Opinion

of the

Scientific Steering Committee

on

BSE-related culling in Cattle

Adopted at the meeting of 14/15 September 2000

1. Executive Summary

The SSC wants to underline that culling is only one of many factors influencing the geographical BSE-risk (see SSC-opinion on the geographical risk of bovine spongiform encephalopathy, 7/7/2000).

1.1 The Question

The SSC was asked to address the following three questions:

- ***What is the expected impact of different culling schemes on the current pre-clinical incidence of BSE and the future clinical incidence?***
- ***Does this effect vary in function of the BSE-incidence in a country as indicated by the BSE-incidence?***
- ***What are therefore the appropriate culling schemes in function of defined levels of incidence ?***

1.2 The Answers

The SSC concludes that the impact of BSE-culling on the current pre-clinical BSE-incidence and the future clinical BSE-incidence is dependent on many factors and cannot easily be assessed. Ideally all cattle exposed to the same feed as the index case should be culled but it seems that this target population cannot normally be identified. The limited available information indicates, however, that already herd culling is having some effect both in terms of eliminating otherwise not identified (pre-clinical) cases and in terms of preventing future cases to appear. However, the data also indicate that largely the same effect can be reached by birth cohort (see definition below) culling, i.e. with only culling about 1/3 of the animals that are culled under a herd-culling scheme[1].

In view of the limited data available the impact of the epidemiological situation in a country on the relative efficiency of practically possible culling schemes cannot be fully assessed. It is, however, likely that birth cohort culling is in most cases the more cost-efficient approach[1].

This position is based on the definition of a birth cohort including, as suggested by the available data, all animals born and/or raised in the same herd as the confirmed case within approximately 12 months before and after the date of birth of the index case. All animals from these cohorts should be traced, killed and destroyed, independent of their current localisation.

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[1] If there is evidence that the entire herd has been exposed to the same contaminated feed as the index case, herd culling would be more appropriate. However, the available data do not suggest that this is generally the case.

The SSC recommends the application of at least birth-cohort culling whenever a domestic index case appears, irrespective of the prevailing epidemiological situation.

The SSC further recommends that all members of these birth cohorts that are older than 24 months are systematically examined for the presence of PrP^{Sc} in their brain or spinal cord using an approved method.

1.3 MAIN ELEMENTS OF THE SCIENTIFIC JUSTIFICATION OF THE ANSWERS

The position of the SSC is founded on the following basic assumptions:

- BSE is NOT horizontally transmitted and the only significant transmission routes are feed and, but by far less important, vertically from an infected dam to its calf. It is hence not comparable to normal infectious diseases.
- It is assumed that infection normally takes place in the first months of life of a calf and calf feed is usually not fed to older cattle.
- As the incubation period of BSE is between 2 and 14 years (mean 60 months) with the vast majority of clinical cases being 4-6 years at clinical onset, the exposure event that lead to the development of a clinical case must have taken place 4-6 years in the past.
- Current diagnostic tools do not allow identifying incubating animals in the early phases of the incubating period. The available methods are, however able to detect PrP^{Sc} and hence diagnose BSE in animals that have not been previously identified as suspects, i.e. in a-symptomatic animals, but only in the late stages of the incubation period.
- BSE is in all cases a rare event. With the exception of the UK in the years of the height of the epidemic, the yearly incidence remained below 0,1 % (1.000/million) of the adult (>24 months) cattle population.

In the light of these basic assumptions the SSC has looked at data from Switzerland, Ireland, Belgium, France and Portugal and at theoretical back-calculations from the UK.

The available data showed that the vast majority of the additional cases found in the population of cattle that were culled under the applied (herd-) culling-scheme while not showing signs of BSE fell indeed into the birth-cohorts as defined above. The Swiss data, being the only available, further indicate that only 1/3 of the cattle culled under a herd culling scheme (natal and present herd) fall into the birth-cohort as defined above.

The UK-back-calculations indicate that indeed appropriate culling in the early nineties would have significantly reduced the number of BSE-cases that finally occurred and the number of undiscovered infected animals that entered the human food chain.

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2. FULL OPINION

2.1 TERMS OF REFERENCE

The SSC wants to underline that culling is only one of many factors influencing the geographical BSE-risk (see SSC-opinion on the geographical risk of bovine spongiform encephalopathy, 7/7/2000).

2.11 The Question

The SSC was asked to address the following three questions:

- ***What is the expected impact of different culling schemes on the current pre-clinical incidence of BSE and the future clinical incidence ?***
- ***Does this effect vary in function of the epidemiological situation of a country as indicated by the BSE-incidence ?***
- ***What are therefore the appropriate culling schemes in function of defined levels of incidence ?***

2.12 The Context of the question

In the European Union most countries have contingency plans for appearance of clinical BSE. These include the one or other form of culling, i.e. killing a-symptomatic animals because of their (assumed) epidemiological relationship to a confirmed case. The basic assumption behind this is that culling will eliminate cattle most likely to have been exposed to the same source of infection as the index case (some of which might be pre-clinical BSE-cases). By this means the current prevalence of BSE-infected animals and the future clinical BSE incidence should be reduced.

It is however noted that BSE occurs in animals up to 18 years of age indicating very long incubation periods (if exposure was in calfhood) or adult exposure. When such old index cases occur birth cohort culls would probably be impossible (no cohort members left, tracing impossible) and herd culls might be inappropriate unless adult exposure and its timing could be substantiated (unlikely).

In the light of the limited data available the agricultural and general public has increasingly questioned the cost/benefit ratio of the applied culling schemes. In order to shed some light on the scientific rationale, and in view of the necessity to develop a European approach to the issue, the Commission services raised the three questions mentioned above.

2.13 Definitions

Culling is the killing of a-symptomatic (or weak symptomatic or not recognised) animals, which are not BSE-suspects, because of their (assumed) higher risk of being infected with BSE due to their epidemiological link to a confirmed case. It is taken for granted that the culled animals are destroyed and do not enter the feed or food chains.

The **objective of any culling** is to eliminate a maximum number of pre-clinical BSE-cases and by this to reduce the current (pre-clinical and clinical) prevalence and hence the future clinical incidence of BSE.

The **effectiveness of a culling scheme** is therefore measured by the (expected, theoretically possible) impact on the current (pre-clinical and clinical) prevalence and hence the future clinical incidence of BSE. A given culling scheme is more effective if the expected number of BSE-incubating (asymptomatic) cattle that are hit and that therefore could not enter the food or feed chain and could not become a clinical BSE-case is higher in relation to the total number of killed animals.

Adult cattle are (in the context of this opinion) all cattle older than 24 months.

Cohorts are groups of animals other than herds that are defined by specified common characteristics. Three types of cohorts are defined as follows:

(a) **Birth cohorts**, i.e. cohort members fall into the same age group as the case, and their place of birth and/or of rearing during its first months of live is related to the case, normally being the same herd.

(b) **Feed cohorts**; i.e. the cohort members are defined in function of their feed source being the same as for the confirmed case.

(c) **Vertical cohorts**, i.e. cohort members are identified in function of their descendence, normally only regarding the maternal link.

2.14 Basic assumptions

- BSE is NOT horizontally transmitted and the only significant transmission routes are feed and, but by far less important, vertically from an infected dam to its calf. It is hence not comparable to normal infectious diseases.
- It is assumed that infection normally takes place in the first months of life of a calf and calf feed is usually not fed to older cattle.
- As the incubation period of BSE is between 2 and 14 years (mean 60 months) with the vast majority of clinical cases being 4-6 years at clinical onset, the exposure event that lead to the development of a clinical case must have taken place 4-6 years in the past.
- Current diagnostic tools do not allow identifying incubating animals in the early phases of the incubating period. The available methods are, however able to detect PrP^{Sc} and hence diagnose BSE in animals that have not been previously identified as suspects, i.e. in a-symptomatic animals, but only in the late stages of the incubation period.
- BSE is in all cases a rare event. With the exception of the UK in the years of the height of the epidemic, the yearly incidence remained below 0,1 % (1.000/million) of the adult (>24 months) cattle population.

2.2 THE ASSESSMENT

This assessment reflects on the scientific rationale of the assumption that culling can reduce the current prevalence and the future incidence, and the extent to which this is possible.

In view of the insufficient database it elucidates, as far as possible, the effect that theoretically could be achieved by different culling schemes in function of their structure and assumed epidemiological situations.

2.21 Theoretically possible culling schemes

In order to achieve its objective, a culling scheme must target those animals carrying the highest risk of being infected while not showing signs compatible with BSE. If a confirmed BSE case is taken as indicator an ideal culling scheme would target those animals that have been exposed to the same feed as the case during its calfhood, normally 4-6 years in the past ("feed cohort"). It should also address those being in direct maternal relation to the case (offspring).

However, in reality it will often not be possible to identify this theoretical target population, the feed cohort, because the potentially contaminated feed-batch usually cannot be identified, and the contaminated feed will most likely have been spread over several herds. It may even be spread over time. How far this distribution reached depends on factors like batch sizes in rendering and in feed production, and the distribution of potentially contaminated feed batches over farms. Also the distribution of contamination within contaminated feed batches is not known.

In Belgium an effort was made to try to identify the animals that could have been exposed to the same feed as a confirmed case. Because of the above-mentioned uncertainties the result was that about 50% of the Belgian national herd could theoretically have been exposed. A result that shows that the approach to target animals potentially exposed to the same feed as the index case is apparently unrealistic, at least in countries with similar situations to those pertaining in Belgium.

2.22 Applied schemes

The following are the main culling schemes that are currently applied, but in each country they are slightly differently implemented. A detailed overview is given in annex.

2.221 Herd-culling

<u>Basic assumption</u>

A confirmed case indicates a higher risk for the other cattle in the herd where the index case was born and raised also to be incubating the disease , and the herd mates are most likely to have been exposed to the same contaminated feed as the index case.

Description

In most cases only the current herd of the confirmed case is culled. In some cases both the natal herd and herd of residence are culled. Herds through which the case passed during its life are normally not culled. Currently, in the Netherlands, all TSE-susceptible animal species on the farm, including cats are culled.

2.222 Cohort culling

Basic assumption

By using specific indicators, groups of cattle other than herds (cohorts) are identified that carry a higher risk to incubate BSE than the current, natal or passed-through herd.

In view of the dominant importance of feed-based transmission the respective cohort-indicator (see below) points to those cattle that are most likely to have been exposed to the same feed-source as the index case. Maternal transmission may also be taken into account. Combinations are possible.

Description:

Different definitions of cohorts are possible:

(a) **Birth cohorts**, i.e. cohort members fall into the same age group as the case, and their place of birth and/or rearing during the first months of live is related to the case, normally being the same herd

The justification to use this cohort is based on the assumption that infection normally takes place in the first months of life of a calf and calf feed is usually not fed to older cattle. The birth cohort is therefore seen to be an approximation to a part of the cattle population that could have been equally exposed as the indicator case.

Different definitions of birth cohorts are applied:

- All cattle in the same herd as the confirmed case and born in the 6 (12) months before and/or after the case, independent of their current place of living.

- All cattle born and raised in the same herd as the confirmed case and born in the 6 (12) months before and/or after the confirmed case but only those present in the same herd as the case when it was reported.

- All cattle born and raised in the 6 (12) months before and/or after the confirmed case in all herds the case passed through during its first 6 (or 12) months of life, independent of their current place of living.

- All cattle born in the 6 (12) months before and/or after the confirmed case in all herds the case passed through during this period but being at present in the same herd as the case.

(b) **Feed cohorts,** i.e. cohort members defined in function of their feed source being the same as for the confirmed case.

This is a theoretical cohort that in reality may not be identifiable. It would include:

- all cattle that could have received feed from the same batches from which the confirmed case has been fed during the first 6 (12, 24,?) months of its life; or
- all cattle that have been exposed to feed from the same feed-mills that have supplied the farm(s) where the confirmed case has been fed during the first 6 (12, 24,?) months of its life.

(c) **Maternal cohorts**, i.e. cohort members are identified in function of their descendence.

This cohort is justified by the risk of maternal transmission that is estimated to be 10% or less. It could include

- all cattle which are direct descendants of female BSE-cases, born within 6 months of clinical onset in the dam; or
- all cattle which are descendants of female BSE-cases, all traceable generations, or
- all cattle descending from confirmed female BSE-cases in first (and second) generation.

2.23 Factors that influence the efficiency of a culling policy

2.231 Ratio of identified number of BSE-cases to the real number of cases

The efficiency of any culling scheme is critically depending on the ratio of identified number of BSE-cases to the real number of cases; however the real number of cases is not known. A high reporting rate increases the potential impact of any culling scheme on the development of the epidemic.

Note: The following comments are apparently logical and supported by practical experience but they are not confirmed and might therefore be regarded to be of a speculative nature. However, because to their potentially decisive importance for the efficiency of the management of the BSE-risk in an affected cattle population, they are outlined hereunder.

It is argued that different culling schemes have different impacts on notification behaviour, as a result of the different perception of farmers and veterinarians.

It seems logical to assume that the willingness of farmers to notify a suspect case is influenced by the impact that this would have on his farm. Culling of a-symptomatic animals will make the impact more severe and less easily acceptable. It could hence reduce the farmer's willingness to report suspects, in particular if the necessity to cull the animals is not evident to the farmer. This effect can be expected to be greater if the impact on the current herd is more severe. A herd culling policy can therefore be assumed to be a greater disincentive to notify a suspect case than a birth-cohort culling, as the latter would in general only affect a part of the current herd or possibly none (if the birth cohort had been sold or was already dead).

On the other hand, culling only parts of the herds could be economically problematic for some farmers, e.g. if the industry denies taking milk or meat from herds where BSE has occurred.

Similar mechanisms can be assumed to influence the motivation of veterinary practitioners to notify suspects with symptoms that are unspecific for BSE but could point towards this direction. If the consequences of such a notification are very severe, any “false alarm” could have very negative impact on the relationship of the practitioner with his clients, the farmers.

Compensation

Appropriate compensation schemes may buffer the impact of the culling scheme on the notification of BSE-suspects to some extent. However, other aspects, such as loosing an entire herd that has taken several years to build-up, can be assumed also to be of importance. The consequent cash flow problems and the duration of the re-establishment of a herd with a similar genetic and productivity make-up may outweigh the one-time compensation payment. A culling policy that includes the culling of all TSE-susceptible animals on an affected farm, could be an additional hindrance to notification.

Cost/Benefit

The acceptance of any culling scheme depends on its assumed cost/benefit ratio. For example, culling entire herds that are affected by a highly contagious disease (list A of OIE) is standard practice and accepted as a drastic but necessary and effective measure by both the general and the agricultural public. It is seen to be the best possible option to prevent a larger epidemic and is therefore regarded to have a good cost/benefit ratio.

If a culling scheme applied to BSE is seen to be similarly effective and necessary in terms of preventing an epidemic, it can be expected to be similarly acceptable to the general and agricultural public.

But if the public is not convinced of this efficiency and necessity, it will not accept such a culling policy, as is the Swiss experience. Convincing and scientifically sound evaluation is needed of the efficiency of different culling schemes with regard to preventing a BSE-epidemic and reducing the risk for man. The latter is, in view of the link to vCJD, very important for the general public perception.

In general terms any culling scheme is costly. The cost can be calculated to a certain extent. They depend mainly on the number of culled animals (and hence the definition of the target population), the compensation paid for each culled animal, and the cost of collecting, culling, testing and disposing of these animals.

However, the cost/benefit ratio depends not only on the cost but also on the "benefits" of a culling scheme. In view of its objective the benefits of culling are determined by its "hit-rate" (the n° of incubating animals per total number of culled animals, and hence the reduction of the current prevalence and of the number of future clinical cases saved per number of animals culled). Given the current inability to identify pre-clinical BSE-cases in the earlier stages of incubation, the hit rate has to be estimated.

2.232 The stage of the epidemic

In general, the likelihood to hit a pre-clinical, undiscovered case by culling animals related to an index case increases with the **extent of the epidemic**.

- As a general rule of thumb the ratio of incubating cattle to all culled cattle, will be higher at an advanced state of the epidemic.

The efficiency in terms of preventing an epidemic is highest during the early phases of such a development in particular if rather large birth cohorts are culled.

The **trend of the epidemic**, if known, should also be taken into account. It is obvious that if the prevalence (of pre-clinical BSE-cases) changes between birth-cohorts (clustering, in time), the likelihood to hit an incubating animal increases if the right birth-cohorts are covered.

If there is evidence that the exposure of the cattle increased over time, more animals born after the index case should be culled and if all birth-cohorts in a herd have been exposed to potentially contaminated feed, the entire herd should be culled.

During the beginning of an epidemic these will be most likely the animals after the index case, after the culmination of the epidemic these would be the animals born before the index case.

2.233 Quality of the surveillance

Culling is by definition linked to index cases. Its efficiency is therefore critically dependent on the ability of the surveillance system to identify these cases and to trace all related animals that should be culled.

If a given culling strategy would reduce the willingness to report suspects (see above) this could outweigh the beneficial effect of culling.

2.24 Assessment of the potential benefits of culling

The following estimations are based on the use of the limited data available.

2.241 Summary and discussion of the available data

With the current diagnostic methods the prevalence of pre-clinical infected cattle cannot be measured because the stage of incubation cannot be recognised.

However, the available methods have proven to be capable to identify incubating animals that are close to the end of the incubation period but would not have been discovered on the basis of clinical signs. The best approximation can therefore be derived from data on the incidence observed with the currently available tests in asymptomatic animals, culled in the context of currently applied culling systems.

In this context it has to be kept in mind that the available data only refer to cattle in the last months of the incubation, but not more than three to six months before clear clinical signs appear. Back-tracing in Switzerland has indeed shown that most, if not all, cattle that were found with the rapid BSE-test had already shown some unspecific symptoms. However, this is the only period in the incubation time when current post-mortem methods are seen to allow BSE-diagnosis in a-symptomatic animals via identification of PRP^{res} accumulation in the brain or the spinal cord or when BSE-diagnosis can be achieved by histopathology of the brain. Currently it cannot be excluded that other animals were in earlier stages of incubation when tested.

Ireland

Data from **Ireland** show that of 15,100 adult (>36 months) cattle, culled in the context of a case herd culling scheme, 14 additional cases were found (0.09% = 900 per million of culled adult animals)

All but one was born in the same birth cohort as the index cases. The birth cohort was defined as including all animals that were either born or reared on the same farm as the index case and exposed to the same exposure risk (i.e. feeding of concentrate-rations) as the case was during the first six months of its life.

Switzerland

Data from **Switzerland** show that of 1,760 cattle culled in the context of a herd culling scheme that targeted the case herd and the herd where the index case was born and raised, 5 additional cases were found.

All additional cases were born in the same herd as the index case, four within 12 months before or after the birth of the case, the fifth one had a 369 days difference in birth date to the index case, but the index case was purchased. Therefore, the fifth is not a real secondary case and should not be taken into account. (0.23% = 2,300 per million of culled animals).

Of about 200 cattle culled so far in the context of a birth cohort[2] culling scheme one additional case has been identified (0.5% = 5,000 per million i.e. the ratio is nearly twice as high as during the herd culling).

Of 350 offspring culled so far none has been found as additional case.

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[2] Born 12 months before or after the index case and born and/or raised in the same herd as the index case. Also those born in the same herd as the index case and within +- 12 months but now in other herds are included.

Portugal

Data from **Portugal** show that of 6,303 cattle culled in the context of a herd culling scheme (case and natal herd) and already examined for BSE, 8 were found BSE+ by histopathology and of 439 (histopathologically inconclusive) 9 were found BSE+ by IHC. The total number of additional cases found within the culled animals is therefore 17 (0.27% = 2,700 per million). No data on the birth cohorts of these additional cases were available.

France

Data from **France** show that of 9,680 animals culled in the context of a herd-culling scheme (case and natal herd), 400 have been examined and one additional BSE-positive case was found (0.25% = 2,500 per million), applying three examination methods.

Within the approximately 200 offspring of BSE-cases that were culled, no additional case was found.

Belgium

Data from **Belgium** show that of 1,399 adult cattle culled in the herd and offspring culling scheme, no additional cases have been found.

The United Kingdom

The only cull that was ever carried out in **the United Kingdom** was a selective cull, carried out since 1997 and being limited to the cattle born in 1989-1993.Under this scheme 77,340 animals have been culled. Additionally 4,940 cattle have been culled in the offspring cull. As these culled animals were not tested for BSE, it is unknown if and how many pre-clinical cases were hit.

2.242 Summary and discussion of the available back-calculations

Theoretical back-calculations (see annex 3) were carried out on the basis of case-incidence data. They show that an appropriate cohort culling, targeting the birth cohorts of confirmed cases, could have saved up-to 57.5% of all cases that finally occurred in the cattle born in the UK in 1987/88. It could not have prevented at least 34% of all clinical cases born in these years because they were not falling into the birth cohorts of confirmed cases. However, the cohort-culling scheme would have had to commence immediately after the confirmation of the first 1987/88 born case to achieve this effect. Commencing only in January 1993 would have reduced the saving to 38.3% of the cases that finally occurred in the UK birth-cohort 1987/88.

R.M.Anderson, in its statement to the BSE inquiry of 26/3/1998[3] came to a similar conclusion. Even a "one-shot" natal-herd culling scheme would have prevented

[3] The BSE-Inquiry, Statement N° 9C. Prof. Roy Anderson FRS, Website: http://www.bse.org.uk

about 55,000 BSE-cases to occur. A repeated scheme implemented end 1989 would have prevented, according to his calculations, even 124,000 future BSE-cases. He also estimates the number of pre-clinically infected cattle that would have been prevented from entering the human food chain to be around 330,000 animals.

2.243 Discussion of the efficiency of different culling schemes in the light of the available data.

Herd-culling versus birth-cohort culling

On the basis of the (limited) available data it can be stated that the number of additional cases found in the context of the different culling exercises remained small in comparison to the number of cattle culled. However, the identified incidence in the sub-population of the culled animals seems to be remarkably higher than the overall case-incidence:

- In Ireland the BSE incidence (cases per million adult cattle) always remained below 40/million while it was 900/million in the sub-population of the culled adult animals. As it is not known how many of the culled animals did fall into the birth-cohort (+- 12 month around the birth date of the index case) no estimation of the incidence in the (theoretical) birth-cohort sub-population is possible.

- In Portugal the case incidence never surpassed 230/million adult cattle. At the same time the incidence found in the sub-population of culled animals was 2,700/million. As for Ireland it is not possible to estimate the incidence in the (theoretical) birth cohort sub-population.

- Similar data are available for Switzerland. While the case incidence before 1999 never surpassed 70/million adult cases, the incidence in the sub-population culled in the context of the herd-culling programme was 2,800 per million.

  For Switzerland it is, however, possible to estimate the incidence in the (theoretical) birth-cohort sub-population. As all additional cases fell into this sub-population (one case having 369 days difference to the index case), and as this sub-population is roughly one third of the herd-cull, the incidence was about 3 times higher than in the sub-population killed under the herd-culling scheme. With other words, if in Switzerland a birth-cohort cull had been executed instead of the herd culling, the same effect would have been reached with only 1/3 of the animals killed.

Therefore it can be concluded that birth-cohort culling is more efficient than herd culling. This conclusion is also supported by theoretical calculations **(see annex 2)** that shows that birth-cohort culling could have saved up-to 57.5% of all cases that occurred in the 1987/88 national birth cohort in the UK, if it had been enacted immediately after the first case in this cohort.

Offspring cull

The data on offspring cull point towards a very low probability to hit undiscovered clinical cases. However, this result should be regarded cautiously as most culled offspring are either too young or too long ago born before the index case developed BSE. It also has to be taken into account that in those countries in which offspring have been culled and examined, the incidence is too low to expect occurrence of a maternally transmitted case within the small numbers examined.

> *Note: In order to verify the maternal transmission hypothesis, it would be useful to put at least the latest the offspring of BSE-dams under restrictions and keep them alive long enough to develop BSE -should they indeed have been infected at birth.*

As a general point it should be stressed once more that the current diagnostic tools do not allow identification of pre-clinical BSE cases until about 3 to 6 month before the end of the incubation period, i.e. the occurrence of **clear** clinical signs of BSE[4]. The numbers of additional cases found in the culled populations is therefore not more than an indicator of exposure in the past. It cannot estimate exposure in the more recent birth cohorts and it will always underestimate a given prevalence, at least as long as the exposure risk continued to exist after the birth date of the index case.

2.3 OPINION

2.31 Response to the questions

1) What is the expected impact of different culling schemes on the current pre-clinical incidence of BSE and the future clinical incidence?

The currently available data show that herds linked to an index case may contain additional undiscovered but discoverable PrP^{res}- positive animals, i.e. pre-clinical BSE-cases. The ratio of total number of culled animals to number of additional cases found is higher for birth cohorts. It is possible that additional infected animals, being in earlier stages of incubation, could be included in the cohorts – but this can currently not be verified or quantified.

Accordingly it is difficult to quantify the expected impact of different culling schemes on the current prevalence and the future incidence. The back-calculation that was carried out on UK-data, however, points towards a significant input on the future incidence (up-to 57% of the cases in the national UK birth cohort 1987/88 could have been eliminated by an early birth-cohort culling). It seems to be important that culling is applied in the early stages of the epidemic, if it starts later the number of prevented cases decreases (in the case of the UK back-calculation to 38.3%). It is therefore not clear if a similarly significant effect can be expected at the later stages of an epidemic

[4] Experience from Switzerland points towards unspecific, early signs of BSE being present in most additional cases found with rapid testing. However, these signs are much more evident in hindsight.

2) Does this effect vary in function of the epidemiological situation of a country as indicated by the BSE-incidence?

Yes, as a general rule of thumb the efficiency of any culling system, measured as its "hit-rate", i.e. the ratio of incubating cattle culled to all culled cattle, will increase with the BSE-prevalence, particularly when the within-cohort prevalence of infection is high. The current incidence, and even more so its trend over the past years, is an indicator for the past prevalence. However, the quality of this indicator is critical dependent of the quality of the surveillance system that generated the figure. It is also important to realise that the incidence figures do not allow concluding on the prevalence during the last 4 to 5 years. The large majority of cases born in these recent years will not have developed signs of BSE yet.

It is essential that, if the clinical incidence has to be used as an indicator, its trend must also be taken into account, as should the quality of surveillance and its development over time. If the trend of the incidence shows that the risk of being infected increases from year to year, a larger proportion of the animals born after an index case should be culled. If the trend is inverse, the majority of culled animals should be born before the index case. Ideally an analysis of the various risk factors[5] that determine the exposure situation in the different years should be carried out over a period of time in order to confirm the trend.

In general it can be assumed that the efficiency of culling in terms of contributing to the prevention of an epidemic from developing is highest during the early phases of an epidemic.

3) What are therefore the appropriate culling schemes in function of defined levels of incidence?

Independent of the actual incidence it seems that cohort culling is more efficient than herd culling. The data from Switzerland indicate that the same effect as with herd culling could have been achieved with only 1/3 of animals culled under a birth cohort-culling scheme.

However, in deciding on a culling scheme, the following should **also** be taken into account:

- As long as it is not possible to identify the exact feed source that has infected the index case it will remain close to impossible to trace all cattle that could have been exposed to the same feed. All culling schemes will therefore remain suboptimal, only hitting a part of the theoretically optimal target population but most likely a large number of animals that were not exposed.
- Within these limitations, culling schemes that target animals epidemiologically linked to the index case and where the likelihood that they have been exposed to the same feed source is highest, are the preferred choice.
- Culling of all cattle born within 12 months before and after an index case and in the same herd, independent of its current herd, is a possible compromise

[5] In particular MBM-feeding to cattle, rendering conditions, fate of SRM and fate of fallen stock

option, as long as tracing is reliable. It will be further improved by including animals that have been reared together with the index calf during the first 12 months of life but were born in another herd.

- If tracing of cohorts is not reliably possible, whole herd culling (preferably the herd where the index case was born and raised during the first year) is the second best option
- Given the critical dependence of the efficiency of a given culling scheme on the quality of the surveillance, the (assumed) impact of a given culling scheme on the willingness to report suspects has to be taken into account. The experience from Switzerland, where the notifications increased when the culling policy changed from herd-to birth-cohort culling indicates a certain preference for the latter.
- Events that significantly modify the risk of a given birth cohort to be infected should be taken into account when defining culling criteria. Examples for such events are the introduction of an MBM-feed ban, a better rendering with a higher capacity to reduce BSE-infectivity, or the introduction of an SRM-ban that reduces the amount of infectivity that could enter rendering (the risk of new infections decreases afterwards, depending on the compliance).

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Annexes

Annex 1 : Currently applied culling policies

Annex 2 : Available data

Annex 3 : Theoretical calculation of the potential impact that appropriate culling could have had on the BSE-epidemic in Great Britain by J.Wilesmith and Judi Ryan Epidemiology Department,VLA Weybridge, August 1999.

Annex1
Currently applied culling policies

	UK	CH	France	Portugal	Ireland
Herd culling					
Case herd		X (until mid99)	X		
Herd where animal born and raised		X (until mid99)	X		
All herds where index case was during its life			(X, first 2 years)		
Additionally cattle which left the herd			X(since 97)		
Additionally other susceptible animals than cattle					
Cohort culling		Cohort = born 12 months before or after index case		Cohort = born 6 months after index case	
Case herd					
Herd where animal born and raised		X (since 99)			
All herds where index case was during lifespan					
Additionally cattle which left the herd	X	X			
Only certain years	X (7/89-6/93)				
Offspring cull					
F1, last direct	X				
F1, all	X(if born after 1/8/96)	X	X		
F1, only specific years	X				
F2					

Annex2
Available Data

SWITZERLAND:

1. Secondary cases before the herd culling (before December 1996)

Before the herd culling, two cases had occurred on seven farms and three cases had occurred on one farm. All second/third cases were born and reared on the same farm as the index case and born one year before or one year after the index case. All brains have been examined using HE and Immunohistochemistry.

date of birth of index case	date of diagnosis	date of birth of 2nd case	date of birth of 3rd case	difference (days) I	difference (days) II
24.11.90	23.01.95	06.01.90		322	-
19.10.91	23.10.95	20.10.91		1	-
22.11.88	15.07.92	04.12.88		12	-
14.12.89	08.01.96	15.12.89		1	-
22.02.88	28.06.92	16.05.88		84	-
30.10.89	30.03.93	02.07.89	28.4.89	120	185
24.09.89	01.06.94	04.09.89		20	-
07.03.90	01.06.94	03.05.90		57	-

2. Secondary cases found through the herd culling (after December 1996)

Switzerland implemented retrospective herd culling in December 1996 (on the farm where the case occurred and were the animal was born and raised).

During the herd slaughtering 1,760 animals were culled and the brains examined. Of these 1,760 cattle, 5 animals from 4 farms were positive. All but one were born within the birth cohort. The animal not born in the birth cohort had a 369 days difference in birth date to the index animal (and was on the farm with 3 cases). Most animals were born in 89 and 90. In one case the index case was born in 1991, the second case in 1992.

All brains have been examined using HE, Immunohistochemistry and Western Blot.

One of the BSE+ animals was histologically negative.

date of birth of index case	date of diagnosis	date of birth of 2nd case	date of birth of 3rd case	difference I (days)	difference II (days)
01.11.89	16.10.96	01.12.89	-	30	-
30.11.91	27.06.95	10.09.92*	-	285	-
30.10.89*	15.03.95	03.11.90	21.01.90	369	286
07.10.89	21.11.94	06.05.90	-	211	-

*purchased

3. Cohort culling (after June 1999)

In July 1999 Switzerland changed from herd culling to cohort culling. The birth cohort is defined as animals, either born or reared on the farm, which was exposed to the same risk (i.e. feeding of concentrate ration) as the index case was, born one year before and one year after the index case. Included are those bought on to the farm as calves and those sold at a later date. Approximately 200 animals have been slaughtered and examined under this scheme – one was found positive (0.5%).

It was noted that following the switch from herd to birth-cohort culling the notification of suspects increased. However, this might also have been triggered by other factors, such as increased awareness of the necessity to indicate any suspicious cow.

4. Slaughtering of offspring (after September 1996)

In September 1996, Switzerland implemented retrospective offspring culling. All direct offspring of the index case have to be culled. Approximately 350 animals have been slaughtered and examined – none positive.

Conclusion: All secondary animals found are born in the same birth cohort as the index case. The only exception was a purchased animal – and was therefore not really a secondary case.
No indication of maternal transmission was found.

If cohort culling instead of herd culling had been introduced in 1996 (or at the beginning of the epidemic) the same number of secondary cases would have been found, but fewer animals would have been killed (in the framework of cohort slaughtering approximately one third of a herd has to be culled in the Swiss situation). Therefore, cohort culling is regarded to have a much better efficiency.

Ireland:

Herd culling and birth cohort culling

Ireland implemented case herd culling in 1990. Since 1996 birth cohorts and UK-imports have been slaughtered retrospectively.

To date, 16.388 adult cattle (3 years old or older) have been slaughtered and obex sampled. 15.100 obexes have been examined to date using HE. To start with, all obexes were also examined using Immunocytochemistry. During 1998, as no additional information was obtained using this method in addition to HE it was decided to examine only birth cohorts and those, which HE appeared inconclusive, with Immunocytochemistry.

Of the 16.388 adult cattle that were culled, 585 fell into birth cohorts, defined as the animal either born or reared on the same farm as the suspect/confirmed case was, and exposed to the same exposure risk (i.e. feeding of concentrate ration) during the first six months of its life as the index case. All animals reared with the BSE+ animal should be considered within this category; including those bought into the farm as calves and those sold out at a later date that received concentrate ration. Calves sold within a few weeks of birth and which did not receive solid food (especially concentrate ration) were considered to be in a low risk group. No tracing of these animals were carried out once it was established that they were sold and that they did not receive concentrate ration).

To date 14 (0.093% or 0.927/1.000) of the 15.100 examined adult cattle that were culled because of their epidemiological link to confirmed BSE-cases, have been diagnosed as BSE+:

- In 5 of the 14 cases nervous clinical signs were recorded at time of slaughter. Sections from different areas of the brain were examined in these animals. They were all categorised as birth cohorts, diagnosed using HE and confirmed by Immunocytochemistry and all but one were animals in the same herd as the index BSE (+).
- 9 animals were diagnosed BSE+ solely by examination of the obex and no nervous signs were recorded at time of slaughter, although it has to be noted that no clinical examination was routinely carried out ante-mortem.
  Of these 9 animals:
  - All but one fell into the category of birth cohorts. For the remaining case, the difference between the index BSE (+) animal and the cohort was one year. This animal was in the same herd as the index BSE (+) and was diagnosed using HE stain.
  - 8 cases were diagnosed with HE stain. One case was diagnosed using Immunocytochemistry techniques. This animal was a birth cohort member and in the same herd as the index BSE(+).
  - 6 were animals in the same herd as the index BSE (+) and 3 were traced cohorts. These 3 animals were birth cohorts and were diagnosed using HE stain.

  Of the 15.100 adult cattle examined, only 3 animals were BSE (+) while having had no known clinical signs and not being in the same herd as the index BSE (+).

Offspring cull
The culling of offspring was implemented in 1996 (?). No data are available.

Portugal:

Herd culling:

Portugal implemented retrospective herd culling (on the farm where the case occurred and where the animal was born and raised) between mid 96 and 1997.

Up to 30 November 1999, 13.557 cattle have been slaughtered under the herd/cohort culling scheme and the brain sampled. They correspond to 789 herds (340 case-herds + 449 related-herds; 631 with local animals + 158 with UK imported animals)

- 6.303 samples have been submitted for histopathogical testing, 353 were discarded as inappropriate and 5.093 samples were still waiting to be tested (Nov. 1999)..
- Out of the 1.210 done, 8 were positive at histopathogical testing. Immunocytochemistry were applied to 627 samples. Until Nov. 1999, 439 of these were tested (9 were found positive) and for the remaining 188 testing was in progress.
- Only suspicious results at histopathological examination are submitted to another test (immunoblotting). They do not further confirm either the positives or the negatives at histopathology.

No data about birth cohorts were available to the SSC.

Offspring cull
Apparently culling of offspring was implemented in 1996. However no detailed data were available.

France:

Herd culling

France implemented voluntary herd culling with compensation since the first case (1990). Herd slaughtering is compulsory since 1994 on both the farm were the case occurred and the farm were the animal was born and raised.

Approximately 9.680 animals in 79 herds have been culled. 400 were examined by histopathology, immuncytochemistry and Western Blot. None was found BSE+.

No data on birth cohorts within the culled and tested animals were available.

Offspring cull
Culling of offspring was implemented in 1996. Approximately 200 offspring of BSE+ dams have been culled and examined. None were found BSE+.

Annex 3

Theoretical calculation of the potential impact that appropriate culling of the 1987/88 national birth cohort could have had on the BSE-epidemic in Great Britain

Preamble

The following represents a brief scooping analysis of the effects of a cull of the most heavily exposed birth cohort[6], namely cattle born between July 1987 and June 1988. It does not rely on detailed tracing of all cases to their natal herd. Data held in the BSE database has been used, and where possible cases have been allocated to their natal herd by the use of the eartag carried at the time of death. This eartag may have been inserted after leaving the natal herd.

The paper does not consider the practical difficulties of dealing with such a cull at a time when the epidemic was at its peak, nor with the lack of disposal capacity which would also have prevented its implementation. It would have been further complicated by the fact that culled cattle would have had to be replaced with purchased cattle that would have been potentially exposed elsewhere.

Data

Using only those cases with a known date of birth, the basic statistics are that there have been 39,192 confirmed cases in animals born in the 1987/88 national birth cohort. These occurred on 14,700 farms (a mean of 2.7 cases born in this cohort/farm). If all cases estimated to have been born in the 1987/88 national birth-cohort are used, the figures are 57,230 cases on 21,011 farms. As this results in no change to the mean number of cases per farm, the analyses are restricted to those with a known date of birth.

The first case was reported in September 1989, and the last case to have occurred on a new farm was reported in May 1999. A spread of 9 years 9 months to date. The full distribution is shown in Table 1. It has to be recognised that while some of the cases presented 11 or 12 years after their birth may have represented the upper range of the incubation period, they may alternatively been exposed and infected in adulthood. Therefore the culling of the birth cohort would not always remove the entire exposed cohort. Some animals would remain alive elsewhere.

The distribution of farms by the number of 1987/88 cases per farm is shown in Table 2, with 7,101 of the 14,700 farms (48.3%) having experienced only one case. The remaining 7,599 farms experiencing multiple cases would have been identified between December 1989 and December 1997.

These figures are based on the farms where the cases were reported, rather than the birth cohorts affected. To retrospectively estimate the effects of a cohort cull, the herdmark of the eartag of the cases has been used to identify the birth cohorts

[6] Birth cohort is here defined as animals born in the same natal herd and the same 12 month period (July to June) as the index case.

affected and then to estimate the likely costs and benefits if such a cull had been initiated on this birth cohort. A total of 572 cases were excluded from the analyses because it was not possible to allocate them to birth cohorts simply by means of ear tag.

This method of identifying cohorts resulted in 38,620 cases in 13,301 cohorts (a mean of 2.9 cases per cohort). Table 3 shows the number of cohorts identified, and the number of subsequent cases occurring in these cohorts, by the quarter year period of restriction of the first case. The subsequent cases have been categorised by those occurring in the same quarter year period as the first case, and those occurring later. The reasoning behind this being that the tracing of cohorts may not be fast enough to prevent those cases which occurred soon after the first case.

Results

If the cull had been initiated in January 1992:

- **16,420** cases would not have been saved, either because they were the first case (13,301), or they occurred shortly afterwards, and before the cohort could have been traced.
- **22,200** cases could have been saved (**57.5%** of the total cases)

If the cull had been initiated in January 1993:

- **23,824** cases would not have been saved
- **14,796** cases could have been saved (**38.3%** of the total cases)

Regardless of when the cull was initiated, approximately 13,301 cohorts would have been traced and slaughtered. The number of animals slaughtered per cohort would depend on the timing of the cull, but as the majority of cohorts would have been identified in 1992 when the cases were approximately 5 years of age, we can assume an average of 15 animals found alive per cohort traced. This results in 199,500 animals slaughtered. Applying this to the two examples above:

If the cull had been initiated in January 1992:

199,500 / 22,200 = **9** animals slaughtered per case saved

If the cull had been initiated in January 1993:

199,500 / 14,796 = **13.5** animals slaughtered per case saved

The assumption in these analyses is that the cohort cull would have been on-going and therefore that all newly identified cohorts would be culled as they arise, right up to the current time. It also presents the best case scenario in assuming that cohorts would be traced and culled immediately, regardless of the size of the backlog. The only time-lag incorporated is for those cases occurring in the same 3 month period as the first case.

The main point arising from these analyses is that 34.4% (13,301/38,620) of the cases which occurred in this birth cohort could not have been prevented by a cohort cull as they identify the cohorts in question.

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August 1999

Month and year of restriction (first case)	Number of farms
1989.09	1
1989.12	1
1990.01	1
1990.02	2
1990.03	2
1990.04	1
1990.05	5
1990.06	4
1990.07	2
1990.08	8
1990.09	10
1990.10	22
1990.11	31
1990.12	41
1991.01	92
1991.02	88
1991.03	148
1991.04	200
1991.05	167
1991.06	180
1991.07	228
1991.08	318
1991.09	361
1991.10	405
1991.11	382
1991.12	391
1992.01	527
1992.02	468
1992.03	514
1992.04	398
1992.05	366
1992.06	384
1992.07	429
1992.08	416
1992.09	443
1992.10	481
1992.11	443
1992.12	415
1993.01	444
1993.02	440
1993.03	458
1993.04	321
1993.05	273
1993.06	261
1993.07	323
1993.08	275
1993.09	308
1993.10	270
1993.11	346
1993.12	230
1994.01	265
1994.02	218
1994.03	226
1994.04	169
1994.05	124
1994.06	108
1994.07	83
1994.08	87
1994.09	75
1994.10	89
1994.11	81
1994.12	86
1995.01	89
1995.02	55
1995.03	59
1995.04	43
1995.05	52
1995.06	33
1995.07	26
1995.08	44
1995.09	23
1995.10	30
1995.11	45
1995.12	16
1996.01	26
1996.02	25
1996.03	25
1996.04	12
1996.05	18
1996.06	16
1996.07	9
1996.08	6
1996.09	8
1996.10	14
1996.11	8
1996.12	4
1997.01	5
1997.02	5
1997.03	7
1997.04	8
1997.05	8
1997.06	6
1997.07	1
1997.08	2
1997.09	3
1997.10	4
1997.11	2
1997.12	4
1998.01	1
1998.02	4
1998.03	2
1998.04	2
1998.06	2
1998.08	3
1998.09	2
1998.10	2
1998.11	2
1998.12	1
1999.04	1
1999.05	2
Total	14,700

Table 1: Distribution of farms with a 1987/88 born case by month and year of restriction of first case

Number of 1987/88 born cases	Number of farms
1	7101
2	2919
3	1476
4	928
5	632
6	424
7	313
8	238
9	165
10	104
11	98
12	66
13	57
14	37
15	27
16	26
17	20
18	18
19	10
20	6
21	8
22	6
23	3
24	3
25	1
26	4
27	3
28	1
29	3
30	1
31	1
38	1
Total	14,700

Table 2: Distribution of farms with a 1987/88 born case by number of cases per farm

Quarter year period of restrictions	No. of new cohorts identified	No. of subsequent cases in same quarter year period*	No. of additional subsequent cases
1989-qtr 3	1	0	0
1989-qtr 4	1	0	2
1990-qtr 1	5	0	24
1990-qtr 2	9	0	63
1990-qtr 3	20	0	154
1990-qtr 4	94	8	833
1991-qtr 1	318	48	2,205
1991-qtr 2	521	78	3,032
1991-qtr 3	859	178	3,960
1991-qtr 4	1,090	237	3,719
1992-qtr 1	1,415	253	3,268
1992-qtr 2	1,061	145	1,811
1992-qtr 3	1,189	148	1,615
1992-qtr 4	1,206	146	1,105
1993-qtr 1	1,169	126	811
1993-qtr 2	741	39	359
1993-qtr 3	795	43	317
1993-qtr 4	760	34	231
1994-qtr 1	612	31	129
1994-qtr 2	332	14	52
1994-qtr 3	225	8	30
1994-qtr 4	220	9	18
1995-qtr 1	184	3	17
1995-qtr 2	102	1	4
1995-qtr 3	76	2	4
1995-qtr 4	86	0	1
1996-qtr 1	64	0	0
1996-qtr 2	32	0	0
1996-qtr 3	22	0	0
1996-qtr 4	27	1	0
1997-qtr 1	15	0	1
1997-qtr 2	12	0	2
1997-qtr 3	5	0	0
1997-qtr 4	8	0	0
1998-qtr 1	5	0	0
1998-qtr 2	2	0	0
1998-qtr 3	6	0	0
1998-qtr 4	5	0	0
1999-qtr 1	2	0	0
1999-qtr 2	4	0	0
1999-qtr 3	1	0	0
1999-qtr 4	0	0	0
Total	**13,301**	**1,552***	**23,767**

** Assumption: these would have occurred too soon after the initial case for the cull to have prevented them*

Table 3: Number of 1987/88 birth cohorts identified by quarter year period of restriction of first case