efficient detection. Testing young animals may allow for an earlier detection of this epidemic.
- An age limit of 24 month in at risk animals would result in: (i) an increased sensitivity of surveillance in case of BSE re-emergence, (ii) an optimised system for early and efficient detection of emerging new TSEs in cattle.

CONCLUSIONS AND RECOMMENDATIONS

CONCLUSIONS

- The purpose of the TSE surveillance in cattle in the EU is mainly to monitor the BSE epidemic.
- Prevention of human exposure to BSE agent mainly relies on SRM removal.
- Prevention of animal exposure and propagation to TSE agents mainly relies on the Feed Ban.
- A statistical model of the future trend of the BSE epidemic was developed to address directly the terms of reference. For further extrapolation of the result of the model into the future, specific assumptions on the efficacy of the control measures since 2008 are required.
- In both the joint EU15 and in each of the individual EU15 countries in which sufficient data are available, the BSE epidemic has been constantly and significantly declining and is converging to the sensitivity limit of the current surveillance system.
- If the age of BSE testing increases to 36, 48 or 60 months of age for healthy slaughtered animals, the modelling shows that less than one case for the first two age limits and less than two cases for the third age limit can be expected to be missed annually in EU15.
- If the age of BSE testing increases to 30, 36, 48 or 60 months of age for at risk animals, the modelling shows that less than one case for the first three age limits and less than three cases for the fourth age limit can be expected to be missed annually in EU15.
- Although the likelihood of detecting new cases in specific age groups is very low, there remains a small probability of detecting one or more cases in some of these groups.
- BSE Passive Surveillance has been demonstrated to be a very insensitive detection system.

- An age limit of 48 months of age in at risk animals would allow for the detection of the majority of the cases if classical BSE re-emerges.
- If a new TSE epidemic emerges in cattle, an optimised active surveillance system for its detection should integrate current knowledge on cattle TSEs and likely hypotheses for early and efficient detection. Testing young animals may allow for an earlier detection of this epidemic.
- An age limit of 24 month in at risk animals would result in: (i) an increased sensitivity of surveillance in case of BSE re-emergence, (ii) an optimised system for early and efficient detection of emerging new TSEs in cattle.
- Targeting at risk population and certain age groups would enable early changes in the trend of BSE epidemic to be detected.
- Since no atypical BSE cases were detected in animals younger than 8 years old in EU15, it is highly unlikely that the increase in age for rapid testing up 60 months will reduce the likelihood of detection of atypical BSE by currently validated BSE rapid tests.
- In view of uncertainties surrounding the sensitivity and specificity of current tests to detect atypical BSE and limited data on the incidence of atypical BSE cases, it is uncertain whether the current BSE surveillance system provides reliable data on the prevalence of atypical BSE.

RECOMMENDATIONS

- The present opinion should be periodically revised based on the accumulation of new information on the 2002, 2003 and subsequent cattle birth cohorts.
- Any future TSE monitoring system in cattle should consider:
  - Ability to follow the current trend of the epidemic;
  - Ability to monitor for atypical BSE, particularly with respect to the sensitivity and specificity of tests and the efficacy and efficiency of the collection, analysis and interpretation of this data form the field;
  - Early and sensitive identification of potential re-emergence of classical BSE or the emergence of a new TSE in cattle population.
- An estimation of the number of undetected BSE infected bovines entering into the food chain would assist in quantifying the residual BSE exposure risk.

DOCUMENTATION PROVIDED TO EFSA

Letter (ref. n. SANCO.E.2/MP/mtd - D(2008) 520029 dated 22/01/2008) from the European Commission with a request for a scientific opinion on the risk for human and animal health related to the revision of the BSE monitoring regime in some Member States.

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APPENDIX A

Number of BSE cases detected through the BSE Surveillance (Active and Passive) and the animals culled in the framework of BSE eradication measures since 2001 per Member State, birth cohort and year of detection.

TABLE OF CONTENTS

Austria

Number of BSE cases detected through the BSE Surveillance (Active and Passive) and the animals culled in the framework of BSE eradication measures in Austria since 2001 per birth cohort and year of detection.

Birth cohort	N° of detected BSE cases per year							Total
	2001	2002	2003	2004	2005	2006	2007	
1980	0	0	0	0	0	0	0	0
1981	0	0	0	0	0	0	0	0
1982	0	0	0	0	0	0	0	0
1983	0	0	0	0	0	0	0	0
1984	0	0	0	0	0	0	0	0
1985	0	0	0	0	0	0	0	0
1986	0	0	0	0	0	0	0	0
1987	0	0	0	0	0	0	0	0
1988	0	0	0	0	0	0	0	0
1989	0	0	0	0	0	0	0	0
1990	0	0	0	0	0	0	0	0
1991	0	0	0	0	0	0	0	0
1992	0	0	0	0	1	0	0	1
1993	0	0	0	0	0	1	0	1
1994	0	0	0	0	1	0	0	1
1995	0	0	0	0	0	0	0	0
1996	1	0	0	0	0	0	1	2
1997	0	0	0	0	0	0	0	0
1998	0	0	0	0	0	0	0	0
1999	0	0	0	0	0	0	0	0
2000	0	0	0	0	0	1	0	1
2001	0	0	0	0	0	0	0	0
2002	0	0	0	0	0	0	0	0
Total	1	0	0	0	2	2	1	6

Belgium

Number of BSE cases detected through the BSE Surveillance (Active and Passive) and the animals culled in the framework of BSE eradication measure in Belgium since 2001 per birth cohort and year of detection.

Birth cohort	N° of detected BSE cases per year							Total
	2001	2002	2003	2004	2005	2006	2007	
1980	0	0	0	0	0	0	0	0
1981	0	0	0	0	0	0	0	0
1982	0	0	0	0	0	0	0	0
1983	0	0	0	0	0	0	0	0
1984	0	0	0	0	0	0	0	0
1985	0	0	0	0	0	0	0	0
1986	0	0	0	0	0	0	0	0
1987	0	0	0	0	0	0	0	0
1988	0	0	0	0	0	0	0	0
1989	0	0	0	0	0	0	0	0
1990	0	0	0	0	0	0	0	0
1991	1	0	1	0	1	0	0	3
1992	1	3	0	0	0	0	0	4
1993	1	1	0	0	0	0	0	2
1994	7	5	2	1	0	1	0	16
1995	18	8	2	0	0	0	0	28
1996	18	13	6	4	0	0	0	41
1997	0	8	3	4	2	0	0	17
1998	0	0	1	2	0	0	0	3
1999	0	0	0	0	0	0	0	0
2000	0	0	0	0	0	1	0	0
2001	0	0	0	0	0	0	0	0
2002	0	0	0	0	0	0	0	0
Total	46	38	15	11	3	1	0	114

Denmark

Number of BSE cases detected through the BSE Surveillance (Active and Passive) and the animals culled in the framework of BSE eradication measures in Denmark since 2001 per birth cohort and year of detection.

Birth cohort	N° of detected BSE cases per year							Total
	2001	2002	2003	2004	2005	2006	2007	
1980	0	0	0	0	0	0	0	0
1981	0	0	0	0	0	0	0	0
1982	0	0	0	0	0	0	0	0
1983	0	0	0	0	0	0	0	0
1984	0	0	0	0	0	0	0	0
1985	0	0	0	0	0	0	0	0
1986	0	0	0	0	0	0	0	0
1987	0	0	0	0	0	0	0	0
1988	0	0	0	0	0	0	0	0
1989	0	0	0	0	0	0	0	0
1990	0	0	0	1	0	0	0	1
1991	0	0	0	0	0	0	0	0
1992	0	0	0	0	0	0	0	0
1993	1	0	0	0	0	0	0	1
1994	0	0	0	0	0	0	0	0
1995	0	0	0	0	0	0	0	0
1996	3	2	1	0	1	0	0	7
1997	1	0	1	0	0	0	0	2
1998	1	1	0	0	0	0	0	2
1999	0	0	0	0	0	0	0	0
2000	0	0	0	0	0	1	0	0
2001	0	0	0	0	0	0	0	0
2002	0	0	0	0	0	0	0	0
Total	6	3	2	1	1	0	0	13

Finland

Number of BSE cases detected through the BSE Surveillance (Active and Passive) and the animals culled in the framework of BSE eradication measures in Finland since 2001 per birth cohort and year of detection.

Birth cohort	N° of detected BSE cases per year							Total
	2001	2002	2003	2004	2005	2006	2007	
1980	0	0	0	0	0	0	0	0
1981	0	0	0	0	0	0	0	0
1982	0	0	0	0	0	0	0	0
1983	0	0	0	0	0	0	0	0
1984	0	0	0	0	0	0	0	0
1985	0	0	0	0	0	0	0	0
1986	0	0	0	0	0	0	0	0
1987	0	0	0	0	0	0	0	0
1988	0	0	0	0	0	0	0	0
1989	0	0	0	0	0	0	0	0
1990	0	0	0	0	0	0	0	0
1991	0	0	0	0	0	0	0	0
1992	0	0	0	0	0	0	0	0
1993	0	0	0	0	0	0	0	0
1994	0	0	0	0	0	0	0	0
1995	1	0	0	0	0	0	0	1
1996	0	0	0	0	0	0	0	0
1997	0	0	0	0	0	0	0	0
1998	0	0	0	0	0	0	0	0
1999	0	0	0	0	0	0	0	0
2000	0	0	0	0	0	0	0	0
2001	0	0	0	0	0	0	0	0
2002	0	0	0	0	0	0	0	0
Total	1	0	0	0	0	0	0	1

France

Number of BSE cases detected through the BSE Surveillance (Active and Passive) and the animals culled in the framework of BSE eradication measures in France since 2001 per birth cohort and year of detection.

Birth cohort	N° of detected BSE cases per year							Total
	2001	2002	2003	2004	2005	2006	2007	
1980	0	0	0	0	0	0	0	0
1981	0	0	0	0	0	0	0	0
1982	0	0	0	0	0	0	0	0
1983	0	0	0	0	0	0	0	0
1984	0	0	0	0	0	0	0	0
1985	0	0	0	0	0	0	0	0
1986	0	0	0	1	0	0	0	1
1987	0	0	1	0	0	0	0	1
1988	0	1	0	0	0	0	0	1
1989	0	0	1	0	0	0	0	1
1990	0	1	1	0	1	0	0	3
1991	0	3	2	0	0	0	0	5
1992	1	5	2	2	2	0	0	12
1993	30	17	7	4	3	1	0	62
1994	87	56	23	12	6	2	0	186
1995	134	103	41	10	7	0	3	298
1996	21	40	13	10	2	0	1	87
1997	4	10	16	4	3	2	1	40
1998	0	4	4	6	0	0	2	16
1999	0	0	0	2	5	2	0	9
2000	0	0	0	0	3	0	0	3
2001	0	0	0	0	0	1	0	1
2002	0	0	0	0	0	0	0	0
Total	277	240	111	51	32	8	5	726

Germany

Number of BSE cases detected through the BSE Surveillance (Active and Passive) and the animals culled in the framework of BSE eradication measures in Germany since 2001 per birth cohort and year of detection.

Birth cohort	N° of detected BSE cases per year							Total
	2001	2002	2003	2004	2005	2006	2007	
1980	0	0	0	0	0	0	0	0
1981	0	0	0	0	0	0	0	0
1982	0	0	0	0	0	0	0	0
1983	0	0	0	0	0	0	0	0
1984	0	0	0	0	0	0	0	0
1985	0	0	0	0	0	0	0	0
1986	0	0	0	0	0	0	0	0
1987	0	1	0	0	0	0	0	1
1988	0	0	0	0	0	0	0	0
1989	0	0	0	0	0	0	0	0
1990	1	1	0	0	0	0	0	2
1991	1	0	0	1	0	0	0	2
1992	1	1	0	0	0	0	0	2
1993	0	3	0	0	0	0	0	3
1994	8	5	0	2	0	0	0	15
1995	40	32	8	2	1	1	0	84
1996	67	44	12	8	3	0	0	134
1997	5	11	13	14	1	0	0	44
1998	2	8	8	10	5	1	0	34
1999	0	0	13	18	11	9	3	54
2000	0	0	0	10	9	5	1	25
2001	0	0	0	0	2	0	0	2
2002	0	0	0	0	0	0	0	0
Total	125	106	54	65	32	16	4	402

Greece

Number of BSE cases detected through the BSE Surveillance (Active and Passive) and the animals culled in the framework of BSE eradication measures in Greece since 2001 per birth cohort and year of detection.

Birth cohort	N° of detected BSE cases per year							Total
	2001	2002	2003	2004	2005	2006	2007	
1980	0	0	0	0	0	0	0	0
1981	0	0	0	0	0	0	0	0
1982	0	0	0	0	0	0	0	0
1983	0	0	0	0	0	0	0	0
1984	0	0	0	0	0	0	0	0
1985	0	0	0	0	0	0	0	0
1986	0	0	0	0	0	0	0	0
1987	0	0	0	0	0	0	0	0
1988	0	0	0	0	0	0	0	0
1989	0	0	0	0	0	0	0	0
1990	0	0	0	0	0	0	0	0
1991	0	0	0	0	0	0	0	0
1992	0	0	0	0	0	0	0	0
1993	0	0	0	0	0	0	0	0
1994	0	0	0	0	0	0	0	0
1995	0	0	0	0	0	0	0	0
1996	1	0	0	0	0	0	0	1
1997	0	0	0	0	0	0	0	0
1998	0	0	0	0	0	0	0	0
1999	0	0	0	0	0	0	0	0
2000	0	0	0	0	0	0	0	0
2001	0	0	0	0	0	0	0	0
2002	0	0	0	0	0	0	0	0
Total	1	0	0	0	0	0	0	1

Ireland

Number of BSE cases detected through the BSE Surveillance (Active and Passive) and the animals culled in the framework of BSE eradication measures in Ireland since 2001 per birth cohort and year of detection.

Birth cohort	N° of detected BSE cases per year							Total
	2001	2002	2003	2004	2005	2006	2007	
1980	0	0	0	0	0	0	0	0
1981	0	0	0	0	0	0	0	0
1982	0	0	0	0	0	0	0	0
1983	0	0	0	0	0	0	0	0
1984	0	0	0	0	0	0	0	0
1985	0	0	0	0	0	0	0	0
1986	2	2	0	1	0	0	0	5
1987	0	2	0	0	0	0	0	2
1988	1	4	0	0	0	0	0	5
1989	2	1	4	3	0	1	0	11
1990	1	10	3	3	0	0	0	17
1991	6	10	6	3	1	2	1	29
1992	8	14	7	12	2	2	0	45
1993	21	40	25	16	11	1	2	116
1994	52	51	31	18	25	6	8	191
1995	110	133	74	43	20	11	5	396
1996	39	60	30	18	10	11	6	174
1997	0	5	3	3	0	2	0	13
1998	0	0	0	4	0	1	1	6
1999	0	2	0	2	3	0	0	7
2000	0	0	0	0	3	0	2	5
2001	0	0	0	0	2	1	0	3
2002	0	0	0	0	0	0	1	1
Total	242	334	183	126	77	38	26	1026

Italy

Number of BSE cases detected through the BSE Surveillance (Active and Passive) and the animals culled in the framework of BSE eradication measures in Italy since 2001 per birth cohort and year of detection.

Birth cohort	N° of detected BSE cases per year							Total
	2001	2002	2003	2004	2005	2006	2007	
1980	0	0	0	0	0	0	0	0
1981	0	0	0	0	0	0	0	0
1982	0	0	0	0	0	0	0	0
1983	0	0	0	0	0	0	0	0
1984	0	0	0	0	0	0	0	0
1985	0	0	0	0	0	0	0	0
1986	0	0	0	0	0	0	0	0
1987	1	0	0	0	0	0	0	1
1988	0	0	2	0	0	0	0	2
1989	0	0	0	0	0	0	0	0
1990	0	0	0	0	0	0	0	0
1991	0	1	0	0	0	0	0	1
1992	0	0	1	0	1	1	1	4
1993	2	0	3	0	0	0	0	5
1994	8	5	1	0	0	0	0	14
1995	12	10	4	0	0	0	0	26
1996	20	14	10	4	3	1	0	52
1997	7	4	9	3	1	1	1	26
1998	0	2	1	0	0	0	0	3
1999	0	0	0	1	2	2	0	5
2000	0	0	0	0	1	1	0	2
2001	0	0	0	0	0	1	0	1
2002	0	0	0	0	0	0	0	0
Total	50	36	31	8	8	7	2	142

Luxemburg

Number of BSE cases detected through the BSE Surveillance (Active and Passive) and the animals culled in the framework of BSE eradication measures in Luxemburg since 2001 per birth cohort and year of detection.

Birth cohort	N° of detected BSE cases per year							Total
	2001	2002	2003	2004	2005	2006	2007	
1980	0	0	0	0	0	0	0	0
1981	0	0	0	0	0	0	0	0
1982	0	0	0	0	0	0	0	0
1983	0	0	0	0	0	0	0	0
1984	0	0	0	0	0	0	0	0
1985	0	0	0	0	0	0	0	0
1986	0	0	0	0	0	0	0	0
1987	0	0	0	0	0	0	0	0
1988	0	0	0	0	0	0	0	0
1989	0	0	0	0	0	0	0	0
1990	0	0	0	0	0	0	0	0
1991	0	0	0	0	0	0	0	0
1992	0	0	0	0	0	0	0	0
1993	0	0	0	0	0	0	0	0
1994	0	0	0	0	0	0	0	0
1995	0	0	0	0	0	0	0	0
1996	0	1	0	0	0	0	0	1
1997	0	0	0	0	0	0	0	0
1998	0	0	0	0	0	0	0	0
1999	0	0	0	0	0	0	0	0
2000	0	0	0	0	0	0	0	0
2001	0	0	0	0	1	0	0	1
2002	0	0	0	0	0	0	0	0
Total	0	1	0	0	1	0	0	2

Netherlands

Number of BSE cases detected through the BSE Surveillance (Active and Passive) and the animals culled in the framework of BSE eradication measures in the Netherlands since 2001 per birth cohort and year of detection.

Birth cohort	N° of detected BSE cases per year							Total
	2001	2002	2003	2004	2005	2006	2007	
1980	0	0	0	0	0	0	0	0
1981	0	0	0	0	0	0	0	0
1982	0	0	0	0	0	0	0	0
1983	0	0	0	0	0	0	0	0
1984	0	0	0	0	0	0	0	0
1985	0	0	0	0	0	0	0	0
1986	0	0	0	0	0	0	0	0
1987	0	0	0	0	0	0	0	0
1988	1	0	0	0	0	0	0	1
1989	0	0	0	0	0	0	0	0
1990	0	0	0	0	0	0	0	0
1991	0	0	1	1	0	0	0	2
1992	1	1	0	0	0	0	0	2
1993	2	1	0	0	0	0	0	3
1994	2	2	0	0	0	0	0	4
1995	4	3	0	0	0	0	0	7
1996	9	10	10	3	0	0	0	32
1997	1	4	5	1	0	1	0	12
1998	0	3	1	1	0	1	0	6
1999	0	0	1	0	0	0	1	2
2000	0	0	0	0	2	0	1	3
2001	0	0	0	0	1	0	0	1
2002	0	0	0	0	0	0	0	0
Total	20	24	18	6	3	2	2	75

Portugal

Number of BSE cases detected through the BSE Surveillance (Active and Passive) and the animals culled in the framework of BSE eradication measures in Portugal since 2001 per birth cohort and year of detection.

Birth cohort	N° of detected BSE cases per year							Total
	2001	2002	2003	2004	2005	2006	2007	
1980	0	0	0	0	0	0	0	0
1981	0	0	0	0	0	0	0	0
1982	0	0	0	0	0	0	0	0
1983	0	0	0	0	0	0	0	0
1984	0	1	0	0	0	0	0	1
1985	0	0	0	0	1	0	0	1
1986	0	0	0	0	0	0	0	0
1987	0	1	1	0	0	0	0	2
1988	0	0	0	0	0	1	0	1
1989	2	0	1	0	0	0	0	3
1990	1	0	1	3	2	3	0	10
1991	0	1	0	1	0	1	0	3
1992	3	1	4	3	2	0	0	13
1993	22	11	24	14	8	3	3	85
1994	38	22	19	13	7	7	2	108
1995	17	19	12	8	6	1	1	64
1996	22	19	23	9	7	2	1	83
1997	5	8	28	23	10	4	2	80
1998	0	1	18	13	7	8	0	47
1999	0	2	1	3	2	2	2	12
2000	0	0	0	1	0	0	0	1
2001	0	0	0	0	0	0	0	0
2002	0	0	0	0	1	0	0	1
Total	110	86	132	91	53	32	11	515

Spain

Number of BSE cases detected through the BSE Surveillance (Active and Passive) and the animals culled in the framework of BSE eradication measures in Spain since 2001 per birth cohort and year of detection.

Birth cohort	N° of detected BSE cases per year							Total
	2001	2002	2003	2004	2005	2006	2007	
1980	0	0	0	0	0	0	0	0
1981	0	0	0	0	0	0	0	0
1982	0	0	0	0	0	0	0	0
1983	0	0	0	0	0	0	0	0
1984	0	0	0	0	0	0	0	0
1985	0	0	0	0	0	0	0	0
1986	1	0	0	0	0	0	0	1
1987	1	0	1	0	0	0	0	2
1988	1	1	1	0	0	0	0	3
1989	1	2	1	0	0	0	1	5
1990	1	0	1	1	0	0	0	3
1991	0	0	0	0	0	0	0	0
1992	1	1	2	1	0	0	1	6
1993	10	12	6	5	1	1	1	36
1994	13	9	9	4	3	1	0	39
1995	22	33	24	9	2	1	3	94
1996	20	33	34	14	7	4	1	113
1997	11	28	57	30	14	10	1	151
1998	0	7	26	49	24	16	6	128
1999	0	1	4	19	25	16	7	72
2000	0	0	1	5	26	21	11	64
2001	0	0	0	0	0	1	0	1
2002	0	0	0	0	1	0	0	1
Total	82	127	167	137	103	71	32	719

Sweden

Number of BSE cases detected through the BSE Surveillance (Active and Passive) and the animals culled in the framework of BSE eradication measures in Sweden since 2001 per birth cohort and year of detection.

Birth cohort	N° of detected BSE cases per year							Total
	2001	2002	2003	2004	2005	2006	2007	
1980	0	0	0	0	0	0	0	0
1981	0	0	0	0	0	0	0	0
1982	0	0	0	0	0	0	0	0
1983	0	0	0	0	0	0	0	0
1984	0	0	0	0	0	0	0	0
1985	0	0	0	0	0	0	0	0
1986	0	0	0	0	0	0	0	0
1987	0	0	0	0	0	0	0	0
1988	0	0	0	0	0	0	0	0
1989	0	0	0	0	0	0	0	0
1990	0	0	0	0	0	0	0	0
1991	0	0	0	0	0	0	0	0
1992	0	0	0	0	0	0	0	0
1993	0	0	0	0	0	0	0	0
1994	0	0	0	0	0	1	0	1
1995	0	0	0	0	0	0	0	0
1996	0	0	0	0	0	0	0	0
1997	0	0	0	0	0	0	0	0
1998	0	0	0	0	0	0	0	0
1999	0	0	0	0	0	0	0	0
2000	0	0	0	0	0	0	0	0
2001	0	0	0	0	0	0	0	0
2002	0	0	0	0	0	0	0	0
Total	0	0	0	0	0	1	0	1

United Kingdom

Number of BSE cases detected through the BSE Surveillance (Active and Passive) and the animals culled in the framework of BSE eradication measures in the United Kingdom since 2001 per birth cohort and year of detection.

Birth cohort	N° of detected BSE cases per year							Total
	2001	2002	2003	2004	2005	2006	2007	
1980	0	1	0	0	0	0	0	1
1981	1	0	0	0	0	0	0	1
1982	0	0	0	0	0	0	0	0
1983	0	0	1	0	0	0	0	1
1984	1	2	0	0	0	1	0	4
1985	1	2	2	0	0	0	0	5
1986	10	8	3	1	1	0	0	23
1987	19	26	6	6	6	1	0	64
1988	17	22	18	6	0	0	0	63
1989	20	34	14	14	5	4	0	91
1990	24	42	16	13	6	4	1	106
1991	58	63	37	21	20	5	0	204
1992	104	130	69	37	29	12	7	388
1993	241	160	114	55	33	20	11	634
1994	362	303	133	72	52	30	16	968
1995	310	275	138	64	31	23	9	850
1996	25	37	24	10	6	7	0	109
1997	9	13	18	4	4	3	1	52
1998	1	4	14	11	9	3	7	49
1999	0	1	5	6	12	5	3	32
2000	0	0	0	2	4	4	2	12
2001	0	0	0	0	2	4	1	7
2002	0	0	0	0	1	1	2	4
Total	1203	1123	612	322	221	127	60	3668

APPENDIX B

Methodology used when performing the calculations with Method 3

Introduction

The BSE risk in various risk categories, age-groups and birth cohorts using a general method as described by de Koeijer (de Koeijer, 2007) was calculated and from that further calculation steps were performed to derive a risk assessment on the requested issues. A summary of the calculation steps is given here, and can be traced back in the excel worksheet that is provided as an Annex to this Opinion.

The case data for all EU15 are pooled together for the period of active surveillance (2001 through 2007). They are ordered by birth cohort and age (into year groups). All cases where the year of birth or age is unknown and all cases older than 155 months are also excluded because their exact age is often unclear from the statistics and their numbers are extremely low. In a later stage a correction was applied for the cases that are ignored in the modelling by adding a small fraction to the cohort estimates.

By organising the data in birth cohorts it is clear that a selection of ages have been fully tested, whereas other ages were not tested at all. A normalised age at onset distribution of BSE in a cohort (up to 155 months) is used to calculate the fraction of cases that is expected to be found in the part of the cohort that has been tested in the period 2001 through 2007. From that the expected number of cases in the full cohort was estimated, subsequently the maximum number of cases using 95% confidence in a binomial sample was calculated (using an add-on excel function downloadable from http://statpages.org/confint.html) (Clopper and Pearson, 1934) and lastly a finite population correction for large samples was applied (Burstein, 1975). Since annually the number of animals tested is of the order of 10 million animals, relatively small variations in this number make no significant difference to the width of the confidence interval, so the 10 million is applied for the number tested throughout the analysis.

Finally the available data was evaluated to determine the proportion of the cases by age group that are found in the healthy slaughter or at risk categories. This proportion is then applied to evaluate the effect of changing surveillance in the various risk categories.

Two scenarios were applied to calculate the future risk of BSE. All scenarios that are included here are based on worst case assumptions. Various other scenarios have been assessed for sensitivity analysis, but details on those scenarios are not included in the spreadsheet or in the Opinion.

1) **Scenario I**: Calculates the upper confidence limit of the incidence in the 2003 birth cohort and assumes all subsequent birth cohorts to have that same incidence. Since the incidence is decreasing significantly each birth cohort since 1995 this is a worst case assumption.
2) **Scenario II**: Estimates the decay rate of the epidemic from all the cohort case incidences by log-linear regression. The incidence in the 2003 cohort onwards is projected forward using the upper 95% confidence interval of the 2002 cohort incidence and the upper confidence limit of the decay rate.

Underlying assumptions and calculation rules

1) BSE infections occur mostly at a very young age.
2) The derived distribution for the age-at-onset is valid for the whole EU15, and will remain valid after 2007.
3) Uncertainty in the distribution of the age-at-onset is negligible
4) Local and regional variation in the age distribution of cattle population is not correlated with the local/regional BSE incidence.
5) The age distribution of cattle is sufficiently constant over the assessed period
6) All detectable BSE cases in the EU15 between 1 January 2001 and 31 December 2007 have been identified and are included in the applied dataset.
7) Animals from birth cohort of year x and age y will appear in the test years x+y and x+y+1. This depends on whether the test is performed before or after the birthday of the animal in a given year. It is assumed this is to be distributed in equal amounts.

Age at onset distribution

Using the age-at-infection and incubation period distributions from Arnold and Wilesmith (Arnold and Wilesmith, 2004) an age at onset distribution can be derived, which is based on reported case data from Great Britain (GB). A preliminary analysis showed that the age-at-onset distribution derived from the GB epidemic data had a lower mean age-at-onset than the observed data from the EU15, so an age-at-onset distribution from the available EU15 case data was derived. To do so, case data for the birth cohorts of 1994-1999 were used. Only the age categories which were fully tested were included. The relative risk of onset for each age category was calculated relative to the 7-year old age-group. Per age group, the average relative risks were determined and subsequently the newly derived age-at-onset distribution was normalized. Thus each of the included birth cohorts had equal weight in the final age-at-onset distribution.

The resulting distribution of the age at onset is given in lines 38 to 40 of each of the excel worksheet.

Sensitivity analyses

Since the age-at-onset distribution could vary between countries due to, for example, differences in the age distribution of the cattle population, a sensitivity analysis was conducted to compare the applied age-at-onset distribution with the GB age-at-onset distribution (Arnold and Wilesmith, 2004). This is considered to be an extreme distribution, which has a much younger age at onset than found anywhere else, probably as a result of the high exposure during the nineteen eighties. It was found that using the GB age-at-onset distribution leads to 56% increase in the expected case numbers in the younger age categories (<48 months). Obviously it then leads to lower predicted case numbers in the older age categories (6 years and older). The EU15 distribution which was derived from the active surveillance data was considered to be the most suitable one to analyse the EU BSE situation since it reflected the age-at-onset of recent EU cases. Calculating the epidemic decay rate from the number of cases in successive birth cohorts (Scenario II) makes little difference in terms of the number of predicted cases in each birth cohort that each age at onset distribution produces for the next 5 birth cohorts. The Scenario II works with the birth cohort data.

It is assumed that prevalence in subsequent birth cohorts can display a wave over time which is a direct effect of a wave in past exposure. This wave blurs the effect of the extended control measures in 2001, since there are only three cohorts available with sufficient cohort data and the wavelength is a full generation long. Thus a time period of at least a full generation is needed in evaluating the growth rate of the epidemic. The applied log-linear regression overcomes the effect of the wave but necessarily uses so many past birth cohorts that the effect of the extra measures in 2001 averages away in the longer period of less pronounced decline.

It was also checked whether using only the healthy slaughter data in the analysis would lead to the same results as an analysis on the complete data, with the subsequent evaluation of the fraction which would appear in healthy slaughter. As can be expected, the calculations are not very sensitive to this assumption.

References

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